SCH527123, a Novel Treatment Option for Severe Neutrophilic Asthma

M. Gaga, MD, PhD[1], P.K. Nair, MD[2], F. Hargreave, MD, PhD[3], J. Sadeh, MD[4], P. Chanez, PU-PH[5]
[1]Athens Chest Hospital - Athens/GR, [2]McMaster University / - Hamilton/CA, [3]McMaster University - Hamilton/CA, [4]Schering Plough - Kenilworth, NJ/US, [5]Université de la méditerranée/INSERM UMR600/CNRS UMR6212 - Marseille/FR

Rationale: There are currently no effective treatments for patients with severe asthma associated with neutrophilic bronchial inflammation. CXCR2 is highly expressed on neutrophils and mediates chemotaxis to inflammatory sites. We investigated the use of SCH527123, a selective CXCR2 antagonist, inhibiting neutrophil migration in patients with severe neutrophilic asthma (SNA).

Design: In a randomized, double blind, parallel study, 34 patients with severe asthma (GINA 2008) and sputum neutrophils > 40% were randomized to SCH527123, 30 mg daily PO or placebo for 4 weeks. Primary endpoints were safety and changes in blood neutrophil counts, secondary endpoints were changes in sputum neutrophils, ACQ score, minor and major exacerbations and lung function.

Results: 22 patients received active treatment (13 female, mean age 48.7, median ICS dose 1738mcg, median OCS dose 11.7mg/day, mean FEV1% pred 67.9) and 12 patients received placebo (7 female, mean age 53.9, mean ICS dose 2740 mcg, median OCS dose 13.8mg/day, mean FEV1% pred 60.4) for 4 weeks. On average, over the 4 weeks there was a 27.7% (p=0.02) decline in blood neutrophils in the active group, which was significant; however, values were quite variable in time and at week 4 the difference between the groups did not reach statistical significance. Sputum neutrophils on the other hand were significantly reduced in the active group by 57% averaged over the 4 weeks (p=0.01). There were no differences in the overall rates of adverse events among the groups although there was an increase in the rate of nasopharyngitis and gastrointestinal side effects which were generally mild. Importantly, there were fewer mild exacerbations (1.3 vs 2.25, p=0.05) and there was a trend for fewer severe exacerbations in the SCH527123 group. ACQ score was improved by 0.42 points in the active group (p=0.053) although the difference did not reach clinical significance and no changes were observed in FEV1.

Conclusions: SCH527123 seems to be a safe treatment option that reduces sputum neutrophils in SNA and shows promise of clinical benefit. Larger studies are needed to evaluate clinical efficacy.