## a. Endpoint of event-free survival

Event-free survival (EFS) is used in about 25% of all clinical trials on leukemia (221). This endpoint is used in about 7% of all oncology clinical trials, where it is used mainly for clinical trials in leukemia and lymphoma, but also sometimes for clinical trials in neuroblastoma, breast cancer, and lung cancer (222). This endpoint is rarely used in clinical trials in colorectal cancer, myelodysplastic disorder, prostate cancer, and melanoma.

Event-free survival (EFS) may be the preferred endpoint, where the investigator wants the endpoint to reflect the primary treatment, and not subsequent treatments that are given where the study drug fails, and not subsequent treatments that are given if relapse occurs (223). Where the study drug fails, subsequent treatments are often not controlled by the investigator. In contrast to the endpoint of EFS, the endpoint of overall survival takes into account second-line treatments that are given where the study drug fails, or where the study drug is unacceptably toxic.

In some clinical trials, EFS may be the preferred endpoint, where the cancer in question can be reliably treated by existing drugs. In this situation, use of *overall survival* as the endpoint would not make much sense, as this particular endpoint would be triggered by so few study subjects. According to Basso et al. (224) recent advances for treating childhood acute lymphocytic leukemia (ALL) allow the "vast majority" of patients to achieve complete remission and then to be cured. In the words of another physician, "[i]n pediatric as opposed to adult oncology, EFS is the preferred end point for almost all of our trials. This is because of the generally high cure rates for our diseases" (225).

Event-free survival has been defined in a number of ways in clinical trials for the various leukemias, as documented in the following bullet points. The author's survey of oncology articles also revealed that a small proportion of articles failed to define EFS (226). Hence, the medical writer should be vigilant and ensure that this definition be included in any Clinical Study Protocols and manuscripts.

[221] Search in *Journal of Clinical Oncology* of all articles published from 1990 to 2011, with "leukemia" as search term in title/abstract, and "event-free survival" as search term in entire text. Search conducted March 9, 2011.

[222] A search in *Journal of Clinical Oncology*, conducted March 7, 2011, probed articles published from 1990 to 2011. Of 1,145 articles containing the term "event-free survival" (anywhere in the article), some 531 articles contained the term "leukemia" or "lymphoma" in the title/abstract, 93 articles contained the term "breast," 89 contained "neuroblastoma," but only 19 contained "myelodysplastic," six contained "melanoma," three contained "prostate," and one contained "pancreatic" or "pancreas" in the title/abstract.

[223] Nachman JB. E-mail of March 10, 2011.

[224] Basso G, Veltroni M, Valsecchi MG, et al. Risk of relapse of childhood acute lymphoblastic leukemia is predicted by flow cytometric measurement of residual disease on day 15 bone marrow. *J Clin Oncol*. 2009;27:5168–5174.

[225] Nachman JB. E-mail of March 10, 2011.

[226] Survey of all 504 articles containing the term "event-free survival" published in *Journal of Clinical Oncology*, in the years 2005 to 2011. This survey was conducted on March 7, 2011.