

of random assignment, and the terminating point was the date when a relapse first occurred or, in the case of persistent disease and other causes of deaths.”

Where data establish that a drug results in DFS of several years, the question arises if it can be concluded that the patient has actually been cured. Commentary from Pui (5) provides the following perspective to this issue. Where a drug results in DFS of three years in about 90% of the study subjects, it is reasonable to require a follow-up time of several more years to establish that a cure had been effected.

II. DIFFERENCE BETWEEN DISEASE-FREE SURVIVAL AND PROGRESSION-FREE SURVIVAL

Where a patient’s cancer is completely removed by surgery, as part of the clinical study protocol, the physician may wonder if progression-free survival (PFS) or DFS is the better endpoint to use. In this situation, these two endpoints are likely to be identical, since immediately after surgery all subjects are considered to be disease free, and all subjects are in a state where the physician is awaiting for the moment when progression is detected (6).

But PFS has a different meaning than DFS. Usually, the endpoint of PFS is used in the context of advanced disease, that is, when the primary treatment had failed to lead to a complete remission, when tumors still linger, and where these tumors are destined to progress (7). PFS implies that detectable disease was present at baseline whereas DFS (or the endpoint of relapse-free survival) has traditionally been used for patients without evidence of disease at baseline (8). Both terms enable the investigator to mark the time from intervention until detectable worsening of the disease. Published reports of PFS describe patients with metastatic disease, whereas published reports of DFS are likely to focus on early stage patients (9).

Disease-free survival is the usual primary endpoint of adjuvant breast cancer trials, since it is considered a good surrogate for the ultimate endpoint, overall survival (10). In breast cancer, DFS is composed of distant and local/regional metastases. According to Dr. Miguel Martin, the endpoint of progression-free survival (PFS) should be reserved for metastatic breast cancer trials, that is, for trials where subjects have advanced cancer at baseline (11).

⁵ Pui C.-H. Toward a total cure for acute lymphoblastic leukemia. *J Clin Oncol.* 2009;27:5121–5123.

⁶ Bepler G. E-mail of August 19, 2010.

⁷ Bepler G. E-mail of August 19, 2010.

⁸ Hudis CA. E-mail of August 19, 2010.

⁹ Hudis CA. E-mail of August 19, 2010.

¹⁰ Martin M. E-mail of August 18, 2010.

¹¹ Martin M. E-mail of August 18, 2010.