Proposal for Review

STICs and STONES: Prospective Assessment of Aspirin in Chemoprevention of high risk Ovarian Cancer (CCTG OV.24)

A RANDOMIZED TRANSLATIONAL WINDOW OF OPPORTUNITY TRIAL

Stephanie Lheureux, Katherine Karakasis, Patricia Shaw, Harriet Richardson, Elisabeth Eisenhauer, Hal Hirte, Daliah Tsoref, Barry Rosen and Amit Oza
A phase II, double blind, placebo-controlled, randomized trial to compare regular use of low-dose aspirin versus placebo in women with germline BRCA1/2 mutations.

In both arms, prophylactic surgery will be performed in the expected timing as part as the standard of care.
**Hypothesis:** Regular use of low-dose aspirin in women with inherited BRCA1/2 mutations will decrease the occurrence of ovarian cancer precursor lesions observed in the fallopian tube at the time of the prophylactic surgery.
Endpoints

- **Primary**

  Presence/absence and numbers of cancer precursor lesions identified by Central Pathology review in the fallopian tube in resected specimens of patients who receive a minimum of 6 months of either low dose aspirin or placebo:
  - Occult (early) carcinoma
  - Serous tubal intraepithelial carcinoma (STIC)

- **Secondary**

  - To identify the non-invasive tubal lesions: the p53 signature
  - To elucidate the linkage between tumorigenesis and microenvironment
    - Hormone stimulation
    - Inflammatory mediators involved in ovulation
    - COX1/2 - VEGF
  - To assess the credibility/acceptance of the drug intervention and monitor serum ASA levels
### Hypothesis

- **Control:** 15% occurrence of pre- & early-malignant lesions
  - 6% occult carcinoma
  - 7-10% STICs
- **Aspirin:** 40% risk reduction

*Geoge SH, Front Oncol 2014*  
*Trabert D, J Natl Cancer Inst 2014*

### Sample Size

<table>
<thead>
<tr>
<th>Placebo Group Pre-lesion rate (%)</th>
<th>Aspirin Group Pre-lesion rate (%)</th>
<th>Absolute difference</th>
<th>Type I error rate</th>
<th>N1:N2 (Total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>9</td>
<td>6.0</td>
<td>0.20</td>
<td>248:124 (372)</td>
</tr>
</tbody>
</table>

2:1 allocation; Type I error 1-sided; 40% relative risk reduction

Drop off 10%: 414 patients for inclusion
Feasibility: Estimated Accrual 200/year

<table>
<thead>
<tr>
<th>Province</th>
<th>Centre</th>
<th>PI</th>
<th># pt with prophylactic salpingo oophorectomy</th>
<th>Eligible subjects annually</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALTA</td>
<td>Cross Cancer Inst</td>
<td>V Capstick</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>BC</td>
<td>BCCA Vancouver</td>
<td>D Miller</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>MB</td>
<td>Cancer Care Manitoba: Winnipeg</td>
<td>L Lotocki</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>NFLD</td>
<td>D.H. Bliss Murphy Cancer Centre</td>
<td>P Power</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>ON</td>
<td>Ottawa Hospital</td>
<td>M Fung Kee Fung</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ON</td>
<td>Jurvinski Cancer Centre</td>
<td></td>
<td></td>
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<tr>
<td>ON</td>
<td>PMH</td>
<td>B Rosen</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>ON</td>
<td>London Health Sciences Centre</td>
<td>J McGee</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td>QC</td>
<td>CHUM</td>
<td>Sauthier</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>QC</td>
<td>CHUQ</td>
<td>M Plante</td>
<td>20</td>
<td>most</td>
</tr>
<tr>
<td>SASK</td>
<td>Saskatoon</td>
<td>C Giede</td>
<td>10</td>
<td>70%</td>
</tr>
</tbody>
</table>

Intergroups: ANZGOG, GINECO, MRC
?? NRG, NSGO
Current Status of Trial

• Protocol written
• Database specifications finalized
• Drug Supply: Discussions ongoing with regulatory authority and drug manufacturer: stability testing and study supply capsule composition
• Planned trial activation in Canada: first quarter 2017
• Collaborating Groups must self fund for participation