Title: International Harmonization of Ovarian Cancer Patient Assessments during and after first line therapy – A Gynecologic Cancer InterGroup (GCIG) survey

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Introduction: There are no internationally agreed upon guidelines for optimal follow-up during and following first line ovarian cancer therapy. Timing of follow-up and types of assessments/ examinations in clinical trials are trial specific and may differ from national guidelines possibly impeding trial participation.

Methods: The GCIG's Harmonization Committee (HC) conducted a survey of its 27 member groups in 22 countries seeking to describe both timings and types of follow-up assessments routinely performed during and after completion of first-line chemotherapy from May 2014 to May 2015.

The survey consisted of six questions posed to the Harmonization Committee representative of each GCIG member group to ascertain the following for each member group:

- If there was existence of national or group specific guidelines.

Comment [KC1]: Need to do full literature search in relation to this. There are ESMO Clinical Practice Guidelines which were published 2013 also found a Cochrane Review published in 2014 "Evaluation of follow-up strategies for patients with epithelial ovarian cancer following completion of primary treatment".
Should we mention about GCIG consensus reviews.
Need to think about having a discussion section.
Could als

Comment [KC2]: Need to check the number of member groups/countries correct.

- Type and frequency of assessments performed at baseline and during therapy.
- Type and frequency of assessment performed following completion of first line chemotherapy.
- Whether the assessments can be performed more frequently than the group's standard practice for patient's enrolled in trials.
- If there were differences in assessment for non-epithelial ovarian cancer patients.
- If groups are using independent assessment of response/progression versus investigator analysis in any of their current ovarian cancer trials.

Results: The following 20 collaborative groups responded to the survey corresponding to 16 countries:

A-AGO(Austria), AGO (Germany) ANZGOG (Australia, New Zealand), BGOG (Belgium), DGOG (Netherlands), GEICO (Spain), GICOM (Mexico), GINECO (France), GOG (USA), G-GOC (USA), GOTIC (Japan), ICORG (Ireland), JGOG (Japan), MANGO (Italy), MITO (Italy), NCIC CTG (Canada), NCRI-MRC (UK), NOGGO (Germany), NSGO (Nordic Countries), SGCTG (Scotland, UK).

12/ 20 groups indicated they have national or group specific guidelines governing assessments for patients with ovarian cancer during and following first line chemotherapy. A number of groups which don't currently have national guidelines in place indicated there are plans to standardize follow-up in their country.

During treatment all groups perform physical examination and CA125. 17/20 groups employ CT/MRI at some point (time-points for scanning varies between groups with some groups performing scans baseline, after 3 and 6 cycles of chemotherapy with other groups only scanning during chemotherapy for patients receiving interval debulking surgery and following completion of chemotherapy). 4/20 groups use ultrasound, and only 1 uses PET.

Follow-up assessments post completion of chemotherapy (0-12 months). 18/20 groups follow-up patients Q3 monthly and 2/20 groups follow-up patients Q4 monthly. Follow-up for all groups include review of symptoms, clinical examination

and CA125 (1/20 groups does not include CA125 assessment as part of follow-up). Variance noted across groups in relation to scanning: 12/20 only scan if clinically indicated e.g. symptoms/signs/raised CA125. With 4/20 scanning Q3-6 monthly, 2 annually.

For subsequent years post chemotherapy years 1-5, follow-up is performed in range Q3 monthly- annually depending Variance noted across groups in relation to scanning with many groups only scanning if clinically indicated e.g. symptoms/signs/raised CA125.

Comment [KC3]: Could break down the FUP frequency by years if this was felt it would be helpful to record further detail.

19/20 groups indicated they can carry out assessments out more frequently for trials than standard practice, however there are factors which need to be addressed/considered:

- Ethics/Regulatory and local approvals required by all groups. For majority of groups/countries it requires to be documented in the application to ethics the assessments which are considered standard with those additional to trial highlighted.
- For 12/20 groups there is requirement for costs of all additional assessments required for trials to be reimbursed to sites.
- A number of groups highlighted requirement for assessment of radiation exposure/risk assessment to be performed as part of ethical approval process. In Germany if frequency of scans more than standard care the protocol for trial requires submitted to German Federal Office for Radiation Protection for approval timelines for this is 9-12 months.

7/20 groups indicated they performed different or additional assessments for non-epithelial ovarian cancer patients. In particular it was highlighted germ cell carcinosarcoma and granulosa cell tumours were treated differently with groups indicating different protocols/guidance followed for the treatment of patients with non epithelial ovarian cancer.

Comment [KC4]: ? Should we detail what different assessments etc that are done – there is limited responses provided.

5/20 groups indicated they were currently using independent assessment vs investigator analysis in any of their current ovarian cancer trials. Independent

assessment of response/progression was being used for a number of trials for primary endpoint of progression free survival.

Conclusions:

The results from this questionnaire indicate that there are not standard assessment procedures or follow-up schedules across countries for ovarian cancer patients during and after first line therapy.

The questionnaire also highlights need to take into consideration other factors highlighted such as requirements for reimbursements of costs for additional tests required for trials.

It is critical all these factors are considered when planning international trial collaboration with a goal towards harmonization.

Comment [KC5]: ? Should we recommend/suggest at planning stage of trial a feasibility questionnaire sent to potential groups to assess if trial will be feasible to be carried out and establish any potential issues which may be encountered this may sit better elsewhere.

Key words:

Ovarian Cancer, Follow Up, GCIG, Harmonization

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References: