Immune checkpoint inhibitors and asymptomatic brain metastases from NSCLC
Case presentation

- 68 years old, male, patient
- ECOG PS 1
- Former smoker (30 cigarettes/d for 50 years);
- Comorbidities: diabetes mellitus type 2, in treatment with Metformin
Clinical Course

- Nov 2014: onset of pain and subsequent paresthesia with functional deficit in the right lower limb;
- Feb 2015: lumbar laminectomy surgery of L3-L4 → bone metastasis from lung adenocarcinoma (TTF1+, p63-), EGFR WT, ALK/ROS1/PD-L1 not evaluable;
- Disease Staging (TNM VIII ed.): cT3 N3 M1c (bone and adrenal gland metastases)
- Mar 2015: post-operative RT on lumbar vertebrae L3-L4 (8 Gy/1 fraction)
- Mar-Sep 2015: 1st line therapy start with Pemetrexed/Carboplatin x4 courses with SD as best response, followed by Pemetrexed maintenance for only 1 cycle, because of hematologic toxicities (anemia G3, thrombocytopenia G4).
- Concomitant Zoledronic acid 4 mg i.v. 4-wk was also started.
- Nov 2015: radiological PD (emergence of pleural effusion, enlargement of lung lesions, and emergence of a single brain metastasis of 13 mm, asymptomatic) with clinical condition deterioration (ECOG PS 1 → ECOG PS 2)
Immune Checkpoint inhibitors & asymptomatic BMs

- In a small, open-label, phase II study, Pembrolizumab showed significant activity in patients with untreated or progressive BMs (5-20 mm in diameter without associated neurological symptoms or the need for corticosteroids) from melanoma or NSCLC with an acceptable safety profile [Goldberg SB, et al. Lancet Oncol 2016];


- Dec 2015: **Start of 2nd line therapy with Nivolumab 3 mg/kg 2-wk i.v.** in the Expanded Access Program (EAP); continued Zoledronic acid 4 mg i.v. 4-wk
Response to Nivolumab

- Mar 2016: after 4 courses of Nivolumab, the CT re-staging showed a PR (RECIST 1.1) with significant reduction of both BM (8 mm vs. 13 mm) and lung lesions (21 mm vs. 45 mm and disappearance of other lesions); bone and adrenal gland metastases remained stable; the ECOG PS improved from 2 to 0.

- Oct 2017: after 39 courses of Nivolumab the patient is still on treatment without relevant toxicities and substantial clinical and radiological SD.
Open questions

- How long should Nivolumab be offered [1]?

- Radiotherapy and immune checkpoint inhibitors: synergistic effect [2]?

- Does immunotherapy increase the rate of radiation necrosis after radiosurgical treatment of brain metastases [3]?

- Upfront use of immunotherapy in asymptomatic BMs pts or delayed after radiation therapy (SRS and/or WBRT)?

Thank you!