



**FIGURE 13.2** Kaplan–Meier plot of overall survival. The *upper curve* represents OS data from subjects receiving gefitinib, while the *lower curve* represents OS data from subjects receiving carboplatin plus paclitaxel.

produced later on in the trial, it might be concluded that gefitinib had superior efficacy to carboplatin plus paclitaxel. But when all the data are taken into account, the difference between the two study arms was not significant ( $P = 0.31$ ).

The difference in OS was also measured by the parameter of median OS. The median survival time was 30.5 months for the gefitinib group, and 23.6 months for the carboplatin plus paclitaxel group. According to this parameter, gefitinib had superior efficacy to carboplatin plus paclitaxel.

To view the big picture, the data on objective response, PFS as measured by the hazard ratio, median PFS, and OS, all show that gefitinib has superior efficacy to carboplatin plus paclitaxel.

As in all clinical trials, roughly equal emphasis was placed on collecting efficacy data and safety data. The Maemondo study revealed that

gefitinib was less toxic, producing diarrhea and rash, while the combination of carboplatin plus paclitaxel was more toxic, producing hematologic and neurologic toxic effects. Thus, the superior efficacy data for gefitinib, in terms of the PFS endpoint, together with gefitinib's lesser toxicity, recommends gefitinib as a preferred chemotherapy for NSCLC. According to more recent review articles, the preferred treatments for NSCLC include gefitinib, cisplatin, or carboplatin, depending on the characteristics of the patient (46,47).

#### d. Methodology Tip—Shapes of Kaplan–Meier Plots in the Maemondo Study

Wittes (48) made an observation regarding Kaplan–Meier plots where two curves, for example, representing study drug arm versus

<sup>46</sup>de Marinis F, Rossi A, Di Maio M, Ricciardi S, Gridelli C. Treatment of advanced non-small-cell lung cancer: Italian Association of Thoracic Oncology (AIOT) clinical practice guidelines. *Lung Cancer*. Mar 24, 2011 [Epub ahead of print].

<sup>47</sup>Keedy VL, Temin S, Somerfield MR, et al. American Society of Clinical Oncology provisional clinical opinion: epidermal growth factor receptor (EGFR) mutation testing for patients with advanced non-small-cell lung cancer considering first-line EGFR tyrosine kinase inhibitor therapy. *J. Clin. Oncol.* April 11, 2011 [Epub ahead of print].

<sup>48</sup>Wittes J. Times to event: why are they hard to visualize? *J. Natl Cancer Inst.* 2008;100:80–1.