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Sarah Lobet, David Ternant, Côme Lepage, Karine Le Malicot, Nicolas Azzopardi, et al.. Analysis of the relationship between body composition and the pharmacokinetics of panitumumab in the treatment of localized squamous cell carcinoma of the anus – An ancillary study of the FFCD0904 phase I and II trial. *Biomedicine and Pharmacotherapy*, 2026, 198, pp.119242. <10.1016/j.biopha.2026.119242>. <hal-05586260>

HAL Id: hal-05586260

<https://hal.science/hal-05586260v1>

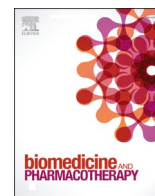
Submitted on 5 May 2026

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Analysis of the relationship between body composition and the pharmacokinetics of panitumumab in the treatment of localized squamous cell carcinoma of the anus – An ancillary study of the FFCD0904 phase I and II trial

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ARTICLE INFO

Keywords:

Panitumumab
Anal squamous cell carcinoma
Pharmacokinetics
Body composition

ABSTRACT

Background and aims: Cancer-related cachexia alters body composition (BC) and organ function, potentially affecting drug pharmacokinetics (PK). This ancillary study of the FFCD0904 phase I/II trial, which evaluated panitumumab-based radiochemotherapy in localized squamous cell carcinoma (SCC) of the anus, explored association between panitumumab PK, BC and its effects.

Methods: Panitumumab PK parameters were estimated using a population PK approach. Pre-treatment CT scans at L3 were used to assess BC. Skin toxicity and efficacy data (tumor response, survival) were analyzed in relation to BC and PK parameters.

Results: Among 54 patients, 35 had panitumumab PK measurements, 42 had baseline CT scans, and 36 had skin toxicity data. In 25 patients with complete BC and PK data, AUC₀₋₁₄ and clearance (CL) tended to be positively correlated with body weight (BW, $p = 0.0025$ and 0.031), fat mass (FM, $p = 0.027$ and 0.033), and fat-free mass (FFM, $p = 0.059$ and 0.049). Non-sarcopenic patients tended to show higher AUC₀₋₁₄ than sarcopenic patients ($p = 0.0016$). Lower albumin appeared to be associated with reduced clearance ($p = 0.015$). Despite these PK associations, neither BC nor panitumumab exposure seems correlated with tumor response, survival, or early skin toxicity.

Conclusion: This exploratory analysis suggests that BW and BC may influence panitumumab PK, with patients who had lower BW, FM and FFM might have reduced exposure and clearance. Interpretation should be cautious due to the small sample size, confounding effect between BC and BW and potential disease-related effects. Larger

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<https://doi.org/10.1016/j.bioph.2026.119242>

Received 4 December 2025; Received in revised form 4 March 2026; Accepted 16 March 2026

Available online 21 March 2026

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studies with longitudinal BC and PK assessments are needed to clarify these relationships and guide dosing strategies.

1. Introduction

Panitumumab is a therapeutic monoclonal antibody (mAb) directed against EGFR that is approved for the treatment of metastatic colorectal cancer. EGFR is overexpressed in the squamous cell carcinomas of the anal canal [1]. Based on this observation, combinations of standard radiochemotherapy and anti-EGFR agents, such as panitumumab or cetuximab, have been theorized to be clinically helpful in locally advanced SCCA. Treatment protocols incorporating these drugs have been tried in a few trials and were associated with unexpected toxicity as well as disappointing efficacy results [2–8].

There has been substantial effort to identify predictors of therapeutic monoclonal antibody effects that could inform personalized treatment. Perhaps the good predictors of panitumumab effects are systemic panitumumab concentrations, or pharmacokinetic (PK) parameters. In oncology, the relationship between mAb concentrations and response is complex and involves several factors, such as baseline disease condition, cancer-related cachexia and tumour burden in addition to target levels [9]. Not accounting for these factors may lead to defaults of evaluation of correlations between concentrations and response [10,11].

The evaluation of body composition (BC) can routinely be achieved using simple radiological biometric parameters [12]. A high variability in the distribution of the two primary tissues of the human body—muscle mass and adipose tissue—has been reported, even among patients with similar body weights [13]. Changes in BC may influence the pharmacokinetics (PK) of chemotherapy agents, potentially affecting both their efficacy and toxicity [14]. While studies have explored the relationship between BC and the PK of certain “cytotoxics” chemotherapy agents, little is known about a possible influence of BC parameters on PK and outcomes of mAbs. This gap in knowledge is particularly problematic given the growing importance of mAbs in oncology. However sarcopenia is known to be associated with worse overall survival in patients with anal cancer [15–17].

The primary aim of this ancillary study of the FFC0904 trial was to investigate the relationship between BC and PK parameters of panitumumab in anal SCC. We hypothesized that differences in panitumumab sera concentrations, could be explained why BC variability in patients and more prone to explain effect variability. As a secondary objective, the relationship between the PK of panitumumab and its clinical outcomes, including skin toxicity and therapeutic efficacy, were studied.

2. Material and methods

2.1. Study design

The present work is an ancillary study of the prospective multicenter FFC0904 phase I and II trials (NCT: 01581840) conducted between June 2012 and June 2025 for phase I, and between January 2016 and November 2017 for phase II. The objective of this trial was to evaluate efficacy as well as tolerance of a chemotherapy regimen based on 5FU, MMC and panitumumab in association with RT for locally advanced SCCA. All patients signed informed consent before the beginning of the study. The phase I study assessed the optimal chemotherapy doses of 5FU, MMC, and panitumumab in association with radiotherapy based on the determination of their maximum tolerated doses (MTD), decreasing the continuous intravenous infusion of 5FU to 400 mg/m² per day over 4 days on weeks 1 and 5 and panitumumab to 3 mg/kg every two weeks while keeping the MMC dose at 10 mg/m² on week 1 and 5 [18]. In the phase II, all patients received a combination of 5FU, MMC, and panitumumab according to the phase I MTD assessment [8].

The outcomes used included tumor response rates at 6, 8 and 16 weeks after the end of treatment on clinical and MRI examinations, recurrence-free survival (RFS) defined as any progression observed on clinical or radiological (MRI, PET-CT, echoendoscopy) evaluations, colostomy-free survival (CFS) defined as the time between the date of inclusion and the date of colostomy or death (from any cause) in the absence of colostomy (alive patients without a colostomy were censored at date of last news), overall survival (OS) and toxicity graded according to the National Cancer Institute Common Adverse Events Criteria v4.0.

2.2. Image analysis

Computerized tomography (CT) images as specified in the study protocol, at baseline, were used to determine BC [12,19]. One axial image of the third lumbar vertebra (L3) was selected for analysis of total skeletal muscle and fat cross-sectional areas. CT image parameters included: without contrast, 1–5 mm slice thickness, 70–120 kVp, and ~100–600 mA. Tissues were identified anatomically and quantified within pre-specified Hounsfield unit (HU) ranges: skeletal muscle (-29 to +150 HU), subcutaneous adipose tissue (-190 to -30 HU), intermuscular adipose tissue (-190 to -30 HU), and visceral adipose tissue (-150 to -50 HU). Total fat cross-sectional area was computed. All images were analysed by a single trained observer with Slice-O-Matic software (v.5.0; Tomovision, Magog, Canada). Total muscle and fat cross-sectional areas (cm²) were computed. Muscle and adipose tissue areas were converted into fat mass (FM) and fat-free mass (FFM) [12].

2.3. Pharmacokinetic analysis

Blood samples were collected to characterize the PK of panitumumab (PANI). In phase I, samples were collected at specific time points: before each panitumumab infusion at weeks 3, 5, 8, and 10; 2 h post-infusion at weeks 1, 3, and 8; 24 h post-infusion at week 1; 7 days after the second infusion at week 4; and after 5-FU administration at weeks 1 and 8, resulting in a total of 11 samples per patient. In phase II, a single sample was collected prior to the third infusion of panitumumab (week 5). Panitumumab serum concentrations were measured by using a validated enzyme-linked immunosorbent assay (ELISA) technique [20]. The limit of detection (LOD) and lower limit of quantification (LLOQ) were 0.033 mg/L and 0.112 mg/L, respectively. Panitumumab serum concentrations measured below the LLOQ were left-censored.

Serum concentrations of panitumumab were analyzed using a population PK approach. The population PK analysis was conducted using Monolix 2024R1, Simulations Plus, doi: 10.5281/zenodo.11401936. The PK of panitumumab has previously been studied using the same approach in metastatic colorectal cancer by Ma *et al.* in 2009 [21]. In this publication, the PK of panitumumab was characterized by a two-compartment model with mixed elimination from the central compartment: clearance (CL), which represents concentration-proportional elimination, and Michaelis-Menten (MM) elimination, indicating a non-linear elimination process. The MM elimination was described using V_{max}, the maximum elimination rate, and the Michaelis constant K_M, the concentration at which the elimination rate is V_{max}/2 (see Fig. 1).

The PopPK model was developed using the full PK dataset (n = 35). Initial parameter values were taken from the population estimates reported by Ma *et al.*, derived from 1200 patients [21]. The Michaelis-Menten constant (K_M) was fixed to the LLOQ (0.1 mg/L) because limited low-concentration data and differences in the bioanalytical method compared with Ma *et al.* made K_M poorly identifiable. Fixing K_M improved model stability and enabled robust estimation of the

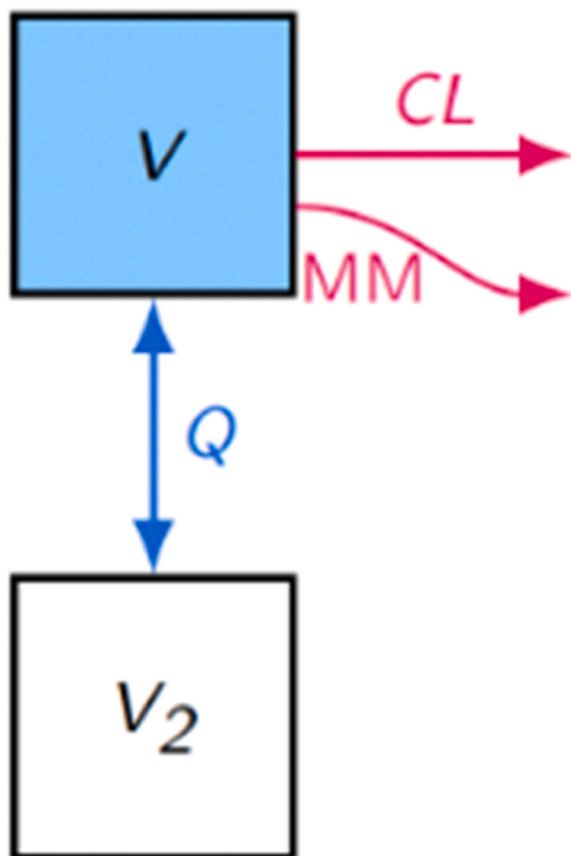


Fig. 1. Representation of the 2-compartment model with mixed elimination. V and V_2 represent the volumes of the central and peripheral compartments, respectively. CL and Q refers to the elimination and distribution clearances of panitumumab from the central compartment, respectively; MM refers to the Michaelis-Menten elimination, characterized by V_{max} , the maximum elimination rate; the Michaelis constant K_M , which is the concentration at which the elimination rate is half of V_{max} .

remaining parameters.

In the initial model (Supplementary Table S1), η -shrinkage exceeded 30% for several IIV terms (V_1 : 64.1%, V_2 : 59.6%, V_m : 58.3%, CL : 50.8%), indicating that individual parameter estimates were largely influenced by population priors rather than individual data, likely due to sparse sampling. To improve model stability and ensure interpretability of empirical Bayes estimates, we applied a predefined criterion whereby IIV terms with shrinkage > 30% were removed sequentially from the highest to the lowest value. Following this procedure, IIV was retained only for clearance (CL), with shrinkage reduced to 20% in the final model. Importantly, removal of high-shrinkage IIV terms did not materially affect fixed-effect estimates, which remained within the confidence intervals of the initial model.

BLQ panitumumab concentrations were treated as left-censored in Monolix, using a likelihood-based approach (M4 method) where each BLQ sample contributes to the likelihood as the probability that the true concentration lies between 0 and the LLOQ.

A formal covariate analysis of structural PK parameters was initially considered. However, due to a high number of missing covariate data, only 25 of the 35 patients with PK measurements had baseline CT scans available for body composition (BC) assessment, restricting the analysis to this subset made it impossible to reliably estimate PopPK parameters. Consequently, the PopPK model was developed using the full dataset of 35 patients, and individual PK parameters were derived from this model to calculate panitumumab exposure, i.e., the area under the concentration-time curve from 0 to 14 days (AUC_{0-14}), corresponding to

Table 1
Patient characteristics.

Characteristics (N = 54)	Median (IQR) ou n (%)
Age (years)	60 [57–68]
Body weight (kg)	62 [55–74]
Height (m)	1.64 [1.60–1.68]
Body mass index (kg/m ²)	24.2 (19.5–27.5)
Tumor size (cm)	40 [34–56]
Albuminemia (g/L)	42 [39–44]
SCC antigen (μ g/L)	2.0 [1.2–4.7]
Sex	Female: 43 (80%) Male: 11 (20%)
WHO status	0: 37 (69%) 1: 17 (31%)
T	T1/T2: 21 (39%) T3/T4: 33 (61%)
N	N1/N2: 25 (46%) N3/N4: 29 (54%)
Body composition parameters (N = 42)	Median (IQR)
Fat Mass (kg)	21 [16–26]
Fat Free Mass (kg)	41 [37–45]
Skeletal muscle index (cm ² /m ²)	42 [38–52]
Sarcopenia	Yes: 20 (48%) No: 22 (52%)
3-year survival (N = 54)	Median [IC 95%]
Recurrence-free survival	65% [53–79]
Colostomy-free survival	70% [59–84]
Overall survival	80% [69–91]
Tumor response at 4 months (N = 54)	n (%)
Complete response	31 (57%)
Partial response	11 (20%)
Stable disease	2 (4%)
Progression	7 (13%)
Not available	3 (6%)
Grade 1/2/3 skin toxicity (N = 36)	n (%)
Acneiform rash	25 (69%)
Desquamation	11 (31%)

the interval between the first and second panitumumab infusions, and the individually predicted clearance (CL). Associations between these individual PK parameters and BC variables were then explored descriptively in the 25 patients with available CT scans and should be considered strictly exploratory, independent of the structural PopPK model.

2.4. Statistical analysis

The potential relationships individual panitumumab pharmacokinetics—assessed by AUC_{0-14} and predicted clearance (CL) with BC, efficacy and skin tolerance, were evaluated using statistical analysis. BC was evaluated using body weight, FFM and FM. Sarcopenia was also considered, defined based on validated cut-off points for skeletal muscle index (SMI): $SMI < 43$ or $53 \text{ cm}^2/\text{m}^2$ for men with BMI below or above $25 \text{ kg}/\text{m}^2$, respectively, and $SMI < 41 \text{ cm}^2/\text{m}^2$ for all women. Patients with an SMI below these cut-points were classified as sarcopenic [22]. Additionally, albuminemia was considered, with a cut-off of $30 \text{ g}/\text{dL}$ for hypoalbuminemia.

Efficacy was assessed based on tumor response at 4 months post-treatment, and on survival at 3 years including, RFS, CFS, and OS. Skin tolerance was evaluated based on toxicity, graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events v4.0. Statistical analyses were conducted to evaluate the associations between these parameters, utilizing correlation analysis (Pearson test for continuous variables, Wilcoxon test for categorical variables) and Cox proportional hazards modeling for survival data. All analyses were performed using R software (version 4.3.3; R Core Team, 2024) [23].

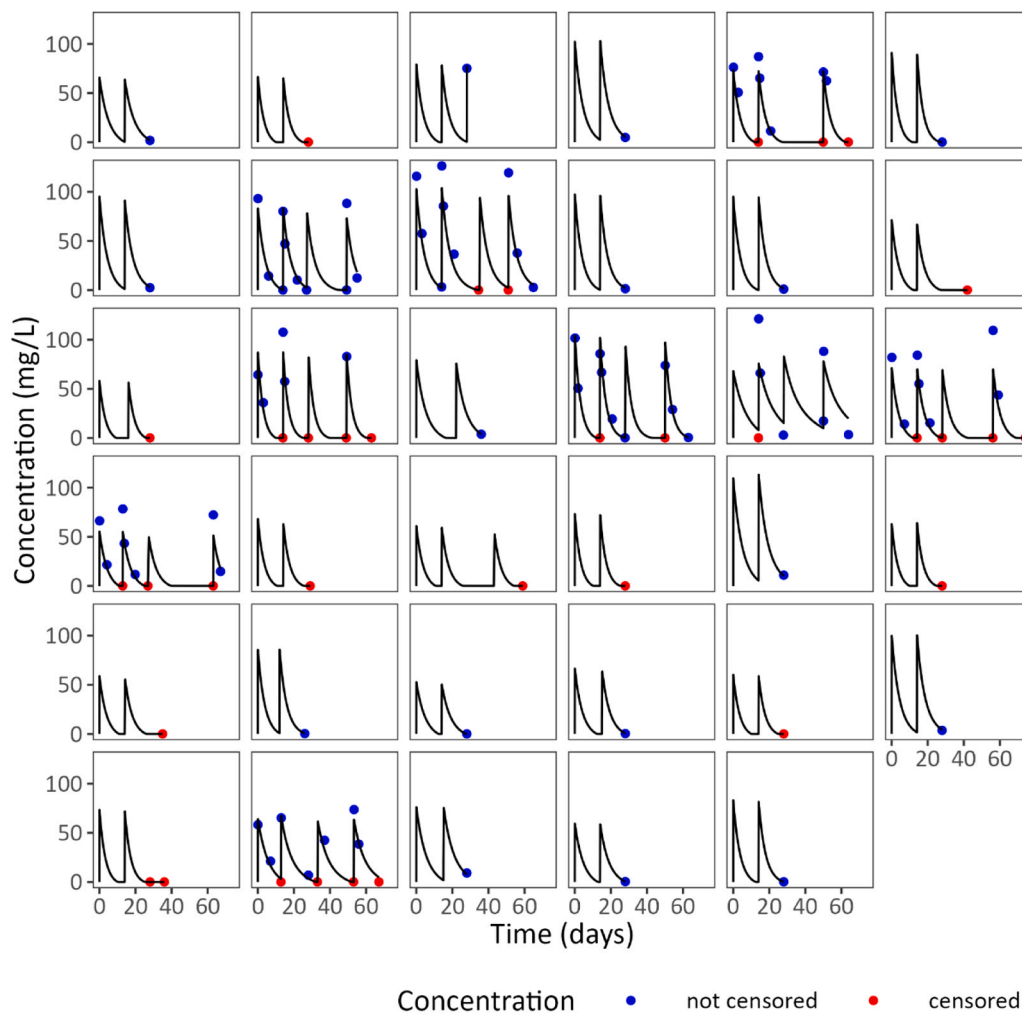


Fig. 2. Individual panitumumab concentration versus time data. Observed individual concentrations (blue) and concentrations below the LLOQ (red, 0.112 mg/L). Simulated individual pharmacokinetic profiles from the model (black lines).

3. Results

3.1. Patient characteristics

In Phase I, ten patients were enrolled, with one excluded for not meeting dose constraints. In Phase II, 45 patients were enrolled, resulting in a total of 54 patients included in the study. Of these 54 patients, 35 had panitumumab measurements available (9 from phase I and 26 from phase II), and baseline CT scans were available for 42 patients. Skin tolerance data were available for 36 patients. Efficacy data were available for all 54 patients. Patient characteristics are summarized in Table 1. A flow chart detailing patient enrollment, exclusions, and data availability is provided in the Supplementary Data.

3.2. Pharmacokinetic analysis

A total of 117 blood samples were collected across both Phase I and Phase II in 35 patients. In Phase I, 90 blood serum concentrations were available from 9 patients, resulting in an average of 10 samples per patient. Of these, 67 and 23 concentration measurements were above and below the LLOQ of 0.112 mg/L, respectively. In Phase II, 27 concentration measurements were available from 26 patients, resulting in an average of 1 sample per patient, with one patient providing two samples. Of these, 16 and 11 concentration measurements were above or below the LLOQ, respectively. Both concentrations above the LLOQ (not censored) and below the LLOQ (censored) were included in the PK

Table 2

PK population parameters obtained using Bayesian estimation based on the estimates from Ma et al. (2009).

Parameters	Our PK model		Ma et al., 2009	
	Estimates	RSE (%)	Estimates	RSE (%)
V_1 (L)	2.51	6.73	3.66	NA
CL (L.day ⁻¹)	0.40	8.67	0.269	NA
Q (L.day ⁻¹)	0.17	23.4	0.389	NA
V_2 (L)	2.91	17.8	2.58	NA
V_{max} (mg.day ⁻¹)	4.26	14.7	10.6	NA
k_M (mg/L)	0.112	fixed	0.401	NA
Interindividual variability parameters				
ω_{Vc}	-	-	0.390	NA
ω_{CL}	0.38	16.5 (shr=20.7%)	0.422	NA
ω_{Vp}	-	-	0.434	NA
ω_{Vmax}	-	-	0.341	NA
ω_{kM}	-	-	0.726	NA
Error model parameters				
σ_{prop}	0.44	9.17	0.428	
σ_{add} (ng/mL)	-	-	22.3	

analysis.

Panitumumab concentrations versus time data were satisfactorily described by the two-compartment model with mixed elimination (Fig. 2, Mlxtran code in supplementary materials) and by diagnostic plot (Figure S1). PK population parameters obtained were similar to the

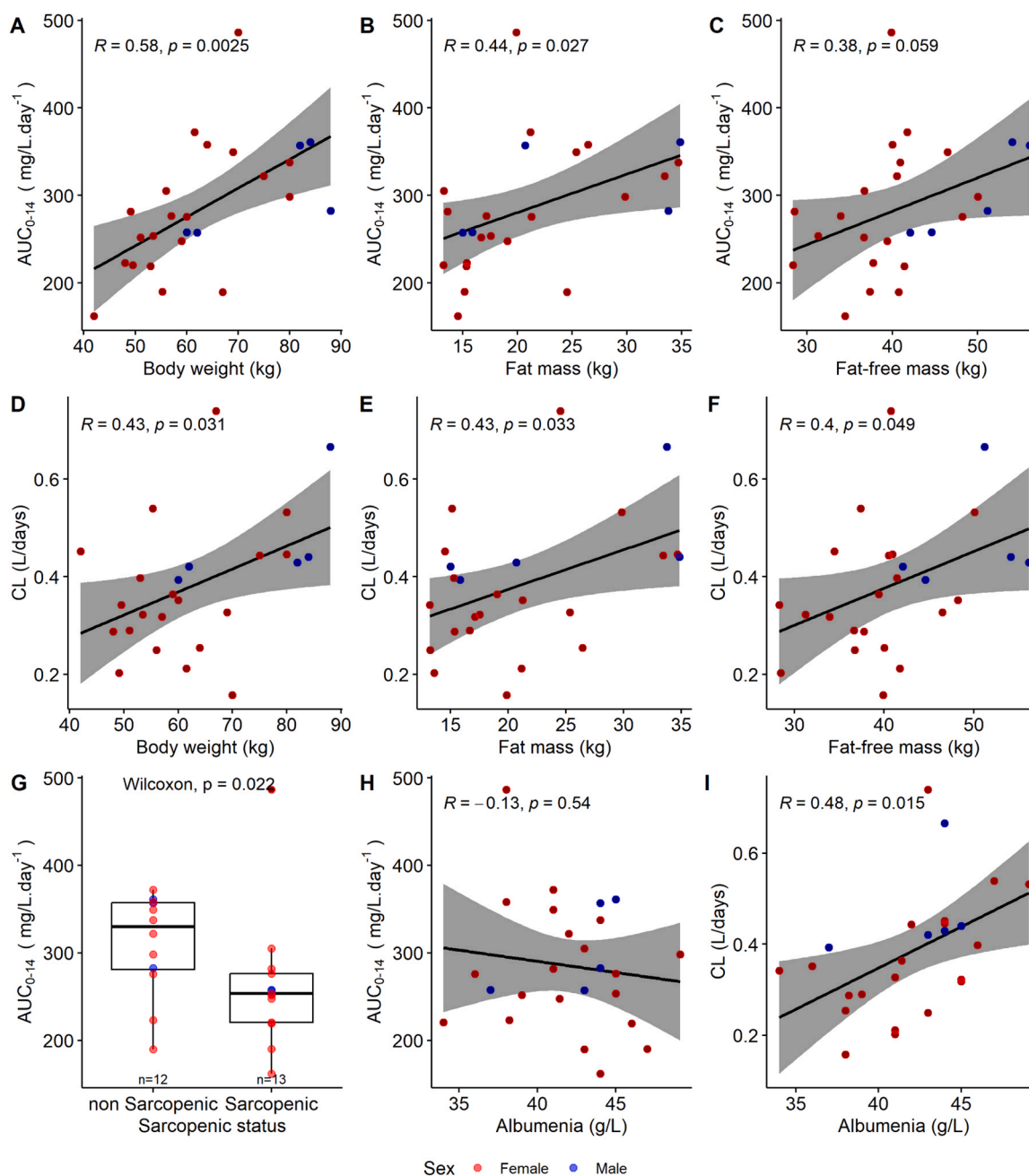


Fig. 3. Impact of Body Composition parameters on PK of Panitumumab ($n = 25$), Correlations between individual AUC_{0-14} and (A) Body weight, (B) Fat Mass, (C) Fat-Free Mass, (H) Albuminemia, and (G) Sarcopenic Status. Correlations between individual CL and (D) Body weight, (E) Fat Mass, (F) Fat-Free Mass, (I) Albuminemia. Pearson's correlation coefficient (R) and p -value (p) were used to assess relationships between continuous variables, testing the null hypothesis of no correlation. For categorical variables, a Wilcoxon test was conducted.

population estimates reported by Ma *et al.*, (Table 2) [21]. The median (5%-95%) derived AUC_{0-14} was 276 (161–486) $\text{mg/L}\cdot\text{day}^{-1}$.

3.3. Primary outcome (body composition influence on PK)

Among the 25 patients with available baseline CT scans, AUC_{0-14} appeared to be positively correlated with BW ($p = 0.0025$, Pearson test), FM ($p = 0.027$, Pearson test) and FFM ($p = 0.059$, Pearson test), with patients who had lower BW, FM and FFM suggesting reduced exposure (Fig. 3A–3C). Similarly, CL seems to be positively correlated with BW ($p = 0.031$, Pearson test), FM ($p = 0.033$, Pearson test), and FFM ($p = 0.049$, Pearson test), with patients who had lower BW, FM and FFM might have reduced clearance (Fig. 3D–3F). Of these patients, 13 were

classified as sarcopenic, while 12 were classified as non-sarcopenic. Non-sarcopenic patients tended to show higher AUC_{0-14} compared to sarcopenic patients ($p = 0.022$, Wilcoxon test) (Fig. 3D). Albumin levels were not clearly associated with exposure ($p = 0.54$, Pearson test, Fig. 3C), but lower albumin appeared to be associated with reduced clearance ($p = 0.015$, Fig. 3I).

3.4. Secondary outcomes (Survival analysis, response rate, panitumumab safety profile)

Tumor response and survival data were available for 54 patients (Table 1). However, the analysis was limited by the availability of PK data for only 35 patients and BC parameters for 42 patients. Neither the

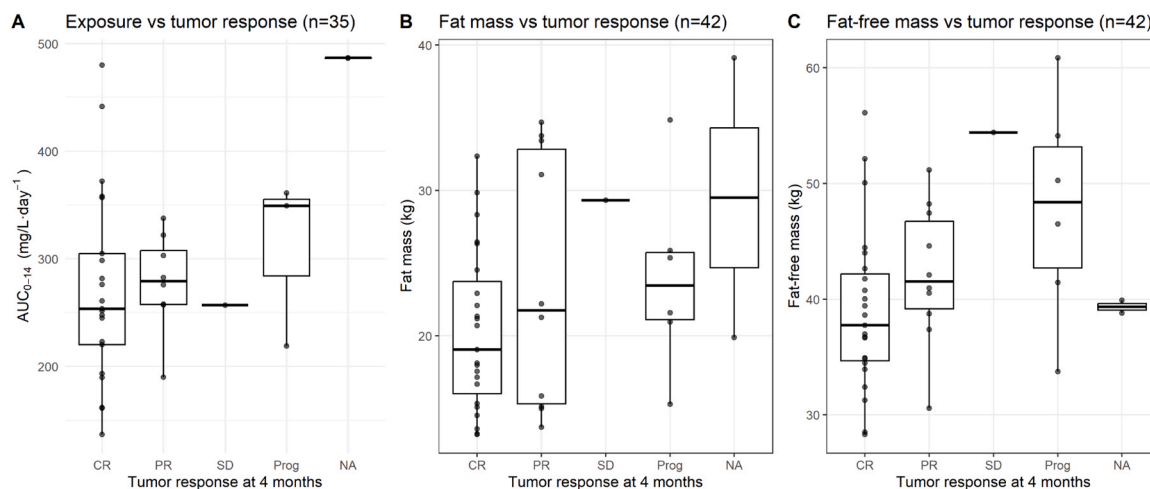


Fig. 4. Impact of PK and Body Composition parameters on response rate of Panitumumab. A) Exposure according tumor response at 4 months ($n = 35$); B) Fat mass according tumor response at 4 months ($n = 42$); C) Fat-free mass according tumor response at 4 months ($n = 42$); CR: complete response; PR: partial response; SD: stable disease; Prog: progression; NA: not available.

Table 3

Impact of PK and Body Composition parameters on survival of Panitumumab.

Summary of Cox Analyses for OS, SSC, and SSR

A) Overall Survival (OS)

Variable	N	Hazard ratio	p
AUC0-14	35	1.00 (0.99, 1.01)	0.52
Fat-free mass (kg)	42	1.07 (0.99, 1.16)	0.09
Fat mass (kg)	42	1.01 (0.93, 1.11)	0.76

B) Colonostomy-free survival (CFS)

Variable	N	Hazard ratio	p
AUC0-14	35	1.00 (0.99, 1.01)	0.77
Fat-free mass (kg)	42	1.06 (1.00, 1.14)	0.06
Fat mass (kg)	42	1.05 (0.97, 1.13)	0.21

C) Recurrence free-survival (RFS)

Variable	N	Hazard ratio	p
AUC0-14	35	1.00 (0.99, 1.01)	0.8
Fat-free mass (kg)	42	1.04 (0.97, 1.11)	0.3
Fat mass (kg)	42	1.02 (0.95, 1.10)	0.6

Hazard Ratio: represents the relative risk of the event occurring (e.g., death or disease progression) for a unit increase in the explanatory variable. An HR > 1 indicates an increased risk, while HR < 1 indicates a decreased risk. The values are median and 95% Confidence Interval (CI): CI represents the range in which the true HR is expected to fall with 95% confidence, where a CI that does not include 1 indicates statistical significance.

exposure of panitumumab nor BC parameters showed significant associations with treatment efficacy, including tumor response (Fig. 4) and survival (Table 3).

Skin toxicity data, including early manifestations like acneiform rash and desquamative rash, were also assessed to evaluate the tolerance of the treatment. Among the 36 patients for whom early toxicity data were available, AUC values were reported for 30, and BC data were available for all 36. Of these 36 patients, 19 patients had a maximum toxicity grade of 1, 16 had a maximum grade of 2, and 1 had a maximum grade of 3. Late skin toxicity could not be tested due to the small sample size (17 patients), all of whom were classified with a maximum toxicity grade of 2. The exposure to panitumumab and BC parameters were not significantly associated with early skin toxicity (Fig. 5).

4. Discussion

To our knowledge, this is the first study that explored the relationship between BC and panitumumab PK. Our exploratory results suggests a possible correlation of BC parameters, including FFM and FM, with panitumumab exposure and clearance. Patients with lower FM and FFM appeared to have lower panitumumab exposure and clearance, suggesting that BC variability may influence panitumumab disposition in patients with localized anal SCC undergoing radiochemotherapy. However, these results are exploratory and should be interpreted cautiously. Due to the small sample size, a formal population PK (PopPK) covariate analysis could not be performed, and FFM and FM were strongly correlated with body weight (BW, $r = 0.61-0.86$), making it difficult to distinguish independent effects of BC from those of total BW. Indeed, BW also seems to be correlated with panitumumab exposure and clearance, with patients with lower BW exhibiting lower

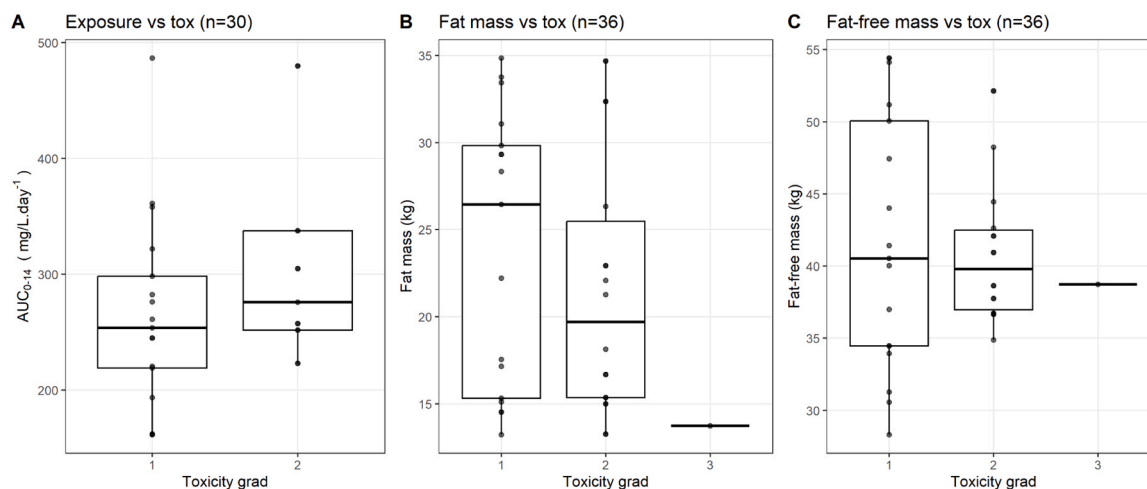


Fig. 5. Impact of PK and Body Composition parameters on skin toxicity of Panitumumab.

exposure and clearance, and a more significant p-value than FFM or FM. This is likely because BW reflects total blood volume and overall patient size, capturing both lean and adipose compartments.

The effect of body weight on PK parameters is consistent with findings by Ma et al., who reported that body weight is positively correlated with clearance (CL), central volume of distribution (V_1), and maximum elimination rate (V_{max}) [21]. In their study, a 50% increase in body weight was associated with 18.1%, 23.8%, and 28.6% increases in CL, V_1 , and V_{max} , respectively.

Sarcopenic patients also tended to have lower AUC_{0-14} compared with non-sarcopenic individuals, further supporting a potential link between reduced muscle mass and decreased panitumumab exposure. Although BC has been widely recognized as a factor influencing efficacy and safety of chemotherapy, relatively few studies have examined this relationship for mAbs in oncology with PK. Ours results align with previous works showing that cachexia can alter the PK of mAbs, such as pembrolizumab [24]. However, sarcopenia may reflect not only reduced FFM but also more severe disease, such as cancer-associated cachexia, systemic inflammation, or increased protein catabolism, which can independently influence drug clearance. Therefore, the observed lower exposure in sarcopenic patients may be partly driven by underlying disease severity rather than BC alone, highlighting a potential confounding effect.

Interestingly, albumin concentration did not significantly correlate with exposure (AUC_{0-14}), but appeared inversely associated with clearance, where patients with lower albumin levels may have reduced CL. This aligns with prior evidence that albumin reflects FcRn-mediated IgG recycling and overall protein catabolism, particularly in patients with cancer or inflammation. However, the interpretation is complicated in oncology since hypoalbuminemia may reflect both disease severity and catabolic activity, potentially confounding PK relationships [25,26].

Despite these exploratory associations of BC on panitumumab exposure, we did not observe meaningful associations between BC parameters, panitumumab PK, and treatment effects - including tumor response, survival, and toxicity. A previous study similarly found no direct link between the loss of muscle or adipose mass and the efficacy or toxicity of bevacizumab [27]. This contrasts with findings from studies on cytotoxic agents, where altered BC, such as sarcopenia, has been shown to affect treatment outcomes [28–30]. However, the design and sample size of our study may have limited our ability to detect such associations. Additionally, the overall lack of efficacy observed in this Phase I/II trial may reflect limitations in the study design or cohort characteristics that precluded detection of significant effects.

As in previous studies, no correlation was observed between panitumumab concentrations and treatment response or safety. Several

factors may explain this. First, the relatively small sample size may have limited statistical power. Second, the use of single-time-point sampling in phase II may not have adequately captured individual PK profiles, potentially weakening observed associations. Third, unmeasured factors such as inter-patient variability in immunes, metabolism or genetic factors, could have played a greater role in determining treatment outcomes.

Moreover, the lack of correlation may reflect a limited efficacy of panitumumab in anal cancer. The retrospective assessment of BC using pre-treatment CT scans also limited our ability to assess BC changes during treatment that may influence both PK and outcomes. Future studies should incorporate longitudinal BC assessments to track dynamic changes in muscle mass and adipose tissue during treatment.

There is a clear need for additional data on the relationship between BC and mAb PK. A panitumumab dosing strategy based on BC rather than body weight could provide a more tailored approach, better reflecting individual differences in drug distribution. BC-based dosing of mAbs may represent a promising avenue for drug optimization. Furthermore, BC analysis offers clinicians a more comprehensive view of patient status, with potential to predict outcomes and guide supportive interventions, such as nutritional and physical activity programs. Further prospective studies are required and longitudinal monitoring of BC changes and drug pharmacokinetics.

In conclusion, our exploratory study suggests that interindividual variability in body weight and body composition may influence panitumumab pharmacokinetics in patients with localized anal SCC. Patients with lower body weight, fat-free mass (FFM), or fat mass (FM) tended to have reduced drug exposure, with sarcopenic individuals showing significantly lower AUC_{0-14} compared with non-sarcopenic patients. However, these results are preliminary and should be interpreted cautiously, given the small sample size, strong correlations between BC and body weight, and potential confounding by disease severity. Despite the observed pharmacokinetic differences, variations in body weight, body composition, or sarcopenia were not associated with treatment efficacy, including tumor response or survival, nor with early skin toxicity. These findings do not allow definitive conclusions. Larger, prospective studies with longitudinal assessment of BC and PK are needed to clarify these relationships and guide optimized, individualized treatment strategies with panitumumab.

CRedit authorship contribution statement

Jérôme Martin-Babau: Writing – review & editing, Investigation. **Astrid Lièvre:** Writing – review & editing, Investigation. **Sarah Lobet:** Writing – original draft, Visualization, Formal analysis, Data curation,

Conceptualization. **Claire Lemanski:** Writing – review & editing, Investigation. **Véronique Vendrely:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Adeline Dolly:** Writing – review & editing, Investigation. **Thierry Lecomte:** Writing – original draft, Supervision, Methodology, Conceptualization. **Franck Nguyen:** Writing – review & editing, Data curation. **Lucie Lagogué:** Writing – review & editing, Data curation. **Louis Bazire:** Writing – review & editing, Investigation. **Christelle De la Fouchardière:** Writing – review & editing, Investigation. **David Ternant:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Formal analysis, Conceptualization. **Come Lepage:** Investigation. **Meher Ben Abdelghani:** Writing – review & editing, Investigation. **Karine Le Malicot:** Writing – review & editing, Supervision, Project administration, Methodology, Data curation, Conceptualization. **Gilles Paintaud:** Writing – review & editing, Visualization, Supervision, Project administration, Methodology, Conceptualization. **Thomas Aparicio:** Writing – review & editing, Investigation. **Nicolas Azzopardi:** Writing – review & editing, Formal analysis.

Funding

AMGEN provided panitumumab treatment.

Declaration of Competing Interest

SL is currently employed by Calvagone SAS; however, this work is part of her PhD thesis, conducted at Tours University, and is independent of her professional duties at Calvagone SAS. DT David Ternant acted as a consultant and has given lectures on behalf of his institution for Astra-Zeneca, Amgen, Boehringer-Ingelheim, Novartis, Pfizer and Sanofi. AL received honoraria for speaking or consulting role from Amgen, Astellas, Bayer, BMS, Esteve, Incyte, MSD, Pierre Fabre, Servier and Takeda; support for congress registration, accommodation and transport from Amgen, Esteve and Viatrix; received research funding from Bayer, Lilly. GP received research grants from Bayer, Lilly, Lundbeck, MabDesign, Merck, Novartis, Pfizer and Regeneron, outside of the submitted work. CL, KLM, NA, AD, FN, LL, LB, CL, MJ, CD, MB, VV declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors thank all the participating centers research, clinical teams and, the patients and their family for their participation in the FFCD0904 trial. Gratitude is also extended to the FFCD for the valuable support throughout the research project. We thank the research clinical networks PRODIGE.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.biopha.2026.119242](https://doi.org/10.1016/j.biopha.2026.119242).

Data availability

Data will be made available on request.

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