

Table 14.1 The Romond study

	Arm A. Control	Arm B. Trastuzumab	Hazard ratio	Significance
DFS at 3 years	75.4%	87.1%	HR = 0.48	P < .0001
Overall survival at 3 years	91.7%	94.3%	HR = 0.67	P = .015

endpoint that has been used for accelerated or regular approval is progression-free survival (PFS).”

IV. DISEASE-FREE SURVIVAL PROVIDES EARLIER RESULTS ON EFFICACY THAN OVERALL SURVIVAL – THE ADD-ON BREAST CANCER STUDY OF ROMOND

In a study of breast cancer, Romond et al. (17) treated women with surgery, and assayed tumor samples for expression of the biomarker, HER2. Only women with overexpressed HER2 were enrolled. These were randomized into two arms, as indicated.

- Arm A. Doxorubicin and cyclophosphamide, followed by paclitaxel
- Arm B. Doxorubicin and cyclophosphamide followed by paclitaxel and concurrent trastuzumab.

To be enrolled in the trial, patients were required to have breast cancer that was surgically treated, where surgery resulted in the complete resection of the primary tumor. Potential subjects with metastasis were not permitted to enroll in the trial.

The endpoints included DFS and overall survival. The endpoint of DFS was tolled as follows. Events determining DFS were local, regional, and distant recurrence; contralateral breast cancer, including ductal carcinoma in situ; other second primary cancers; and death before recurrence or a second primary cancer. It should be noted that the value for DFS was expressed as the value found at the 3-year time point, and that the value was not expressed in terms of median DFS.

The results for both endpoints, that is, DFS and overall survival, appear in [Table 14.1](#) and demonstrate the advantage of including the antibody in the treatment scheme.

Disease-free survival for the trastuzumab arm and control arm is shown in the first Kaplan-Meier plot ([Fig. 14.1](#), Panel A). This plot shows that trastuzumab provides a dramatic early advantage over the control treatment.

Overall survival for the trastuzumab arm and control arm is shown in the second Kaplan-Meier plot ([Fig. 14.1](#), Panel B). This plot shows that trastuzumab also provides a dramatic advantage over the control treatment. But according to this endpoint, this advantage is not evident until four years have passed.

¹⁷ Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *New Engl J Med.* 2005;353:1673–1684.