World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

Pharmacotherapy of Systemic Sclerosis: A Comparison of Skin Score with Fresolimumab and Tocilizumab

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World Journal of Biology Pharmacy and Health Sciences, 2024, 20(02), 637–639

Publication history: Received on 12 October 2024; revised on 22 November 2024; accepted on 24 November 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.20.2.0928

Abstract

Systemic Sclerosis is a disease that affects millions worldwide. Research indicates that people suffering from systemic sclerosis 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 systemic sclerosis 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 using modified Rodnan skin scores (mRSS) for those taking tocilizumab was then compared to the findings of another study which assessed the disease activity with those taking fresolimumab.

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

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

Keywords: Systemic Sclerosis; Tocilizumab; Fresolimumab; Autoimmune Disease; Monoclonal Antibody Therapy; Inflammatory Skin Disease

1. Introduction

There is sufficient information to suggest that persons suffering from systemic sclerosis respond well to monoclonal antibody therapy (1). Two prominent monoclonal antibody treatments for the treatment of systemic sclerosis are the anti-TGF-β agents such as fresolimumab and the anti-interleukin-6 (anti-IL-6) agents such as tocilizumab (1,2).

Anti-TGF-β agents such as fresolimumab are directed towards tumor growth transformation factor-β, which has previously been found to be upregulated in vitro in terms of profibrotic activity, and thus believed to be strongly implicated in the pathogenesis of systemic sclerosis (1). IL-6 inhibitors such as tocilizumab inhibit IL-6, which is known to be elevated in those with systemic sclerosis (2). It is believed that by inhibiting IL-6, the hepatic synthesis of C reactive

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protein (CRP) and platelet levels will be decreased and thus correlating to a decreased disease severity (2). Inhibition of IL-6 has been shown to be able to prevent the development of inflammation-driven dermal fibrosis induced by bleomycin in mice (2).

It is well known that both of these monoclonal antibody therapies could have effects in reducing modified Rodnan skin scores (mRSS) for those with systemic sclerosis, 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 systemic sclerosis.

2. Methods

For the study conducted using fresolimumab (1):

A total of 15 patients with systemic sclerosis were enrolled in an open-label trial of fresolimumab, a high-affinity neutralizing antibody that targets all 3 TGF-β isoforms. Seven patients received two 1 mg/kg doses of fresolimumab, and eight patients received one 5 mg/kg dose of fresolimumab. Degree of disease activity was measured using the modified Rodnan skin score (mRSS).

For the study conducted using tocilizumab (2):

Ninety-three patients with SSc treated with tocilizumab and 3180 patients with systemic sclerosis were included in a randomized-placebo observational study. Degree of disease activity was measured using the modified Rodnan skin score (mRSS). Patients had baseline and follow-up visits at 12±3 months, and mRSS was a primary endpoint

3. Results

For the study conducted using fresolimumab (1):

The primary clinical outcome in this trial, the MRSS, declined rapidly in most patients, generally within several weeks of the infusion. The median change in MRSS, using data across both dose groups, was most striking at weeks 11 and 17, −6 (p = 0.0005) and −9.5 (p = 0.0024), respectively

For the study conducted using tocilizumab (2):

MRSS was lower in the tocilizumab group, however the difference was not statistically significant (difference −1.0, 95% CI −3.7 to 1.8, p=0.48).

Table 1 MRSS Results of Each Treatment

Treatment Group	Difference in mRSS	p-value
Fresolimumab	-9.5	0.0024
Tocilizumab	-1.0	0.48

The above (**Table 1**) depicts the differences in mRSS that each treatment had when compared to the respective control groups. The difference in mRSS was far more notable for those treated with fresolimumab (-9.5) as compared to tocilizumab (-1.0).

4. Conclusion

Our analysis suggests that while both fresolimumab and tocilizumab are likely effective in reducing systemic sclerosis disease activity, fresolimumab did so by more than nine times that of the tocilizumab-treated group. This also indicates that transformation growth factor-β is likely more implicated in systemic sclerosis than interleukin-6. The analyses are limited in the sense that they both couldn't accurately control for the severity of systemic sclerosis 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 systemic sclerosis than transformation growth

factor-β and interleukin-6. Also, further studies must be conducted with larger sample sizes controlling for age and other demographic factors. While fresolimumab shows promising results, there is plenty more investigation that must be conducted to find the most effective monoclonal antibody treatment for systemic sclerosis.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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