m. 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. (81) 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 three 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 three days of follow-up.

Analysis of the ITT population (120 subjects) showed a significant difference of average pain intensity between gabapentin and placebo group ($P = .0250$). Modified ITT analysis also demonstrated a significant difference in pain intensity between the gabapentin group and placebo group ($P = .0257$).

n. Modified ITT group based on a subgroup of study subjects – the Gralla study

In a study of chemotherapy-induced vomiting, Gralla et al. (82) provided patients with a control anti-emetic regimen, or with an anti-emetic regimen that included an additional drug, namely, aprepitant. There were 1,043 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 post-treatment assessment.

The criterion for receiving post-treatment assessment was that the patient receives 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 1,043 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 expressly referred to this group as the modified ITT group, 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

[81] 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;22:2909–2917.

[82] 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;104:864–868.