respiratory tract infection, sore throat, and bronchitis were seen in the lansoprazole-treated subjects. Activity-related bone fractures were slightly increased in the lansoprazole-treated subjects.

REVIEWER COMMENTS. The same investigators have shown similar results in adults. This study contributes to the questioning of the true association between asthma and GER disease in children and adults and potential overuse of PPI therapy in patients without symptomatic GER. These data were obtained in asthmatic children without symptomatic GER and may not be comparable in children with active GER symptoms. Impedance monitoring was not done and the results cannot be extrapolated to the possible effect of non-acid reflux on asthma control. Increased fracture risk has been reported in adults on long-term PPI therapy. This is the first large study to suggest possible association in children, although specific cause-and-effect was not investigated.

Omalizumab and the Risk of Malignancy: Results From a Pooled Analysis

PURPOSE OF THE STUDY. Omalizumab, a humanized anti-IgE monoclonal antibody, is an approved treatment for severe persistent asthma in patients 12 years or older. Previous pooled data showed an increased number of malignancies in treated patients compared to control subjects (0.5% vs 0.2%, respectively). This study reexamined the malignancy risk from the use of omalizumab.

STUDY POPULATION. Sixty-seven phase I to IV clinical trials sponsored by the medicine’s manufacturers and their extension periods were pooled for analysis.

METHODS. Studies were categorized as randomized, double-blind, placebo-controlled (RDBPC, 32/67), controlled clinical trials (40/67), or all clinical trials. Patients with a prior history of malignancy were included in 11 trials. A global safety database maintained by the manufacturer was also used to identify any omalizumab-treated patients with events that occurred after the clinical trials ended and after last exposure during a clinical trial (ARGUS). Potential malignancies (including cysts, polyps, and nevi) were identified and then blindly screened by 2 physicians with exclusion of events deemed benign by both. The remaining cases were blindly reviewed by an independent oncology panel. Cases of “definite” and “possible” malignancy were included.

RESULTS. There were 11,459 patients in all clinical trials (7789 on omalizumab/5800 patient-years; 3670 placebo-treated patients/2168 patient-years), 9424 in controlled trials (6246 on omalizumab/2978 patient-years; 3178 placebo-treated patients/2168 patient-years), and 7432 in RDBPC trials (4254 on omalizumab/2144 patient-years; 3178 placebo-treated patients/1689 patient-years). Across all clinical trials and the ARGUS database, 177 patients had 209 potential malignancies identified. After the blinded review, 56 patients (43 omalizumab-treated and 13 control patients) had a total of 62 malignancies. Twelve of the 56 patients were identified from the ARGUS database (11 omalizumab, 1 control). In the RDBPC trials (including events identified from the ARGUS database), malignancies were identified in 14 omalizumab-treated patients and 11 placebo-treated subjects (4.14 and 4.45/1000 patient-years, respectively; rate ratio = 0.93). When patients identified from the ARGUS database were excluded and only events recorded during the RDBPC trials were considered, the rate ratio for malignancy in omalizumab versus control subjects was 0.73. When all trials were examined, the incidence rates of malignancy were similar but the corresponding rate ratios were 1.35 and 1.13, respectively. The time from study entry to malignancy diagnosis was the same in treated and control patients. The dose and duration of omalizumab treatment did not affect the malignancy rate.

CONCLUSIONS. There is no association between omalizumab treatment and risk of malignancy in patients with severe persistent asthma.

REVIEWER COMMENTS. This study provides reassurance about the long-term safety of omalizumab.

IMMUNOTHERAPY

A Novel Approach in Allergen-Specific Immunotherapy: Combination of Sublingual and Subcutaneous Route

PURPOSE OF THE STUDY. To compare the efficacy and safety of a novel combination of subcutaneous immunotherapy (SCIT) for induction and sublingual immunotherapy (SLIT) for maintenance, to immunotherapy via a single method (either SCIT or SLIT) for both induction and maintenance.

STUDY POPULATION. Investigators enrolled 60 children, aged 5 to 12 years, monosensitized to house dust mite (HDM), who had been followed at a pediatric allergy immunology clinic in Istanbul for mild persistent to moderate asthma or rhinitis, with persistent symptoms despite inhaled or intranasal steroids for 2 years.
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Mitchell R. Lester

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