#6747 - Sites of metastases prior to systemic treatment influence progression patterns and survival in stage IV melanoma patients

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Background

- Different metastatic sites have distinct response rates to immune checkpoint inhibitors (ICI), suggesting that anatomical locations play a role in treatment response and survival (Pires da Silva *et al.*, 2022).

Objectives

To investigate the association between sites of metastases at baseline and:

- sites of progression in patients who failed first-line anti-PD1 vs first line BRAF/MEK inhibitors (BRAF/MEKi),
- sites of progression in patients who failed first-line anti-PD1 with innate vs acquired resistance, and
- survival of all patients, from time of first line treatment to last follow-up.

Methods

- 557 patients with stage IV melanoma diagnosed between 2010-2021 were identified in the Melanoma Institute Australia research database.
- All patients had first-line treatment - 189 anti-PD1 alone, 158 anti-PD1 + anti-CTLA4, and 210 BRAF/MEKi therapy.
- First-line treatment was administered no later than 90 days after the earliest metastatic event prior to therapy.

Results

- Graph representation of anatomical progression captures sites of metastases at baseline and those after treatment failure.

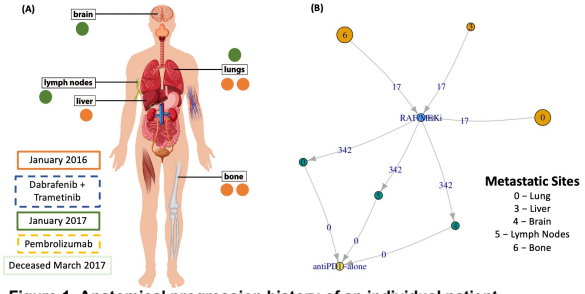

Figure 1. Anatomical progression history of an individual patient.

Results

- Sites of metastasis at baseline influence the pattern of progression in patients that fail first-line systemic therapy.

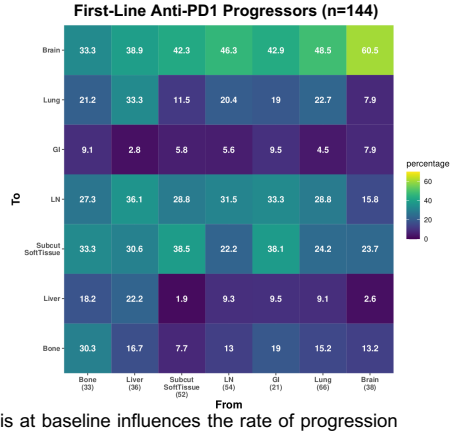

Figure 2. Rates of progression at anatomical sites (%) in patients that failed anti-PD1. *Rows:* metastatic sites at baseline. *Columns:* metastatic sites occurring immediately after first-line treatment.

- Brain metastasis at baseline influences the rate of progression to the brain.

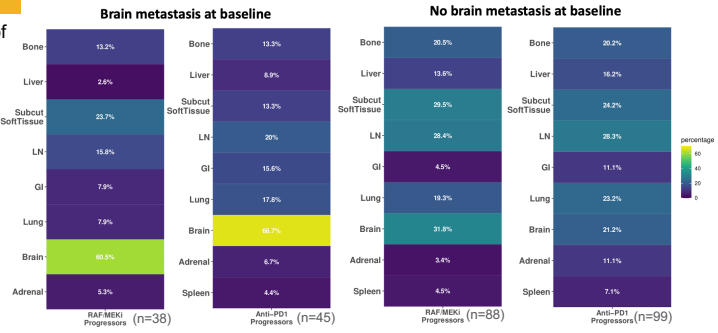

Figure 3. Rates of progression at anatomical sites (%) in patients that failed treatment with (left) and without (right) brain metastasis at baseline.

Results

- Brain metastasis at baseline influences the rate of progression to the brain in patients with innate resistance.

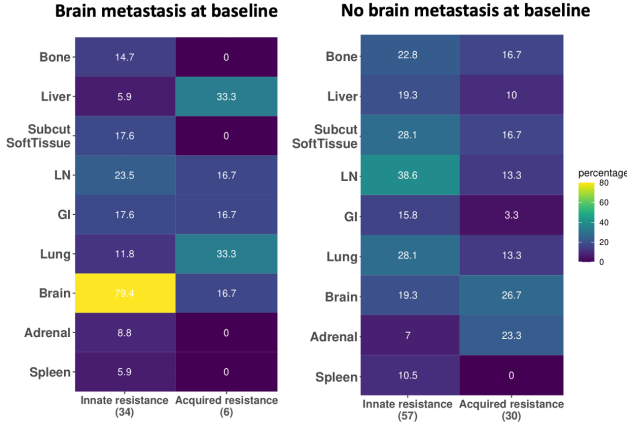

Figure 4. Rates of progression at anatomical sites (%) in patients with innate and acquired resistance after anti-PD1 first-line treatment with (left) and without (right) brain metastasis at baseline.

- Sites of metastases at baseline impact the survival of patients.

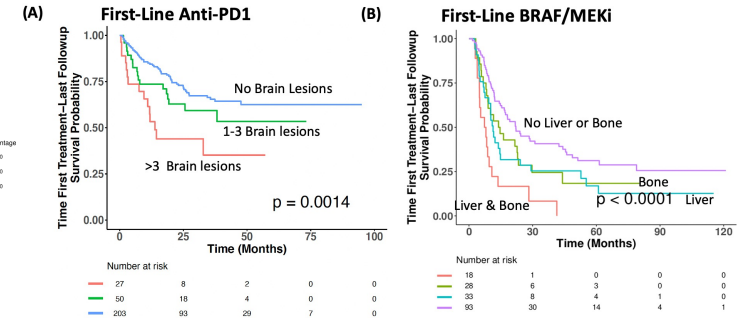

Figure 5. Survival association of metastatic sites at baseline. Survival of patients exposed to (A) anti-PD1 first-line treatment, and (B) BRAF/MEKi first-line treatment.

Conclusions and Future Directions

- Different sites of metastases at baseline have a distinct effect on the progression patterns and survival of patients who received BRAF/MEKi or anti-PD1 as first-line treatment.
- Graph representation of metastatic progression is generally applicable and is being
  - used for the development of a time-dependent predictor of brain metastases, and
  - utilised to characterise the clinical progression history of patients presenting with in-transit metastasis and with toxicity profiles after ICI administration.

References

- Pires da Silva I, *et al.* Clinical Models to Define Response and Survival With Anti-PD-1 Antibodies Alone or Combined With Ipilimumab in Metastatic Melanoma. J Clin Oncol. 2022

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