cancer)." According to Dr. T.G. Roberts (50) and Prof. T.J. Lynch (51) oncology clinical trials that are called "second-line trials" require patients to have been exposed to a first-line regimen (before enrolling in the second-line trial). One reason for this requirement is to help ensure a homogeneous group of study subjects (52). Another reason is to give study subjects a chance to have the best available treatment prior to enrolling in the second-line trial. Regarding this reason, the FDA may mandate, for ethical reasons, that prior therapy be one of the inclusion criteria (53).

The inclusion/exclusion criteria for many thousands of clinical trials are available on www.clinicaltrials.gov. About 500 of these clinical trials concern 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" (54). 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 (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 (56) 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. (57) "[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."

[50] Roberts Jr. TG. E-mail of January 14, 2011.
[51] Lynch TJ. E-mail of January 17, 2011.
[52] Roberts Jr. TG. E-mail of January 14, 2011.
[53] Roberts Jr. TG. E-mail of January 14, 2011.
[54] Clinicaltrials.gov identifier NCT00474786.
[55] 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;13:1120–1127.
[56] Wakelee H, Belani CP. Optimizing first-line treatment options for patients with advanced NSCLC. *Oncologist*. 2005;10(suppl 3):1–10.
[57] Hennessy BT, Hanrahan EO, Breathnach OS. Chemotherapy options for the elderly patient with advanced non-small cell lung cancer. *Oncologist*. 2003;8:270–277.