Lepto-Meningeal metastases in the modern era of melanoma treatment. A mono-institutional experience

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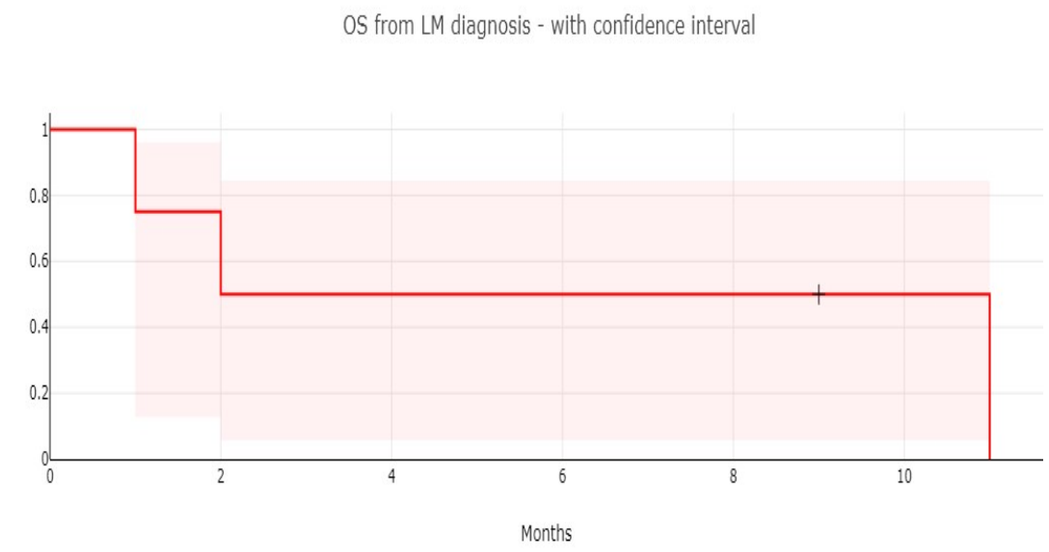
Background

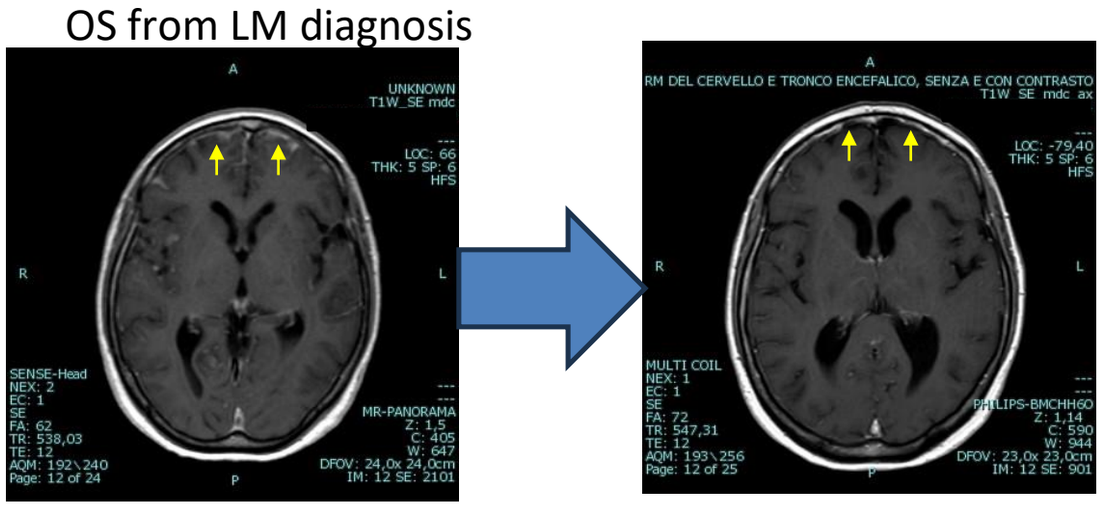
- Leptomeningeal metastases (LM) occur in around 5-10% of metastatic melanoma (MM) patients.
- The prognosis of LM is poor with a median OS of 2-3 months from diagnosis. LM occur most frequently in BRAF muted MM (60%).
- Since 2022, the combination of Ipilimumab + Nivolumab (I+N) and Encorafenib + Binimetinib (E+B) are reimbursed by the Italian medicine agency (AIFA), for the treatment of MM. To date no evidence exists regarding the treatment of LM with those combinations.
- We hereby report a mono-institutional case series of patients diagnosed with LM, treated with either I+N, E+B or both.

Patients and methods

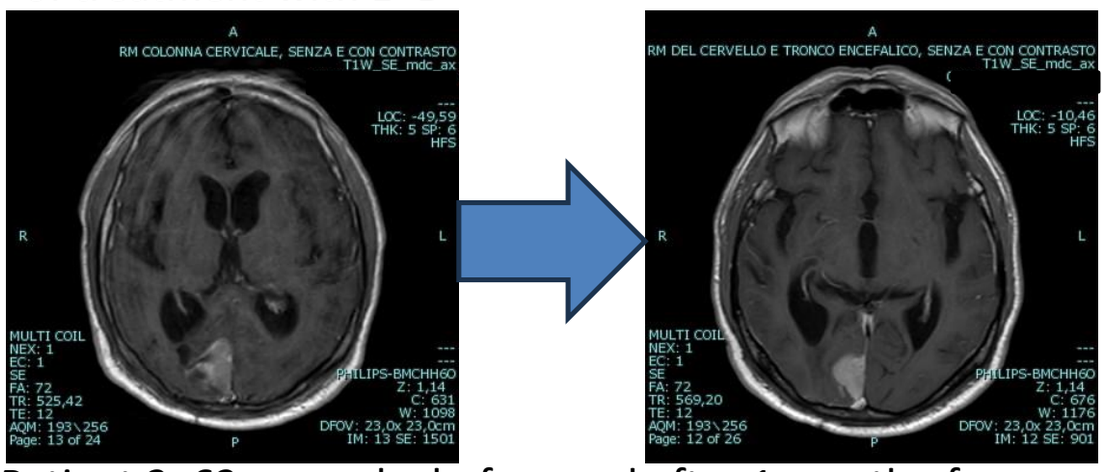
- A retrospective chart review of patients with LM in MM was performed at one institution.
- Patients were eligible if they had evidence of LM according to EANO-ESMO LM classification and were treated with either I+N, E+B or both.
- Response evaluation was performed with revised LM-EANO criteria. Survival analysis was performed with Kaplan Meier method.



OS from LM diagnosis



Patient 1, 47 yo, female, before and after 2 month of treatment with E+B



Patient 2, 63 yo, male, before and after 1 month of treatment with E+B

Results

- From January 2022, 4/76 MM (5.2%) patients with available data developed LM.
- Median age of LM patients was 60 years, 2/4 patients were male, 3/4 BRAF V600E muted (BRAFmut), 2/4 had concomitant brain metastases, 1/4 had LM at diagnosis, 2/4 had concomitant brain metastases, 2/4 had a previous brain metastasis surgery, 0/4 had concomitant visceral metastases.
- 1/4 had LM at diagnosis, 2/4 had EANO-ESMO-LM I class LM (cyto-histological confirmation of LM), 2/4 had EANO-ESMO-LM II (radiological confirmation of LM) 3/4 patients received high dose steroids.
- 2/3 BRAFmut patients received E+B, 1/3 BRAFmut patients received both E+B and I+N.
- Of 3/4 patients treated with I+N, no disease control was achieved.
- Of two patients treated with E+B one achieved a PR and one a SD as a best response. One of two patients treated with E+B reduced baseline steroid dose .
- Median OS from LM diagnosis was 5.5 months.
- Median PFS was 5.7 weeks.
- One patient treated with E+B had a PFS of 24

Conclusions

- In our case series, LM confirms to be a disease with a dismal prognosis.
- Immunotherapy with double I+N was not effective in the treatment of LM, according with preclinical findings of an immunosuppressive microenvironment of LM.
- Patients with BRAF V600E mutation may derive benefit from E+B treatment.
- Larger collaborations are welcomed to define the clinical behaviour in this rare group of patients

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