COI Disclosure

Ian Wilson is an:
Employee of Invitae
Shareholder in Invitae

ASCO – This material was presented previously, in part, and was recognized as “Best of ASCO 2017”
Beyond BRCA:

Germline genetic testing in prostate cancer: Do we need disease-specific guidelines?

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Background

• ~180,000 cases of prostate cancer are diagnosed each year in the United States

• 5-10% of patients with prostate cancer have a genetic variant that increases their risk of developing the disease

• These cases are associated with more aggressive disease and potentially an increased risk of future cancers
Background

• Pathogenic germline mutations in DNA repair genes have been found to be more common in men with metastatic disease than those with non-metastatic disease.

• Men with a germline defect in DNA repair genes are twice as likely to have a FHx of other cancers—detailed histories are important!
Prostate genes - tumor risks

The same genes that can increase the risk of prostate cancer also increase the risk of other cancers.
Testing criteria/guidelines

Personal Hx Prostate (Gleason ≥7)
AND

• ≥1 relative with ovarian (any age)
  family Hx breast ≤ 50
OR
• ≥2 close relatives with breast, prostate
  (Gleason ≥7), or pancreatic

Other personal Hx, family Hx
(OR Gleason ≤ 7)
PLUS

• Personal Hx MBC
• Pancreatic w/ AJ ancestry, ≥1 relative w/ OvCa or
  BrCa, OR ≥2 relatives w/ cancer
• 1st or 2nd degree relative that meets HBOC criteria
• 3rd degree relative w/ BrCa and/or OvCa and ≥2
  relatives w/ breast cancer (one ≤50) and/or OvCa
Question

• Are current guidelines and testing criteria (BRCA1/2 only) able to adequately capture sufficient patients with inherited risks of prostate cancer?
Methods

• Results and records reviewed for 1,158 men with a personal history of prostate cancer and germline genetic testing (2013-2016).

• Genes analyzed were selected by ordering providers and ranged from 2 to 80 genes per order.
  
  ● Majority of orders included the 14 genes on the PCa Panel

<table>
<thead>
<tr>
<th>ATM</th>
<th>BRCA1</th>
<th>BRCA2</th>
<th>CHEK2</th>
<th>EPCAM</th>
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<tbody>
<tr>
<td>HOXB13</td>
<td>MLH1</td>
<td>MSH2</td>
<td>MSH6</td>
<td>NBN</td>
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<tr>
<td>PMS2</td>
<td>TP53</td>
<td>PALB2*</td>
<td>RAD51D*</td>
<td></td>
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</tbody>
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Results

• 77% of P/LP/RA variants detected were in genes offered on an expertly curated PCa panel.

• 42.5% of P/LP/RA variants in genes on the PCa panel were not in BRCA1/2.
Results
Results

- Patients with positive findings
- Evaluating submitted data and records for those patients that met HBOC guidelines for testing
Results

- No, but...
- Primarily because of missing Gleason scores, but also:
  - Relatives’ Gleasons unknown
  - Prostate + AJ insufficient
- Details matter!
Case 1

- BRCA2+
- PrCA; 55 years old
- Gleason 7
Case 2

- BRCA1+
- PrCa; 45 years old
- Gleason 6
- Fhx of gastric, colorectal, brain, hematological malignancies
Case 3

- HOXB13+
- PrCa; 65 years old
- Gleason 7
Case 4

- PMS2+
- Gleason 9 PrCa
- Extensive Hx, Gleason scores unknown
Takeaway points/Action items

• Current guidelines need to be re-visited to capture more patients with inherited risk of PrCa.
• The impact of positive findings to patients’ families should not be underestimated.
• Broader education of clinical colleagues (urologists, surgeons) will drive testing uptake.
Acknowledgements

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