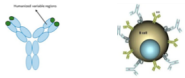
Long-term effectiveness and safety of ocrelizumab: A single centre real-worls study

Lucia Moiola[1], Tiziana Zaccone[1], Simone Guerrieri[1], Agostino Nozzolillo[1], Chiara Zanetta[1], Irene Gattuso[1], Angela Genchi[1], Federica Esposito[1], Paola Maria V Rancoita[2], Maria Giovanna Scarale[2], Maria Assunta Rocca[1, 2, 3], Massimo Filippi[1, 2, 3, 4, 5]

[1]*Neurology Unit, Multiple Sclerosis Center, IRCCS San Raffaele Scientific Institute, Milan, Italy,*
[2]*Vita-Salute San Raffaele University, Milan, Italy,*
[3]*Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy,*
[4]*Neurorehabilitation Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy,*
[5]*Neurophysiology Service, IRCCS San Raffaele Scientific Institute, Milan, Italy*

Introduction and Aims:

Ocrelizumab (OCR) is a recombinant humanized anti- CD20 monoclonal antibody approved as a high efficacy treatment (HET) for the treatment of MS. Long-term studies about effectiveness and tolerability of OCR in clinical practice remain scanty.



Aim of this work was to evaluate the effectiveness and safety of OCR in relapsing multiple sclerosis (RMS) and primary progressive MS (PPMS) and identified predictors of treatment response

Methods: the present study is:

- Retrospective
- Observational
- Single-center

Data from all patients receiving OCR for MS at San Raffaele Hospital of Milan were collected

Results:

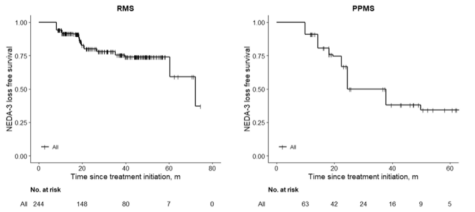
We included 260 RMS and 73 PPMS patients treated with OCR for ≥1 year at MS Center until May 2024.

	RMS (n=260)	PPMS (n=73)
Females, n (%)	**159 (65.2%)**	**23 (32.4%)**
Age at OCR start (years), mean±SD	**37.15 [30.10 - 45.52]**	**44.67 [37.45 - 50.80]**
Disease duration at OCR start, (years), mean±SD	**10.55 [4.70 - 18.33]**	**5.92 [3.49 - 8.88]**
EDSS at OCR start, mean (range)	**2.5 [1.5 – 4.0]**	**4.5 [3.5 – 6.0]**
Previous DMTs, n (%)	**Naïve 38 (14.6%) 1 DMT 49 (18.9%) 2 DMT 60 (23.1%) ≥ 3 DMT 113 (43.5%)**	**Naïve 32 (43.8%) 1 DMT 25 (34.3%) 2 DMT 10 (13.7%) ≥ 3 DMT 6 (8.2%)**

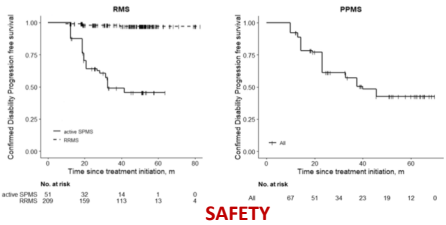
EFFECTIVENESS

- Median follow-up was 3.90 years for RMS and 4.23 years for PPMS
- Within 2 years from treatment initiation, annualized relapse rate (ARR) decreased from 0.412 to 0.014 and was maintained low throughout follow-up in RMS, with no relapses in PPMS
- MRI activity significantly declined and was maintained in both groups (p<0.0001)
- After 3 years, CDP-free survival was high in RR-MS (>97%) and lower in SP-MS (48.9%) and PPMS (57.2%)
- Predictors of OCR inefficacy included higher baseline EDSS, older age and longer disease duration in RMS; male sex, older age and prior lower-efficacy treatments in PPMS

NEDA-3 loss-free survival in RMS and PPMS patients



CDP-free survival in RRMS, active SPMS and PPMS patients



SAFETY

The drug was well tolerated with good quality of life. 22 pregnancies occurred in 17 RMS patients during OCR treatment with most resulted in live births. Adverse events were in line with previous clinical studies, with hypogammaglobulinemia and recurrent infections being the most frequent.

Severity and type of hypogammaglobulinemia

	RMS (n=260)	PPMS (n=73)	p-value	Adjusted p-value
Hypogammaglobulinemia				
No	167 (64.23%)	55 (75.34%)		
Mild	87 (33.46%)	18 (24.66%)	0.1427	0.7133
Moderate (n. patients, %)	6 (2.31%)	0 (0%)		
Hypogammaglobulinemia IgG (n. patients, %)	42 (16.15%)	6 (8.22%)	0.0933	0.4663
Hypogammaglobulinemia IgA (n. patients, %)	14 (5.38%)	4 (5.48%)	1.0000	1.0000
Hypogammaglobulinemia IgM (n. patients, %)	78 (30%)	15 (20.55%)	0.1396	0.6979

Uncommon adverse events

	RMS (n=260)	PPMS (n=73)
Febrile neutropenia[a]	5	0
Malignancies		
Breast cancer	2	1
Urothelial carcinoma	1	0
Diffuse large B-cell lymphoma	1	0
Melanoma	0	1
Lung adenocarcinoma	0	1
Transient hepatic alterations	15	2
Drug-induced pneumonia	2	0
Alopecia		
Alopecia barbae	1	0
Alopecia areata	0	1
Atopic dermatitis	1	0
Psoriasis exacerbation	0	1
Deep vein thrombosis	1	1
Autoimmune cerebellitis	1	0
Lower limb vasculitis[b]	1	0

[a]Febrile neutropenia required specific treatment with G-CSF, none of these patients experienced fatal outcomes or MS disease activity

[b]Vasculitis requiring leg amputaion

CONCLUSIONS

We confirm OCR sustained efficacy in controlling inflammatory disease activity, with greater impact in RMS, with a favourable safety profile. Early treatment initiation is crucial to prevent irreversible disability accumulation

DIsclosures: *LM received compensations for speaking activities and/or for participating to advisory board from Merck, Celgene, Biogen, Sanofi, Novartis, Roche, Alexion, and Amgen. TZ, IG, AN, MGS, PMVR have nothing to disclose has nothing to disclose SG received compensation for speaking activities from Bristol Squibb Meyer, Novartis, Merck. CZ received compensation for speaking activities, and/or consulting services, from Alexion, AstraZeneca, Biogen, Bristol Myers Squibb, Janssen, Merck, Novartis, Roche, Sanofi. AG received compensation for speaking activities from Novartis. FE received consulting and speaking fees from Novartis and Sanofi Genzyme. M.A. Rocca received consulting fees and/or speaker honoraria from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, AstraZeneca, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono, Novartis, Sanofi and Teva. M. Filippi received compensation for consulting services and/or participation in Advisory Boards from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi; speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme.*