Introduction

- Inherited cancer syndromes account for ~5-10% of cancers
  - A hallmark is an autosomal dominant pattern of inheritance with incomplete penetrance
  - Diagnosed with germline testing of DNA
- Germline testing is traditionally done with genetic counseling
  - Often performed when a familial cancer syndrome is suspected based on family history or cancer type (i.e. triple negative breast cancers)
- Genomic testing of tumors is used frequently in community & academic oncology practices
  - Can indicate targetable mutations, with implications for treatment and prognosis
- Identification of possible germline mutations within genomic testing may be a clue to presence of inherited cancer syndromes

Aims

1. To determine the incidence of potential germline mutations detected via genomic testing at an academic medical center
2. To identify the referral rates for genetic counseling and germline testing for patients with potentially actionable incidental findings

Methods

Study population
Cancer diagnosis + genomic testing of tumor tissue through FoundationOne at an academic medical center

Results: Incidental findings

- 44 pathogenic mutations known to predispose to familial cancer syndromes found in 118/143 patients (Table 1)
- Multiple mutations in potential germline genes reported for the majority of patients (Figure 1)

Table 1: Mutations in genes associated with hereditary cancer

<table>
<thead>
<tr>
<th>Gene</th>
<th>Patients with mutations</th>
<th>Gene</th>
<th>Patients with mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP53</td>
<td>79 (55.24%)</td>
<td>BRCA2</td>
<td>2 (1.40%)</td>
</tr>
<tr>
<td>CDKN2A</td>
<td>36 (25.17%)</td>
<td>MADH4</td>
<td>2 (1.40%)</td>
</tr>
<tr>
<td>RB1</td>
<td>16 (11.19%)</td>
<td>MET</td>
<td>2 (1.40%)</td>
</tr>
<tr>
<td>PTEN</td>
<td>14 (9.79%)</td>
<td>MUTYH</td>
<td>2 (1.40%)</td>
</tr>
<tr>
<td>STK11</td>
<td>14 (9.79%)</td>
<td>PALB2</td>
<td>2 (1.40%)</td>
</tr>
<tr>
<td>APC</td>
<td>12 (8.39%)</td>
<td>CDH1</td>
<td>1 (0.70%)</td>
</tr>
<tr>
<td>NF1</td>
<td>9 (6.29%)</td>
<td>MSH2</td>
<td>1 (0.70%)</td>
</tr>
<tr>
<td>CDK4</td>
<td>5 (3.50%)</td>
<td>NF2</td>
<td>1 (0.70%)</td>
</tr>
<tr>
<td>BRCA1</td>
<td>4 (2.80%)</td>
<td>RET</td>
<td>1 (0.70%)</td>
</tr>
<tr>
<td>FANCA</td>
<td>3 (2.10%)</td>
<td>SDHC</td>
<td>1 (0.70%)</td>
</tr>
<tr>
<td>MSH6</td>
<td>3 (2.10%)</td>
<td>TSC2</td>
<td>1 (0.70%)</td>
</tr>
<tr>
<td>WT1</td>
<td>3 (2.10%)</td>
<td>TGBFR2</td>
<td>1 (0.70%)</td>
</tr>
</tbody>
</table>

Figure 1: Patients with potential germline mutations

- Patients with 1+ potential germline mutation(s)
- Patients with no identified mutations

Results: Follow-up referrals

- There was a low rate of referral for follow-up genetic counseling among the 118 patients with potentially actionable germline mutations (Figure 2)

Figure 2: Patients with potential germline mutations referred for genetic counseling

- Germline testing outcomes:
  - Germline testing was completed for 73% (11/15) of patients referred for genetic counselling (9% of all patients with potentially actionable germline mutations)
  - In those that underwent germline testing, 27% (3/11) were found to have positive germline mutations
    - Positive mutations included BRCA1, MUTYH, PMS2

Conclusions

- Genomic testing has implications for identification of hereditary cancers
- The low rate of referral for genetic counseling represents a potential missed opportunity for our patients and their families

Next steps

- Follow-up of individuals with potential germline mutations
- Provider education of the germline impact of genomic testing

References