GCIG **Harmonization Committee** **Statistical Section**

Sunday, Nov. 17, 2013

UCL Education Centre Room5

MINUTES

Chair: Jim Paul (james.paul@glasgow.ac.uk) – SGCTG (JP)
Co-Chair: Byung Ho Nam (byunghonam@ncc.rc.kr) – KGOG (BHN)

Present:
Andrew Embleton (a.embleton@ctu.mrc.ac.uk) – MRC/NCRI (AE)
Mark Brady (brady@gogstats.org) – GOG (MB)
Alexander Reuss (Alexander.reuss@kks.uni-marburg.de) – AGO (AR)
Dongsheng Tu (dtu@ctg.queensu.ca) – NCIC (DT)
Tetsutaro Hamano (hamato@insti.kitasato-u.ac.jp)– GOTIG (TH)
Roldano Fossati (roldano.fossati@marionegri.it) – MaNGO (RF)

Welcome & Introductions (C.O.I. declaration)

No conflicts of interest were declared.

1. Discussion of study designs from the Rare Tumour Working Groups Brainstorming

JP presents a summary of the study designs presented at the RTWG the previous day:-

Max Parmar had made the following recommendations:-

- Concentrate on superiority trials
- Randomisation essential
- Make arms as different as possible (maximize likelihood of "success")
- Consider more than one experimental arm
- To make study size/duration feasible may have to compromise on type I error
- The degree of compromise should take into account consequences of a wrong decision in face the toxicity of the experimental regimen or difficulty in adding other agents to experimental regimen

JP had outlined Bayesian methods for combining study data with external evidence and subjective opinion in order to reach decisions. Also recommended:-

- Maximising information by using factorial designs
- Randomising at presentation and at relapse in the same protocol
- Stopping early - incorporation of formal futility stopping rules
- Looking for molecular target signals across conventional anatomical/histological subdivisions
- Making sure certain minimum number of rare histology to give a "reliable" signal within an "all-comer" study e.g. adenocarcinoma in cervical cancer study

MB agreed to finalise our position paper on study designs for rare tumour in light of the RTWG presentations.

Action MB

2. Proposals for discussion topics at future meetings (All)

The following topics for discussion were considered for discussion at the next meeting:-

a. The PFS/OS endpoint controversy for phase III trials (MB).
b. The use of futility boundaries in clinical trials (MB)
c. Response adaptive designs
d. The timing of scans for progression

After further discussion it was agreed that the next meeting would look at statistical Issues in scanning to assess progression:-

- Must it be the same across the whole study?
- How frequent does scanning have to be?
    - How does this impact on power?
    - How does it impact on the estimate of the HR
- What if scans don't happen at scheduled times? Adjustment?
- Assessment for bias in treatment comparisons from differences in scan timing
- Need for central review?

BHN (KGOG) and AR (AGO) agreed to take a lead on this.

Action BHN/AR

4. AoB

There was no AoB.