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<b>Study No:</b> 574		
<b>Title:</b> A study to determine the pharmacokinetic profiles of amoxicillin and clavulanate over a 12 hour dosing interval in paediatric patients in the weight range of 5 to 40 kg receiving Augmentin at 45/3.2 mg/kg orally every 12 hours for up to 10 days.		
<b>Rationale:</b> For beta-lactam antibiotics, time above minimum inhibitory concentration (T>MIC) is the pharmacokinetic parameter most closely related to efficacy. This study, using the Augmentin '600' form at a ratio of 14:1 amoxicillin:clavulanate, was designed to assess T>MIC for amoxicillin (for an amoxicillin MIC of 4µg/mL) and the pharmacokinetics of amoxicillin and clavulanic acid in subjects in the weight range 5 to 40 kg, aged from at least three months to 12 years (no older than their 12 <sup>th</sup> birthday).		
<b>Phase:</b> I		
<b>Study Period:</b> 12 April 2000 to 19 September 2000.		
<b>Study Design:</b> Open-label, single period study.		
<b>Centres:</b> Three centres; 1 in Australia and 2 in the United States.		
<b>Indication:</b> Bacterial infection which could benefit from amoxicillin/clavulanate treatment.		
<b>Treatment:</b> Subjects were dosed with amoxicillin/clavulanate '600' at 45/3.2 mg/kg every 12 hours for up to 10 days via oral syringe. As the reconstituted suspension contained 600 mg amoxicillin per 5 mL (i.e. 120 mg/mL) and the dose was 45 mg amoxicillin per kg, the specific dose amount in mL for each subject was calculated based on weight, according to the following formula: (body weight x 45) / 120.		
<b>Objectives:</b> To obtain pharmacokinetic data on amoxicillin and clavulanate, plus T>MIC data for amoxicillin when amoxicillin/clavulanate '600' is given orally twice per day to subjects in the weight range of 5 to 40 kg.		
<b>Statistical Methods:</b> Subjects were included in the summary statistics provided that they had evaluable pharmacokinetic data. All subjects who received at least one dose of study medication were included in the evaluation of clinical safety and tolerability. As no statistical hypotheses were to be tested, the sample size was not based on formal power calculations. The initial sample size target of 15 subjects (up to a maximum of 20 subjects) was based on feasibility. All primary and secondary pharmacokinetic parameters were listed and summarized descriptively.		
<b>Study Population:</b> Subjects aged at least three months and no more than 12 years (no older than their 12 <sup>th</sup> birthday), who were in the weight range of 5 to 40 kg and with a bacterial infection which could benefit from amoxicillin/clavulanate treatment. At least three subjects had to be in the age range of three months to two years (no older than their 2 <sup>nd</sup> birthday) and, as far as possible, subjects of different ages and weights throughout the permitted range were entered into the study.		
<b>Number of Subjects:</b>		<b>All Subjects</b>
Planned, N		15-20
Dosed, N		24
Completed, n (%)		21 (87.5)
Total Number Subjects Withdrawn, n (%)		3 (12.5)
Withdrawn due to Adverse Events, n (%)		0
Withdrawn due to Lack of Efficacy, n (%)		0
Withdrawn for Other Reasons, n (%)		3 (12.5)
<b>Demographics</b>		
N (All Subjects)		24
Females: Males		10: 14
Mean Age in Years (SD)		5 (3.4)
Mean Weight in Kg (SD)		21.0 (9.4)
White, n (%)		13 (54.2)
<b>Pharmacokinetic (PK) Results: (PK Population)</b>		
<b>PK parameter</b>	<b>Amoxicillin (n=18)</b>	<b>Clavulanate (n=18)</b>
T>MIC (h), arithmetic mean (SD)	5.5 (1.25)	Not applicable
T>MIC <sup>a</sup> (%), arithmetic mean (SD)	46 (10)	Not applicable
C <sub>max</sub> [maximum plasma concentration] (µg/mL), arithmetic mean (SD)	16.5 (7.1)	1.73 (0.87)

T <sub>max</sub> [time to maximum plasma concentration] (h), median (range)	2.00 (1.00-4.02)	1.07 (0.98-4.00)
AUC <sub>(0-t)</sub> [area under the plasma concentration time curve from zero to the last quantifiable plasma concentration] (μg.h/mL), arithmetic mean (SD)	62.6 (16.3)	4.13 (1.86)
T <sub>½</sub> [terminal half-life] (h), arithmetic mean (SD)	1.36 (0.35)	1.10 (0.29) <sup>b</sup>
CL/F [apparent oral plasma clearance] (L/h/kg), arithmetic mean (SD)	0.77 (0.26)	1.11 (1.09) <sup>b</sup>
a T>MIC is based on amoxicillin MIC of 4 ug/mL		
b n=17.		
<b>Safety Results: (All Subjects)</b> Adverse events (AEs) and serious adverse events (SAEs) were collected throughout treatment until follow-up (within 3 days of final dose).		
<b>Adverse Events</b>	<b>All Subjects</b>	
N (All Subjects)	24	
No. subjects with AEs, n (%)	4 (17)	
<b>Serious Adverse Events (SAEs), n (%) [# considered by the investigator to be related to study medication]:</b>		
N	24	
No. subjects with non-fatal-SAEs, n (%) [related]	0	
No. subjects with fatal-SAEs, n (%) [related]	0	

**Publications:**

No publication

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