

Ocrelizumab, serum immunoglobulin levels and serious infections

Overview¹



Impact on IgG and IgM



SI types and outcomes



Ig levels and SI incidence

- After 12 years of continuous treatment, IgG and IgM levels remained normal for most patients
- For IgG in particular, levels remained normal for >85% of patients over 12 years

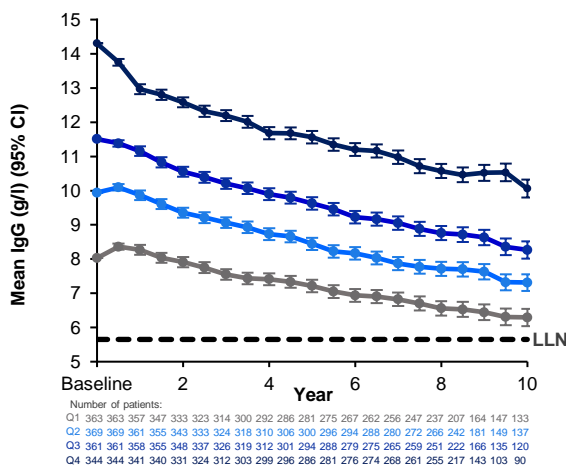
- The type, severity, latency and duration of SIs observed during episodes of IgG<LLN were consistent with the overall SIs observed in patients treated with OCR
- Longer exposure to OCR did not lead to an increased risk of SIs regardless of IgG status

- Over a period of up to 12 years, discontinuations due to low IgG, or due to SIs associated with low IgG, were observed in less than 1% of patients
- Low numbers (n=12, 0.6%) discontinued due to SIs during periods of low IgM (<0.4 g/L)

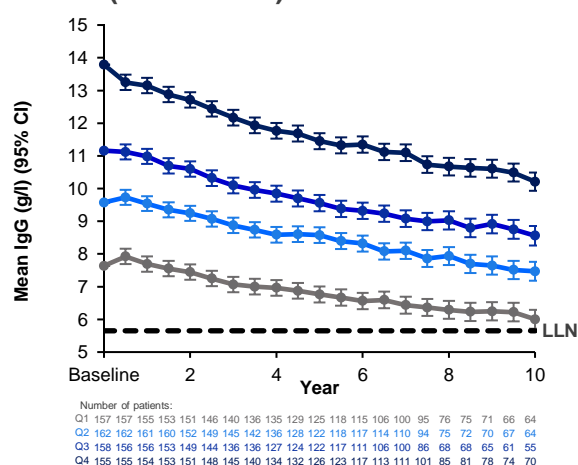
Clinical trial population: Change in serum IgG and IgM levels over 10 years¹

Figure 1: Change in serum IgG levels in RMS (A) and PMS (B) populations*

A. RMS (OPERA)



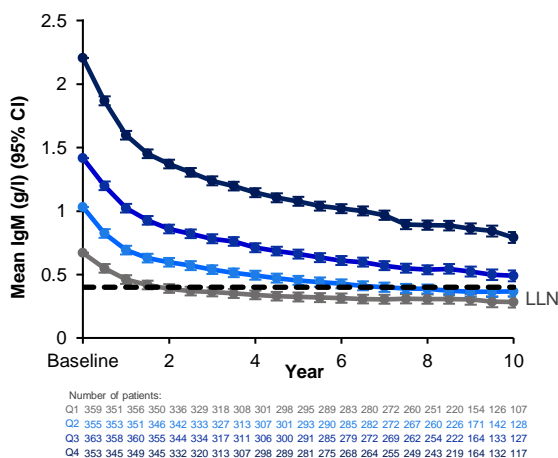
B. PMS (ORATORIO)



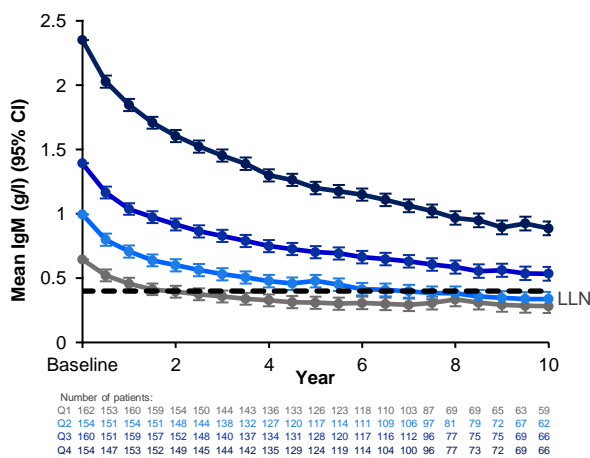
Legend: Q1 (brown), Q2 (light blue), Q3 (dark blue), Q4 (black)

Figure 2: Change in serum IgM levels in RMS (A) and PMS (B) populations*

A. RMS (OPERA)



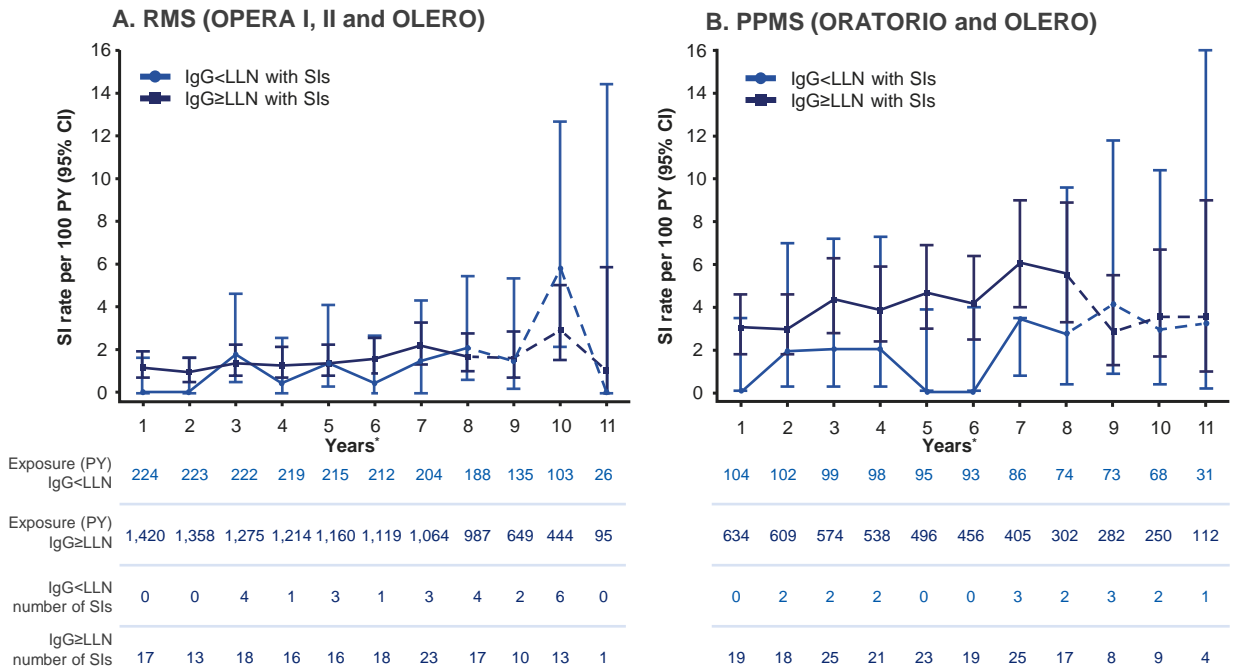
B. PMS (ORATORIO)



Legend: Q1 (brown), Q2 (light blue), Q3 (dark blue), Q4 (black)

Clinical trial population: Relationship between SI rates and Ig levels¹

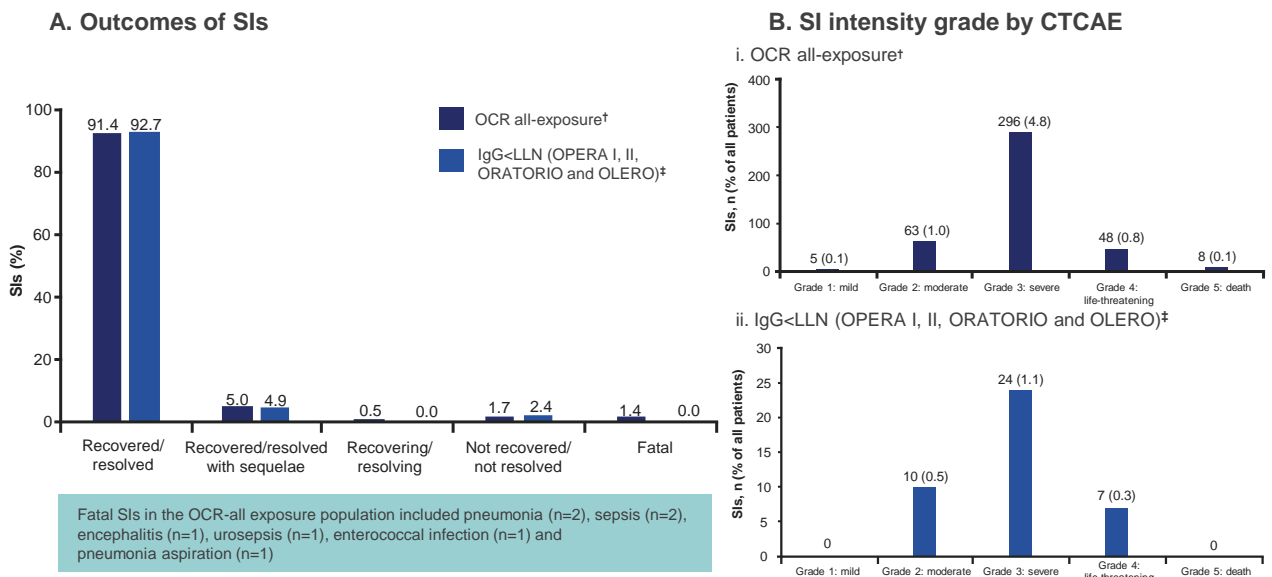
Figure 3: SI rate per 100 PY in RMS (A) and PPMS (B) populations



- In both RMS and PPMS populations, longer exposure to OCR did not lead to an increased risk of SIs regardless of **IgG status** (normal levels or levels below the LLN)
- The **type, severity, latency and duration of SIs** observed during episodes of IgG<LLN were consistent with the overall SIs observed in patients treated with OCR

For more information on the rate of infections with OCR treatment, please visit the [Ocrelizumab and infections](#) webpage

Figure 4: Outcomes of SIs (A) and SI intensity grade by CTCAE* (B, excluding COVID-19) in (i) OCR all-exposure[†] and (ii) IgG<LLN (OPERA I, II, ORATORIO and OLERO)[‡] populations



- The majority of SIs were of **Grade 3 intensity**; **>90% had resolved (regardless of IgG status) and were not treatment limiting**

Footnotes

Figures 1 & 2

*Includes patients who received any dose of OCR during the CTP and associated OLE periods of the Phase III OPERA and ORATORIO studies, including patients originally randomised to comparator (IFN β -1a or placebo) who switched to open-label OCR treatment (data as of November 2022).

Figure 3

COVID-19 related AEs were excluded from this analysis, but patients continued to contribute to the incidence of all other AEs.

[†]The exposure in PY during Years 8–11 is limited for meaningful interpretation, so these data are presented in the plots with dotted lines.

Figure 4

COVID-19 related AEs were excluded from this analysis, but patients continued to contribute to the incidence of all other AEs.

*Grade 1 (mild): Asymptomatic or mild symptoms/clinical or diagnostic observation only/intervention not indicated; Grade 2 (moderate): Minimal, local or non-invasive intervention indicated/limiting age-appropriate instrumental ADL; Grade 3 (severe): Severe or medically significant but not immediately life-threatening/hospitalisation or prolongation of hospitalisation indicated/disabling/limiting self-care ADL; Grade 4 (life-threatening): Life-threatening consequences/urgent intervention required; Grade 5 (death): Death related to AE (not applicable for all AEs); percentages are calculated using the number of patients that experienced any number of SIs (counting multiple occurrences once), by the number of patients;

[†]Includes patients who received any dose of OCR during the CTP and associated OLE periods of the Phase II and Phase III studies plus VELOCE, CHORDS, CASTING, OBOE, ENSEMBLE, LIBERTO, CONSONANCE, CHIMES and OLERO (total N=6,155 patients);

[‡]Single-drop method (total N=2,092).

Abbreviations

ADL, activities of daily living; AE, adverse event; CI, confidence interval; COVID-19, coronavirus disease 2019; CTCAE, Common Terminology Criteria for Adverse Events; CTP, controlled treatment period; Ig, immunoglobulin; LLN, lower limit of normal; OCR, ocrelizumab; OLE, open-label extension; PMS, progressive MS; PPMS, primary progressive MS; pwMS, patients with MS; PY, patient-years; Q, quarter; RMS, relapsing MS; SI, serious infection.

Reference

1. Hauser SL, et al. Presented atECTRIMS 2023 (Poster P304).