Protocol. Instead, the modified ITT group was based on a predetermined subgroup of the study population. To view the big picture, it is almost always the case that clinical trials stratify the study population into various subgroups, such as by age, gender, or location of the clinic. In the Gralla study, subgroups were defined, not during the event of stratification, but according to a criterion that was applicable only after therapy had commenced, where this criterion was the need to administer doxorubicin or cyclophosphamide. For subgroups defined by any technique, or for subgroups defined either before or after initiation of the clinical trial, analysis by this subgroup will fall under the category of modified ITT analysis or PP analysis.

VIII. START DATE FOR ENDPOINTS IN CLINICAL STUDIES

In a survey, Mathoulin-Pelissier et al. (83) revealed that published clinical studies often fail to define the start date, or fail to provide a clear definition of an endpoint. These particular problems encumber at least a quarter of published clinical studies. Deviations from the proper start date, as set forth by ICH Guidelines (date of randomization), are documented below.

Endpoints have a start date and a date of measurement, where what is measured can be an objective endpoint such as tumor number, a biochemical parameter, or a clinical endpoint such as change in performance status score. As documented below, the start dates may vary in different studies. The start date may be the date of diagnosis, the date of randomization, the date of surgery, or a date that is exactly six months after surgery (84). Hence, the medical writer needs to be vigilant, not only in ensuring that the start date is identified in regulatory submissions and manuscripts, but also when comparing publications on clinical trials.

The most usual start date is the date of randomization. For example, date of randomization was used as the start date in studies of colon cancer by van Geelan et al. (85) and by Gill et al. (86) studies of breast cancer by Goss et al. (87) by Schmid

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