Megadatabase Report

General Assembly Report

Lisbon 2016

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.

We would like to change our name to:

The Meta-Analysis Group - GCIG MA

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

- OS is the gold standard but challenges/limitations so PFS is often selected as the primary endpoint
  - To be of valid clinical significance it must be a surrogate of overall survival or it must be associated with prolonged improvement or maintenance of quality of life.
- 5th OCCC
  - PFS can serve as a primary endpoint instead of overall survival (OS), provided that secondary endpoints such as quality of life support the superiority of the investigated treatment. T
  - Various pathological, clinical covariates and biomarkers should be collected at baseline as they may modify the treatment effect
- (Buyse et al. 2000)
  - But low sample sizes (few trials), Heterogeneous assessment of progression, only cytotoxic agents
- No assessment as yet of the surrogacy of GCIG CA125 criteria of progression
- The relationship between the dynamic evolution (time to increase, nadir velocity of increase etc.) of CA 125 and response and progression by RECIST and has not been investigated so far in surrogacy evaluation framework
- Treatment effect is usually reported through Hazard ratio and median survival
  - The restricted mean survival time (RMST) –may be a better endpoint

Objectives

To assess surrogate endpoints for OS

- Progression free survival defined by RECIST alone
- Progression free survival defined by GCIG criteria

Secondary

- To assess surrogate value of $RMST_{PFS}$ for $RMST_{OS}$
- To investigate the surrogate value of different dynamic measures of CA125
- Response by RECIST 1.1
- To evaluate the sensitivity of such PFS/OS (or CA-125/PFS) relationships according to
  - Maintenance, induction
  - Prognostic factors (age, cytoreductive status…)
  - Year of the clinical trial

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

- 33 trials identified
- Several groups have expressed interest in joining the study
- Next steps
  - Finalise the protocol – end of Nov
  - Set up the steering committee
  - Data requests to groups/investigators
  - Aim to give an initial study report in Chicago

Next Steps 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

Structure and Processes

- GCIG mega-database group:
  - Representative from each GCIG group and from the harmonisation and stastitics groups
  - Remit: to discuss develop and review proposals from individual groups for new projects
  - We need to agree the rules for how a project is approved or projects are prioritised ie majority vote
  - 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 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
  - Are able to propose secondary analyses but these must be agreed by all the contributing groups
- Secretariat
  - 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