Case Presentation 2

Michelle Harrison

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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
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

Referred for opinion: Peritonectomy and HIPEC
Management options

1. Peritoneectomy and HIPEC then chemotherapy

2. Chemotherapy then peritoneectomy 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)
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
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
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

<table>
<thead>
<tr>
<th>Purity (% Tumour Cells)</th>
<th>Tumour Mutation Burden</th>
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<tbody>
<tr>
<td>74%</td>
<td>2.3 Mut/Mb (normal range 2.3-13.5 Mut/Mb)</td>
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</table>

**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.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Alteration</th>
<th>Evidence of Pathogenicity</th>
<th>Tier</th>
<th>Therapy</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>No actionable variants found</td>
<td></td>
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**Other findings of interest**

<table>
<thead>
<tr>
<th>Alteration</th>
<th>Evidence of Pathogenicity</th>
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<tbody>
<tr>
<td>KRAS p.G13D</td>
<td>Reported in COSMIC 5583 times and is considered pathogenic in ClinVar. This is a known gain of function mutation in oncogene KRAS.</td>
</tr>
<tr>
<td>NM_004985.3 c.38G&gt;A</td>
<td></td>
</tr>
<tr>
<td>CDKN2A biallelic loss</td>
<td>Biallelic loss of tumour suppressor CDKN2A.</td>
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</table>

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/

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.

<table>
<thead>
<tr>
<th>Gene Mutations</th>
<th>Level-associated cancer type(s) Citation(s)</th>
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<tbody>
<tr>
<td>KRAS</td>
<td>Oncogenic Mutations</td>
</tr>
<tr>
<td></td>
<td>All Tumors</td>
</tr>
</tbody>
</table>

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

Levels

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

BGB-283 Phase 1A/1B: Best Objective Responses in K-RAS Mutated Cancers (Excluding CRC)

* On Treatment

As of Sep 17, 2016

Desai et al AACR 2017

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

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