**INTRODUCTION AND PURPOSE**

- Ocrelizumab (OCR) is a recombinant, humanised, monoclonal antibody that selectively targets CD20 B cells.
- OCR has demonstrated superior efficacy to interferon (IFN)-β-1a in patients with relapsing multiple sclerosis (RMS) and to placebo in patients with primary progressive multiple sclerosis (PPMS) in Phase III trials.
- The proportions of patients with adverse events (AEs) or serious AEs were similar across the OCR IFN-β-1a and placebo groups.

- Pooled trial data indicated an imbalance in malignancies between the OCR and control arms, which was driven by a higher number of female breast cancer events in the OCR group.
- Further data are needed to characterise the long-term safety of OCR in the post-marketing setting, and a programme comprising observational studies—MANUSCRIPT and VERISMO—was developed to fulfil regulatory requirements (U.S. Food and Drug Administration and European Medicines Agency).
- The CONFIDENCE study will collect data to be included in the global post-authorisation safety (PAS) studies MANUSCRIPT and VERISMO.
- CONFIDENCE will assess long-term safety data (e.g., incidence of malignancies and serious-risk profile in patients with multiple sclerosis (MS)) newly exposed to OCR in Germany.

**OVERALL AIMS**

- To further assess and characterise the long-term safety profile of OCR, including malignancy, in patients with MS in a real-world setting.

**METHODS**

**Study Design**

- MANUSCRIPT and VERISMO are multi-source, multi-country, noninterventional, longitudinal cohort PAS studies on patients with MS who have newly initiated treatment with OCR (and other MS disease-modifying therapies (DMTs)) (see Figure 1 for data sources and overview of study flow).

**Findings**

- The objectives and populations of the studies are provided in Table 1 and Figure 2.
- Participants will be followed up for as long as possible, and up to 10 years, or until censoring, loss to follow-up or death.

**Table 1. MANUSCRIPT and VERISMO study objectives and patient populations**

<table>
<thead>
<tr>
<th>Study</th>
<th>Objectives</th>
<th>Population</th>
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<tbody>
<tr>
<td>MANUSCRIPT</td>
<td>Expected to enrol 6,050 patients (aged ≥18 years) with MS who have newly initiated treatment with OCR or another DMT during the study period, or patients with MS not on DMT in routine clinical practice.</td>
<td>N=4,300 OCR treated (n=3,400) Non-OCR treated (n=1,500) German centres</td>
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<tr>
<td>VERISMO</td>
<td>Expected to enrol 6,300 patients (aged ≥18 years) with MS who have newly initiated treatment with OCR or with another DMT in the US</td>
<td>N=4,360 OCR treated (n=3,600) Non-OCR treated (n=1,500) US (n=1,000) Non-OCR DMT treated (n=2,000)</td>
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**Figure 1. Overall study flow**

**RESULTS**

- **CONFIDENCE** data collected de novo will be integrated with existing data from MS registries, providing large-scale data sets for long-term safety assessment studies.

**CONCLUSIONS**

- The post-marketing studies MANUSCRIPT and VERISMO will further characterise the safety profile of ocrelizumab in patients with MS newly exposed to the drug, with a focus on malignancy.
- CONFIDENCE evaluates the long-term safety follow-up, including the risk of malignancies and serious infections.
- CONFIDENCE data collected de novo will be integrated with existing data from MS registries, providing large-scale data sets for long-term safety assessment studies.

**ACKNOWLEDGEMENTS**

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