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BRCA mutation testing in ovarian cancer
DISCLOSURE OF INTEREST

- Nil
Clinical presentation

- 47 yo female
- Presented with abdominal bloating and fatigue
- HGSOC Stage IIIC

- PMH: T2N0M0 TN Breast Ca aged 39
- FH: Paternal aunt with Breast Ca in 30s
Management

- Upfront complete debulking surgery – R0 resection
- Adjuvant chemotherapy – CarboTaxol
- Pt recruited to 100,000 Genomes Project
- Pathogenic germline BRCA1 mutation identified – c.4485-1G>A
- Mutation confirmed in accredited diagnostics lab

<table>
<thead>
<tr>
<th>Gene</th>
<th>GRCh38 coordinates ref/alt allele</th>
<th>Transcript</th>
<th>CDS change and protein change</th>
<th>Predicted consequences</th>
<th>Population germline allele frequency (1KG</th>
<th>gnomAD)</th>
<th>Genomics England germline allele frequency</th>
<th>Alt allele/total read depth</th>
<th>Genotype</th>
<th>ClinVar ID</th>
<th>Gene mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA1</td>
<td>17:43074522 C&gt;T</td>
<td>ENST00000357654</td>
<td>c.4485-1G&gt;A</td>
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<td>20/36</td>
<td>0/1</td>
<td>RCV000235386 RCV000112343 RCV000496665 RCV000580034</td>
<td>tumour suppressor</td>
</tr>
</tbody>
</table>
2 Domain 1 variants identified: RB1 and TP53

Circos plot shows multiple CNAs

Mutational signature shows prevalence of Signature 3:
  - failure of DNA double-strand break-repair by homologous recombination
Clinical Impact

- Eligible for PARP inhibitors – as treatment or maintenance
- Eligible for trials open to BRCA mutation positive patients
- Cascade screening for BRCA1 mutation in relatives
  - 1 sister and 2 daughters – refer to clinical genetics
  - Relatives can be offered increased screening & medical/surgical prophylaxis
- Should she have had BRCA mutation testing after diagnosis of breast cancer?
  - might have had risk-reducing surgery and prevented HGSOC
Thank you for your attention