analysis, the efficacy results are similar to each other.

Why was the efficacy of the active control greater in the PP group than in the ITT group? Efficacy was measured by the parameter of "treatment failure" which, in turn, was defined as the summation of, "patients who were lost to follow-up, those who dropped out owing to adverse events," and those with actual disease according to analysis of trypanosomal DNA in the blood. A large proportion (one-third) of the patients had treatment failure. Of the 26 patients in the study drug group, 9 had treatment failure, where 5 of these withdrew because of adverse events and 4 were lost to follow-up.

The take-home lesson is as follows. If a *large proportion* of the subjects enrolled in a clinical trial is excluded from the PP analysis group (and included in the ITT analysis group), and where the most prevalent reason for exclusion was for lack of "efficacy," then it will likely be the case that efficacy results from the PP group and ITT group will be different.

b. ITT Analysis Versus PP Analysis—The Sethi Study

In a study of bronchitis infections, Sethi et al. (24) used both ITT analysis and PP analysis, and defined the PP population to exclude patients who violated any aspect of the study protocol to a degree that might affect assessment of treatment efficacy. Protocol violations that might affect assessment were determined prior to beginning the study and included violation of exclusion criteria (including age), serious or complicating infection or disease, active alcohol or drug abuse, use of prohibited concomitant medication, compromising adverse event, medication or visit noncompliance, failure to meet the inclusion criterion of acute exacerbations of chronic bronchitis, and an outcome of "unable to determine."

c. ITT Analysis Versus PP Analysis—The Abrial Study

In a study of chemotherapy for breast cancer, Abrial et al. (25) used both ITT analysis and PP analysis. Per protocol analysis was conducted because a large fraction of the study subjects did not receive the entire treatment. Eight subjects out of 50 did not receive the entire treatment because of allergy or toxicity. Hence, the clinical results and data from mammograms and ultrasound were calculated on both an ITT basis (50 subjects) and PP basis (42 subjects).

Data from PP analysis were somewhat more favorable than with ITT analysis. Regarding clinical evaluation of efficacy, complete response was found in 26% of the ITT subjects and in 31% of the PP subjects. Regarding the objective evaluation of efficacy (mammograms), complete response was found in 18% of the ITT subjects, while complete response was found in 21.4% of the PP subjects. ITT analysis and PP analysis showed similar efficacy results.

[24]Sethi S, Breton J, Wynne B. Efficacy and safety of pharmacokinetically enhanced amoxicillin-clavulanate at 2,000/125 milligrams twice daily for 5 days versus amoxicillin-clavulanate at 875/125 milligrams twice daily for 7 days in the treatment of acute exacerbations of chronic bronchitis. Antimicrob. Agents Chemother. 2005;49:153–60.

[25]Abrial C, van Praagh I, Delva R, et al. Pathological and clinical response of a primary chemotherapy regimen combining vinorelbine, epirubicin, and paclitaxel as neoadjuvant treatment in patients with operable breast cancer. Oncologist 2005;10:242–9.