MALIGNANT MELANOMA DEVELOPMENT DURING OCRELIZUMAB TREATMENT IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS: A CASE SERIES

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Poster code: 690

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Background and aims

Long-term and post-marketing studies currently available do not indicate an increased cancer risk during ocrelizumab administration in patient with multiple sclerosis (pwMS).
We report three cases of malignant melanoma during ocrelizumab treatment.

Materials and methods

We retrospectively identified pwMS receiving anti-CD20 treatment among our single center cohort and we monitored three patients who were diagnosed with melanoma during ocrelizumab therapy. Clinical, staging and treatment data related to melanoma management and anti-CD20 rechallenge were collected.

Results

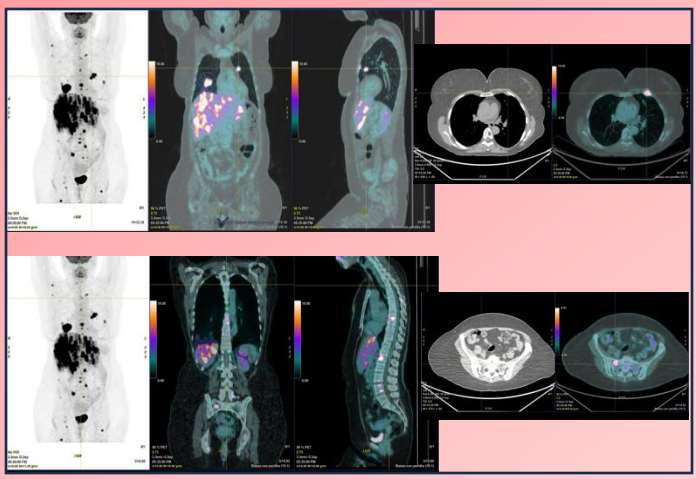
Table 1. Demographic and clinical characteristic of our patients.

Patients' characteristics (n=3)	Median (range) or n (%)
Age (years)	54 (49-59)
Sex	Female 1 (33.3%)
EDSS	5 (3.5-6)
Relapsing-remitting	3 (100%)
Ocrelizumab	3 (100%)
Anti-CD20 cycles	5 (2-7)
Time after beginning treatment with anti-CD20 (months)	27 (7-41)

Table 2. Oncological characteristics of our patients.

Melanoma staging (n=3)	
Stage I	1 (33%)
Stage III	1 (33%)
Stage IV	1 (33%)
Treatment	
Surgical	3 (100%)
Dabrafenib and Trametinib	2 (66.6%)
Anti-CD20 discontinuation	2 (66.6%)

Figure 1. Stage IV melanoma. ^{18}FDG-PET/TC scans show bilateral lung, liver, left adrenal, skeletal, muscular and subcutaneous secondarisms.



Patients' demographic characteristics are summarized in **Table 1**.
Only one patient had a previous melanoma diagnosis in medical history. No signs of dermatological atipias were detected at the preliminary evaluation time.
The histological diagnosis of melanoma occurred with a median time of 27 months after the first cycle administration. One patient had local tumor, one a lymph node metastasis, while the third (**Figure 1**) a plurimetastatic melanoma.

Patients were treated according to their oncological staging with wide local excision, sentinel lymph node biopsy and in two cases with dabrafenib and trametinib (**Table 2**).
In the melanoma in situ case, treatment with ocrelizumab has not been interrupted.
The patient affected by stage IIIC melanoma was switched to dimethyl fumarate, with evidence of stable disease at one-year follow up.
DMT has been discontinued in stage IV melanoma according to patient's preference.

Discussion

The ocrelizumab-treated cohort in phase 3 OPERA I/II trials reported one case of malignant melanoma in relapsing-remitting MS patients, a second case was detected during the open-label extension study approximately 1 year after ocrelizumab exposure. Regarding progressive MS patients, phase III ORATORIO trial did not report melanoma cases among the observed malignancies and no melanomas were described in the extension trial for ocrelizumab with 6.5 years follow up. Subsequent analysis of post-marketing data and clinical trial demonstrated no increased risk of malignancy in participants receiving long-term treatment compared to MS Danish cohort and the general population.

Conclusions Our case series underlines the importance of screening and monitoring of malignant melanoma development in pwMS during ocrelizumab treatment.

References
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Disdosures
A. Favero: received funding for travel from Fidia.
L. Rossi: received funding for travel/accomodation/course participation from Novartis, Roche, Sandoz, Merzand and AbbVie.
A. Sartori: received funding for travel and/or speaker honoraria from Biogen, Novartis, Roche; she is Principal Investigator in clinical trials of Novartis and Roche.
A. Bosco: received funding for travel from Biogen, Roche, Sanofi and MBS.
A. Bratina: received speaker honoraria from Argenx.
P.Manganotti: nothing to disdose.