



**Figure 13.3** Schematic representation of Kaplan-Meier plot. This was a 1-arm study. All patients received gefitinib. The two curves show TTP for the subgroup of 25 patients with high EGFR (FISH positive), and TTP for the subgroup of 11 patients with low EGFR (FISH negative)

greater efficacy was demonstrated with the endpoints of objective response, TTP, and overall survival.

The Cappuzzo study provides the take-home lesson that, to forestall data acquisition problems due to short follow-up times, it is wise to include endpoints that can be fully captured early in the clinical trial. Suitable endpoints that can be captured early in the trial include objective response (RECIST criteria) and TTP.

A schematic representation of the Kaplan-Meier plot demonstrates the striking differences in TTP that were associated with the change in EGFR gene copy number (Fig. 13.3). The authors concluded that EGFR FISH analysis is an accurate predictor for efficacy with gefitinib therapy against lung cancer. To conclude, the Cappuzzo study demonstrates that EGFR is a useful biomarker. Other biomarkers, such as HER2 and KRAS, are described in this book in the chapter on biomarkers and personalized medicine.

## IX. METHODOLOGY TIP – ADVANTAGE OF USING AN ENDPOINT THAT INCORPORATES A “MEDIAN” TIME

The data of Cappuzzo et al. (28) as disclosed above, were incomplete for the endpoint of overall survival, as indicated in Table 13.4. As explained by the authors, “the median follow-up time was too short...for significant tests of differences in survival outcomes.”

But one might ask how a clinical trial can be too short to calculate results of median overall survival, but not be too short to calculate median TTP. The following

<sup>28</sup> Cappuzzo F, Ligorio C, Jänne PA, et al. Prospective study of gefitinib in epidermal growth factor receptor fluorescence in situ hybridization-positive/phospho-Akt-positive or never smoker patients with advanced non-small-cell lung cancer: the ONCOBELL trial. *J Clin Oncol.* 2007;25:2248–2255.