Support Care Cancer (2017) 25:2715–2722
DOI 10.1007/s00520-017-3680-1

ORIGINAL ARTICLE

A scoring system to guide the decision for a new systemic treatment after at least two lines of palliative chemotherapy for metastatic cancers: a prospective study

Brice Chanez[1] · François Bertucci[1,2] · Marine Gilabert[1] · Anne Madroszyk[1] · Frédérique Rousseau[1] · Delphine Perrot[1] · Patrice Viens[1,2] · Jean-Luc Raoul[1]

Received: 7 December 2016 / Accepted: 15 March 2017 / Published online: 28 March 2017

Abstract
Purpose A four-parameter score has been identified as associated with overall survival (OS) in patients with advanced cancer with an estimated survival inferior to 6 months. Here, we tested its prognostic value for OS in patients who had received more than two lines of systemic therapy.
Methods We prospectively enrolled patients with advanced cancer who were going to receive a third or more therapeutic line outside classical clinical guidelines. The four parameters (Eastern Cooperative Oncology Group performance status, number of metastatic sites, serum LDH, and serum albumin) were collected at baseline, allowing to calculate the score, which sorted the patients in three groups, A, B, and C (low, intermediate, and high score, respectively). We then searched for correlations between this grouping and clinicopathological features particularly OS.
Results From August 2013 to March 2014, 65 patients were enrolled and corresponded after determining their score to 26 patients in group A, 30 in B, and 9 in C. The median OS of the cohort was 4.4 months, and the 6-month OS was 42%. Overall survival was different between the three groups, with respective 6-month OS equal to 80% in group A, 17% in group B, and 0% in group C and respective median OS of 9, 2.3, and 1.6 months. Such prognostic value persisted in multivariate analysis. Similar OS differences were observed in patients with PS ≤2.
Conclusion This simple scoring should help oncologists identify which patients, after at least two lines of systemic therapy, might benefit from best supportive care alone.

Keywords Cancer · End of life · Chemotherapy · Prognostic score · Supportive care · Palliative care

Introduction

In most metastatic cancers, systemic treatments are only palliative and aim to improve the duration and quality of life. Usually, only two or three lines of chemotherapy have demonstrated efficacy. Beyond these recognized therapeutic options, the risk of worsening the quality of life is not acceptable outside of clinical trials. In 2012, the American Society of Clinical Oncology expert panel [1] considered the number one item in a top-five list of items in oncology to be the following: "don't use cancer-directed therapy for solid tumor patients with the following characteristics: low performance status (3 or 4), no benefit from prior evidence-based interventions, not eligible for a clinical trial, and no strong evidence supporting the clinical value of further anti-cancer treatment."

However, patients frequently desire chemotherapy, even at the risk of severe side effects. In a study conducted in patients with non-small cell lung cancer who had previously been treated with cisplatinum-based chemotherapy, different scenarios were proposed to the patients to determine the minimum survival benefit needed to accept the toxicity of chemotherapy [2]: 6% of patients would accept toxic chemotherapy for a survival benefit of only 1 week. In the first-line setting, many patients with cancer were willing to accept intensive

Presented at the ESMO 2014 meeting, Madrid, Spain

✉ Jean-Luc Raoul
raouljl@ipc.unicancer.fr

[1] Department of Medical Oncology, Institut Paoli-Calmettes, Marseille, France

[2] Aix-Marseille University, Marseille, France

chemotherapy for a very small chance of benefit (chance of a cure of only 1% or life prolongation of 12 months) [3], but would be unwilling to accept the same treatment for an increase in life expectancy without a cure [4]. For oncologists, it is thus crucial to determine when to stop aggressive anticancer treatment and to propose the best supportive care alone; it is also important to avoid collusion in the doctor-patient communication [5].

The National Cancer Policy Board has defined poor-quality care [6] as "when practices of known effectiveness are being underused, practices of known ineffectiveness are being overused, and when services of equivocal effectiveness are being used in accordance with provider rather than patient preference". A review [7] focused on the theme of overly aggressive cancer treatment, which potentially indicates poor-quality care; crucial points included the overuse of chemotherapy near death, the possible misuse of treatment, resulting in high rates of emergency room visits or hospitalization for end-stage patients, and the underuse of hospice services. A simple score based on four parameters [8] was previously defined in a series of 177 hospitalized patients with different cancers with an estimated survival inferior to 6 months and showed an excellent prognostic value. By providing objectivity in medical and ethical decisions and the patient-physician relationship, this scoring system might be of importance about the treatment plan and life projections during this critical period, for example, by defining patients with poor prognosis for whom the life expectancy is short and may not benefit from additional anti-cancer treatment such as chemotherapy. The authors concluded that their prognostic score needed further validation before its application in the daily practice.

Here, we prospectively assessed this scoring system to determine its usefulness in cancer patients who will receive a new line of systemic chemotherapy after the second line, that is, beyond the definite guidelines.

Patients and methods

Study design

In this prospective, unicentric study, we enrolled patients older than 18 years who were treated at our Comprehensive Cancer Center for a solid tumor and who would receive at least a third line of systemic chemotherapy outside of clinical guidelines and clinical trial. We excluded patients treated for breast cancer because of the great number of systemic therapeutic lines demonstrated as effective after the second line [9], as well as those included in a prospective trial. The study was approved by our Institutional Review Board (no. 15-005).

Scoring system

The scoring system, developed by Barbot et al. [8], is based on four parameters: performance status (PS), number of metastatic sites, and serum levels of LDH and albumin. The clinical parameters (PS and metastatic sites) were determined the first day of the new line of chemotherapy, and the biological parameters (LDH and albumin) were measured in the blood test collected the day before. In the seminal paper, PS was evaluated using Karnofsky Performance Status (KPS); in this study, we used the Eastern Cooperative Oncology Group (ECOG) scale [10] and its equivalence with the KPS scale previously published [11]: ECOG PS 0 = KPS 100%, PS 1 = KPS 90–80%, PS 2 = KPS 70–60%, PS 3 = KPS 50–40%, and PS 4 = KPS 30–10%. These parameters were scored as follows: ECOG PS 0–1, 0 point (pt); ECOG PS 2, 2 pts.; ECOG PS 3–4, 4 pts.; 1 metastatic site, 0 pt.; ≥2 sites, 2 pts.; LDH <600 UI/L 0 pt., ≥600 UI/L 1 pt.; and albumin ≥33 g/L −3 pts., <33 g/L 0 pt. The final score was (PS + metastatic sites + LDH + albumin) +3. The results ranged from 0 to 10. Based on this score, we defined three groups: group A, from 0 to 3 points; group B, from 4 to 7 points; and group C, from 8 to 10 points.

Statistical analysis

Baseline patient and disease characteristics were summarized using descriptive analysis and compared between groups using the Fisher's exact test. Our primary end-point was the overall survival (OS), calculated from the first day of enrollment to death from any cause. Patients who were alive at the end of study were censored at the date of last contact. The follow-up was calculated from the first day of enrollment to the last contact for event-free patients. Survival curves for each group were estimated using the Kaplan-Meier method and were compared between groups with the log-rank test. Univariate and multivariate analyses for OS were done using Cox regression analysis (Wald test). Multivariate analysis incorporated all variables with a p value inferior to 5% in univariate analysis. The prediction performance was assessed using Harrell's concordance index (C-index) [12], and sensitivity, specificity, and area under the receiver-operating characteristics curve (AUC) for 2-, 4-, and 6-month OS. All statistical tests were two-sided at the 5% level of significance. Statistical analysis was done using the survival package (version 2.30) in the R software (version 2.9.1).

Results

Patients' characteristics

We prospectively enrolled 65 patients with metastatic solid tumors who were hospitalized for starting a third or more line

of systemic chemotherapy at our center between August 2013 and March 2014. They included 35 males and 30 females, and the median age at inclusion was 63 years (Table 1). The primary tumor types included colorectal cancer (22%), sarcoma (20%), lung cancer (17%), ovarian cancer (17%), pancreatic cancer (11%), and other cancers (14%). Patients had received a median of three therapeutic lines (range 2–5) before inclusion. During the previous lines, 42% of patients had never achieved any objective response, 12% had achieved a stable disease, and 46% had achieved a partial or complete response as their best response. The new treatment regimen was single-agent chemotherapy, polychemotherapy, or a targeted therapy in 49, 45, and 6% of the cases, respectively. The 65 patients were sorted into three groups based on the scoring system: group A included 26 patients, group B included 30 patients, and group C included 9 patients. The therapeutic response to this new therapeutic line was assessable in 61 patients (four patients, one in group A, and three in group B, died a few days after the first administration). The assessment was both clinical and radiological and planned every 3 cycles of chemotherapy or 2 months of targeted therapy. In case of obvious clinical progression, the radiological assessment was not done: four patients (all in group A) showed disease stabilization for at least 6–8 weeks, and three (two in group A and one in group B) achieved partial response. All patients from group C showed disease progression at first clinical assessment. As shown in Table 1, there was no significant difference between the three groups for all tested variables, except for patients' sex, with more women in group A than groups B and C, and as expected for the four parameters defining the score.

Overall survival in the whole cohort

The median follow-up of the whole cohort was 7.4 months (range, 0.4 to 13). The median OS was 4.4 months (range, 0.4 to 13), and the 2-, 4-, and 6-month OS rates were 70% (95% CI 60–82), 52% (95% CI 41–66), and 42% (95% CI 31–56), respectively (Fig. 1a). The causes of death were difficult to determine since in several cases, we could not differentiate patients who died from toxicity from those who died from

Table 1 Baseline characteristics of patients

Characteristics		Whole cohort ($N = 65$) N (%)	Group A ($N = 26$) N (%)	Group B ($N = 30$) N (%)	Group C ($N = 9$) N (%)	p value[a]
Median age	Years (range)	65 (25.2–86.0)	62.6 (38.0–79.0)	67.8 (41.5–86.0)	62.5 (25.2–79.0)	0.08
Sex	Female	30 (46)	20 (77)	8 (26.7)	2 (22)	0.0002
	Male	35 (54)	6 (23)	22 (73.3)	7 (79)	
Primary tumor type	Colorectal	14 (21.5)	4 (15)	8 (26.7)	2 (22)	0.35
	Ovary	11 (17)	6 (23)	4 (13)	1 (11)	
	Lung	11 (17)	4 (15)	3 (10)	4 (44)	
	Sarcoma	13 (20)	7 (27)	6 (20)	0 (0)	
	Other	16 (25)	5 (19)	9 (30)	2 (22)	
Median number of previous therapeutic lines	2	34 (52)	11 (42)	18 (60)	5 (56)	0.77
	3	16 (25)	9 (35)	5 (17)	2 (22)	
	4	6 (9)	3 (11.5)	2 (7)	1 (11)	
	≥5	9 (14)	3 (11.5)	5 (17)	1 (11)	
Best response obtained with previous therapy	CR	3 (5)	3 (11.5)	0 (0)	0 (0)	0.5
	PR	27 (41.5)	10 (38.5)	14 (47)	3 (33)	
	SD	8 (12)	2 (8)	5 (17)	1 (11)	
	PD	27 (41.5)	11 (42)	11 (37)	5 (56)	
New systemic treatment	Mono-CT	32 (49)	13 (50)	14 (47)	5 (56)	0.99
	Poly-CT	29 (45)	11 (42)	14 (47)	4 (44)	
	Targeted therapy	4 (6)	2 (8)	2 (7)	0 (0)	
Best response with new systemic treatment	PR	3 (5)	2 (8)	1 (3)	0 (0)	0.14
	SD	4 (6)	4 (16)	0 (0)	0 (0)	
	PD	54 (83)	19 (73)	26 (87)	9 (100)	
ECOG performance status	0–1	32 (49)	25 (96)	7 (23)	0 (0)	1.59E−11
	2	19 (29)	1 (4)	16 (53)	2 (22)	
	3–4	14 (21.5)	0 (0)	7 (23)	7 (78)	
Number of metastatic sites	0–1	24 (37)	12 (46)	12 (40)	0 (0)	0.037
	≥2	41 (63)	14 (54)	18 (60)	9 (100)	
Serum LDH level	<600 UI/L	51 (78.5)	23 (88.5)	24 (80)	4 (44)	0.030
	≥600 UI/L	14 (21.5)	3 (11.5)	6 (20)	5 (56)	
Serum albumin level	≥33 g/L	32 (49)	26 (100)	6 (20)	0 (0)	7.28E−13
	<33 g/dL	33 (51)	0 (0)	24 (80)	9 (100)	

PD progressive disease, *PR* partial response, *CR* complete response, *SD* stable disease, *CT* chemotherapy

[a] p value for statistical comparison between the three groups A, B, and C

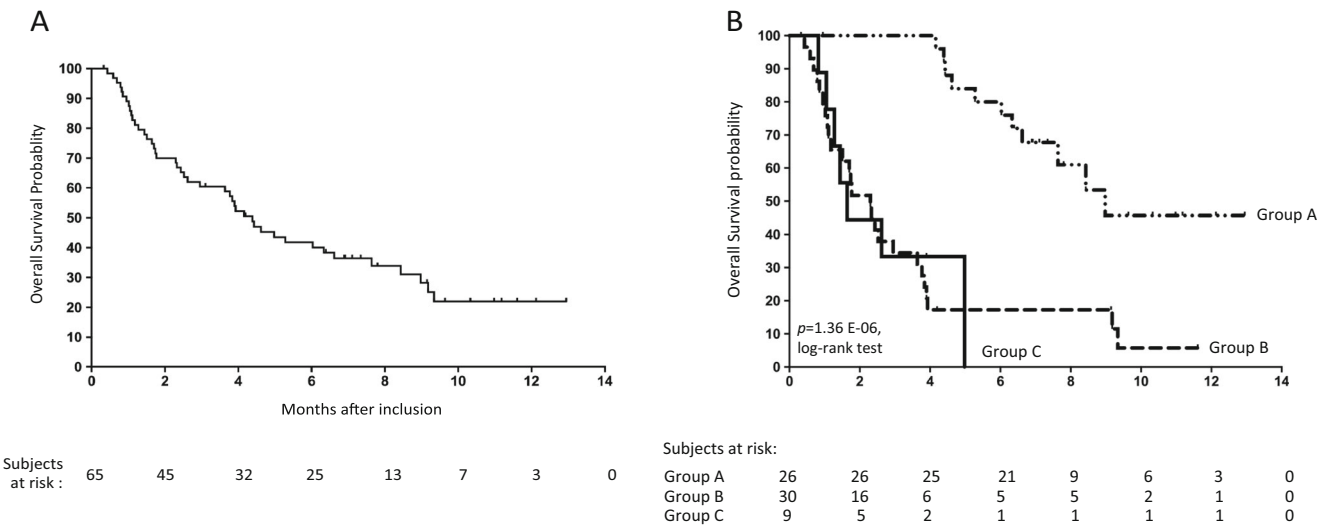

Fig. 1 Overall survival in the whole cohort of patients. **a** Kaplan-Meier OS curves in 65 patients treated with a new systemic therapy in a third or more line. **b** Similar to **a**, but according to the three scoring groups A, B, and C

disease evolution. The median OS for groups A, B, and C were 9 months (range, 4.2 to 13), 2.3 months (range, 0.4 to 11.6), and 1.6 months (range, 1 to 5), respectively. The 2-, 4-, and 6-month OS rates were 100% (95% CI 100–100), 100% (95% CI 100–100), and 80% (95% CI 66–97), respectively, in group A, 52% (95% CI 36–74), 17% (95% CI 8–38), and 17% (95% CI 8–38), respectively, in group B, and 44% (95% CI 21–92), 33% (95% CI 13–84), and 0% (95% CI NA-NA), respectively, in group C (Fig. 1b). Differences were significant between groups B and A (hazard ratio HR = 5.44, 95% CI 2.62–11.3; $p < 0.0001$) and between groups C and A (HR = 6.41, 95% CI 2.36–17.4; $p < 0.0001$), but not between groups B and C. The C-index was 84%. The sensitivity, specificity, and AUC values were 95, 55, and 80%, respectively, for the 2-month OS; 97, 72, and 87%, respectively, for the 4-month OS; and 84, 70, and 85% for the 6-month OS.

We tested all baseline characteristics in an exploratory prognostic analysis for OS. In univariate analysis (Table 2), the female sex, the colorectal primary tumor site, and group A were favorable prognostic variables, whereas the patients' age, the best response to previous therapies, and the number and the type of current therapeutic line were not associated

Table 2 Univariate prognostic analysis for OS

Characteristics		HR [95% CI]	*p* value
Age		1.01 [0.98–1.04]	0.53
Sex	Male vs. female	3.29 [1.72–6.28]	3.00E−04
Primary tumor type	Lung vs. colorectal	0.49 [0.18–1.31]	0.047
	Ovary vs. colorectal	0.23 [0.08–0.67]	
	Sarcoma vs. colorectal	0.42 [0.17–1.04]	
	Other vs. colorectal	0.87 [0.39–1.95]	
Median number of previous therapeutic lines	3 vs. 2	0.69 [0.32–1.45]	0.31
	4 vs. 2	0.60 [0.20–1.74]	
	5 vs. 2	1.89 [0.65–5.48]	
	6 vs. 2	0.41 [0.10–1.77]	
	7 vs. 2	2.77 [0.36–21.19]	
Best response obtained with previous therapy	PR vs. PD	0.74 [0.39–1.42]	0.63
	SD vs. PD	1.29 [0.54–3.10]	
New systemic treatment	Poly-CT vs. mono-CT	1.11 [0.60–2.05]	0.76
	Targeted therapy vs. mono-CT	0.71 [0.21–2.44]	
Score-based group	B vs. A	5.44 [2.62–11.3]	1.24E−05
	C vs. A	6.41 [2.36–17.4]	

PD progressive disease, *PR* partial response, *CR* complete response, *SD* stable disease, *CT* chemotherapy

with OS. In multivariate analysis (Table 3), the score-based grouping was the sole independent prognostic variable.

Overall survival in patients with PS inferior or equal to 2

At inclusion, 14 patients (7 out of 30 from group B and 7 out of 9 from group C) had a very poor performance status of 3–4, usually contra-indicating systemic chemotherapy. Thus, we did a post hoc unplanned subgroup analysis of survival in the 51 patients with a PS 0–2. The median OS were 6.3 months (range, 0.4 to 13) for all patients, 9 months (range, 1 to 13) in group A (26 patients), and 2.5 months (range, 0.3 to 11.6) in group B (23 patients). The 4-month OS was 100% (95% CI 100–100) in group A and 23% (95% CI 11–49) in group B ($p = 2.49E{-}05$, log-rank test; Fig. 2). Group C was not included in the per-group analysis because of the small number of patients ($N = 2$).

Discussion

This prospective analysis confirmed the prognostic value of the previously developed scoring system [8] in a population of heavily pretreated cancer patients who had received a new line of systemic chemotherapy beyond at least the second line and the usual guidelines.

This score is very easy to calculate and is based on two clinical (PS, number of metastatic sites) and two biological (serum LDH and albumin levels) parameters. In the seminal study, the score produced three different groups of patients in a palliative care setting, one with a very poor survival (score 8–10, group C; 8.3% 2-month OS), one with an intermediate survival (score 4–7, group B; 42.7% 2-month OS), and one with a better survival (score 0 to 3, group A; 92.2% 2-month OS). In our population of patients who had progressed after at least two validated chemotherapy regimens, the clinical outcome was very poor with a median OS equal to 4.4 months. Interestingly, the same score-based patients' grouping identified three groups with different survival and might be helpful to better tailor treatment: group A patients had a median OS of 9 months, better than those of groups B and C with, respectively, median OS of 2.3 and 1.6 months. This difference was also robust among patients who had a performance status of 0–2 at inclusion with a median OS of 9 months in group A (100% 4-month OS) versus 2.7 months in group B (23% 4-month OS). Regarding the scoring system, we have used the ECOG performance status (PS) in this analysis, whereas the Karnofsky Performance Score (KPS) was the criteria used by Barbot et al. But these scores are interconvertible [13] with published equivalence rules that we used here [11].

Several scores have been developed to evaluate the life expectancy of patients in the palliative setting. The most used and validated score is the Palliative Prognostic Score (PaP Score) [14], based on six predictive factors: dyspnea, anorexia, KPS, total white blood cell count, lymphocyte percentage, and clinical prediction of survival (CPS). The PaP Score is expressed as the probability of survival at 30 days. The Victoria Hospital developed a palliative performance score (PPS) in 1996 and updated it in 2006. This score is derived from the KPS and includes in the second version the ambulation capacity, activity, and evidence of disease importance, self-care, food intake, and the consciousness level of the patient. The score is expressed from 0 (death) to 100% (no limitation and no evidence of disease). The score has been used several times with moderate accuracy to predict survival [15, 16]. PPS was also used in a retrospective setting to study the performance status of patients before the start of a new chemotherapy cycle for advanced cancer. The conclusion was that few patients with a poor PS could begin a new line of chemotherapy. Another score, the prognostic palliative index (PPI), was developed and validated in Japan for terminally ill patients and included more physical symptoms than other scores; it was based on oral intake, resting dyspnea, delirium, performance status, and the severity of edema [17]. The PPI was also validated in an Irish cohort in a prospective setting and identified patients with a median survival between 68 days (PPI <4) and 5 days (PPI >6) [18]. Finally, studies that compared these scores concluded that they were not substantially different in terms of accuracy in predicting death and could even be interchangeable with the ECOG or KPS [19]. Interestingly, a recent study [20] showed that these prognostic scores, which incorporate objective clinical and biological variables, are more accurate than a subjective variable such as the CPS, further supporting their use.

However, our study was conducted not only to assess the prognosis of patients near the end of their life but also to provide physicians and cancer patients with information allowing avoiding unproven systemic treatment in patients who had previously received at least two chemotherapy lines. We did not include breast cancer patients because multiple lines of systemic therapy exist and are more numerous than in the other solid tumors treated in our institute. Such situation is very frequent, and a recent review concerning the

Table 3 Multivariate prognostic analysis for OS

Characteristics		HR [95% CI]	*p* value
Sex	Male vs. female	1.26 [0.51–3.12]	0.62
Primary tumor type	Lung vs. colorectal	0.38 [0.12–1.24]	0.11
	Ovary vs. colorectal	0.28 [0.07–1.03]	0.06
	Sarcoma vs. colorectal	0.55 [0.21–1.41]	0.21
	Other vs. colorectal	0.81 [0.35–1.86]	0.62
Score-based group	B vs. A	4.64 [1.92–11.21]	6.5E−04
	C vs. A	7.15 [2.01–25.41]	2.4E−03

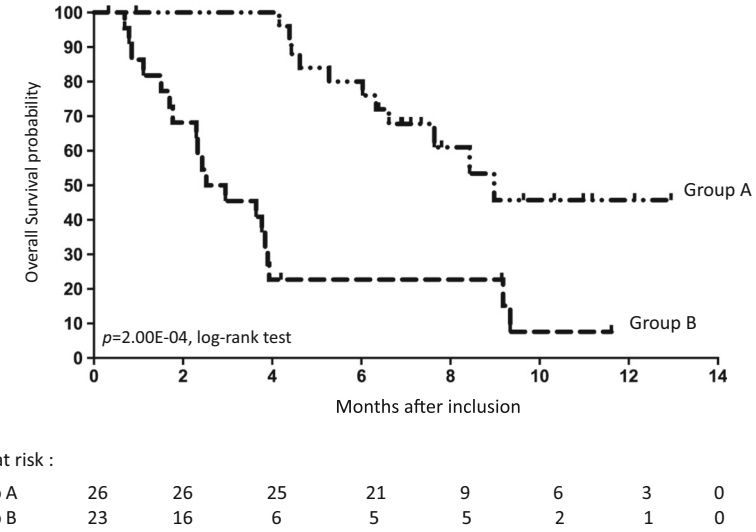

Fig. 2 Survival curves of the subgroup of patients with PS 0–2. Kaplan-Meier OS curves in 49 patients with PS 0–2 of groups A and B. Patients from group C were excluded from the figure because of the small number ($N = 2$)

aggressiveness of cancer care near the end of life [7] reported that, from the SEER results, the proportion of patients still receiving chemotherapy within 14 days before death rose from 9.7% in 1993 to 11.6% in 1999, despite data showing that overly aggressive cancer treatment potentially indicates poor-quality care. The authors suggested different explanations for such decisions [21]. For the physician, they could be seen as a source of hope, they were often easier to recommend, and they could be driven by anecdotal experience. On the other hand, the patients may request an aggressive treatment because they have unrealistic expectations about their actual prognosis and the benefit of chemotherapy. More recently, a cohort study from Ontario [22] confirmed that the aggressiveness of cancer care near the end of life increased with time and that patients were currently more likely to receive chemotherapy, to visit the emergency department, and to be admitted to the intensive care unit. However, these rates, and particularly those of chemotherapy and intensive care unit admissions, were far less common in Canada than in the USA, perhaps due to differences in health system characteristics. In Korea, this trend was also described by Lee et al. [23], who showed that the likelihood of receiving chemotherapy during the last month of life increased in 2005 (2-fold) and 2010 (4.4-fold) compared with that in the year 2000. In a recent study of 1193 US patients [4], 69% of those with lung cancer and 81% of those with colorectal cancer did not report understanding that chemotherapy was not at all likely to cure their cancer, thus compromising their ability to make informed treatment decisions. Moreover, if a physician improved the understanding of the patient, this action could come at the cost of the patient's satisfaction with the physician. Indeed, patients who reported a higher score for physician communication were at a higher risk for inaccurate expectations.

However, some studies have shown that if some cancer patients could accept toxic treatment for even a 1% of chance of a cure, most would be unwilling to accept the same treatment for a benefit in life expectancy without a cure. This misunderstanding could represent an obstacle to optimal end-of-life planning and care. However, in a study focused on cancer patients' role in treatment decisions [24], the shared control between physicians and patients was great when there was good evidence to support the treatment, but when there was either no evidence for or evidence against a treatment, the physician control was greater than the patient control. The authors concluded that "better strategies for shared decision making may be needed when there is no evidence to support benefit of a treatment or when patients have terminal illnesses that cannot be cured." Thus, our target must be physicians. However, in a recent series of 722 patients with metastatic lung or colorectal cancer [25], 18% received chemotherapy in the last month of life; surprisingly, this percentage was the same for those who knew that chemotherapy was not at all likely to cure their cancer (21.7%) and for those who did not (15.8%).

The score we prospectively studied here in this short series could help physicians to identify the patients who will die shortly after initiation of this "new therapeutic line" and who might be spared the constraints and toxicity of treatment and be immediately directed towards the best supportive care [26]. It could also help patients in their decision-making [27]. Taking into account the small sample size of our study, it will be of interest to go further with a better designed study including more patients to have "evidence-based" data in this specific setting. Of course, this score does not provide information to determine whether a patient with a better prognosis will actually derive benefit from this treatment. However, a recent prospective study [28] examined the effect of chemotherapy use on the quality of the last 2 weeks of life in a cohort of 312 patients, of whom 51% received chemotherapy and 49% did not. Chemotherapy use was not associated with patient

survival; it was more common in patients with good performance status (PS 0–1) at study entry. However, among these PS 0–1 patients, chemotherapy use was associated with a lower quality of life near death than was non-use. In patients with moderate (PS 2) or poor (PS 3) baseline performance status, the use of chemotherapy did not improve quality of life near death. The authors concluded that the quality of life near death in patients with end-stage cancer is not improved and can be harmed by chemotherapy use near death, even in patients with good performance status. In a commentary concerning this paper, Blanke and Fromme [29] said that equating treatment with hope is inappropriate and that, if an oncologist suspects the death of a patient within the subsequent 6 months, the default should be no active treatment.

In conclusion, this simple score based on four parameters (performance status, number of sites, serum LDH, and albumin) has a prognostic value in patients with different types of solid cancers who receive systemic chemotherapy beyond the second line. The main limitations of our study include the small sample size and the heterogeneity of population in terms of types of primary tumor and of number of previous lines of chemotherapy (between 2 and 5). But our goal was to assess this score. There was not previous sample size justification because our objective was to test in a limited and predetermined period of time the hypothesis that this score could be of interest even in a small cohort of patients. Of course, our results need to be confirmed in a prospective larger study, but yet they suggest that this score could be useful to help patients and physicians refrain from giving systemic chemotherapy when it will likely be harmful and inefficient.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Schnipper LE, Smith TJ, Raghavan D et al (2012) American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the top five list for oncology. J Clin Oncol 30:1715–1724. doi:10.1200/JCO.2012.42.8375
2. Silvestri G, Pritchard R, Welch HG (1998) Preferences for chemotherapy in patients with advanced non-small cell lung cancer: descriptive study based on scripted interviews. BMJ 317:771–775. doi:10.1136/bmj.317.7161.771
3. Slevin ML, Stubbs L, Plant HJ et al (1990) Attitudes to chemotherapy: comparing views of patients with cancer with those of doctors, nurses, and general public. BMJ 300:1458–1460
4. Weeks JC, Catalano PJ, Cronin A et al (2012) Patients' expectations about effects of chemotherapy for advanced cancer. N Engl J Med 367:1616–1625. doi:10.1056/NEJMoa1204410
5. The AM, Hak T, Koëter G, van Der Wal G (2000) Collusion in doctor-patient communication about imminent death: an ethnographic study. BMJ 321:1376–1381
6. Institute of Medicine (US) and National Research Council (US) National Cancer Policy Board (1999) Ensuring quality cancer care. National Academies Press (US), Washington
7. Earle CC, Landrum MB, Souza JM et al (2008) Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? J Clin Oncol 26:3860–3866. doi:10.1200/JCO.2007.15.8253
8. Barbot A-C, Mussault P, Ingrand P, Tourani J-M (2008) Assessing 2-month clinical prognosis in hospitalized patients with advanced solid tumors. J Clin Oncol 26:2538–2543. doi:10.1200/JCO.2007.14.9518
9. Cortes J, O'Shaughnessy J, Loesch D et al (2011) Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet 377:914–923. doi:10.1016/S0140-6736(11)60070-6
10. Oken MM, Creech RH, Tormey DC et al (1982) Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649–655
11. Buccheri G, Ferrigno D, Tamburini M (1996) Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. Eur J Cancer 1990 32A:1135–1141
12. Harrell FE, Lee KL, Mark DB (1996) Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 15:361–387. doi:10.1002/(SICI)1097-0258(19960229)15:4<361::AID-SIM168>3.0.CO;2-4
13. Ma C, Bandukwala S, Burman D et al (2010) Interconversion of three measures of performance status: an empirical analysis. Eur J Cancer 1990 46:3175–3183. doi:10.1016/j.ejca.2010.06.126
14. Maltoni M, Nanni O, Pirovano M et al (1999) Successful validation of the palliative prognostic score in terminally ill cancer patients. Italian multicenter study group on palliative care. J Pain Symptom Manag 17:240–247
15. Maltoni M, Scarpi E, Pittureri C et al (2012) Prospective comparison of prognostic scores in palliative care cancer populations. Oncologist 17:446–454. doi:10.1634/theoncologist.2011-0397
16. O'Mahony S, Nathan S, Mohajer R et al (2016) Survival prediction in ambulatory patients with stage III/IV non-small cell lung cancer using the palliative performance scale, ECOG, and lung cancer symptom scale. Am J Hosp Palliat Care 33:374–380. doi:10.1177/1049909115570707
17. Morita T, Tsunoda J, Inoue S, Chihara S (2001) Improved accuracy of physicians' survival prediction for terminally ill cancer patients using the Palliative Prognostic Index. Palliat Med 15:419–424
18. Stone CA, Tiernan E, Dooley BA (2008) Prospective validation of the palliative prognostic index in patients with cancer. J Pain Symptom Manag 35:617–622. doi:10.1016/j.jpainsymman.2007.07.006
19. de Kock I, Mirhosseini M, Lau F et al (2013) Conversion of Karnofsky Performance Status (KPS) and Eastern Cooperative Oncology Group Performance Status (ECOG) to Palliative Performance Scale (PPS), and the interchangeability of PPS and KPS in prognostic tools. J Palliat Care 29:163–169
20. Hui D, Park M, Liu D et al (2016) Clinician prediction of survival versus the Palliative Prognostic Score: which approach is more accurate? Eur J Cancer 1990 64:89–95. doi:10.1016/j.ejca.2016.05.009
21. Chan W, Lam K, Siu W, Yuen K (2016) Chemotherapy at end-of-life: an integration of oncology and palliative team. Support Care Cancer 24:1421–1427. doi:10.1007/s00520-015-3031-z
22. Ho TH, Barbera L, Saskin R et al (2011) Trends in the aggressiveness of end-of-life cancer care in the universal health care system of Ontario, Canada. J Clin Oncol 29:1587–1591. doi:10.1200/JCO.2010.31.9897
23. Lee HS, Chun KH, Moon D et al (2015) Trends in receiving chemotherapy for advanced cancer patients at the end of life. BMC Palliat Care 14:4. doi:10.1186/s12904-015-0001-7

24. Keating NL, Beth Landrum M, Arora NK et al (2010) Cancer patients' roles in treatment decisions: do characteristics of the decision influence roles? J Clin Oncol 28:4364–4370. doi:10.1200/JCO.2009.26.8870
25. Mack JW, Walling A, Dy S et al (2015) Patient beliefs that chemotherapy may be curative and care received at the end of life among patients with metastatic lung and colorectal cancer. Cancer 121:1891–1897. doi:10.1002/cncr.29250
26. Assi T, El Rassy E, Tabchi S et al (2016) Treatment of cancer patients in their last month of life: aimless chemotherapy. Support Care Cancer 24:1603–1608. doi:10.1007/s00520-015-2959-3
27. Delgado-Guay MO, Rodriguez-Nunez A, De la Cruz V et al (2016) Advanced cancer patients' reported wishes at the end of life: a randomized controlled trial. Support Care Cancer 24:4273–4281. doi:10.1007/s00520-016-3260-9
28. Prigerson HG, Bao Y, Shah MA et al (2015) CHemotherapy use, performance status, and quality of life at the end of life. JAMA Oncol 1:778–784. doi:10.1001/jamaoncol.2015.2378
29. Blanke CD, Fromme EK (2015) Chemotherapy near the end of life: first—and third and fourth (line)—do no harm. JAMA Oncol 1:785–786. doi:10.1001/jamaoncol.2015.2379