Review Article

The Consideration of At-Home Administration of Omalizumab

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Part of every pharmacist's job involves selecting the safest medication regimen to fit each patient's medical needs and achieve compatibility with individual lifestyles. Over time, developments in monoclonal antibody therapies have provided symptom control benefits for patients living with severe allergic asthma. Omalizumab (Xolair®), a monoclonal antibody medication for IgE-mediated asthma, was approved by the FDA for in-clinic use in 2003. In 2018, the European Commission approved this agent's use for at-home self-administration; this supported increased access and fewer in-clinic trips for patients.[1] However, in the United States, omalizumab largely remains administered in the clinic only.

Due to the COVID-19 pandemic, there has been a recent push to decrease the amount of in-person clinic visits. Over the past 17 years, practitioners in the United States have applied cautionary measures in prescribing omalizumab for at-home use due to its black-box warning for anaphylaxis. However, in August of 2020, Novartis announced the FDA acceptance of a supplemental Biologics License Application for an omalizumab (Xolair®) pre-filled syringe for self-administration, and it will be up for approval in quarter 1 of 2021.[2] With patient access and safety in mind, this clinical inquiry explores the rates and risk factors associated with anaphylaxis that have been reported in the literature for omalizumab.

Evidence Summary

In a one-arm observational case study, 25 patients newly started on omalizumab were observed for the safety outcomes of at-home administration.[3] Patients were given one or two doses in-clinic, and, once a patient could demonstrate ability to self-administer, they were approved for at-home administration of therapy. Inclusion criteria encompassed patients with uncontrolled IgE-mediated asthma for greater than or equal to 1 year. Twenty-five patients were included and observed over a 2-month to 4-year time period to assess for severe adverse events. Results showed that no patients reported anaphylaxis or the need to use epinephrine or antihistamines during the total of 1,017 omalizumab at-home doses reported. Limitations of this study relate to its one-arm nature, because there is no comparator group and no ability to measure the portion of effect due to variables other than the intervention. The authors demonstrated the potential of implementing an at-home administration framework.

A 2017 observational study assessed real-life adverse effects from omalizumab administration in-clinic over a 9-year period.[4] Inclusion criteria included patients greater than or equal to 12 years of age with uncontrolled severe persistent asthma, defined by the 2017 GINA report, who had at least 1 injection of omalizumab. Ninety-one patients were included, and this group of patients received 10,472 injections over the study period. There were no anaphylaxis events reported throughout the study. A weakness is that the clinical conclusions are limited due to the lack of a comparator group. This study might support the low rate of anaphylaxis due to omalizumab.

In a post-marketing surveillance report covering data from 2003 to 2005, authors assessed anaphylaxis events reported to Genentech omalizumab (Xolair®).[5] Inclusion criteria included patients with asthma on omalizumab (n = 39,510) and those who had an anaphylactic reaction to omalizumab. The authors identified criteria for an anaphylactic reaction based on the National Institute of Allergy and Infectious Diseases and the Food Allergy and Anaphylaxis Network's (NIAID/FAAN) definition.[6] The outcome was determined to be 35 patients with anaphylaxis observed at a rate of 0.09%.[5] In this report, authors noted that 75% of anaphylaxis cases occurred within 2 hours after injection for the first 3 injections, and within 30 minutes for the fourth injection and beyond. In addition, a post-marketing adverse event report covering data from 2003 to 2006 was published with similar inclusion criteria and definition of anaphylaxis as the previous report (n = 57,300).[7] Authors assessed the frequency and properties of anaphylactic reactions, and the outcome was determined to be 124 cases of anaphylaxis observed at a rate of 0.2%. Of note, this data summary reported anaphylactic reactions that took place up to 4 days after injection (5 out of 124 cases). A limitation of both studies is the risk for confounding due to severity bias, as patients with more severe disease might influence the outcome of anaphylaxis separately. Another limitation of these studies is that there was no control over mandating the patients and/or healthcare providers to report all cases of anaphylaxis; therefore, the study is at risk for information bias.

In a 2020 pharmacoeconomic evaluation, historical data from 2016 to 2018 was used to estimate the cost effectiveness of at-home versus in-clinic administration of omalizumab and mepolizumab.[8] This study performed the analysis by an incremental cost-effectiveness ratio (ICER) comparison. The analysis was calculated from that of the societal and health system perspective. Direct and indirect costs of the injection, distance traveled by the patient, and risk of anaphylaxis were compared in each setting. The data sources used for safety risks were determined based on prescribing information, drug approval status from Europe, and two retrospective studies. The number of simulations in the model was 10,000. The results of the ICER, from

the health care perspective, for in-clinic to at-home administration was $445,861,774 per fatality prevented and from the societal perspective $500,648,430 per fatality prevented. One limitation of this study is that adherence to at-home therapy was unaccounted for and assumed to be at 100%, which is not a realistic assumption. This analysis attempted to address the theoretical cost savings and justification for at-home administration.

In a series of letters to the editor, small case reports have shared various characteristics that might be associated with a higher risk of anaphylaxis when taking omalizumab.[9-11] This compiled data indicated reactions to be more likely to occur within 2 hours of the first 3 doses, within 30 minutes from the fourth dose on, or with a previous history of anaphylaxis. Weaknesses within these reports come from the risk for confounding due to limited controls, and the concern for overreporting in patients with severe allergic asthma; however, these findings can provide more information when considering each patient individually as a candidate for at-home use.

Recommendations from Others

The 2020 Global Initiative for Asthma (GINA) report addresses recommendations for management of asthma in adults and children greater than 5 years old.[12] When considering omalizumab therapy, the report states that it is indicated as add-on therapy for patients who still have uncontrolled IgE-mediated asthma despite other treatments. It additionally outlines that self-administration is an option if the agent meets acceptable criteria from local payers and prescribers, and education is provided to identify adverse effects, including hypersensitivity reactions. Overall, the GINA report stresses the role of the individualized patient-and-asthma-team relationship in supporting and educating patients to strengthen self-confidence in managing asthma therapies day to day.

Evidence-Based Answer

Home-administration may have a similar safety profile compared to in-clinic administration regarding risk of anaphylaxis in patients living with asthma on omalizumab therapy. (Strength of recommendation = B, based on lower quality evidence of observational studies, post-marketing surveillance reports, a pharmacoeconomic analysis, and letters to the editor with patient-oriented outcomes.) Further research and evaluation of at-home administration is necessary to increase practitioner confidence in the safety profile for omalizumab. For clinicians considering the transition of patients to at-home administration, there should be adequate risk-benefit discussions, patient education and demonstration in injection technique, and education in allergic reaction medication administration for each patient. Furthermore, all adverse reactions should be well-documented, reported, and electronically retrievable for quick and reportable population-health data.

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