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Title: Efficacy and safety of AZD5069, a CXCR2 antagonist, in adult bronchiectasis

Prof. Ian 31550 Pavord ian.pavord@uhl-tr.nhs.uk MD [1], Dr. Anthony 31551 De Soyza anthony.de-soyza@ncl.ac.uk MD [2], Prof. J. Stuart 31552 Elborn s.elborn@qub.ac.uk MD [3], Dr. David 31553 Smith david.smith@nbt.nhs.uk MD [4], Heather 31554 Wray heather.wray@astrazeneca.com [5], Margareta 31555 Puu margareta.puu@astrazeneca.com [5], Bengt 31556 Larsson bengt.larsson@astrazeneca.com [5] and Prof. Robert 31582 Stockley rob.stockley@uhb.nhs.uk MD [6]. [1] Department of Respiratory Medicine, Thoracic Surgery and Allergy, Glenfield Hospital, Leicester, United Kingdom ; [2] Institute of Cellular Medicine, Freeman Hospital & Newcastle University, Newcastle upon Tyne, United Kingdom ; [3] Adult CF Centre, Belfast City Hospital, Belfast, United Kingdom ; [4] Respiratory Research Unit, Southmead Hospital, Bristol, United Kingdom ; [5] R&D, AstraZeneca, Mölndal, Sweden and [6] Lung Function and Sleep Department, Queen Elizabeth Hospital, Birmingham, United Kingdom .

Body: Rationale: CXCR2 antagonist AZD5069 may be useful for neutrophilic airway diseases, including bronchiectasis. This early phase study assessed the effects of AZD5069 on sputum neutrophil numbers, a range of biomarkers, other variables and safety in bronchiectasis patients (pts). Methods: Pts with radiological bronchiectasis entered a randomised, double-blind, parallel-group, multicentre study (NCT01255592) of oral AZD5069 80 mg (n=26) or placebo (PBO; n=26) twice daily for 4 weeks. The primary outcome was relative change in absolute sputum neutrophil count. Results: Table 1 summarises baseline demographics and effects of treatment. AZD5069 reduced neutrophil counts by 69% vs PBO (p=0.004). There were no clinically relevant effects on secondary variables. Biomarkers (sputum IL-6, GRO-α; serum GRO-α, IL-1β, IL-8) increased with AZD5069 vs PBO ($p \leq 0.001$), but this was not considered to affect AZD5069 efficacy (since effect on the primary target was confirmed by reduced sputum neutrophils). More pts receiving AZD5069 reported adverse events (23 vs 16). Incidence of infections was similar with AZD5069 and PBO but infections led to more study discontinuations with AZD5069 (4 vs 0).

	Placebo (n=26)	**AZD5069 (n=26)**
Demographics		
Mean age (yrs) (SD)	65 (8.8)	66 (6.6)
Males (% pts)	53.8	38.5
Mean FEV1 on Day 1 (L) (SD)	1.9 (0.9)	1.5 (0.5)

Results		
Ratio of end of treatment to baseline absolute neutrophil count in sputum (90% CI)	1.00 (0.66,1.51)	0.31 (0.20,0.50)
Any adverse events (n)	16	23
Infections (n)	8	9
Discontinuations due to infection (n)	0	4

Conclusions:AZD5069 resulted in a statistically significant reduction in sputum neutrophils vs PBO. Clinical status was not improved in this short-term study.