1. Complete Response (CR): Disappearance of all target lesions.
2. Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.
3. Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered progression.
4. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

b. Objective response – Demetri's example of partial response

The clinical trial of Demetri et al. (34) concerned gastrointestinal stromal tumors (GIST). Patients received imatinib, a small molecule that inhibits a small group of related tyrosine kinases, including the KIT receptor tyrosine kinase. The clinical trial contained two arms, where patients in arm A received 400 mg imatinib daily, and arm B received 600 mg imatinib daily.

There was no control group. But data from earlier clinical trials demonstrated that responses of this type of cancer to standard forms of chemotherapy were low. The documented objective response rate was 5%, and the overall survival in unresectable patients was less than 12 months (35). Subsequent clinical trials assessing the safety and efficacy of imatinib for GIST also did not contain any control group, for example the clinical trial of Heinrich et al. (36).

The following provides some background information regarding GIST. Most GISTs result from activating mutations in the KIT receptor tyrosine kinase, where this activating mutation is the mechanism responsible for about 85% of GIST patients. In about 8% of GIST patients, the mechanism responsible for the cancer is an activating mutation in a related enzyme, namely, platelet-derived growth factor receptor-alpha (PDGFRA) (37). The survival of metastatic GIST patients is dramatically improved by treatment with the KIT and PDGFRA inhibitor imatinib, a small molecule that

[34] Demetri GD, von Mehren M, Blanke CD, et al. Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *New Engl J Med*. 2002;347:472–480.

[35] von Mehren M. E-mail of May 2, 2011.

[36] Heinrich MC, Owzar K, Corless CL, et al. Correlation of kinase genotype and clinical outcome in the North American Intergroup Phase III Trial of imatinib mesylate for treatment of advanced gastrointestinal stromal tumor: CALGB 150105 Study by Cancer and Leukemia Group B and Southwest Oncology Group. *J Clin Oncol*. 2008;26:5360–5367.

[37] Demetri GD, Heinrich MC, Fletcher JA, et al. Molecular target modulation, imaging, and clinical evaluation of gastrointestinal stromal tumor patients treated with sunitinib malate after imatinib failure. *Clin Cancer Res*. 2009;15:5902–5909.