2. Synopsis

Clinical Study Synopsis: Study B3M-MC-S006

Title: Cefaclor 40 mg/kg versus Amoxicillin/clavulanate 45 mg/kg in the 10-day Treatment of Acute Otitis Media

Investigators: This multicenter study included 15 principal investigators.

Study Centers: There were 15 study centers.

Dates of Study: 18 September 2000 to 19 April 2001

Clinical Phase: Phase IV

Objectives: The primary objective of this study was to test the hypothesis that the therapeutic effects of cefaclor for 10 days were at least equivalent to the therapeutic effects of amoxicillin/clavulanate, 7:1 ratio, for the 10 day treatment of acute otitis media (AOM). The secondary objectives were to compare the safety and gastrointestinal tolerability.

Methodology: Multicenter, single-blind (investigator-blinded), randomized, parallel treatment group study

Number of Patients: Cefaclor: Male 60, Female 44, Total 104
Amoxicillin/clavulanate: Male 60, Female 43, Total 103

Diagnosis and Inclusion Criteria: See Sections 3.4.2 (Criteria for Enrollment) and 3.4.3 (Disease Diagnostic Criteria) of the Protocol.

Dosage and Administration: Test Product
Cefaclor: 40 mg/kg/day given in two divided doses (with a maximum of 1 g/day)
Reference Therapy
Amoxicillin/clavulanate (7:1 ratio): 45 mg/kg/day given in two divided doses (dose based on the amoxicillin component)

Duration of Treatment:
- Cefaclor: 10 days
- Amoxicillin/clavulanate: 10 days

Criteria for Evaluation:
**Efficacy**—
- Pretherapy (within 48 hours of the first dose): Demographics, previous medical history, assessment of AOM signs and symptoms
- During Therapy (Day 3 to 5 after start of therapy): Symptoms by telephone visit and/or optional clinical visit
- End of Therapy (Day 8 to 12 after start of therapy): Evaluation and clinical response determined
- Posttherapy (Day 14 to 28 after start of therapy): Test-of-Cure visit – follow-up evaluation and clinical response determined

**Safety**—
Adverse events and gastrointestinal (GI) tolerability were monitored throughout the study.

Statistical Methods:
- All statistical significance tests were two-sided. Statistical significance was taken at the 5% level. Symptomatic responses were compared between the treatments by constructing a 90% confidence interval about the difference between proportions of success in each treatment group. Summary statistics for GI tolerability scores and sign and symptom severity scores were generated by visit and treatment. The incidence of GI events was compared between treatment groups by constructing a contingency table of treatment and score, and treatments were compared using a Kruskal-Wallis Test. Sign and symptom scores were also compared between the treatment groups using a Kruskal-Wallis Test. Fisher's exact test was used to compare adverse event frequencies between the treatment groups.

Summary and Conclusions:
Cefaclor had an equivalent therapeutic effect to amoxicillin/clavulanate when given over 10 days for the treatment of acute otitis media. For the All Patients Population-Termination Response, indeterminate responses excluded, the observed success rates (cure or improvement) were 95.9% for cefaclor patients and 93.9% for amoxicillin/clavulanate patients. The noninferiority of
cefaclor with reference to amoxicillin/clavulanate was formally demonstrated for the 10-day treatment of AOM. As for the safety profile, there were no statistically significant differences found between cefaclor and amoxicillin/clavulanate for unsolicited adverse events. Diarrhea of a mild or moderate severity was reported statistically more often by patients receiving amoxicillin/clavulanate as evaluated by the use of the solicited GI questionnaire.