Case Presentation 2

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Case study

SH, age 31

- Right cystectomy x 2 (age 15 and 17)

Pathology: Benign

- Right SO and appendectomy (age 19)

Pathology: Mucinous borderline ovarian cancer with focal areas of intraepithelial carcinoma

- Left cystectomy (age 21)

Pathology: Mucinous borderline ovarian cancer

Case study

Sept 2017:

- US with left cyst and hydrosalpinx

January 2018:

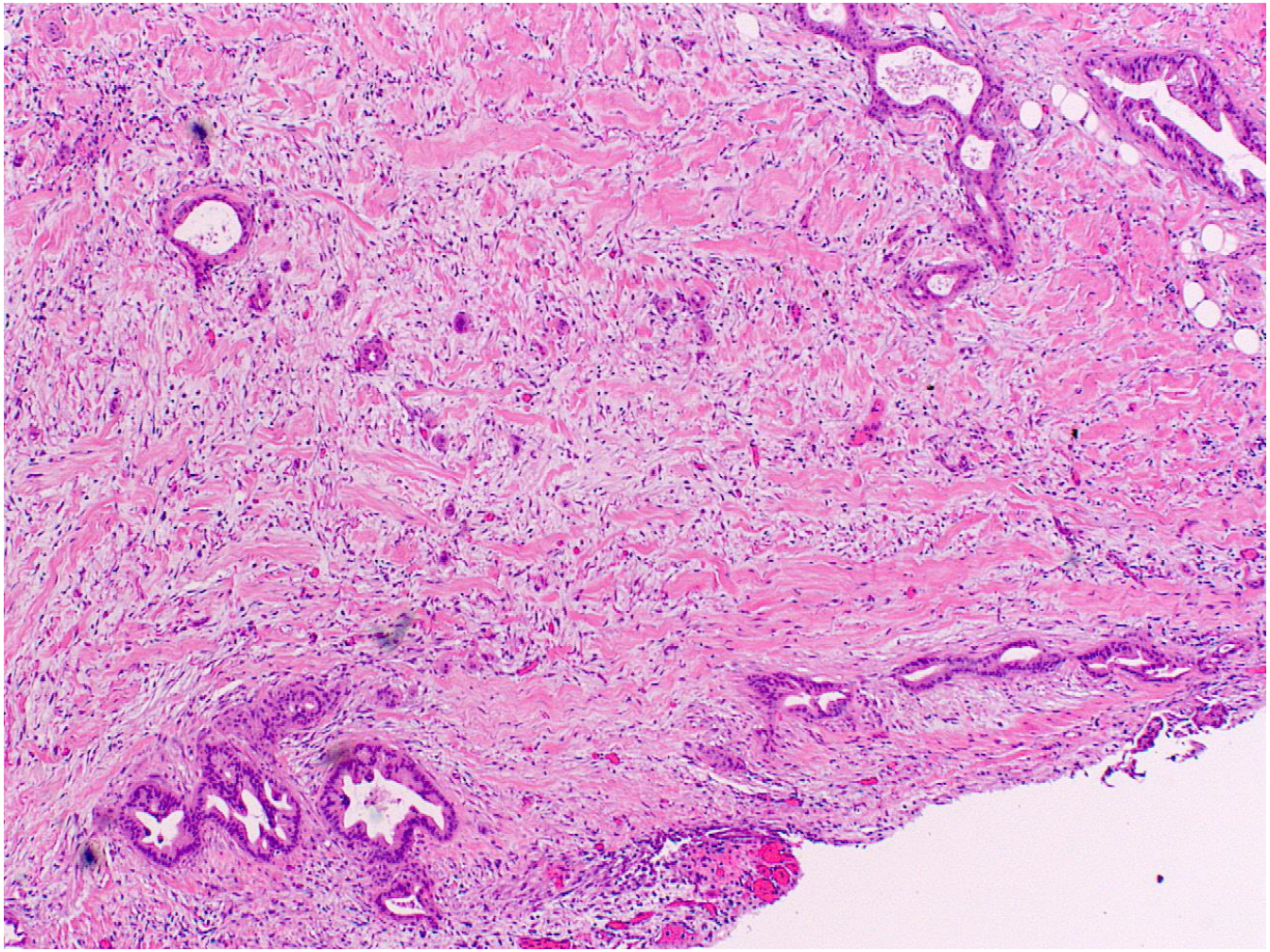
- Increasing lower abdominal discomfort
- CT with left ovarian cyst
- Ca125 17, Ca 19.9 1743, CEA normal

Case study

Laparotomy and Left SO, omentectomy, pelvic and peritoneal biopsies and endometrial curettings.

- Deposits in the upper abdomen, pelvic brim, right abdominal wall and small bowel serosa

Case study



Case study

Referred for opinion: Peritonectomy and HIPEC

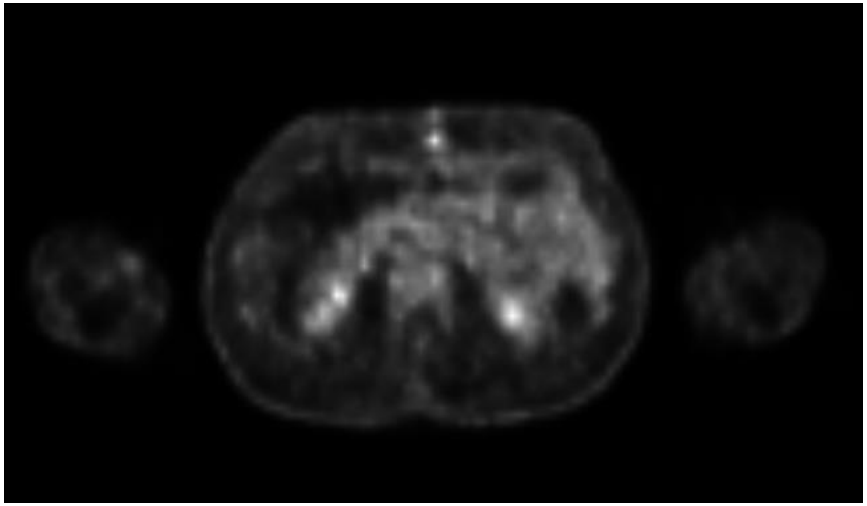
Management options

1. Peritonectomy and HIPEC then chemotherapy

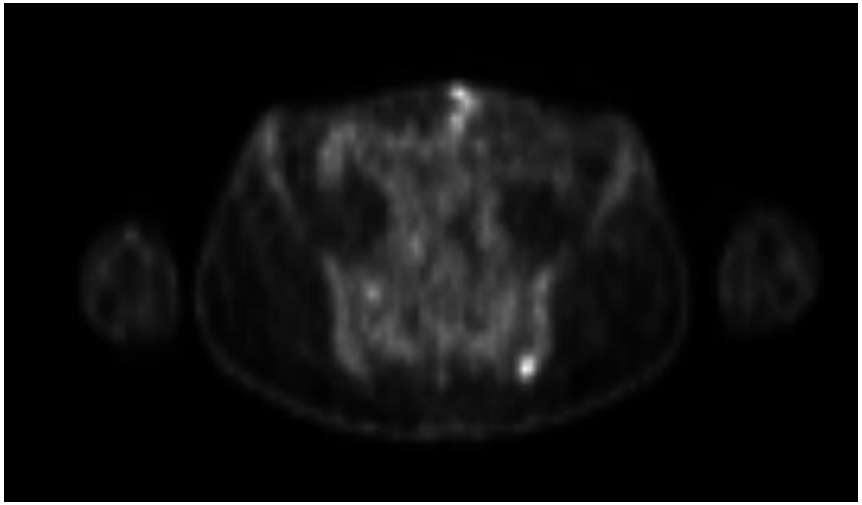
2. Chemotherapy then peritonectomy and HIPEC

3. Chemotherapy and no HIPEC

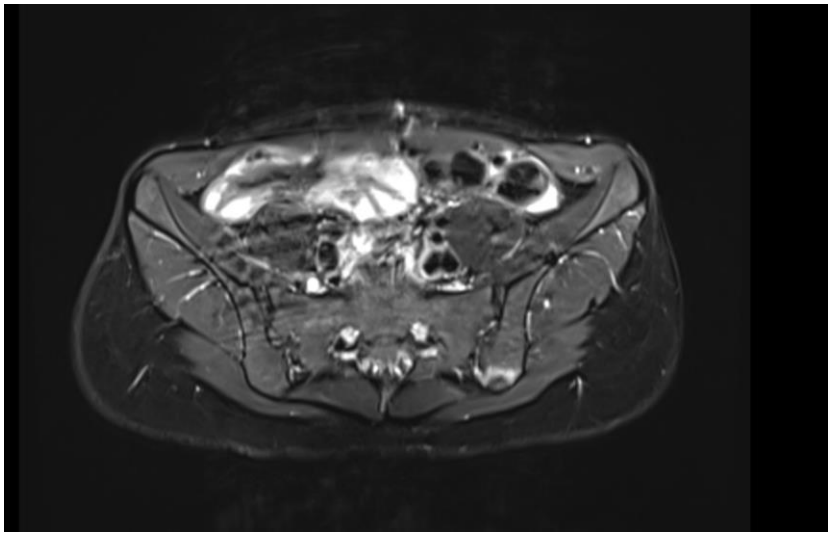
Case study



Diffuse uptake
- Soft tissues of the pelvis adjacent to the bowel
- Peritoneum
- Surface of the liver
- Pelvic bone

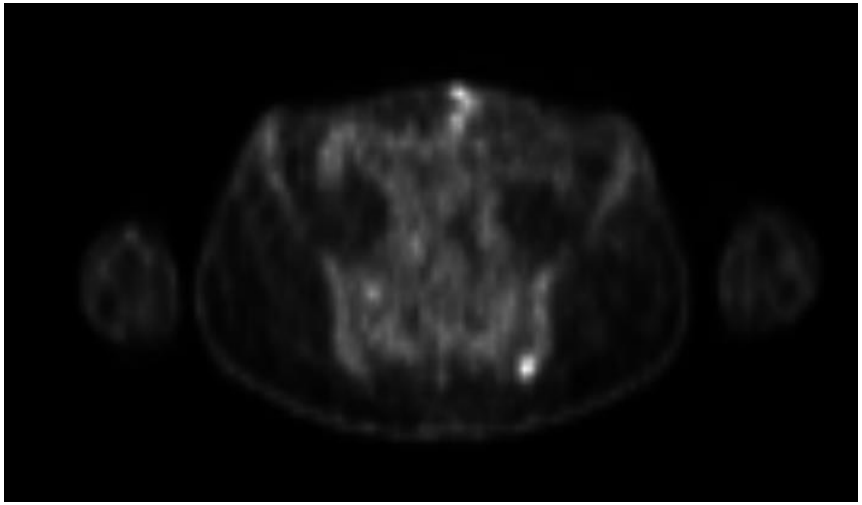


Case study



MRI scan

- At least 3 ill-defined osseous lesions
- Highly suggestive of metastasis



Management options

1. Carboplatin and Paclitaxel
2. Carboplatin, Paclitaxel and Bevacizumab
3. Oxaliplatin and 5FU / Capecitabine
4. Oxaliplatin and 5FU / Capecitabine and Bevacizumab
5. Chemotherapy then peritonectomy and HIPEC (if responds)

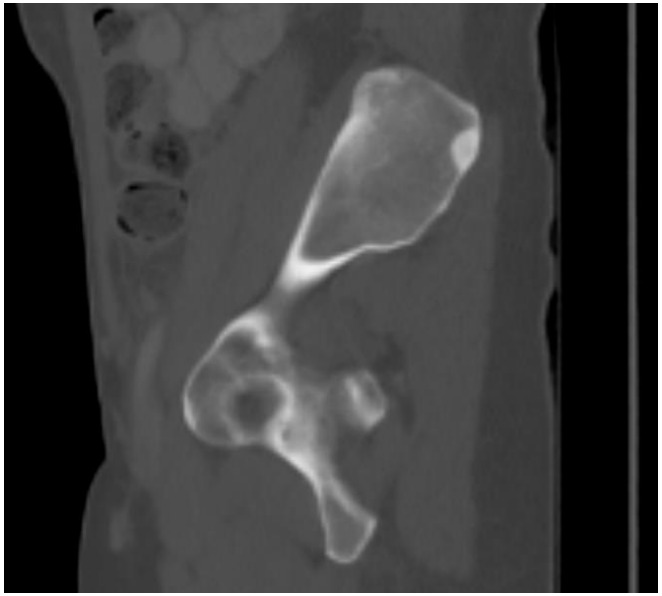
Case study

Oxaliplatin and Capecitabine

Progress imaging after 3 cycles:

- No evidence of residual peritoneal or serosal liver disease

-Increasing size and number of bone metastasis in the pelvis

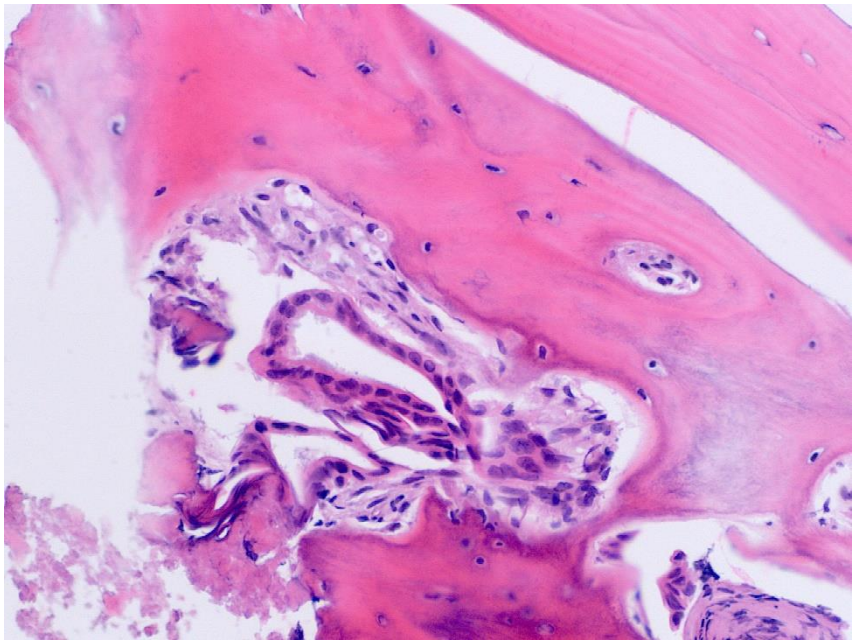


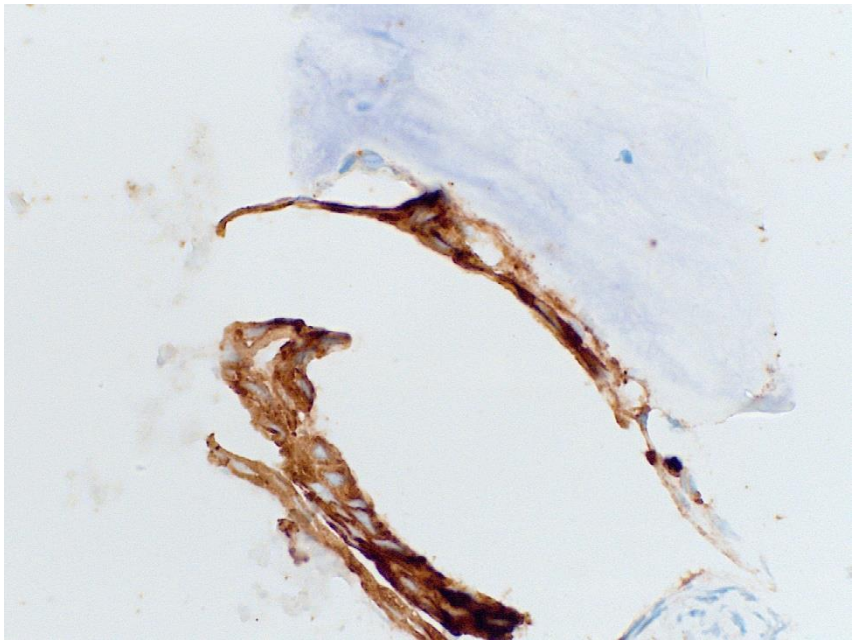
Management options

1. Continue Oxaliplatin and Capecitabine
2. Switch to Carboplatin and Paclitaxel
3. Pelvic radiotherapy
4. Biopsy bone lesion and Peritonectomy and HIPEC if negative
5. Look for clinical trial options

Case study

Biopsy performed





Case study

Continued Oxaliplatin and Capecitabine

Referred to MoST

Progress imaging after 6 cycles:

-Stable appearances

-No new sites of disease

Clinically well with no disease symptoms

Neuropathy with Oxaliplatin

Case study

MoST report

Purity (% Tumour Cells)	Tumour Mutation Burden
74%	2.3 Mut/Mb (normal range 2.3-13.5 Mut/Mb)

Molecular Tumour Board Recommendation

Based on the genomic profile of your patient's tumour, the Molecular Tumour Board's interpretation suggests the following ranked potential therapeutic interventions. These recommendations are made in a research context, from a molecular screen that is not clinically accredited.

Rank	Alteration	Evidence of Pathogenicity	Tier	Therapy
	No actionable variants found			

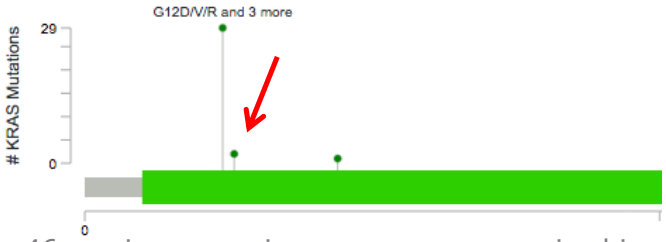
Other findings of interest

Alteration	Evidence of Pathogenicity
KRAS p.G13D NM_004985.3 c.38G>A	Reported in COSMIC 5583 times and is considered pathogenic in ClinVar. This is a known gain of function mutation in oncogene KRAS.
CDKN2A biallelic loss	Biallelic loss of tumour suppressor CDKN2A.

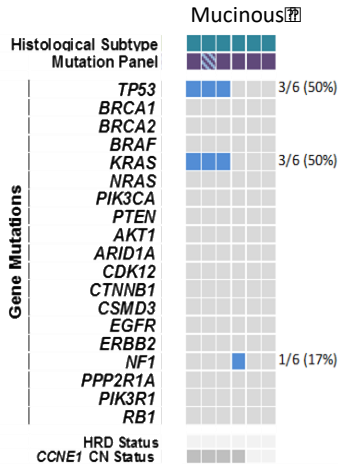
These variants were discussed at the molecular tumour board, however no related therapeutic recommendations could be made for this patient. Nevertheless, the variants may have important roles in the underlying tumour biology.

KRAS p.G13D

KRAS mutations are common in mucinous ovarian cancer
KRAS p.G13D is oncogenic, not the most common 'hot-spot' mutation



46 mucinous ovarian cancer cases, genie.cbioportal.org/



INOVATe

Gene Mutations
Pathogenic/Likely Pathogenic
Not Detected
Not Tested

KRAS G13D in mucinous ovarian cancer

CLINICAL IMPLICATIONS	BIOLOGICAL EFFECT
Oncogenic	Gain-of-function

KRAS, a GTPase which functions as an upstream regulator of the MAPK and PI3K pathways, is frequently mutated in a diverse range of cancers including pancreatic, colorectal and lung cancers.

The KRAS G13D mutation is known to be oncogenic.

Laboratory and preliminary clinical data suggest that KRAS-mutant cancers may be sensitive to MEK or ERK inhibitors.

Level	Alteration(s)	Drug(s)	Level-associated cancer type(s)	Citation(s)
4	Oncogenic Mutations	Binimetinib, Cobimetinib, Trametinib	All Tumors	

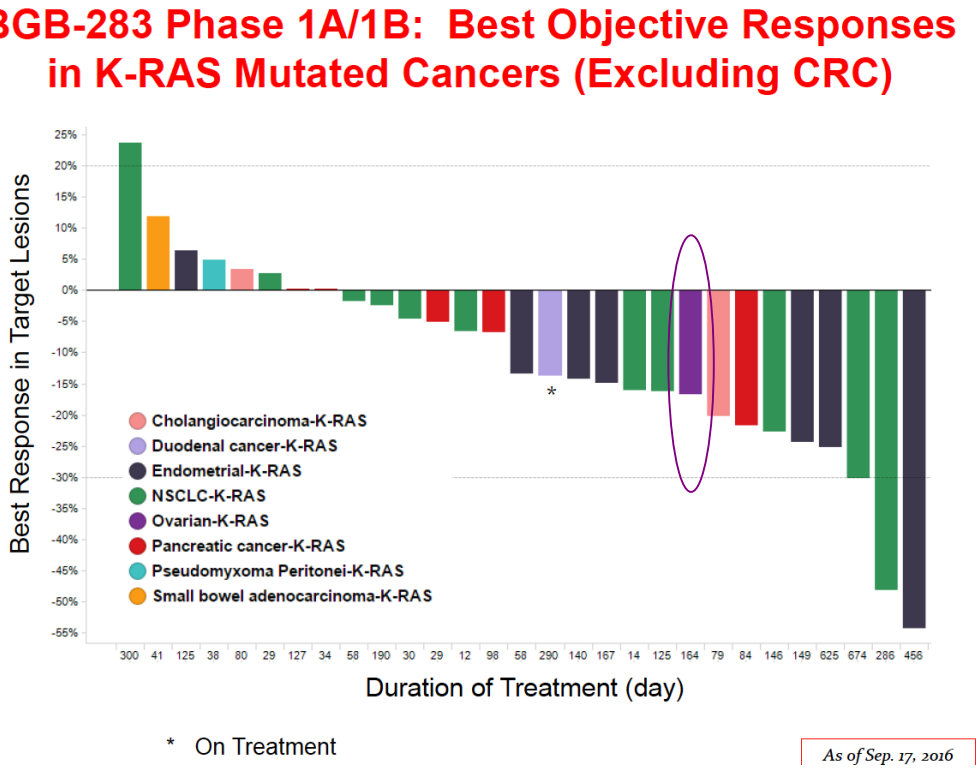
The information above is intended for research purposes only and should not be used as a substitute for professional diagnosis and treatment.

Levels

OncoKB

Feedback

RAF-dimer inhibitor (BGB-283) in *KRAS* mutated cancers



Desai et al AACR 2017

Option - New Trial: Phase I combination RAF-dimer inhibitor and MEK-inhibitor

Hope or Hype?

Where to next?

Management options

1. Carboplatin and Paclitaxel
2. Carboplatin
3. Capecitabine
4. Other “GI style” chemotherapy regimen
5. No further treatment