Tocilizumab more effective than Rituximab in RA patients with low B-cell levels

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New research discovered that tocilizumab is more effective than rituximab in achieving low disease activity in patients with rheumatoid arthritis whose synovial tissue show a low level of B cell infiltration and did not respond to conventional synthetic disease-modifying anti-rheumatic drugs (conventional synthetic DMARDs) or tumor necrosis factor (TNFi) inhibitors first (Abstract# 2911).

Rheumatoid arthritis (RA) is the most common type of autoimmune arthritis. It is a chronic disease that causes joint pain, stiffness, swelling and decreased movement of the joints. Small joints in the hands and feet are most commonly affected. Sometimes RA can affect your organs, such as eyes, skin or lungs.

"Approximately half of RA patients lack treatment responses to expensive biologic therapies that also carry the risk of side effects. Predictive markers of response could help stratify RA," said Costantino Pitzalis MD, Ph.D., FRCP, director of the Center for Experimental Medicine and Rheumatology at Barts and the London School of Medicine and Dentistry, and the study's lead author. "This leaves a major unmet clinical need and an urgent necessity to identify markers of treatment response to avoid delays in disease control, unnecessary exposure to potentially toxic drugs and considerable waste of resources."

B-cells are pivotal to RA pathogenesis, validated by the efficacy of the B cell-depleting agent rituximab, which is approved for use in RA patients after inadequate response to conventional synthetic DMARDs and TNFi.

However, only 30 percent of these difficult to treat patients achieve a 50 percent improvement (ACR50 response) in disease activity, at six months after starting rituximab.

In a previous trial, the study's researchers found that, in patients with early RA, more than 50 percent had low levels or an absence of B-cell infiltration in their synovial tissue. For this study being presented at the 2019 ACR/ARP Annual Meeting, we hypothesized that alternative B cell independent pathways drive inflammation in this subgroup, and that alternative biologic agents to rituximab should work more effectively in these patients.

This 48-week, phase four, open-label randomized controlled trial evaluated whether or not stratifying RA patients according to synovial B-cell rich or poor status would help predict response to rituximab. Patients were recruited from 19 European medical centers who did not respond, or were intolerant, to conventional synthetic DMARD therapy and at least one TNFi l. Researchers obtained synovial tissue samples at the beginning of the trial, and histologically classified them as either B-cell rich or B-cell poor to balance the randomization of 164 patients in equal groups to receive either rituximab or tocilizumab.

The researchers tested the superiority of tocilizumab over rituximab at 16 weeks in the B-cell poor patient population. The study's primary endpoint was a Clinical Disease Activity Index (CDAI) improvement of 50 percent or higher from baseline. The co-primary endpoint was the Major Treatment Response, which was equal to CDAI improvement of 50 percent or higher along with a CDAI of 10.1 or lower. The secondary outcomes included an assessment of CDAI response in the B-cell rich patient cohort, where they evaluated the non-inferiority of rituximab compared to tocilizumab. They also reported safety data for the therapies up to week 48 of the trial.

The researchers found that 81 of 83 patients who received rituximab and 73 of 81 patients who received tocilizumab completed treatment to week 16 of the trial. Baseline characteristics among the two treatment groups were similar. In the B-cell poor cohort, a numerically higher proportion of patients responded to tocilizumab (56.1 percent) compared to rituximab (44.7 percent) considering the primary outcome. A significantly greater proportion of patients responded to tocilizumab (46.3 percent) compared to rituximab (23.7 percent) considering the co-primary outcome as well as several additional secondary endpoints including the proportion of patients in remission at 36.6 percent versus 15.8 percent. The number of patients reaching moderate or good EULAR response was 87.8 percent versus 65.8 percent, respectively.

In the B-cell rich cohort, the researchers found no significant difference in the majority of endpoints. Patients treated with tocilizumab also had a higher number of adverse and serious adverse events, such as infections, compared to those treated with rituximab.

Overall, tocilizumab was more effective than rituximab at achieving both low levels and significant falls in disease activity in RA patients classified as B-cell poor who have failed conventional synthetic DMARDs and TNFi therapy, the study's findings show.

"These findings are important as they indicate that patients with low level of B cells in the synovial tissue are less likely to respond to rituximab and should be treated with alternative medications," said Dr. Pitzalis.

More information: Study: A Randomized, Open Labelled Clinical Trial to Investigate Synovial Mechanisms Determining Response - Resistance to Rituximab versus Tocilizumab in Rheumatoid Arthritis Patients Failing TNF Inhibitor Therapy

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