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Assessing the real-world effectiveness of ocrelizumab in patients with multiple sclerosis – CONFIDENCE one-year interim analysis

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BACKGROUND

- With more than 170,000 patients treated with ocrelizumab (OCR) worldwide as of July 2020[1], real-world effectiveness data are of relevance
- The safety and efficacy of OCR, a humanized monoclonal antibody selectively targeting CD20+ B-cells, in patients with multiple sclerosis (MS) have been characterised in Phase II and Phase III clinical trials[2–4]
- However, data on the safety and effectiveness of OCR in a real-world setting are currently limited
- CONFIDENCE (ML39632, EUPAS22951) is a non-interventional post-authorization safety study collecting real-world safety and effectiveness data for patients with relapsing MS (RMS) or primary progressive MS (PPMS) newly treated with OCR for up to 10 years[5]

OBJECTIVES

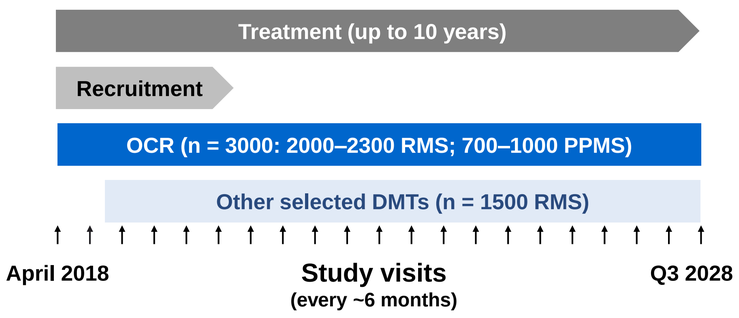
- Here, we present results of the interim analysis of effectiveness data from patients treated with OCR with an observational period of approximately one year

METHODS

Study design

- CONFIDENCE aims to collect data for 3000 OCR-treated patients and 1500 patients treated with other disease-modifying treatments* (DMTs) according to label at ~250 centers in Germany
- Study visits will be approximately every 6 months for up to 10 years regardless of discontinuation of study medication (**Figure 1**)

Figure 1. CONFIDENCE study design



*Other DMTs include: alemtuzumab, cladribine, dimethyl fumarate, fingolimod, natalizumab and teriflunomide;
DMTs, disease-modifying treatments; MS, multiple sclerosis; PPMS, primary progressive MS; RMS, relapsing MS

- The objectives of CONFIDENCE are to:
  - assess the long-term safety of OCR (primary objective)
  - estimate long-term effectiveness of OCR and the incidence of serious infections and malignancies (secondary objectives)

CONFIDENCE interim analysis

- Here, we analyze secondary effectiveness outcomes in OCR-treated patients with one baseline visit and two follow-up visits (~1 year of treatment; data cutoff 1 April 2020)
- Safety outcomes (primary outcome) are presented separately at this congress[6]

Effectiveness outcomes

- The proportion of patients who remained relapse free
- The mean expanded disability status scale (EDSS) was used to quantify disability
- Confirmed disability progression (CDP) and confirmed disability improvement (CDI) were defined as an increase or decrease, respectively, in EDSS score of
  - ≥1.0 point from baseline if the baseline EDSS was ≤5.5
  - ≥0.5 point from baseline if the baseline EDSS was >5.5
  - Disability progression or improvement were considered confirmed when the change in the EDSS was confirmed at a visit at least 24 weeks after the initial documentation
- Treatment success was defined as the proportion of patients with no clinical disease activity measured by relapse or disease progression and no discontinuation of current treatment due to adverse event or lack of effectiveness
- Patient reported outcomes were measured by an adapted Multiple Sclerosis Impact Scale (MSIS)-29†
- Statistical analyses are mainly descriptive and exploratory
  - Error is reported as standard deviation unless stated otherwise

RESULTS

Population and baseline characteristics

- As of 17 August 2020, 2,227 patients have been recruited for OCR treatment in CONFIDENCE, of which 559 are included in this interim analysis
- Patients with RMS (mean age 43.9 ± 11.2 years) were younger than patients with PPMS (mean age 52.8 ± 9.7 years) (**Table 1**)
- 87.9% of patients with RMS and 29.1% of patients with PPMS had at least one prior disease-modifying MS-specific therapy
- Mean EDSS at baseline was 3.3 ±1.9 for patients with RMS (n = 390) and 4.5 ± 1.7 for patients with PPMS (n = 87)
- Further baseline characteristics are presented separately at this congress[6]

Table 1. Baseline characteristics

Characteristic	RMS (n = 456)	PPMS (n = 103)
Female, n (%)	303 (66.4)	57 (55.3)
Age, years		
Mean (SD)	43.9 (11.2)	52.8 (9.7)
Median (IQR)	44.0 (35.0; 53.0)	53.0 (47.0; 58.0)
Time since first symptoms, years		
Mean (SD)	12.2 (9.3)	8.8 (8.1)
Median (IQR)	10.5 (4.31; 18.5)	5.8 (3.2; 11.8)
Time since diagnosis, years		
Mean (SD)	10.2 (8.2)	6.1 (7.3)
Median (IQR)	8.4 (3.1; 15.7)	3.5 (1.1; 8.6)
EDSS		
Mean (SD)	3.3 (1.9)	4.5 (1.7)
Median (IQR)	3.0 (2.0; 5.0)	4.5 (3.0; 6.0)

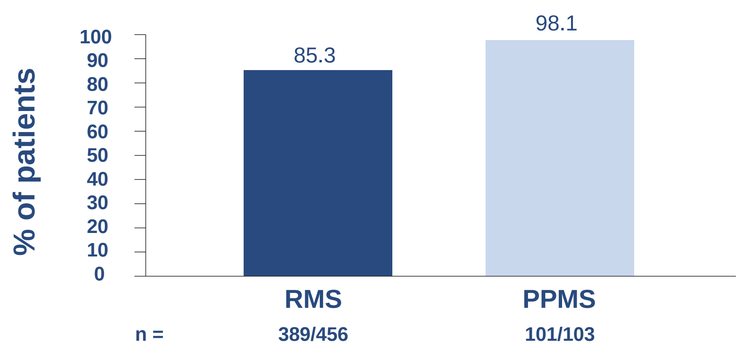
EDSS, expanded disability status scale; IQR, interquartile range; MS, multiple sclerosis; PPMS, primary progressive MS; RMS, relapsing MS; SD, standard deviation.

Effectiveness outcomes

Patients who remained relapse free

- Overall, 389 patients (85.3%) with RMS treated with OCR remained relapse free during one year of treatment (**Figure 2**)
  - The annualized relapse rate was 0.20 ± 0.54
- A total of 101 (98.1%) patients with PPMS remained relapse free during one year of treatment (**Figure 2**)
  - The annualized relapse rate was 0.02 ± 0.14

Figure 2. Patients who remained relapse-free over one year

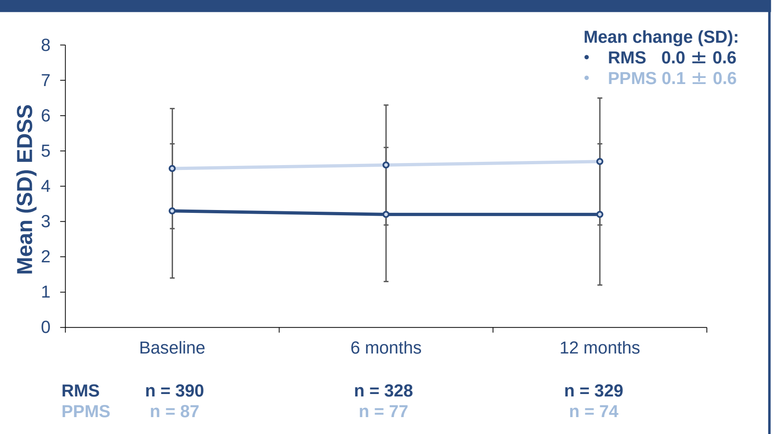


MS, multiple sclerosis; PPMS, primary progressive MS; RMS, relapsing MS

Effectiveness according to EDSS

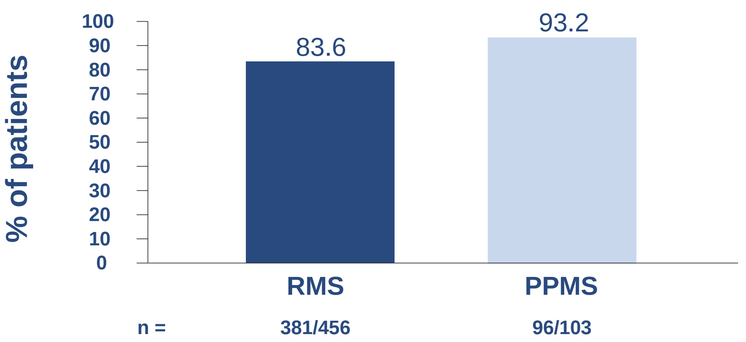
- Overall, mean EDSS remained largely constant over one year of OCR treatment (**Figure 3**)
- Most patients experienced treatment success over one year of OCR treatment (**Figure 4**)
- 2.3% of patients with RMS experienced CDP, while 5.1% of patients experienced CDI (**Figure 5**)
- 5.7% of patients with PPMS experienced CDP, while 2.3% of patients experienced CDI (**Figure 5**)

Figure 3. Mean (SD) EDSS over one year



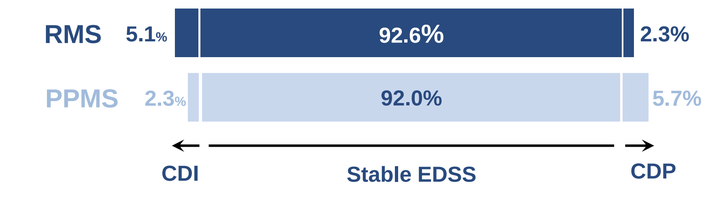
EDSS, expanded disability status scale; MS, multiple sclerosis; PPMS, primary progressive MS; RMS, relapsing MS; SD, standard deviation.

Figure 4. Patients who experienced treatment success‡



‡Treatment success was defined as patients with no clinical disease activity measured by relapse or disease progression and no discontinuation of current treatment due to adverse event or lack of effectiveness; Two patients with RMS (0.4%) discontinued due to adverse events and one patient due to lack of effectiveness. No patients with PPMS discontinued treatment due to adverse events or lack of effectiveness. MS, multiple sclerosis; PPMS, primary progressive MS; RMS, relapsing MS.

Figure 5. Proportion of patients with CDI and CDP at 12 months

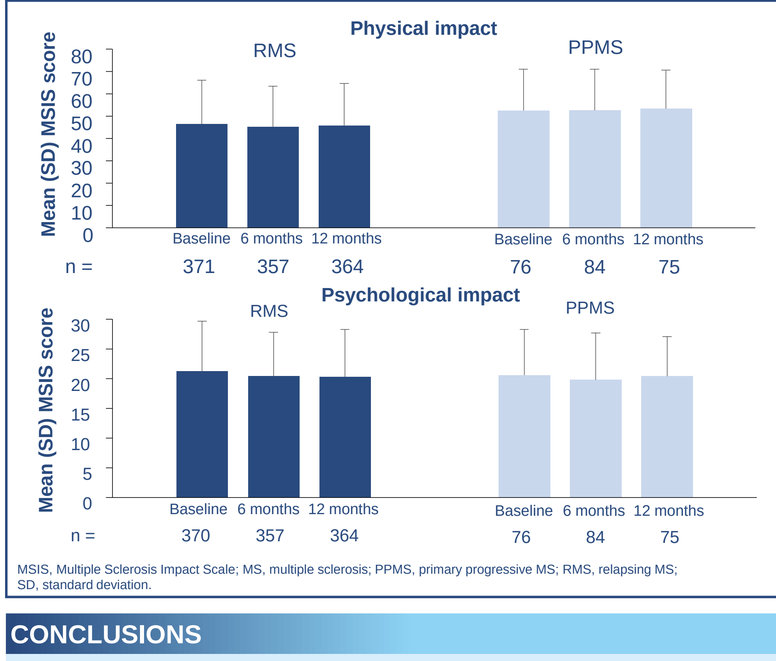


CDP and CDI, defined as an increase or decrease, respectively, in EDSS score of ≥1.0 point from baseline if the baseline EDSS was ≤5.5 or ≥0.5 point from baseline if the baseline EDSS was >5.5. CDP, confirmed disability progression; CDI, confirmed disability improvement; EDSS, expanded disability status scale;
MS, multiple sclerosis; PPMS, primary progressive MS; RMS, relapsing MS.

Patient-reported outcomes

- Overall, the physical and psychological impact of MS as reported by the MSIS-29† score remained constant throughout one year of treatment (**Figure 6**)
- Decreases in MSIS-29† scores indicate improvements
  - Patients with RMS had a –0.4 ± 12.3 (n = 321) change in physical impact score and a –1.0 ± 6.5 (n = 320) change in psychological impact score
  - Patients with PPMS had a 2.4 ± 15.1 change in physical impact score and a 0.5 ± 7.0 change in psychological impact score (n = 64 for both)

Figure 6. Mean MSIS-29† score over one year



MSIS, Multiple Sclerosis Impact Scale; MS, multiple sclerosis; PPMS, primary progressive MS; RMS, relapsing MS; SD, standard deviation.

CONCLUSIONS

- **CONFIDENCE represents a real-world cohort of MS patients**
  - **At baseline, patients with RMS and PPMS in CONFIDENCE were on average ~7 and ~8 years older, respectively, than those in the pivotal trials[3,4]**
  - **Patients with RMS had higher mean baseline EDSS and patients with PPMS had slightly lower mean baseline EDSS than patients in the pivotal trials[3,4]**
- **EDSS and MSIS-29† remained constant over the first year of OCR treatment**
- **The majority of patients in this analysis experienced treatment success**
- **This one-year interim analysis in the CONFIDENCE study indicates the effectiveness of OCR in a real-world population**
  - **Safety outcomes (IP021) are presented separately at this congress[6]**

ACKNOWLEDGEMENTS

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For more information on the CONFIDENCE study, please visit:

www.encepp.eu/encepp/viewResource.htm?id=23845

DISCLOSURES

The following authors hereby declare that since 1 Nov 2019 they have or have had business, personal or material relationships with the following companies, consulting firms or medical institutions and sponsors thereof: **MB**; Bayer, Biogen, Boehringer, Celgene, Coloplast, Daiichi-Sankyo, Das Fortbildungskolleg, Merck, Novartis, Roche, Sanofi and Teva // honoraria for lecturing, consulting and/or travel expenses for attending meetings; **JCE, PD, SHS, JL**: Roche Pharma AG // employee and shareholder; **SGM:** Almirall, Amicus Therapeutics Germany, Bayer Health Care, Biogen, Celgene, Diamed, Genzyme, MedDay Pharmaceuticals, Merck Serono, Novartis, Novo Nordisk, ONO Pharma, Roche, Sanofi-Aventis, Chugai Pharma, QuintilesIMS and Teva // honoraria for lecturing, and travel expenses for attending meetings; German Ministry for Education and Research (BMBF), Bundesinstitut für Risikobewertung (BfR), Deutsche Forschungsgemeinschaft (DFG), Else Kröner Fresenius Foundation, Gemeinsamer Bundesausschuss (G-BA), German Academic Exchange Service, Hertie Foundation, Interdisciplinary Center for Clinical Studies (IZKF) Muenster, German Foundation Neurology and Alexion, Almirall, Amicus Therapeutics Germany, Biogen, Diamed, Fresenius Medical Care, Genzyme, HERZ Burgdorf, Merck Serono, Novartis, ONO Pharma, Roche, and Teva // research funding; **TZ**: Biogen, Roche, Merck, TEVA, and Almirall // grants and personal fees from grants; Genzyme and Novartis; and personal fees from Bayer, BAT, Celgene and Gilead // personal fees and non-financial support.

MSW hereby declares that since 1 Nov 2019 he has had no business, personal or material relationships with companies, consulting firms or medical institutions and sponsors thereof, in regard to this study.

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Effectiveness

Safety

†On the adapted MSIS-29, items were translated into German and scored on a 5-point scale ranging from 1 to 5; decreases in MSIS-29† scores indicate improvements.