laboratory tests are available. Patients are enrolled in anti-infective trials when presenting with appropriate symptoms, and it might take too long to get a culture result back before treating them. Later, the culture might show they did not have the type of infection the drug was intended to treat, and they may be excluded from the primary efficacy analysis (70). This is in contrast to the situation in oncology clinical trials, where analysis of a tumor biopsy is required for enrollment. Moreover, it should be pointed out that bacterial infections sometimes take the form of a medical emergency, in contrast to the situation with cancer.

In a study of pneumonia treated with either monotherapy (levofloxacin) or combination therapy (cefotaxine plus ofloxin), Leroy et al. (71) conducted a modified ITT analysis and PP analysis. The ITT group contained 398 randomized patients. The modified ITT group (308 patients) excluded patients where the infection had been misdiagnosed. In all, 62 patients had been misdiagnosed. The PP group (271 patients), which excluded patients with major protocol violations, required that a causative pathogen for pneumonia was isolated on study inclusion. A number of misdiagnosed subjects, excluded from the modified ITT group, had been admitted to an intensive care unit on an emergency basis, where misdiagnosis was due to pulmonary embolism or heart failure, which can mimic the symptoms of pneumonia (72).

g. Exclusion of study subjects because of failure to satisfy the inclusion criteria, and for withdrawing consent – the Dupont study

In a study of antibiotic treatment against peritonitis, Dupont et al. (73) conducted an ITT analysis, modified ITT analysis, and PP analysis. ITT analysis was conducted on 227 subjects.

For modified ITT analysis, subjects in which infection was not proven were later excluded. Twenty-three subjects were excluded. Also, 14 patients of the subjects in the randomized group were excluded from the ITT group, after they withdrew their consent.

Per protocol analysis excluded subjects who had major deviations from the clinical study protocol. For the PP analysis, 45 more subjects were excluded.

[70] Bittman R. E-mail of July 14, 2010.

[71] Leroy O, Saux P, Bédos JP, Caulin E. Comparison of levofloxacin and cefotaxime combined with ofloxacin for ICU patients with community-acquired pneumonia who do not require vasopressors. *Chest*. 2005;128:172–183.

[72] Leroy O. E-mail of August 31, 2010.

[73] Dupont H, Carbon C, Carlet J. Monotherapy with a broad-spectrum beta-lactam is as effective as its combination with an aminoglycoside in treatment of severe generalized peritonitis: a multicenter randomized controlled trial. *Antimicrob Agents Chemother.* 2000;44:2028–2033.