GCIG Harmonization Committee - Statistical Section
Saturday, December 1, 2012, 3:30pm – 5:30pm
Wassenaar Room, Holiday Inn, Leiden

MINUTES

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

Present:
Andrew Embleton (a.embleton@ctu.mrc.ac.uk) – MRC/NCRI;
Dongsheng Tu (dtu@ctg.queensu.ca) – NCIC CTG;
Tetsutaro Hamano (hamamo@insti.kitasato-u.ac.jp) – GOTIC/JGOG;
Mark Brady (brady@gogstats.org) – GOG;
Alexander Reuss (Alexander.reuss@kks.uni-marburg.de) - AGO

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

No conflicts of interest were declared.

1. Approaches to the design of phase II trials of targeted agents

JP presented a number of different approaches to this (slide set attached).

Design 1 - Restricted to "target" group
Design 2 – Partially Enriched - Gateway Testing
Design 3 – Partially Enriched - Fall-Back Testing
Design 4 - Randomized Phase II Trial Designs With Biomarkers Boris Freidlin, Lisa M. McShane, Mei-Yin C. Polley, and Edward L. Korn J Clin Oncol 30:3304-3309.2012

In the discussion it was agreed that a phase II of a new targeted agent with associated biomarker should only be restricted to the "target" patient group (biomarker +ve) if the background scientific evidence was utterly compelling that the targeted agents effect was restricted to that particular "target" group. This was uncommon.

It would usually necessary to "enrich" the phase II trial wit patients form the putative biomarker +ve group.

The preliminary choice of biomarker will be based on:-

- Biological rationale
- Laboratory data (in vitro/in vivo)
- PD from phase I

Nevertheless still uncertainty that biomarker is correct:-

- Measuring the wrong thing
- Have the wrong cut-off
- Not required

For a successful biomarker/targeted agent combination, biomarker specificity was key.

2. Consensus on approaches to phase III trials for rare tumours - review of document prepared following 2011 GCIG meeting in Chicago

The document prepared following 2011 GCIG meeting in Chicago was circulated for discussion. It was agreed to look at the possibility of including phase II designs in this.

3. Proposals for discussion topics at future meetings:

a) The PFS/OS endpoint controversy for phase III trials (Brady)
b) The use of futility boundaries in clinical trials (Brady)
c) Response adaptive designs
d) Allowing/adjusting for treatment cross-over after progression in assessing effect of a new treatment on OS (Tetsutaro)

It was agreed that topic d) would be discussed at the next meeting..

4. AoB

None