“Sufficient Life Expectancy”: An Amazing Inclusion Criterion in Cancer Phase II-III Trials

To the Editor: A tremendous change in eligibility criteria has been observed during the past two decades in the majority of clinical trials. The number of eligibility criteria has notably increased and they are more and more factual. They may include the biologic signature of the tumor. For example, some ongoing studies investigating HER or KIT antagonists consider only patients without k-ras or with specific KIT (D816H/V) mutations. In such a context of sophistication of eligibility criteria, the concept of sufficient life expectancy (SLE) appears as an amazing and rather subjective eligibility criterion. With this in mind, we reviewed all the study protocols of phase II or III trials (n = 123) carried out in our institution between 1991 and 2008. We assessed how frequently the SLE criterion was requested and which types of studies required it. Eighty-four studies (68%) were phase II trials, and 81 (66%) were industry sponsored. In one study protocol, the SLE criterion coexisted with 51 other eligibility criteria. The primary end points were response rate (86 trials; 70%), survival (19 trials; 16%), and quality-of-life measurements (18 trials; 14%). The most frequent tumors were breast cancers (27 trials; 22%), sarcomas (13 trials; 10%), and colorectal cancers (10 trials; 8%). The SLE criterion was required in 75 of 123 trials (61%). The most frequent SLE cut-offs were 4 and 6 months (24% and 33%, respectively). All these 75 study protocols required both the SLE criteria and a “good performance status.” None of them provided any tool or relevant reference that could enlighten the investigator in properly assessing the SLE. Overall, the SLE criterion was significantly more frequent in industry-sponsored studies (odds ratio [OR], 6.1; range, 2.7 to 13.8), in trials written after 2003 (OR, 3.4; range, 1.5 to 7.7), and in those with response rate as the primary objective (OR, 2.4; range, 1.1 to 5.3).

Therefore, this review confirms that this SLE criterion still remains frequently requested, especially in industry-sponsored studies and in studies considering the response rate as the primary end point. Surprisingly, despite the abovementioned increasing sophistication in eligibility assessment, this SLE criterion was more frequent in recent studies. The SLE criterion remains based on the sole subjective clinical evaluation. We do not deny the underlying philosophy of using this criterion. Excluding frail patients with a foreseeable life expectancy that does not seem long enough to assess the treatment effects is logical. However, especially for performance status, there are speculations about the real value of such a criterion. It is worth it to note that, at least in phase I studies, recent efforts have been made for rational selection of patients, using objective and measurable parameters that predict survival at baseline.1,2 Similar efforts are awaited for phase II and III trials.

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