Safety and Efficacy of Reslizumab for Children and Adolescents With Eosinophilic Esophagitis Treated for 9 Years

Markowitz JE, Jobe L, Miller M, Frost C, Laney Z, Eke R. *J Pediatr Gastroenterol Nutr*. 2018;66(6):893–897

PURPOSE OF THE STUDY: To report the efficacy and long-term safety of reslizumab (RSZ) for the treatment of pediatric eosinophilic esophagitis (EoE).

STUDY POPULATION: This was a single-center study including 12 patients (7–16 years old) previously enrolled in a parent multicenter randomized controlled trial receiving either 2 mg/kg RSZ or placebo. All patients had active EoE, esophageal symptoms, and endoscopic findings at enrollment and were permitted to be on a proton pump inhibitor and dietary avoidance. None were on topical steroids. Of the initial 12 patients, 8 patients elected to receive RSZ in an expanded access program (open label and compassionate use) from July 2008 to January 2012, with 3 remaining until 2017 and using RSZ for 9 years.

METHODS: The patients participating in the extension program were treated with 2 mg/kg intravenous RSZ every 28 days and were re-evaluated annually. During the monthly infusion encounters, patients were assessed through a questionnaire, and adverse events were recorded. If clinically indicated, RSZ could be increased to 3 mg/kg. Clinical remission was defined as resolution of all EoE symptoms, normal endoscopic findings, and histology <5 eosinophils per high-power field.

RESULTS: Over the 9-year study, the 12 patients received ~501 doses of RSZ (1–3 mg/kg intravenously). RSZ treatment median duration was 3 years, and all patients reported improved esophageal symptoms at follow-up. Ninety-two percent of patients demonstrated a reduced eosinophil count to <5 eosinophils per high-power field ($P < .001$). The 3 subjects who remained on prolonged RSZ also continued to have histologic remission. RSZ was well tolerated and safe throughout the duration of the study. Five patients (42%) experienced at least 1 adverse event, including nasal congestion or cough. None of the patients experienced adverse events that were attributed to or required the discontinuation of RSZ.

CONCLUSIONS: RSZ shows promise as an effective and safe long-term treatment of pediatric EoE.

REVIEWER COMMENTS: RSZ is an interleukin-5 antagonist approved for adults for the treatment of severe asthma. This study is limited by its small sample size, restricting its opportunity to detect differences. Another confounding variable is that participants were allowed to restrict food triggers and take a proton pump inhibitor, both of which are treatments for EoE. The authors importantly recognized the declining participation but noted it was not related to any adverse events. Despite these limitations, RSZ seems to be an effective and safe drug for a select pediatric EoE population.

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Asthma

RISK FACTORS

Birth Weight for Gestational Age and the Risk of Asthma in Childhood and Adolescence: A Retrospective Cohort Study

Carter JH, Woolcott CG, Liu L, Kuhle S. *Arch Dis Child*. 2019;104(2):179–183

PURPOSE OF THE STUDY: To evaluate the possible correlation between birth weight for gestational age and asthma in childhood and adolescents.

STUDY POPULATION: This was a cohort of all children of a term (≥37 weeks), singleton gestation born in the Canadian province Nova Scotia between January 1, 1989, and December 31, 2014.

METHODS: The retrospective cohort was created through the Nova Scotia Atlee Perinatal Database and with provincial administrative health data. Linkage was conducted by Health Data Nova Scotia on the basis of the health card number. Infants were categorized as small for gestational age (SGA; < 10th percentile), large for gestational age (LGA; >90th percentile), or appropriate for gestational age (10th–90th percentile). Birth weight *z* scores were calculated by using sex- and gestational age–specific means and SDs from the same reference population. Confounders included the following: maternal age, area of residence (urban versus rural), area-level income quintile at birth, parity, prepregnancy weight status (normal, overweight, or obese), asthma during pregnancy, mode of delivery (vaginal delivery versus cesarean delivery), and smoking in pregnancy (yes or no). Unadjusted and adjusted Cox proportional hazards regression with robust SEs was used to estimate the association between birth weight for gestational age and asthma. Associations between birth weight for gestational age and smoking in pregnancy were also examined.

RESULTS: The final sample included 40 727 children. Of those, 10 155 children (23.6%) had asthma by 6 years of life, and 12 997 children (30.2%) had asthma during the first 18 years of life. LGA was not associated with the risk of developing asthma. There was an additive interaction between SGA and smoking. In mothers who smoked, there was an increased risk for asthma in children with low birth weight. However, in mothers who do not smoke, there was no increased risk of asthma across the birth weight spectrum among children.

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