the steady dropout of subjects due to gastrointestinal distress, aversion to the taste of the study drug, had the consequence that the modified ITT group was only 175 subjects, and the PP group was only 153 subjects.

o. Excluding Subjects Who Failed to Receive the Assigned Treatment Because of Adverse Events—The Caraceni Study

In a study of neuropathic pain, Caraceni et al. (84) analyzed the data by ITT analysis and by modified ITT analysis.

The ITT population consisted of all subjects with at least one administration of gabapentin or placebo. The modified ITT population consisted of 115 patients, where the inclusion criterion for this analysis was at least 3 days of pain assessments. Reasons for withdrawing patients from the trial were adverse events in six patients (7.6%) receiving gabapentin and in three patients receiving placebo (7.3%). Five patients (two in the placebo group and three in the gabapentin group) had less than 3 days of follow-up.

Analysis of the ITT population (120 subjects) showed a significant difference of average pain intensity between gabapentin and placebo group ($P = 0.0250$). Modified ITT analysis also demonstrated a significant difference in pain intensity between the gabapentin group and placebo group ($P = 0.0257$).

p. Modified ITT Group Based on a Subgroup of Study Subjects—The Gralla Study

In a study of chemotherapy-induced vomiting, Gralla et al. (85) provided patients with a control antiemetic regimen, or with an antiemetic regimen that included an additional drug, namely, aprepitant. There were 1043 study subjects in all. Aprepitant is a small organic molecule. A modified ITT approach was used to analyze the data, and included all patients who received cisplatin, took study drug, and had at least one posttreatment assessment.

The criterion for receiving posttreatment assessment was that the patient receive only the most emetogenic (vomiting-inducing) combination of chemotherapeutic drugs. This combination involved doxorubicin and cyclophosphamide.

This criterion resulted in only 142 study subjects (out of 1043 subjects) being included in the modified ITT analysis.

Results from the ITT group, and from the modified ITT group, showed that including aprepitant was effective in reducing vomiting, where a more dramatic result came from analysis of the modified ITT group. Gralla referred to this group as, "A modified intent-to-treat approach."

The Gralla study provides an example where the definition of the modified ITT group was not based on the usual criterion of compliance with the Clinical Study 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

[84]Caraceni A, Zecca E, Bonezzi C, et al. Gabapentin for neuropathic cancer pain: a randomized controlled trial from the Gabapentin Cancer Pain Study Group. J. Clin. Oncol. 2004;22:2909–17.

[85]Gralla RJ, de Wit R, Herrstedt J. Antiemetic efficacy of the neurokinin-1 antagonist, aprepitant, plus a 5HT3 antagonist and a corticosteroid in patients receiving anthracyclines or cyclophosphamide in addition to high-dose cisplatin. Cancer 2005;104:864–8.