Regarding this reason, FDA may mandate, for ethical reasons, that prior therapy be one of the inclusion criteria (71).

The inclusion/exclusion criteria for many thousands of clinical trials are available on www.clinicaltrials.gov. About 500 of these clinical trials concerns second-line therapy, that is, therapy for patients where a previous treatment has failed. The following is only one example of many. The example is from the trial, "Temsirolimus Versus Sorafenib as Second-Line Therapy in Patients with Advanced RCC Who Have Failed First-Line Sunitinib" (72). The list of inclusion criteria requires that, "subjects must have at least 1 cycle of sunitinib therapy." Another example, from a publication by the FDA, is a trial on multiple myeloma (73).

TABLE 4.1 ECOG Performance Status[a]

Grade	ECOG Performance Status
0	Fully active, able to carry on all predisease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, eg, light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

[a]*Oken MM, Creech RH, Tormey DC., et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am. J. Clin. Oncol. 1982;5:649–55.*

i. Poor Performance Status as a Basis for Exclusion

Potential subjects who have already been exposed to first-line therapy may have a declined performance status, due to drugs or radiation administered during the first-line therapy. Poor performance status has been defined as a score of 2 on the ECOG rating scale, as shown in Table 4.1. According to Wakelee and Belani (74), patients with poor performance status, as assessed by ECOG performance status, "are often excluded from clinical trials. They tend to have poorer responses to treatment and shorter survival than their counterparts with PS scores of 0–1. It is also generally believed that they are at greater risk for toxicity." Similarly, according to Hennesy et al. (75), "[e]lderly patients and patients with poorer performance statuses are often excluded from clinical trials … where it was generally considered that these patients experienced higher toxicity rates … [e]lderly patients often have comorbid conditions."

j. Irreversible and Cumulative Toxicity as a Basis for Exclusion

Although most chemotherapeutic agents have an associated toxicity, reversible side effects

[71]T.G. Roberts, Jr. e-mail of January 14, 2011.

[72]Clinicaltrials.gov identifier NCT00474786.

[73]Hazarika M, Rock E, Williams G, et al. Lenalidomide in combination with dexamethasone for the treatment of multiple myeloma after one prior therapy. Oncologist 2008;13:1120–7.

[74]Wakelee H, Belani CP. Optimizing first-line treatment options for patients with advanced NSCLC. Oncologist 2005;10 (Suppl. 3):1–10.

[75]Hennessy BT, Hanrahan EO, Breathnach OS. Chemotherapy options for the elderly patient with advanced non-small cell lung cancer. Oncologist. 2003;8:270–7.