

Ocrelizumab and Serum Ig Levels

Overview¹



Impact on IgG

- As of January 2020, following regular, 6-monthly dosing of OCR 600 mg, a mean reduction in serum IgG levels of approximately 3% per year was seen
- IgG levels remained above LLN for the majority of patients (>90%), over a period of up to 7 years



SI types and outcomes

- The type, severity, duration, and outcome of SIs observed during episodes of Ig <LLN were similar to the overall population treated with OCR, and to the general MS population



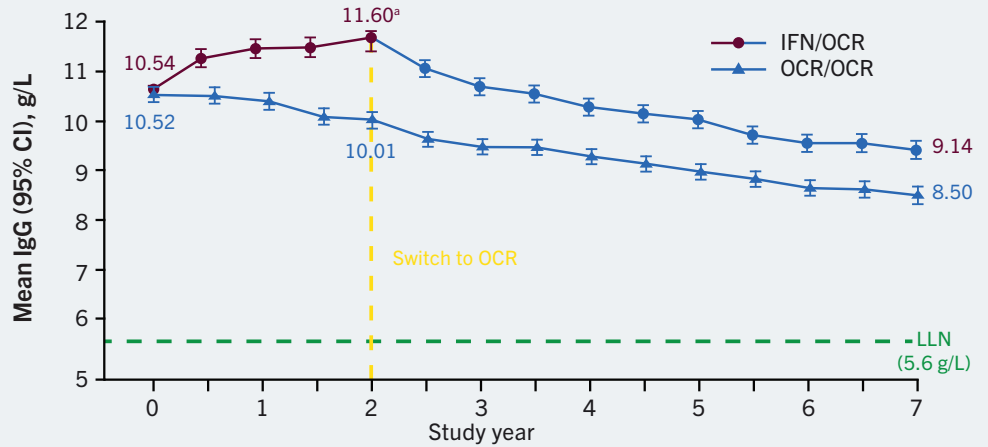
Ig levels and SI incidence

- While incidence of SIs was low, an apparent association between decreased IgG and SIs was observed (but less apparent for IgM and IgA)
- All patients with a SI associated with low IgG recovered
- Few patients had to discontinue OCR due to a SI associated with Ig <LLN

Clinical Trial Population: Change in Serum Ig Levels

A. OPERA

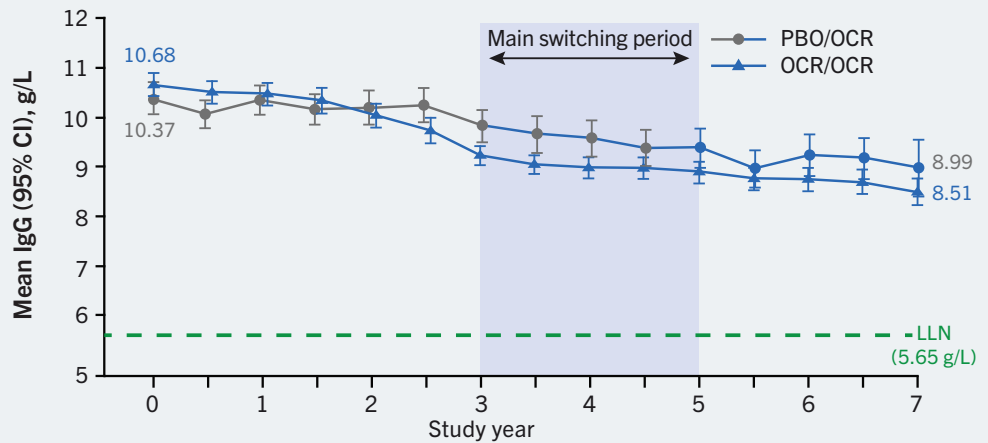
Change in serum IgG levels in patients with RMS



N of patients/weeks	BL	24	48	72	96	120	144	168	192	216	240	264	288	312	336
IFN/OCR	824	772	711	677	653	602	587	575	563	551	545	537	523	513	508
OCR/OCR	823	781	757	741	719	698	664	646	628	622	607	593	582	575	566
Proportion of patients with IgG levels <LLN (%)															
IFN/OCR	0.5				0.3				1.1						2.9
OCR/OCR	0.5				1.5			4.0							7.7

B. ORATORIO

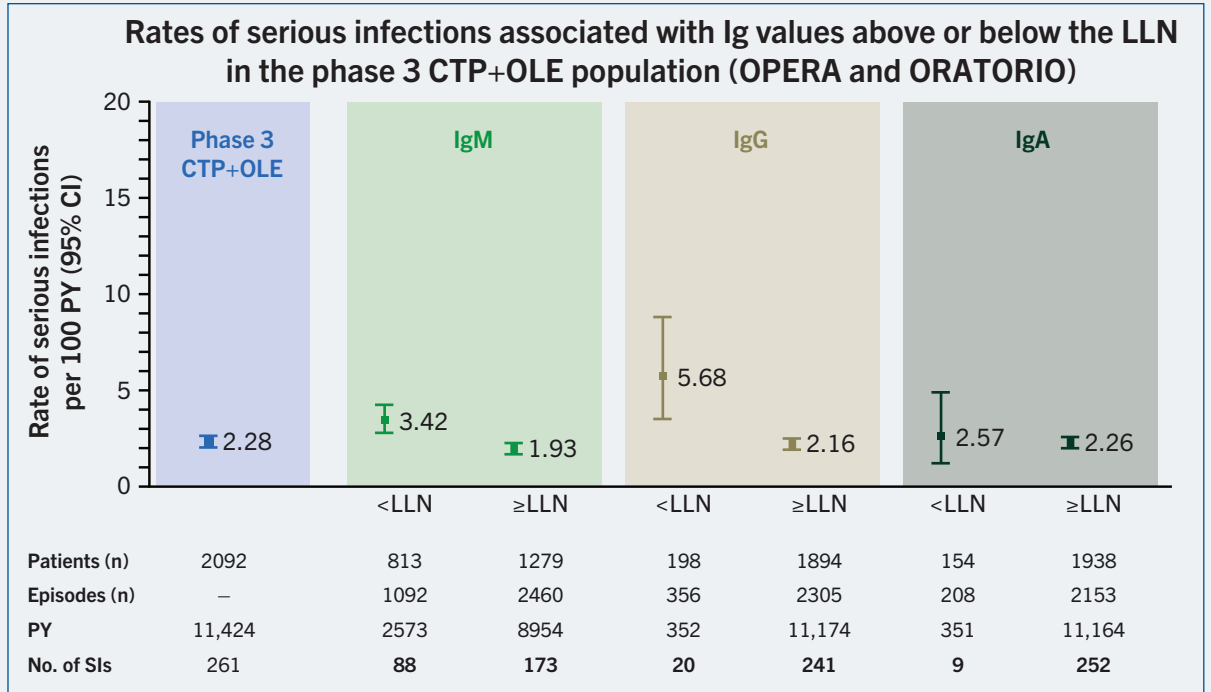
Change in serum IgG levels in patients with PPMS



N of patients/weeks	BL	24	48	72	96	120	144	168	192	216	240	264	288	312	336
PBO/OCR	239	218	206	192	172	162	154	139	133	119	101	107	105	109	69
OCR/OCR	484	430	430	407	402	371	397	384	364	343	330	310	291	276	252
Proportion of patients with IgG levels <LLN (%)															
PBO/OCR	0.4					1.2			2.3						4.6
OCR/OCR	0					1.1		4.1							5.1

¹In patients treated with IFN, an increase in serum IgG levels was observed over a 2-year period. This is consistent with previous findings from other groups.² Data on proportion of patients with immunoglobulin levels <LLN shown only until Week 312, as data at Week 336 are not mature. The proportion of patients randomized to OCR in the OPERA population with IgG levels <LLN was 1.5% at Week 96, and 7.7% at Week 312 (OCR/OCR data). Similarly, the proportion of patients randomized to OCR in the ORATORIO population with IgG levels <LLN was 1.1% at Week 120, and 5.1% at Week 312 (OCR/OCR data).

Clinical Trial Population: Relationship Between Rates of SIs and Ig Values



The [Prescribing Information](#) is the primary source of information on the known and potential risks associated with ocrelizumab.

Abbreviations:

BL=baseline; CTP=controlled treatment period; IFN=interferon; Ig=immunoglobulin; LLN=lower limit of normal; MS=multiple sclerosis; OCR=ocrelizumab; OLE=open-label extension; PBO=placebo; PPMS=primary progressive MS; PY=patient-years; RMS=relapsing MS; SI=serious infection.

References:

1. Hauser SL, et al. *Neurology*. 2021;doi:10.1212/WNL.000000000012700.
2. Mehling M, et al. *PLoS ONE*. 2013;8:e78532.