at least 80% or took more than 120% of the prescribed dose. Adherence was checked by pill count at visit 4 (day 0) for the placebo run-in phase and at visit 5 (6 weeks) and visit 6 (12 weeks) for the treatment phase. Patients found not to have adhered to the clinical trial regimen at visits 5 or 6 were not included in the PP analysis. One hundred and forty-three subjects were used for the ITT analysis, while 129 were used for PP analysis. The authors found no differences in the results with either analysis.

e. ITT analysis vs. PP analysis – the Geddes study

Geddes et al. (27) defined PP analysis as all treated subjects with clinical signs and symptoms of sepsis and proven infection, excluding major protocol violators. Major protocol violators, who were not included in the PP population, were subjects with incorrect entry diagnosis, incorrect treatment duration, antibiotic pre-treatment, or a missing post-treatment clinical evaluation. The investigators conducted both ITT analysis and PP analysis in their clinical study of two different antibiotic treatments. According to ITT analysis, the cure rate for levofloxacin (77%) was higher than that for imipenem/cilastatin (68%). According to PP analysis, the cure rate for levofloxacin (89%) was similar to that for imipenem/cilastatin (85%). Thus, the Geddes study documents an example where ITT analysis and PP analysis resulted in different conclusions regarding efficacy.

f. ITT analysis vs. PP analysis – the Chauffert study

In a study of pancreatic cancer, Chauffert et al. (28) PP analysis was defined as patients without major protocol deviations who received >75% of the planned dose of radiotherapy or >75% of the induction dose of gemcitabine. According to PP analysis, the therapeutic results for the gemcitabine arm were slightly more favorable, with respect to the radiotherapy arm. In this clinical trial, PP analysis had a confirmatory role in this study.

III. DISADVANTAGES OF ITT ANALYSIS

Most comments regarding ITT analysis versus PP analysis dwell on biases that occur with use of PP analysis. But biases can also result when ITT analysis is used. According to Neuesch et al. (29) ITT analysis can introduce bias into the analysis of the clinical

[27] Geddes A, Thaler M, Schonwald S, Härkönen M, Jacobs F, Nowotny I. Levofloxacin in the empirical treatment of patients with suspected bacteraemia/sepsis: comparison with imipenem/cilastatin in an open, randomized trial. *J Antimicrob Chemother.* 1999;44:799–810.

[28] Chauffert B, Mornex F, Bonnetain F, et al. Phase III trial comparing intensive induction chemoradiotherapy (60 Gy, infusional 5-FU and intermittent cisplatin) followed by maintenance gemcitabine with gemcitabine alone for locally advanced unresectable pancreatic cancer. *Ann Oncology.* 2008;19:1592–1599.

[29] Nüesch E, Trelle S, Reichenbach S, et al. The effects of excluding patients from the analysis in randomised controlled trials: meta-epidemiological study. *Brit Med J.* 2009;339:b3244.