FINAL

GYNECOLOGIC CANCER INTERGROUP (GCIG)

META-ANALYSIS working group

Thursday, October 27, 2016, 5:30pm – 6:30pm

AUGUSTA II ROOM, DoubleTree Fontana Hotel, Lisbon

Chair: R. Glasspool **Co-Chairs: BH Nam/X.Paoletti**

MINUTES

Present (as per sign-in sheets): R.Glasspool (Chair & SGCTG), BH Nam (KGOG), B.Votan & X. Paoletti (GINECO), A.Reuss (AGO), PJ Chang, A. Folkins & T. Longacre (for Berek COGi), R. Bekkers (DGOG), A. Casado & N. Ottevanger (EORTC-GCG), E. Peeraer (for Kridelka BGOG), N. Yanaihara & T. Kagimura (for Sagae JGOG), D Tu (CCTG), E. Avall-Lundqvist, T. Juhler-Nottrup & E. Roennengart (NSGO), M. Brady & B. Stonebraker (GOG), K. Fujiwara (GOTIC), H. Mackay (PMHC), T. Levy (ISGO).
Non-registered: R. Chekerov (NOGGO), C. Lee (ANZGOG).
Absent: AGOG, C. Grimm (AGO-Au), J. Pfisterer (AGO), GEICO, Onate (GICOM), P.Ramirez (G-GOC), D. O'Donnell (ICORG), R. Fossati (MaNGO), D. Gennaro (MITO), I. McNeish (NCRI), E. Braicu (NOGGO), RTOG, X. Wang (SGOG), NCI US, K.Carty (Harm. Ops & SGCTG).

Welcome and Introductions: Ros Glasspool (RG) welcomed everyone. Nearly all the groups have now nominated a representative for the group.

The report of the last meeting presented at the general assembly in Chicago 2016 was approved

RG outlined the aims of the group:

- To perform individual patient level meta-analyses in order to address questions that cannot be answered by individual trials.
- To identify key questions and develop projects to address them
- To create an infrastructure that will facilitate meta-analysis projects between GCIG groups.
  - Agree terms of reference for how projects will be reviewed and run
  - Agree authorship rules that fairly reflect the contribution of data from groups and the work done by the team managing and executing an individual project.

- Develop a GCIG data-sharing agreement template that is broadly acceptable to all groups to reduce the bureaucracy and costs of individual projects.

RG reiterated that the aim was not to create a permanent database but to perform analyses on a project by project basis. Groups will remain in control of the data that they contribute with any further analyses only being performed with their specific agreement.

It was proposed that the group should be known as the **Meta-Analysis Group** rather than the Mega-Database group and all agreed.

RG thanked the harmonisation group for the opportunity to present the draft data sharing agreement in their meeting and for their offer help to develop this further.

An initial "pilot" project is planned that will start in parallel with developing the structure/processes of the group, in order to demonstrate the potential of the approach and to help identify the issues that need to be addressed when developing this structure.

Projects:

Xavier Paoletti (GINECO) and Ros Glasspool (SGCTG) presented the first project proposal for the group:

Meta-analysis of randomized trials to assess the surrogacy of intermediate endpoints of overall survival in newly diagnosed advanced Ovarian Epithelial, Fallopian Tube and primary peritoneal cancer
(see slides on website for further details)

The concept was supported by everyone present at the meeting.

Several groups have expressed interest in contributing to meta-analyses projects through the GCIG including the GINECO, EORTC, SGCTG, MRC, ANZGOG, NOGGO, MITO and JGOG

The AGO have stated that their involvement is conditional on the data-sharing agreement and in particular the authorship rules.

Terms of Reference, Structure and Process and Authorship Rules:

1. The terms of reference were circulated in July after the Chicago meeting. It was proposed that the term PI should be replaced by "PI as representative of the trial leading cooperative group or any other responsible representative of the sponsor". A revised draft with this change will be circulated for final comments.
2. The proposed structure and processes were reviewed:
   - GCIG Meta-analysis group:
     - Representative from each GCIG group and from the harmonisation ops and statistics groups
     - Remit: to discuss develop and review proposals from individual groups for new projects

  - The rules for how a project is approved or projects are prioritised need to be defined.
  - Proposals can be made by any member group. If the proposal is adopted, the proposer would then take on the responsibility of international principal co-ordinator (IPC). They will take overall responsibility for the study including sourcing funding
- Project Steering Committee
  - Representative from each GCIG group that agrees to contribute data to a particular project
  - Responsible for agreeing the final protocol, reviewing and discussing the results and writing the manuscript
  - Are able to propose secondary analyses but these must be agreed by all the contributing groups
- Consortium
  - Representative for every trial that is contributed to a particular project
  - Responsible for reviewing and agreeing the results of the analysis and approving the manuscript with the project steering committee
  - Are able to propose secondary analyses but these must be agreed by all the contributing groups
- Secretariat – established for each project. Proposed that there might be several secretariats based in different groups/institutions and these may take the lead on different tumour sites eg ovarian, endometrial, cervical/vulvar, rare tumours, PROs or translational. Any group will be able to propose that they host a secretariat if they have the necessary expertise, security and platforms for the project.

  - Members will include:
    - the Senior statistician
    - IPC
    - Junior Statistician (decided by the institution performing the meta-analysis)
    - Medical Advisor (who helps with protocol writing, trial selection, data collection, with medical questions at the time of data management etc decided by the IPC/institution performing the meta-analysis)
  - Responsible for the protocol development, the data collection, cleaning, safe storage, the analysis
  - Are able to propose secondary analyses but these must be agreed by all the contributing groups

4. Authorship rules were discussed and different models for acknowledging groups contributing data considered. The authorship rules need to reflect the contributions of both the team executing a particular project and by the groups sharing data. All present agreed that the first and last authorships should be reserved for the senior statistician and the IPC given the large amount of work and expertise involved in these projects. In

addition 2 authorships should be available to a junior statistician and a medical advisor who fulfil a major role on any project.

Different models for the contributing groups were discussed

- Model A
  1 author for every trial contributed (regardless of size of the trial)
- Model B
  1 author for every group contributing data and subsequent authors depend on the percentage of the total contributed by that group
- Model C
  1 author for every trial contributed with additional authors for the group depending on the percentage of the total contributed
- Model D
  There are no authors – it is published in the name of the GCIG Meta-analysis Group and all contributors are listed in an appendix with their roles

Model A or Model C were the favoured options for those at the meeting. In order to encourage data sharing it is important that all trials contributed are included in authorship or there will be no incentive. It is important to the process to include as many relevant trials as possible. It was agreed that there could be some flexibility for different projects which might depend on the number of trials included. ie Model A or C could be used. The percentage of patients contributed required to merit an additional author can be discussed further but 20% was proposed.

5. Order of authors: Proposal

1st author/last author : IPC/Senior Statistician or visa versa

- There has been a suggestion that the senior author should be given to the group contributing the largest number of patients (as per ENGOT rules) but this was not supported by those present as it is important to reflect the additional work and added value of those responsible for co-ordinating and executing the project

If secondary analyses are proposed and agreed by all contributing data then the first author will be the proposer and the statistician the second author.

Contributing group positions will depend on the percentage of patients contributed.

If group A has the highest patient number, group B the 2nd highest recruitment number, group C the 3rd highest, and group D the lowest, 3rd author would be appointed by group A, 4th author by group B etc. until all trials have been represented. The medical advisor (MA) and junior statistician (JS) will be included before the second of the groups authors.

International Principal Coordinator, A1, B1, C1, D, E, MA and JS A2, B2, C2, A3, B3, C3, A4, B4, B5, Senior Statistician

Rare Tumour Projects:

The rare tumour group are keen to explore projects in rare tumours. Some ideas were discussed.

Potential Ideas

- Ovarian Germ Cell Tumours
    - Develop better prognostic classifications to identify who needs adjuvant therapy and who needs more intensive first-line therapy
    - Outcomes following surveillance and delayed chemotherapy for relapse. Can it be safely extended to Stage I a or b grade 2 and 3 or stage IC?
- Sex Cord Stromal Tumours
    - Identification of risk factors for relapse after complete cytoreductive surgery
- Adenocarcinoma of cervix
    - Does prognosis and response to treatment differ from squamous ca cervix?
- Ovarian histological subtypes
    - Do LGS and or CCC benefit from the addition of angiogenesis inhibitors to standard chemotherapy?
    - Limited by the quality of the path review in old studies: numbers may still be too small.
- Joint Translational/Rare Tumour group project
    - Are there sample sets in rare tumours with molecular data sitting within GCIG groups that we could usefully share to address questions that they cannot do alone eg potential molecular prognostic and predictive factors?

Next Steps:

For the Surrogacy Project:

- Circulate and finalize protocol (by end of November)
- Agree authorship rules
- Set up the Project Steering Committee
- Launch data collection
- Submit data request to each targeted group using their data sharing template
- Initial funding provided by XP's research grants on meta-analysis
- Targeted first report: June 2017

For the group as a whole

- Find a name to the initiative- The GCIG MA
- Finalize the GCIG data sharing agreement (Harmonization op. committee)
- Confirm the process for selecting and prioritizing projects by the GCIG MA group
- Update the draft terms of reference and authorship rules
- Evaluate pilot study process
- Identify sources of funding

ADJOURN