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CON EDITORIAL

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Has survival increased in cancer patients admitted to the ICU? No

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For a contrasting viewpoint, please go to
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As stated by Mokart, Pastores and Darmon in this issue [1], a number of studies have convincingly argued that the overall outcome of cancer patients in the intensive care unit (ICU) has improved over the last two decades [2]. Although we believe this is true for a significant number of critically ill cancer patients, this finding relies on cohorts of heterogeneous populations, and unrestricted application to all cancer patients would certainly be inaccurate. Table 1 illustrates this heterogeneity focusing on underlying diagnoses, severity of illness and especially the proportion of patients under mechanical ventilation which-is closely related to outcome. Although non-invasive ventilation (NIV) is assumed to have a beneficial effect on outcome if employed in cancer patients with acute respiratory failure, the failure rate is high yielding a grim prognosis, even worse than that of patients who undergo immediate invasive mechanical ventilation [3]. So only a small proportion of 10–20 % of patients are likely to be successfully managed by NIV [4, 5]. As the outcome of invasively mechanically ventilated patients is improving [3, 6], new trials are needed to address the current benefits of NIV in this population.

As a matter of fact, some subgroups of critically ill cancer patients remain affected with a desperately low survival rate, in relation with the characteristics of underlying malignancies and/or with the type of acute complication warranting ICU admission. For instance, patients with lung cancer still carry very high in-ICU mortality rates, especially when poor performance status, airway obstruction or extensive (non-resectable) disease are present [7]. Furthermore, the in-hospital mortality is high among ICU survivors, and maintenance of optimal treatment of lung cancer is most often jeopardized in such patients with severely impaired functional status or residual organ dysfunctions. However, not all types of lung cancer display the same prognosis. Inaugural small cell lung cancer is usually highly susceptible to chemotherapy with a potential for reversal of related acute complications. Subsets of lung adenocarcinoma with mutations within the epidermal growth factor receptor or the ALK tyrosine kinase are now affordable to emerging targeted agents. The long-term outcomes of these latter diseases will be reappraised, thereby justifying a broader ICU admission policy than beforehand. Hematopoietic stem cell transplantation (HSCT) recipients also remain viewed as a high-risk subgroup in the ICU that seemingly

Table 1 Study populations in critically ill cancer patients during recent years

Study	PY	*n*	Population (%): hematol./solid/HSCT	MV (%)	Severity of illness scores	Survival: ICU/hospital/1-year
Staudinger et al. [12]	2000	414	58/42/9	62	APACHE III: 33	53/NR/23
Azoulay et al. [13]	2001	237	71/29/18	80	SAPS II: 58	30/27 (day 30)/NR
Kroschinsky et al. [14]	2002	104	100/0/NR	52	SAPS II: 46	56/NR/29
Maschmeyer et al. [11]	2003	189	46/54/14	50	NR	69/46/NR
Soares et al. [6]	2010	717	7/93/2	27	SAPS II: 32	79/70/NR
Azoulay et al. [15]	2010	220	84/16/25	37	LOD: 5	NR/69 (day 28)/NR
Bird et al. [16]	2012	199	100/0/42	52	APACHE II: 21	66/54/41 (6-month)
Legrand et al. [17]	2012	428	84/16/20	54	SAPS II: 56	60/50/37
Mokart et al. [18]	2012	70	94/6/20	94	SAPS II: 52	27/NR/13
Azoulay et al. [2]	2013	1,011	100/0/25	48	NR	72/61/43
Azevedo et al. [3]	2014	263	14/87/3	85	SAPS III: 54	46/33/NR

PY publication year, *MV* invasive mechanical ventilation, *HSCT* hematopoietic stem cell transplantation, *NR* not reported, *ICU* intensive care unit

did not benefit from the general improvement in outcome. Nonetheless this represents a good example of how a crude consideration of an underlying condition may lead to general conclusions irrelevant to particular subgroups. Indeed, not all HSCT recipients carry the same risk in the ICU. Treatment-related morbidity and mortality of autologous HSCT are low. In contrast, allogeneic HSCT is associated with a grossly 20 % risk of ICU admission subsequently associated with a high fatality rate, especially when invasive ventilation is required. Furthermore, some important features related to the procedure have delineated some prognostic subgroups. Basically, corticosteroid-resistant graft-versus-host disease (GVHD) remains associated with dismal survival rates while complications occurring within the engraftment period might be associated with decent survival rates [8].

Beyond the prognosis related to the underlying malignancy itself, some acute complications remain challenging. Multiple organ failure (MOF) is the most common mechanism of death in ICU cancer patients and is usually associated with poor outcomes if not reversible in the first week of treatment. However, MOF is not a disease by itself but a syndrome that should be balanced relative to its primary etiology. Bacterial infections often present with higher severity but have a potential of reversal [9]. In contrast, the prognosis of invasive fungal infections in critically ill cancer patients, and especially invasive aspergillosis, remains poor despite the development of new molecular tools likely to improve and to shorten the diagnostic process, as well as less toxic and probably more efficient antifungal drugs [10, 11]. Sinusoidal obstruction syndrome complicating HSCT remains a devastating condition for which the treatment with defibrotide did not fulfil its initial promise in most severe patients. Furthermore, the absence of definite diagnosis for the acute complication is commonly associated with increased risk of death. This might be related in part to patients subjected to therapeutic limitations and who therefore did not undergo appropriate diagnostic procedures, but this clearly represents a major area of improvement. We would even argue that ICU admission could be justified in order to perform appropriate diagnostic work-up.

Definitive assertions deserve caution since they may lead to simplistic attitudes towards the decision-making process of ICU admission in such patients. In other words, how should we understand the high fatality rate in such patients? Multiple prognostic studies published for more than two decades have allowed some reliable prognostic subgroups of patients to be defined. So should we now restrict ICU admission to patients with good anticipated survival rates? We believe that it would definitely represent a step backward. Indeed, most of our current knowledge about management of critically ill cancer patients arose from cohorts that included various patients with different prognosis ranging from the worst to the best. Advances in the field have been made possible through the still necessary selection of patients with a realistic oncologic project and a decent functional status, but also through improved management of the most severe patients who were affected with very high mortality rate in the past. As a result, some patients who would have been declined ICU admission a few years ago for the reason of futility may now exhibit reasonable survival rates. Finally we would like to stress the particular situation of patients with advanced-stage malignancies enrolled in therapeutic trials addressing the efficiency of new drugs or new treatment protocols. Undoubtedly, such patients are prone to early therapeutic limitations and a high mortality rate, but it is our commitment to support advances in the treatment of cancer and accurate assessment of complications related to new drugs.

Conflicts of interest The authors state that they have no competing interest with the subject.

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