A Founder CHEK2 Pathogenic Variant in Association with Kidney Cancer

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Purpose

To support the association between IVS2+1G>A in CHEK2 and an increased lifetime risk of developing renal cancer

Proband

The patient is a 59-year-old Caucasian male who presented with:
- clear cell renal cancer at age 46
- gastric cancer at age 56

Genetic Testing Results

- 59 gene panel through Invitae Genetics
- Pathogenic variant in CHEK2 (c.444+1G>A), also known as IVS2+1G>A
  - Previously known increased lifetime risk to develop female breast and colon cancer only

Implications

- If this association is confirmed it will be important to consider CHEK2 pathogenic variants in families with renal cancer especially in combination with breast and colorectal cancer.
- Consider increased monitoring for renal cancer in patients with this specific CHEK2 pathogenic variant

Table 1: ESTABLISHED CHEK2 CANCER RISKS

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Increased lifetime risk</th>
<th>General population risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female breast</td>
<td>25-39%</td>
<td>12%</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Up to 12%</td>
<td>5%</td>
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<tr>
<td>Thyroid, prostate, male breast</td>
<td>Elevated, exact risk is unknown</td>
<td>N/A</td>
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</tbody>
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Family History

- Affected, living brother and unaffected, living brother and sister found to have IVS2+1G>A in CHEK2
- Note: Most affected family members are deceased and therefore unavailable for testing
- CHEK2 has previously been established to cause an increased lifetime risk of developing female breast and colon cancer (table 1)
  - Here we provide initial support that CHEK2 is also associated with renal cancer

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