that it is often characterized by rapid onset and short duration [6] making it highly amenable to the use of short acting opioids.

We thank the authors for pointing out the one controlled trial dealing with nursing interventions in lung cancer patients which demonstrated efficacy in nonpharmacological interventions especially patient education. Referring to the Cochrane review conducted by Bausewein et al., it is important to appreciate that most of the enrolled studies have been conducted in COPD patients, with only a few studies including participants with other conditions. Furthermore, that review is out of date and has been withdrawn in April 2014. We stand by our statement 'Little evidence but sufficient clinical consensus is available concerning non-pharmacological interventions. They should be offered before starting pharmacological interventions and should accompany them afterwards'.

Regarding the methodology of European Society for Medical Oncology (ESMO) Guideline production, we recently published details on its pivotal features along with the target audience, their purpose and scope in an editorial in this journal [7]. We welcome further critiques and suggestions with the hope that subsequent versions will be progressively more robust.

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disclosure

MK has been investigator of the Effendys Study sponsored by TEVA Pharmaceutical Industries and is member of the advisory board of this company; AC: Speakers’ bureau: Roche and Merck Serono; Advisory boards: Merck Serono, Roche, Amgen, Bayer and Lilly. All remaining authors have declared no conflicts of interest.

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Trabectedin is an effective second-line treatment in soft tissue sarcoma patients

Demetri et al. have conducted the first randomized phase III trial assessing the efficacy of trabectedin in soft tissue sarcoma patients [1]. This trial demonstrated that treatment with trabectedin (n = 345), when compared with dacarbazine therapy (n = 173), was associated with a statistically significant improvement in progression-free survival [4.2 versus 1.5 months; hazard ratio, 0.55 (0.44–0.70), P = 0.001] but no significant improvement in overall survival (12.4 versus 12.9 months; hazard ratio, 0.87, P = 0.37). One could analyze this trial as a negative trial because trabectedin did not meet the planned primary end point of improvement in overall survival [1]. However, the choice of overall survival as the primary end point in this clinical circumstance is controversial. In a recent meta-analysis, adjuvant chemotherapy failed to improve overall survival [2]. In the most recently published clinical trial, first-line combination chemotherapy (doxorubicin/ifosfamide) compared with doxorubicin alone improved the progression-free survival (7.4 versus 4.6 months, hazard ratio 0.74, P = 0.003) but did not improve overall survival (14.3 versus 12.8 months, hazard ratio 0.83, P = 0.076) [3]. In our systematic literature review, we found only one study of a second-line chemotherapy regimen or targeted therapy that improved overall survival [4]. Indeed, the currently approved drugs for this indication do not improve overall survival [4]. For example, in the PALETTE trial, treatment with pazopanib compared with placebo did not improve survival (median overall survival 12.5 versus 10.7 months; hazard ratio 0.86; P = 0.25) [5]. The only exception is one randomized phase II trial that was not designed to demonstrate overall survival benefits. In this study, treatment with gemcitabine/dacarbazine was associated with a longer overall survival compared with treatment with dacarbazine alone (median overall survival was 16.8 versus 8.2 months; hazard ratio, 0.56; P = 0.14); clearly, the results of this trial need to be confirmed [6]. In light of the existing evidence, we think that overall survival is not an appropriate end point for assessing the efficacy of new treatments in advanced metastatic soft tissue sarcoma.

When we summarized the available data, we found that all of the randomized trials assessing the activity of trabectedin in a second-line treatment demonstrated significant improvement in progression-free survival (Table 1) [1, 7–9]. This primary end point is regarded by authorities as an appropriate end point for approving new drugs for this indication. There is no doubt that trabectedin is an effective drug in soft tissue
sarcoma patients who have already received a doxorubicin-based regimen [1, 7–9].

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