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<b>Study No.:</b> 25000/563			
<b>Title:</b> A single-blind, randomized, multicentre, parallel group study to compare the efficacy and safety of Augmentin 500/125mg po bid versus Cefaclor 250mg po tid versus Cefuroxime 250mg po bid in the treatment of acute exacerbations of chronic bronchitis in Chinese adult patients.			
<b>Rationale:</b> This study was designed to determine whether amoxicillin/clavulanate is at least as effective as a regimen of either cefaclor or cefuroxime orally (po) for the treatment of acute exacerbations of chronic bronchitis (AECB).			
<b>Phase:</b> IV			
<b>Study Period:</b> 20 June 2000 to 31 October 2000.			
<b>Study Design:</b> A randomised, single-blind, multicentre, parallel group study.			
<b>Centres:</b> 13 centres in China			
<b>Indication:</b> AECB.			
<b>Treatment:</b> Subjects were randomised (1:1:1) to receive amoxicillin/clavulanate 500/125mg twice daily (bid) po or cefaclor 250mg three times daily (tid) po or cefuroxime 250mg bid po. Treatment continued for a period of 7 days.			
<b>Objectives:</b> The primary objective was to compare the clinical efficacy and safety of amoxicillin/clavulanate 500/125mg po bid versus cefaclor 250mg po tid versus cefuroxime 250mg po bid in the treatment of AECB in Chinese adult subjects.			
<b>Primary Outcome/Efficacy Variable:</b> The primary efficacy variable was clinical response (cure, improvement, failure, recurrence, or indeterminate) at the end of therapy visit (Day 7-8) evaluated by the investigator based on symptoms of sputum purulence, cough, and dyspnoea.			
<b>Secondary Outcome/Efficacy Variable(s):</b> The secondary efficacy variable was bacteriological response at the end of therapy visit (Day 7-8). For each pathogen actually identified in an evaluable sputum at screening, the pathogen bacteriological outcome at the end of therapy visit was categorised as bacteriological eradication, presumed bacteriological eradication, persistence, presumed persistence, new infection, colonisation, or unable to evaluate.			
<b>Statistical Methods:</b> Efficacy variables were compared between the amoxicillin/clavulanate and cefaclor treatment groups and between the amoxicillin/clavulanate and cefuroxime treatment groups in the clinical per-protocol (PP) population. Treatments were compared using 90% confidence interval (CI) estimates of differences with the intention of demonstrating 'non-inferiority'. An overall significance level of 5% was used. Safety population were defined as a person who took at least one dose of investigational medication The per-protocol (PP) population: The patient completed all visits as specified by the protocol. No major protocol violation existed with regard to Inclusion / Exclusion criteria. 100% compliance for the first 72 hours and 80% - 120% overall compliance with study medication had been achieved			
<b>Study Population:</b> Male and female subjects aged 18 to 75 years (inclusive) were recruited if they had a history of chronic bronchitis characterised by cough and sputum production for more than 2 consecutive years and for most days in a consecutive 3-month period.			
	<b>Amoxicillin/ clavulanate</b>	<b>Cefaclor</b>	<b>Cefuroxime</b>
Number of Subjects:			
Planned, N	112	112	112
Randomised, N	121	119	120
Completed, n (%)	115 (95)	116 (97)	115 (96)
Total Number Subjects Withdrawn, n (%)	6 (5)	3 (3)	5 (4)
Withdrawn due to Adverse Events, n (%)	2 (2)	0	1 (1)
Withdrawn due to Lack of Efficacy, n (%)	3 (2)	1 (1)	2 (2)
Withdrawn for Other Reasons, n (%)	1 (1)	2 (2)	2 (2)
<b>Demographics</b>			
N (All Subjects)	121	119	120
Females: Males	47: 74	58: 61	56: 64
Mean Age, years (SD)	57.2 (12.59)	56.7 (12.34)	57.7 (11.4)
Chinese, n (%)	121 (100)	119 (100)	120 (100)
<b>Primary Efficacy Results: (Clinical PP Population)</b>			

	<b>Amoxicillin/ clavulanate (N=121)</b>	<b>Cefaclor (N=119)</b>	<b>Cefuroxime (N=120)</b>
<b>Clinical response at end of therapy visit</b>			
Clinical success (clinical cure + improvement), n (%)	112 (93)	111 (93)	110 (92)
Clinical failure (failure + recurrence + clinical outcome indeterminate), n (%)	9 (7)	8 (7)	10 (8)
Treatment comparison, 90% CI of difference (one tailed, lower limit)	Amoxicillin/ clavulanate VS Cefaclor -2.74%		Amoxicillin/ clavulanate VS Cefuroxime -1.42%
p-value	Amoxicillin/ clavulanate VS Cefaclor 0.89		Amoxicillin/ clavulanate VS Cefuroxime 0.89
<b>Secondary Outcome Variable(s): population had positive results of pathogen culture of sputum at entry, a bacteriological outcome was given at On Therapy visit.</b>			
	<b>Amoxicillin/ clavulanate (N=65)</b>	<b>Cefaclor (N=62)</b>	<b>Cefuroxime (N=63)</b>
<b>Bacteriological response at end of therapy visit</b>			
Proven eradication, n (%)	20 (31)	26 (42)	14 (22)
Presumed eradication, n (%)	39 (60)	29 (47)	44 (70)
Persistence, n (%)	5 (8)	4 (6)	5 (8)
New infection, n (%)	1 (2)	3 (5)	0
Bacteriological success rate, n (%)	59 (91)	55 (89)	58 (92)
Bacteriological failure rate, n (%)	6 (9)	7 (11)	5 (8)
Proven eradication, n (%)	20 (31)	26 (42)	14 (22)
Treatment comparison, 90% CI of difference (one tailed, lower limit)	Amoxicillin/ clavulanate VS Cefaclor -2.48%		Amoxicillin/ clavulanate VS Cefuroxime -5.48%
<b>Safety Results: (Safety Population) From enrollment to the end of therapy (Day 7-8, visit 3)</b>			
	<b>Amoxicillin/ clavulanate (N=121)</b>	<b>Cefaclor (N=119)</b>	<b>Cefuroxime (N=120)</b>
<b>Most Frequent Adverse Events – On-Therapy</b>			
Subjects with any AE(s), n (%)	15 (12.4)	6 (5.0)	10 (5.8)
Nausea	4 (3)	0	1 (1)
Increase in white blood cell count	2 (2)	0	0
Positive glucose in urine	1 (1)	0	2 (2)
Discomfort in upper abdomen	1 (1)	1 (1)	1 (1)
Diarrhoea	1 (1)	1 (1)	0
Rash	1 (1)	1 (1)	0
Constipation	1 (1)	0	0
Decrease in white blood cell count	1 (1)	0	0
Dizziness	1 (1)	0	0
Increase in platelet count	1 (1)	0	0
Lethargy	1 (1)	0	0
Elevation of total bilirubin	0	1 (1)	2 (2)
Abdominal pain	0	1 (1)	0
Decrease in platelet count	0	1 (1)	0
Anorexia	0	0	1 (1)
Elevation of alanine transaminase	0	0	1 (1)
Infection of upper respiratory tract	0	0	1 (1)
Sleepy	0	0	1 (1)
<b>Serious Adverse Events - On-Therapy n (%) [n considered by the investigator to be related to study medication]</b>			
	<b>Amoxicillin/ clavulanate (N=121)</b>	<b>Cefaclor (N=119)</b>	<b>Cefuroxime (N=120)</b>
Subjects with non-fatal SAEs, n (%)	0	0	0

Subjects with fatal SAEs, n (%)	0	0	0
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**Conclusion:**

There was no statistically significant difference in the incidence of clinical success between amoxicillin/ clavulanate and cefaclor and and Cefuroxime. By calculating the lower limits of 90% CI of the difference in clinical success rates between Augmentin and Cefaclor and Cefuroxime, the lower limits were by far greater than -15% in both the ITT and PP Population. It was concluded that clinical efficacy of Augmentin was non-inferior to Cefaclor and Cefuroxime in the study.

AEs were reported by 15 (12.4%) amoxicillin/ clavulanate-treated subjects, 6 (5.0%) cefaclor-treated subjects and 10 (5.8%) cefuroxime-treated subjects. The most commonly reported AEs were nausea and increase in white blood cell count in the amoxicillin/ clavulanate group, and elevation of total bilirubin and positive glucose in urine in the cefuroxime group. No AEs were reported by more than 1 subject in the cefaclor group. There were no fatal or non-fatal SAEs.

**Publications:**

No Publication

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