Long-term safety of mepolizumab for the treatment of hypereosinophilic syndromes.

Hypereosinophilic syndromes (HESs) are chronic disorders that require long-term therapy to suppress eosinophilia and clinical manifestations. Corticosteroids are usually effective, yet many patients become corticosteroid refractory or develop corticosteroid toxicity. Mepolizumab, a humanized monoclonal anti-IL-5 antibody, showed corticosteroid-sparing effects in a double-blind, placebo-controlled study of FIP1L1/PDGFRA-negative, corticosteroid-responsive subjects with HESs. We evaluated long-term safety and efficacy of mepolizumab (750 mg) in HES. MHE100901 is an open-label extension study. The primary endpoint was the frequency of adverse events (AEs). Optimal dosing frequency, corticosteroid-sparing effect of mepolizumab, and development of antimepolizumab antibodies were also explored. Seventy-eight subjects received 1 to 66 mepolizumab infusions each (including mepolizumab infusions received in the placebo-controlled trial). Mean exposure was 251 weeks (range, 4-302 weeks). The most common dosing interval was 9 to 12 weeks. The incidence of AEs was 932 events per 100 subject-years in the first year,
declining to 461 events per 100 subject-years after 48 months. Serious AEs, including 1 death, were reported by the investigator as possibly due to mepolizumab in 3 subjects. The median daily prednisone dose decreased from 20.0 to 0 mg in the first 24 weeks. The median average daily dose for all subjects over the course of the study was 1.8 mg. Sixty-two percent of subjects were prednisone free without other HES medications for ≥ 12 consecutive weeks. No neutralizing antibodies were detected. Twenty-four subjects withdrew before study completion for death (n = 4), lack of efficacy (n = 6), or other reasons. Mepolizumab was well tolerated and effective as a long-term corticosteroid-sparing agent in PDGFRA-negative HES.