Ocrelizumab in a difficult-to-treat rheumatoid arthritis patient

Sirs,

Over the past twenty years, the increasing availability of biological and targeted disease-modifying anti-rheumatic drugs (DMARDs) has significantly improved the outcomes for patients with rheumatoid arthritis (RA). However, managing patients with a variable proportion of those defined as difficult-to-treat (D2T) still remains problematic and requires access to multiple drugs (1, 2). B (CD20) cells play a central role in RA pathogenesis. Rituximab (RTX), a chimeric monoclonal anti-CD20 antibody has been shown to be an effective and safe treatment for RA. It has been approved in patients with an inadequate response to conventional DMARDS (2). Ocrelizumab (OCR), a humanised monoclonal anti-CD20 antibody, has proven its efficacy for the treatment of relapsing multiple sclerosis and is approved in France since 2019 (3). Although five randomised controlled trials evaluating OCR in RA, OCR has never been approved for use in RA elsewhere due to safety concerns (4-8).

We present the case of a 58-year-old woman who was diagnosed with seropositive, erosive RA in 1997. After receiving several conventional DMARDS (methotrexate and sulfasalazine), she was given biological DMARDs: etanercept for three months stopped for hypersensitivity reaction, followed by adalimumab for four years, which was stopped due to the appearing of a large B-cell lymphoma in 2015. Following successful treatment for her haematological malignancy with R-CHOP, the patient underwent rituximab treatment for RA, resulting in significant improvement between 2015 and 2020. Unfortunately, three months after the last infusion, she developed cutaneous sarcoidosis (skin sarcoids with histopathological evidence of granumolatous lesion) without pulmonary or ganglionic involvement. RTX was suspected and stopped (9). Other biological DMARDS compatible with her history of lymphoma were tried: tocilizumab (ineffective), sarilumab (significant local reaction at the injection site). In 2024, RA relapsed with high disease activity (DAS28-CRP 5.83).

The patient started treatment with OCR (300 mg, two intravenous infusions with a 14-day interval) alone in January 2025. The pre-therapeutic assessment did not reveal contraindications (normal blood formula, a gamma globulin level at 13.7 g/L). Premedication consisted of 100 mg IV methylprednisolone, acetaminophen and antihistamine. There was no complication during or after both infusions. Four months later, RA was in remission (DAS28-CRP 2.7). At six months, a single 600 mg intravenous OCR infusion was systematically re-administered as maintenance therapy. The level of gamma globulin before the second administration was normal (11.8 g/dL). There were no adverse events, particularly infectious one, nor relapse of sarcoidosis.

OCR in association with methotrexate has proven its efficacy in RA patients who exhibit resistance to methotrexate or TNF inhibitors according a metanalysis of five RCT reported in 2017 (10). Serious adverse events were comparable between OCR and placebo. Although no face-to-face trial has evaluated RTX *versus* OCR in RA patients, a non-inferiority analysis of a Danish registry comparing OCR *versus* RTX in patients with remitting multiple sclerosis reported in 2023 found that persistence (reflecting both efficacy and safety) was higher with OCR than with RTX.

In conclusion, OCR should remain a therapeutic off-label option for difficult-to-treat RA patients who experience adverse effects after receiving RTX, particularly those with haematological malignancies, for whom treatment options are limited.

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