A case of right-sided colonic adenocarcinoma with pulmonary metastases and an unusual molecular profile
Disclosure of interest

- None
Case presentation

- 76-year-old ♀
- Never-smoker
- Arterial hypertension
- Family history of cancer (brother and sister)

Jan 2019:
- Feeling of tiredness and weakness
Diagnostic work-up

1. CBC ➔ anaemia (Hg=10.3 g/dL); CEA=18.7
2. Colonoscopy ➔ diverticulae of left colon and sigmoid
3. Abdominal CT scan ➔ luminal stenosis of the right colon above the cecum extending for 7 cm and a renal lesion
4. Thorax CT scan ➔ 17 spiculate nodular lesions disseminated in both lungs (0.5–1.8 cm)
5. GI MDT Discussion
6. Fit, w/o curative intent – disease control
Histology & Molecular findings

- Feb 2019: right hemicolecotomy
- Histology report: low-grade adenocarcinoma at 3 cm from ileocecal valve (5.5 cm X 5 cm)
  - Infiltration of pericolic adipose tissue: **T3**
  - 1/18 LN +ve: **N1a**
  - Multiple pulmonary lesions on CT scan of the thorax: **M1**
- Tissue NGS (23-gene panel): **KRAS^Q22K**, **BRAF^G466E**, also **SMAD** and **TP53** mutations
- MSI testing: MSS

Plasma BEAMing Digital PCR (research protocol): **KRAS** and **NRAS** exons 2, 3, 4 codons 12, 13, 59, 61, 117, 146 ➔ No mutation detected
Treatment & Response

Feb–Aug 2019:
8 cycles of CapOx + Bev
(well tolerated)

Re-evaluation
CT scan ➔ PR

Sep 2019–present:
Maintenance Cap + Bev
Food for thought…

- Why did a non-rectal tumour spread to the lung having skipped the liver?
- What is the biological impact of the rare KRAS and BRAF mutations observed in this tumour?
- How to explain co-existence of mutually exclusive KRAS and BRAF mutations?
Lung-only colorectal cancer metastases


The ASCRS Textbook of Colon and Rectal Surgery. Springer, Cham (2016)

KRAS Q22K

- Activating mutation of the Ras pathway *in vitro* ➔ anti-EFGR resistance
- In CRC, 0.009% or 7/73000 (COSMIC)
- JM Loree (2017): 8609 mCRC cases: 0.2%

RAS wild-type 50.7%
RAS mutant 49.3%

Typical RAS mutations 48%
Atypical RAS mutations other than Q22K 1.1%
KRAS Q22K 0.2%
**BRAF G466E**

- In CRC, 2/73000 (COSMIC)
- Belongs to Class 3 of BRAF mutants with low/absent kinase activity
  - Co-exist with aberrations in upstream molecules of the Ras pathway such as **RAS**, **NF1** or receptor tyrosine kinases (RTK)
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  - *Yao Z et al. Nat (2017)*

- Promise for response to therapeutic inhibition of the Ras/Raf pathway
Take-home message

- The existence of rare *KRAS* and *BRAF* mutations in a patient with colorectal cancer points to the limitations of hotspot mutation analysis, as such mutations may have implications in the patient’s treatment and clinical course.
Thank you for your attention!