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Toxicity and Clinical Outcomes in HER2-Positive Metastatic Breast Cancer Treated with Trastuzumab Deruxtecan: Does Body Composition Matter?

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Abstract

Purpose.

This study aimed to evaluate the association between early changes in body composition and T-DXd treatment-related toxicity and outcomes.

Patients and Methods. This retrospective multicentre observational study included 50 MBC patients treated with T-DXd at ASST Spedali Civili di Brescia and Sant'Anna Hospital of Como. Body composition parameters—skeletal muscle area (SMA), subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and intramuscular adipose tissue (IMAT)—were assessed on CT scans at baseline and after 3 months (Δt0–t1). Toxicities were graded according to CTCAE v5.0. Associations between body composition changes, toxicity, progression-free survival (PFS), and overall survival (OS) were analyzed.

Results Early changes in body composition were observed, with a significant increase in VAT (+ 15.3%, $p = 0.05$) and non-significant increases in SAT and IMAT, alongside a decline in SMA. Increased SAT (Δt0–t1), particularly above the median, was significantly associated with higher grades of fatigue ($p = 0.02$) and nausea ($p = 0.04$), while muscle loss showed a trend toward increased fatigue severity ($p = 0.06$). Increases in SAT and VAT were associated with worse OS ($p < 0.01$), and VAT increase was also associated with shorter PFS ($p = 0.02$). No association was found between body composition changes and dose reductions.

Conclusion. Early alterations in body composition, particularly adipose tissue expansion, are associated with treatment-related toxicity and poorer outcomes in patients receiving T-DXd. These findings support longitudinal CT body composition assessment as a dynamic imaging biomarker of host response to therapy, providing prognostic information beyond conventional anthropometric measures.

Introduction

Breast cancer is the most commonly diagnosed malignancy among women worldwide and remains a leading cause of cancer-related death [1]. Despite remarkable advances in screening and treatment that have substantially improved survival, metastatic disease continues to be largely incurable [1]. The introduction of Trastuzumab Deruxtecan (T-DXd) has significantly reshaped the treatment landscape of both HER2-positive and HER2-low metastatic breast cancer (MBC), demonstrating improvements in response rate, progression-free survival, and overall survival. [2], [3]. The safety profile of T-DXd in advanced breast cancer was established in pivotal trials, where grade ≥ 3 adverse events (CTCAE v5.0) were predominantly hematologic (e.g., anemia) and gastrointestinal, particularly nausea. Notably, fatigue was reported in approximately 45% of patients in the pivotal trials [2], [3], emerging as one of the most frequent toxicities and a key determinant of patient-reported outcomes and quality of life.

Real-world studies have confirmed this safety profile, consistently reporting nausea, fatigue/asthenia, and neutropenia among the most common adverse events [4].

Body composition, including lean mass and adipose tissue, is increasingly recognized as a key determinant of cancer outcomes, although evidence in MBC remains limited [5], [6], [7]. Sarcopenia is associated with higher treatment toxicity, reduced tolerance, and poorer survival, while the role of fat mass is less clearly defined despite its association with inflammation and tumor progression [5], [7]. Body composition may also influence drug pharmacokinetics, affecting treatment efficacy and toxicity [5]. In particular, myosteatosis has been linked to increased chemotherapy-related toxicity, dose reductions, and higher cardiovascular risk [5]. Radiomic analysis of computed tomography images (CT scan) represents a promising tool for assessing these parameters and their clinical implications [6], [8], [9]. The primary aim of this study was to assess modification of body composition parameters during treatment with TDX-D. Secondary objectives included evaluating the impact of baseline body composition and early changes in body composition on treatment-related toxicity and clinical outcomes.

Materials and Methods

Study Design

This study is a retrospective, multicentre, observational study evaluating Her2-positive MBC patients treated with T-DXd at the Oncology Division of ASST Spedali Civili of Brescia and Sant'Anna Hospital of Como. The retrospective collection of data followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline [10]. The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice (GCP) principles, and current regulatory requirements. Approval was obtained from the appropriate local Ethics Committee prior to data collection.

Participants

Eligible patients treated from August 2023 to November 2025 were identified through institutional databases. Clinical information regarding demographic characteristics, oncologic history, tumor features, treatment details, toxicity data, and survival outcomes was retrospectively extracted from electronic medical records and recorded in a pseudonymized electronic dataset.

Eligibility criteria included treatment with T-DXd regardless of line of therapy, at least one computed tomography (CT) scan obtained at baseline (prior to treatment initiation) and at 3 months after treatment start, provision of written informed consent, and adequate compliance.

Toxicity and outcome evaluation

Toxicity and outcome evaluation
The incidence and severity of treatment-related adverse events (AEs) were assessed using the common terminology criteria for adverse events (CTCAE v5.0) and categorized as grades 1–2 (mild to moderate) or grades 3–4 (severe).

Progression-free survival (PFS) was defined as the time from treatment initiation to documented disease progression or death from any cause, whichever occurred first.

Overall survival (OS) was defined as the time from treatment initiation to death from any cause. Patients without events were censored at the date of last follow-up.

Anthropometric parameters measured

Anthropometric parameters were assessed using standardized procedures, with participants wearing light clothing and no shoes, both at baseline and after 3 months of T-DXd therapy. Height and weight were measured using a wall-mounted stadiometer and a calibrated digital scale respectively. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2) and categorized according to World Health Organization (WHO) criteria as underweight (< 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (≥ 30.0 kg/m^2).

Body composition analysis

Body composition parameters were evaluated through the analysis of CT images acquired as part of routine clinical care before starting treatment with TDX-d and after 3–4 months during treatment. Cross-sectional images at the level of the third lumbar vertebra (L3) were used to quantify skeletal muscle (SMA), subcutaneous adipose tissue (SAT), visceral adipose tissue (VAT), and intramuscular adipose tissue (IMAT), according to validated radiological methods. Image segmentation was performed using 3D Slicer software, enabling quantitative assessment of tissue areas (cm^2) [11].

Statistical Analysis

Patients' characteristics were summarized using descriptive statistics. Continuous variables were reported as median and interquartile range (IQR), while categorical variables were expressed as absolute frequencies and percentages. Longitudinal changes were assessed using paired non-parametric tests. Correlations between BMI and body composition indices were evaluated using Spearman's rank correlation coefficient. Associations between body composition parameters and treatment-related toxicity categorized as mild (grade 1) and severe (grade 3 and 4) were analyzed using the Wilcoxon rank-sum test. Overall survival (OS) was defined as the time from the diagnosis of metastatic disease to death from any cause or last follow-up. The association between body composition variables and OS was investigated using univariate Cox proportional hazards models. Due to the limited sample size, multivariable analyses were not performed. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant. Statistical analyses were conducted using Stata software, version 18.0 (StataCorp, College Station, TX, USA).

Results

Patient and Treatment Characteristics

Fifty MBC patients treated with T-DXd at the Breast Unit and Oncology of the ASST-Spedali Civili of Brescia and at the Oncology of St. Anna Hospital from 2018 to 2020 were included in the study (**Fig.1**).

The characteristics of patients are described in table 1. The median age at T-DXd initiation was 59 years (range 28–80). Most patients had estrogen receptor (ER)-positive disease (66%). HER2 expression was assessed on tissue samples obtained at diagnosis and was HER2 3+ in 36% of patients, HER2-low in 36%, and HER2-negative in 10%, while HER2 status was unavailable in 18% of cases. Approximately half of the patients presented with a high disease burden (≥4 metastatic sites). The most common sites of metastasis were liver (58%) and bone (54%), nearly 20% of patients had brain metastases. T-DXd was mainly administered in the second- or third-line setting (48% of cases). Regarding treatment modifications, dose reductions were required in 28 patients (56%). **The primary reason for dose reduction was treatment-related toxicity (42%), while in a minority of cases (4%) it was due to worsening general clinical conditions.**

Table 1 – Patients characteristics at the start of TDX-d

Characteristics	N=50 (%)
Median age at metastatic disease diagnosis [range]	54 [27–72]
Median age at TDX-d start [range]	59 [28-80]
Estrogen receptors (ER)	
Negative (<10%)	17 (34)
Positive (≥10%)	33 (66)
Progesteron receptors (PgR)	
Negative (<10%)	32 (64)
Positive (≥10%)	18 (36)
Ki67	
< 20%	4 (8)
≥ 20%	31 (62)
NA	15 (30)
HER2 on metastatic site	
0	5 (10)
1+	12 (24)
2+	6 (12)
3+	18 (36)
NA	9 (18)
Metastatic disease onset	13 (26)
PS ECOG at T-DXd start	
0	39 (78)
1	11 (22)
Number of metastatic sites at T-DXd start	
1	6 (12)
2	24 (48)
3	14 (28)
4	6 (12)
Metastatic disease sites at T-DXd start	
Brain	10 (20)

Lung	18 (36)
Liver	29 (58)
Peritoneal carcinosis	1 (2)
Skin/soft tissues	9 (18)
Bone	27 (54)
Lymphnodes	25 (50)
Line of T-DXd therapy	
1	1 (2)
2-3	24 (48)
4-5	18 (36)
≥ 6	7 (14)
Dose reduction during T-DXd	28 (56)
% of dose reduction	
First dose reduction 4,4 mg/kg	14 (28)
Second dose reduction 3,2 mg/kg	14 (28)
Reason for dose reduction	
Adverse events	21 (42)
Unfit patient	2 (4)
Other	2 (4)
NA	3 (6)

Treatment-related toxicities observed during T-DXd therapy are reported in Table 2. The most frequently observed adverse event was fatigue, occurring in 43 out of 50 patients (86%), predominantly grade 1–2, with only 4% developing grade 3 fatigue. Nausea occurred in 29 patients (58%), mostly grade 1–2, whereas vomiting was reported in only 10% of cases. Other toxicities included abdominal cramps, constipation, and diarrhea, each reported in 16% of patients, as well as mucositis (8%), dysgeusia (10%), and anemia (10%).

Table 2. Toxicity during T-DXd treatment.

Adverse events during T-DXd	Total N=50 (%)	G1/G2	G3
Fatigue	43 (86)	41 (82)	2 (4)
Nausea	29 (58)	28 (56)	1 (3)
Vomiting	5 (10)	5 (10)	0
Abdominal cramps	8 (16)		
Constipation	8 (16)		
Diarrhoea	8 (16)		
Mucosyte	4 (8)		
Dysgeusia	5 (10)		
Anaemia	5 (10)		

Changes in anthropometric parameters during TDX-D treatment

Data on body weight, height, and BMI were collected at baseline (t0, before the first cycle of T-DXd) and after 3 months of treatment (t1). A statistically significant association was observed between BMI and both SAT area ($p < 0.01$) and VAT area ($p < 0.01$), whereas no significant association was found between BMI with SMA ($p=0.583$) and IMAT area ($p = 0.95$) (Table 3).

Table 3. Correlation between BMI and body composition parameters

Body composition parameters	n	Spearman's ρ	p-value
SMA area	38	0.092	0.583
SAT surface area	38	0.698	<0.001
VAT surface area	38	0.517	0.001
IMAT surface area	38	0.010	0.953

Spearman rank correlation. M= muscle; SAT = subcutaneous adipose tissue; VAT = visceral adipose tissue; IMAT = intermuscular adipose tissue

Median body weight at t0 was 56.5 kg (range 40–85 kg), with a median BMI of 21.6 kg/m² (range 15.1–36.6 kg/m²). At baseline, 29 patients (58%) were classified as normal weight, 16 (32%) as overweight, and 5 (10%) as obese. At t1, median body weight decreased to 56 kg (range 40–82 kg) and median BMI to 21.1 kg/m² (range 15.8–32.4 kg/m²), indicating an overall reduction compared with baseline values.

Longitudinal changes in Body Composition During Treatment with TDX-d.

Median changes in body composition parameters are reported in Table 4. Among the 50 patients included in the study, 34 had undergone a first disease reassessment (t1) at the time of analysis. In these patients, a reduction in SMA was observed, decreasing from 240.4 cm² at baseline to 228.4 cm² at t1 (p=0.28). Conversely, adipose tissue compartments showed an overall increase, with SAT rising from 432.3 cm² to 434.8 cm² (p=0.97) and VAT from 139.2 cm² to 169.5 cm² (p=0.05). IMAT showed a slight decrease, from 10.6 cm² to 10.3 cm² (p=0.18).

Table 4. Body composition changes parameter (Area-cm2)

Body composition parameters	**t0**	**t1**
N°	50	34
Skeletal Muscle Area (SMA), (cm²)	240.4 (26.8–473.8)	228.4 (153.5–294.1)
Subcutaneous adipose tissue (SAT), (cm²)	432.3 (67.5–874.6)	434.76 (82.3–719.4)
Visceral adipose tissue (VAT), (cm²)	139.2 (18.2–523.8)	169.5 (20.7–348.7)
Intramuscolar adipose tissue (IMAT), superficie (cm²)	10.6 (0.5–45.4)	10.27 (1.8–71.6)

As reported the increase in VAT alone reached statistical significance, with a median increase of 15.3% (Table 5).

Table 5. Two-timepoint area comparison (t0-t1).

	t0	**t1**	**Median modification % Area (Δt0–t1)**	**Interquartile range (p25–p75)**	**p value**
N°	50	34			
SMA area	240.4 (26.8–473.8)	228.4 (153.5–294.1)	-3.7	-12.9 – 6.2	0.28
SAT area	432.3 (67.5–874.6)	434.76 (82.3–719.4)	1.2	-12.2 – 14.5	0.97
VAT area	139.2 (18.2–523.8)	169.5 (20.7–348.7)	15.3	-4.7 – 40.9	0.05
IMAT area	10.6 (0.5–45.4)	10.27 (1.8–71.6)	32.9	-24.1 – 91.1	0.18

Changes in body composition and TDX-d correlated adverse events.

Of the 34 patients who had undergone a first restaging, 31 (91%) had complete documentation of adverse events and were included in the toxicity analysis; 3 patients were excluded due to unavailable clinical records. The correlation between fatigue and percentage changes in body composition at Δt0–t1 was evaluated and described in Table 6. Changes in SAT from t0 to t1 were significantly associated with both fatigue severity and nausea. In particular, a 1.2% increase in SAT was linked to higher fatigue grade ($p = 0.003$) and to the occurrence of nausea ($p = 0.035$). A trend toward an association between greater muscle loss and increased fatigue grade was also observed, although it just failed to reach the statistical significance ($p = 0.057$). No significant associations were found between SMA, VAT, or IMAT and the occurrence of fatigue or nausea.

Table 6. Values expressed as median (Q1; Q3) of the percentage change in surface areas from T0 to T1 and their correlation with adverse events. Mann–Whitney test.

Parameter	**Total**	**Asthenia**			**Nausea**		
	(N=31)	**Grade 0–1** (N=22)	**Grade 2–3** (n=9)	**p**	**Grade 0** (n=12)	**Grade 1+** (n=19)	**p**
SMA	−3.7 (−12.9; +6.2)	−1.8 (−7.4; +6.2)	−18.4 (−24.6; +0.9)	0.057	−1.8 (−16.8; +9.4)	−4.1 (−10.5; +6.0)	1.000
SAT	1.2 (−12.2; +14.5)	8.8 (−5.2; +19.8)	−15.1 (−34.0; −8.6)	**0.003**	13.7 (−4.7; +20.6)	−5.2 (−15.1; +9.1)	**0.035**
VAT	15.3 (−4.7; +40.9)	23.7 (−1.6; +40.9)	14.9 (−33.4; +32.3)	0.428	33.3 (−3.3; +42.8)	4.7 (−6.1; +38.7)	0.346
IMAT	32.9 (−24.1; +91.1)	33.1 (−24.5; +67.4)	1.8 (−19.4; +170.9)	0.716	18.5 (−21.7; +121.9)	32.9 (−24.5; +67.4)	0.921

Prognostic effect of body composition parameters and TDX-d treatment.

In the univariable analysis for PFS, an increase in VAT from t0 to t1 was significantly associated with a higher risk of progression (HR 1.06; 95% CI 1.01–1.08; $p = 0.02$), whereas no significant associations were observed for the other body composition parameters (**Fig. 2).**

Similarly, univariable analysis for OS showed that increases in both SAT and VAT from t0 to t1 were significantly associated with worse survival outcomes (SAT: HR 1.03; 95% CI 1.01–1.06; $p < 0.01$; VAT: HR 1.01; 95% CI 1.00–1.02; $p < 0.01$). IMAT also showed a trend toward an association with OS, although statistical significance was not reached (HR 1.00; 95% CI 0.99–1.01; $p = 0.082$) (**Fig. 3).**

DISCUSSION

The present multicentre real-world study demonstrates that early longitudinal changes in body composition are closely associated with treatment tolerability and clinical outcomes in patients with HER2-positive and HER2-low metastatic breast cancer receiving trastuzumab deruxtecan (T-DXd). More importantly, our findings suggest that body composition should no longer be regarded simply as a static patient characteristic but rather as a dynamic imaging biomarker of host response to therapy. To our knowledge, this is among the first studies showing that early remodeling of skeletal muscle and adipose tissue during T-DXd treatment identifies patients at increased risk of toxicity and poor survival, thereby supporting the concept of CT-based host phenotyping as a complementary approach to tumour assessment.

Current imaging in metastatic breast cancer is almost exclusively focused on tumour burden and response according to RECIST criteria. However, cancer progression and treatment efficacy are determined not only by tumour biology but also by the biological response of the host. Body composition analysis offers the opportunity to characterize this response through routinely acquired CT scans, providing information on the metabolic and functional status of the patient that is not captured by tumour imaging alone. In this perspective, longitudinal body composition assessment should be considered an integral component of host phenotyping, reflecting the dynamic interaction between tumour biology, systemic therapy and patient resilience.

The principal finding of our study is that body composition evolves rapidly during the first months of T-DXd therapy. Patients developed a characteristic pattern consisting of progressive skeletal muscle depletion accompanied by expansion of adipose tissue, particularly visceral adipose tissue (VAT). Rather than representing isolated anthropometric changes, this pattern probably reflects the complex interaction between tumour biology, systemic inflammation, endocrine and metabolic dysregulation, reduced physical activity, nutritional alterations, corticosteroid exposure and treatment-related effects [12], [13]. Consequently, body composition remodeling may represent the phenotypic expression of the host response to advanced cancer and systemic treatment rather than a simple consequence of weight fluctuations.

This interpretation has important biological implications. Patients capable of maintaining skeletal muscle mass while avoiding excessive adipose tissue accumulation may possess greater physiological reserve, metabolic flexibility and capacity to tolerate treatment. Conversely, patients developing early adverse body composition remodeling may represent a biologically vulnerable subgroup characterized by reduced resilience to both disease and therapy. Thus, longitudinal body composition assessment provides information extending beyond conventional prognostic variables by capturing dynamic biological adaptations occurring during treatment.

Evidence regarding longitudinal body composition changes during T-DXd therapy remains limited. Molfino et al. reported progressive skeletal muscle depletion together with reductions in most adipose tissue compartments, whereas VAT remained substantially unchanged [14]. Conversely, our cohort demonstrated a significant increase in VAT during treatment. Similarly, Yaacobi Peretz et al. identified

significant associations between body composition parameters and treatment outcome, although the patterns of tissue remodeling differed from those observed in our population [15]. Although heterogeneous in their specific findings, all available studies consistently indicate that body composition is dynamically modified during T-DXd therapy and that these changes carry clinically relevant information. Therefore, differences among studies should probably be interpreted as reflecting distinct patient populations, disease characteristics and analytical methodologies rather than conflicting biological evidence.

One of the most clinically relevant observations of the present study is the association between adipose tissue expansion and treatment-related toxicity. Patients experiencing greater increases in subcutaneous adipose tissue (SAT) developed significantly more fatigue and nausea, whereas skeletal muscle loss showed only a borderline association with fatigue severity. Notably, toxicity correlated with dynamic changes in body composition rather than with baseline anthropometric characteristics, suggesting that metabolic remodeling occurring during treatment is more informative than static baseline measurements for identifying patients at increased risk of treatment intolerance.

Several mechanisms may explain these observations. Adipose tissue is increasingly recognized as an active endocrine organ capable of producing adipokines and pro-inflammatory cytokines that promote chronic inflammation, mitochondrial dysfunction and impaired physical performance [16], [17]. These mechanisms are well-established contributors to cancer-related fatigue and reduced functional capacity. In addition, T-DXd contains a membrane-permeable lipophilic payload whose tissue distribution could theoretically be influenced by adipose tissue expansion [14], [15]. A larger adipose compartment might modify drug distribution, tissue retention and systemic exposure, thereby contributing to toxicity independently of administered dose. Although this hypothesis remains speculative, it deserves prospective pharmacokinetic and translational investigation.

Perhaps the most important finding of our study is the strong association between adipose tissue expansion and survival outcomes. Increases in both SAT and VAT were associated with poorer overall survival, while VAT increase also predicted shorter progression-free survival. Interestingly, skeletal muscle depletion alone was not significantly associated with prognosis. These observations suggest that, in patients receiving T-DXd, adipose tissue remodeling may represent a stronger marker of clinical outcome than muscle loss itself.

This finding is biologically plausible. Visceral and subcutaneous adipose tissue actively participate in chronic inflammation, insulin resistance, immune dysregulation and activation of tumour-promoting signalling pathways [18], [19]. Consequently, adipose tissue expansion should not be considered merely an epiphenomenon accompanying disease progression but rather a surrogate marker of biological processes that may favour tumour aggressiveness and reduce treatment efficacy. In this context, adipose tissue becomes an active component of tumour-host interactions rather than simply an energy storage compartment.

Our findings are partially consistent with those reported by Yaacobi Peretz et al., who demonstrated an association between increased adiposity and lower objective response rates during T-DXd therapy [15]. Conversely, Molfino et al. identified skeletal muscle depletion as the principal determinant of overall survival[14]. Additional evidence from broader breast cancer populations has also demonstrated the adverse prognostic impact of visceral and subcutaneous adiposity irrespective of treatment modality [20]. Collectively, these observations reinforce the concept that longitudinal body composition assessment captures clinically meaningful aspects of host biology that complement traditional tumour-centred biomarkers.

The clinical implications of these findings extend beyond prognostic stratification. Unlike body mass index, which provides only a crude estimate of body size, CT-derived body composition analysis offers a quantitative assessment of the patient's metabolic phenotype and its evolution during therapy[11]. Since CT imaging is routinely performed in metastatic breast cancer, body composition assessment can be implemented without additional imaging procedures, radiation exposure or costs. More importantly, identifying patients with an unfavourable body composition trajectory may allow early implementation of nutritional counselling, structured exercise programmes and multimodal supportive interventions before clinically overt deterioration develops. Thus, body composition assessment has the potential to become not only a prognostic biomarker but also an actionable biomarker, capable of identifying patients who may benefit from personalized supportive care strategies.

From a broader perspective, these findings support a paradigm shift in oncologic imaging. While precision oncology has largely focused on molecular characterization of the tumour, equal attention should be devoted to characterization of the host. Integrating tumour phenotyping with host phenotyping may provide a more comprehensive representation of treatment response, recognizing that clinical outcomes result from the interaction between tumour biology and patient biology rather than from either component alone. Routine CT scans may therefore simultaneously provide information on tumour evolution and on host adaptation, substantially increasing the clinical value of imaging already acquired in standard practice.

Several limitations should be acknowledged. The retrospective design introduces the possibility of selection bias and residual confounding. The relatively small sample size precluded multivariable analyses and limits the generalizability of our findings. Furthermore, body composition changes may partly reflect disease progression rather than direct treatment effects. Accordingly, our findings should be regarded as hypothesis-generating. Nevertheless, the consistency of the associations observed across treatment-related toxicity, progression-free survival and overall survival, together with their biological plausibility, provides a strong rationale for prospective validation.

In conclusion, our study suggests that early body composition remodeling during T-DXd therapy represents more than a simple metabolic consequence of treatment. Dynamic changes in adipose tissue identify patients at increased risk of toxicity and poor survival, supporting the concept that longitudinal CT-derived body composition assessment may serve as a dynamic imaging biomarker of host response

to therapy. Because this information can be extracted from routinely acquired CT scans without additional costs or patient burden, its integration into clinical practice appears readily feasible. Future prospective studies should determine whether modifying unfavorable body composition trajectories through nutritional, exercise-based and multimodal supportive interventions can improve treatment tolerance and ultimately translate into better clinical outcomes.

Declarations

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All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Giulia Scartabellati, Benedetta Trevisan, Rebecca Pedersini, Francesco Donato. The first draft of the manuscript was written by Giulia Scartabellati and Benedetta Trevisan and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

The datasets generated during and/or analysed during the current study are not publicly available due to privacy reasons, but are available from the corresponding author on reasonable request.

Clinical trial number: not applicable.

This study was performed in line with the principles of the Declaration of Helsinki. Ethical approval was granted by the Territorial Ethics Committee Lombardia 6 (Comitato Etico Territoriale Lombardia 6), based at Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, on 10/02/2026 (protocol number NP 6831).

Informed consent

was obtained from all individual participants included in the study.

Author Contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by G.S., B.T., R.P., and F.D. The first draft of the manuscript was written by G.S. and B.T., and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability

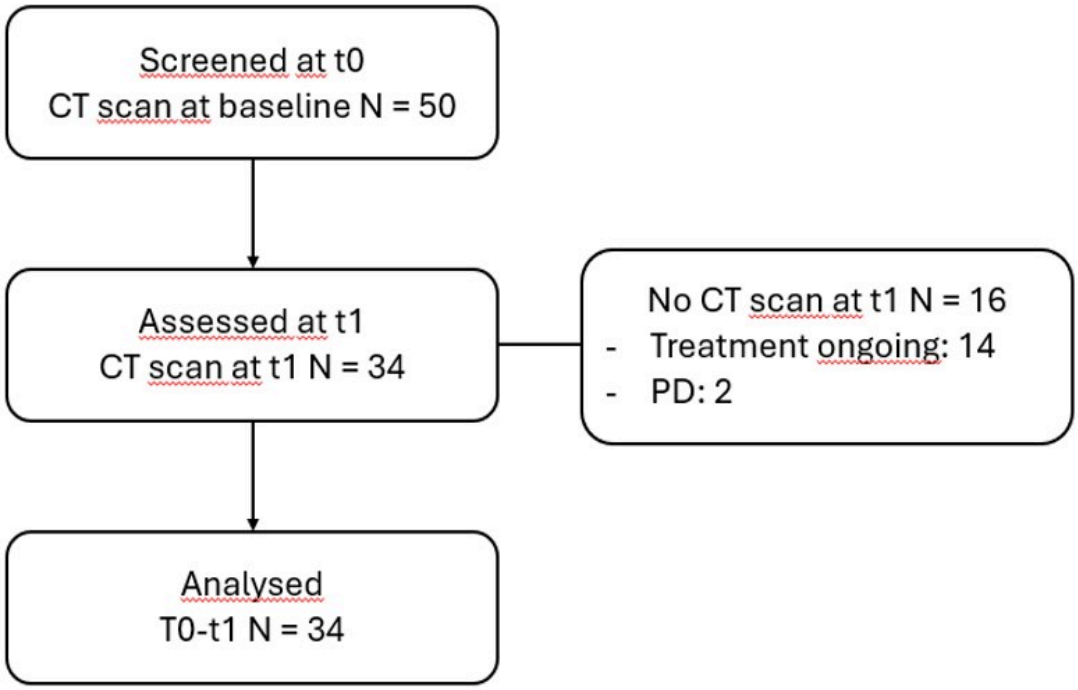
The datasets generated during and/or analysed during the current study are not publicly available due to privacy reasons, but are available from the corresponding author on reasonable request.

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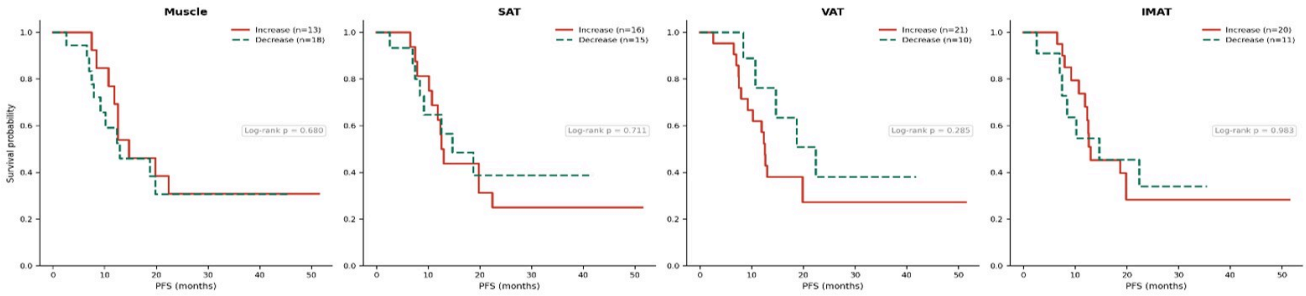
Figures



CT scan: computed tomography images, T0: baseline assessment; T1: three months after treatment start, PD: progression disease

Figure 1

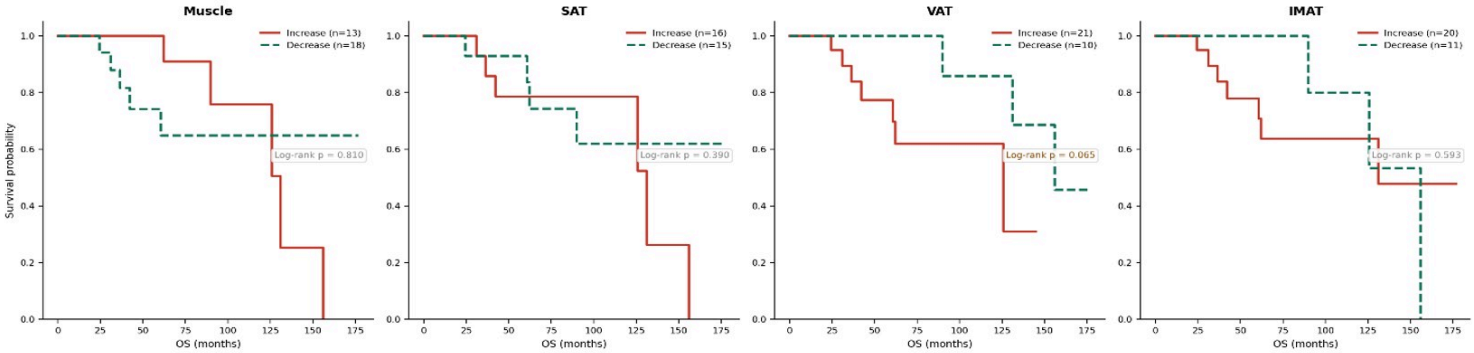
Consort diagram of the study population.).



Patients stratified by increase (≥0%) vs decrease (<0%) in surface area from T0 to T1. Log-rank p shown. Hazard ratios from univariable Cox proportional hazard models (reported in text).

Figure 2

Kaplan-Meier curves. Body composition changes and PFS.



Patients stratified by increase (≥0%) vs decrease (<0%) in surface area from T0 to T1. Log-rank p shown. Hazard ratios from univariable Cox proportional hazard models (reported in text).

Figure 3

Kaplan-Meier curves. Body composition changes and OS).