These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert in the country of prescription. Ketek is not indicated in this patient population

Sponsor / Company: sanofi-aventis **Drug substance(s):**Telithromycin (HMR3647)	**Study Identifier:** NCT00174811 **Study code:** EFC6131
Title of the study: Multinational, randomized, double-blind, double-dummy, comparative study to evaluate the efficacy and safety of telithromycin 25 mg/kg given once daily for 5 or 10 days depending on age and previous treatment history versus cefuroxime axetil 15 mg/kg, given twice daily for 10 days, in children with acute otitis media	
Study center(s): Multicenter, international study in 15 countries (enrolling: Argentina, Chile, Costa Rica, Dominican Republic, France, Guatemala, Mexico, Panama, Peru, Portugal, Russian Federation, Taiwan, United States; not enrolling: Brazil, Germany) with a total of 43 active centers	
Study period: Date first subject/patient enrolled: 20 Jun 2005 Date last subject/patient completed: 27 Jun 2006	
Phase of development: Phase 3	
Objectives: Primary objective of this study was to demonstrate the noninferiority of telithromycin with respect to cefuroxime axetil in clinical efficacy at the posttherapy/test-of cure (TOC) Visit 3 (Day 13 to 17) in the per protocol population (PPc) for analysis of clinical outcome in children with acute otitis media (AOM).	
Methodology: Multicenter, international, randomized, double-blind, double-dummy, comparative study	
Number of subjects/patients:	
Planned: 900; Randomized: 639 (the study was terminated on 20 September 2007 before enrollment was completed)	
Treated: 633; Evaluated: 633 for efficacy; 633 for safety; 27 for pharmacokinetics	
Diagnosis and criteria for inclusion: Patients between 6 and 60 months of age with confirmed AOM with the following inclusion criteria participated: • Recent and rapid onset of AOM signs and symptoms • The presence of middle ear fluid (MEF) on otoscopy • Otalgia or ear tugging or touching • At least 1 of the following clinical findings not specific to AOM: fever, vomiting, diarrhea, anorexia, sleep disturbance, or irritability • Tympanocentesis performed per protocol with MEF sample collected.	

Investigational product: Telithromycin 50 mg/mL oral suspension

Dose: 25 mg/kg (oral suspension 50 mg/mL to a maximum of 1200 mg/day) once a day

Administration: Oral

Duration of treatment: Telithromycin: 10 days for high risk patients (≤24 months of age who received antibacterials for AOM within the past 30 days) and 5 days all other patients

Duration of observation: 28 days

Reference therapy: Cefuroxime axetil 15 mg/mL oral suspension

Dose: : 15 mg/kg (oral suspension 15 mg/mL not to exceed 500 mg/day or 1000 mg/day, depending on local health authority guidelines) twice daily for 10 days

Administration: Oral

Placebo: Powder for oral suspension matching that which contained the excipients of telithromycin or cefuroxime.

Administration: Oral

Criteria for evaluation:

Efficacy/pharmacodynamic:

The primary efficacy assessment was clinical efficacy at the posttherapy/TOC visit (Day 13 to Day 17) in the clinically evaluable per protocol population. A patient was considered to be clinically cured if the following criteria were met:

- AOM-related fever was absent
- Otoscopic examination of the tympanic membrane improvement
- No surgical procedure and no subsequent antibacterial were administered for AOM or its complications

Safety:

The safety assessments were adverse events (AEs), vital sign measurements and clinical laboratory variables. In addition, specific alert terms also defined as adverse event of special interest (AESI) identified as critical to the safety evaluation of the product, were subject to expedited reporting and included cardiac, hepatic, and visual AEs.

Pharmacokinetics:

Plasma and MEF samples were collected for the determination of telithromycin concentrations.

Health outcomes:

Quality of life variables included unscheduled office visits or emergency room visits, days missed from school, number of days the caregiver missed work or usual activities and the additional hours of child care.

Statistical methods:

Because this study was terminated after randomization of 639 of the planned 900 patients, consequently, the type II error was not controlled as planned, and only descriptive statistics were generated. No inferential statistical tests for noninferiority or superiority were carried out.

Analysis of safety measurements (vital signs, laboratory values, and AEs reported) was performed according to internal guidelines for the analysis and reporting of safety data from clinical trials on all patients who received at least 1 dose of study medication by treatment taken. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA Version 10.0).

Summary:

Because of the early termination of the study and limited data, no definite efficacy conclusions can be drawn.

Six hundred thirty-nine (639) patients were randomized and 520 (81.4%) were included in the PPc population at posttherapy (Day 13 to Day 17).

Efficacy/pharmacodynamic results:

The primary efficacy assessment of clinical outcome at posttherapy for the PPc population showed that the clinical cure rate for telithromycin was 90.0 % (235 of 261) and for cefuroxime 92.7% (240 of 259). The observed cure rates in both PPc and mITT populations were similar between the 2 treatment groups.

Safety results:

No deaths were reported during the study.

A total of 7 patients in the telithromycin group and 5 patients in the cefuroxime group experienced serious TEAEs. Two serious TEAEs in each treatment group were associated with the hepatobiliary system (telithromycin: increase in bilirubin and hepatic enzyme, Cefuroxime: hepatotoxocoity and increased alanine aminotransferase). One serious TEAE, "staring" was reported in 1 patient in each treatment group.

The most frequently reported TEAEs in either treatment group were gastrointestinal disorders (diarrhea, vomiting), infections (upper respiratory tract infection, nasopharyngitis, and gastroenteritis), and skin disorders (dermatitis and rash). Disorders of the eye were reported in 6 patients (conjunctivitis) in the telithromycin group and 2 patients (myopia and blurred vision) in the cefuroxime group.

Study treatment discontinuations due to TEAEs (telithromycin 13, cefuroxime 6) were mostly due to vomiting (8 events in the telithromycin group, 3 events in the cefuroxime group and) or skin disorders (3 events in the telithromycin group and none in the cefuroxime group).

For AESIs, the reporting of hepatic (telithromycin 4 and cefuroxime 5) and visual events (telithromycin 1and cefuroxime 3) were similar between treatment groups, and no cardiac AESIs were reported.

Postbaseline alanine aminotransferase (ALT) elevation >3 upper limit of normal (ULN) was noted; 1 in the telithromycin and 2 in the cefuroxime treatment group. One (1) patient in the telithromycin group had bilirubin elevation >2 ULN without ≥3 ULN increase in ALT. No patient in the cefuroxime group had elevated bilirubin. The number of patients with platelets >1.5 ULN was 22-in the telithromycin and 13 in the cefuroxime treatment group.

Pharmacokinetic results**:**

Due to the early termination of the study, pharmacokinetic samples were limited to 27 patients. Therefore, the pharmacokinetic/pharmacodynamic analyses were not performed.

Health Outcomes: Because of the early termination of the study, no conclusions can be drawn.

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