a. Use of the Word "Rate"

As mentioned in Chapter 12, the term "rate" is often used when reporting objective response, PFS, and other endpoints. This is potentially confusing because in general, as in the fields of chemistry, physics, and physiology (42), the word rate always refers to the ratio of [events]/[unit of time]. The unit of objective response is not a rate, or at least, it is not the same kind of rate as used in chemistry, physics, and physiology. In clinical trial reporting, the word "rate," as it applies to endpoints, actually refers to "percent" or "proportion" (43).

b. Endpoint Keyed to One Specific Time Point—6-Month PFS

When reporting data from clinical trials, PFS can be expressed in terms of "median PFS," which is the data when exactly half of the subjects have experienced this endpoint. The unit for this time point is months. Alternatively, PFS can be expressed in terms of a specific date, such as "6-month PFS." Six-month PFS means the percent of all of the study subjects who have experienced PFS by the 6-month time point in the clinical trial. The unit for this time point is percent.

Lamborn et al. (44) point out an advantage of using PFS that is tied to a specific time point, "[w]hen PFS is used as the primary efficacy end point, a fixed time point (in this case 6 months) reduces time-dependent assessment bias, such as that caused by visit or imaging frequency."

c. Data on PFS may be More Significant Than Data on Overall Survival—The Maemondo Study

In a study on nonsmall-cell lung cancer (NSCLC), Maemondo et al. (45) divided study subjects into two arms:

- Arm A. Gefitinib (study drug).
- Arm B. Carboplatin plus paclitaxel combination (standard treatment).

Chemotherapy was for 9 weeks and, in some cases longer, and following chemotherapy subjects were followed for about 42 months. During this follow-up period, the response of the tumors to chemotherapy was assessed by computed tomography at 2-month intervals. Analysis by computed tomography enabled the measurement of size and number of lung tumors, and comparison of the size and number with the RECIST criteria. In conducting this comparison, the researchers classified the objective response as partial response, complete response, stable disease, or progressive disease.

The endpoints in the Maemondo study included objective response, PFS, and OS. The results for objective response are shown in Table 13.1. These results demonstrate that geftinib worked better than the carboplatin−paclitaxel combination, in terms of all of the parameters. For example, the percent of subjects experiencing partial reponse was about twice as great in the geftinib arm as in the carboplatin plus paclitaxel arm. The percent of subjects experiencing progressive disease

[42]Reaction rate, heart rate, blood cell sedimentation rate.

[43]Eisenhauer EA. E-mail of September 11, 2010.

[44]Lamborn KR, Yung WK, Chang SM, et al. Progression-free survival: an important end point in evaluating therapy for recurrent high-grade gliomas. Neuro. Oncol. 2008;10:162−70.

[45]Maemondo M, Inoue A, Kobayashi K, et al. Gefitinib or chemotherapy for non-small-cell lung cancer with mutated EGFR. New Engl. J. Med. 2010;362:2380−8.