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(REVIEW ARTICLE)

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Pharmacotherapy of Sjogren's syndrome: A comparison of disease activity with Iscalimab and Ianalumab

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Abstract

Sjögren's Syndrome is a disease that affects millions worldwide. Research indicates that people suffering from Sjögren's Syndrome respond well to monoclonal antibody treatment aimed at characteristic immune cell markers. By targeting immune cell markers, the immune system is subsequently suppressed in a way such that disease activity is decreased. Monoclonal antibody treatments targeted towards a variety of immune cell markers have historically been shown to result in decreases in Sjögren's Syndrome disease activity. Many studies have assessed disease activity with monoclonal antibody treatments, but few have compared different treatments.

A systematic review of a study that assessed the disease activity for those taking iscalimab was then compared to the findings of another study which assessed the disease activity with those taking ianalumab.

The patients treated with iscalimab had significantly decreased Sjögren's Syndrome disease when compared with other matched controls. Those who were treated with ianalumab had significantly decreased disease activity when compared with other matched controls. However, those who were treated with iscalimab had a greater reduction of disease activity as compared to control groups than did those who were treated with ianalumab.

Monoclonal antibody treatments for Sjögren's Syndrome are widespread. It is critical that these treatments are compared in order to find those with the greatest efficacy. For this review, iscalimab seemed to have a greater reduction of disease activity than did ianalumab. Further studies with greater sample sizes are needed to conclude which has greater efficacy.

Keywords: Ianalumab; Rituximab; Sjögren's Syndrome; Autoimmune Disease; Monoclonal Antibody Therapy; Inflammatory Skin Disease

1. Introduction

There is sufficient information to suggest that persons suffering from Sjögren's Syndrome respond well to monoclonal antibody therapy (1). Two prominent monoclonal antibody treatments for the treatment of Sjögren's Syndrome are the anti-CD40 agents such as iscalimab and the anti-B-cell activating factor receptor (anti-BAFF receptor) agents such as ianalumab (1,2).

Anti-CD40 agents such as iscalimab are directed towards the CD40 cellular marker, which induces CD40–CD154-mediated T cell–B cell interaction which contribute to aberrant lymphocyte activation in inflamed tissue, leading to sialadenitis and other tissue injury (1). Anti-BAFF receptor agents such as ianalumab inhibit the BAFF-mediated

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signaling for B-cell maturation, proliferation, and survival, which has been previously implicated in the pathogenesis of Sjögren's Syndrome (2).

It is well known that both of these monoclonal antibody therapies have significant effects in reducing Sjögren's syndrome disease activity index (ESSDAI) score's, but little has been done to compare their efficacies (1,2). This is especially important to know such that a physician can prescribe the best pharmacological intervention to treat a patient with Sjögren's Syndrome.

2. Methods

For the study conducted using iscalimab (1):

This multicentre, randomized, double-blind, placebo-controlled, proof-of-concept study took place at ten investigational sites across Europe (UK, n=4; Germany, Switzerland, and Hungary, n=1 each) and the USA (n=3). Eligible patients were aged 18–75 years and fulfilled the 2002 American European consensus group diagnostic classification criteria for primary Sjögren's syndrome. In the double-blind phase of the trial, patients were randomly assigned (2:1) via computer-generated unique randomisation numbers to receive subcutaneous iscalimab (3 mg/kg) or placebo at weeks 0, 2, 4, and 8 (cohort 1) or intravenous iscalimab (10 mg/kg) or placebo at weeks 0, 2, 4, and 8 (cohort 2). At week 12, patients in both cohorts received open-label iscalimab (same dose and route) for 12 weeks. Clinical disease activity was measured by a change in European League Against Rheumatism Sjögren's syndrome disease activity index (ESSDAI) score after 12 weeks of treatment.

For the study conducted using ianalumab (2):

This was a randomized, parallel, double-blind, placebo-controlled, phase 2b dose-finding study. Eligible patients were 18–75 years old and met the American European Consensus Group classification criteria for primary Sjögren's syndrome. Between June 27, 2017, and Dec 06, 2018, 293 patients were screened, 190 of whom were randomly assigned (placebo n=49, ianalumab 5 mg n=47, ianalumab 50 mg n=47, ianalumab 300 mg n=47). The primary outcome was the change in ESSDAI score from baseline to 24 weeks in all randomly assigned patients. Dose-related change in disease activity (ESSDAI) from baseline at week 24 was assessed by multiple comparison procedures with modeling analysis.

3. Results:

For the study conducted using iscalimab (1):

Intravenous treatment with iscalimab resulted in a mean reduction of 5·21 points (95% CI 0·96–9·46; one-sided p=0·0090) in ESSDAI score compared with placebo. There was no signficiant difference in ESSDAI score between subcutaneous iscalimab and placebo.

For the study conducted using ianalumab (2):

Statistically significant dose-responses were seen for overall disease activity (ESSDAI score) in four of the five dose-response models tested (p<0·025 in four models, p=0·060 in one model). The ESSDAI score decreased from baseline in all ianalumab groups, with the maximal ESSDAI score change from baseline observed in the ianalumab 300 mg group: placebo-adjusted least-squares mean change from baseline −1·92 points (95% CI −4·15 to 0·32; p=0·092).

Table 1 ESSDAI Results for Both Treatments

Treatment	Change in ESSDAI (pts.)	p-value
Iscalimab (IV)	-5.21	0.009
Ianalumab (300mg)	-1.92	0.025

The above table (Table 1) depicts the percentage achieving ESSDAI and p-values for each of the treatment groups in each study. All groups treated with monoclonal antibodies had statistically significant decreases in ESSDAI when compared to placebo groups.

4. Conclusion

Our analysis suggests that while both iscalimab and ianalumab are effective in reducing Sjögren's Syndrome disease activity, iscalimab did so by almost 3 times more than the ianalumab group. This also indicates that the CD40–CD154-mediated T cell–B cell interaction is likely more implicated in Sjögren's Syndrome than B-cell proliferation. The analyses are limited in the sense that they both couldn't accurately control for the severity of Sjögren's Syndrome and comorbidities. Additionally, the length of both research studies could not be controlled. There is also the likelihood that there is another immune marker that may be even more implicated in the pathogenesis of Sjögren's Syndrome than CD40 and the B-cell activating factor receptor. Also, further studies must be conducted with larger sample sizes controlling for age and other demographic factors. While iscalimab shows promising results, there is plenty more investigation that must be conducted to find the most effective monoclonal antibody treatment for Sjögren's Syndrome.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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