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Study No.: 25000/559		
Title: Efficacy and tolerability of amoxicillin/clavulanate versus cefaclor for a period of 10 days in the treatment of recurrent acute otitis media in children.		
Rationale: Amoxicillin is recommended for treatment of acute otitis media (AOM) but, in recurrent episodes, resistance may develop. The aim of this study was to compare the efficacy and tolerability of amoxicillin/clavulanate versus cefaclor in the treatment of recurrent acute otitis media (AOM) in children.		
Phase: IV		
Study Period: 10 January 2000 to 7 July 2002.		
Study Design: Multicentre, randomised, parallel group, single blind study.		
Centres: 31 centres in Italy.		
Indication: Recurrent AOM.		
Treatment: Subjects received 10 days of treatment with either amoxicillin/clavulanate 50mg/12.5mg/kg/day in 2 doses (every 12 hours), or with cefaclor 40mg/Kg/day in 3 doses (every 8 hours).		
Objectives: The primary objective was to evaluate the efficacy and tolerability of amoxicillin/clavulanate versus cefaclor for 10 days in the treatment of recurrent AOM in children.		
Primary Outcome/Efficacy Variable: The primary efficacy variable was the clinical response (recovery, improvement or failure) determined by the investigator at the end of treatment (Visit 2; 11-15 days after Visit 1).		
Secondary Outcome/Efficacy Variable(s): The secondary efficacy variables were: the clinical response (recovery, persistence of tympanic effusion or recurrence) determined at follow-up (Visit 3 and Visit 4, respectively 30-35 days and 90-95 days after the end of treatment); the average number of days with tympanic effusion; the number of recovered subjects at impedenziometric examination at each visit; and the number of asymptomatic subjects during the study.		
Statistical Methods: For the efficacy variables, differences between the treatment groups were analysed using the Student t-test and/or analysis of variance (ANOVA) for parametric variables, and the Mann-Whitney test for non-parametric variables. The intent-to-treat (ITT) population included all randomised subjects who took at least 1 dose of study medication. The safety population was the same as the ITT population.		
Study Population: Male and females aged between 6 months and 12 years with a diagnosis of recurrent AOM were enrolled. Subjects were excluded if they had known hypersensitivity to antibiotic beta-lactamase, in particular to amoxicillin/clavulanate and cefaclor; had otorrhoea due to perforation of the ear drum; had treatment with any antibiotic in the 7 days prior to enrolment; had medical conditions that had to be treated with other antibiotics; had human immunodeficiency virus (HIV), kidney failure, thrombocytopenia or hepatic insufficiency.		
	Amoxicillin/clavulanate	Cefaclor
Number of Subjects:		
Planned, N	300	300
Randomised, N	293	303
Completed, n (%)	276 (94)	289 (95)
Total Number Subjects Withdrawn, n (%)	17 (6)	14 (5)
Withdrawn due to Adverse Events, n (%)	6 (2)	1 (<1)
Withdrawn due to Lack of Efficacy, n (%)	1 (<1)	0
Withdrawn for Other Reasons, n (%)	10 (3)	13 (4)
Demographics		
N (All subjects)	293	303
Females: Males	131: 162	121: 182
Mean Age, months (SD)	61.4 (32.5)	58.9 (29.1)
Race, n (%)	n/a	n/a
Primary Efficacy Results: (ITT Population)		
Clinical response at Visit 2	Amoxicillin/clavulanate (N=286)	Cefaclor (N=297)
Recovery, n (%)	115 (40.2)	78 (26.3)
Improvement, n (%)	155 (54.2)	182 (61.3)

Failure, n (%)	12 (4.2)	29 (9.8)
Not evaluable, n (%)	4 (1.4)	8 (2.7)
Treatment difference, (95% Confidence Interval [CI])	n/a	
p-value	0.0006	
Secondary Outcome Variable(s): (ITT Population)		
	Amoxicillin/clavulanate (N=286)	Cefaclor (N=297)
Clinical response at Visit 3		
N, evaluable	280	293
Recovery, n (%)	213 (76.1)	185 (63.1)
Persistence of tympanic effusion, n (%)	50 (17.8)	91 (31.0)
Recurrence, n (%)	14 (5.0)	16 (5.4)
Treatment difference, (95% CI)	n/a	
Clinical response at Visit 4		
N, evaluable	276	289
Recovery, n (%)	239 (86.6)	218 (75.4)
Persistence of tympanic effusion, n (%)	27 (9.8)	53 (18.3)
Recurrence, n (%)	9 (3.3)	16 (5.5)
Treatment difference, (95% CI)	n/a	
Days with tympanic effusion		
Mean days	33.8	45.1
Recovered subjects at impedenziometric examination (Visit 2)		
N, evaluable	189	184
Recovery, n (%)	78 (41.3)	35 (19.0)
Recovered subjects at impedenziometric examination (Visit 3)		
N, evaluable	190	189
Recovery, n (%)	134 (70.5)	108 (57.1)
Recovered subjects at impedenziometric examination (Visit 4)		
N, evaluable	189	186
Recovery, n (%)	156 (82.5)	133 (71.5)
Asymptomatic subjects (Visit 2)		
N, evaluable	286	297
Asymptomatic, n (%)	96 (33.6)	83 (27.9)
Asymptomatic subjects (Visit 3)		
N, evaluable	280	295
Asymptomatic, n (%)	176 (62.9)	164 (55.6)
Asymptomatic subjects (Visit 4)		
N, evaluable	276	293
Asymptomatic, n (%)	210 (76.1)	192 (65.5)
Safety Results: (Safety Population) - Adverse events (AEs) and serious adverse events (SAEs) occurring during the study were recorded.		
The safety population consist of all subjects who received at least one dose of study medication (randomized subjects) were assessed for clinical safety and were included in the safety analyses.		
	Amoxicillin/clavulanate (N=293)	Cefaclor (N= 303)
Most Frequent Adverse Events – On-Therapy	n (%)	n (%)
Subjects with any AE(s), n (%)	39 (13.3)	45 (14.8)
Vomiting	8 (2.7)	3 (1.0)
Diarrhoea	8 (2.7)	1 (0.3)
Otalgia	5 (1.7)	4 (1.3)
Irritability	5 (1.7)	3 (1.0)
Anorexia	3 (1.0)	9 (3.0)
Epigastralgia	3 (1.0)	4 (1.3)
Pyrexia	3 (1.0)	2 (0.7)

Rhinitis	2 (0.7)	5 (1.6)
Rhiynorrhoea	2 (0.7)	2 (0.7)
Cough	2 (0.7)	2 (0.7)
Erythema	2 (0.7)	0
Urticaria	2 (0.7)	1 (0.3)
Varicella	1 (0.3)	3 (1.0)
Otitis	0	4 (1.3)
Asthenia	0	3 (1.0)
Bronchitis	0	3 (1.0)
Tonsillitis	0	3 (1.0)
Serious Adverse Events (SAEs) - On-Therapy		
n (%) [n considered by the investigator to be related to study medication]		
	Amoxicillin/clavulanate (N=293)	Cefaclor (N= 303)
Subjects with non-fatal SAEs, n (%)	1 (0.3)	0
	n (%) [related]	n (%) [related]
Gastroenteritis	1 (0.3) [0]	0
Subjects with fatal SAEs, n (%)	0	0

Conclusion:

The percentage of subjects achieving recovery at Visit 2 was statistically significantly higher in subjects receiving amoxicillin/clavulanate compared with those receiving cefaclor. AEs were reported by 39 (13.3%) subjects in the amoxicillin/clavulanate group and 45 (14.8%) subjects in the cefaclor group. The most commonly reported AEs were vomiting and diarrhoea in the amoxicillin/clavulanate group and anorexia in the cefaclor group. One non-fatal SAE was reported following amoxicillin/clavulanate treatment.

Publications:

No Publication

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