

Associations of body composition and physical activity with treatment burden during weekly paclitaxel for breast cancer: an exploratory prospective cohort study

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Abstract

Purpose

To characterise treatment burden regarding adverse events, relative dose intensity and treatment modifications and their associations with body composition, physical activity, and paclitaxel exposure in breast cancer patients.

Methods

This prospective cohort included 20 women with breast cancer receiving 12 cycles of weekly paclitaxel. Body composition was assessed by computed tomography, dual-energy X-ray absorptiometry, and bioelectrical impedance; physical activity by accelerometry. Patient-reported outcomes, medical-record adverse events, relative dose intensity, treatment modifications and paclitaxel concentrations were documented. Baseline-adjusted mixed-effects models examined body composition and physical activity markers.

Results

From baseline to final follow-up, sensory neuropathy and fatigue increased by 10.0, 95% CI [4.8, 15.1] and 19.4 points, 95% CI [9.5, 29.3], while physical functioning and global health declined by 10.4, 95% CI [2.8, 18.0] and 10.7 points, 95% CI [1.5–19.8]. No adverse event reached Common Terminology Criteria for Adverse Events grade ≥ 3 ; yet 65% of participants had a toxicity-attributed treatment modification. Higher adiposity markers across imaging modalities and body mass index were associated with worse sensory neuropathy. Per 1,000 additional steps/day, fatigue was 4.54 points lower, 95% CI [– 8.42, – 0.66], physical functioning 1.92 higher, 95% CI [0.23, 3.61], and global health 2.48 higher, 95% CI [0.33, 4.63]. No consistent associations were observed with relative dose intensity, modification count, or adverse-event burden.

Conclusion

Weekly paclitaxel was accompanied by clinically important patient-reported deterioration and frequent treatment modifications despite no CTCAE grade ≥ 3 events. Greater adiposity and lower physical activity were associated with higher patient-reported burden; the design does not support causal or clinical inference.

Trial registration

ClinicalTrials.gov NCT06387901, registered 29 April 2024.

Introduction

Paclitaxel (PTX) is a central component of systemic treatment for breast cancer [1, 2]. Its use is accompanied by cumulative adverse events such as chemotherapy-induced peripheral neuropathy (CIPN) (a condition characterized primarily by sensory neuropathy), haematological or hepatic toxicity, fatigue, and deterioration in physical functioning and health-related quality of life [3–6]. These effects may lead to dose reductions, delays, interruptions, or premature discontinuation and thereby reduced relative dose intensity (RDI), which has been associated with worse outcomes in several breast-cancer settings [7–9].

Patient-reported outcomes (PROs) complement routine toxicity assessment by quantifying symptoms, functioning, and perceived health directly from the patient's perspective [10–12]. This is particularly relevant during weekly PTX, when neuropathy and fatigue may accumulate gradually and lower-grade toxicities may prompt treatment modification [3, 5, 6]. Clinician-recorded adverse events, treatment delivery, and PROs therefore represent related but distinct dimensions of burden.

Body size is conventionally represented by body surface area for cytotoxic dosing, although this does not capture interindividual differences in lean tissue and adiposity [13–15]. Patients with similar body weight, body mass index (BMI), or body surface area can differ substantially in skeletal muscle, total and visceral adiposity, and muscle quality [16–18]. Low muscle mass and greater adiposity have been associated with chemotherapy toxicity and poorer outcomes in breast cancer, suggesting body composition [19–23], and muscle mass itself may influence systemic exposure and treatment-limiting neuropathy [20, 21, 23, 24]. Imaging- and impedance-derived phenotypes may consequently provide information beyond BMI alone [16–18].

Objectively measured physical activity provides complementary information about a patient's functioning during treatment [25–27]. Higher physical activity may reflect greater functional reserve, whereas treatment-related fatigue, neuropathy, and deconditioning may also reduce physical activity [28]. Associations between physical activity during treatment and PROs may therefore operate in both directions and should not be interpreted causally. Integrating host phenotype, physical activity, and PTX exposure may nevertheless help characterise heterogeneity in treatment burden.

The PABTOX cohort investigated interactions between PTX dosing, body composition, physical activity, and toxicity in women with breast cancer receiving 12 weekly PTX doses [29]. This exploratory analysis aimed to characterise treatment burden using repeated PROs, adverse events, toxicity attributed treatment modifications, and RDI, and to examine their associations with baseline body composition, objective physical activity during treatment, and post-infusion PTX concentration.

Methods

Study design, ethics, and participants

PABTOX was a prospective, single-centre translational observational cohort study conducted at Universitair Ziekenhuis Brussel (UZ Brussel), Belgium, from September 2024 to January 2026 (ClinicalTrials.gov NCT06387901). Women aged 18 years or older with breast cancer were eligible when scheduled to receive 12 weekly PTX doses of 80 mg/m². Concomitant targeted therapy was permitted when no clinically relevant overlapping toxicity was expected. Exclusion criteria were cognitive impairment interfering with participation, enrolment in an investigational medicinal product trial, PTX intolerance or allergy, medication expected to interact with PTX or study assessments, unresolved neuropathy from previous treatment, and diabetes with peripheral neuropathy. Full eligibility criteria and planned procedures were published previously [29]. All participants provided written informed consent. The Medical Ethics Committee of UZ Brussel approved the study (BUN 1432024000096).

The protocol target was 40 participants. Recruitment ended in January 2026 after 20 participants had been enrolled at the end of the prespecified recruitment period, in accordance with funding and stakeholder contractual timelines. No separate power calculation was performed for this analysis. Reporting followed STROBE guidelines [30], its checklist and protocol-to-analysis differences are described in Online Resource 1.

Assessment schedule and treatment delivery

Study assessments were scheduled around PTX administration on weeks 1, 6, 9, and 12 (T1–T4). RDI was calculated as delivered dose intensity divided by planned standard dose intensity and expressed as a percentage. PTX dose reductions, delays, interruptions, discontinuations, and granulocyte colony-stimulating factor administration were recorded.

Medical record derived adverse events and treatment modifications

Adverse events were retrospectively abstracted from unstructured electronic medical records and mapped to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 terms and grades [31]. Adverse event burden was the number of distinct abstracted events per participant, retained at the highest documented grade. The published protocol described dose limiting toxicities (DLTs) as clinically relevant CTCAE grade ≥ 3 toxicities [29]. Separately, a treatment modification attributed to PTX toxicity was defined as an adverse event documented as contributing to PTX dose reduction, delay, or discontinuation, irrespective of the CTCAE grade. Any versus no attributed modification was a binary sensitivity outcome.

Patient-reported outcomes

The EORTC QLQ-C30 and QLQ-CIPN20 questionnaires were completed on Day 1 and Day 7 of T1–T4, yielding eight scheduled occasions [32, 33]. Sensory neuropathy, fatigue, physical functioning, and global health status/quality of life were scored and linearly transformed to 0–100 scales following EORTC

procedures. Higher sensory neuropathy and fatigue scores indicate worse symptoms; higher physical-functioning and global health scores indicate better outcomes. T1 Day 1 was considered the baseline assessment; the seven subsequent occasions constituted patient follow-up. Adverse QLQ-C30 changes were interpreted using domain-specific group-level thresholds: fatigue increases of 5–10, > 10–20, and > 20 points indicated small, medium, and large deterioration, respectively; physical-functioning decreases of 5–10 and > 10 points indicated small and medium deterioration; and global health/QoL decreases of 5–15 and > 15 points indicated small and medium deterioration [34]. For the QLQ-CIPN20 sensory subscale, the distribution-based minimal clinically important difference range for worsening was an increase of 2.5–5.9 points [35].

Body composition and physical activity

Body composition was assessed using dual energy X-ray absorptiometry (DXA; Hologic QDR 4500, Bedford, MA, USA), bioelectrical impedance (BIA; InBody S10, Ltd., Seoul, Republic of Korea), and routinely acquired computed tomography (CT; Siemens Biograph128 and 20). DXA provided appendicular lean mass (ALM) and total fat mass, operationalised as ALM divided by BMI (ALM/BMI) and fat mass index (FMI, fat mass/height²), respectively. BIA provided phase angle, analysed as a raw bioelectrical marker. Pre-treatment CT provided L3 skeletal muscle area, total adipose tissue area, visceral adipose tissue area, and mean skeletal muscle attenuation. The corresponding areas were normalised to height squared to derive the CT L3 skeletal muscle index (CT-SMI), total adipose tissue index (CT-TATI), and visceral adipose tissue index (CT-VATI); mean muscle attenuation was expressed in Hounsfield units (HU). CT images acquired two to four weeks before PTX initiation were analysed at L3 using a GE HealthCare Volume Viewer (GE HealthCare, Chicago, IL, USA) research prototype with artificial intelligence-based segmentation. Study specific attenuation ranges were 0–100 HU for skeletal muscle and – 190 to – 30 HU for visceral adipose tissue. The rationale for the selection of body composition markers is in Online Resource 2.

Objective physical activity was measured with a hip-worn ActiGraph GT3X+ (ActiGraph LLC, Pensacola, FL, USA) and processed in ActiLife 6.11.9 using 60-s epochs. Non-wear was ≥ 60 consecutive zero-count minutes, allowing interruptions ≤ 2 min. A valid day required ≥ 10 h wear and a valid period ≥ 4 days, including ≥ 1 weekend day. Principal measures were mean steps/day and counts per minute (CPM). T1 described baseline activity; means across valid T1–T4 periods represented concurrent treatment-period activity. The EHIS-PAQ assessed self-reported activity [36].

Paclitaxel sampling and exposure estimation

Samples were scheduled within 10 min after infusion and 16–26 h later [24]. The first ten participants provided paired capillary dried blood spot (DBS) and venous plasma samples; subsequent participants provided DBS only. Actual post-infusion sampling extended to approximately 1 h. PTX was quantified using a validated UPLC–MS/MS method [37]. Sampling time-specific blood-to-plasma ratios were derived in six paired-sample participants and assessed internally in four. Time above 0.05 $\mu\text{mol/L}$

($T_c > 0.05$) was estimated from the two concentrations and recorded times assuming first-order elimination and one-compartmental kinetics. Full procedures are in Online Resource 5.

Statistical analysis

Continuous variables were summarised as mean with standard deviation when normally distributed, or as median with interquartile range; categorical variables as n/N (%). PRO trajectories across the seven follow-up occasions were analysed using linear mixed-effects models with time as a categorical variable and a participant random intercept. Time, considered as a continuous variable was examined as a sensitivity analysis.

The main explanatory analyses used separate baseline adjusted linear mixed-effects models for each PRO (IBM SPSS Statistics version 27). Each model included follow-up time, the corresponding baseline PRO score, and one body composition or physical activity marker, with a participant random intercept. Models were estimated using restricted maximum likelihood. Markers were evaluated separately; no mutually adjusted marker model, random slopes, or stepwise selection was used. Models included all available follow-up outcomes from participants with non-missing baseline outcome and model-specific marker data under their likelihood-based missing-at-random assumption. Participants missing either were excluded from that model. No explicit imputation or last-observation-carried-forward was applied. No multiplicity adjustment was used. Interpretation emphasized coefficients, 95% confidence intervals (CI), and analysis-specific sample sizes rather than isolated p-values.

Secondary analyses used Spearman rank correlations to examine post-infusion PTX concentration, body composition markers and changes, physical activity, RDI, treatment modification count, and adverse event count (R version 4.5.2). Correlations used pairwise complete observations. Any versus no treatment modification was examined descriptively using Mann–Whitney U tests (Online Resource 6).

Results

Participant flow and baseline characteristics

Of 105 women were screened, 42 were considered potentially eligible. Of 28 women approached, four were subsequently ineligible because the final regimen included PTX plus carboplatin, three were not enrolled because of anxiety or psychological distress, and one cancelled treatment. Twenty participants provided consent and comprised the cohort (Fig. 1).

Median age was 50.0 years (IQR 44.5–66.0) and median BMI was 26.0 kg/m² (IQR 21.0–33.5). Baseline accelerometry yielded a median 5111 steps/day (IQR 3080–6691; n = 16) and 261 CPM (IQR 211–374; n = 17); 10 of 19 participants reported less than 600 MET-min/week (Table 1). All participants were prescribed cryotherapy.

Table 1
Baseline clinical, body composition, and physical activity characteristics.

Characteristic	Result
Patient	
Age, years (IQR)	50.0 (44.5–66.0)
Caucasian	17/20
Middle Eastern/North African	3/20
Tumour	
Oestrogen-receptor positive	17/20
Progesterone-receptor positive	11/20
HER2-positive tumour	9/20
Paclitaxel monotherapy	11/20
Paclitaxel with trastuzumab-based therapy	9/20
Previous cyclophosphamide-containing chemotherapy	10/20
Body size	
Height, cm (IQR)	165.0 (161.8–169.0)
Body weight, kg (IQR)	72.0 (61.0–85.7)
Body surface area, m ² (IQR)	1.84 (1.70–1.93)
BMI, kg/m ² (IQR)	26.0 (21.0–33.5)
Normal body fat category	4/18
Overweight, non-obese body fat category	6/18
Obese body-fat category	8/18
Physical activity	
Actigraph® mean counts per minute, counts/min, (range)	261.4 (211.1–373.9)
Actigraph® mean steps/day, steps/day (range)	5111.2 (3080.3–6690.6)
EHIS-PAQ low activity (< 600 MET-min/week)	10/19
Note. Values are median (interquartile range) for continuous variables and n/N for categorical variables; previous cyclophosphamide-containing chemotherapy comprised cyclophosphamide with either epirubicin or methotrexate/fluorouracil; EHIS-PAQ, European Health Interview Survey–Physical Activity Questionnaire; HER2, human epidermal growth factor receptor 2; IQR, interquartile range; MET, metabolic equivalent of task.	

Characteristic	Result
Patient	
EHIS-PAQ moderate activity (≥ 600 MET-min/week)	9/19
Note. Values are median (interquartile range) for continuous variables and n/N for categorical variables; previous cyclophosphamide-containing chemotherapy comprised cyclophosphamide with either epirubicin or methotrexate/fluorouracil; EHIS-PAQ, European Health Interview Survey–Physical Activity Questionnaire; HER2, human epidermal growth factor receptor 2; IQR, interquartile range; MET, metabolic equivalent of task.	

Treatment delivery, adverse events, and toxicity burden

Median RDI was 89% (IQR 79–95); 6/20 participants had an RDI below 85%. Two participants had at least one treatment delay, and three discontinued the 12-week treatment plan early. Medical record abstraction yielded 135 adverse event terms: 125 grade 1 and 10 grade 2. No event reached CTCAE grade ≥ 3 .

Fifteen participants (75%) had at least one treatment modification. Across these participants, 22 different types of adverse events were documented, resulting in a treatment modification (median two modification events per patient, IQR 1–2). Sensory neuropathy (n = 9), neutropenia (n = 4), and increased alanine aminotransferase (n = 3) were the most frequently recorded toxicities. A decreased neutrophil count was abstracted from the medical records for four participants, whereas systematic grading of absolute neutrophil counts identified neutropenia in eight participants (grade 1, n = 4; grade 2, n = 4). Eleven participants received short-acting granulocyte colony-stimulating factor. Treatment delivery and toxicity results are summarized in Table 2; the full adverse event distribution is provided in Online Resource 3.

From T1 Day 1 to T4 Day 7, model-estimated mean sensory neuropathy and fatigue scores increased by 10.0 and 19.4 points, respectively, while physical-functioning and global health/QoL scores decreased by 10.4 and 10.7 points, respectively (Table 2). Based on the point estimates, sensory neuropathy worsening exceeded the published minimal clinically important difference range, fatigue and physical functioning showed medium deterioration, and global health/QoL showed small deterioration. Descriptive trajectories across all eight scheduled assessments are presented in Online Resource 4.

Table 2

Treatment delivery, adverse events, toxicity-related treatment modifications, and patient-reported toxicity

Domain	Result
Treatment delivery	
Administered paclitaxel dose per infusion, mg	145 (131–150)
Relative dose intensity, %	89 (79–95)
Relative dose intensity < 85%	6/20
At least one treatment delay	2/20
Did not complete all 12 cycles	3/20
Adverse events	
Total adverse events (record-derived, any grade)	135
- Grade 1	125
- Grade 2	10
- Grade ≥ 3	0
Adverse events per patient (record-derived, any grade)	3 (1–4)
Peripheral sensory neuropathy (record-derived, any grade)	17/20
Fatigue (record-derived, any grade)	17/20
Neutropenia (record-derived, any grade)	4/20
Laboratory-derived neutropenia	8/20
Short-acting G-CSF administered	11/20
Any treatment modification	15/20
Treatment modification count per participant	1 (1–2); range 0–4
Treatment modification events	33
Note. Values are median (interquartile range) or n/N, or counts. A toxicity-attributed treatment modification was an adverse event documented as contributing to PTX dose reduction, delay, interruption, or discontinuation, irrespective of grade. The 22 participant–toxicity attributions represent documented reasons for modification rather than 22 separate modification actions. Laboratory-derived neutropenia was graded independently from absolute neutrophil counts and therefore differs from the four participants for whom “neutrophil count decreased” was explicitly identified in narrative records. Patient-reported outcomes were scored from 0 to 100. Positive change indicates worsening for sensory neuropathy and fatigue; negative change indicates worsening for physical functioning and global health status/quality of life.	
Abbreviations: ALT, alanine aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; G-CSF, granulocyte colony-stimulating factor; IQR, interquartile range; T1–T4, paclitaxel assessment weeks 1, 6, 9, and 12.	

Domain	Result
Treatment delivery	
- Dose reduction	28
- Treatment discontinuation	2
- Treatment delay	3
Different types of adverse events associated with treatment modifications	22
- Peripheral sensory neuropathy	9
- Neutropenia (record and laboratory-derived)	6
- ALT increase	3
- Abdominal cramps	1
- Back pain	1
- Productive cough	1
- Myalgia	1
Patient-reported change in PTX toxicity burden, T1D1 to T4D7	
Sensory neuropathy, points	+ 10.0 (worse)
Fatigue, points	+ 19.4 (worse)
Physical functioning, points	-10.4 (worse)
Global health status/quality of life, points	-10.7 (worse)
Note. Values are median (interquartile range) or n/N, or counts. A toxicity-attributed treatment modification was an adverse event documented as contributing to PTX dose reduction, delay, interruption, or discontinuation, irrespective of grade. The 22 participant–toxicity attributions represent documented reasons for modification rather than 22 separate modification actions. Laboratory-derived neutropenia was graded independently from absolute neutrophil counts and therefore differs from the four participants for whom “neutrophil count decreased” was explicitly identified in narrative records. Patient-reported outcomes were scored from 0 to 100. Positive change indicates worsening for sensory neuropathy and fatigue; negative change indicates worsening for physical functioning and global health status/quality of life.	
Abbreviations: ALT, alanine aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; G-CSF, granulocyte colony-stimulating factor; IQR, interquartile range; T1–T4, paclitaxel assessment weeks 1, 6, 9, and 12.	

Baseline adjusted patient-reported outcomes

In separate baseline-PRO- and occasion-adjusted models, higher CT total adipose tissue index ($\beta = 0.57$ per 10 cm²/m², 95% CI [0.03, 1.10]), CT visceral adipose tissue index ($\beta = 1.30$ per 10 cm²/m², 95% CI

[0.16, 2.44]), DXA fat mass index ($\beta = 1.09$ per kg/m^2 , 95% CI [0.24, 1.93]), and BMI ($\beta = 0.78$ per kg/m^2 , 95% CI [0.24, 1.32]) were associated with higher follow-up sensory neuropathy scores (Fig. 2). All 95% CIs for body composition coefficients in the fatigue models included zero.

Higher BMI was associated with lower physical functioning during follow-up ($\beta = -1.29$ per kg/m^2 , 95% CI [- 2.47, - 0.11]. Higher DXA fat mass index ($\beta = -1.65$ per kg/m^2 , 95% CI [- 2.74, - 0.56] and BMI ($\beta = -0.98$ per kg/m^2 , 95% CI [- 1.91, - 0.05] were associated with lower follow-up global health scores.

Per 1,000 additional mean steps/day, fatigue was 4.54 points lower, 95% CI [- 8.42, - 0.66], physical functioning 1.92 higher, 95% CI [0.23–3.61], and global health 2.48 higher, 95% CI [0.33–4.63]. Global health was also higher per 100 CPM ($\beta = 6.52$, 95% CI [1.43, 11.61]. Remaining activity-model CIs included zero; analysis-specific sample sizes are in Fig. 2.

Paclitaxel samples and exposure

Overall, 138 DBS and 71 plasma samples were available; missingness and reasons are detailed in Online Resource 5. Sixty-nine paired DBS–plasma observations from ten participants informed the blood-to-plasma analysis. Mean ratios increased from 0.81 post-infusion to 1.42 approximately 24 h later ($p < 0.001$); conversion-factor agreement was assessed internally in four participants (Online Resource 5). Median observed or DBS-estimated plasma concentrations were 1.57 $\mu\text{mol}/\text{L}$ post-infusion and 0.023 $\mu\text{mol}/\text{L}$ at delayed sampling; median approximate $T_{c>0.05}$ was 18.5 h. Exposure summaries did not progressively increase across T1–T4 (Fig. 3).

Secondary unadjusted associations

Median post-infusion DBS PTX concentration was not associated with RDI, toxicity-attributed modification-action count, or adverse-event burden. Higher baseline BMI ($p = -0.541$, $n = 20$, $p = .014$) and BIA-derived visceral fat ($p = -0.462$, $n = 19$, $p = .046$) were associated with lower RDI, whereas greater preservation or increase in DXA lean mass was associated with higher RDI ($p = 0.612$, $n = 14$, $p = .020$). Mean steps/day and CPM were not associated with RDI. No binary comparison of any versus no toxicity-attributed modification yielded a nominal $p < .05$. Complete estimates and pairwise sample sizes are in Online Resource 6.

Discussion

In this prospective cohort, weekly paclitaxel was accompanied by clinically important worsening of sensory neuropathy, fatigue, physical functioning, and global health. Thirteen out of 20 patients underwent a toxicity-related treatment modification despite no documented CTCAE grade ≥ 3 event. Thus, lower-grade symptoms altered treatment delivery and substantially affect patients. Greater adiposity was associated with greater sensory neuropathy; higher BMI with poorer physical functioning

and global health, and higher FMI with poorer global health. Higher physical activity was associated with less fatigue and better functioning and global health. No associations emerged with treatment modification or adverse event counts; post-infusion concentration was unrelated to toxicity measures or RDI.

Treatment was often modified while the corresponding clinician-reported toxicities remained grade 1 or 2. These adaptations may have reduced subsequent doses, and thus exposure, and may have prevented progression to higher-grade toxicity, thereby restricting variation in both severe toxicity and exposure dependent outcomes. Consequently, the absence of associations of PTX exposure or host factors with treatment delivery and toxicity should not be interpreted as evidence that these factors are unrelated to biological toxicity. Because the timing and clinical thresholds for modification were neither standardised nor formally modelled, early or proactive treatment adaptation remains a plausible explanation rather than a demonstrated mechanism.

Adiposity was the most consistent body composition correlate of poorer outcomes. Higher CT total and visceral adipose tissue indices, DXA FMI, and BMI were associated with worse follow-up sensory neuropathy; higher FMI and BMI also related to poorer global health status/quality of life. Higher baseline BMI and BIA-derived visceral fat correlated with lower RDI. Concordance across modalities makes a single-instrument artefact less likely. This aligns with studies linking higher overall or visceral adiposity to chemotherapy toxicity and an increased risk of treatment modifications [17–20, 22, 23]. Potential mechanisms include altered distribution, metabolic and inflammatory vulnerability, and reduced physiological reserve [18], none directly tested here. Muscle markers were less informative, contrasting with studies associating low muscle mass with taxane toxicity or PTX exposure [20, 21, 23, 24]. Limited between-participant variation and smaller analysis-specific samples owing to missing muscle measurements, together with imaging's inability to capture strength or cardiorespiratory reserve, may partly explain this.

Higher step count per day was associated with lower fatigue, better physical functioning, and global health. Likewise, higher step counts per minute were associated with better global health. This aligns with literature relating physical activity to higher physical functioning and quality of life during cancer treatment [25–27]. However, physical activity and PROs were measured concurrently, therefore, directionality cannot be established and toxicity may have reduced physical activity. These physical activity measures should therefore be interpreted as functional indicators in this cohort, although intervention studies suggest physical activity and exercise may prevent toxicity and improve PROs during chemotherapy [38].

Median post-infusion PTX concentration was not associated with RDI, treatment modification count, or adverse event burden. Similarly, no relationship between post-infusion PTX concentration and occurrence of sensory neuropathy was identified, consistent with findings reported by Hertz et al. [23, 24]. Although the median estimated $T_c > 0.05$ of 18.5 h exceeded the 14.06 h threshold associated with CIPN-related treatment disruption in the Hertz study, this comparison should be interpreted cautiously.

Hertz et al. evaluated neuropathy-induced treatment disruption longitudinally, whereas the present study assessed broader toxicity-related treatment modifications and did not capture recurrent events during 12 weekly PTX treatment. Furthermore, the limited number of neuropathy-related treatment disruptions, proactive dose adaptations, and the small sample size may have reduced the ability to detect exposure-toxicity relationships. Consequently, observing an exposure-neuropathy signal comparable to that reported by Hertz et al. was considered less likely in this cohort. Sampling up to approximately 1 h after infusion did not provide a standardised peak concentration, and $T_{c>0.05}$ was reconstructed from only two concentrations under an apparent first-order approximation. The mean blood-to-plasma ratio differed between post-infusion and delayed sampling (0.81 versus 1.42), which was accounted for by time-specific conversion factors. The lower blood-to-plasma ratio post-infusion might be explained by the use of cryotherapy reducing finger perfusion during sampling.

Strengths include prospective repeated PRO assessment, objective accelerometry, body composition characterization using CT, DXA, and BIA, and integration of adverse event burden with treatment delivery, alongside PTX sampling. Adjustment for the corresponding baseline PRO reduced the risk that follow-up associations merely reflected pre-existing symptom or functional differences.

Limitations include the small single-centre sample, limiting precision. Mixed-effects models adjusted for time and the corresponding baseline outcome, but not age, clinical status, concomitant therapy, or supportive care. Multiple marker–outcome models and secondary correlations were examined without multiplicity correction; nominal findings may therefore reflect chance. This exploratory strategy was retained because the sample was too small for stable mutually adjusted models and the markers represented alternative measures of host phenotype. Markers were entered separately in baseline outcome-adjusted models without data-driven selection, and complete estimates and 95% confidence intervals were reported. Interpretation emphasised consistency across measurement methods rather than isolated p-values; the findings nevertheless require validation. Physical activity during treatment could not establish temporal direction.

Larger studies should prospectively standardize CTCAE grading and record the timing, type, clinical threshold, and reason for each treatment modification. Repeated PROs should be retained alongside clinical and laboratory toxicity measures. Population PK-PD modelling is needed to determine whether body composition and physical activity add predictive information beyond baseline symptoms and clinical treatment decisions.

Conclusion

In this small prospective cohort, weekly paclitaxel was accompanied by clinically important deterioration in sensory neuropathy, fatigue, physical functioning, and global health, while 13/20 participants had toxicity-attributed treatment modification despite no CTCAE grade ≥ 3 event. Greater adiposity and lower physical activity were associated with higher patient-reported burden. These exploratory associations highlight potentially clinically relevant relationships and provide a basis for further investigation,

although they should not be interpreted as causal or used for risk stratification or dose individualisation without external validation.

Declarations

Author contributions CRediT

Conceptualization: Len De Nys, Stephanie Wuyts, Pieter-Jan De Sutter, Nele Adriaenssens; Methodology: Len De Nys, Stephanie Wuyts, Pieter-Jan De Sutter, Minhua Xu, Gil Awada, David Beckwée, Nele Adriaenssens; Formal analysis: Len De Nys, Stephanie Wuyts, Pieter-Jan De Sutter, Minhua Xu; Investigation: Len De Nys, Stephanie Wuyts, Nele Adriaenssens, Sofie Vande Castele; Writing - original draft preparation: Len De Nys, Stephanie Wuyts, Minhua Xu; Writing - review and editing: Len De Nys, Stephanie Wuyts, Gil Awada, Pieter-Jan De Sutter, Stephane Steurbaut, Nele Adriaenssens, Minhua Xu, Sofie Vande Castele, Steven Provyn; Funding acquisition: Nele Adriaenssens, Stephanie Wuyts, Steven Provyn, David Beckwée, Stephane Steurbaut; Supervision: Steven Provyn, David Beckwée, Stephanie Wuyts, Nele Adriaenssens

Ethics approval

The study was approved by the Medical Ethics Committee of Universitair Ziekenhuis Brussel, Belgium (BUN 1432024000096), and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study. The authors affirm that human research participants provided informed consent for publication of the data used in this manuscript.

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Author Contribution

Conceptualization: LDN, SW, PJDS, NA; Methodology: LDN, SW, PJDS, MX, GA, DB, NA; Formal analysis: LDN, SW, PJDS, MX; Investigation: LDN, SW, NA, SVC; Writing – original draft preparation: LDN, SW, MX; Writing – review and editing: LDN, SW, GA, PJDS, SS, NA, MX, SVC, SP; Funding acquisition: NA, SW, SP, DB, SS; Supervision: SP, DB, SW, NA. Shared last-authorship: SW, NA; All authors reviewed the manuscript.

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Data Availability

The PABTOX data that support the findings of this study are available upon request (Len.de.nys@vub.be).

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Figures

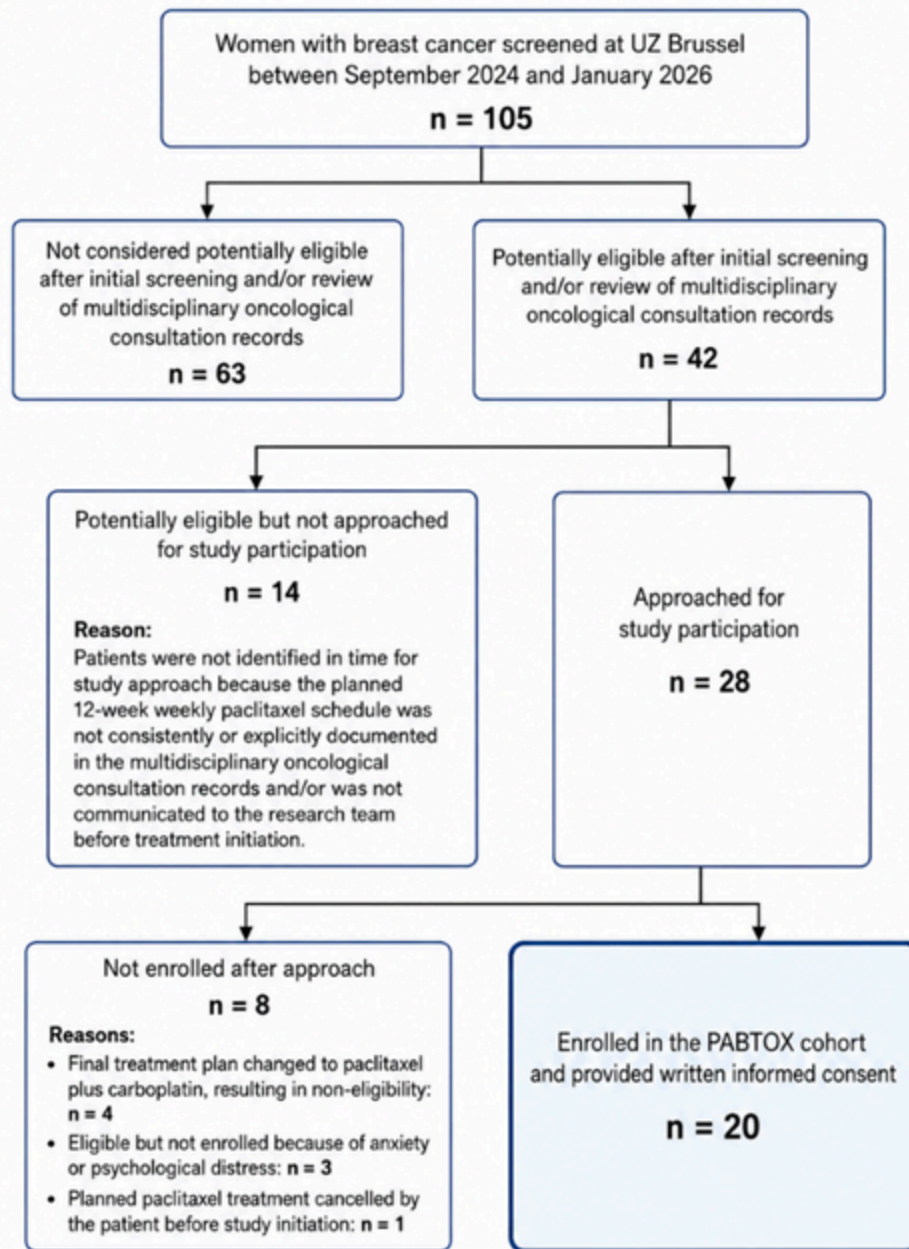


Figure 1

Participant flow in the PABTOX cohort.

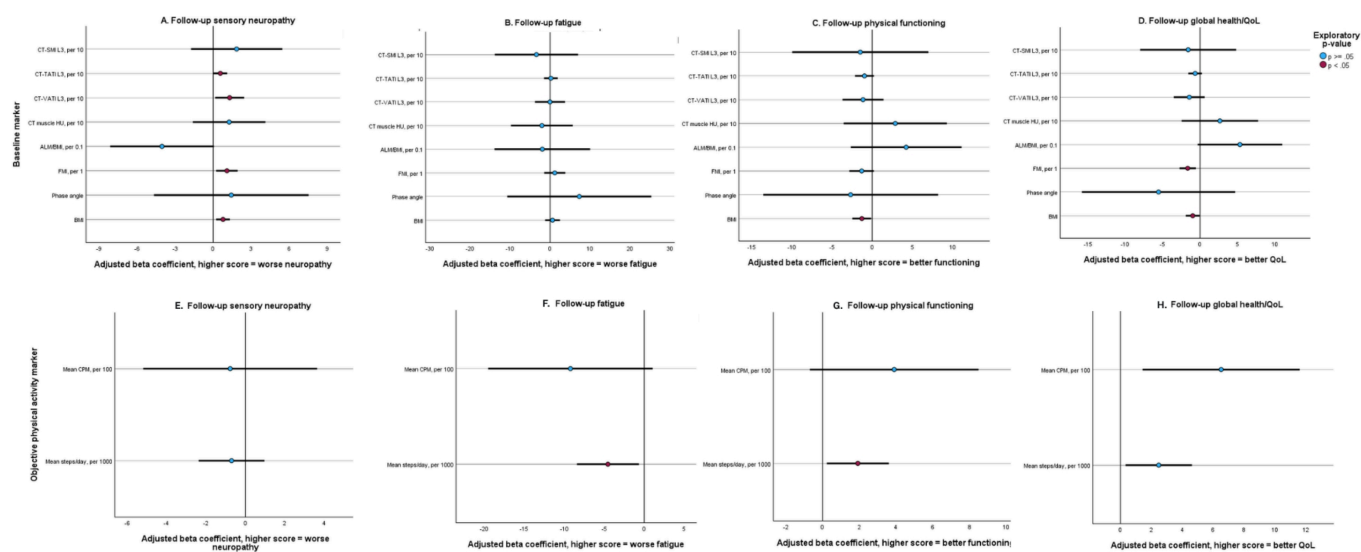


Figure 2

Associations of body-composition markers with patient-reported outcomes. Forest plots show β coefficients and 95% confidence intervals from separate linear mixed-effects models containing categorical follow-up occasion, the outcome-specific T1D1 baseline score, one predictor, and a participant-specific random intercept. Coefficients are expressed in EORTC 0–100 points per predictor unit indicated in the row label. Positive coefficients indicate worse chemotherapy-induced peripheral neuropathy or fatigue but better physical functioning or global health status/quality of life; negative coefficients indicate the opposite. The vertical line represents no association. All p-values are two-sided nominal exploratory values. ALM/BMI, appendicular lean mass divided by body mass index; BMI, body mass index; CPM, counts per minute; CT, computed tomography; FMI, fat mass index; HU, Hounsfield units; L3, third lumbar vertebral level; QoL, quality of life; SMI, skeletal muscle index; TATI, total adipose tissue index; VATI, visceral adipose tissue index.

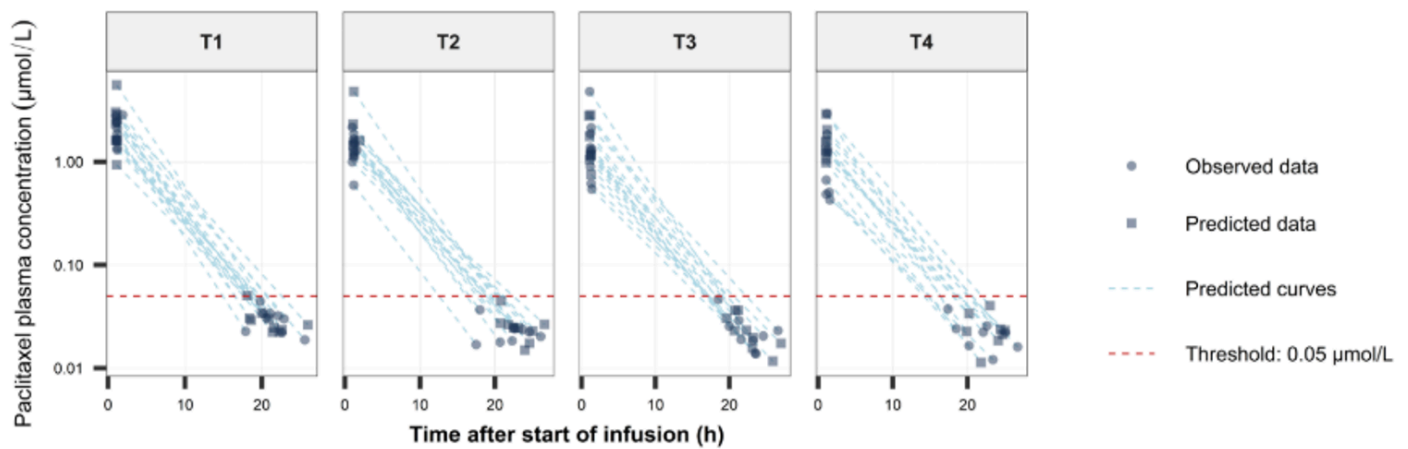


Figure 3

Individual paclitaxel (PTX) plasma concentration–time profiles stratified by treatment cycle. Individual PTX plasma concentration–time profiles by treatment occasion. T1–T4 correspond to treatment weeks 1, 6, 9, and 12. Circles represent measured plasma concentrations and squares plasma concentrations predicted from DBS using sampling time specific blood-to-plasma ratios. Dashed lines represent individual first-order elimination curves reconstructed from the immediate and delayed concentrations. The horizontal line indicates 0.05 $\mu\text{mol/L}$; the concentration axis is logarithmic.

Supplementary Files

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