

## Statistical Analysis Report

***DISSPO Parcours Dig' study: Prospective evaluation of a program for early identification of needs and multidisciplinary intervention in supportive care in Digestive Oncology***

**Confidential paper: don't broadcast until the final version**

|                          | NAME                                 | FONCTION                       | DATE       |
|--------------------------|--------------------------------------|--------------------------------|------------|
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### Document history

| Version | Date       | Nature of modifications                                                                                                     |
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| 1       | 21/11/2023 | First draft edition                                                                                                         |
| 2       | 17/10/2025 | Updated version (addition of descriptive parameters related to malnutrition and sarcopenia in tables 1-3, and tables 5b-5d) |
|         |            |                                                                                                                             |

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## Protocol summary

|                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
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## Study background and rationale

### Epidemiology and management of gastrointestinal cancer (GI) patients

Colorectal cancer (CRC), pancreatic cancer, and esogastric cancer are the most common **GI cancers** <sup>1</sup>. In France, CRC is the second leading cause of cancer deaths after lung cancer <sup>1</sup>. Pancreatic ductal adenocarcinoma (PDAC) incidence is dramatically increasing worldwide; it is expected to become the second cause of cancer deaths in 2030 <sup>2,3</sup>.

Metastases (at diagnosis or during disease evolution) occur in more than 50% of patients with GI cancer, the liver being the most frequent metastatic site. Despite significant therapeutic progress over the two last decades, overall survival (OS) of patients with GI cancer at the metastatic stage remains poor, with the 5-year OS rate ranging from less than 5% (PDAC) to 10%-15% (CRC) <sup>4</sup>. The Eastern Cooperative Oncology Group performance status (ECOG PS)

is a strong prognostic factor associated with significantly shorter OS when ECOG PS is  $\geq 2$ , consistently across GI cancer types (<http://ecog-acrin.org/resources/ecog-performance-status>).

The therapeutic management of patients with advanced/metastatic GI cancer (CRC, PDAC, and esogastric cancer) relies on supportive care and systemic anticancer therapy (mainly, chemotherapy and targeted therapy; [www.tncc.org](http://www.tncc.org)). Supportive care aims to prevent and ameliorate suffering while ensuring optimal health-related quality of life (HRQoL). It includes the treatment of biliary and digestive tract obstructions, tumor-associated pain, anxiety and depression, fatigue, cancer cachexia and denutrition, as well as thromboembolic disease treatment and prevention in high-risk patients. HRQoL has been reported to be a prognostic indicator of survival in various cancers <sup>5,6</sup>. Interventions aiming to improve HRQoL and, ultimately, survival in GI cancer patients are an innovative complementary approach that is receiving growing interest.

#### Our consortium and expertise from previous studies

Our consortium (C. Neuzillet, clinician/A. Anota, methodologist) is pioneer and leader in France in the field of clinical trials evaluating APA in GI cancer patients, with the APACaP (NCT02184663) and APACaPop-PRODIGE 56 (NCT03400072) national multicenter trials, which evaluate the effects of APA programs on HRQoL in patients with advanced and resected pancreatic cancers, respectively <sup>38</sup>. More than 280 patients have been included in the APACaP trial to date, showing the feasibility of such studies even in a palliative setting.

Curie Institute also has an extensive expertise in this field, notably through the Activ program, consisting in a combined nutrition and APA behavioral intervention for breast cancer patients in the adjuvant setting.

#### Hypothesis and study aims

The **Parcours Dig' study** aims to assess the feasibility of a program for early identification of needs and multidisciplinary intervention in supportive care in Digestive Oncology in patients with advanced GI cancer (non-colorectal cancer, or colorectal cancer with nutritional risk factors) receiving first-line palliative chemotherapy.

#### Study design

##### General design

Monocentric, single-arm, study to evaluate the feasibility and effects of an early multidisciplinary assessment and intervention in addition to usual patient care.

**This type of intervention complies with the standards recommended by the National Cancer Institute (INCa) to promote the practice of physical activity during and after treatment in oncology (RIPH 2).**

#### Study interventions

Patients will receive usual care, including:

- Chemotherapy at the investigator's choice,
- Outpatient clinical visits according to the regular schedule,
- Tumor evaluation based on tumor marker serum levels (e.g. carbohydrate antigen 19-9 [CA19-9] and/or carcinoembryonic antigen [CEA] and/or others), as appropriate, and TAP-CT with intravenous contrast injection every 8 weeks.

In addition, all patients will be assessed for their needs in supportive care and receive multidisciplinary intervention including nutritional support and APA.

**Nutritional support** will consist of:

- A nutrition assessment by a dietician including a VAS of food intakes at baseline, at W4 and W8 (plus additional visits if required),
- Nutritional intervention according to the Société Francophone de Nutrition Clinique et Métabolisme (SFNEP) guidelines, including dietetic counseling for all patients, and oral supplementation, enteral tube feeding and/or parenteral nutrition to provide 30-35 kcal/kg/day with 1,2-1,5 g/kg/day of proteins.

**APA support** will consist of:

- A physical condition assessment by an APA professional including physical tests (6-minute walking test, handgrip test, chair stand fitness test, get-up and go test, balance in single-leg and bipodal stance) at baseline and W8,
- Personalized unsupervised program combining aerobic (e.g. walking, nordic walking) and resistance exercises.

A physical condition assessment by a APA professional including physical tests to evaluate: cardiorespiratory endurance (6-minute walking test), gripping strength (handgrip test), endurance of the lower limbs (chair stand fitness test & get-up and go test) and static

balance (balance in single-leg and bipodal stance) at baseline and W8. The aim of the fitness tests is to measure the efficiency of the physical activity unsupervised program.

The personalized unsupervised physical activity program will be home-based and consist of the combination of aerobic exercises using large muscle groups (e.g. walking, nordic walking, swimming, cycling) to improve aerobic capacity and resistance exercises targeting all major muscle groups (e.g. free weights, elastics, weight-bearing functional tasks) to maintain or gain muscle mass and strength. The goal of this program is to decrease sedentary times and increase the exercise tolerance. Physical activity sessions comprise exercises for warming-up followed by aerobic or resistance exercises and a recuperation period. The warming-up and recuperation periods account for at least 30% of the session duration. The aim of the APA program is to gradually reach a total of 30 minutes of aerobic training, three to five times per week (according to physical condition), and to perform strengthening activities at least twice a week for all the major muscle groups, excluding the warming-up and recuperation periods.

#### Sample size calculation

Feasibility study will be performed on patients recruited over a 2-month time period, with a one-month follow-up.

If  $\geq 80\%$  of patients with advanced GI cancers included in the program complete the baseline, W4 and W8 assessments.

With an expected number of 3-4 new patients/week -> about 30 screened patients -> objective to reach 24 patients with baseline, W4 and W8 assessments.

## Statistical considerations

Continuous variables will be summarized using descriptive statistics, i.e. number of patients with available data, median and 25%-75% quartile (Q1-Q3). Continuous variables could be transformed to categorical variables using the median or using conventional cut-offs from bibliography or clinical practice.

Medians between two subgroups will be compared using Wilcoxon's-test.

Categorical variables will be presented by absolute and relative frequencies and missing modality. Frequencies between subgroups will be compared using chi-square test (or Fisher exact test, if appropriate).

Primary endpoint will be estimated with a binomial proportion with its 95% confidence interval (CI) by Wilson score method.

For the secondary endpoints, absolute and relative changes from baseline will be calculated between inclusion and end of intervention (W8).

The Kaplan-Meier method will be used to estimate time to event endpoints (OS, PFS). Median event-free times will be reported with 95% CI. The standard error will be estimated by the Greenwood formula and the log-log transformation will be used to compute confidence intervals. Median follow-up with its 95% CI will be estimated using the reverse Kaplan-Meier method for OS. Log rank test will be used to compare survival between subgroups.

All statistical tests will be two-sided and p-value < 0.05 to be considered statistical significant. All analyses will be performed using SAS version 9.4 (SAS Institute, Cary NC).

## Flowchart

### Evaluability for the primary objective:

In order to be evaluable for the primary endpoint, a patient must be in success or failure for this criterion. As defined in the protocol (definition 1):

- A success will be defined as patients having a complete multidisciplinary intervention i.e. receiving a nutritional support at inclusion, week 4 ( $\pm 7$  days) and week 8 ( $\pm 7$  days), and an APA support at inclusion and week 8 ( $\pm 7$  days)
- A failure will be defined as patients having an incomplete multidisciplinary intervention, i.e. at least one missing (nutritional or APA) support at the concerned visits or at least one visit delay  $> 7$  days.

Another definition (definition 2) will be considered for the sensitivity analysis:

- A success will be defined as patients having a complete multidisciplinary intervention i.e. receiving a nutritional support at the 3 visits (inclusion, intervention, end of intervention), and an APA support at the 2 visits (inclusion, end of intervention)
- A failure will be defined as patients having an incomplete multidisciplinary intervention, i.e. at least one missing (nutritional or APA) support at the concerned visits.

A patient will be considered as non-evaluable for the primary endpoint in case of premature end of the study due to death or lost to follow-up or withdrawal of consent before the end of intervention visit (W8).

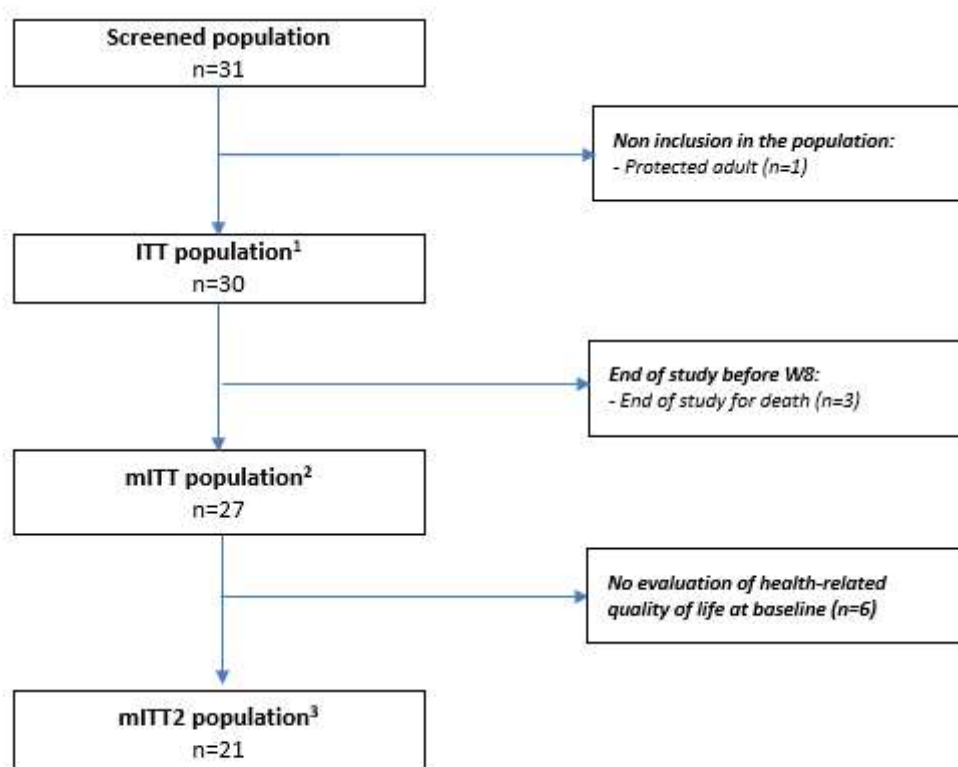
### Analysis populations:

- Intention-to-treat (ITT) population: including all patients regardless of their eligibility, i.e. patients with advanced GI cancer (non-colorectal cancer, or colorectal cancer with nutritional risk factors) receiving first-line palliative chemotherapy
- Modified intention-to-treat (mITT) population for primary endpoint analysis: including ITT population evaluable for the primary endpoint
- Modified intention-to-treat (mITT2) population for HRQoL analysis: including mITT population with an evaluation of health-related quality of life (HRQoL) at baseline.

Primary analysis will be performed on the mITT population considering evaluability for the primary endpoint with definition 1. A sensitivity analysis will be performed considering evaluability for the primary endpoint with definition 2.

Secondary analyses will be performed on the ITT, mITT and mITT2 populations for all secondary objectives

Figure 1. Flow-chart of the study



## Description of the population

Table 1. Patient characteristics according to the type of cancer in the ITT population (n=30)

|                        |                                                                        | Global<br>(n=30)<br>N(%) or median[IQR] | Localized cancer<br>(n=12)<br>N(%) or<br>median[IQR] | Metastatic cancer<br>(n=18)<br>N(%) or<br>median[IQR] | p            |
|------------------------|------------------------------------------------------------------------|-----------------------------------------|------------------------------------------------------|-------------------------------------------------------|--------------|
| <b>Fragility score</b> |                                                                        |                                         |                                                      |                                                       |              |
| Chemotherapy type      | mono chemotherapy                                                      | 6 (20)                                  | 0 (0)                                                | 6 (33.3)                                              | <b>0.001</b> |
|                        | bi chemotherapy                                                        | 9 (30)                                  | 1 (8.3)                                              | 8 (44.4)                                              |              |
|                        | tri chemotherapy                                                       | 15 (50)                                 | 11 (91.7)                                            | 4 (22.2)                                              |              |
| Nutritional status     | no denutrition                                                         | 9 (30)                                  | 4 (33.3)                                             | 5 (27.8)                                              | 0.258        |
|                        | moderate denutrition                                                   | 11 (36.7)                               | 6 (50)                                               | 5 (27.8)                                              |              |
|                        | severe denutrition                                                     | 10 (33.3)                               | 2 (16.7)                                             | 8 (44.4)                                              |              |
| Comorbidities          | No comorbidity                                                         | 1 (.)                                   | 0 (.)                                                | 1 (.)                                                 | 0.652        |
|                        | One significant comorbidity                                            | 13 (44.8)                               | 5 (41.7)                                             | 8 (47.1)                                              |              |
|                        | At least two significant comorbidities                                 | 12 (41.4)                               | 6 (50)                                               | 6 (35.3)                                              |              |
| Symptoms               | no symptom                                                             | 4 (13.8)                                | 1 (8.3)                                              | 3 (17.6)                                              | 0.765        |
|                        | Symptoms controlled by oral treatments<br>requiring regular assessment | 7 (23.3)                                | 2 (16.7)                                             | 5 (27.8)                                              |              |
|                        | Symptoms not controlled by oral treatments                             | 21 (70)                                 | 9 (75)                                               | 12 (66.7)                                             |              |
| Age-related fragility  | patient < 75 years old                                                 | 2 (6.7)                                 | 1 (8.3)                                              | 1 (5.6)                                               | <b>0.034</b> |
|                        | patient > 75 years old and G8 score ≤ 14                               | 21 (70)                                 | 11 (91.7)                                            | 10 (55.6)                                             |              |
|                        | patient > 75 years old and G8 score ≤ 14                               | 9 (30)                                  | 1 (8.3)                                              | 8 (44.4)                                              |              |
| Fragility score        | 4                                                                      | 10 (33.3)                               | 8 (66.7)                                             | 2 (11.1)                                              | <b>0.006</b> |
|                        | 5                                                                      | 5 (16.7)                                | 2 (16.7)                                             | 3 (16.7)                                              |              |
|                        | 6                                                                      | 7 (23.3)                                | 2 (16.7)                                             | 5 (27.8)                                              |              |
| Fragility score        | 7                                                                      | 8 (26.7)                                | 0 (0)                                                | 8 (44.4)                                              |              |
|                        | moderate fragility                                                     | 30 (100)                                | 12 (100)                                             | 18 (100)                                              |              |
|                        |                                                                        |                                         |                                                      |                                                       |              |

## Screening

### Comorbidities

#### Comorbidities

#### Comorbidities type: cardiac

|     |           |           |           |       |
|-----|-----------|-----------|-----------|-------|
| no  | 13 (43.3) | 7 (58.3)  | 6 (33.3)  | 0.176 |
| yes | 17 (56.7) | 5 (41.7)  | 12 (66.7) |       |
| no  | 23 (76.7) | 11 (91.7) | 12 (66.7) | 0.113 |
| yes | 7 (23.3)  | 1 (8.3)   | 6 (33.3)  |       |
|     | 3 (.)     | 0 (.)     | 3 (.)     |       |

#### atrial fibrillation

#### aortic bioprosthesis

#### pacemaker

#### rhythm disturbances

#### Comorbidities type: pulmonary

#### Comorbidities type: neurologic

|        |           |           |           |       |
|--------|-----------|-----------|-----------|-------|
| no     | 30 (100)  | 12 (100)  | 18 (100)  |       |
| no     | 26 (86.7) | 11 (91.7) | 15 (83.3) | 0.511 |
| yes    | 4 (13.3)  | 1 (8.3)   | 3 (16.7)  |       |
| stroke | 3 (75)    | 1 (100)   | 2 (66.7)  |       |

#### normal pressure hydrocephalus

#### High blood pressure

|     |         |        |          |       |
|-----|---------|--------|----------|-------|
| no  | 1 (25)  | 0 (0)  | 1 (33.3) |       |
| yes | 18 (60) | 9 (75) | 9 (50)   | 0.171 |

#### Obesity

|     |           |          |           |       |
|-----|-----------|----------|-----------|-------|
| no  | 12 (40)   | 3 (25)   | 9 (50)    |       |
| yes | 29 (96.7) | 12 (100) | 17 (94.4) | 0.406 |

#### other comorbidity

|          |           |           |           |       |
|----------|-----------|-----------|-----------|-------|
| no       | 1 (3.3)   | 0 (0)     | 1 (5.6)   |       |
| yes      | 25 (83.3) | 10 (83.3) | 15 (83.3) | 1.000 |
| diabetes | 5 (16.7)  | 2 (16.7)  | 3 (16.7)  |       |

#### diabetes

#### history of leukemia and melanoma

#### prostate cancer

#### localized

#### locally advanced

#### metastatic

#### Pathology stage

|                                  |          |          |           |       |
|----------------------------------|----------|----------|-----------|-------|
| no                               | 3 (60)   | 1 (50)   | 2 (66.6)  |       |
| yes                              | 1 (20)   | 1 (50)   | 0 (0)     |       |
| history of leukemia and melanoma | 1 (20)   | 0 (0)    | 1 (33.3)  |       |
| prostate cancer                  | 7 (23.3) | 6 (50)   | 1 (5.6)   | 0.001 |
| localized                        | 8 (26.7) | 5 (41.7) | 3 (16.7)  |       |
| locally advanced                 | 15 (50)  | 1 (8.3)  | 14 (77.8) |       |
| metastatic                       | 2 (.)    | 1 (.)    | 1 (.)     | 0.206 |

#### Pathology

#### adenocarcinoma

#### epidermoide carcinoma

#### Differentiation grade

|                |           |           |          |       |
|----------------|-----------|-----------|----------|-------|
| no             | 27 (96.4) | 10 (90.9) | 17 (100) |       |
| yes            | 1 (3.6)   | 1 (9.1)   | 0 (0)    |       |
| adenocarcinoma | 10 (.)    | 4 (.)     | 6 (.)    | 0.893 |

|                                               |                           |                      |             |                |              |
|-----------------------------------------------|---------------------------|----------------------|-------------|----------------|--------------|
| Type of adenocarcinoma                        | Poorly differentiated     | 11 (55)              | 4 (50)      | 7 (58.3)       | 0.018        |
|                                               | Moderately differentiated | 5 (25)               | 2 (25)      | 3 (25)         |              |
|                                               | Well differentiated       | 4 (20)               | 2 (25)      | 2 (16.7)       |              |
|                                               |                           | 6 (.)                | 3 (.)       | 3 (.)          |              |
|                                               | stomach                   | 4 (16.7)             | 4 (44.4)    | 0 (0)          | 0.136        |
|                                               | liver/biliary tract       | 2 (8.3)              | 0 (0)       | 2 (13.3)       |              |
|                                               | pancreas                  | 10 (41.7)            | 4 (44.4)    | 6 (40)         |              |
|                                               | colorectal cancer         | 8 (33.3)             | 1 (11.1)    | 7 (46.7)       |              |
| Type of epidermoid carcinoma                  |                           | 30 (.)               | 12 (.)      | 18 (.)         | 0.232        |
| Type of endocrine carcinoma                   |                           | 30 (.)               | 12 (.)      | 18 (.)         |              |
| Other type of endocrine carcinoma             |                           | 30 (.)               | 12 (.)      | 18 (.)         |              |
|                                               |                           |                      |             |                |              |
| <b><u>History of the pathology</u></b>        |                           |                      |             |                |              |
| Time since primary diagnosis (months)         |                           | 1 [0.8-1.9] (n=30)   | 1 [0.8-1.7] | 1.1 [0.8-2.1]  | 0.866        |
| Surgery                                       | no                        | 26 (86.7)            | 12 (100)    | 14 (77.8)      | <b>0.079</b> |
|                                               | yes                       | 4 (13.3)             | 0 (0)       | 4 (22.2)       |              |
| If yes, type of surgery                       | right colectomy           | 1 (25)               | 0 (0)       | 1 (25)         |              |
|                                               | left colectomy            | 1 (25)               | 0 (0)       | 1 (25)         |              |
|                                               | partial hepatectomy       | 1 (25)               | 0 (0)       | 1 (25)         | 0.136        |
|                                               | SPG                       | 1 (25)               | 0 (0)       | 1 (25)         |              |
| Time since primary surgery (months)           |                           | 2.4 [1.8-32.6] (n=4) | .-.-        | 2.4 [1.8-32.6] |              |
| pTNM                                          |                           | 28 (.)               | 12 (.)      | 16 (.)         |              |
| Chemotherapy                                  | pT3N0                     | 1 (50)               | 0 (0)       | 1 (50)         | 0.406        |
|                                               | pTXN+M1                   | 1 (50)               | 0 (0)       | 1 (50)         |              |
|                                               | no                        | 27 (90)              | 12 (100)    | 15 (83.3)      |              |
|                                               | yes                       | 3 (10)               | 0 (0)       | 3 (16.7)       |              |
| Type of chemotherapy : neoadjuvant            | no                        | 29 (96.7)            | 12 (100)    | 17 (94.4)      | 0.232        |
|                                               | yes                       | 1 (3.3)              | 0 (0)       | 1 (5.6)        |              |
| Type of chemotherapy : adjuvant               | no                        | 28 (93.3)            | 12 (100)    | 16 (88.9)      |              |
|                                               | yes                       | 2 (6.7)              | 0 (0)       | 2 (11.1)       |              |
| Duration of neoadjuvant chemotherapy (months) |                           | 1.7 [1.7-1.7] (n=1)  | .-.-        | 1.7 [1.7-1.7]  | 0.018        |
| Duration of adjuvant chemotherapy (months)    |                           | 4.9 [2.4-7.4] (n=2)  | .-.-        | 4.9 [2.4-7.4]  |              |

|                                               |     |                     |           |               |              |
|-----------------------------------------------|-----|---------------------|-----------|---------------|--------------|
| Radiotherapy                                  | No  | 29 (96.7)           | 12 (100)  | 17 (94.4)     | 0.406        |
|                                               | Yes | 1 (3.3)             | 0 (0)     | 1 (5.6)       |              |
| Type of radiotherapy : neoadjuvant            | No  | 29 (96.7)           | 12 (100)  | 17 (94.4)     | 0.406        |
|                                               | Yes | 1 (3.3)             | 0 (0)     | 1 (5.6)       |              |
| Duration of neoadjuvant radiotherapy (months) |     | 1.3 [1.3-1.3] (n=1) | . [-.]    | 1.3 [1.3-1.3] |              |
| <b>Physical examination</b>                   |     |                     |           |               |              |
| ECOG PS                                       |     |                     |           |               | <b>0.105</b> |
| 0                                             |     | 1 (.)               | 0 (.)     | 1 (.)         |              |
| 1                                             |     | 8 (27.6)            | 6 (50)    | 2 (11.8)      |              |
| 2                                             |     | 14 (48.3)           | 5 (41.7)  | 9 (52.9)      |              |
| 3                                             |     | 6 (20.7)            | 1 (8.3)   | 5 (29.4)      |              |
|                                               |     | 1 (3.4)             | 0 (0)     | 1 (5.9)       |              |
| No                                            |     | 9 (30)              | 3 (25)    | 6 (33.3)      | 0.626        |
| Yes                                           |     | 21 (70)             | 9 (75)    | 12 (66.7)     |              |
| At least one symptom at screening visit       |     |                     |           |               |              |
| Symptoms :                                    |     |                     |           |               |              |
| Pain                                          | No  | 18 (60)             | 8 (66.7)  | 10 (55.6)     | 0.543        |
|                                               | Yes | 12 (40)             | 4 (33.3)  | 8 (44.4)      |              |
| Asthenia                                      | No  | 26 (86.7)           | 12 (100)  | 14 (77.8)     | 0.079        |
|                                               | Yes | 4 (13.3)            | 0 (0)     | 4 (22.2)      |              |
| Anorexia                                      | No  | 26 (86.7)           | 9 (75)    | 17 (94.4)     | 0.125        |
|                                               | Yes | 4 (13.3)            | 3 (25)    | 1 (5.6)       |              |
| Nausea                                        | No  | 29 (96.7)           | 12 (100)  | 17 (94.4)     | 0.406        |
|                                               | Yes | 1 (3.3)             | 0 (0)     | 1 (5.6)       |              |
| Vomiting                                      | No  | 29 (96.7)           | 11 (91.7) | 18 (100)      | 0.213        |
|                                               | Yes | 1 (3.3)             | 1 (8.3)   | 0 (0)         |              |
| Transit disorders                             | No  | 25 (83.3)           | 10 (83.3) | 15 (83.3)     | 1.000        |
|                                               | Yes | 5 (16.7)            | 2 (16.7)  | 3 (16.7)      |              |
| RGO-oesophagite                               | No  | 30 (100)            | 12 (100)  | 18 (100)      |              |
| Dysphagia                                     | No  | 29 (96.7)           | 11 (91.7) | 18 (100)      | 0.213        |
|                                               | Yes | 1 (3.3)             | 1 (8.3)   | 0 (0)         |              |
| Icterus (ou jaundice ?)                       | No  | 28 (93.3)           | 11 (91.7) | 17 (94.4)     | 0.765        |
|                                               | Yes | 2 (6.7)             | 1 (8.3)   | 1 (5.6)       |              |

|                                              |                              |                         |                |                |              |
|----------------------------------------------|------------------------------|-------------------------|----------------|----------------|--------------|
| Ascites                                      | No                           | 29 (96.7)               | 11 (91.7)      | 18 (100)       | 0.213        |
|                                              | Yes                          | 1 (3.3)                 | 1 (8.3)        | 0 (0)          |              |
| Occlusion                                    | No                           | 30 (100)                | 12 (100)       | 18 (100)       |              |
| Other symptoms                               | No                           | 25 (83.3)               | 9 (75)         | 16 (88.9)      | 0.317        |
|                                              | Yes                          | 5 (16.7)                | 3 (25)         | 2 (11.1)       |              |
|                                              | bloating                     | 1 (20)                  | 0 (0)          | 1 (50)         |              |
|                                              | dyspnea                      | 1 (20)                  | 0 (0)          | 1 (50)         |              |
|                                              | budding ulcer mass (primary) | 1 (20)                  | 1 (33.3)       | 0 (0)          |              |
|                                              | rash                         | 1 (20)                  | 1 (33.3)       | 0 (0)          |              |
|                                              | rectal bleeding              | 1 (20)                  | 1 (33.3)       | 0 (0)          |              |
|                                              |                              | 4 (.)                   | 2 (.)          | 2 (.)          | 0.271        |
| Electro-cardiogram done                      | no                           | 21 (80.8)               | 7 (70)         | 14 (87.5)      |              |
|                                              | yes                          | 5 (19.2)                | 3 (30)         | 2 (12.5)       |              |
|                                              |                              | 1 (.)                   | 1 (.)          | 0 (.)          | 0.248        |
| If yes, result                               | anormal                      | 1 (25)                  | 0 (0)          | 1 (50)         |              |
|                                              | normal                       | 3 (75)                  | 2 (100)        | 1 (50)         |              |
| <b><u>Biological assessment</u></b>          |                              |                         |                |                |              |
| CA19.9                                       |                              | 16 [10-258] (n=19)      | 21 [11-29.6]   | 15.1 [10-301]  | 0.838        |
| ACE                                          |                              | 3 [1.3-5] (n=21)        | 2.1 [1-4]      | 3.7 [1.8-19.3] | 0.212        |
| <b>Inclusion</b>                             |                              |                         |                |                |              |
| Sex                                          | Female                       | 12 (40)                 | 5 (41.7)       | 7 (38.9)       | 0.879        |
|                                              | Male                         | 18 (60)                 | 7 (58.3)       | 11 (61.1)      |              |
| Age (years)                                  |                              | 70.4 [59.3-78.8] (n=30) | 59.8 [58.5-73] | 72.9 [62.8-82] | <b>0.086</b> |
| <b><u>Physical examination</u></b>           |                              |                         |                |                |              |
| Weight loss between M-6 and baseline         |                              | 7 [4.5-11] (n=28)       | 6 [5-10]       | 7.5 [2-13]     | 0.907        |
| Weight loss between M-6 and baseline (class) | No weight loss               | 2 (.)                   | 0 (.)          | 2 (.)          | 0.393        |
|                                              | 0<Weight loss<10             | 2 (7.1)                 | 0 (0)          | 2 (12.5)       |              |
|                                              | Weight loss≥10               | 16 (57.1)               | 8 (66.7)       | 8 (50)         |              |
|                                              |                              | 10 (35.7)               | 4 (33.3)       | 6 (37.5)       |              |
| Weight loss between M-1 and baseline         |                              | 2 [-2-4.5] (n=28)       | -1.5 [-2-3]    | 2 [0.5-5]      | 0.102        |

| Weight loss between M-1 and baseline (class) | 2 (.)                 | 0 (.)          | 2 (.)            | 0.202 |
|----------------------------------------------|-----------------------|----------------|------------------|-------|
| No weight loss                               | 11 (39.3)             | 7 (58.3)       | 4 (25)           |       |
| 0<Weight loss<5                              | 10 (35.7)             | 3 (25)         | 7 (43.8)         |       |
| Weight loss≥5                                | 7 (25)                | 2 (16.7)       | 5 (31.3)         |       |
| No                                           | 10 (33.3)             | 5 (41.7)       | 5 (27.8)         | 0.429 |
| Yes                                          | 20 (66.7)             | 7 (58.3)       | 13 (72.2)        |       |
| BMI (kg/m2)                                  | 22.7 [20.7-25] (n=19) | 22 [20.7-24.6] | 23.4 [20.8-24.6] | 0.792 |
| BMI                                          | 11 (.)                | 6 (.)          | 5 (.)            | 0.563 |
| Normal weight                                | 14 (73.7)             | 4 (66.7)       | 10 (76.9)        |       |
| Overweight                                   | 4 (21.1)              | 2 (33.3)       | 2 (15.4)         |       |
| Obesity                                      | 1 (5.3)               | 0 (0)          | 1 (7.7)          |       |
| Underweight                                  | 11 (.)                | 6 (.)          | 5 (.)            | 0.637 |
| No                                           | 14 (73.7)             | 4 (66.7)       | 10 (76.9)        |       |
| Yes                                          | 5 (26.3)              | 2 (33.3)       | 3 (23.1)         |       |
| Overweight                                   | 11 (.)                | 6 (.)          | 5 (.)            | 0.637 |
| No                                           | 14 (73.7)             | 4 (66.7)       | 10 (76.9)        |       |
| Yes                                          | 5 (26.3)              | 2 (33.3)       | 3 (23.1)         |       |
| Obesity                                      | 11 (.)                | 6 (.)          | 5 (.)            | 0.485 |
| No                                           | 18 (94.7)             | 6 (100)        | 12 (92.3)        |       |
| Yes                                          | 1 (5.3)               | 0 (0)          | 1 (7.7)          |       |
| ECOG PS                                      | 2 (.)                 | 0 (.)          | 2 (.)            | 0.048 |
| 0                                            | 6 (21.4)              | 5 (41.7)       | 1 (6.3)          |       |
| 1                                            | 13 (46.4)             | 6 (50)         | 7 (43.8)         |       |
| 2                                            | 7 (25)                | 1 (8.3)        | 6 (37.5)         |       |
| 3                                            | 2 (7.1)               | 0 (0)          | 2 (12.5)         |       |
| ECG                                          | 3 (.)                 | 0 (.)          | 3 (.)            | 0.187 |
| No                                           | 8 (29.6)              | 2 (16.7)       | 6 (40)           |       |
| Yes                                          | 19 (70.4)             | 10 (83.3)      | 9 (60)           |       |
| If yes, results                              | 1 (.)                 | 0 (.)          | 1 (.)            |       |
| Abnormal                                     | 4 (22.2)              | 1 (10)         | 3 (37.5)         |       |
| Normal                                       | 14 (77.8)             | 9 (90)         | 5 (62.5)         |       |
| At least one symptom at inclusion            | 11 (36.7)             | 5 (41.7)       | 6 (33.3)         | 0.643 |
| No                                           |                       |                |                  |       |

|                    |     |           |           |           |       |
|--------------------|-----|-----------|-----------|-----------|-------|
| Symptoms :         | Yes | 19 (63.3) | 7 (58.3)  | 12 (66.7) |       |
|                    | No  | 1 (.)     | 0 (.)     | 1 (.)     | 0.979 |
| Pain               | No  | 17 (58.6) | 7 (58.3)  | 10 (58.8) |       |
|                    | Yes | 12 (41.4) | 5 (41.7)  | 7 (41.2)  |       |
| asthenia           | No  | 1 (.)     | 0 (.)     | 1 (.)     | 0.653 |
|                    | Yes | 23 (79.3) | 10 (83.3) | 13 (76.5) |       |
| anorexia           | No  | 6 (20.7)  | 2 (16.7)  | 4 (23.5)  |       |
|                    | Yes | 1 (.)     | 0 (.)     | 1 (.)     | 0.474 |
| nausea             | No  | 25 (86.2) | 11 (91.7) | 14 (82.4) |       |
|                    | Yes | 4 (13.8)  | 1 (8.3)   | 3 (17.6)  |       |
| vomiting           | No  | 1 (.)     | 0 (.)     | 1 (.)     | 0.226 |
|                    | Yes | 28 (96.6) | 11 (91.7) | 17 (100)  |       |
| transit disorders  | No  | 1 (3.4)   | 1 (8.3)   | 0 (0)     |       |
|                    | Yes | 1 (.)     | 0 (.)     | 1 (.)     | 0.798 |
| transit disorders  | No  | 27 (93.1) | 11 (91.7) | 16 (94.1) |       |
|                    | Yes | 2 (6.9)   | 1 (8.3)   | 1 (5.9)   |       |
| transit disorders  | No  | 1 (.)     | 0 (.)     | 1 (.)     | 0.286 |
|                    | Yes | 24 (82.8) | 11 (91.7) | 13 (76.5) |       |
| GERD               | No  | 5 (17.2)  | 1 (8.3)   | 4 (23.5)  |       |
|                    | Yes | 1 (.)     | 0 (.)     | 1 (.)     |       |
| icterus / jaundice | No  | 29 (100)  | 12 (100)  | 17 (100)  |       |
|                    | Yes | 1 (.)     | 0 (.)     | 1 (.)     | 0.226 |
| ascites            | No  | 28 (96.6) | 11 (91.7) | 17 (100)  |       |
|                    | Yes | 1 (3.4)   | 1 (8.3)   | 0 (0)     |       |
| occlusion          | No  | 1 (.)     | 0 (.)     | 1 (.)     |       |
|                    | Yes | 29 (100)  | 12 (100)  | 17 (100)  |       |
| other              | No  | 1 (.)     | 0 (.)     | 1 (.)     |       |
|                    | Yes | 29 (100)  | 12 (100)  | 17 (100)  | 0.798 |

|                                  |                  |           |           |           |       |
|----------------------------------|------------------|-----------|-----------|-----------|-------|
|                                  | No               | 27 (93.1) | 11 (91.7) | 16 (94.1) |       |
|                                  | Yes              | 2 (6.9)   | 1 (8.3)   | 1 (5.9)   |       |
|                                  | Dyspnea          | 1 (50)    | 0 (0)     | 1 (100)   |       |
|                                  | Rectal bleeding  | 1 (50)    | 1 (100)   | 0 (0)     |       |
| <b><u>Chemotherapy</u></b>       |                  |           |           |           |       |
| Ongoing chemotherapy             | No               | 2 (.)     | 0 (.)     | 2 (.)     | 0.743 |
|                                  | Yes              | 13 (46.4) | 6 (50)    | 7 (43.8)  |       |
| If yes, administration mode      | Yes              | 15 (53.6) | 6 (50)    | 9 (56.3)  | 0.398 |
|                                  | Unique           | 1 (6.7)   | 0 (0)     | 1 (11.1)  |       |
|                                  | Combined         | 14 (93.3) | 6 (100)   | 8 (88.9)  |       |
|                                  | 5FU              | 1 (100)   | 0 (0)     | 1 (100)   |       |
| If unique,                       | No               | 1 (7.1)   | 0 (0)     | 1 (12.5)  | 0.369 |
|                                  | If combined: 5FU | 13 (92.9) | 6 (100)   | 7 (87.5)  |       |
| If combined : IRINOTECAN         | No               | 8 (57.1)  | 2 (33.3)  | 6 (75)    | 0.119 |
|                                  | Yes              | 6 (42.9)  | 4 (66.7)  | 2 (25)    |       |
| If combined : OXALIPLATINE       | No               | 2 (14.3)  | 0 (0)     | 2 (25)    | 0.186 |
|                                  | Yes              | 12 (85.7) | 6 (100)   | 6 (75)    |       |
| If combined : GEMCITABINE        | No               | 13 (92.9) | 6 (100)   | 7 (87.5)  | 0.369 |
|                                  | Yes              | 1 (7.1)   | 0 (0)     | 1 (12.5)  |       |
| If combined : other chemotherapy | No               | 12 (85.7) | 4 (66.7)  | 8 (100)   | 0.078 |
|                                  | Yes              | 2 (14.3)  | 2 (33.3)  | 0 (0)     |       |
| Chemotherapy: dose reduction     | Taxotere         | 2 (100)   | 2 (100)   | 0 (0)     | 0.475 |
|                                  | No               | 11 (73.3) | 5 (83.3)  | 6 (66.7)  |       |
|                                  | Yes              | 4 (26.7)  | 1 (16.7)  | 3 (33.3)  |       |
|                                  |                  |           |           |           |       |
| <b><u>Targeted therapies</u></b> |                  |           |           |           |       |
| Targeted therapies?              | No               | 3 (.)     | 1 (.)     | 2 (.)     | 0.223 |
|                                  | Yes              | 25 (92.6) | 11 (100)  | 14 (87.5) |       |
|                                  | BEVACIZUMAB      | 2 (7.4)   | 0 (0)     | 2 (12.5)  |       |
|                                  | PANITUMUMAB      | 1 (50)    | 0 (0)     | 1 (50)    |       |
| Pain                             |                  | 1 (50)    | 0 (0)     | 1 (50)    | 0.446 |
|                                  |                  | 3 (.)     | 1 (.)     | 2 (.)     |       |
|                                  | No               | 20 (74.1) | 9 (81.8)  | 11 (68.8) |       |
|                                  |                  |           |           |           |       |

|                      |                                              |                         |                  |                  |              |
|----------------------|----------------------------------------------|-------------------------|------------------|------------------|--------------|
| Third level antalgic | Yes                                          | 7 (25.9)                | 2 (18.2)         | 5 (31.3)         | 0.290        |
|                      | No                                           | 23 (.)                  | 10 (.)           | 13 (.)           |              |
|                      | Yes                                          | 5 (71.4)                | 2 (100)          | 3 (60)           |              |
|                      | SKENAN                                       | 2 (28.6)                | 0 (0)            | 2 (40)           |              |
| <b>Biochemistry</b>  |                                              | 2 (100)                 | 0 (0)            | 2 (100)          |              |
|                      | Leukocytes (10 <sup>9</sup> /l)              | 8.5 [6-12.2] (n=27)     | 7.8 [5.6-10.3]   | 8.7 [6.1-16.5]   | 0.449        |
|                      | Hemoglobin (g/dL)                            | 11.5 [10.7-14.4] (n=27) | 13.4 [11.9-15.3] | 10.9 [10.5-11.7] | <b>0.008</b> |
|                      | Platelets (10 <sup>9</sup> /l)               | 304 [247-506] (n=27)    | 291 [246-519]    | 309 [247-479]    | 0.961        |
|                      | Polynuclear neutrophils (10 <sup>9</sup> /l) | 5.4 [3.8-8] (n=27)      | 5 [4-7.3]        | 5.6 [3.8-11]     | 0.626        |
|                      | Lymphocytes (10 <sup>9</sup> /l)             | 1.6 [1.1-2.1] (n=25)    | 1.8 [1.5-2.2]    | 1.5 [0.9-1.9]    | 0.114        |
|                      | Monocytes (10 <sup>9</sup> /l)               | 0.6 [0.4-0.9] (n=25)    | 0.4 [0.3-0.5]    | 0.7 [0.6-1.2]    | 0.127        |
|                      | Polynuclear eosinophils (10 <sup>9</sup> /l) | 0.2 [0.1-0.3] (n=22)    | 0.2 [0.2-0.3]    | 0.1 [0.1-0.3]    | 0.229        |
|                      | Polynuclear basophils (10 <sup>9</sup> /l)   | 0.1 [0-0.1] (n=21)      | 0.1 [0.1-0.1]    | 0 [0-0.1]        | 0.108        |
|                      | Neutrophil/Lymphocyte Ration                 | 4 [1.9-5.9] (n=25)      | 3.1 [1.4-4.1]    | 4.7 [2.4-12.2]   | 0.046        |
|                      | Creatinine (μmol/l)                          | 70 [64-80.5] (n=26)     | 69 [66-81]       | 70 [60-80.5]     | 0.856        |
|                      | Calcemia (mmol/l)                            | 2.4 [2.4-2.5] (n=21)    | 2.4 [2.4-2.5]    | 2.5 [2.3-2.5]    | 0.404        |
|                      | Phosphore (mmol/l)                           | 1.1 [1-1.3] (n=21)      | 1.2 [1.1-1.4]    | 1.1 [1-1.2]      | 0.109        |
|                      | Magnesium (mmol/l)                           | 0.9 [0.8-0.9] (n=19)    | 0.9 [0.8-0.9]    | 0.9 [0.8-0.9]    | 0.646        |
|                      | CRP (mg/l)                                   | 5.2 [1-44] (n=22)       | 2.3 [1-6]        | 20.5 [2.9-69.5]  | <b>0.137</b> |
|                      | CRP class                                    | 8 (.)                   | 2 (.)            | 6 (.)            | <b>0.069</b> |
|                      |                                              | 13 (59.1)               | 8 (80)           | 5 (41.7)         |              |
|                      |                                              | 9 (40.9)                | 2 (20)           | 7 (58.3)         |              |
|                      | Total bilirubine (μmol/l)                    | 9.5 [7-14] (n=24)       | 9.5 [7-13]       | 9.5 [7.4-15]     | 0.770        |
|                      | Phosphatase (U/l)                            | 104 [78-248] (n=25)     | 88 [56-234]      | 119.5 [86-336]   | 0.147        |
|                      | LDH (U/l)                                    | 207 [194-244] (n=11)    | 213 [207-222]    | 201 [185-266]    | 0.648        |
|                      | ASAT (U/l)                                   | 30.5 [23-39] (n=26)     | 28.5 [23-38.5]   | 32.5 [25-40]     | 0.571        |
|                      | ALAT (U/l)                                   | 29.5 [19-40] (n=26)     | 31.5 [21.5-39]   | 29 [19-54]       | 0.979        |
|                      | Albumine (g/l)                               | 37.9 [31.9-41] (n=22)   | 39.6 [37.7-45]   | 33.5 [28.8-38.5] | <b>0.052</b> |
|                      | Albumine class                               | 8 (.)                   | 2 (.)            | 6 (.)            | <b>0.019</b> |
|                      |                                              | 14 (63.6)               | 9 (90)           | 5 (41.7)         |              |
|                      |                                              | 8 (36.4)                | 1 (10)           | 7 (58.3)         |              |
|                      | ≥36                                          |                         |                  |                  |              |
|                      | <36                                          |                         |                  |                  |              |

## Albumine class

|     |                         |                   |                   |       |
|-----|-------------------------|-------------------|-------------------|-------|
| ≥30 | 8 (.)                   | 2 (.)             | 6 (.)             | 0.364 |
| <30 | 18 (81.8)               | 9 (90)            | 9 (75)            |       |
|     | 4 (18.2)                | 1 (10)            | 3 (25)            |       |
|     | 0.2 [0.1-0.3] (n=12)    | 0.3 [0.2-0.3]     | 0.1 [0.1-0.3]     | 0.254 |
|     | 15 (.)                  | 5 (.)             | 10 (.)            | 0.051 |
| 0   | 8 (53.3)                | 6 (85.7)          | 2 (25)            |       |
| 1   | 3 (20)                  | 0 (0)             | 3 (37.5)          |       |
| 2   | 4 (26.7)                | 1 (14.3)          | 3 (37.5)          |       |
|     | 13.7 [11.2-14.8] (n=8)  | 11.3 [11-13.5]    | 14.3 [13.8-15.3]  | 0.177 |
|     | 11.8 [9.3-20.7] (n=8)   | 16.4 [9-33.2]     | 11 [9.3-16.1]     | 0.665 |
|     | 373 [247.5-489.5] (n=8) | 373 [237.5-419.5] | 409.5 [247.5-717] | 0.665 |
|     | 20.8 [13-38] (n=6)      | 16.3 [11.6-28.8]  | 33.5 [22-45]      | 0.247 |
|     | 359 [91-1056] (n=11)    | 344 [62-359]      | 707 [197-1056]    | 0.411 |
|     | 19 [13-30.2] (n=7)      | 30.2 [22-33]      | 14.5 [10-17.5]    | 0.052 |

## Transferrin saturation coefficient

## Imagery

Measure of muscular surface of L3 (m2/m2)

Measure of muscular surface of L3 (class)

≥34,4 for Female or ≥45,4 for Male

<34,4 for Female or <45,4 for Male

Number of metastatic sites at inclusion

|   |                         |                  |                  |       |
|---|-------------------------|------------------|------------------|-------|
| 0 | 5 (.)                   | 1 (.)            | 4 (.)            | 0.006 |
| 1 | 10 (40)                 | 9 (81.8)         | 1 (7.1)          |       |
| 2 | 7 (28)                  | 1 (9.1)          | 6 (42.9)         |       |
| 3 | 6 (24)                  | 1 (9.1)          | 5 (35.7)         |       |
| 4 | 1 (4)                   | 0 (0)            | 1 (7.1)          |       |
|   | 1 (4)                   | 0 (0)            | 1 (7.1)          |       |
|   | 30.7 [28.3-33] (n=2)    | 30.7 [28.3-33]   | . [-.]           |       |
|   | 16.5 [14.1-18.5] (n=26) | 16.7 [13.4-21.5] | 16.5 [14.6-18.3] | 0.979 |
|   | 4 (.)                   | 2 (.)            | 2 (.)            |       |
|   | 26 (100)                | 10 (100)         | 16 (100)         |       |
|   | 28 [26-30] (n=23)       | 28 [27-31]       | 27.8 [25-29]     | 0.281 |
|   | 44 [42-45] (n=22)       | 43.5 [42-45]     | 44 [42-49]       | 0.918 |
|   | 30.7 [26-33.9] (n=26)   | 31.8 [30.1-33.9] | 29.1 [25.5-35.2] | 0.429 |

Muscle Area Index (cm2/m2)

Muscle Mass Index (kg/m2)

Muscle Mass Index (class)

≥5,5 for Female or ≥7 for Male

Arm Circumference (cm)

Thigh circumference (cm)

Fat mass (%)

|                                                |                       |                   |                |       |
|------------------------------------------------|-----------------------|-------------------|----------------|-------|
| Lean mass (%)                                  | 69.5 [67.9-74] (n=25) | 68.3 [66.1-69.9]  | 72 [68.1-75.1] | 0.267 |
| Weight loss at M1 (%)                          | 1 [0-3.4]             | 2.8 [0-3.7]       | 0 [0-2.4]      | 0.173 |
| Weight loss at M1 (%) in class                 | 5 (.)                 | 1 (.)             | 4 (.)          | 0.098 |
| No weight loss                                 | 12 (48)               | 3 (27.3)          | 9 (64.3)       |       |
| 0<Weight loss<5                                | 10 (40)               | 7 (63.6)          | 3 (21.4)       |       |
| Weight loss>=5                                 | 3 (12)                | 1 (9.1)           | 2 (14.3)       |       |
| Weight loss at M6 (%)                          | 3.6 [0-7.3]           | 5.8 [2.5-9.5]     | 1.1 [-1.3-4.3] | 0.075 |
| Weight loss at M6 (%) in class                 | 10 (.)                | 2 (.)             | 8 (.)          | 0.185 |
| No weight loss                                 | 7 (35)                | 2 (20)            | 5 (50)         |       |
| 0<Weight loss<10                               | 11 (55)               | 6 (60)            | 5 (50)         |       |
| Weight loss>=10                                | 2 (10)                | 2 (20)            | 0 (0)          |       |
| <b><u>Nutritional evaluation</u></b>           |                       |                   |                |       |
| VAS of food intakes                            | 7 [5-9] (n=26)        | 8.5 [7-9]         | 6 [5-10]       | 0.331 |
| Nutritional support: dietary advice            | 1 (.)                 | 0 (.)             | 1 (.)          | 0.474 |
| No                                             | 4 (13.8)              | 1 (8.3)           | 3 (17.6)       |       |
| Yes                                            | 25 (86.2)             | 11 (91.7)         | 14 (82.4)      |       |
| Nutritional support: oral nutrition supplement | 1 (.)                 | 0 (.)             | 1 (.)          | 0.269 |
| No                                             | 8 (27.6)              | 2 (16.7)          | 6 (35.3)       |       |
| Yes                                            | 21 (72.4)             | 10 (83.3)         | 11 (64.7)      |       |
| Nutritional support: enteral nutrition         | 1 (.)                 | 0 (.)             | 1 (.)          | 0.765 |
| No                                             | 26 (89.7)             | 11 (91.7)         | 15 (88.2)      |       |
| Yes                                            | 3 (10.3)              | 1 (8.3)           | 2 (11.8)       |       |
| Nutritional support: parenteral nutrition      | 1 (.)                 | 0 (.)             | 1 (.)          |       |
| No                                             | 29 (100)              | 12 (100)          | 17 (100)       |       |
| <b><u>Physical evaluation</u></b>              |                       |                   |                |       |
| 6-minute walking test (m)                      | 367 [231-420]         | 419 [362.5-440.5] | 255 [168-409]  | 0.021 |
| Borg scale                                     | 3 [2-3]               | 3 [2-3]           | 3 [3-3]        | 0.107 |
| Handgrip Test (kg)                             | 25 [22-37]            | 26 [22-38]        | 24.5 [22.5-30] | 0.824 |
| Get up and Go test (sec)                       | 7 [6-9]               | 6 [5-8]           | 8.5 [7-12]     | 0.034 |
| chair stand fitness test (nb in 30 sec)        | 9 [8-11]              | 10 [9-12]         | 8 [7-10]       | 0.109 |

balance in single-leg (sec)  
balance in bipodal stance (sec)

38 [4-60]  
60 [60-60]

60 [10-60]  
60 [60-60]

4 [1-60]  
60 [60-60]

0.032  
0.179

## Nutrition and APA

### Nutrition

Currently, are you following a diet?

No  
Yes

Was this diet prescribed to you by a health professional: general practitioner, specialist doctor (nutritionist or endocrinologist), dietician?

Yes

Why are you following this diet?  
For a medical reason unrelated to an overweight problem (food allergy, salt-free diet, etc.)

No  
Yes

Why are you following this diet? To lose weight

No

Why are you following this diet?  
To not gain weight

No

Why are you following this diet? To stay fit

No  
Yes

Can you indicate the amounts of food you are currently eating, by placing the slider between "I am eating nothing at all" and "I am eating as usual"?

Please indicate the portion consumed during your last meal (noon or evening)

3  
5

9 (.)  
17 (81)  
4 (19)

1 (.)  
7 (63.6)  
4 (36.4)

8 (.)  
10 (100)  
0 (0)

26 (.)  
4 (100)

8 (.)  
4 (100)

1 (.)  
27 (93.1)  
2 (6.9)

0 (.)  
10 (83.3)  
2 (16.7)

1 (.)  
29 (100)

0 (.)  
12 (100)

1 (.)  
29 (100)

1 (.)  
27 (93.1)  
2 (6.9)

75 [50-90] (n=19)

8 (.)  
2 (9.1)  
4 (18.2)

80.5 [68-90]

1 (.)  
0 (0)  
0 (0)

50 [20-89]

7 (.)  
2 (18.2)  
4 (36.4)

0.034

0.081

0.081

0.287  
0.123

|     |                                                                                                                                                                                                       |           |           |           |       |
|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------|-----------|-------|
| 7   |                                                                                                                                                                                                       | 3 (13.6)  | 2 (18.2)  | 1 (9.1)   |       |
| 8   |                                                                                                                                                                                                       | 3 (13.6)  | 2 (18.2)  | 1 (9.1)   |       |
| 9   |                                                                                                                                                                                                       | 1 (4.5)   | 1 (9.1)   | 0 (0)     |       |
| 10  |                                                                                                                                                                                                       | 9 (40.9)  | 6 (54.5)  | 3 (27.3)  |       |
|     | Have you heard about the existence of anti-cancer diet?                                                                                                                                               | 8 (.)     | 1 (.)     | 7 (.)     | 0.193 |
| No  |                                                                                                                                                                                                       | 13 (59.1) | 5 (45.5)  | 8 (72.7)  |       |
| Yes |                                                                                                                                                                                                       | 9 (40.9)  | 6 (54.5)  | 3 (27.3)  |       |
|     | Have you heard about the existence of foods to avoid or favor to prevent the occurrence of cancer?                                                                                                    | 21 (.)    | 6 (.)     | 15 (.)    | 0.571 |
| No  |                                                                                                                                                                                                       | 2 (22.2)  | 1 (16.7)  | 1 (33.3)  |       |
| Yes |                                                                                                                                                                                                       | 7 (77.8)  | 5 (83.3)  | 2 (66.7)  |       |
|     | Have you heard of diets to follow when cancer is present in order to slow down its progression or help cure it? (example therapeutic fasting during chemotherapy, avoidance of sugar, ketogenic diet) | 21 (.)    | 6 (.)     | 15 (.)    | 0.343 |
| No  |                                                                                                                                                                                                       | 4 (44.4)  | 2 (33.3)  | 2 (66.7)  |       |
| Yes |                                                                                                                                                                                                       | 5 (55.6)  | 4 (66.7)  | 1 (33.3)  |       |
|     | Which diet? Ketogenic diet                                                                                                                                                                            | 1 (.)     | 0 (.)     | 1 (.)     |       |
| No  |                                                                                                                                                                                                       | 29 (100)  | 12 (100)  | 17 (100)  |       |
|     | Which diet? Therapeutic fasting                                                                                                                                                                       | 1 (.)     | 0 (.)     | 1 (.)     | 0.393 |
| No  |                                                                                                                                                                                                       | 28 (96.6) | 12 (100)  | 16 (94.1) |       |
| Yes |                                                                                                                                                                                                       | 1 (3.4)   | 0 (0)     | 1 (5.9)   |       |
|     | Which diet? Sugar-free diet                                                                                                                                                                           | 1 (.)     | 0 (.)     | 1 (.)     | 0.029 |
| No  |                                                                                                                                                                                                       | 26 (89.7) | 9 (75)    | 17 (100)  |       |
| Yes |                                                                                                                                                                                                       | 3 (10.3)  | 3 (25)    | 0 (0)     |       |
|     | Which diet? other                                                                                                                                                                                     | 1 (.)     | 0 (.)     | 1 (.)     | 0.226 |
| No  |                                                                                                                                                                                                       | 28 (96.6) | 11 (91.7) | 17 (100)  |       |
| Yes |                                                                                                                                                                                                       | 1 (3.4)   | 1 (8.3)   | 0 (0)     |       |
|     | What is your opinion on the subject?                                                                                                                                                                  | 1 (100)   | 1 (100)   | 0 (0)     |       |
|     | Proteins                                                                                                                                                                                              | 25 (.)    | 8 (.)     | 17 (.)    | 0.361 |

|                                                                                                                        |                                                                                                                                  |                  |                 |                  |              |
|------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|------------------|-----------------|------------------|--------------|
| Was this diet recommended to you by anyone?                                                                            | I don't have an opinion                                                                                                          | 3 (60)           | 2 (50)          | 1 (100)          |              |
|                                                                                                                        | I have a favorable opinion of it (I think that there is no particular risk in doing this diet in combination with my treatments) | 2 (40)           | 2 (50)          | 0 (0)            |              |
| Was it by a health professional: general practitioner, specialist doctor (nutritionist or endocrinologist), dietician? | No                                                                                                                               | 25 (.)           | 8 (.)           | 17 (.)           | 0.576        |
|                                                                                                                        | Yes                                                                                                                              | 1 (20)           | 1 (25)          | 0 (0)            |              |
|                                                                                                                        |                                                                                                                                  | 4 (80)           | 3 (75)          | 1 (100)          |              |
| Was this diet recommended to you by an acquaintance/family member/friends?                                             | No                                                                                                                               | 26 (.)           | 9 (.)           | 17 (.)           | 0.505        |
|                                                                                                                        | Yes                                                                                                                              | 1 (25)           | 1 (33.3)        | 0 (0)            |              |
|                                                                                                                        |                                                                                                                                  | 3 (75)           | 2 (66.7)        | 1 (100)          |              |
| Do you intend to follow a special diet during your treatment or have you already started one?                          | No                                                                                                                               | 28 (.)           | 11 (.)          | 17 (.)           | 0.157        |
|                                                                                                                        | Yes                                                                                                                              | 1 (50)           | 0 (0)           | 1 (100)          |              |
|                                                                                                                        |                                                                                                                                  | 1 (50)           | 1 (100)         | 0 (0)            |              |
|                                                                                                                        | No                                                                                                                               | 13 (.)           | 2 (.)           | 11 (.)           | 0.252        |
|                                                                                                                        | Yes                                                                                                                              | 12 (70.6)        | 6 (60)          | 6 (85.7)         |              |
|                                                                                                                        |                                                                                                                                  | 5 (29.4)         | 4 (40)          | 1 (14.3)         |              |
| <b>Quality of life (Eortc Qla C30)</b>                                                                                 |                                                                                                                                  |                  |                 |                  |              |
| Physical functioning                                                                                                   |                                                                                                                                  | 93.3 [80-100]    | 100 [100-100]   | 80 [53.3-93.3]   | <0.001       |
| Role Functioning                                                                                                       |                                                                                                                                  | 100 [66.7-100]   | 100 [83.3-100]  | 75 [66.7-100]    | 0.133        |
| Cognitive functioning                                                                                                  |                                                                                                                                  | 100 [83.3-100]   | 100 [83.3-100]  | 100 [83.3-100]   | 1.000        |
| Emotional functioning                                                                                                  |                                                                                                                                  | 72.2 [58.3-95.8] | 91.7 [58.3-100] | 66.7 [58.3-91.7] | 0.337        |
| Social functioning                                                                                                     |                                                                                                                                  | 83.3 [66.7-100]  | 91.7 [83.3-100] | 83.3 [66.7-100]  | 0.444        |
| Fatigue                                                                                                                |                                                                                                                                  | 33.3 [0-50]      | 0 [0-22.2]      | 50 [33.3-66.7]   | <b>0.001</b> |
| Pain                                                                                                                   |                                                                                                                                  | 0 [0-33.3]       | 0 [0-16.7]      | 0 [0-33.3]       | 0.556        |
| Nausea and vomiting                                                                                                    |                                                                                                                                  | 0 [0-16.7]       | 0 [0-0]         | 0 [0-16.7]       | 0.076        |
| Insomnia                                                                                                               |                                                                                                                                  | 33.3 [0-66.7]    | 16.7 [0-33.3]   | 33.3 [0-66.7]    | 0.364        |
| Constipation                                                                                                           |                                                                                                                                  | 0 [0-33.3]       | 0 [0-33.3]      | 16.7 [0-66.7]    | 0.303        |
| Dyspnoea                                                                                                               |                                                                                                                                  | 0 [0-33.3]       | 0 [0-33.3]      | 0 [0-33.3]       | 0.716        |

|                          |            |                  |               |              |
|--------------------------|------------|------------------|---------------|--------------|
| Diarrhoea                | 0 [0-50]   | 0 [0-33.3]       | 33.3 [0-66.7] | 0.142        |
| Appetite loss            | 0 [0-33.3] | 0 [0-0]          | 33.3 [0-66.7] | <b>0.025</b> |
| Financial difficulties   | 0 [0-0]    | 0 [0-0]          | 0 [0-0]       | 1.000        |
| Global health status/QoL | 50 [50-75] | 70.8 [58.3-83.3] | 50 [41.7-50]  | <b>0.009</b> |

Table 2. Patient characteristics according to the availability of HRQoL evaluation at baseline in the ITT population (n=30)

| Table 2. Patient characteristics according to the fragility score and to the assessment of the oral treatment requirement (n=30) |                  |                                                |  |                                           |  |       |
|----------------------------------------------------------------------------------------------------------------------------------|------------------|------------------------------------------------|--|-------------------------------------------|--|-------|
| Fragility score                                                                                                                  | Global<br>(n=30) | No HRQoL<br>evaluation at<br>baseline<br>(n=9) |  | HRQoL evaluation<br>at baseline<br>(n=21) |  | p     |
|                                                                                                                                  |                  | N(%) or median[IQR]                            |  | N(%) or<br>median[IQR]                    |  |       |
| Chemotherapy type                                                                                                                |                  |                                                |  |                                           |  | 0.013 |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
| Nutritional status                                                                                                               |                  |                                                |  |                                           |  | 0.038 |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
| Comorbidities                                                                                                                    |                  |                                                |  |                                           |  | 0.337 |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
| Symptoms                                                                                                                         |                  |                                                |  |                                           |  | 0.518 |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
| Age-related fragility                                                                                                            |                  |                                                |  |                                           |  | 0.258 |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
| Fragility score                                                                                                                  |                  |                                                |  |                                           |  | 0.036 |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |
|                                                                                                                                  |                  |                                                |  |                                           |  |       |

|                                |                                  |           |          |           |
|--------------------------------|----------------------------------|-----------|----------|-----------|
| Fragility score                | 6                                | 7 (23.3)  | 2 (22.2) | 5 (23.8)  |
|                                | 7                                | 8 (26.7)  | 5 (55.6) | 3 (14.3)  |
|                                | moderate fragility               | 30 (100)  | 9 (100)  | 21 (100)  |
| Screening                      |                                  |           |          |           |
| Comorbidities                  |                                  |           |          |           |
| Comorbidities                  |                                  |           |          |           |
| Comorbidities type: cardiac    | no                               | 13 (43.3) | 5 (55.6) | 8 (38.1)  |
|                                | yes                              | 17 (56.7) | 4 (44.4) | 13 (61.9) |
|                                |                                  |           |          | 0.376     |
| Comorbidities type: cardiac    | no                               | 23 (76.7) | 5 (55.6) | 18 (85.7) |
|                                | yes                              | 7 (23.3)  | 4 (44.4) | 3 (14.3)  |
|                                |                                  |           |          | 0.073     |
| Comorbidities type: cardiac    | atrial fibrillation              | 3 (.)     | 2 (.)    | 1 (.)     |
|                                | aortic bioprosthesis             | 1 (25)    | 0 (0)    | 1 (50)    |
|                                | pacemaker                        | 1 (25)    | 1 (50)   | 0 (0)     |
| Comorbidities type: cardiac    | rhythm disturbances              | 1 (25)    | 0 (0)    | 1 (50)    |
|                                |                                  |           |          | 0 (0)     |
|                                |                                  |           |          | 0 (0)     |
| Comorbidities type: pulmonary  | no                               | 30 (100)  | 9 (100)  | 21 (100)  |
|                                | no                               | 26 (86.7) | 7 (77.8) | 19 (90.5) |
|                                | yes                              | 4 (13.3)  | 2 (22.2) | 2 (9.5)   |
| Comorbidities type: neurologic | stroke                           | 3 (75)    | 2 (100)  | 1 (50)    |
|                                | normal pressure hydrocephalus    | 1 (25)    | 0 (0)    | 1 (50)    |
|                                |                                  |           |          | 0.348     |
| High blood pressure            | no                               | 18 (60)   | 5 (55.6) | 13 (61.9) |
|                                | yes                              | 12 (40)   | 4 (44.4) | 8 (38.1)  |
|                                |                                  |           |          | 0.745     |
| Obesity                        | no                               | 29 (96.7) | 8 (88.9) | 21 (100)  |
|                                | yes                              | 1 (3.3)   | 1 (11.1) | 0 (0)     |
|                                |                                  |           |          | 0.120     |
| other comorbidity              | no                               | 25 (83.3) | 8 (88.9) | 17 (81)   |
|                                | yes                              | 5 (16.7)  | 1 (11.1) | 4 (19)    |
|                                |                                  |           |          | 0.593     |
| Pathology stage                | diabetes                         | 3 (60)    | 1 (50)   | 2 (66.6)  |
|                                | history of leukemia and melanoma | 1 (20)    | 0 (0)    | 1 (25)    |
|                                | prostate cancer                  | 1 (20)    | 0 (0)    | 1 (25)    |
| Pathology stage                | localized                        | 7 (23.3)  | 0 (0)    | 7 (33.3)  |
|                                | locally advanced                 | 8 (26.7)  | 3 (33.3) | 5 (23.8)  |
|                                | metastatic                       | 15 (50)   | 6 (66.7) | 9 (42.9)  |
|                                |                                  |           |          | 0.140     |

|                                       |                |               |               |       |
|---------------------------------------|----------------|---------------|---------------|-------|
| Pathology                             | 2 (.)          | 1 (.)         | 1 (.)         | 0.107 |
| adenocarcinoma                        | 27 (96.4)      | 7 (87.5)      | 20 (100)      |       |
| epidermoïde carcinoma                 | 1 (3.6)        | 1 (12.5)      | 0 (0)         |       |
| Differentiation grade                 | 10 (.)         | 1 (.)         | 9 (.)         | 0.064 |
| Poorly differentiated                 | 11 (55)        | 5 (62.5)      | 6 (50)        |       |
| Moderately differentiated             | 5 (25)         | 0 (0)         | 5 (41.7)      |       |
| Well differentiated                   | 4 (20)         | 3 (37.5)      | 1 (8.3)       |       |
| Type of adenocarcinoma                | 6 (.)          | 2 (.)         | 4 (.)         | 0.505 |
| stomach                               | 4 (16.7)       | 0 (0)         | 4 (23.5)      |       |
| liver/biliary tract                   | 2 (8.3)        | 1 (14.3)      | 1 (5.9)       |       |
| pancreas                              | 10 (41.7)      | 3 (42.9)      | 7 (41.2)      |       |
| colorectal cancer                     | 8 (33.3)       | 3 (42.9)      | 5 (29.4)      |       |
| Type of epidermoid carcinoma          | 30 (.)         | 9 (.)         | 21 (.)        |       |
| Type of endocrine carcinoma           | 30 (.)         | 9 (.)         | 21 (.)        |       |
| Other type of endocrine carcinoma     | 30 (.)         | 9 (.)         | 21 (.)        |       |
| <b>History of the pathology</b>       |                |               |               |       |
| Time since primary diagnosis (months) | 1 [0.8-1.9]    | 1.1 [0.8-1.9] | 1 [0.8-1.7]   | 0.821 |
| Surgery                               | 26 (86.7)      | 7 (77.8)      | 19 (90.5)     | 0.348 |
| no                                    | 4 (13.3)       | 2 (22.2)      | 2 (9.5)       |       |
| yes                                   | 1 (25)         | 1 (50)        | 0 (0)         |       |
| right colectomy                       | 1 (25)         | 0 (0)         | 1 (50)        |       |
| left colectomy                        | 1 (25)         | 0 (0)         | 1 (50)        |       |
| partial hepatectomy                   | 1 (25)         | 0 (0)         | 1 (50)        |       |
| SPG                                   | 1 (25)         | 1 (50)        | 0 (0)         |       |
| Time since primary surgery (months)   | 2.4 [1.8-32.6] | 32 [1.6-62.5] | 2.4 [2.1-2.8] |       |
| pTNM                                  | 28 (.)         | 9 (.)         | 19 (.)        |       |
| pT3N0                                 | 1 (50)         | 0 (0)         | 1 (50)        |       |
| pTXN+M1                               | 1 (50)         | 0 (0)         | 1 (50)        |       |
| Chemotherapy                          | 27 (90)        | 8 (88.9)      | 19 (90.5)     | 0.894 |
| no                                    | 3 (10)         | 1 (11.1)      | 2 (9.5)       |       |
| yes                                   | 29 (96.7)      | 9 (100)       | 20 (95.2)     | 0.506 |
| Type of chemotherapy : neoadjuvant    | 1 (3.3)        | 0 (0)         | 1 (4.8)       |       |
| no                                    | 28 (93.3)      | 8 (88.9)      | 20 (95.2)     | 0.523 |
| Type of chemotherapy : adjuvant       |                |               |               |       |

|                                               |               |               |               |  |       |
|-----------------------------------------------|---------------|---------------|---------------|--|-------|
| yes                                           |               |               |               |  |       |
| Duration of neoadjuvant chemotherapy (months) | 2 (6.7)       | 1 (11.1)      | 1 (4.8)       |  |       |
| Duration of adjuvant chemotherapy (months)    | 1.7 [1.7-1.7] | . [-.]        | 1.7 [1.7-1.7] |  |       |
| Radiotherapy                                  | 4.9 [2.4-7.4] | 2.4 [2.4-2.4] | 7.4 [7.4-7.4] |  |       |
|                                               | 29 (96.7)     | 9 (100)       | 20 (95.2)     |  | 0.506 |
| Yes                                           | 1 (3.3)       | 0 (0)         | 1 (4.8)       |  |       |
| No                                            | 29 (96.7)     | 9 (100)       | 20 (95.2)     |  | 0.506 |
| Type of radiotherapy : neoadjuvant            | 1 (3.3)       | 0 (0)         | 1 (4.8)       |  |       |
| Yes                                           | 1.3 [1.3-1.3] | . [-.]        | 1.3 [1.3-1.3] |  |       |
| Duration of neoadjuvant radiotherapy (months) |               |               |               |  |       |
| <b>Physical examination</b>                   |               |               |               |  |       |
| ECOG PS                                       | 1 (.)         | 1 (.)         | 0 (.)         |  | 0.066 |
| 0                                             | 8 (27.6)      | 0 (0)         | 8 (38.1)      |  |       |
| 1                                             | 14 (48.3)     | 4 (50)        | 10 (47.6)     |  |       |
| 2                                             | 6 (20.7)      | 3 (37.5)      | 3 (14.3)      |  |       |
| 3                                             | 1 (3.4)       | 1 (12.5)      | 0 (0)         |  |       |
| No                                            | 9 (30)        | 1 (11.1)      | 8 (38.1)      |  | 0.139 |
| Yes                                           | 21 (70)       | 8 (88.9)      | 13 (61.9)     |  |       |
| At least one symptom at screening visit       |               |               |               |  |       |
| Symptoms :                                    |               |               |               |  |       |
| Pain                                          | 18 (60)       | 3 (33.3)      | 15 (71.4)     |  | 0.051 |
| Yes                                           | 12 (40)       | 6 (66.7)      | 6 (28.6)      |  |       |
| Asthenia                                      | 26 (86.7)     | 6 (66.7)      | 20 (95.2)     |  | 0.035 |
| Yes                                           | 4 (13.3)      | 3 (33.3)      | 1 (4.8)       |  |       |
| Anorexia                                      | 26 (86.7)     | 7 (77.8)      | 19 (90.5)     |  | 0.348 |
| Yes                                           | 4 (13.3)      | 2 (22.2)      | 2 (9.5)       |  |       |
| Nausea                                        | 29 (96.7)     | 8 (88.9)      | 21 (100)      |  | 0.120 |
| Yes                                           | 1 (3.3)       | 1 (11.1)      | 0 (0)         |  |       |
| Vomiting                                      | 29 (96.7)     | 9 (100)       | 20 (95.2)     |  | 0.506 |
| Yes                                           | 1 (3.3)       | 0 (0)         | 1 (4.8)       |  |       |
| Transit disorders                             | 25 (83.3)     | 7 (77.8)      | 18 (85.7)     |  | 0.593 |
| Yes                                           | 5 (16.7)      | 2 (22.2)      | 3 (14.3)      |  |       |
| RGO-oesophagite                               | 30 (100)      | 9 (100)       | 21 (100)      |  |       |
| Dysphagia                                     | 29 (96.7)     | 9 (100)       | 20 (95.2)     |  | 0.506 |

|                                      |                                              |                  |                  |                  |       |
|--------------------------------------|----------------------------------------------|------------------|------------------|------------------|-------|
| Icterus (ou jaundice ?)              | Yes                                          | 1 (3.3)          | 0 (0)            | 1 (4.8)          |       |
|                                      | No                                           | 28 (93.3)        | 9 (100)          | 19 (90.5)        | 0.338 |
|                                      | Yes                                          | 2 (6.7)          | 0 (0)            | 2 (9.5)          |       |
|                                      | No                                           | 29 (96.7)        | 9 (100)          | 20 (95.2)        | 0.506 |
|                                      | Yes                                          | 1 (3.3)          | 0 (0)            | 1 (4.8)          |       |
| Ascites                              | No                                           | 30 (100)         | 9 (100)          | 21 (100)         |       |
|                                      | Yes                                          | 25 (83.3)        | 7 (77.8)         | 18 (85.7)        | 0.593 |
| Occlusion                            | No                                           | 5 (16.7)         | 2 (22.2)         | 3 (14.3)         |       |
|                                      | Yes                                          | 1 (20)           | 0 (0)            | 1 (33.3)         |       |
|                                      | bloating                                     | 1 (20)           | 1 (50)           | 0 (0)            |       |
|                                      | dyspnea                                      | 1 (20)           | 1 (50)           | 0 (0)            |       |
|                                      | budding ulcer mass (primary)                 | 1 (20)           | 0 (0)            | 1 (33.3)         |       |
| Other symptoms                       | rash                                         | 1 (20)           | 0 (0)            | 1 (33.3)         |       |
|                                      | rectal bleeding                              | 4 (.)            | 3 (.)            | 1 (.)            | 0.318 |
|                                      | no                                           | 21 (80.8)        | 4 (66.7)         | 17 (85)          |       |
|                                      | yes                                          | 5 (19.2)         | 2 (33.3)         | 3 (15)           |       |
| Electro-cardiogram done              | normal                                       | 1 (.)            | 1 (.)            | 0 (.)            |       |
|                                      | anormal                                      | 1 (25)           | 1 (50)           | 0 (0)            |       |
|                                      | normal                                       | 3 (75)           | 1 (50)           | 2 (100)          |       |
|                                      |                                              |                  |                  |                  |       |
| <b>Biological assessment</b>         |                                              |                  |                  |                  |       |
| CA19.9                               |                                              | 16 [10-258]      | 15.1 [10-304]    | 18.5 [10-182.5]  | 1.000 |
|                                      | ACE                                          | 3 [1.3-5]        | 18.5 [2.7-327.5] | 2.5 [1-4]        | 0.193 |
| <b>Inclusion</b>                     |                                              |                  |                  |                  |       |
| Sex                                  | Female                                       | 12 (40)          | 4 (44.4)         | 8 (38.1)         | 0.745 |
|                                      | Male                                         | 18 (60)          | 5 (55.6)         | 13 (61.9)        |       |
| Age (years)                          |                                              | 70.4 [59.3-78.8] | 72.7 [60.8-82]   | 68.3 [59.3-74.1] | 0.651 |
| <b>Physical examination</b>          |                                              |                  |                  |                  |       |
| Weight loss between M-6 and baseline |                                              | 7 [4.5-11]       | 7 [4-11]         | 7 [5-11]         | 0.915 |
|                                      | Weight loss between M-6 and baseline (class) | 2 (.)            | 2 (.)            | 0 (.)            | 0.567 |
| No weight loss                       |                                              | 2 (7.1)          | 0 (0)            | 2 (9.5)          |       |
|                                      | 0<Weight loss<10                             | 16 (57.1)        | 5 (71.4)         | 11 (52.4)        |       |

|                                                                                      |                     |                |                  |                |       |
|--------------------------------------------------------------------------------------|---------------------|----------------|------------------|----------------|-------|
| Weight loss between M-1 and baseline<br>Weight loss between M-1 and baseline (class) | Weight loss ≥10     | 10 (35.7)      | 2 (28.6)         | 8 (38.1)       | 0.729 |
|                                                                                      |                     | 2 [-2-4.5]     | 2 [-2-3]         | 2 [-2-5]       |       |
| Malnutrition                                                                         | No weight loss      | 2 (.)          | 2 (.)            | 0 (.)          | 0.386 |
|                                                                                      | 0 < Weight loss < 5 | 11 (39.3)      | 2 (28.6)         | 9 (42.9)       |       |
| BMI (kg/m2)<br>BMI                                                                   | Weight loss ≥5      | 10 (35.7)      | 4 (57.1)         | 6 (28.6)       |       |
|                                                                                      | No                  | 7 (25)         | 1 (14.3)         | 6 (28.6)       | 1.000 |
|                                                                                      | Yes                 | 10 (33.3)      | 3 (33.3)         | 7 (33.3)       |       |
|                                                                                      |                     | 20 (66.7)      | 6 (66.7)         | 14 (66.7)      |       |
|                                                                                      |                     | 22.7 [20.7-25] | 23.1 [20.7-24.6] | 22.1 [20.8-25] | 1.000 |
|                                                                                      |                     | 11 (.)         | 3 (.)            | 8 (.)          | 0.127 |
| Underweight                                                                          | Normal weight       | 14 (73.7)      | 5 (83.3)         | 9 (69.2)       |       |
|                                                                                      | Overweight          | 4 (21.1)       | 0 (0)            | 4 (30.8)       |       |
|                                                                                      | Obesity             | 1 (5.3)        | 1 (16.7)         | 0 (0)          |       |
|                                                                                      |                     | 11 (.)         | 3 (.)            | 8 (.)          | 0.516 |
| Overweight                                                                           | No                  | 14 (73.7)      | 5 (83.3)         | 9 (69.2)       |       |
|                                                                                      | Yes                 | 5 (26.3)       | 1 (16.7)         | 4 (30.8)       |       |
|                                                                                      |                     | 11 (.)         | 3 (.)            | 8 (.)          | 0.516 |
|                                                                                      |                     | 14 (73.7)      | 5 (83.3)         | 9 (69.2)       |       |
| Obesity                                                                              | No                  | 5 (26.3)       | 1 (16.7)         | 4 (30.8)       |       |
|                                                                                      | Yes                 | 11 (.)         | 3 (.)            | 8 (.)          | 0.130 |
|                                                                                      |                     | 18 (94.7)      | 5 (83.3)         | 13 (100)       |       |
|                                                                                      |                     | 1 (5.3)        | 1 (16.7)         | 0 (0)          |       |
| ECOG PS                                                                              | 0                   | 2 (.)          | 2 (.)            | 0 (.)          | 0.020 |
|                                                                                      | 1                   | 6 (21.4)       | 0 (0)            | 6 (28.6)       |       |
|                                                                                      | 2                   | 13 (46.4)      | 2 (28.6)         | 11 (52.4)      |       |
|                                                                                      | 3                   | 7 (25)         | 3 (42.9)         | 4 (19)         |       |
| ECG                                                                                  | No                  | 2 (7.1)        | 2 (28.6)         | 0 (0)          |       |
|                                                                                      | Yes                 | 3 (.)          | 2 (.)            | 1 (.)          | 0.373 |
|                                                                                      |                     | 8 (29.6)       | 3 (42.9)         | 5 (25)         |       |
|                                                                                      |                     | 19 (70.4)      | 4 (57.1)         | 15 (75)        |       |
| If yes, results                                                                      | Abnormal            | 1 (.)          | 0 (.)            | 1 (.)          | 0.163 |
|                                                                                      |                     | 4 (22.2)       | 2 (50)           | 2 (14.3)       |       |

| At least one symptom at inclusion | Normal |           |          |           |
|-----------------------------------|--------|-----------|----------|-----------|
| Symptoms :                        |        |           |          |           |
| Pain                              |        |           |          |           |
|                                   | No     | 1 (.)     | 2 (50)   | 12 (85.7) |
|                                   | Yes    | 17 (58.6) | 2 (22.2) | 9 (42.9)  |
|                                   |        | 12 (41.4) | 7 (77.8) | 12 (57.1) |
| asthenia                          |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 23 (79.3) | 5 (62.5) | 18 (85.7) |
|                                   |        | 6 (20.7)  | 3 (37.5) | 3 (14.3)  |
| anorexia                          |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 25 (86.2) | 6 (75)   | 19 (90.5) |
|                                   |        | 4 (13.8)  | 2 (25)   | 2 (9.5)   |
| nausea                            |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 28 (96.6) | 7 (87.5) | 21 (100)  |
|                                   |        | 1 (3.4)   | 1 (12.5) | 0 (0)     |
| vomiting                          |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 27 (93.1) | 8 (100)  | 19 (90.5) |
|                                   |        | 2 (6.9)   | 0 (0)    | 2 (9.5)   |
| transit disorders                 |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 24 (82.8) | 7 (87.5) | 17 (81)   |
|                                   |        | 5 (17.2)  | 1 (12.5) | 4 (19)    |
| transit disorders                 |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 29 (100)  | 8 (100)  | 21 (100)  |
| GERD                              |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 28 (96.6) | 8 (100)  | 20 (95.2) |
|                                   |        | 1 (3.4)   |          | 1 (4.8)   |
| icterus / jaundice                |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 29 (100)  | 8 (100)  | 21 (100)  |
| ascites                           |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |
|                                   | Yes    | 29 (100)  | 8 (100)  | 21 (100)  |
| occlusion                         |        |           |          |           |
|                                   | No     | 1 (.)     | 1 (.)    | 0 (.)     |

|                                  |             |           |          |           |       |
|----------------------------------|-------------|-----------|----------|-----------|-------|
| other                            |             |           |          |           |       |
| No                               | No          | 29 (100)  | 8 (100)  | 21 (100)  | 0.462 |
|                                  |             | 1 (.)     | 1 (.)    | 0 (.)     |       |
| No                               | No          | 27 (93.1) | 7 (87.5) | 20 (95.2) |       |
| Yes                              | Yes         | 2 (6.9)   | 1 (12.5) | 1 (4.8)   |       |
| Dyspnea                          |             | 1 (50)    | 1 (100)  | 0 (0)     |       |
| Rectal bleeding                  |             | 1 (50)    | 0 (0)    | 1 (100)   |       |
| <b><u>Chemotherapy</u></b>       |             |           |          |           |       |
| Ongoing chemotherapy             |             | 2 (.)     | 2 (.)    | 0 (.)     | 0.512 |
|                                  | No          | 13 (46.4) | 4 (57.1) | 9 (42.9)  |       |
|                                  | Yes         | 15 (53.6) | 3 (42.9) | 12 (57.1) |       |
| If yes, administration mode      | Unique      | 1 (6.7)   | 1 (33.3) | 0 (0)     | 0.038 |
|                                  | Combined    | 14 (93.3) | 2 (66.7) | 12 (100)  |       |
| If unique,                       | 5FU         | 1 (100)   | 1 (100)  | 0 (0)     |       |
| If combined: 5FU                 | No          | 1 (7.1)   | 0 (0)    | 1 (8.3)   | 0.672 |
|                                  | Yes         | 13 (92.9) | 2 (100)  | 11 (91.7) |       |
| If combined : IRINOTECAN         | No          | 8 (57.1)  | 2 (100)  | 6 (50)    | 0.186 |
|                                  | Yes         | 6 (42.9)  | 0 (0)    | 6 (50)    |       |
| If combined : OXALIPLATINE       | No          | 2 (14.3)  | 0 (0)    | 2 (16.7)  | 0.533 |
|                                  | Yes         | 12 (85.7) | 2 (100)  | 10 (83.3) |       |
| If combined : GEMCITABINE        | No          | 13 (92.9) | 2 (100)  | 11 (91.7) | 0.672 |
|                                  | Yes         | 1 (7.1)   | 0 (0)    | 1 (8.3)   |       |
| If combined : other chemotherapy | No          | 12 (85.7) | 2 (100)  | 10 (83.3) | 0.533 |
|                                  | Yes         | 2 (14.3)  | 0 (0)    | 2 (16.7)  |       |
| Chemotherapy: dose reduction     | Taxotere    | 2 (100)   | 0 (0)    | 2 (100)   |       |
|                                  | No          | 11 (73.3) | 3 (100)  | 8 (66.7)  | 0.243 |
|                                  | Yes         | 4 (26.7)  | 0 (0)    | 4 (33.3)  |       |
| <b><u>Targeted therapies</u></b> |             |           |          |           |       |
| Targeted therapies?              |             | 3 (.)     | 2 (.)    | 1 (.)     | 0.419 |
|                                  | No          | 25 (92.6) | 6 (85.7) | 19 (95)   |       |
|                                  | Yes         | 2 (7.4)   | 1 (14.3) | 1 (5)     |       |
|                                  | BEVACIZUMAB | 1 (50)    | 0 (0)    | 1 (100)   |       |
|                                  | PANITUMUMAB | 1 (50)    | 1 (100)  | 0 (0)     |       |

|                                              |     |                  |                     |       |
|----------------------------------------------|-----|------------------|---------------------|-------|
| Pain                                         | No  | 2 (.)            | 1 (.)               | 0.029 |
|                                              | Yes | 3 (42.9)         | 17 (85)             |       |
|                                              |     | 4 (57.1)         | 3 (15)              |       |
|                                              |     | 5 (.)            | 18 (.)              | 0.809 |
| Third level antalgic                         | No  | 3 (75)           | 2 (66.7)            |       |
|                                              | Yes | 1 (25)           | 1 (33.3)            |       |
|                                              |     | 1 (100)          | 1 (100)             |       |
|                                              |     |                  |                     |       |
| <b>Biochemistry</b>                          |     |                  |                     |       |
| Leukocytes (10 <sup>9</sup> /l)              |     | 12.2 [7.7-26.6]  | 7.2 [5.6-10.3]      | 0.128 |
| Hemoglobin (g/dL)                            |     | 10.6 [8.7-11.2]  | 12.6 [11.2-14.6]    | 0.005 |
| Platelets (10 <sup>9</sup> /l)               |     | 310 [273-525]    | 298 [243-492.5]     | 0.489 |
| Polynuclear neutrophils (10 <sup>9</sup> /l) |     | 7.3 [5.2-17.2]   | 4.5 [3.3-7]         | 0.064 |
| Lymphocytes (10 <sup>9</sup> /l)             |     | 1.6 [1.4-3.1]    | 1.5 [1.1-2.1]       | 0.414 |
| Monocytes (10 <sup>9</sup> /l)               |     | 1 [0.7-1.9]      | 0.5 [0.3-0.7]       | 0.039 |
| Polynuclear eosinophils (10 <sup>9</sup> /l) |     | 0.3 [0.2-0.5]    | 0.2 [0.1-0.3]       | 0.183 |
| Polynuclear basophils (10 <sup>9</sup> /l)   |     | 0.1 [0-0.1]      | 0.1 [0-0.1]         | 0.213 |
| Neutrophil/Lymphocyte Ratio                  |     | 3.3 [2.4-8.5]    | 4.1 [1.9-4.8]       | 0.976 |
| Creatinine (μmol/l)                          |     | 73 [55-93]       | 69.9 [64-79.7]      | 0.664 |
| Calcemia (mmol/l)                            |     | 2.4 [2.4-2.5]    | 2.4 [2.3-2.5]       | 0.938 |
| Phosphore (mmol/l)                           |     | 1 [0.9-1.1]      | 1.2 [1.1-1.3]       | 0.051 |
| Magnesium (mmol/l)                           |     | 0.8 [0.8-0.8]    | 0.9 [0.9-0.9]       | 0.156 |
| CRP (mg/l)                                   |     | 20.5 [6-44]      | 3.5 [1-41.1]        | 0.318 |
| CRP class                                    |     | 3 (.)            | 5 (.)               | 0.132 |
|                                              | ≤11 | 2 (33.3)         | 11 (68.8)           |       |
|                                              | >11 | 4 (66.7)         | 5 (31.3)            |       |
| Total bilirubine (μmol/l)                    |     | 9 [7.4-15]       | 10 [7-13]           | 0.924 |
| Phosphatase (UI/l)                           |     | 248 [209-612]    | 87 [72-114]         | 0.007 |
| LDH (UI/l)                                   |     | 244 [200-456]    | 204.5 [189.5-217.5] | 0.262 |
| ASAT (UI/l)                                  |     | 39 [31-54]       | 27 [23-38]          | 0.032 |
| ALAT (UI/l)                                  |     | 30 [24-34]       | 29 [17-48]          | 0.817 |
| Albumine (g/l)                               |     | 36.1 [24.2-37.7] | 39 [32.1-43.2]      | 0.071 |
| Albumine class                               |     | 3 (.)            | 5 (.)               | 0.416 |

|                                           |                   |                  |                  |       |
|-------------------------------------------|-------------------|------------------|------------------|-------|
| ≥36                                       | 14 (63.6)         | 3 (50)           | 11 (68.8)        |       |
| <36                                       | 8 (36.4)          | 3 (50)           | 5 (31.3)         |       |
|                                           | 8 (.)             | 3 (.)            | 5 (.)            | 0.259 |
| ≥30                                       | 18 (81.8)         | 4 (66.7)         | 14 (87.5)        |       |
| <30                                       | 4 (18.2)          | 2 (33.3)         | 2 (12.5)         |       |
|                                           | 0.2 [0.1-0.3]     | 0.1 [0.1-0.2]    | 0.3 [0.1-0.3]    | 0.173 |
|                                           | 15 (.)            | 4 (.)            | 11 (.)           | 0.087 |
| 0                                         | 8 (53.3)          | 2 (40)           | 6 (60)           |       |
| 1                                         | 3 (20)            | 0 (0)            | 3 (30)           |       |
| 2                                         | 4 (26.7)          | 3 (60)           | 1 (10)           |       |
|                                           | 13.7 [11.2-14.8]  | 13.9 [13.5-14.3] | 12.6 [11-15.3]   | 0.867 |
| Quick time (sec)                          | 11.8 [9.3-20.7]   | 12.1 [6.5-45]    | 11.4 [9.8-20]    | 1.000 |
| Vitamin B9 (nmol/l)                       | 373 [247.5-489.5] | 305 [213-397]    | 395.5 [282-537]  | 0.617 |
| Vitamin B12 (pmol/l)                      | 20.8 [13-38]      | 41.5 [38-45]     | 16.3 [11.6-20.8] | 0.105 |
| Vitamin D (ng/ml)                         | 359 [91-1056]     | 359 [344-460]    | 575.5 [62-1210]  | 1.000 |
| Ferritin level (ng/ml)                    | 19 [13-30.2]      | 16 [10-20.5]     | 30.2 [16-33]     | 0.216 |
| Transferrin saturation coefficient        |                   |                  |                  |       |
| <b>Imagery</b>                            |                   |                  |                  |       |
| Measure of muscular surface of L3 (m2/m2) | 38.1 [34.4-47.6]  | 35.1 [33.1-45]   | 38.5 [36.4-47.7] | 0.446 |
| Measure of muscular surface of L3 (class) | 6 (.)             | 2 (.)            | 4 (.)            | 0.178 |
|                                           | 12 (50)           | 2 (28.6)         | 10 (58.8)        |       |
| ≥34,4 for Female or ≥45,4 for Male        | 12 (50)           | 5 (71.4)         | 7 (41.2)         |       |
| <34,4 for Female or <45,4 for Male        | 5 (.)             | 3 (.)            | 2 (.)            | 0.295 |
| Number of metastatic sites at inclusion   | 10 (40)           | 1 (16.7)         | 9 (47.4)         |       |
| 0                                         | 7 (28)            | 2 (33.3)         | 5 (26.3)         |       |
| 1                                         | 6 (24)            | 2 (33.3)         | 4 (21.1)         |       |
| 2                                         | 1 (4)             | 0 (0)            | 1 (5.3)          |       |
| 3                                         | 1 (4)             | 1 (16.7)         | 0 (0)            |       |
| 4                                         | 30.7 [28.3-33]    | . [-]            | 30.7 [28.3-33]   |       |
| Muscle Area Index (cm2/m2)                | 16.5 [14.1-18.5]  | 16 [14.1-18.5]   | 16.5 [14.2-18.5] | 0.715 |
| Muscle Mass Index (kg/m2)                 | 4 (.)             | 3 (.)            | 1 (.)            |       |
| Muscle Mass Index (class)                 | 26 (100)          | 6 (100)          | 20 (100)         |       |
| ≥5,5 for Female or ≥7 for Male            | 28 [26-30]        | 29 [27-31.5]     | 28 [26-29]       | 0.462 |
| Arm Circumference (cm)                    |                   |                  |                  |       |

|                                                |                |                  |                  |       |
|------------------------------------------------|----------------|------------------|------------------|-------|
| Thigh circumference (cm)                       | 44 [42-45]     | 45.5 [40.5-49.5] | 44 [42-45]       | 0.966 |
| Fat mass (%)                                   | 30.7 [26-33.9] | 32.2 [26-39.4]   | 30.7 [26-32.6]   | 0.715 |
| Lean mass (%)                                  | 69.5 [67.9-74] | 67.8 [60.6-74]   | 69.5 [67.9-75.1] | 0.567 |
| Weight loss at M1 (%)                          | 1 [0-3.4]      | 0 [0-1.4]        | 1.4 [0-3.6]      | 0.782 |
| Weight loss at M1 (%)                          | 5 (.)          | 4 (.)            | 1 (.)            | 0.626 |
| No weight loss                                 | 12 (48)        | 3 (60)           | 9 (45)           |       |
| 0<Weight loss<5                                | 10 (40)        | 2 (40)           | 8 (40)           |       |
| Weight loss>=5                                 | 3 (12)         | 0 (0)            | 3 (15)           |       |
| Weight loss at M6 (%)                          | 3.6 [0-7.3]    | 0 [-7.2-4.3]     | 4 [0-7.5]        | 0.244 |
| Weight loss at M6 (%)                          | 10 (.)         | 6 (.)            | 4 (.)            | 0.435 |
| No weight loss                                 | 7 (35)         | 2 (66.7)         | 5 (29.4)         |       |
| 0<Weight loss<10                               | 11 (55)        | 1 (33.3)         | 10 (58.8)        |       |
| Weight loss>=10                                | 2 (10)         | 0 (0)            | 2 (11.8)         |       |
| <b><u>Nutritional evaluation</u></b>           |                |                  |                  |       |
| VAS of food intakes                            | 7 [5-9]        | 7 [5-10]         | 7 [5-9]          | 0.813 |
| Nutritional support: dietary advice            | 1 (.)          | 1 (.)            | 0 (.)            | 0.280 |
| No                                             | 4 (13.8)       | 2 (25)           | 2 (9.5)          |       |
| Yes                                            | 25 (86.2)      | 6 (75)           | 19 (90.5)        |       |
| Nutritional support: oral nutrition supplement | 1 (.)          | 1 (.)            | 0 (.)            | 0.461 |
| No                                             | 8 (27.6)       | 3 (37.5)         | 5 (23.8)         |       |
| Yes                                            | 21 (72.4)      | 5 (62.5)         | 16 (76.2)        |       |
| Nutritional support: enteral nutrition         | 1 (.)          | 1 (.)            | 0 (.)            | 0.110 |
| No                                             | 26 (89.7)      | 6 (75)           | 20 (95.2)        |       |
| Yes                                            | 3 (10.3)       | 2 (25)           | 1 (4.8)          |       |
| Nutritional support: parenteral nutrition      | 1 (.)          | 1 (.)            | 0 (.)            |       |
| No                                             | 29 (100)       | 8 (100)          | 21 (100)         |       |
| <b><u>Physical evaluation</u></b>              |                |                  |                  |       |
| 6-minute walking test (m)                      | 367 [231-420]  | 243 [219-279.5]  | 409 [273-420]    | 0.099 |
| Borg scale                                     | 3 [2-3]        | 3 [3-3]          | 3 [2-3]          | 0.597 |
| Handgrip Test (kg)                             | 25 [22-37]     | 26 [22-31]       | 25 [23-37]       | 0.884 |

Get up and Go test (sec)  
chair stand fitness test (nb in 30 sec)  
balance in single-leg (sec)  
balance in bipodal stance (sec)

|            |              |            |       |
|------------|--------------|------------|-------|
| 7 [6-9]    | 8 [6.5-10.5] | 7 [6-9]    | 0.627 |
| 9 [8-11]   | 7 [6-8.5]    | 10 [8-12]  | 0.061 |
| 38 [4-60]  | 24 [5.5-49]  | 60 [4-60]  | 0.670 |
| 60 [60-60] | 60 [60-60]   | 60 [60-60] | 1.000 |

Table 3. Patient characteristics according to the primary endpoint (definition 1) in the mITT population (n=27)

|                                                                        | Global<br>(n=27) | Primary efficacy<br>endpoint:<br>success<br>(n=12)<br>N(%) or<br>median[IQR] | Primary efficacy<br>endpoint: failure<br>(n=15)<br>N(%) or<br>median[IQR] | p     |
|------------------------------------------------------------------------|------------------|------------------------------------------------------------------------------|---------------------------------------------------------------------------|-------|
| <b>Fragility score</b>                                                 |                  |                                                                              |                                                                           |       |
| Chemotherapy type                                                      |                  |                                                                              |                                                                           |       |
| mono chemotherapy                                                      | 4 (14.8)         | 1 (8.3)                                                                      | 3 (20)                                                                    | 0.690 |
| bi chemotherapy                                                        | 8 (29.6)         | 4 (33.3)                                                                     | 4 (26.7)                                                                  |       |
| tri chemotherapy                                                       | 15 (55.6)        | 7 (58.3)                                                                     | 8 (53.3)                                                                  |       |
| no denutrition                                                         | 9 (33.3)         | 4 (33.3)                                                                     | 5 (33.3)                                                                  | 0.869 |
| moderate denutrition                                                   | 10 (37)          | 5 (41.7)                                                                     | 5 (33.3)                                                                  |       |
| severe denutrition                                                     | 8 (29.6)         | 3 (25)                                                                       | 5 (33.3)                                                                  |       |
| Comorbidities                                                          | 1 (.)            | 0 (.)                                                                        | 1 (.)                                                                     | 0.512 |
| No comorbidity                                                         | 12 (46.2)        | 7 (58.3)                                                                     | 5 (35.7)                                                                  |       |
| One significant comorbidity                                            | 11 (42.3)        | 4 (33.3)                                                                     | 7 (50)                                                                    |       |
| At least two significant comorbidities                                 | 3 (11.5)         | 1 (8.3)                                                                      | 2 (14.3)                                                                  |       |
| no symptom                                                             | 7 (25.9)         | 3 (25)                                                                       | 4 (26.7)                                                                  | 0.522 |
| Symptoms                                                               |                  |                                                                              |                                                                           |       |
| Symptoms controlled by oral treatments<br>requiring regular assessment | 19 (70.4)        | 8 (66.7)                                                                     | 11 (73.3)                                                                 |       |
| Symptoms not controlled by oral<br>treatments                          | 1 (3.7)          | 1 (8.3)                                                                      | 0 (0)                                                                     |       |
| Age-related fragility                                                  |                  |                                                                              |                                                                           |       |
| patient < 75 years old                                                 | 19 (70.4)        | 9 (75)                                                                       | 10 (66.7)                                                                 | 0.637 |
| patient > 75 years old and G8 score ≤ 14                               | 8 (29.6)         | 3 (25)                                                                       | 5 (33.3)                                                                  |       |
| Fragility score                                                        | 10 (37)          | 4 (33.3)                                                                     | 6 (40)                                                                    | 0.525 |
|                                                                        | 5 (18.5)         | 1 (8.3)                                                                      | 4 (26.7)                                                                  |       |

|                                                                 |                                   |           |           |           |        |
|-----------------------------------------------------------------|-----------------------------------|-----------|-----------|-----------|--------|
| Fragility score<br>Type of cancer vs fragility score            | 6                                 | 7 (25.9)  | 4 (33.3)  | 3 (20)    | 0.191  |
|                                                                 | 7                                 | 5 (18.5)  | 3 (25)    | 2 (13.3)  |        |
|                                                                 | moderate fragility                | 27 (100)  | 12 (100)  | 15 (100)  |        |
|                                                                 | Metastatic with frailty score <=6 | 10 (37)   | 6 (50)    | 4 (26.7)  |        |
|                                                                 | Metastatic with frailty score=7   | 5 (18.5)  | 3 (25)    | 2 (13.3)  |        |
| Non metastatic                                                  |                                   |           |           |           | 9 (60) |
| Screening                                                       |                                   |           |           |           |        |
| Comorbidities<br>Comorbidities type: cardiac                    | no                                | 12 (44.4) | 4 (33.3)  | 8 (53.3)  | 0.299  |
|                                                                 | yes                               | 15 (55.6) | 8 (66.7)  | 7 (46.7)  |        |
|                                                                 | no                                | 22 (81.5) | 10 (83.3) | 12 (80)   |        |
|                                                                 | yes                               | 5 (18.5)  | 2 (16.7)  | 3 (20)    |        |
|                                                                 |                                   | 2 (.)     | 1 (.)     | 1 (.)     |        |
| Comorbidities type: pulmonary<br>Comorbidities type: neurologic | atrial fibrillation               | 1 (33.3)  | 0 (0)     | 1 (50)    | 0.411  |
|                                                                 | pacemaker                         | 1 (33.3)  | 1 (100)   | 0 (0)     |        |
|                                                                 | rhythm disturbances               | 1 (33.3)  | 0 (0)     | 1 (50)    |        |
|                                                                 | no                                | 27 (100)  | 12 (100)  | 15 (100)  |        |
|                                                                 | no                                | 24 (88.9) | 10 (83.3) | 14 (93.3) |        |
| High blood pressure                                             | yes                               | 3 (11.1)  | 2 (16.7)  | 1 (6.7)   | 0.722  |
|                                                                 | stroke                            | 2 (66.7)  | 1 (50)    | 1 (100)   |        |
|                                                                 | normal pressure hydrocephalus     | 1 (33.3)  | 1 (50)    | 0 (0)     |        |
|                                                                 | no                                | 17 (63)   | 8 (66.7)  | 9 (60)    |        |
|                                                                 | yes                               | 10 (37)   | 4 (33.3)  | 6 (40)    |        |
| Obesity                                                         | no                                | 26 (96.3) | 12 (100)  | 14 (93.3) | 0.362  |
|                                                                 | yes                               | 1 (3.7)   | 0 (0)     | 1 (6.7)   |        |
|                                                                 | no                                | 22 (81.5) | 10 (83.3) | 12 (80)   |        |
|                                                                 | yes                               | 5 (18.5)  | 2 (16.7)  | 3 (20)    |        |
|                                                                 |                                   | 3 (60)    | 1 (50)    | 2 (66.6)  |        |
| other comorbidity                                               | diabetes                          | 1 (20)    | 0 (0)     | 1 (33.3)  | 0.825  |
|                                                                 | history of leukemia and melanoma  | 1 (20)    | 1 (50)    | 0 (0)     |        |
|                                                                 | prostate cancer                   | 1 (20)    | 1 (50)    | 0 (0)     |        |
|                                                                 | localized                         | 7 (25.9)  | 3 (25)    | 4 (26.7)  |        |
|                                                                 | Pathology stage                   |           |           |           |        |

|                                     |                           |                |               |                 |       |
|-------------------------------------|---------------------------|----------------|---------------|-----------------|-------|
| Pathology                           | locally advanced          | 7 (25.9)       | 2 (16.7)      | 5 (33.3)        | 0.366 |
|                                     | metastatic                | 13 (48.1)      | 7 (58.3)      | 6 (40)          |       |
|                                     | adenocarcinoma            | 2 (.)          | 1 (.)         | 1 (.)           |       |
|                                     | epidermoïde carcinoma     | 24 (96)        | 11 (100)      | 13 (92.9)       |       |
| Differentiation grade               | Poorly differentiated     | 1 (4)          | 0 (0)         | 1 (7.1)         | 0.056 |
|                                     | Moderately differentiated | 10 (.)         | 4 (.)         | 6 (.)           |       |
|                                     | Well differentiated       | 8 (47.1)       | 4 (50)        | 4 (44.4)        |       |
|                                     |                           | 5 (29.4)       | 4 (50)        | 1 (11.1)        |       |
| Type of adenocarcinoma              | stomach                   | 4 (23.5)       | 0 (0)         | 4 (44.4)        | 0.975 |
|                                     | liver/biliary tract       | 6 (.)          | 3 (.)         | 3 (.)           |       |
|                                     | pancreas                  | 4 (19)         | 2 (22.2)      | 2 (16.7)        |       |
|                                     | colorectal cancer         | 2 (9.5)        | 1 (11.1)      | 1 (8.3)         |       |
| History of the pathology            |                           | 7 (33.3)       | 3 (33.3)      | 4 (33.3)        | 0.034 |
|                                     |                           | 8 (38.1)       | 3 (33.3)      | 5 (41.7)        |       |
|                                     | no                        | 1.1 [0.8-1.9]  | 0.9 [0.8-1.2] | 1.6 [0.9-2.8]   |       |
|                                     | yes                       | 24 (88.9)      | 11 (91.7)     | 13 (86.7)       |       |
| If yes, type of surgery             | right colectomy           | 3 (11.1)       | 1 (8.3)       | 2 (13.3)        | 0.681 |
|                                     | left colectomy            | 1 (33.3)       | 0 (0)         | 1 (50)          |       |
|                                     | partial hepatectomy       | 1 (33.3)       | 0 (0)         | 1 (50)          |       |
|                                     |                           | 1 (33.3)       | 1 (100)       | 0 (0)           |       |
| Time since primary surgery (months) | pTNM                      | 2.8 [2.1-62.5] | 2.1 [2.1-2.1] | 32.6 [2.8-62.5] | 0.540 |
|                                     | pT3N0                     | 25 (.)         | 11 (.)        | 14 (.)          |       |
|                                     | pTXN+M1                   | 1 (50)         | 0 (0)         | 1 (100)         |       |
|                                     | no                        | 1 (50)         | 1 (100)       | 0 (0)           |       |
| Chemotherapy                        | yes                       | 24 (88.9)      | 11 (91.7)     | 13 (86.7)       | 0.681 |
|                                     | no                        | 3 (11.1)       | 1 (8.3)       | 2 (13.3)        |       |
|                                     | yes                       | 26 (96.3)      | 12 (100)      | 14 (93.3)       |       |
|                                     | no                        | 1 (3.7)        | 0 (0)         | 1 (6.7)         |       |
| Type of chemotherapy : neoadjuvant  | yes                       | 25 (92.6)      | 11 (91.7)     | 14 (93.3)       | 0.869 |
|                                     | no                        | 2 (7.4)        | 1 (8.3)       | 1 (6.7)         |       |

|                                               |     |               |               |               |       |
|-----------------------------------------------|-----|---------------|---------------|---------------|-------|
| Duration of neoadjuvant chemotherapy (months) |     |               |               |               |       |
| Duration of adjuvant chemotherapy (months)    |     |               |               |               |       |
| Radiotherapy                                  | No  | 1.7 [1.7-1.7] | . [-.]        | 1.7 [1.7-1.7] |       |
|                                               | Yes | 4.9 [2.4-7.4] | 7.4 [7.4-7.4] | 2.4 [2.4-2.4] | 0.362 |
|                                               |     | 26 (96.3)     | 12 (100)      | 14 (93.3)     |       |
|                                               |     | 1 (3.7)       | 0 (0)         | 1 (6.7)       |       |
| Type of radiotherapy : neoadjuvant            | No  | 26 (96.3)     | 12 (100)      | 14 (93.3)     | 0.362 |
|                                               | Yes | 1 (3.7)       | 0 (0)         | 1 (6.7)       |       |
| Duration of neoadjuvant radiotherapy (months) |     | 1.3 [1.3-1.3] | . [-.]        | 1.3 [1.3-1.3] |       |
| <b>Physical examination</b>                   |     |               |               |               |       |
| ECOG PS                                       | 0   | 8 (29.6)      | 5 (41.7)      | 3 (20)        | 0.533 |
|                                               | 1   | 12 (44.4)     | 5 (41.7)      | 7 (46.7)      |       |
|                                               | 2   | 6 (22.2)      | 2 (16.7)      | 4 (26.7)      |       |
|                                               | 3   | 1 (3.7)       | 0 (0)         | 1 (6.7)       |       |
| At least one symptom at screening visit       | No  | 8 (29.6)      | 5 (41.7)      | 3 (20)        | 0.221 |
|                                               | Yes | 19 (70.4)     | 7 (58.3)      | 12 (80)       |       |
| <b>Symptoms :</b>                             |     |               |               |               |       |
| Pain                                          | No  | 17 (63)       | 8 (66.7)      | 9 (60)        | 0.722 |
|                                               | Yes | 10 (37)       | 4 (33.3)      | 6 (40)        |       |
| Asthenia                                      | No  | 24 (88.9)     | 11 (91.7)     | 13 (86.7)     | 0.681 |
|                                               | Yes | 3 (11.1)      | 1 (8.3)       | 2 (13.3)      |       |
| Anorexia                                      | No  | 24 (88.9)     | 11 (91.7)     | 13 (86.7)     | 0.681 |
|                                               | Yes | 3 (11.1)      | 1 (8.3)       | 2 (13.3)      |       |
| Nausea                                        | No  | 27 (100)      | 12 (100)      | 15 (100)      |       |
| Vomiting                                      | No  | 26 (96.3)     | 11 (91.7)     | 15 (100)      | 0.255 |
|                                               | Yes | 1 (3.7)       | 1 (8.3)       | 0 (0)         |       |
| Transit disorders                             | No  | 22 (81.5)     | 10 (83.3)     | 12 (80)       | 0.825 |
|                                               | Yes | 5 (18.5)      | 2 (16.7)      | 3 (20)        |       |
| RGO-oesophagite                               | No  | 27 (100)      | 12 (100)      | 15 (100)      |       |
| Dysphagia                                     | No  | 26 (96.3)     | 11 (91.7)     | 15 (100)      | 0.255 |
|                                               | Yes | 1 (3.7)       | 1 (8.3)       | 0 (0)         |       |
| Icterus (ou jaundice ?)                       | No  | 25 (92.6)     | 11 (91.7)     | 14 (93.3)     | 0.869 |
|                                               | Yes | 2 (7.4)       | 1 (8.3)       | 1 (6.7)       |       |

|                                              |                              |                  |                |                |       |
|----------------------------------------------|------------------------------|------------------|----------------|----------------|-------|
| Ascites                                      | No                           | 26 (96.3)        | 12 (100)       | 14 (93.3)      | 0.362 |
|                                              | Yes                          | 1 (3.7)          | 0 (0)          | 1 (6.7)        |       |
| Occlusion                                    | No                           | 27 (100)         | 12 (100)       | 15 (100)       |       |
| Other symptoms                               | No                           | 22 (81.5)        | 12 (100)       | 10 (66.7)      | 0.027 |
|                                              | Yes                          | 5 (18.5)         | 0 (0)          | 5 (33.3)       |       |
|                                              | bloating                     | 1 (20)           |                | 1 (20)         |       |
|                                              | dyspnea                      | 1 (20)           |                | 1 (20)         |       |
|                                              | budding ulcer mass (primary) | 1 (20)           |                | 1 (20)         |       |
|                                              | rash                         | 1 (20)           |                | 1 (20)         |       |
|                                              | rectal bleeding              | 1 (20)           |                | 1 (20)         |       |
| Electro-cardiogram done                      |                              | 3 (.)            | 0 (.)          | 3 (.)          | 1.000 |
|                                              | no                           | 20 (83.3)        | 10 (83.3)      | 10 (83.3)      |       |
|                                              | yes                          | 4 (16.7)         | 2 (16.7)       | 2 (16.7)       |       |
| If yes, result                               | anormal                      | 1 (.)            | 1 (.)          | 0 (.)          | 0.386 |
|                                              | normal                       | 1 (33.3)         | 0 (0)          | 1 (50)         |       |
|                                              |                              | 2 (66.7)         | 1 (100)        | 1 (50)         |       |
| <b><u>Biological assessment</u></b>          |                              |                  |                |                |       |
| CA19.9                                       |                              | 16 [10-258]      | 15 [9-258]     | 18.5 [11-107]  | 0.838 |
| ACE                                          |                              | 2.8 [1.2-4.5]    | 2.5 [1-4]      | 3 [1.3-5]      | 0.732 |
| <b>Inclusion</b>                             |                              |                  |                |                |       |
| Sex                                          | Female                       | 10 (37)          | 4 (33.3)       | 6 (40)         | 0.722 |
|                                              | Male                         | 17 (63)          | 8 (66.7)       | 9 (60)         |       |
| Age (years)                                  |                              | 68.3 [58.9-81.4] | 68.2 [57-75.9] | 72.5 [58.9-82] | 0.542 |
| <b><u>Physical examination</u></b>           |                              |                  |                |                |       |
| Weight loss between M-6 and baseline         |                              | 7 [5-11]         | 10.5 [4-15]    | 5.5 [5-8]      | 0.156 |
| Weight loss between M-6 and baseline (class) |                              | 1 (.)            | 0 (.)          | 1 (.)          | 0.133 |
|                                              | No weight loss               | 2 (7.7)          | 1 (8.3)        | 1 (7.1)        |       |
|                                              | 0<Weight loss<10             | 14 (53.8)        | 4 (33.3)       | 10 (71.4)      |       |
|                                              | Weight loss≥10               | 10 (38.5)        | 7 (58.3)       | 3 (21.4)       |       |
| Weight loss between M-1 and baseline         |                              | 2 [-2-5]         | 3 [-0.5-5.5]   | 0.5 [-2-2]     | 0.114 |
| Weight loss between M-1 and baseline (class) |                              | 1 (.)            | 0 (.)          | 1 (.)          | 0.292 |

|                 |                                   |                |              |                |       |
|-----------------|-----------------------------------|----------------|--------------|----------------|-------|
| Malnutrition    | No weight loss                    | 11 (42.3)      | 4 (33.3)     | 7 (50)         | 0.637 |
|                 | 0<Weight loss<5                   | 8 (30.8)       | 3 (25)       | 5 (35.7)       |       |
|                 | Weight loss≥5                     | 7 (26.9)       | 5 (41.7)     | 2 (14.3)       |       |
|                 | No                                | 8 (29.6)       | 3 (25)       | 5 (33.3)       |       |
|                 | Yes                               | 19 (70.4)      | 9 (75)       | 10 (66.7)      |       |
| BMI (kg/m2)     |                                   | 22.1 [20.7-25] | 23 [21.2-25] | 21.9 [19.8-24] | 0.470 |
|                 | BMI                               | 10 (.)         | 4 (.)        | 6 (.)          |       |
|                 | Normal weight                     | 12 (70.6)      | 5 (62.5)     | 7 (77.8)       |       |
|                 | Overweight                        | 4 (23.5)       | 3 (37.5)     | 1 (11.1)       |       |
|                 | Obesity                           | 1 (5.9)        | 0 (0)        | 1 (11.1)       |       |
| Underweight     |                                   | 10 (.)         | 4 (.)        | 6 (.)          | 0.707 |
|                 | No                                | 12 (70.6)      | 6 (75)       | 6 (66.7)       |       |
|                 | Yes                               | 5 (29.4)       | 2 (25)       | 3 (33.3)       |       |
|                 |                                   | 10 (.)         | 4 (.)        | 6 (.)          |       |
|                 | Overweight                        | 12 (70.6)      | 5 (62.5)     | 7 (77.8)       |       |
| Obesity         |                                   | 5 (29.4)       | 3 (37.5)     | 2 (22.2)       | 0.331 |
|                 | Obesity                           | 10 (.)         | 4 (.)        | 6 (.)          |       |
|                 | No                                | 16 (94.1)      | 8 (100)      | 8 (88.9)       |       |
|                 | Yes                               | 1 (5.9)        | 0 (0)        | 1 (11.1)       |       |
|                 |                                   | 1 (.)          | 0 (.)        | 1 (.)          |       |
| ECOG PS         |                                   | 6 (23.1)       | 4 (33.3)     | 2 (14.3)       | 0.528 |
|                 | 0                                 | 13 (50)        | 5 (41.7)     | 8 (57.1)       |       |
|                 | 1                                 | 6 (23.1)       | 3 (25)       | 3 (21.4)       |       |
|                 | 2                                 | 1 (3.8)        | 0 (0)        | 1 (7.1)        |       |
|                 | 3                                 | 2 (.)          | 0 (0)        | 2 (.)          |       |
| ECG             |                                   | 7 (28)         | 3 (25)       | 4 (30.8)       | 0.748 |
|                 | No                                | 18 (72)        | 9 (75)       | 9 (69.2)       |       |
|                 | Yes                               | 1 (.)          | 1 (.)        | 0 (.)          |       |
|                 | Abnormal                          | 4 (23.5)       | 1 (12.5)     | 3 (33.3)       |       |
|                 | Normal                            | 13 (76.5)      | 7 (87.5)     | 6 (66.7)       |       |
| If yes, results |                                   | 10 (37)        | 4 (33.3)     | 6 (40)         | 0.312 |
|                 | No                                |                |              |                |       |
|                 | At least one symptom at inclusion |                |              |                |       |
|                 |                                   |                |              |                |       |
|                 |                                   |                |              |                |       |

|                             |          |           |           |           |
|-----------------------------|----------|-----------|-----------|-----------|
| Symptoms :                  |          |           |           |           |
| Pain                        | Yes      | 17 (63)   | 8 (66.7)  | 9 (60)    |
|                             | No       | 17 (63)   | 8 (66.7)  | 9 (60)    |
| asthenia                    | Yes      | 10 (37)   | 4 (33.3)  | 6 (40)    |
|                             | No       | 22 (81.5) | 10 (83.3) | 12 (80)   |
| anorexia                    | Yes      | 5 (18.5)  | 2 (16.7)  | 3 (20)    |
|                             | No       | 25 (92.6) | 11 (91.7) | 14 (93.3) |
| nausea                      | Yes      | 2 (7.4)   | 1 (8.3)   | 1 (6.7)   |
|                             | No       | 26 (96.3) | 12 (100)  | 14 (93.3) |
| vomiting                    | Yes      | 1 (3.7)   | 0 (0)     | 1 (6.7)   |
|                             | No       | 25 (92.6) | 10 (83.3) | 15 (100)  |
| transit disorders           | Yes      | 2 (7.4)   | 2 (16.7)  | 0 (0)     |
|                             | No       | 23 (85.2) | 10 (83.3) | 13 (86.7) |
| transit disorders           | Yes      | 4 (14.8)  | 2 (16.7)  | 2 (13.3)  |
| GERD                        | No       | 27 (100)  | 12 (100)  | 15 (100)  |
|                             | No       | 26 (96.3) | 11 (91.7) | 15 (100)  |
| icterus / jaundice          | Yes      | 1 (3.7)   | 1 (8.3)   | 0 (0)     |
| ascites                     | No       | 27 (100)  | 12 (100)  | 15 (100)  |
| occlusion                   | No       | 27 (100)  | 12 (100)  | 15 (100)  |
| other                       | No       | 25 (92.6) | 12 (100)  | 13 (86.7) |
|                             | Yes      | 2 (7.4)   | 0 (0)     | 2 (13.3)  |
| Dyspnea                     |          | 1 (50)    | 0 (0)     | 1 (50)    |
| Rectal bleeding             |          | 1 (50)    | 0 (0)     | 1 (50)    |
| <b>Chemotherapy</b>         |          |           |           |           |
| Ongoing chemotherapy        | No       | 1 (.)     | 0 (0)     | 1 (.)     |
|                             | Yes      | 11 (42.3) | 7 (58.3)  | 4 (28.6)  |
| If yes, administration mode | Unique   | 15 (57.7) | 5 (41.7)  | 10 (71.4) |
|                             | Combined | 1 (6.7)   | 0 (0)     | 1 (10)    |
| If unique, 5FU              |          | 14 (93.3) | 5 (100)   | 9 (90)    |
|                             | No       | 1 (100)   | 0 (0)     | 1 (100)   |
| If combined: 5FU            |          | 1 (7.1)   | 0 (0)     | 1 (11.1)  |
|                             |          |           |           | 0.439     |

Ongoing chemotherapy

If yes, administration mode

If unique, 5FU

If combined: 5FU

|                                              |     |                  |                  |                  |       |
|----------------------------------------------|-----|------------------|------------------|------------------|-------|
| If combined : IRINOTECAN                     | Yes | 13 (92.9)        | 5 (100)          | 8 (88.9)         | 0.334 |
|                                              | No  | 8 (57.1)         | 2 (40)           | 6 (66.7)         |       |
|                                              | Yes | 6 (42.9)         | 3 (60)           | 3 (33.3)         |       |
|                                              | No  | 2 (14.3)         | 0 (0)            | 2 (22.2)         |       |
| If combined : OXALIPLATINE                   | Yes | 12 (85.7)        | 5 (100)          | 7 (77.8)         | 0.255 |
|                                              | No  | 13 (92.9)        | 5 (100)          | 8 (88.9)         |       |
|                                              | Yes | 1 (7.1)          | 0 (0)            | 1 (11.1)         |       |
|                                              | No  | 12 (85.7)        | 5 (100)          | 7 (77.8)         |       |
| If combined : GEMCITABINE                    | Yes | 2 (14.3)         | 0 (0)            | 2 (22.2)         | 0.439 |
|                                              | No  | 2 (100)          | 0 (0)            | 2 (100)          |       |
|                                              | Yes | 11 (73.3)        | 2 (40)           | 9 (90)           |       |
|                                              | No  | 4 (26.7)         | 3 (60)           | 1 (10)           |       |
| If combined : other chemotherapy             | Yes | 2 (.)            | 0 (.)            | 2 (.)            | 0.039 |
|                                              | No  | 23 (92)          | 12 (100)         | 11 (84.6)        |       |
|                                              | Yes | 2 (8)            | 0 (0)            | 2 (15.4)         |       |
|                                              | No  | 1 (50)           | 0 (0)            | 1 (50)           |       |
| Chemotherapy: dose reduction                 | Yes | 1 (50)           | 0 (0)            | 1 (50)           | 0.689 |
|                                              | No  | 2 (.)            | 0 (.)            | 2 (.)            |       |
|                                              | Yes | 20 (80)          | 10 (83.3)        | 10 (76.9)        |       |
|                                              | No  | 5 (20)           | 2 (16.7)         | 3 (23.1)         |       |
| Targeted therapies                           | Yes | 22 (.)           | 10 (.)           | 12 (.)           | 0.171 |
|                                              | No  | 4 (80)           | 1 (50)           | 3 (100)          |       |
|                                              | Yes | 1 (20)           | 1 (50)           | 0 (0)            |       |
|                                              | No  | 1 (100)          | 1 (100)          | 0 (0)            |       |
| Targeted therapies?                          | Yes | 8.5 [6-11.1]     | 7.2 [6-16.5]     | 8.6 [5.9-10.8]   | 0.642 |
|                                              | No  | 11.7 [10.9-14.4] | 11.7 [10.9-14.4] | 11.9 [10.6-14.6] |       |
|                                              | Yes | 304 [247-506]    | 309 [247-506]    | 301 [239-513]    |       |
|                                              | No  | 5.4 [3.8-7.3]    | 4.5 [3.8-8.7]    | 6.1 [2.8-7.3]    |       |
| Pain                                         | Yes | 1.6 [1.1-2.2]    | 1.3 [0.9-2.2]    | 1.8 [1.5-2.1]    | 0.805 |
|                                              | No  | 0.6 [0.3-0.9]    | 0.6 [0.3-0.9]    | 0.5 [0.4-0.8]    |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |
| Third level antalgic                         | Yes |                  |                  |                  | 0.277 |
|                                              | No  |                  |                  |                  |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |
| Biochemistry                                 | Yes |                  |                  |                  | 0.456 |
|                                              | No  |                  |                  |                  |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |
| Leukocytes (10 <sup>9</sup> /l)              | Yes |                  |                  |                  | 0.000 |
|                                              | No  |                  |                  |                  |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |
| Hemoglobin (g/dL)                            | Yes |                  |                  |                  | 0.891 |
|                                              | No  |                  |                  |                  |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |
| Platelets (10 <sup>9</sup> /l)               | Yes |                  |                  |                  | 0.805 |
|                                              | No  |                  |                  |                  |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |
| Polynuclear neutrophils (10 <sup>9</sup> /l) | Yes |                  |                  |                  | 0.277 |
|                                              | No  |                  |                  |                  |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |
| Lymphocytes (10 <sup>9</sup> /l)             | Yes |                  |                  |                  | 0.456 |
|                                              | No  |                  |                  |                  |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |
| Monocytes (10 <sup>9</sup> /l)               | Yes |                  |                  |                  | 0.456 |
|                                              | No  |                  |                  |                  |       |
|                                              | Yes |                  |                  |                  |       |
|                                              | No  |                  |                  |                  |       |

|                                              |                   |                 |                   |       |
|----------------------------------------------|-------------------|-----------------|-------------------|-------|
| Polynuclear eosinophils (10 <sup>9</sup> /l) | 0.2 [0.1-0.3]     | 0.2 [0.1-0.3]   | 0.2 [0.1-0.3]     | 0.841 |
| Polynuclear basophils (10 <sup>9</sup> /l)   | 0.1 [0-0.1]       | 0.1 [0-0.1]     | 0.1 [0-0.1]       | 0.799 |
| Neutrophil/Lymphocyte Ration                 | 4 [1.9-5.9]       | 4.1 [1.9-12.2]  | 3.7 [1.4-4.7]     | 0.162 |
| Creatinine (μmol/l)                          | 70 [64.5-80.8]    | 68 [60-79.7]    | 71.1 [67-87]      | 0.369 |
| Calcemia (mmol/l)                            | 2.4 [2.3-2.5]     | 2.5 [2.3-2.5]   | 2.4 [2.4-2.4]     | 0.438 |
| Phosphore (mmol/l)                           | 1.1 [1-1.3]       | 1.2 [1.1-1.3]   | 1 [0.9-1.4]       | 0.176 |
| Magnesium (mmol/l)                           | 0.9 [0.8-0.9]     | 0.9 [0.9-0.9]   | 0.8 [0.8-0.9]     | 0.130 |
| CRP (mg/l)                                   | 4.4 [1-32.6]      | 4.7 [1.4-69]    | 3 [1-21]          | 0.286 |
| CRP class                                    | 7 (.)             | 3 (.)           | 4 (.)             | 0.423 |
|                                              | ≤11               | 5 (55.6)        | 8 (72.7)          |       |
|                                              | >11               | 4 (44.4)        | 3 (27.3)          |       |
| Total bilirubine (μmol/l)                    | 9.5 [7-13]        | 12.6 [10-16.6]  | 7.2 [5.4-10.1]    | 0.012 |
| Phospatase (U/l)                             | 96 [75-234]       | 88 [78-135]     | 108 [75-234]      | 0.925 |
| LDH (U/l)                                    | 207 [194-222]     | 207 [202-222]   | 203.5 [183-228.5] | 0.713 |
| ASAT (U/l)                                   | 29 [23-39]        | 31.5 [20-40]    | 29 [25-38]        | 0.860 |
| ALAT (U/l)                                   | 29.5 [18.5-44]    | 27 [16-56]      | 32 [24-38]        | 0.930 |
| Albumine (g/l)                               | 38.3 [32.1-41.7]  | 37 [31.9-40.1]  | 38.6 [34.6-45]    | 0.403 |
| Albumine class                               | 7 (.)             | 3 (.)           | 4 (.)             | 0.423 |
|                                              | ≥36               | 5 (55.6)        | 8 (72.7)          |       |
|                                              | <36               | 4 (44.4)        | 3 (27.3)          |       |
| Albumine class                               | 7 (.)             | 3 (.)           | 4 (.)             | 0.660 |
|                                              | ≥30               | 8 (88.9)        | 9 (81.8)          |       |
|                                              | <30               | 1 (11.1)        | 2 (18.2)          |       |
| Pre albumine (g/l)                           | 0.3 [0.1-0.3]     | 0.2 [0.1-0.3]   | 0.3 [0.2-0.3]     | 0.453 |
| GPS score                                    | 13 (.)            | 7 (.)           | 6 (.)             | 0.436 |
|                                              | 0                 | 8 (57.1)        | 6 (66.7)          |       |
|                                              | 1                 | 3 (21.4)        | 1 (11.1)          |       |
|                                              | 2                 | 3 (21.4)        | 2 (22.2)          |       |
| Quick time (sec)                             | 13.5 [11-15.3]    | 15.3 [11-82]    | 12.4 [11.2-13.7]  | 0.476 |
| Vitamin B9 (nmol/l)                          | 11.8 [9.3-20.7]   | 10.6 [9.3-15.7] | 16.8 [9.3-33.2]   | 0.470 |
| Vitamin B12 (pmol/l)                         | 373 [247.5-489.5] | 443 [315.5-717] | 305 [169.5-419.5] | 0.312 |
| Vitamin D (ng/ml)                            | 19.6 [13-22]      | 13 [10.2-22]    | 28.8 [19.6-38]    | 0.386 |

|                                           |                  |                  |                    |       |
|-------------------------------------------|------------------|------------------|--------------------|-------|
| Ferritin level (ng/ml)                    | 344 [91-954]     | 954 [197-1210]   | 217.5 [70.5-351.5] | 0.270 |
| Transferrin saturation coefficient        | 22 [16-30.2]     | 24.5 [16-33]     | 22 [7-30.2]        | 0.773 |
| <b><u>Imagery</u></b>                     |                  |                  |                    |       |
| Measure of muscular surface of L3 (m2/m2) | 38.1 [35.1-47.7] | 38.1 [36.7-50.7] | 37.7 [32.6-46.4]   | 0.339 |
| Measure of muscular surface of L3 (class) | 5 (.)            | 2 (.)            | 3 (.)              | 0.184 |
|                                           | 12 (54.5)        | 7 (70)           | 5 (41.7)           |       |
| ≥34,4 for Female or ≥45,4 for Male        | 10 (45.5)        | 3 (30)           | 7 (58.3)           |       |
| <34,4 for Female or <45,4 for Male        | 4 (.)            | 1 (.)            | 3 (.)              | 0.715 |
| Number of metastatic sites at inclusion   | 10 (43.5)        | 4 (36.4)         | 6 (50)             |       |
| 0                                         | 6 (26.1)         | 3 (27.3)         | 3 (25)             |       |
| 1                                         | 6 (26.1)         | 3 (27.3)         | 3 (25)             |       |
| 2                                         | 1 (4.3)          | 1 (9.1)          | 0 (0)              |       |
| 3                                         | 30.7 [28.3-33]   | 33 [33-33]       | 28.3 [28.3-28.3]   |       |
| Muscle Area Index (cm2/m2)                | 16.5 [14.1-18.5] | 16.5 [15.4-18.9] | 16.1 [13.4-17.5]   | 0.258 |
| Muscle Mass Index (kg/m2)                 | 3 (.)            | 1 (.)            | 2 (.)              |       |
| Muscle Mass Index (class)                 | 24 (100)         | 11 (100)         | 13 (100)           |       |
| ≥5,5 for Female or ≥7 for Male            | 28 [26-30]       | 28 [24-29]       | 28 [26-30.5]       | 0.664 |
| Arm Circumference (cm)                    | 44 [42-45]       | 44 [42-52]       | 43 [41-45]         | 0.409 |
| Thigh circumference (cm)                  | 30.7 [26-33.5]   | 30.5 [24.7-35.1] | 30.9 [26.6-33]     | 0.862 |
| Fat mass (%)                              | 69.5 [67.9-74]   | 69.9 [67.9-75.7] | 69.1 [67-73.5]     | 0.558 |
| Lean mass (%)                             |                  |                  |                    |       |
| Weight loss at M1 (%)                     | 1 [0-3.4]        | 1.4 [0-4.5]      | 0 [0-3]            | 0.507 |
| Weight loss at M1 (%)                     | 2 (.)            | 0 (.)            | 2 (.)              | 0.157 |
| No weight loss                            | 12 (48)          | 5 (41.7)         | 7 (53.8)           |       |
| 0<Weight loss<5                           | 10 (40)          | 4 (33.3)         | 6 (46.2)           |       |
| Weight loss>=5                            | 3 (12)           | 3 (25)           | 0 (0)              |       |
| Weight loss at M6 (%)                     | 3.6 [0-7.3]      | 2.3 [-1.3-4]     | 5.9 [0-9.5]        | 0.088 |
| Weight loss at M6 (%)                     | 7 (.)            | 2 (.)            | 5 (.)              | 0.327 |
| No weight loss                            | 7 (35)           | 4 (40)           | 3 (30)             |       |
| 0<Weight loss<10                          | 11 (55)          | 6 (60)           | 5 (50)             |       |
| Weight loss>=10                           | 2 (10)           | 0 (0)            | 2 (20)             |       |

### Nutritional evaluation

|                                                |     |  |  |           |           |
|------------------------------------------------|-----|--|--|-----------|-----------|
| VAS of food intakes                            |     |  |  |           |           |
| Nutritional support: dietary advice            | No  |  |  | 5 [5-10]  | 8 [7-9]   |
|                                                | Yes |  |  | 1 (8.3)   | 2 (13.3)  |
|                                                |     |  |  | 11 (91.7) | 13 (86.7) |
| Nutritional support: oral nutrition supplement | No  |  |  | 2 (16.7)  | 5 (33.3)  |
|                                                | Yes |  |  | 10 (83.3) | 10 (66.7) |
| Nutritional support: enteral nutrition         | No  |  |  | 11 (91.7) | 14 (93.3) |
|                                                | Yes |  |  | 1 (8.3)   | 1 (6.7)   |
| Nutritional support: parenteral nutrition      | No  |  |  | 12 (100)  | 15 (100)  |

### Physical evaluation

|                                         |  |  |  |                |               |
|-----------------------------------------|--|--|--|----------------|---------------|
| 6-minute walking test (m)               |  |  |  | 388 [168-420]  | 399 [304-420] |
| Borg scale                              |  |  |  | 3 [3-3]        | 2 [1-3]       |
| Handgrip Test (kg)                      |  |  |  | 26 [23.5-39.5] | 24 [22-30]    |
| Get up and Go test (sec)                |  |  |  | 8 [5.5-12]     | 7 [6-8]       |
| chair stand fitness test (nb in 30 sec) |  |  |  | 9.5 [7.5-12]   | 9 [8-10.5]    |
| balance in single-leg (sec)             |  |  |  | 7 [2.5-60]     | 60 [14-60]    |
| balance in bipodal stance (sec)         |  |  |  | 60 [60-60]     | 60 [60-60]    |

### Nutrition and APA

|                                                                                                                                                 |     |  |  |           |           |
|-------------------------------------------------------------------------------------------------------------------------------------------------|-----|--|--|-----------|-----------|
| <b>Nutrition</b>                                                                                                                                |     |  |  |           |           |
| Currently, are you following a diet?                                                                                                            | No  |  |  | 1 (.)     | 5 (.)     |
|                                                                                                                                                 | Yes |  |  | 9 (81.8)  | 8 (80)    |
|                                                                                                                                                 |     |  |  | 2 (18.2)  | 2 (20)    |
| Was this diet prescribed to you by a health professional: general practitioner, specialist doctor (nutritionist or endocrinologist), dietician? | Yes |  |  | 10 (.)    | 13 (.)    |
|                                                                                                                                                 |     |  |  | 2 (100)   | 2 (100)   |
| Why are you following this diet?                                                                                                                |     |  |  |           |           |
| For a medical reason unrelated to an overweight problem (food allergy, salt-free diet, etc.)                                                    | No  |  |  | 11 (91.7) | 14 (93.3) |
|                                                                                                                                                 | Yes |  |  | 1 (8.3)   | 1 (6.7)   |

|                                                                                                                                                                                                          |     |            |            |            |       |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|------------|------------|------------|-------|
| Why are you following this diet? To lose weight                                                                                                                                                          | No  | 27 (100)   | 12 (100)   | 15 (100)   |       |
| Why are you following this diet?                                                                                                                                                                         | No  | 27 (100)   | 12 (100)   | 15 (100)   |       |
| To not gain weight                                                                                                                                                                                       | No  | 25 (92.6)  | 11 (91.7)  | 14 (93.3)  | 0.869 |
| Why are you following this diet? To stay fit                                                                                                                                                             | Yes | 2 (7.4)    | 1 (8.3)    | 1 (6.7)    |       |
| Can you indicate the amounts of food you are currently eating, by placing the slider between "I am eating nothing at all" and "I am eating as usual"?                                                    |     | 75 [50-90] | 50 [20-76] | 88 [75-90] | 0.045 |
| Please indicate the portion consumed during your last meal (noon or evening)                                                                                                                             |     | 5 (.)      | 0 (.)      | 5 (.)      | 0.066 |
| 3                                                                                                                                                                                                        |     | 2 (9.1)    | 2 (16.7)   | 0 (0)      |       |
| 5                                                                                                                                                                                                        |     | 4 (18.2)   | 4 (33.3)   | 0 (0)      |       |
| 7                                                                                                                                                                                                        |     | 3 (13.6)   | 2 (16.7)   | 1 (10)     |       |
| 8                                                                                                                                                                                                        |     | 3 (13.6)   | 0 (0)      | 3 (30)     |       |
| 9                                                                                                                                                                                                        |     | 1 (4.5)    | 0 (0)      | 1 (10)     |       |
| 10                                                                                                                                                                                                       |     | 9 (40.9)   | 4 (33.3)   | 5 (50)     |       |
| Have you heard about the existence of anti-cancer diet?                                                                                                                                                  |     | 5 (.)      | 0 (.)      | 5 (.)      | 0.429 |
| No                                                                                                                                                                                                       |     | 13 (59.1)  | 8 (66.7)   | 5 (50)     |       |
| Yes                                                                                                                                                                                                      |     | 9 (40.9)   | 4 (33.3)   | 5 (50)     |       |
| Have you heard about the existence of foods to avoid or favor to prevent the occurrence of cancer?                                                                                                       |     | 18 (.)     | 8 (.)      | 10 (.)     | 0.858 |
| No                                                                                                                                                                                                       |     | 2 (22.2)   | 1 (25)     | 1 (20)     |       |
| Yes                                                                                                                                                                                                      |     | 7 (77.8)   | 3 (75)     | 4 (80)     |       |
| Have you heard of diets to follow when cancer is present in order to slow down its progression or help cure it?<br>(example therapeutic fasting during chemotherapy, avoidance of sugar, ketogenic diet) |     | 18 (.)     | 8 (.)      | 10 (.)     | 0.099 |
| No                                                                                                                                                                                                       |     | 4 (44.4)   | 3 (75)     | 1 (20)     |       |
| Yes                                                                                                                                                                                                      |     | 5 (55.6)   | 1 (25)     | 4 (80)     |       |
| Which diet? Ketogenic diet                                                                                                                                                                               | No  | 27 (100)   | 12 (100)   | 15 (100)   |       |
| Which diet? Therapeutic fasting                                                                                                                                                                          | No  | 26 (96.3)  | 11 (91.7)  | 15 (100)   | 0.255 |

|                                                                                                                                  |                         |                  |                  |                 |              |
|----------------------------------------------------------------------------------------------------------------------------------|-------------------------|------------------|------------------|-----------------|--------------|
| Which diet? Sugar-free diet                                                                                                      | Yes                     | 1 (3.7)          | 1 (8.3)          | 0 (0)           |              |
|                                                                                                                                  | No                      | 24 (88.9)        | 12 (100)         | 12 (80)         | 0.100        |
| Which diet? other                                                                                                                | Yes                     | 3 (11.1)         | 0 (0)            | 3 (20)          |              |
|                                                                                                                                  | No                      | 26 (96.3)        | 12 (100)         | 14 (93.3)       | 0.362        |
| Yes                                                                                                                              | Yes                     | 1 (3.7)          | 0 (0)            | 1 (6.7)         |              |
|                                                                                                                                  | Proteins                | 1 (100)          | 0 (0)            | 1 (100)         |              |
| What is your opinion on the subject?                                                                                             |                         | 22 (.)           | 11 (.)           | 11 (.)          | 0.361        |
|                                                                                                                                  | I don't have an opinion | 3 (60)           | 1 (100)          | 2 (50)          |              |
| I have a favorable opinion of it (I think that there is no particular risk in doing this diet in combination with my treatments) |                         | 2 (40)           | 0 (0)            | 2 (50)          |              |
|                                                                                                                                  | No                      | 22 (.)           | 11 (.)           | 11 (.)          | 0.576        |
| Was this diet recommended to you by anyone?                                                                                      | No                      | 1 (20)           | 0 (0)            | 1 (25)          |              |
|                                                                                                                                  | Yes                     | 4 (80)           | 1 (100)          | 3 (75)          |              |
| Was it by a health professional: general practitioner, specialist doctor (nutritionist or endocrinologist), dietician?           | No                      | 23 (.)           | 11 (.)           | 12 (.)          | 0.505        |
|                                                                                                                                  | Yes                     | 1 (25)           | 0 (0)            | 1 (33.3)        |              |
| Was this diet recommended to you by an acquaintance/family member/friends?                                                       |                         | 3 (75)           | 1 (100)          | 2 (66.7)        |              |
|                                                                                                                                  | No                      | 25 (.)           | 11 (.)           | 14 (.)          | 0.157        |
| Do you intend to follow a special diet during your treatment or have you already started one?                                    | No                      | 1 (50)           | 1 (100)          | 0 (0)           |              |
|                                                                                                                                  | Yes                     | 1 (50)           | 0 (0)            | 1 (100)         |              |
|                                                                                                                                  | No                      | 10 (.)           | 4 (.)            | 6 (.)           | 0.490        |
|                                                                                                                                  | Yes                     | 12 (70.6)        | 5 (62.5)         | 7 (77.8)        |              |
|                                                                                                                                  |                         | 5 (29.4)         | 3 (37.5)         | 2 (22.2)        |              |
| <b>Quality of life (Eortc Qlq C30)</b>                                                                                           |                         |                  |                  |                 |              |
| Physical functioning                                                                                                             |                         | 93.3 [80-100]    | 90 [53.3-100]    | 100 [93.3-100]  | <b>0.090</b> |
| Role Functioning                                                                                                                 |                         | 100 [66.7-100]   | 66.7 [66.7-100]  | 100 [100-100]   | <b>0.048</b> |
| Cognitive functioning                                                                                                            |                         | 100 [83.3-100]   | 100 [83.3-100]   | 100 [100-100]   | 0.604        |
| Emotional functioning                                                                                                            |                         | 72.2 [58.3-95.8] | 77.8 [66.7-91.7] | 66.7 [50-100]   | 0.643        |
| Social functioning                                                                                                               |                         | 83.3 [66.7-100]  | 83.3 [66.7-100]  | 83.3 [66.7-100] | 1.000        |

|                          |               |                  |                |              |
|--------------------------|---------------|------------------|----------------|--------------|
| Fatigue                  | 33.3 [0-50]   | 38.9 [11.1-66.7] | 22.2 [0-33.3]  | <b>0.120</b> |
| Pain                     | 0 [0-33.3]    | 0 [0-33.3]       | 0 [0-16.7]     | 0.812        |
| Nausea and vomiting      | 0 [0-16.7]    | 8.3 [0-16.7]     | 0 [0-0]        | <b>0.018</b> |
| Insomnia                 | 33.3 [0-66.7] | 0 [0-50]         | 33.3 [0-66.7]  | 0.445        |
| Constipation             | 0 [0-33.3]    | 0 [0-33.3]       | 0 [0-33.3]     | 0.698        |
| Dyspnoea                 | 0 [0-33.3]    | 16.7 [0-33.3]    | 0 [0-33.3]     | 0.415        |
| Diarrhoea                | 0 [0-50]      | 0 [0-66.7]       | 0 [0-33.3]     | 0.933        |
| Appetite loss            | 0 [0-33.3]    | 33.3 [0-66.7]    | 0 [0-0]        | <b>0.057</b> |
| Financial difficulties   | 0 [0-0]       | 0 [0-0]          | 0 [0-0]        | 0.215        |
| Global health status/QoL | 50 [50-75]    | 50 [45.8-70.8]   | 58.3 [50-83.3] | 0.213        |

## Primary endpoint

Primary efficacy endpoint is:

- Rate of patients having a complete multidisciplinary intervention i.e. receiving a nutritional support at inclusion, week 4 ( $\pm 7$  days) and week 8 ( $\pm 7$  days), and an APA support at inclusion and week 8 ( $\pm 7$  days) among patients followed until end of intervention visit or later (definition 1).

Another definition will be used for sensitivity analysis:

- Rate of patients having a complete multidisciplinary intervention i.e. receiving a nutritional support at the 3 visits (inclusion, intervention, end of intervention), and an APA support at the 2 visits (inclusion, end of intervention) among patients followed until end of intervention visit or later (definition 2).

Table 4. Primary efficacy endpoint according to the definition (n=27)

|                           |                                                 | Definition 1<br>(n=27)<br>n(%) | Definition 2<br>(n=27)<br>n(%) |
|---------------------------|-------------------------------------------------|--------------------------------|--------------------------------|
| Primary efficacy endpoint | Success                                         | 12 (44.4; 95%CI: 25.5-64.7)    | 17 (63 ; 95%CI: 42.4-80.6)     |
|                           | Failure                                         | 15 (55.6)                      | 10 (37)                        |
| Reason*                   | Incomplete program: nutritional and APA support | 5 (33.3)                       | 5 (50)                         |
|                           | Incomplete program: APA support                 | 4 (26.7)                       | 4 (40)                         |
|                           | Incomplete program: nutritional support         | 1 (6.7)                        | 1 (10)                         |
|                           | Visit delay > 7 days                            | 5 (33.3)                       | -                              |

\*Reason for visit delay > 7 days will be counted only in case of complete program (realized nutritional and APA supports)

Among the 3 patients considered as non-evaluable for the primary endpoint for death before end of intervention visit (W8), 2 patients could be considered with a “complete program” during their available follow-up (cf. swimmer plot).

Table 5.a. Primary efficacy endpoint according to the type of cancer (n=27)

|                                             |                                                 | Global<br>cancer<br>(n=27)<br>n(%) | Localized<br>cancer<br>(n=12)<br>n(%) | Metastatic<br>cancer<br>(n=15)<br>n(%) | p     |
|---------------------------------------------|-------------------------------------------------|------------------------------------|---------------------------------------|----------------------------------------|-------|
| Primary efficacy<br>endpoint (definition 1) | Success                                         | 12 (44.4)                          | 3 (25)                                | 9 (60)                                 | 0.121 |
|                                             | Failure                                         | 15 (55.6)                          | 9 (75)                                | 6 (40)                                 |       |
| If failure, reason*                         | Incomplete program: nutritional and APA support | 5 (33.3)                           | 2 (22.2)                              | 3 (50)                                 | 0.401 |
|                                             | Incomplete program: APA support                 | 4 (26.7)                           | 3 (33.3)                              | 1 (16.7)                               |       |
|                                             | Incomplete program: nutritional support         | 1 (6.7)                            | 0 (0)                                 | 1 (16.7)                               |       |
|                                             | Visit delay > 7 days                            | 5 (33.3)                           | 4 (44.4)                              | 1 (16.7)                               |       |
| Primary efficacy<br>endpoint (definition 2) | Success                                         | 17 (63)                            | 7 (58.3)                              | 10 (66.7)                              | 0.656 |
|                                             | Failure                                         | 10 (37)                            | 5 (41.7)                              | 5 (33.3)                               |       |
| If failure, reason                          | Incomplete program: nutritional and APA support | 5 (50)                             | 2 (40)                                | 3 (60)                                 | 0.524 |
|                                             | Incomplete program: APA support                 | 4 (40)                             | 3 (60)                                | 1 (20)                                 |       |
|                                             | Incomplete program: nutritional support         | 1 (10)                             | 0 (0)                                 | 1 (20)                                 |       |

\*Reason for visit delay > 7 days will be counted only in case of complete program (realized nutritional and APA supports)

Table 5.b. Primary efficacy endpoint according to the type of cancer & frailty score (n=27)

|                                          |         | Global<br>cancer<br>(n=27)<br>n(%) | Localized<br>cancer<br>(n=12)<br>n(%) | Metastatic<br>cancer with<br>frailty score <7<br>(n=10)<br>n(%) | Metastatic<br>cancer with<br>frailty score =7<br>(n=5)<br>n(%) | p     |
|------------------------------------------|---------|------------------------------------|---------------------------------------|-----------------------------------------------------------------|----------------------------------------------------------------|-------|
| Primary efficacy endpoint (definition 1) | Success | 12 (44.4)                          | 3 (25)                                | 6 (60)                                                          | 3 (60)                                                         | 0.208 |
|                                          | Failure | 15 (55.6)                          | 9 (75)                                | 4 (40)                                                          | 2 (40)                                                         |       |

|                                                                                                                           |                                                 |           |          |          |        |       |
|---------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|-----------|----------|----------|--------|-------|
|                                                                                                                           | Failure                                         | 15 (55.6) | 9 (75)   | 4 (40)   | 2 (40) |       |
| If failure, reason*                                                                                                       | Incomplete program: nutritional and APA support | 5 (33.3)  | 2 (22.2) | 2 (50)   | 1 (50) | 0.519 |
|                                                                                                                           | Incomplete program: APA support                 | 4 (26.7)  | 3 (33.3) | 0 (0)    | 1 (50) |       |
|                                                                                                                           | Incomplete program: nutritional support         | 1 (6.7)   | 0 (0)    | 1 (25)   | 0 (0)  |       |
|                                                                                                                           | Visit delay > 7 days                            | 5 (33.3)  | 4 (44.4) | 1 (25)   | 0 (0)  |       |
|                                                                                                                           | Primary efficacy endpoint (definition 2)        | 17 (63)   | 7 (58.3) | 7 (70)   | 3 (60) |       |
|                                                                                                                           | Failure                                         | 10 (37)   | 5 (41.7) | 3 (30)   | 2 (40) |       |
| If failure, reason                                                                                                        | Incomplete program: nutritional and APA support | 5 (50)    | 2 (40)   | 2 (66.7) | 1 (50) | 0.595 |
|                                                                                                                           | Incomplete program: APA support                 | 4 (40)    | 3 (60)   | 0 (0)    | 1 (50) |       |
|                                                                                                                           | Incomplete program: nutritional support         | 1 (10)    | 0 (0)    | 1 (33.3) | 0 (0)  |       |
| *Reason for visit delay > 7 days will be counted only in case of complete program (realized nutritional and APA supports) |                                                 |           |          |          |        |       |

\*Reason for visit delay > 7 days will be counted only in case of complete program (realized nutritional and APA supports)

Table 5.c. Primary efficacy endpoint according to the malnutrition status (n=27)

|                                             | Global<br>(n=27)                                | Manutrition: |               | Manutrition: |               | p |
|---------------------------------------------|-------------------------------------------------|--------------|---------------|--------------|---------------|---|
|                                             |                                                 | no<br>(n=8)  | yes<br>(n=19) | no<br>(n=8)  | yes<br>(n=19) |   |
| Primary efficacy endpoint<br>(definition 1) |                                                 | n(%)         | n(%)          | n(%)         | n(%)          |   |
|                                             | Success                                         | 12 (44.4)    | 3 (37.5)      | 9 (47.4)     | 0.696         |   |
| If failure, reason*                         | Failure                                         | 15 (55.6)    | 5 (62.5)      | 10 (52.6)    |               |   |
|                                             | Incomplete program: nutritional and APA support | 5 (33.3)     | 2 (40)        | 3 (30)       | 0.867         |   |
|                                             | Incomplete program: APA support                 | 4 (26.7)     | 2 (40)        | 2 (20)       |               |   |
|                                             | Incomplete program: nutritional support         | 1 (6.7)      | 0 (0)         | 1 (10)       |               |   |
|                                             | Visit delay > 7 days                            | 5 (33.3)     | 1 (20)        | 4 (40)       |               |   |
| <hr/>                                       |                                                 |              |               |              |               |   |
| Primary efficacy endpoint<br>(definition 2) |                                                 |              |               |              |               |   |
|                                             | Success                                         | 17 (63)      | 4 (50)        | 13 (68.4)    | 0.415         |   |
| If failure, reason                          | Failure                                         | 10 (37)      | 4 (50)        | 6 (31.6)     |               |   |
|                                             | Incomplete program: nutritional and APA support | 5 (50)       | 2 (50)        | 3 (50)       | 0.659         |   |

Incomplete program: APA support  
Incomplete program: nutritional support

\*Reason for visit delay > 7 days will be counted only in case of complete program (realized nutritional and APA supports)

Malnutrition status defined according to HAS 2019:

- BMI < 18,5 kg/m<sup>2</sup> if age < 70 ; BMI < 21 kg/m<sup>2</sup> if age ≥ 70
- Weight loss ≥ 5% of BW in 1 month
- Weight loss ≥ 10% of BW in 6 months
- Albumin < 35 g/L

Table 5.d. Primary efficacy endpoint according to the muscular surface of L3 (n=22)

|                                                 | Global**<br>(n=22) | muscular<br>surface of<br>L3: Low<br>(n=10) | muscular<br>surface of<br>L3: High<br>(n=12) | p     |
|-------------------------------------------------|--------------------|---------------------------------------------|----------------------------------------------|-------|
|                                                 | n(%)               | n(%)                                        | n(%)                                         |       |
| Primary efficacy endpoint<br>(definition 1)     |                    |                                             |                                              |       |
| Success                                         | 10 (45.4)          | 3 (30)                                      | 7 (58.3)                                     | 0.231 |
| Failure                                         | 12 (54.6)          | 7 (70)                                      | 5 (41.7)                                     |       |
| If failure, reason*                             |                    |                                             |                                              |       |
| Incomplete program: nutritional and APA support | 5 (41.7)           | 4 (57.1)                                    | 1 (20)                                       | 0.356 |
| Incomplete program: APA support                 | 3 (25)             | 2 (28.6)                                    | 1 (20)                                       |       |
| Incomplete program: nutritional support         | 0 (0)              | 0 (0)                                       | 0 (0)                                        |       |
| Visit delay > 7 days                            | 4 (33.3)           | 1 (14.3)                                    | 3 (60)                                       |       |
| Primary efficacy endpoint<br>(definition 2)     |                    |                                             |                                              |       |
| Success                                         | 14 (63.6)          | 4 (40)                                      | 10 (83.3)                                    | 0.074 |
| Failure                                         | 8 (36.4)           | 6 (60)                                      | 2 (16.7)                                     |       |
| If failure, reason                              |                    |                                             |                                              |       |
| Incomplete program: nutritional and APA support | 5 (62.5)           | 4 (66.7)                                    | 1 (50)                                       | 0.673 |
| Incomplete program: APA support                 | 3 (37.5)           | 2 (33.3)                                    | 1 (50)                                       |       |
| Incomplete program: nutritional support         | 0 (0)              | 0 (0)                                       | 0 (0)                                        |       |

\*Reason for visit delay > 7 days will be counted only in case of complete program (realized nutritional and APA supports)

\*\*5 patients without muscular surface of L3 at baseline

Cut-offs considered to define low/high for L3 muscular surface: ≥34,4 for Female or ≥45,4 for Male

Table 6. Primary efficacy endpoint according to the availability of HRQoL evaluation at baseline (n=27)

|                                             |                                                 | Global<br>(n=27) | No HRQoL<br>evaluation at<br>baseline<br>(n=6) | HRQoL<br>evaluation at<br>baseline<br>(n=21) | p     |
|---------------------------------------------|-------------------------------------------------|------------------|------------------------------------------------|----------------------------------------------|-------|
|                                             |                                                 | n(%)             | n(%)                                           | n(%)                                         |       |
| Primary efficacy<br>endpoint (definition 1) | Success                                         | 12 (44.4)        | 0 (0)                                          | 12 (57.1)                                    | 0.013 |
|                                             | Failure                                         | 15 (55.6)        | 6 (100)                                        | 9 (42.9)                                     |       |
|                                             | Incomplete program: nutritional and APA support | 5 (33.3)         | 2 (33.3)                                       | 3 (33.3)                                     | 0.841 |
|                                             | Incomplete program: APA support                 | 4 (26.7)         | 2 (33.3)                                       | 2 (22.2)                                     |       |
|                                             | Incomplete program: nutritional support         | 1 (6.7)          | 0 (0)                                          | 1 (11.1)                                     |       |
| Visit delay > 7 days                        | 5 (33.3)                                        | 2 (33.3)         | 3 (33.3)                                       |                                              |       |
|                                             |                                                 |                  |                                                |                                              |       |
| Primary efficacy<br>endpoint (definition 2) | Success                                         | 17 (63)          | 2 (33.3)                                       | 15 (71.4)                                    | 0.088 |
|                                             | Failure                                         | 10 (37)          | 4 (66.7)                                       | 6 (28.6)                                     |       |
| If failure, reason                          | Incomplete program: nutritional and APA support | 5 (50)           | 2 (50)                                         | 3 (50)                                       | 0.659 |
|                                             | Incomplete program: APA support                 | 4 (40)           | 2 (50)                                         | 2 (33.3)                                     |       |
|                                             | Incomplete program: nutritional support         | 1 (10)           | 0 (0)                                          | 1 (16.7)                                     |       |

## Secondary endpoints

### Health-related quality of life

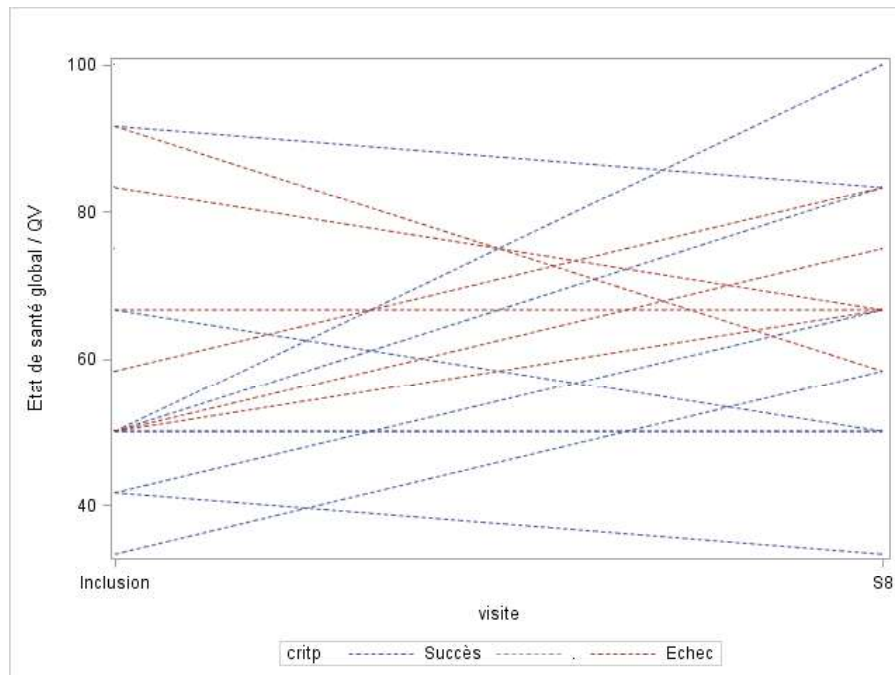
Analysis on the mITT2 population (21 patients with an evaluation of health-related quality of life (HRQoL) at baseline).

Absolute and relative changes from baseline are presented for HRQoL PF functional scale, AP symptom scale and global health status (QoL).

#### Global health status/QoL (QL)

| QL at baseline                   |       |   |      |         |        |                |                |
|----------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Critère principal (définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
| Succès                           | 9     | 9 | 52.8 | 17.2    | 50.0   | 41.7           | 50.0           |
| Echec                            | 6     | 6 | 66.7 | 17.5    | 62.5   | 50.0           | 83.3           |

| QL at W8                         |       |   |      |         |        |                |                |
|----------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Critère principal (définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
| Succès                           | 9     | 9 | 63.9 | 21.2    | 58.3   | 50.0           | 83.3           |
| Echec                            | 6     | 6 | 69.4 | 8.6     | 66.7   | 66.7           | 75.0           |



#### Absolute change for QL from baseline to W8

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 12    | 9 | 11.1 | 22.8    | 0.0    | -8.3           | 25.0           |
| Echec                               | 9     | 6 | 2.8  | 24.0    | 8.3    | -16.7          | 25.0           |

|                                                |                | Global<br>(n=21)<br>N(%) | Primary efficacy<br>endpoint: success<br>(n=12)<br>N(%) | Primary efficacy<br>endpoint: failure<br>(n=9)<br>N(%) | p     |
|------------------------------------------------|----------------|--------------------------|---------------------------------------------------------|--------------------------------------------------------|-------|
| <b>Absolute change from<br/>baseline to W8</b> |                |                          |                                                         |                                                        |       |
| QL                                             |                | 6 (.)                    | 3 (.)                                                   | 3 (.)                                                  | 1.000 |
|                                                | Deterioration  | 5 (33.3)                 | 3 (33.3)                                                | 2 (33.3)                                               |       |
|                                                | No difference* | 3 (20)                   | 2 (22.2)                                                | 1 (16.7)                                               |       |
|                                                | Improvement    | 7 (46.7)                 | 4 (44.4)                                                | 3 (50)                                                 |       |

\*if -5≤QL<5

#### Relative change (%) for QL from baseline to W8

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 12    | 9 | 27.5 | 47.4    | 0.0    | -9.1           | 66.7           |
| Echec                               | 9     | 6 | 11.6 | 35.7    | 16.7   | -20.0          | 42.9           |

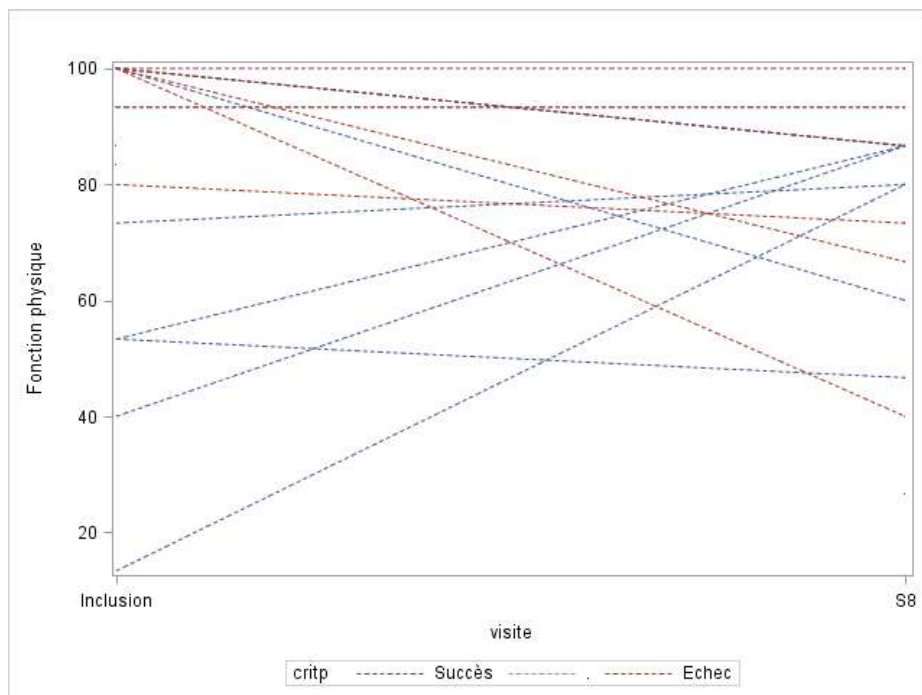
## Physical functioning (PF)

### PF at baseline

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 9     | 9 | 69.6 | 31.5    | 73.3   | 53.3           | 100.0          |
| Echec                               | 6     | 6 | 95.6 | 8.1     | 100.0  | 93.3           | 100.0          |

### PF at W8

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 9     | 9 | 78.5 | 15.2    | 86.7   | 80.0           | 86.7           |
| Echec                               | 6     | 6 | 76.7 | 21.8    | 80.0   | 66.7           | 93.3           |



### Absolute change for PF from baseline to W8

| Critère principal<br>(définition 1) | N Obs | N | Mean  | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|-------|---------|--------|----------------|----------------|
| Succès                              | 12    | 9 | 8.9   | 33.7    | 0.0    | -13.3          | 33.3           |
| Echec                               | 9     | 6 | -18.9 | 23.6    | -10.0  | -33.3          | 0.0            |

|                                                | Global<br>(n=21)<br>N(%) | Primary efficacy<br>endpoint: success<br>(n=12)<br>N(%) | Primary efficacy<br>endpoint: failure<br>(n=9)<br>N(%) | p     |
|------------------------------------------------|--------------------------|---------------------------------------------------------|--------------------------------------------------------|-------|
| <b>Absolute change from<br/>baseline to W8</b> |                          |                                                         |                                                        |       |
| PF                                             | 6 (.)                    | 3 (.)                                                   | 3 (.)                                                  | 0.155 |
| Deterioration                                  | 8 (53.3)                 | 4 (44.4)                                                | 4 (66.7)                                               |       |
| No difference*                                 | 3 (20)                   | 1 (11.1)                                                | 2 (33.3)                                               |       |
| Improvement                                    | 4 (26.7)                 | 4 (44.4)                                                | 0 (0)                                                  |       |

\*if  $-5 \leq \text{PF} < 2$

#### Relative change (%) for PF from baseline to W8

| Critère principal<br>(définition 1) | N Obs | N | Mean  | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|-------|---------|--------|----------------|----------------|
| Succès                              | 12    | 9 | 67.7  | 169.0   | 0.0    | -13.3          | 62.5           |
| Echec                               | 9     | 6 | -19.2 | 23.5    | -10.8  | -33.3          | 0.0            |

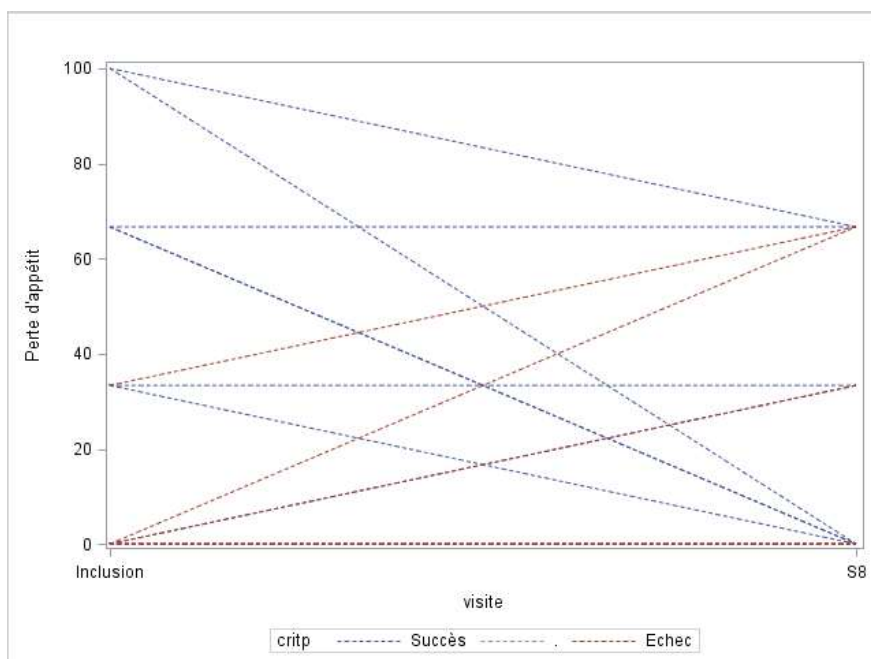
#### Appetite loss (AP)

##### AP at baseline

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 9     | 9 | 51.9 | 37.7    | 66.7   | 33.3           | 66.7           |
| Echec                               | 6     | 6 | 5.6  | 13.6    | 0.0    | 0.0            | 0.0            |

##### AP at W8

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 9     | 9 | 22.2 | 28.9    | 0.0    | 0.0            | 33.3           |
| Echec                               | 6     | 6 | 27.8 | 32.8    | 16.7   | 0.0            | 66.7           |



#### Absolute change for AP from baseline to W8

| Critère principal<br>(définition 1) | N  | Obs | N | Mean  | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|----|-----|---|-------|---------|--------|----------------|----------------|
| Succès                              | 12 | 9   |   | -29.6 | 42.3    | -33.3  | -66.7          | 0.0            |
| Echec                               | 9  | 6   |   | 22.2  | 27.2    | 16.7   | 0.0            | 33.3           |

|                                            |                | Global<br>(n=21)<br>N(%) | Primary efficacy<br>endpoint: success<br>(n=12)<br>N(%) | Primary efficacy<br>endpoint: failure<br>(n=9)<br>N(%) | p     |
|--------------------------------------------|----------------|--------------------------|---------------------------------------------------------|--------------------------------------------------------|-------|
| <b>Absolute change from baseline to W8</b> |                |                          |                                                         |                                                        |       |
| AP                                         |                | 6 (.)                    | 3 (.)                                                   | 3 (.)                                                  | 0.069 |
|                                            | Deterioration  | 5 (33.3)                 | 5 (55.6)                                                | 0 (0)                                                  |       |
|                                            | No difference* | 6 (40)                   | 3 (33.3)                                                | 3 (50)                                                 |       |
|                                            | Improvement    | 4 (26.7)                 | 1 (11.1)                                                | 3 (50)                                                 |       |

\*if  $-2 \leq PF < 7$

#### Relative change (%) for AP from baseline to W8

| Critère principal<br>(définition 1) | N  | Obs | N | Mean  | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|----|-----|---|-------|---------|--------|----------------|----------------|
| Succès                              | 12 | 7   |   | -61.9 | 48.8    | -100.0 | -100.0         | 0.0            |
| Echec                               | 9  | 1   |   | 100.0 | .       | 100.0  | 100.0          | 100.0          |

## Body composition

Relative changes from baseline are presented for body composition (weight, MMS, MMI).

### Weight

| weight at baseline               |       |    |      |         |        |                |                |
|----------------------------------|-------|----|------|---------|--------|----------------|----------------|
| Critère principal (définition 1) | N Obs | N  | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
| Succès                           | 12    | 12 | 70.3 | 14.0    | 69.5   | 62.0           | 79.0           |
| Echec                            | 10    | 10 | 65.7 | 15.4    | 65.0   | 53.0           | 71.0           |

| weight at W8                     |       |    |      |         |        |                |                |
|----------------------------------|-------|----|------|---------|--------|----------------|----------------|
| Critère principal (définition 1) | N Obs | N  | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
| Succès                           | 12    | 12 | 68.3 | 13.5    | 69.0   | 60.0           | 78.0           |
| Echec                            | 10    | 10 | 64.1 | 15.3    | 63.0   | 50.0           | 72.0           |

| Relative change (%) for weight from baseline to W8 |       |    |      |         |        |                |                |
|----------------------------------------------------|-------|----|------|---------|--------|----------------|----------------|
| Critère principal (définition 1)                   | N Obs | N  | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
| Succès                                             | 12    | 12 | -2.8 | 5.1     | -2.8   | -7.3           | 0.2            |
| Echec                                              | 15    | 10 | -2.5 | 3.4     | -2.5   | -3.8           | -1.6           |

## Measure of muscular surface of L3 (cm<sup>2</sup>/m<sup>2</sup>)

| Measure of muscular surface of L3 (cm <sup>2</sup> /m <sup>2</sup> ) at baseline |       |   |      |         |        |                |                |
|----------------------------------------------------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Critère principal (définition 1)                                                 | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
| Succès                                                                           | 9     | 9 | 44.3 | 10.4    | 38.5   | 36.8           | 50.7           |
| Echec                                                                            | 8     | 8 | 42.8 | 12.1    | 40.8   | 33.5           | 48.4           |

| Measure of muscular surface of L3 (cm <sup>2</sup> /m <sup>2</sup> ) at W8 |       |   |      |         |        |                |                |
|----------------------------------------------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Critère principal (définition 1)                                           | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
| Succès                                                                     | 9     | 9 | 42.4 | 12.5    | 37.5   | 32.5           | 53.0           |
| Echec                                                                      | 8     | 8 | 40.7 | 14.2    | 41.0   | 29.8           | 45.5           |

#### Relative change (%) for measure of muscular surface of L3 from baseline to W8

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 12    | 9 | -5.3 | 6.9     | -6.7   | -10.7          | -2.4           |
| Echec                               | 15    | 8 | -6.2 | 9.9     | -4.6   | -10.0          | -0.6           |

#### Muscle Mass Index (kg/m<sup>2</sup>)

##### Muscle Mass Index (kg/m<sup>2</sup>) at baseline

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 9     | 9 | 16.6 | 2.0     | 16.4   | 15.4           | 17.7           |
| Echec                               | 7     | 7 | 16.1 | 3.6     | 16.1   | 12.5           | 19.5           |

##### Muscle Mass Index (kg/m<sup>2</sup>) at W8

| critp  | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|--------|-------|---|------|---------|--------|----------------|----------------|
| Succès | 9     | 9 | 19.4 | 3.9     | 18.0   | 17.0           | 22.3           |
| Echec  | 7     | 7 | 27.7 | 16.0    | 19.7   | 15.4           | 43.5           |

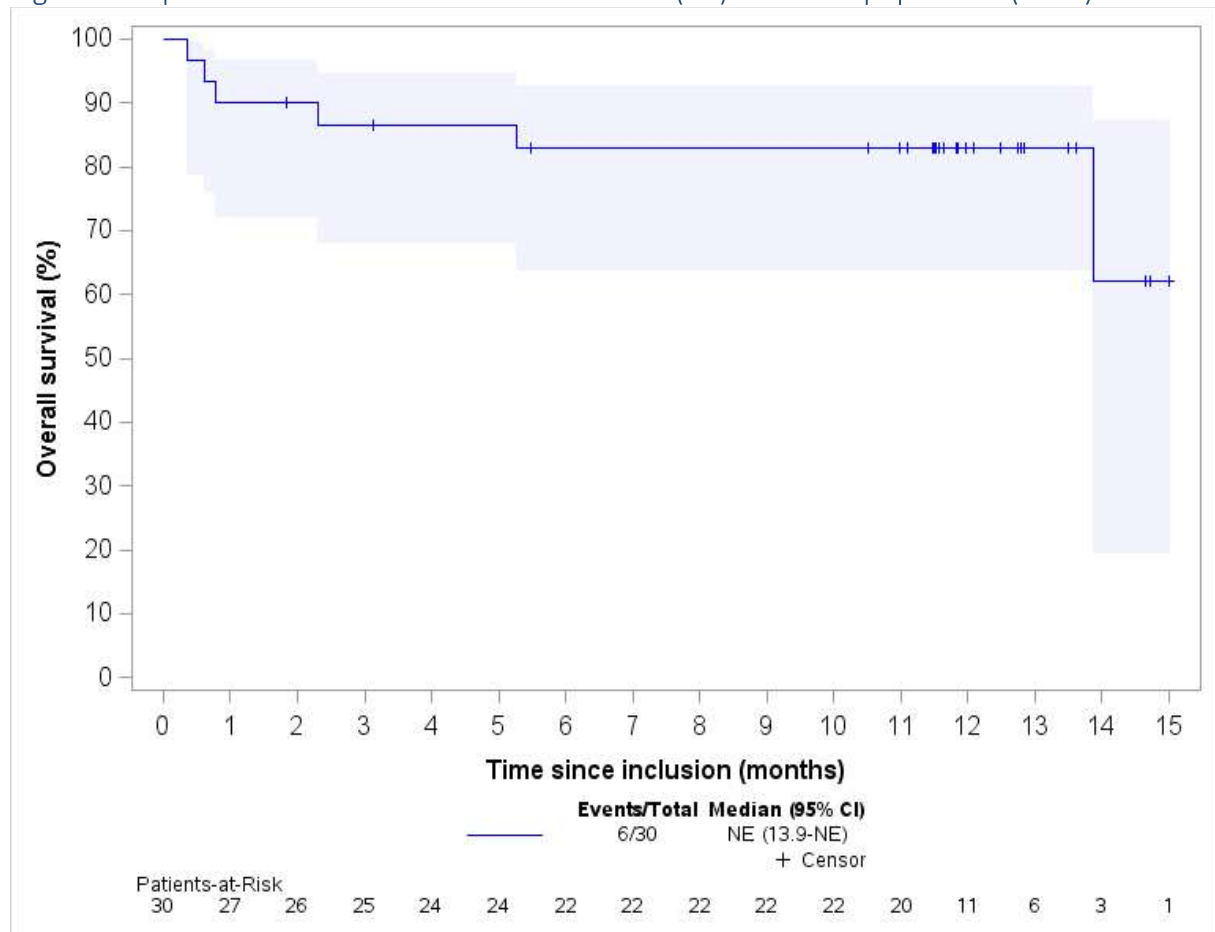
#### Relative change (%) for Muscle Mass Index from baseline to W8

| Critère principal<br>(définition 1) | N Obs | N | Mean | Std Dev | Median | Lower Quartile | Upper Quartile |
|-------------------------------------|-------|---|------|---------|--------|----------------|----------------|
| Succès                              | 12    | 9 | 18.4 | 28.3    | 5.0    | 0.0            | 39.4           |
| Echec                               | 15    | 7 | 75.1 | 91.4    | 57.6   | -4.7           | 170.2          |

## Overall survival (OS)

OS is defined as the time between chemotherapy initiation and death (from any cause) or the last date the patients was known to be alive. Patients alive at last report will be censored at the endpoint.

Figure 2: Kaplan-Meier estimates of overall survival (OS) in the ITT population (n=30)



Median follow-up (95% CI): 11.9(11.5-12.8) months.

Figure 3: Kaplan-Meier estimates of overall survival (OS) according to the type of cancer in the ITT population (n=30)

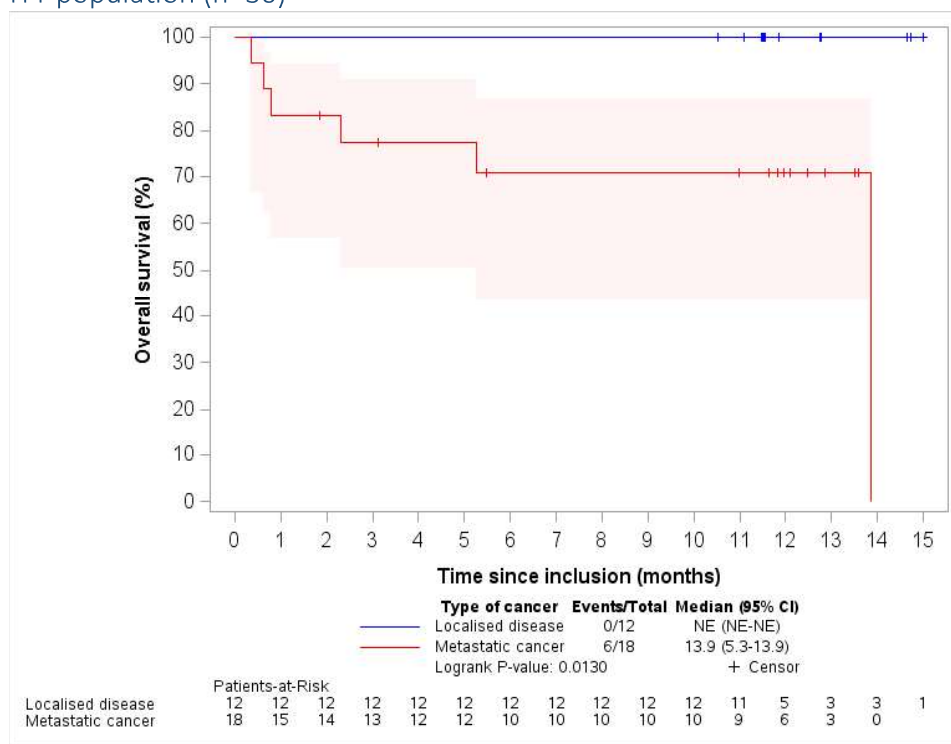


Figure 4: Kaplan-Meier estimates of overall survival (OS) according to the primary endpoint (definition 1) in the mITT population (n=27)

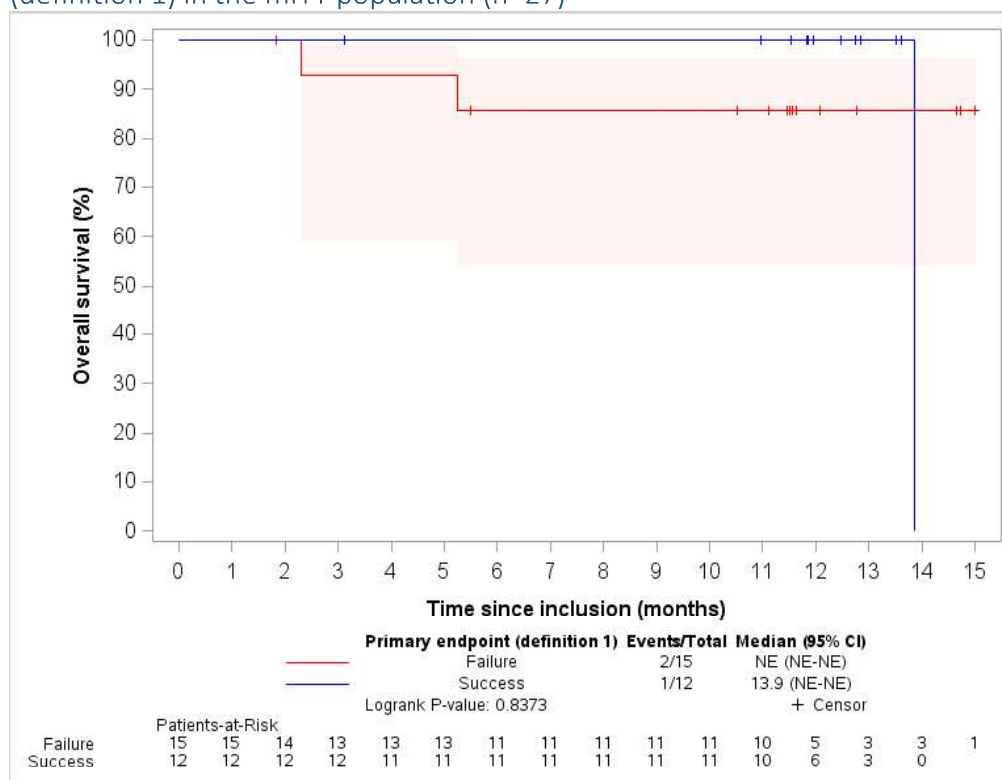


Figure 5: Kaplan-Meier estimates of overall survival (OS) according to the primary endpoint (definition 2) in the mITT population (n=27)

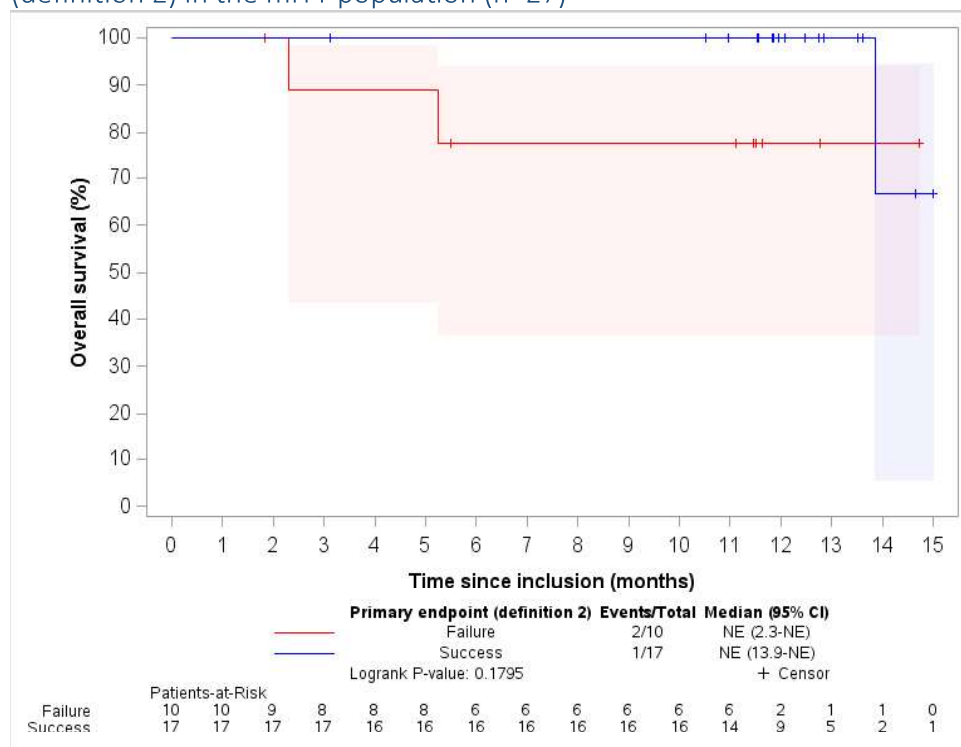
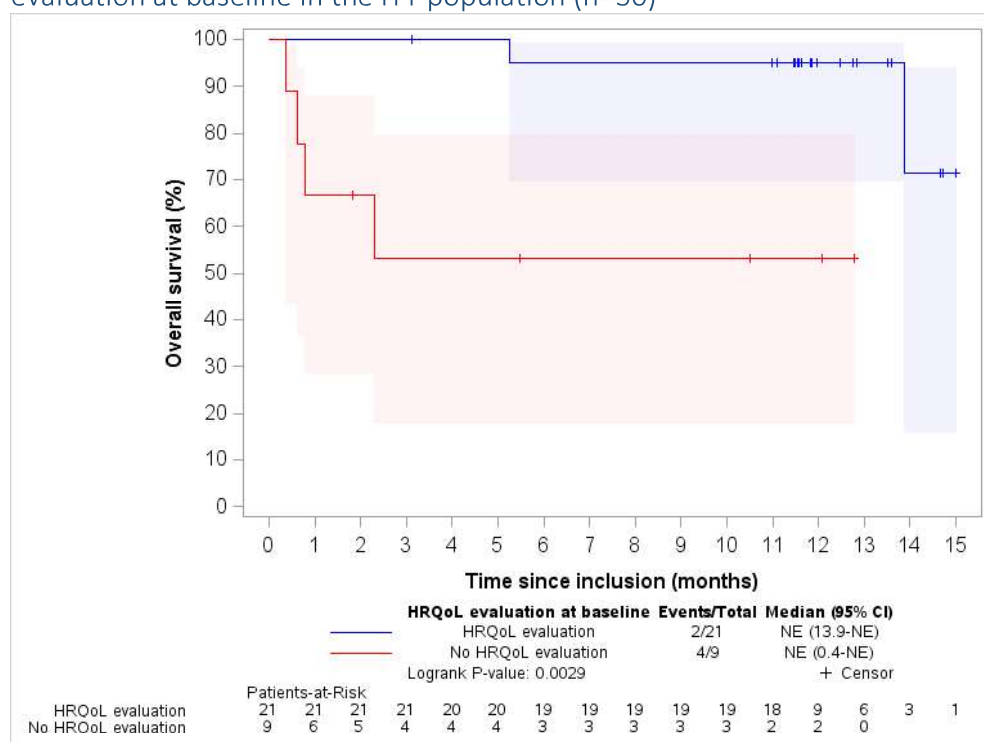


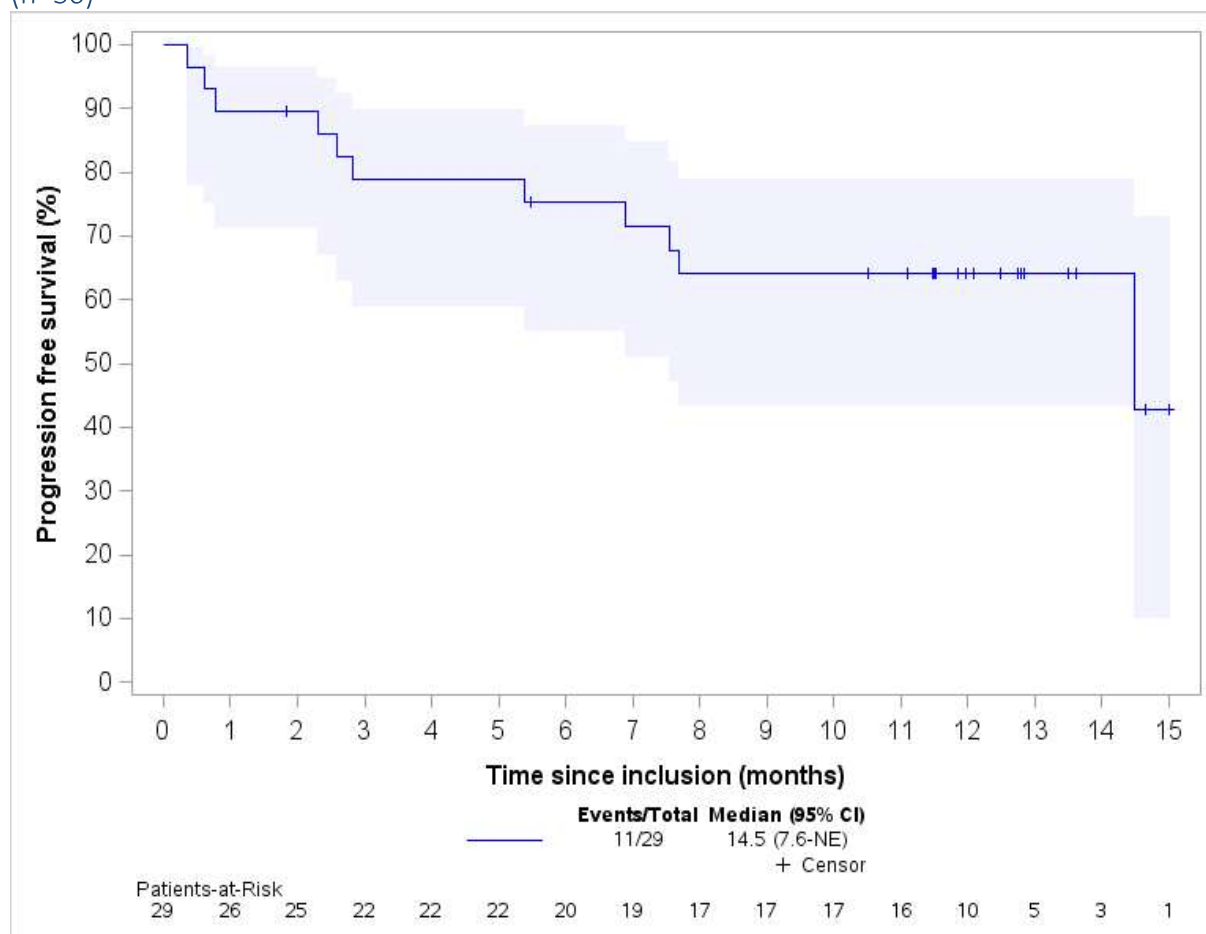
Figure 6: Kaplan-Meier estimates of overall survival (OS) according to the availability of HRQoL evaluation at baseline in the ITT population (n=30)



### Progression-free survival (PFS)

PFS is defined as the time between chemotherapy initiation and disease progression or death from any cause whichever occurs first. Patients alive and without progression at last tumor assessment will be censored at the endpoint.

Figure 7: Kaplan-Meier estimates of progression-free survival (PFS) in the ITT population (n=30)



NB: 1 patient with a missing date of progression will be not considered in survival analysis.

Figure 8: Kaplan-Meier estimates of progression-free survival (PFS) according to the type of cancer in the ITT population (n=30)

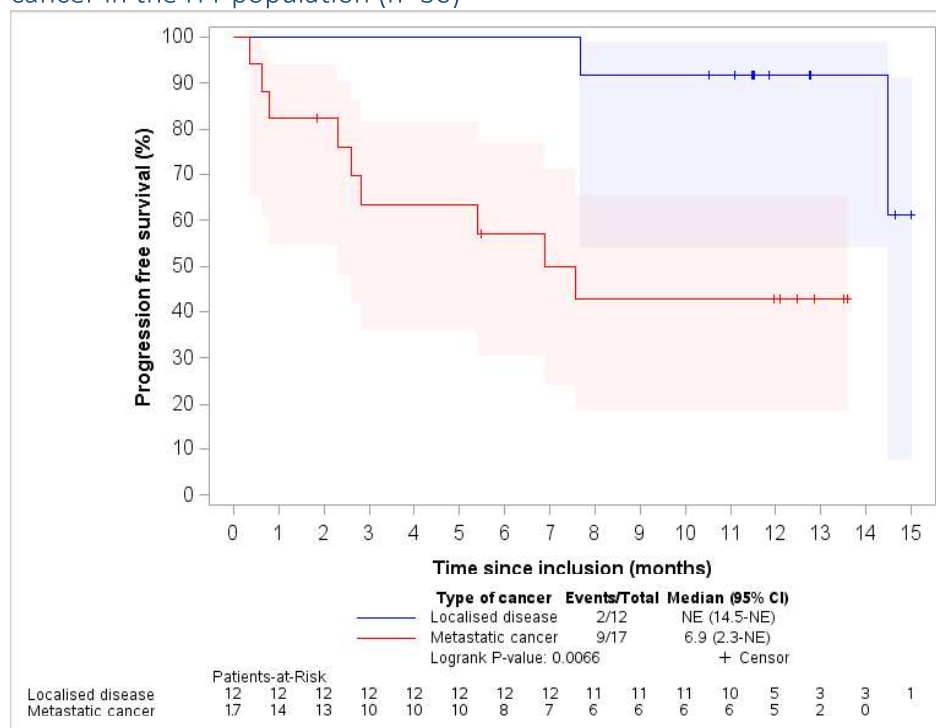


Figure 9: Kaplan-Meier estimates of progression-free survival (PFS) according to the primary endpoint (definition 1) in the mITT population (n=30)

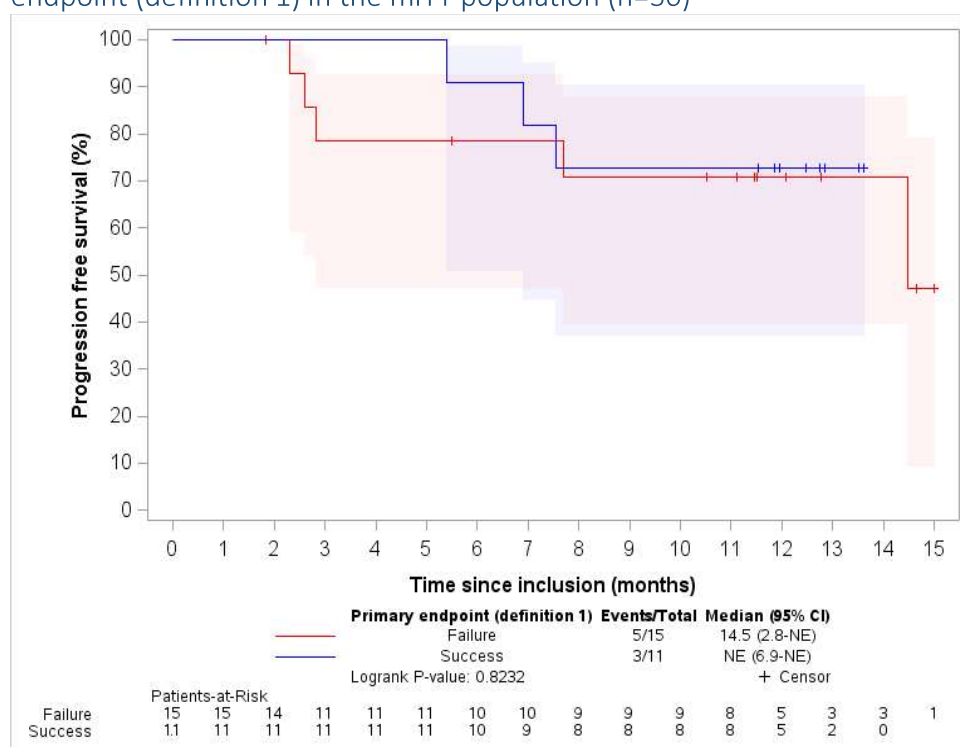


Figure 10: Kaplan-Meier estimates of progression-free survival (PFS) according to the primary endpoint (definition 2) in the mITT population (n=30)

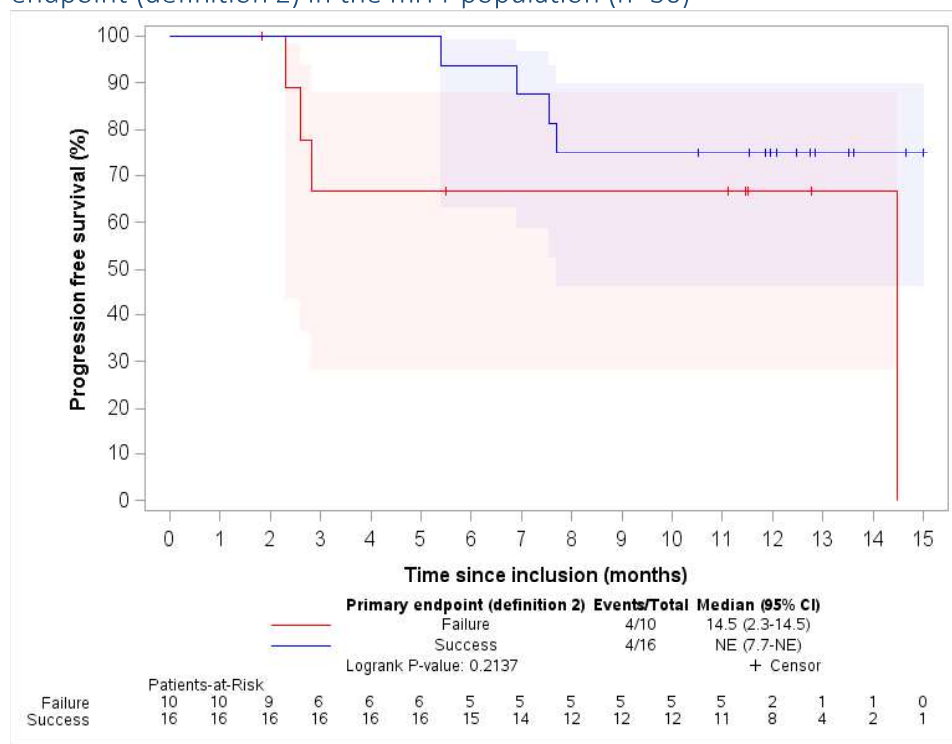
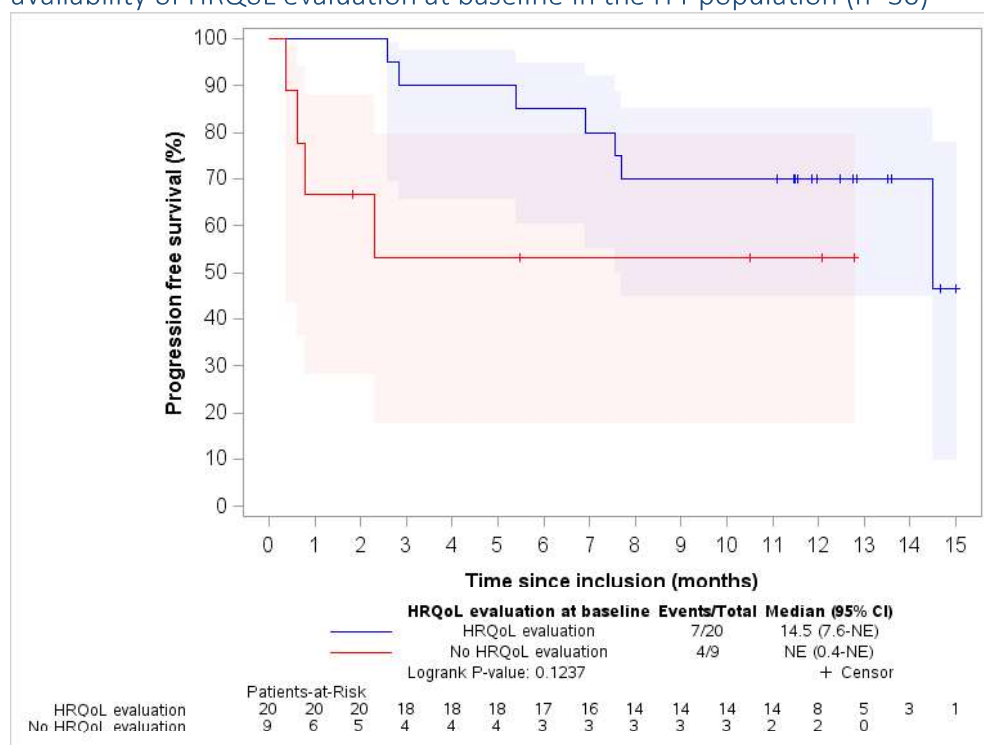


Figure 11: Kaplan-Meier estimates of progression-free survival (PFS) according to the availability of HRQoL evaluation at baseline in the ITT population (n=30)



## Tolerance

Table 7. Tolerance according to the type of cancer in the ITT population (n=30)

|                                         |     | Global<br>(n=30) | Localized<br>cancer<br>(n=12) | Metastatic<br>cancer<br>(n=18) |       |
|-----------------------------------------|-----|------------------|-------------------------------|--------------------------------|-------|
|                                         |     | N(%)             | N(%)                          | N(%)                           | p     |
| Treatment exposure                      |     |                  |                               |                                |       |
| At least one dose delay or deleted dose | No  | 19 (63.3)        | 6 (50)                        | 13 (72.2)                      | 0.216 |
|                                         | Yes | 11 (36.7)        | 6 (50)                        | 5 (27.8)                       |       |
| At least one dose delay                 | No  | 23 (76.7)        | 8 (66.7)                      | 15 (83.3)                      | 0.290 |
|                                         | Yes | 7 (23.3)         | 4 (33.3)                      | 3 (16.7)                       |       |
| At least one deleted dose               | No  | 25 (83.3)        | 10 (83.3)                     | 15 (83.3)                      | 1.000 |
|                                         | Yes | 5 (16.7)         | 2 (16.7)                      | 3 (16.7)                       |       |
| At least one dose reduction             | No  | 16 (53.3)        | 7 (58.3)                      | 9 (50)                         | 0.654 |
|                                         | Yes | 14 (46.7)        | 5 (41.7)                      | 9 (50)                         |       |
| Adverse events                          |     |                  |                               |                                |       |
| At least one AE                         | No  | 23 (76.7)        | 10 (83.3)                     | 13 (72.2)                      | 0.481 |
|                                         | Yes | 7 (23.3)         | 2 (16.7)                      | 5 (27.8)                       |       |
| Number of AE by patient                 | 0   | 23 (76.7)        | 10 (83.3)                     | 13 (72.2)                      | 0.640 |
|                                         | 1   | 6 (20)           | 2 (16.7)                      | 4 (22.2)                       |       |
|                                         | 2   | 1 (3.3)          | 0 (0)                         | 1 (5.6)                        |       |

Table 8. Tolerance according to the primary endpoint (definition 1) in the mITT population (n=27)

|  |  | Global<br>(n=27)<br><br>N(%) | Primary endpoint:<br>success<br>(n=12)<br><br>N(%) | Primary endpoint:<br>failure<br>(n=15)<br><br>N(%) | <br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br><br>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Table 9. Tolerance according to the availability of HRQoL evaluation at baseline in the ITT population (n=30)

|                                         |     | Global<br>(n=30) | No HRQoL<br>evaluation at<br>baseline<br>(n=9) | HRQoL evaluation<br>at baseline<br>(n=21) |       |
|-----------------------------------------|-----|------------------|------------------------------------------------|-------------------------------------------|-------|
|                                         |     | N(%)             | N(%)                                           | N(%)                                      | p     |
| Treatment exposure                      |     |                  |                                                |                                           |       |
| At least one dose delay or deleted dose | No  | 19 (63.3)        | 6 (66.7)                                       | 13 (61.9)                                 | 0.804 |
|                                         | Yes | 11 (36.7)        | 3 (33.3)                                       | 8 (38.1)                                  |       |
| At least one dose delay                 | No  | 23 (76.7)        | 7 (77.8)                                       | 16 (76.2)                                 | 0.925 |
|                                         | Yes | 7 (23.3)         | 2 (22.2)                                       | 5 (23.8)                                  |       |
| At least one deleted dose               | No  | 25 (83.3)        | 8 (88.9)                                       | 17 (81)                                   | 0.593 |
|                                         | Yes | 5 (16.7)         | 1 (11.1)                                       | 4 (19)                                    |       |
| At least one dose reduction             | No  | 16 (53.3)        | 6 (66.7)                                       | 10 (47.6)                                 | 0.338 |
|                                         | Yes | 14 (46.7)        | 3 (33.3)                                       | 11 (52.4)                                 |       |
| Adverse events                          |     |                  |                                                |                                           |       |
| At least one AE                         | No  | 23 (76.7)        | 5 (55.6)                                       | 18 (85.7)                                 | 0.073 |
|                                         | Yes | 7 (23.3)         | 4 (44.4)                                       | 3 (14.3)                                  |       |
| Number of AE by patient                 | 0   | 23 (76.7)        | 5 (55.6)                                       | 18 (85.7)                                 | 0.121 |
|                                         | 1   | 6 (20)           | 3 (33.3)                                       | 3 (14.3)                                  |       |
|                                         | 2   | 1 (3.3)          | 1 (11.1)                                       | 0 (0)                                     |       |

## Individual patient trajectories over time representation

Figure 12. Swimmer plot for individual profile with the principal characteristics and outcomes in the ITT population (n=30)

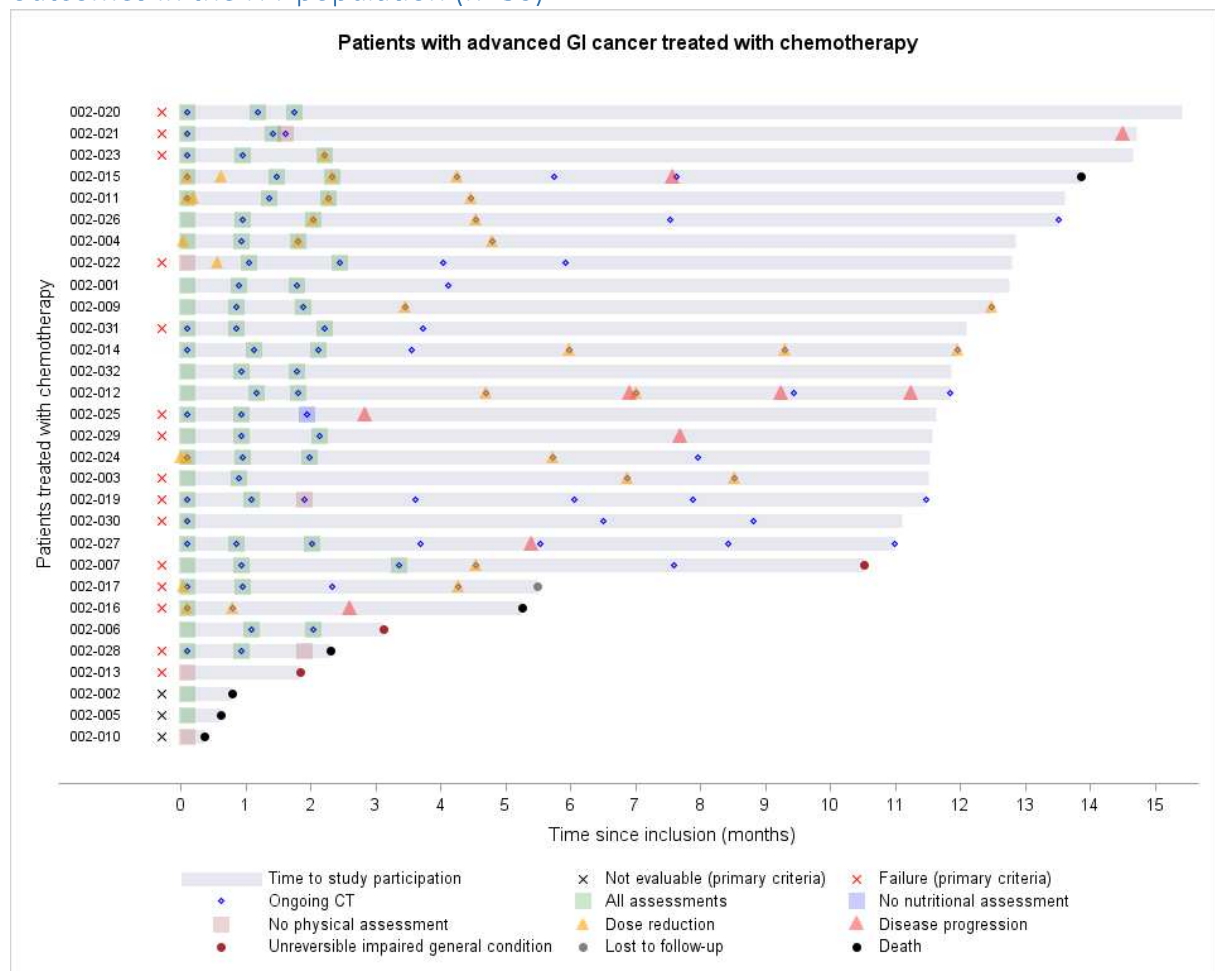


Figure 13. Swimmer plot for individual profile with the principal characteristics and outcomes according to the type of cancer (localized, metastatic) in the ITT population (n=30)

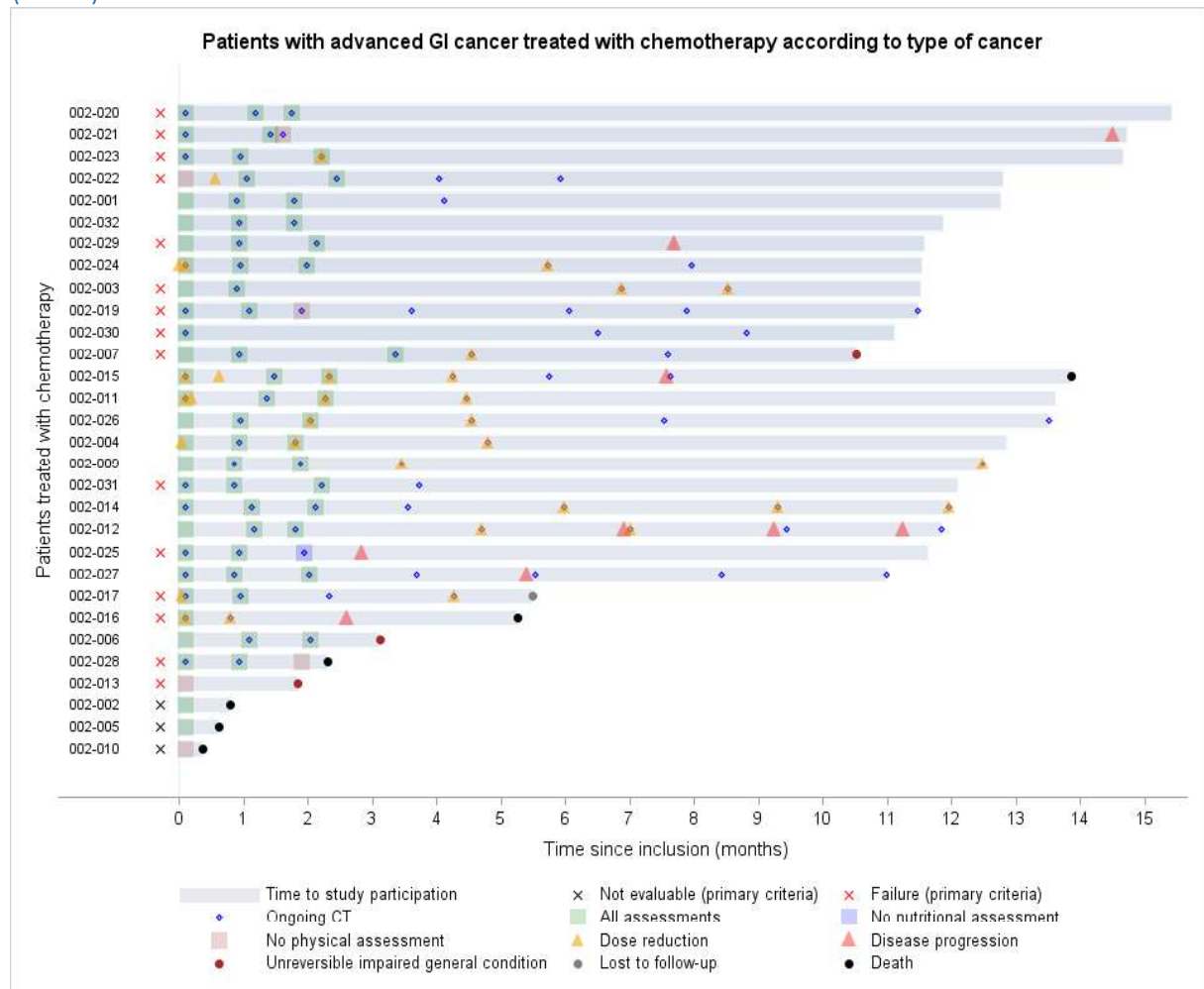
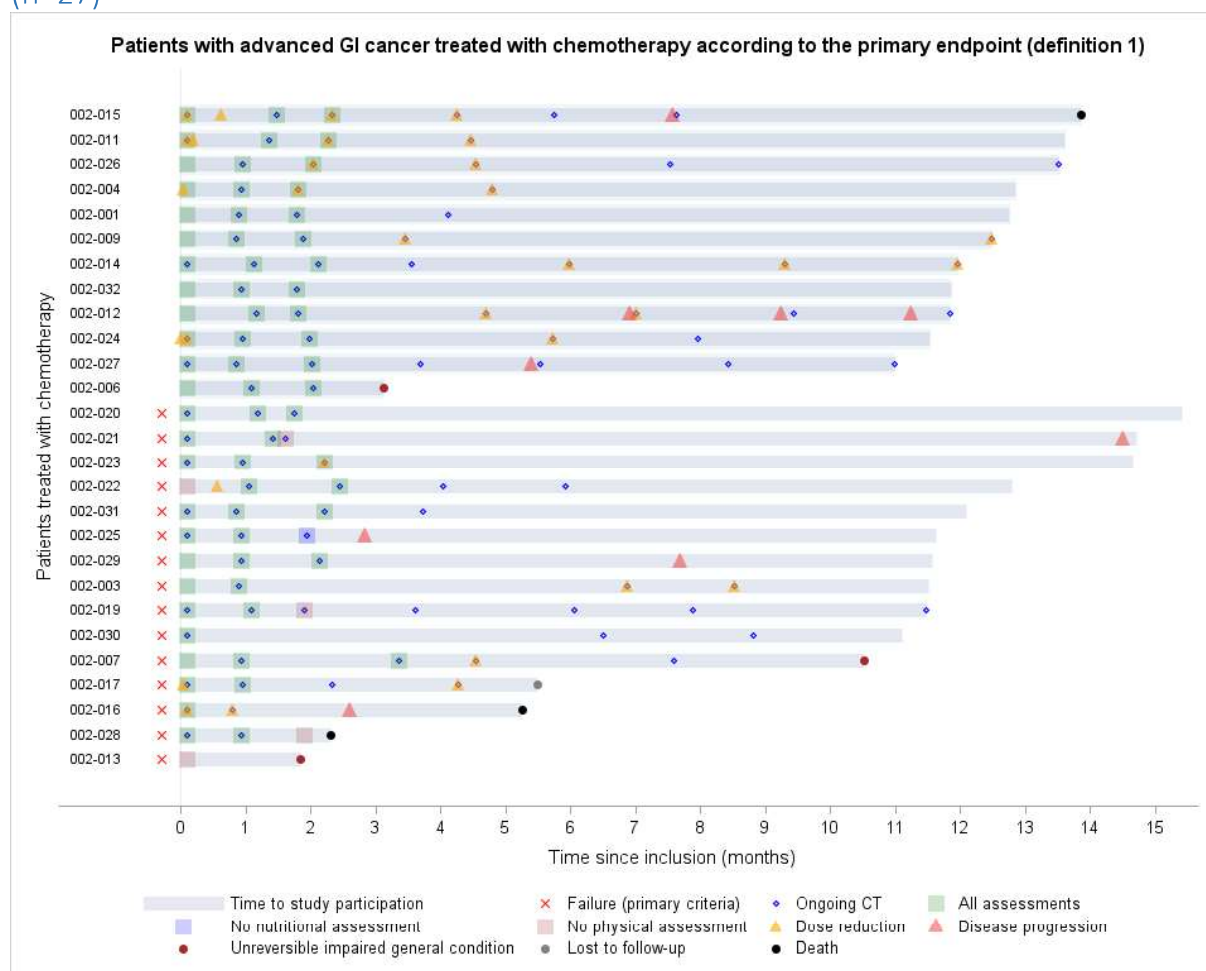


Figure 14. Swimmer plot for individual profile with the principal characteristics and outcomes according to the primary endpoint (definition 1) in the mITT population (n=27)



Of note, we have no information about the end of chemotherapy and a possible posterior line of treatment.