Sarcopenia and body mass index predict sunitinib-induced early dose-limiting toxicities in renal cancer patients

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Background: Little is known on factors predicting sunitinib toxicity. Recently, the condition of low muscle mass, named sarcopenia, was identified as a significant predictor of toxicity in metastatic renal cell cancer (mRCC) patients treated with sorafenib. We investigated whether sarcopenia could predict early dose-limiting toxicities (DLTs) occurrence in mRCC patients treated with sunitinib.

Methods: Consecutive mRCC patients treated with sunitinib were retrospectively reviewed. A DLT was defined as any toxicity leading to dose reduction or treatment discontinuation. Body composition was evaluated using CT scan obtained within 1 month before treatment initiation.

Results: Among 61 patients eligible for analysis, 52.5% were sarcopenic and 32.8% had both sarcopenia and a body mass index (BMI) < 25 kg m⁻². Eighteen patients (29.5%) experienced a DLT during the first cycle. Sarcopenic patients with a BMI < 25 kg m⁻² experienced more DLTs (P = 0.01; odds ratio = 4.1; 95% CI: 1.3–13.3), more cumulative grade 2 or 3 toxicities (P = 0.008), more grade 3 toxicities (P = 0.04) and more acute vascular toxicities (P = 0.009).

Conclusion: Patients with sarcopenia and a BMI < 25 kg m⁻² experienced significantly more DLTs during the first cycle of treatment.

Renal cancer accounts for more than 64 000 new cases per year in the United States, and causes approximately 13 500 deaths yearly (Siegel et al., 2012). Worldwide incidence and mortality rates are rising at approximately 2–3% per decade (Gupta et al., 2008). Sunitinib (Sutent; Pfizer, New York, NY, USA) is an orally active, multi-targeted inhibitor of VEGFR1-3, PDGFR, KIT, FLT3, CSF-1 and RET (Chow and Eckhardt, 2007), approved for the treatment of metastatic renal cell cancer (mRCC; Motzer et al., 2007). Importantly, sunitinib-induced toxicities (mainly diarrhoea, hand-foot syndrome, fatigue and hypertension) may limit the patient’s ability to receive full-dose treatment. In the sunitinib arm of the pivotal phase III trial, these toxicities resulted in dose reductions in 50% and treatment termination in 19% of the patients (Motzer et al., 2009).

Little is known on factors predicting sunitinib toxicity. Polymorphisms in CYP3A5 (rs776746) might identify a subset of patients prone to toxicity-related dose reductions (Garcia-Donas et al., 2011). However, these polymorphisms are not routinely assessed in daily practice.

Recently, the condition of low muscle mass, named sarcopenia (Cruz-Jentoft et al, 2010; Fearon et al., 2011), has been studied in cancer patients, in whom sex-specific cut-off values based on mortality risks have been determined (Prado et al., 2008). Sarcopenia is a significant predictor of toxicity in mRCC patients.
We hypothesised that an increased toxicity would be observed in sarcopenia could predict the occurrence of early dose-limiting toxicities (DLTs) in mRCC patients treated with sunitinib. The purpose of the present analysis was to investigate whether sarcopenia could predict the occurrence of early dose-limiting toxicities (DLTs) in mRCC patients treated with sunitinib. We hypothesised that an increased toxicity would be observed in sarcopenic patients.

**MATERIALS AND METHODS**

**Participants.** We performed a retrospective, electronic, medical record review of all consecutive mRCC patients treated with sunitinib in our institution from June 2006 to March 2012.

**Ethics.** The study was approved by the local ethics board according to good clinical practice and applicable laws, and the declaration of Helsinki.

**Treatment, toxicity and activity assessment.** Adult mRCC out-patients received sunitinib at a starting dose of 50 mg per day, 4 weeks/6, 37.5 mg continuous daily dosing (CDD) or 25 mg CDD according to their Eastern Cooperative Oncology Group performance status (ECOG PS) and co-morbidities, at the discretion of the treating physician, as described by other authors (Escudier et al, 2009; Barrios et al, 2012). Toxicity was assessed at each visit, every 2 weeks (or before if clinically indicated) during the first cycle, then monthly.

In the case of grade 3 or 4 toxicity according to the National Cancer Institute Common Terminology Criteria v3.0, sunitinib was discontinued, except for patients with grade 3 hypertension in whom antihypertensive drugs were introduced according to current guidelines (Izzedine et al, 2009). Depending on toxicity resolution, sunitinib was resumed at full dose or at decreased doses, or permanently discontinued, at the discretion of the treating physician.

A DLT was defined as any toxicity leading to a dose reduction, temporary or permanent discontinuation of treatment. Following the design of a previous study (Prado et al, 2009), only DLTs occurring during the first cycle of treatment were examined for the present analysis. A cycle of treatment was determined as a period of 6 weeks.

Treatment activity was assessed every two cycles by CT scan, or before if clinically indicated, according to RECIST v1.0 (Therasse et al, 2000).

**Anthropometric measurements.** Weight was measured with a medical balance beam scale, and height was measured with a stadiometer. The BMI was calculated (weight (kg)/height$^2$ (m$^2$)) and the World Health Organization categories were used: underweight, BMI < 18.5; normal, 18.5 ≤ BMI ≤ 24.9; overweight, 25 ≤ BMI < 29.9; obesity, BMI ≥ 30. Body surface area (BSA) was calculated using the Mosteller formula: BSA (m$^2$) = ((height (cm) × weight (kg))/3600)$^{1/2}$.

**Image analysis.** Body composition was evaluated by assessing muscle tissue areas on CT-scan images, as previously described (Heysmield et al, 1997; Mitsiopoulos et al, 1998). CT scans had been performed for diagnostic or follow-up purposes within no more than 30 days before initiation of sunitinib. Images were analysed using Imagej software v1.42q (National Institutes of Health, http://rsb.info.nih.gov/ij). The third lumbar vertebra (L3) was chosen as a standard landmark, as previously described (Antoun et al, 2010a). Muscles were identified based on their anatomic features, and the structure of those specific muscles was quantified based on pre-established thresholds of skeletal muscle tissue (−29 to +150 Hounsfield units; Mitsiopoulos et al, 1998). Cross-sectional areas (cm$^2$) of the sum of all of these muscles were computed and the mean value for two consecutive images was computed for each patient. These values were normalised for stature (Mourtzakis et al, 2008; Prado et al, 2008) and expressed in units of cm$^2$ m$^{-2}$. The sex-specific cutoff values for sarcopenia (55.4 cm$^2$ m$^{-2}$ for males and 38.9 cm$^2$ m$^{-2}$ for females) determined in cancer patients were used as done by others in mRCC patients (Antoun et al, 2010a). The total lumbar–skeletal muscle cross-sectional area is linearly related to the whole-body muscle (Shen et al, 2004; Mourtzakis et al, 2008) and the total lean body mass (LBM) was estimated from muscle cross-sectional areas as described by Mourtzakis et al (2008): LBM (kg) = (0.30 × (skeletal muscle area at L3 using CT (cm$^2$)) + 6.06). As the body composition analysis was done a posteriori, treating physicians were blinded to patients’ body composition status (sarcopenic or not).

**Statistical analysis.** Prevalence of toxicity was compared using Fisher’s exact test, and Mann–Whitney’s test was used for the comparison of continuous variables. All P-values were two-sided, and the level of significance was P<0.05. Multivariate analysis of factors predicting early DLTs was conducted using logistic regression with 3000 bootstrap iterations, including only factors predicting the occurrence of DLTs with a P-value<0.05 by univariate analysis. Progression-free survival (PFS) and overall survival (OS) were measured from the date of first treatment administration to the date of disease progression or death for the former, and the date of death for the latter. Kaplan–Meier

![Figure 1. Patients selection for analysis.](image-url)
estimates of the distribution of times from baseline to outcome were computed, and the groups were compared using the log-rank test. Calculations were performed with NCSS 2007 software (NCSS, Kaysville, UT, USA).

RESULTS

Patients’ characteristics. From June 2006 to March 2012, 84 mRCC patients received sunitinib, among which 61 (73%) met all criteria for study analysis (Figure 1).

Baseline characteristics of patients treated with sunitinib are presented in Table 1. Briefly, 32 patients (52.5%) were sarcopenic and 20 (32.8%) were sarcopenic, and had a BMI < 25 kg m\(^{-2}\). The variables needed to assign a Memorial Sloan Kettering Cancer Center (MSKCC) risk score were missing for 11 patients, and those needed to assign a Heng score were missing for 15 patients. Some patients could be correctly assigned even with some missing data; for the others the most likely values were derived.

Sunitinib toxicity. Eighteen patients (29.5%) experienced a DLT during the first cycle of treatment (Table 2). In all cases but two, patients had multiple toxic effects of grade 2 and/or 3. Sunitinib was discontinued and resumed either at the same dose in three cases (16.5%) or at a lower dose in eight cases (44.5%). For the seven remaining patients (39%), sunitinib was permanently discontinued. Table 2 shows therapy adjustments and the duration of subsequent sunitinib treatment after the occurrence of a DLT (median for the whole cohort: 31 weeks, range 6–150). Sunitinib was resumed in 40% of patients with sarcopenia and low BMI (for a median duration of 33 weeks, range 16–85), and in 75% of

| Characteristics | Males (n = 38) | Females (n = 23) | Total (n = 61) |
|-----------------|---------------|-----------------|---------------|
| Age (years), median (range) | 60 (29–83) | 59 (30–79) | 60 (29–83) |
| ECOG PS, n (%) | | | |
| 0 | 14 (36.8) | 5 (21.7) | 19 (31.2) |
| 1 | 19 (50) | 12 (52.2) | 31 (50.8) |
| ≥2 | 5 (13.2) | 6 (26.1) | 11 (18) |
| Metastatic sites, n (%) | | | |
| 1 | 16 (42.1) | 11 (47.8) | 27 (44.3) |
| 2 | 8 (21.1) | 6 (26.2) | 14 (23) |
| 3 | 7 (18.4) | 5 (21.7) | 12 (19.7) |
| ≥4 | 7 (18.4) | 1 (4.3) | 8 (13) |
| Specific metastatic sites, n (%) | | | |
| Lung | 22 (57.9) | 11 (47.8) | 33 (54.1) |
| Liver | 2 (5.3) | 2 (8.7) | 4 (6.6) |
| Bone | 20 (52.6) | 9 (39.1) | 29 (47.5) |
| MSKCC prognostic risk, n (%) | | | |
| Low risk | 5 (13.2) | 5 (21.7) | 10 (16.4) |
| Intermediate risk | 28 (73.6) | 13 (56.6) | 41 (67.2) |
| High risk | 5 (13.2) | 5 (21.7) | 10 (16.4) |
| Heng prognostic group, n (%) | | | |
| Favourable | 5 (13.2) | 5 (21.7) | 10 (16.4) |
| Intermediate | 23 (60.5) | 13 (56.6) | 36 (59) |
| Poor | 10 (26.3) | 5 (21.7) | 15 (24.6) |
| Weight (kg), median (range) | 78 (50–124) | 62 (44–91) | 73 (44–124) |
| BMI (kg m\(^{-2}\)), median (range) | 25.9 (17.3–43.4) | 24.2 (17.1–36.5) | 24.9 (17.1–43.4) |
| Underweight (BMI<18.5), n (%) | 2 (5.3) | 3 (13) | 5 (8.2) |
| Normal weight (18.5≤BMI<24.9), n (%) | 14 (36.8) | 13 (56.5) | 27 (44.3) |
| Overweight (25≤BMI<29.9), n (%) | 12 (31.6) | 4 (17.5) | 16 (26.2) |
| Obese (30≤BMI), n (%) | 10 (26.3) | 3 (13) | 13 (21.3) |
| LBM (kg), median (range) | 49.3 (32.2–65.9) | 33.5 (24.9–40.3) | 42.7 (24.9–65.9) |
| Skeletal muscle L3 area (cm\(^2\)), median (range) | 158 (101–214) | 105 (77–128) | 136 (77–214) |
| Skeletal muscle L3 index (cm\(^2\) m\(^{-2}\)), median (range) | 51.6 (35.0–67.5) | 40.9 (27.2–47.2) | 46.2 (27.2–67.5) |
| Sarcopenic, n (%) | 24 (63.2) | 8 (34.8) | 32 (52.5) |
| Sarcopenic and BMI <25, n (%) | 13 (34.2) | 7 (30.4) | 20 (32.8) |

Abbreviations: ECOG PS = Eastern Cooperative Oncology Group performance status; MSKCC = Memorial Sloan Kettering Cancer Center; BMI = body mass index (weight/height\(^2\)); LBM = lean body mass; CT = computed tomography. LBM calculated from the regression equation: whole LBM (kg) = 0.30 × (skeletal muscle at L3 using CT (cm\(^2\)) + 6.06).
patients in the remaining patients (median duration: 31 weeks, range 6–150), \( P = 0.06 \).

The comparison of anthropometric parameters between patients with or without early DLT is summarised in Table 3. Significant differences were observed regarding age (\( P = 0.006 \)), weight (\( P = 0.007 \)), BSA (\( P = 0.004 \)), LBM (\( P = 0.006 \)) and skeletal muscle L3 index (\( P = 0.02 \)). No difference was found regarding BMI or sarcopenia. The prevalence of DLT did not significantly differ in patients receiving 50 mg, 4 weeks/6, or CDD 50 mg per day (\( P = 0.31 \)).

The comparison between patients with both sarcopenia and BMI < 25 kg m\(^{-2}\) with the remaining patients is summarised in Table 4. No difference was found regarding the starting dose, ECOG PS at beginning of treatment or classification according to the MSKCC risk group. Figures 2A and B illustrate the distribution of BMI, muscle index and early DLT for men and women, respectively. Overall, sarcopenic patients with BMI < 25 kg m\(^{-2}\) experienced significantly more DLTs (\( P = 0.01 \); odds ratio = 4.1; 95% CI: (1.3–13.3)), more cumulative grade 2 or 3 toxicities (\( P = 0.008 \)) and more grade 3 toxicities (\( P = 0.04 \)) during the first cycle. Permanent termination of sunitinib during the first cycle occurred in 30% of these patients compared with 2.4% of the remaining patients (\( P = 0.01 \)). Of note, acute vascular toxicities (microangiopathic haemolytic anaemia, thrombotic microangiopathy or reversible posterior leukoencephalopathy syndrome) were more frequent during the first cycle of treatment in this subset of patients (\( P = 0.009 \)). By multivariate analysis, the combination of sarcopenia and BMI < 25 kg m\(^{-2}\) was the only independent predictor of early DLTs (\( P = 0.04 \)).

**Survival analysis.** The median PFS and OS for the study population (\( n = 61 \)) were 9.0 (95% CI: 6.4–11.8) and 22.1 months (95% CI: 14.0–26.0), respectively. No significant differences were observed between patients with sarcopenia and BMI < 25 kg m\(^{-2}\), and the remaining patients regarding median PFS (7.5 (95% CI: 3.9–10.1) vs 9.4 months (95% CI: 6.3–16.2), respectively; \( P = 0.11 \); Figure 3A) and median OS (19.3 (95% CI: 14.0–20) vs 23.5 months (95% CI: 12.5–40.7), respectively; \( P = 0.21 \); Figure 3B).

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**Table 2. Description of DLTs and therapy adjustments**

| Patient | Starting dose | Grade 3 toxicities | Grade 2 toxicities | Sarcopenia and BMI <25 | Therapy adjustment | Sunitinib after DLT (weeks) |
|---------|---------------|--------------------|--------------------|------------------------|-------------------|---------------------------|
| 1       | 37.5 mg CDD   | Proteinuria        | 0                  | No                     | 37.5 mg CDD       | 6                         |
| 2       | 25 mg CDD and 37.5 mg CDD after 2 weeks | 0                | Nausea             | Proteinuria            | Hypertension       | Asthenia  | Yes | 37.5 mg CDD | 8 |
| 3       | 50 mg 4w/6    | Thrombocytopenia   | Hypertension       | Yes                    | 37.5 mg CDD       | 50                        |
| 4       | 50 mg 4w/6    | MAHA               | 0                  | Yes                    | PT, switch to everolimus | 0 |
| 5       | 50 mg 4w/6    | Hypothyroidism     | Asthenia           | 0                      | Yes               | PT, switch to everolimus | 0 |
| 6       | 50 mg 4w/6    | Hypertension       | Proteinuria        | No                     | 37.5 mg CDD       | 37 (ongoing)              |
| 7       | 37.5 mg CDD   | Hand-foot syndrome | Stomatitis         | Diarrhoea              | No                | 25 mg CDD                | 21 |
| 8       | 37.5 mg CDD   | Asthenia           | 0                  | No                     | 25 mg CDD         | 150                       |
| 9       | 50 mg 4w/6    | Stomatitis         | Thrombocytopenia   | No                     | 37.5 mg CDD       | 22                        |
| 10      | 50 mg 4w/6    | Proteinuria        | MAS                | Asthenia               | No                | 50 mg 4w/6                | 33 |
| 11      | 50 mg 4w/6    | Asthenia           | TMA                | Yes                    | PT                | 0                         |
| 12      | 50 mg 4w/6    | TMA                | Hypertension       | Asthenia               | Yes               | PT, switch to everolimus | 0 |
| 13      | 25 mg CDD     | Hypertension       | Stomatitis         | Hypothyroidism         | Edema             | Yes                      | PT, switch to everolimus | 0 |
| 14      | 50 mg 4w/6    | Stomatitis         | Rash               | 0                      | Yes               | 37.5 mg CDD               | 16 (ongoing) |
| 15      | 50 mg 4w/6    | Haemorrhagic rectocolitis | 0       | No                     | PT, switch to sorafenib | 0 |
| 16      | 50 mg 4w/6    | Asthenia           | Anorexia           | Proteinuria            | No                | 25 mg CDD                | 31 |
| 17      | 50 mg 4w/6    | RPLS               | Asthenia           | 0                      | Yes               | PT                        | 0 |
| 18      | 50 mg 4w/6    | Nausea             | Hypertension       | Hand-foot syndrome     | Asthenia          | Yes                      | 37.5 mg CDD               | 85 |

**Abbreviations:** DLT = dose-limiting toxicity; PT = permanent termination; CDD = continuous daily dosing; MAHA = microangiopathic haemolytic anaemia; TMA = thrombotic microangiopathy; MAS = macrophage activation syndrome; RPLS = reversible posterior leukoencephalopathy syndrome; 50 mg 4w/6 = 50 mg of sunitinib daily, 4 weeks on and 2 weeks off.
This retrospective analysis is the first evaluating the relationship between sarcopenia and early toxicity in patients treated with sunitinib for mRCC. We found that patients with sarcopenia and a BMI < 25 kg m⁻² experienced significantly more DLTs, more cumulative grade 2 or 3 toxicities and more grade 3 toxicities during the first cycle.

Baseline characteristics of patients included in this analysis were similar to those observed in previous studies in mRCC patients considering sarcopenic and non-sarcopenic patients, no significant differences were observed regarding PFS (P = 0.71) or OS (P = 0.75).

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|                                | Sarcopenic and BMI < 25 kg m⁻² (n = 20) | Non-sarcopenic or BMI > 25 kg m⁻² (n = 41) | P-value |
|--------------------------------|----------------------------------------|-------------------------------------------|---------|
| **Sunitinib starting dose, n (%)** |                                        |                                           |         |
| 25 or 37.5 mg, CDD              | 2 (10)                                 | 10 (24.4)                                 | 0.30    |
| 50 mg, 4 weeks/6                | 18 (90)                                | 31 (75.6)                                 |         |
| **ECOG PS, n (%)**              |                                        |                                           |         |
| 0–1                            | 14 (70)                                | 36 (87.8)                                 | 0.15    |
| ≥2                             | 6 (30)                                 | 5 (12.2)                                  |         |
| **MSKCC prognostic score, n (%)** |                                        |                                           |         |
| Low risk                       | 2 (10)                                 | 8 (19.5)                                  | 0.39    |
| Intermediate risk              | 13 (65)                                | 28 (68.3)                                 |         |
| High risk                      | 5 (25)                                 | 5 (12.2)                                  |         |
| **Heng prognostic score, n (%)** |                                        |                                           |         |
| Favourable                     | 1 (5)                                  | 9 (22)                                    | 0.07    |
| Intermediate                   | 11 (55)                                | 25 (61)                                   |         |
| Poor                           | 8 (40)                                 | 7 (17)                                    |         |
| **Characteristics, median (range)** |                                        |                                           |         |
| Age (years)                    | 61 (35–79)                             | 58 (29–83)                                | 0.46    |
| Weight (kg)                    | 64 (50–79)                             | 78 (44–124)                               | 0.0001  |
| Height (m)                     | 1.73 (1.58–1.87)                       | 1.70 (1.50–1.92)                          | 0.44    |
| BMI (kg m⁻²)                   | 23.0 (17.3–24.9)                       | 27.1 (17.1–43.4)                          | <0.001  |
| BSA (m²)                       | 1.75 (1.54–1.99)                       | 1.96 (1.39–2.53)                          | 0.009   |
| Haemoglobin (g dl⁻¹)           | 12.1 (7.2–15.2)                        | 12.7 (8.4–16.6)                           | 0.43    |
| Lymphocytes (× 10⁹/l)          | 1545 (310–2110)                        | 1400 (560–4872)                           | 0.93    |
| Platelets (× 10⁹/l)            | 361 (222–725)                          | 271 (124–517)                             | 0.06    |
| Albuminaemia (g l⁻¹)           | 40 (26–46)                             | 39 (28–45)                                | 0.98    |
| CRP (g l⁻¹)                    | 32.5 (1–147.1)                         | 18 (1–298)                                | 0.87    |
| Creatininaemia (µM)            | 84.5 (45–136.3)                        | 98.5 (53–167.3)                           | 0.02    |
| Lumbar skeletal muscle index (cm² m⁻²) | 41.4 (27.2–54.5)                       | 47.7 (37.7–67.5)                          | <0.001  |
| LBM (kg)                       | 42.0 (24.9–53.1)                       | 46.7 (32.3–65.9)                          | 0.01    |
| **DLT, n (%)**                 |                                        |                                           |         |
| Present                        | 10 (50)                                | 8 (19.5)                                  | 0.01    |
| Absent                         | 10 (50)                                | 33 (80.5)                                 |         |
| **Permanent termination of sunitinib owing to toxicity, n (%)** |                                        |                                           | 0.003   |
| Present                        | 6 (30)                                 | 1 (2.4)                                   |         |
| Absent                         | 14 (70)                                | 40 (97.6)                                 |         |
| **Prevalence of selected toxicities, n (%)** |                                        |                                           |         |
| Diarrhoea, grade 2–3           | 0                                      | 4 (9.8)                                   | 0.29    |
| Grade 3 diarrhoea              | 0                                      | 0                                         | 1       |
| Hypertension, grade 2–3        | 12 (60)                                | 14 (34.1)                                 | 0.09    |
| Grade 3 hypertension           | 6 (30)                                 | 9 (22)                                    | 0.53    |
| Asthenia, grade 2–3            | 10 (50)                                | 16 (39)                                   | 0.58    |
| Grade 3 asthenia               | 3 (15)                                 | 4 (9.8)                                   | 0.67    |
| Hand–foot syndrome, grade 2–3  | 2 (10)                                 | 2 (4.8)                                   | 0.59    |
| Grade 3 hand–foot syndrome     | 0                                      | 1 (2.4)                                   | 0       |
| Acute vascular toxicity (MAHA, TMA, RPLS), n (%) | 4 (20)                                 | 0                                         | 0.009   |
| Number of grade 2 or 3 toxicities per patient, n (%) | 0                                      | 0                                         | 0.0008  |
| 0                              | 1 (5)                                  | 13 (31.7)                                 | 0.02    |
| 1                              | 5 (25)                                 | 11 (26.8)                                 | 1       |
| 2                              | 8 (40)                                 | 11 (26.8)                                 | 0.37    |
| 3                              | 2 (10)                                 | 6 (14.7)                                  | 0       |
| 4                              | 4 (20)                                 | 0                                         | 0.009   |
| 0–1                            | 6 (30)                                 | 24 (58.5)                                 | 0.055   |
| ≥2                             | 14 (70)                                | 17 (41.5)                                 |         |
| Number of grade 3 toxicities per patient, n (%) | 0                                      | 0                                         | 0.04    |
| 0                              | 6 (30)                                 | 23 (56.1)                                 | 0.06    |
| 1                              | 8 (40)                                 | 15 (36.6)                                 | 0       |
| ≥2                             | 6 (30)                                 | 3 (7.3)                                   | 0.04    |

Abbreviations: BMI = body mass index; BSA = body surface area; CDD = continuous daily dosing; DLT = dose-limiting toxicity; ECOG PS = Eastern Cooperative Oncology Group criteria performance status; MSKCC = Memorial Sloan Kettering Cancer Center; CRP = C-reactive protein; LBM = lean body mass; MAHA = microangiopathic haemolytic anaemia; TMA = thrombotic microangiopathy; RPLS = reversible posterior leukoencephalopathy syndrome. Bold entries indicate statistically significant values (P < 0.05).
therefore, avoid severe toxicities by early dose adjustments or therapeutic interventions when needed.

Conversely, patients devoid of sarcopenia and BMI \( < 25 \text{ kg m}^{-2} \) could probably be treated with full-dose sunitinib without excessive risk, even when ECOG PS exceeds 1.

In conclusion, our results highlight the importance of assessing body composition, and suggest that the combination of sarcopenia and low BMI predicts early DLTs in mRCC patients treated with sunitinib.

ACKNOWLEDGEMENTS

We thank Dr Romain Coriat, the nurses, residents and clinical research staff at the Cochin Teaching Hospital.

CONFLICT OF INTEREST

Dr Mir has acted as an advisory board member for Sanofi-Aventis, Ferring Pharmaceuticals, Ipsen and Janssen. Professor Goldwasser has acted as a paid consultant for Roche, Amgen, Bayer Healthcare and Pfizer. All other authors declare no conflict of interest.

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