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JOURNAL CLUB

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ARTICLE

Safety and efficacy of rituximab in systemic sclerosis (DESIRES): a double-blind, investigator-initiated, randomised, placebo-controlled trial, The Lancet Rheumatology, Volume 3, Issue 7, 2021, Pages e489-e497, ISSN 2665-9913, https://doi.org/10.1016/S2665-9913(21)00107-7.

CLINICAL QUESTION

Is rituximab is effective in treating patients with systemic sclerosis with skin disease and ILD?

SUMMARY

Studies have shown that B-cell abnormalities, such as sustained abnormal activation of B-cells, particularly memory B-cells, are important in the development of systemic sclerosis. [1.2.3] B-cell-targeted therapies could be effective against this disease.

This is a double-blind, investigator-initiated, randomised, placebo-controlled trial at four hospitals in Japan. Patients aged 20–79 years, who fulfilled the 2013 American College of Rheumatology and European League Against Rheumatism classification criteria for systemic sclerosis, with a modified Rodnan Skin Score (mRSS) of 10 or greater, and an expected survival of at least 6 months were randomly assigned (1:1) to receive intravenous rituximab (375 mg/m2) or placebo once per week for 4 weeks. Patients and investigators were masked to treatment allocation.

The primary endpoint was the absolute change in mRSS 24 weeks after initiation of study treatment, measured in all patients who received at least one dose of study treatment and had one endpoint assessment.

The secondary endpoints included: percentage of predicted forced vital capacity (FVC% predicted), percentage diffusing capacity for carbon monoxide (%DLCO; corrected for hemoglobin), total lung capacity (TLC); quality of life assessment using the medical outcomes study 36-item short-form general health survey (SF-36); and health assessment questionnaire disability index (HAQ-DI).

In the DESIRES trial, the mean baseline mRSS in the placebo group was 15·7, resulting in a mean increase of 2·14 points at 24 weeks.

The rituximab group had a mean change in mRSS of −6·30 at 24 weeks from baseline and a difference of −8·44 (95% CI −11·00 to −5·88) compared with the placebo group. 25 (89%) of 28 patients in the rituximab group and 23 (88%) of 26 patients in the placebo group had interstitial lung disease.

FVC% predicted decreased to the same extent in both groups until 12 weeks of follow-up.

In the rituximab group, it increased by 1·22% from 12 weeks to 24 weeks, whereas in the placebo group it continued to decline.

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Consequently, the change in percentage of predicted forced vital capacity at 24 weeks from baseline was significantly improved in the rituximab group compared with the placebo group (0·09% vs −2·87%; difference 2·96% [95% CI 0·08–5·84]; p=0·044).

This study is registered with ClinicalTrials.gov, NCT04274257, and UMIN-CTR, UMIN000030139.

GROUP OPINION

Rituximab appears to be an effective and safe treatment for systemic sclerosis.

Perhaps head-to-head trials (H2H) can be helpful to determine the most efficacious therapy. These studies test rituximab against other therapies that are already on the market and can determine which one is a better option for our patients.

Combination therapies have been used in clinical practice for years but we do not have trials that help us to determine the right combinations.

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