Ocrelizumab Treatment Interruption in Clinically Stable Multiple Sclerosis: Prospective Evidence Supporting a Time-Limited Treatment Pause

Authors: Franz Felix Konen,[1] Franziska Axhausen,[2] Stephanie Wolff,[2] Pauline Mühlenbrock,[2] Stefan Gingele,[1] Konstantin Fritz Jendretzky,[1] Sandra Nay,[1] Lea Martha Grote-Levi,[1] Philipp Schwenkenbecher,[1] Sven G. Meuth,[3] *Thomas Skripuletz,[1] Steffen Pfeuffer[2]

1. Department of Neurology, Hannover Medical School, Germany
2. Department of Neurology, Justus Liebig University Giessen, Germany
3. Department of Neurology, University hospital Münster, Germany

*Correspondence to skripuletz.thomas@mh-hannover.de

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SUMMARY OF KEY FINDINGS

Background

Anti-cluster of differentiation (CD)20 therapies such as ocrelizumab constitute effective treatment options for relapsing multiple sclerosis (MS).[1,2] While continuous B cell depletion effectively suppresses inflammatory disease activity, prolonged treatment may be associated with cumulative infection risk, hypogammaglobulinaemia, and increasing healthcare costs.[1-3] Consequently, there is growing interest in determining whether treatment can be safely paused in carefully selected patients with stable disease.[4]

Konen et al.[5] addressed this question in a prospective, multicentre, observational cohort study conducted at two German MS centres. Patients who received ocrelizumab for at least 12 months and remained free of inflammatory disease activity during the preceding year were eligible. Outcomes of patients who interrupted treatment were compared with those who continued therapy using 4:1 propensity score matching.[5]

Findings

Among 655 eligible patients, 290 were included in the matched analysis, comprising 58 patients who interrupted ocrelizumab treatment and 232 who continued therapy.[5] Median follow-up after treatment interruption was 28.5 months.[5] The primary outcomes were combined inflammatory activity (clinical relapse and/or new MRI lesions) and progression independent of relapse activity.[5]

Inflammatory disease activity remained largely suppressed during the first 2 years after treatment interruption.[5] No statistically significant increase in combined inflammatory activity or disability progression was observed compared with patients who remained on continuous treatment.[5] Receiver operating characteristic analyses further suggested that the anti-inflammatory benefit of ocrelizumab plateaued after approximately 29–30 months of therapy, whereas the likelihood of recurrent disease activity increased after approximately 30–32 months without treatment, indicating that protection gradually wanes during prolonged treatment interruption.[5]

At the time of treatment interruption, more than 90% of patients demonstrated complete peripheral B cell depletion. During the treatment-free period, $CD19^+$ B cells gradually repopulated, with recovery beginning within the first year and continuing for up to 48 months.[5] Serum IgG concentrations also increased progressively, suggesting partial recovery from treatment-associated hypogammaglobulinaemia.[5]

Conclusion

These prospective data suggest that, in carefully selected patients with clinically stable MS, a planned interruption of ocrelizumab following approximately 30 months of treatment may represent a feasible short-term management strategy without an immediate increase in inflammatory disease activity.[5] Importantly, these findings support treatment pausing rather than permanent discontinuation and emphasise the need for ongoing clinical and MRI monitoring, particularly beyond 2 years after treatment interruption.[5]

WHAT CHALLENGE DOES THIS ADDRESS?

The optimal duration of anti-CD20 therapy remains uncertain, and clinicians increasingly face the challenge of balancing sustained disease control against the risks associated with long-term immunosuppression. This study addressed the unmet need for prospective evidence informing whether temporary interruption of ocrelizumab may reduce cumulative treatment burden while maintaining disease stability in selected patients.

RELEVANCE TO EUROPEAN PRACTICE

Across Europe, neurologists are increasingly considering personalised treatment strategies that minimise long-term safety risks without compromising efficacy. These findings provided important prospective evidence supporting individualised treatment pauses in clinically stable patients receiving ocrelizumab. Although treatment interruption should not yet be considered routine practice, the results may help inform shared decision-making regarding treatment duration, particularly in patients at increased risk of infections or hypogammaglobulinaemia. The study also reinforced the importance of structured clinical and MRI surveillance during treatment-free intervals.

WHAT ARE THE NEXT STEPS FOR THE RESEARCH?

Further prospective studies with larger patient populations and longer follow-up are needed to confirm these findings and better define which patients are most suitable for treatment interruption. Future research should also establish biomarkers including B cell kinetics and Ig recovery that may help individualise the timing of treatment re-initiation. Ultimately, RCTs comparing continuous treatment with biomarker-guided treatment pauses will be required before treatment interruption can be incorporated into routine clinical practice.

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