Terms of Reference -
Somatic BRCA ad hoc working group

Approved by the CCMG Board of Directors – November 13, 2019

Brief Description

In 2016 Health Canada has approved use of PARP inhibitors for the treatment of high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer positive for BRCA1 or BRCA2 mutation (somatic or germline). Clinical trials have shown that women with both germline and somatic BRCA1 /2 mutations respond well to PARP-inhibitors therapy. Laboratories in Canada started in 2018 to validate and offer somatic BRCA testing as a tumour-first testing approach. BRCA1/2 mutations in ovarian tumors are important for the following reasons: 1) Presence of the BRCA mutation (somatic or germline) is associated with favorable response to the PARP inhibitors therapy 2) a mutation identified in tumor could be germline in origin, and if confirmed to be germline is important for cascade testing of relatives and appropriate management. While Canadian laboratories are experienced with BRCA germline testing for familial cancer risks, BRCA tumor testing is relatively novel. There is a significant gap in the availability of published recommendations/guidelines on the optimal laboratory testing approaches, and the reporting of genetic results for tumor testing when there is a high likelihood that the identified mutation could be germline in origin.

Mandate

The purpose of this CCMG Ad hoc Working Group is to develop and publish guidelines for laboratory testing analysis, variant classification and reporting of BRCA1 and BRCA2 variants in the somatic context of ovarian tumors.

These recommendations will promote consistency in somatic BRCA1/2 testing and reporting across Canada.

Timeline

March 2019: Forming the somatic BRCA ad hoc working group was proposed by Laboratory Practice to the CCMG board of directors (BoD).

April 2019: The request for forming of the work group was approved by CCMG BoD.

May 2019: Potential members of the group we approached from laboratories familiar with germline and somatic BRCA testing across Canada.

June 2019: Face to face meeting of members of working group at Niagara Falls CCMG meeting. In addition the Tumor-First Testing Workshop was organized by Tracy Stockley and Daria Grafodatskaya. Feedback was sought from workshop participants on the topic related to somatic *BRCA t*esting and notes were taken (by Darci Butcher) to assist with generating the guidelines document.

October/November 2019: TOR finalized and approved by BoD**,** work group member will be assigned to topics of the preliminary draft.

December 2019/February 2020 assemble first draft

February 2020: Approach CAP to invite pathologists to the working group.

March/April 2020: Incorporate aspects relevant to pathology into the manuscript.

May/June 2020: Submit draft to BoD to distribute to CCMG committees/external organizations for feedback.

July/August 2020: Incorporation of the feedback, submission to BoD for final approval

September 2020: Manuscript submission to the Journal.

The working group will disband after the manuscript is completed and accepted for the publication.

Membership

- 6-8 CCMG laboratory scientists (CCMG molecular certified). Preference will be given to those members who oversee labs preforming tumor BRCA testing, in addition at least two CCMG scientists will be from the laboratories performing germline BRCA testing.
- 1 Molecular Genetics Fellow in training, will also assist with minutes taking during workshop(s), teleconference meetings.
- 2-4 CAP pathologists (Note: The membership from CAP pathologists will be sought at a later date when part of the manuscript related to genetic testing is completed).

Appointment and term of chair

Two co-chairs will be selected from the membership of the Ad Hoc Working group for the duration of the existence of the Working Group.

Conduct of Meetings

- The co-chairs will convene regular zoom meetings of the Ad Hoc Working Group, with approximately one meeting held each month or more frequent if required.
- Quorum for decisions will be at least 50% of Working Group members
- Draft minutes of all meetings will be prepared and circulated to the Working group members for comment, ideally within 10 working days of the meeting.
- All meeting minutes will be made available to CCMG Board of Directors via the Board of Directors Representative.

Reporting

The co-chairs will report to the CCMG Board of Directors via the Board representative for monthly updates.

After completion of the manuscript it will be submitted to CCMG Board of Directors to seek the feedback from appropriate CCMG committees (suggested: **Laboratory Practice Committee, Clinical Practice Committee**) and external organizations (suggested: **Canadian Association of Pathologists, Canadian Association of Genetic Counsellors, Society of Gynecologic Oncology of Canada**).

The final manuscript will be submitted to BoD for approval.