

EDITORIAL



## The good physician and the great physician: why a physician should consider the ESMO guidelines on the management of cancer cachexia?

Fifty years after passage of the National Cancer Act and right now when strategies are put forward to implement the European Union initiative Europe's Beating Cancer, it might be important to assess whether new areas of synergic intervention, including nutrition support, should be implemented. It is acknowledged that patients with newly diagnosed cancer now face a reduced risk of rapid tumor progression and premature mortality.<sup>1</sup> Significant challenges remain, however, which may jeopardize the perception of the benefits so far obtained. Among them, the issues of quality of life and the clinical benefit gap between trials and the real world should have priority in the planning of the optimal management of patients with cancer for the next decades.

It is genuinely believed that offering longer survival by implementing new therapies would translate to improved quality of life. Unfortunately, this reasoning is not supported by the evidence,<sup>2</sup> which may also suggest that survival *per se* may not represent the optimal outcome measure to capture the efficiency of anticancer therapies.<sup>3</sup> Highlighting this gap, quality of life is not a parameter frequently reported in registration trials.<sup>4</sup> It is understood that disease-modifying therapies, i.e. chemotherapy, radiotherapy, surgery, immunotherapy, etc., target cancer cells and aim at extending survival. Nevertheless, it has been reported that 10% of the survival benefit achieved by implementing anticancer therapies may be spent in hospital rather than at home.<sup>5</sup> This may not represent the benefit to which most patients with advanced cancer may aspire when starting their journeys. Suboptimal and late implementation of supportive care may explain not only the poor performance of anticancer therapies as far as quality of life is considered, but also the discrepancy observed between survival benefits obtained in registration trials and those reported in the real world.

Cancer care is based on two major strategies; disease-modifying therapies and supportive care. Although they should be concurrently implemented, data from real life show an unacceptable delay in starting supportive care.<sup>6</sup> Understanding the reasons for this delay may help in devising proactive clinical protocols. Patients with cancer are frequently polymorbid, and the number of comorbidities significantly worsens clinical outcomes and prevents enrollment in clinical trials.<sup>7</sup> Malnutrition is a frequent

comorbidity of patients with cancer, with a negative impact on outcome.<sup>8</sup> In contrast with other comorbidities, malnutrition is preventable and treatable when addressed in a timely manner,<sup>9</sup> thereby possibly contributing to better quality of life and extended survival. Unfortunately, prevention and treatment of cancer-associated malnutrition is not considered as a key component of anticancer therapies. Nicely designed and conducted clinical trials are becoming available in the literature, however, and suggest that patient-tailored modulation of nutritional intake improves quality of life and may enhance the efficacy of anticancer therapies.<sup>10</sup>

In this changing scenario, in which the apparent discrepancy between disease-modifying therapies and supportive care is being reconciled, the European Society for Medical Oncology (ESMO) guidelines on treatment of cancer cachexia mark a true landmark considering the evolving holistic approach to patients with cancer.<sup>11</sup> Although they acknowledge the limitations imposed by the soft supporting literature, they still recommend that patients with cancer should be screened for the presence of malnutrition upon their first oncological visit, and referred to health care specialists in case of malnutrition risk. Beyond the clinical benefits for patients receiving anticancer therapies, early nutritional care may help to reduce the proportion of patients with cancer who are currently ineligible for optimal treatment. A new framework for cancer therapies, in which biological age plays a key role, has been proposed.<sup>12</sup> Sarcopenia is a reliable clinical index of biological age,<sup>12</sup> and robust evidence shows that it is modifiable,<sup>13</sup> even in the last phase of the clinical journey of patients with cancer.<sup>14</sup> Clinical conditions associated with sarcopenia and frailty, however, increase toxicities<sup>15</sup> and impede evidence-based therapies.<sup>16</sup> Prevention and reversal of sarcopenia by early nutritional care may contribute to effectively address these relevant clinical issues.

ESMO guidelines are based on a clinically-driven and pragmatic approach: considering the negative impact of malnutrition, it is preferable to take the risk that nutritional support is minimally effective, rather than accepting the certainty that patients will suffer the clinical consequences of malnutrition. Should then all patients with cancer be referred for nutritional support? Of course not. Nutritional support is a medical therapy and as such should be implemented when the possible benefits outweigh the potential harms. ESMO guidelines show once more that the target of clinical decisions is the patient with cancer, whose needs and aspirations should be considered from the beginning of their long clinical

journey. To quote Dr. William Osler, ‘the good physician treats the disease, the great physician treats the patient who has the disease’.

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## DISCLOSURE

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