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 amyotrophic lateral sclerosis. We sought to examine if Dexpramipexole is an oral investigational drug lowering blood and tissue eosinophils among patients than is currently indicated with approved biologics, including both moderate and high magnitude eosinophil lowering but minimal lowering in blood. This suggests the possibility that dexpramipexole may have utility in eosinophilic disease.

Results

Dexpramipexole effectively lowers blood eosinophils

Conclusions

1. Dexpramipexole administration resulted in significant and high magnitude eosinophil lowering in both blood and nasal polyp 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.

Discussion

This suggests that dexpramipexole may have utility in eosinophilic asthma and other eosinophil-associated diseases.

Two subjects were noted to have substantial polyp tissue eosinophil lowering but minimal lowering in blood. This suggests the possibility that dexpramipexole may have direct activity on tissue eosinophils.

Study Design/Methods

- Entry criteria:
  - Age 18-65 years
  - Confirmed diagnosis of CRSwNP
  - Total polyp score ≥4
  - Eosinophilic nasal polyps (≥50% eosinophils in tissue biopsies)
  - Polyp biopsies containing tissue eosinophils

- Study design:
  - Aim was to determine if dexpramipexole lowered blood and tissue eosinophils in an eosinophilic associated chronic nasal sinusitis with nasal polyps (CRSwNP).
  - Multi-center, double-blind, placebo-controlled 16-week label clinical trial was performed in which subjects received dexpramipexole 150 mg BID for 6 months. At 6 months blood and tissue eosinophil lowering activity was as great or greater than seen with current biologics.
  - Heterogeneity of eosinophil lowering among subjects was examined with approved biologics, including both moderate and high eosinophil lowering.

- Statistical analysis:
  - Eosinophil reduction ratio
  - Eosinophil reduction ratio was defined as change from baseline in Total Polyp Score (TPS) as the primary endpoint.
  - Blood absolute eosinophil count (AEC) ≥0.30x10^9/L and polyp eosinophilia.
  - Polyp tissue eosinophil count (M2) was calculated as follows:
    - M2 = (M3-M4)/M3
    - Polyp tissue eosinophil reduction ratio was calculated as change from baseline in Total Polyp Score (TPS) and Total Polyp Score.

- Results:
  - Dexpramipexole was well tolerated and without dose-limiting side effects.