



ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

Oligometastatic progression following elective discontinuation of anti-PD-1 therapy

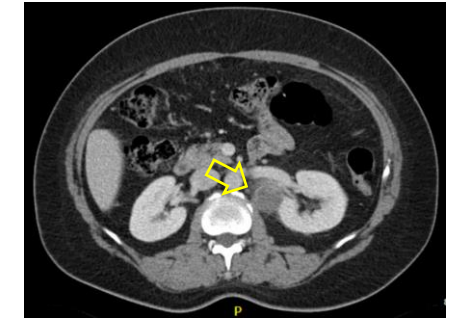
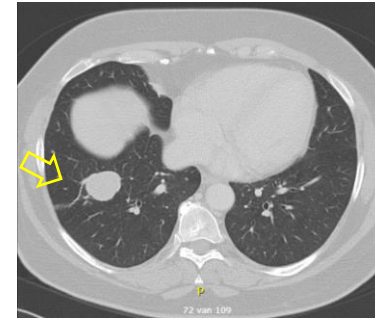
BRAF V600E Mutant Melanoma patient case

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Initial diagnosis

- **07/2012**
56y F, diagnosis of stage IV-M1c (T0, sc, lung, kidney, peritoneal M+; nl LDH) BRAF V600E mutant melanoma
- **10/8/2012**
Start vemurafenib (Phase 4 study)
- **07/03/2014**
Switch to dabrafenib/trametinib because of vemurafenib related skin photosensitivity
AE: neutrophilic panniculitis (G1)

07/2012

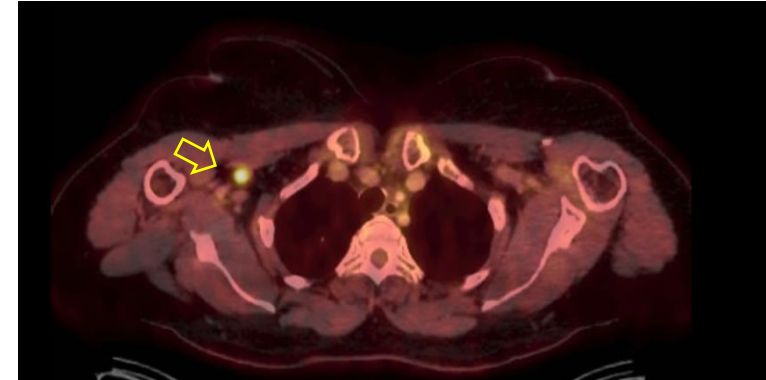


07/2013



Progression on BRAF-/MEKi, switch to anti-PD-1

- **18/7/2017**
Solitary new FDG-avid sc lesion R-upper-arm (9 mm)
 - Resection = melanoma metastasis, BRAF V600mut
 - Continue on Dabrafenib/Trametinib
- **27/11/2017**
CMR on 18F-FDG PET/CT
- **25/10/2018**
Suspect FDG-avid axillary lymph node
 - Switch therapy to pembrolizumab
 - 27/12/2018: CMR, no AE



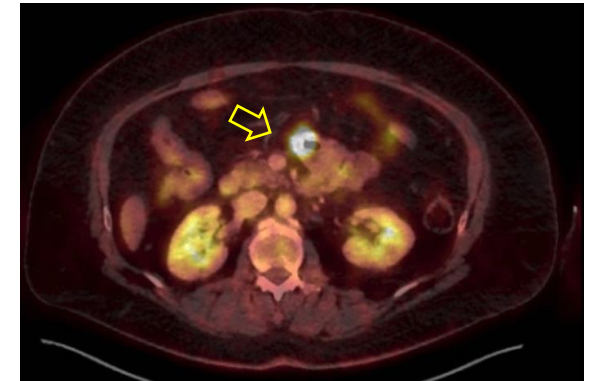
Oligo-metastatic PD on anti-PD-1

▶ **26/09/2019**

Asymptomatic FDG-avid small bowel lesion

- Confirmed on video capsule endoscopy as jejunal bleeding metastasis
- 23/10/2019: robot assisted metastasectomy (end-to-side anastomosis)

▶ **18/12/2019: CR**



What would you do next ?

POLLING QUESTION

1. Resume BRAF/MEK inhibition
2. Resume anti-PD1 therapy
3. Resection (metastasectomy) without further systemic therapy
4. Start nivolumab + ipilimumab combination
5. I'm not an expert but I'm happy to learn more about the subject



A laparoscopic resection of the small bowel metastasis with an end-to-end anastomosis was performed.

No further therapy was administered.

Confirmed CR up to the latest FU in January 2021



The value of local therapy in treatment of solitary melanoma progression upon ICI

Background & Methodology

- Retrospective multi-institutional analysis (17 centers, 9 countries)
- **Aim:** to evaluate the value of local therapy for the treatment of solitary melanoma progression (SP) during or after cessation of ICI.
- **Patient population:**
294 stage IV melanoma patients, with \geq stable disease (SD) as best overall response (BOR) upon ICI, and with SP on ICI therapy.
Best overall response to ICI:
 - 15% stable disease (SD)
 - 55% partial response (PR)
 - 30% complete responseThe median follow-up from start ICI was 43 months.
- **Solitary progression (SP):**
median time to development of SP in overall population was 13 months.
Treatment of SP:
 - 42% local + systemic therapy
 - 36% local therapy
 - 18% systemic therapy

Results

Median time to second progression after treatment of solitary progression (TTSP) in overall population 33 months.

Median overall survival (OS) during ICI was not reached; estimated 3-year OS was 79%.

During ICI therapy solitary progression occurred in 143 patients - median time to development: 11 months

- Median TTSP after treatment of solitary progression: 29 months
- 3 years TTSP was **similar** (P=0.971) for: **local therapy + ICI continuation** (N=94), local therapy only (N=15) or ICI continuation only (N=14)
- **Local therapy + ICI continuation did improve OS** at 3 years (p=0.020)

After ICI cessation solitary progression occurred in 151 patients - median time to development: 17 months from start ICI and 9 months from stop ICI

- Median TTSP after treatment of solitary progression: 35 months
- Combined **local therapy + ICI restart** (n=22) was **superior** (P=0.002) to local therapy (n=90) or to ICI restart (n=18) **in delaying TTSP**
- Combined **local therapy + ICI restart did not improve OS** so far compared to single modality treatment

Conclusions and Key Takeaways

These data suggest that local therapy might benefit patients with stage IV melanoma and solitary progression

