investigator of the Tarhini study stated that only data from the second examination were reported, where these data served to confirm data from the first examination (54).

Another methodological point is as follows. This concerns the relationship between the endpoints of PFS and overall survival. According to Gradishar et al. (55) "[p]atient survival data were not mature at the time of data cutoff for this publication." This statement reveals an advantage of endpoints such as progression-free survival, time to progression (TTP), and disease-free survival (DFS), over the endpoint of overall survival. The advantage is that PFS, TTP, and DFS can be calculated long before enough data are available for calculating overall survival. Progression of a tumor, or a corresponding parameter in clinical trials on fatal infections, can occur long before the event (death) used for calculating the endpoint of overall survival. Investigators might not have enough information to calculate overall survival because study subjects continue to live beyond the timeframe originally expected by the investigators, because of the need to terminate the trial early due to a dwindling supply of potential enrollees, or because of a need for immediate publication in a journal. For all of these reasons, the endpoints of PFS, TTP, and DFS are advantageous over the endpoint of overall survival.

4. The endpoint of PFS may have an advantage, where PFS data are more statistically significant than overall survival data – the Robert study

In a study of breast cancer, Robert et al. (56) enrolled subjects into two arms, as indicated below. Only subjects with overexpressed HER2, as measured in tumor biopsies, were enrolled in the trial. The level of HER2 overexpression was either 2+ or 3+. The investigators documented whether each subject expressed HER2 at the 2+ level or 3+ level, enabling separate analysis of the study results according to these two subgroups of subjects. The two arms were as follows. Arm A is the same as arm B, except that arm A includes carboplatin:

- Arm A. Trastuzumab, paclitaxel, and carboplatin (TPC)
- Arm B. Trastuzumab and paclitaxel (TP).

Trastuzumab (Herceptin®) is an antibody that specifically binds to human epidermal growth factor receptor type-2 (HER2). This receptor is a membrane-bound protein located on the surface of tumor cells. HER2, which is overexpressed in about 25–30% of breast cancer patients, is a biomarker for poor prognosis (57). Techniques for

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