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Role of Nemolizumab and Omalizumab in management of atopic dermatitis: A review

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REVIEW

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ABSTRACT

Background
Nemolizumab (CIM331) is a monoclonal antibody that binds the IL-31 receptor α component. This inhibits IL-31 from acting on neurons that constrains the initialization of the sense of pruritus in cases of atopic dermatitis.

Aims
To summarize the results of reported studies evaluating the role of nemolizumab and omalizumab in management of atopic dermatitis.

Methods
This is a systematic review was carried out, including PubMed, Google Scholar, and EBSCO that examining randomized controlled trials, observational, and experimental studies which study role of nemolizumab in management of atopic dermatitis.

Results
The review included 8 randomized studies reported efficacy of both nemolizumab and omalizumab for management of atopic dermatitis.

Conclusion
Other studies with large numbers of patients with AD are necessary to define the adverse effects of both drugs in the treatment of AD.

Key Words
Nemolizumab, Omalizumab, atopic dermatitis

What this review adds:

1. What is known about this subject?
Nemolizumab is a subcutaneously administered humanized monoclonal antibody against interleukin-31 receptor which is involved in pruritus and inflammation in atopic dermatitis. Omalizumab is a biologic drug known for treating atopic patients with moderate to severe persistent allergic asthma.

2. What new information is offered in this study?
Both nemolizumab as well as omalizumab, significantly improve the symptoms of AD and subsequently improve

patients QoL.

3. What are the implications for research, policy, or practice?

Approving the efficacy of these drugs and evaluating their adverse effects to assess benefit and of drugs in treated patients.

Background

Atopic dermatitis (AD) is a mutual, chronic skin condition that can considerably influence the quality of life of the cases as well as their families. It causes substantial morbidity and unpleasantly disturbs quality of life. The occurrence of AD has augmented over the past 30 years. It is presently predictable that 10–20% of children and 1–3% of adults in industrialized countries are affected by the disease.[1]

Itching, the main clinical feature of AD, is intermediated by the binding of the pro-inflammatory cytokine interleukin (IL)-31 to IL-31 receptor A on sensual neurons and long-lasting pruritus aggravated disorder over the itch–scratch cycle. Management choices are restricted for cases with AD not improved by topical treatments, for example the corticosteroids and calcineurin inhibitors, which form the mainstay of treatment.[2]

Nemolizumab is an anti-IL-31 receptor A humanized monoclonal antibody, which chunks IL-31-mediated signalling and motivate pruritus, IL-31 which has a part in continuation of the inflammatory reaction and non-organization of the somatic and functional possessions of the skin barrier together leading to the progression of the disease.[3] Nemolizumab established improvements in pruritus, illness severity and sleep disruption in a phase II, 12-week, randomized, double-blind, placebo-controlled, dose-finding research paper (Part A) in adults with moderate to severe AD inefficiently treated by local therapeutics.[4]

Method

A systematic review was carried out, including PubMed, Google Scholar, and EBSCO using the following terms in different combinations: nemolizumab in atopic dermatitis, omalizumab in atopic dermatitis, efficacy of nemolizumab in AD. We included all full texts [randomized controlled trials, observational, and experimental studies]. The authors extracted the data, and then the author's names, year and region of publication, the study type, period of study, and the result were reported (Table 1).

Results

The search of the mentioned databases returned a total of 39 studies that were included for title screening. 37 of them were included for abstract screening, which lead to the exclusion of 22 articles. The remaining 15 publications full-texts were reviewed. The full-text revision lead to the exclusion of seven studies, and 8 were enrolled for final data extraction (Table 1).

Kabashima et al. in a 16-week, double-blind, phase 3 trial in 2020 At week 16, the mean percent change in the VAS score was -42.8% in the nemolizumab group and -21.4% in the placebo group (P<0.001). The mean percent change in the EASI score was -45.9% with nemolizumab and -33.2% with placebo.[5]

Silverberg, a phase IIb clinical trial reported a dose-dependent increase in mild asthma exacerbations in subjects treated with nemolizumab. Two subjects discontinued the study due to elevations in creatine kinase levels.[6]

Mihara et al. in a former 24 weeks follow up study, discussed in Table 1 reviewed that; patients receiving nemolizumab every four weeks showed great work Productivity in week 12 as atopic dermatitis improved until week 64 of trial.[2]

Kabashima reported no severe adverse events occurred for up to 64 weeks after treatment with nemolizumab. Most adverse events were mild and included headache, lower extremity edema, increased creatine phosphokinase levels (CPK), nasopharyngitis, and upper respiratory tract infections.[7]

Heil et al.[8] reported reduction in free serum IgE with omalizomab, lowering in surface IgE and FcεRI expression on different peripheral blood mononuclear cells, reduction in the saturation of FcεRI with IgE, increase in the number of free FcεRI and lowered number of IgE+, but not of FcεRI+ cells in skin.

Iyengar et al.[9] found that omalizumab decreased levels of TSLP, OX40L, TARC and interleukin (IL)-9. Marked increase in IL-10, a tolerogenic cytokine was notable in the omalizumab-treated group.

Sheinkopf et al.[10] studied 21 patients and reported that all patients showed clinical and statistically significant improvement of their atopic dermatitis (p<0.00052).

Discussion

AD affect the quality of life (QoL). Pruritus is the main symptom of AD, leading to insomnia and compact the health related QoL in individuals with AD. Itching correspondingly results in reduced the health related QoL, symptoms of depression and competing the day-to-day functioning comprising the capability to work productively and study.[12] A previous study reported reduction in DLQI scores observed during part A of the study and prolonged alleviation of the effect of symptoms on daily life. Improvements in efficacy of nemolizumab were observed after patients switched from placebo to nemolizumab which was consistent with the early improvement in pruritus observed within week 1 of nemolizumab treatment in part A of the study.[13]

AD is associated with elevated serum levels of IgE, circulating activated T cells and serum L-selectin correlates with AD disease severity. Acute AD is dominated by a Th2/Th17-reaction pattern that can be continued by IgE and allergen contact. Chronic AD is characterized by a Th-1 signature.[14] A recent study by Schroeder et al. demonstrated that omalizumab treatment significantly decreased cat-allergen- specific T cell proliferation and Th2 cytokine expression by approximately 25 and 50%, respectively. This suggests that IgE facilitates allergen presentation by DCs in vivo and possibly regulates DC-dependent T cell cytokines during effector phases of allergic disease.[15] A recent study by our group investigating 11 children treated with omalizumab while undergoing oral immunotherapy revealed near elimination of the CD4+ T cell response to milk within a week of treatment.[16] Iyengar et al.[9] reported that omalizumab effectively reduced free IgE levels, even in patients with serum IgE levels up to 1,890IU/ml, as free serum IgE levels decreased early on in the study period. In addition, all patients receiving omalizumab had decreased levels of TSLP, TARC, OX40L and IL-9. Another study found that omalizumab treatment dramatically reduces serum levels of free IgE and decreases surface-bound IgE.[17] Interestingly, in Lane's study, the AD of one patient (IgE=2890IU/mL) responded very well to omalizumab dosed at 300mg every two weeks.[18]

Conclusion

Previous randomized clinical trials reported efficacy of both nemolizumab and omalizumab for management of atopic dermatitis. Other studies with large numbers of patients with AD are necessary to define the adverse effects of both drugs in the treatment of AD.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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None

Table 1: Author, year of publication, study type, and study outcome

Author	Year of publication	Study type	Outcome
Kabashima et al.[5]	2020	A 16-week, double-blind, phase 3 clinical trial	Nemolizumab S.C with topical products results in reduction in pruritus and greater injection-site reactions than placebo plus topical agents in management of atopic dermatitis.
Silverberg et al.[6]	2020	A 24-week, randomized, double-blind, multicenter study	Nemolizumab occasioned in rapid and continuous improvements in inflammation of pruritus in patients with AD, with greatest effectiveness at 30 mg with an acceptable safety profile.
Mihara et al.[2]	2019	A two-part, phase II, randomized control trial.	Nemolizumab treated patients with moderate to severe atopic dermatitis with enhanced Work Productivity.
Kabashima et al.[7]	2018	Randomized, phase II, long-term extension study	Nemolizumab was efficacious and well tolerated in patients with moderate-to-severe atopic dermatitis when topical drugs are not effective.
Heil et al.[8]	2010	A randomized, placebo-controlled and double blind pilot study	Interference with immediate and delayed skin type testing can mean that the clinical advantage of omalizumab therapy, if any, will be found in patients with acute instead of chronic types of the condition.
Iyengar et al.[9]	2013	A randomized, double-blind, placebo-controlled study of 8 patients	Anti-IgE treatment with omalizumab lowers the levels of cytokines implicated in Th2 polarization and allergic inflammation, including TSLP, TARC and OX40L.
Sheinkopf et al.[10]	2008	A pilot study	Omalizumab is effective in treating AD in patients with moderate to severe persistent allergic asthma.
Kim et al. [11]	2013	Clinical trial	Omalizumab has proven useful in treating AD as well as other allergic conditions