Dexpramipexole Effectively Lowers Blood and Tissue Eosinophils in Subjects with Chronic Rhinosinusitis with Nasal Polyps

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Abstract

Introduction

Dexpramipexole is an oral investigational drug serendipitously noted to lower blood eosinophils in prior clinical studies in symptomatic allergic asthma. At open label dose of 300 mg/day for 6 months, mean blood eosinophils was lowered by 76% at month 6 in subjects with chronic rhinosinusitis with nasal polyps (CRSwNP). The primary endpoint was change in total polyop score (TPS) from baseline to month 6. Change in nasal poly eosinophils was an exploratory endpoint. Data are shown from a 6-month, open-label, phase 2 study of 16 subjects with severe CRSwNP (CRS #16) who achieved ≥40% reduction in TPS at month 6. There were no significant reduction in TPS in the 12 subjects who did not achieve ≥40% reduction in TPS. There were no significant adverse events. TPS was not significantly reduced at month 6 in subjects with endobronchial eosinophilic inflammation (EoE). Given the strong trend toward clinical benefit and TPS lowering in the asthma population, we elected to perform this study in the CRSwNP population.

Results

Conclusions

Dexpramipexole lowers blood eosinophils in the asthma population. Variability of eosinophil lowering among subjects was seen in both the blood and polyp tissue.

Discussion

1. Dexpramipexole administration resulted in significant and high magnitude eosinophil lowering in both blood and nasal polype tissue
2. Dexpramipexole eosinophil lowering was maximal after 2 months.
3. Heterogeneity of eosinophil lowering among subjects was seen in both the blood and polyp tissue.
4. Dexpramipexole administration did not have a significant effect on total polyp score.
5. Dexpramipexole was well tolerated and without dose-limiting side effects.

Study Design/Methods

Total Polyp Score

Conclusions

Co-primary endpoint

Study Demographics, to 16 subjects

Dexpramipexole Effectively Lowers Blood and Tissue Eosinophils

Dexpramipexole effectively lowers blood eosinophils

Results

Study Design

Entry criteria:
- Age 18-65 years
- Confirmed diagnosis of CRSwNP
- Total poly score ≥7
- Endobronchial eosinophilic inflammation (EoE)
- Polyp biopsy containing endobronchial eosinophilic inflammation

Study Design

An open label trial was performed in which subjects received dexpramipexole 150 mg BID for 6 months. At 6 months, the TPS was calculated as (mean of M2 to M6 AEC)/(mean screening and baseline AEC) and polyp tissue eosinophils were calculated as (mean of M2-M6 M4-M5 screening and baseline AEC). Polyp tissue eosinophils reduction ratio were calculated as (mean of M2-M6 M4-M5 screening and baseline AEC). AEC at month 6 was 0.20% (H,N reduction (p=0.001). Ten of the 16 subjects had eosinophilic scores reduced to 0.20% (H,N reduction (p=0.001). There were no significant adverse events. TPS was not significantly reduced at month 6 in the 16 subjects who did not achieve ≥40% reduction in TPS. There were no significant reduction in TPS in the 12 subjects who did not achieve ≥40% reduction in TPS. There were no significant adverse events. TPS was not significantly reduced at month 6 in subjects with endobronchial eosinophilic inflammation (EoE). Given the strong trend toward clinical benefit and TPS lowering in the asthma population, we elected to perform this study in the CRSwNP population.

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