Meeting Minutes
Friday November 14, 2008

Gynecologic Cancer Intergroup
Harmonization Committee, Statistical Subcommittee
Liverpool Convention Center
Liverpool England

Participants: Mark Brady, Elizabeth Eisenhauer, Max Parmar, Natalie Le Fur, Jim Paul, Wendi Qian and Alexander Reuss,.

The meeting of the Statistical Section of the GCIG Harmonization Committee was called to order at 4:00 pm, on Friday, November 14, 2008 at the Liverpool Convention Center, Liverpool, England. Mark Brady indicated that there were primarily two items on the agenda for discussion: data sharing and treatment unblinding,

1. **Data sharing**: At the previous GCIG meeting, which was held in Chicago, there was a presentation and discussion on the Breast Cancer DataMart. This is a project which aggregates data from several cooperative groups conducting clinical trials to study treatments for breast cancer. These groups are sponsored by the National Cancer Institute. The stated purpose of DataMart is to provide researchers a database for conducting meta-analyses and data-mining. The question posed to the Harmonization Committee is: Should the GCIG develop a similar database for aggregating data from trials involving women treated for gynecologic cancers?

There was general agreement among the meeting participants that members of the GCIG have been very successful implementing a prospective approach for aggregating data for meta-analyses and other projects. Successful projects include: Concomitant chemo-radiation treatment for cervical cancer, Adjuvant chemotherapy for soft-tissue sarcoma, Safety and efficacy of ESAs in the treatment of cervical cancer, and the prognosis of women with advanced stage uncommon tumors of the ovary. These projects took a prospective approach which is different from DataMart. They are considered prospective because they first identify the study objectives, and then determine the appropriate trials and data items for the analyses. Since the study objectives determine the required data items and how they are defined, this approach tends to be efficient. No effort is spent collecting data items that will not be incorporated into the analyses. The investigators who are contemplating a contribution to the study have an opportunity to assess the scientific merit of the data-mining project, determine whether the inclusion of their trial-data into the study are appropriate, and then evaluate the resources needed to complete the project.

If a DataMart-like process to be developed, then the committee members recommended consideration for the following issues:

a. A prospectively defined meta-analysis typically aggregates well-defined datasets from all of the trials that relate to the objective. It is unlikely that a DataMart project would include all of the trials needed for a specific meta-analysis (ie chemoradiation in cervical cancer, or adjuvant treatment of soft tissue sarcomas). Therefore, DataMart-like datasets are primarily useful for only opportunistic data-mining projects.

b. It is currently unclear how successful DataMart has been. Have the results from any of its data-mining studies had the clinical impact comparable to a prospectively defined meta-analysis?

c. The advantages of the DataMart approach may not out weight its disadvantages. The primary advantage of the DataMart approach is that the data can be made available once the data-mining project has been approved. However, the cost of this advantage is that the dataset is determined without regard to the specific data-mining objectives and therefore the collected data items or their definitions may not be entirely appropriate for the analyses.

c. Some administrative issues should also be considered:

i. A standardized list of data items would need to be established and agreed upon by all contributors. On one hand, this list is limited by the number of items that are common to most clinical trials. However, it would need to be relatively extensive in order to serve the yet undetermined purposes of data-mining.

ii. Quality control procedures need to be developed to ensure that the data items are interpreted consistently across trials.

iii. Each cooperative group that wishes to participate in the project should have an opportunity to provide input into the content of the common dataset and its administration.

iv. A committee with by-laws defining the objectives, procedures and membership criteria needs to be established to review data-mining proposals and administer the DataMart project.

v. Funds for creating the DataMart database have not yet been identified. Conceivably, this could be an ongoing project that involves updating event dates (PFS, survival, or late AEs), adding new trials as they mature, or redefining and proposing new data items.

d. Some GCIG group members expressed concern for the informed consent issues involved in projects with undefined objectives. The IRBs that govern some groups may not approve even anonymized data to such a project.

f. The committee members did not discuss establishing a biologic specimen bank with corresponding clinical data, since this is currently not a DataMart function.

2. **Unblinding:** Jim Paul lead a discussion of the reasons for treatment unblinding during the conduct of a clinical trial. He distinguished between two different levels of unblinding, patient-level and trial-level. When a patient experiences a SUSAR or SAE, then the treating physician or the DSMB may be informed of which treatment that the patient was receiving when the event occurred. The treating physician could use this information to guide the patient's future care, and the DSMB may use the information to guide their recommendation for an amendment to the protocol. Trial-level unblinding occurs when annual reports of SAEs or SUSARs are submitted to a regulatory agency while the trial is active, or the DSMB reviews efficacy results for interim analyses. In trial-level unblinding the summaries are reported separately for each of the randomized treatment groups, however, the treatment groups may be identified or masked.

Jim posed several situations when treatment unblinding could be considered and asked a member from each of the cooperative groups to explain their standard operating procedure for each of these cases. It was apparent that there was considerable heterogeneity in the procedures used by the groups. For instants, some groups reported SUSARs to regulating agencies with the study treatments identified, while others do not identify the study treatment. Some groups present interim analyses to the DSMB with study treatments identified, but other groups conceal the treatment identifiers until the DSMB states their rationale for unblinding and describes a process using this information.

The discussion of unblinding will be taken up at the next Harmonization Committee Statistical Subcommittee meeting to determine whether it would useful to develop some recommended guidelines for unblinding

The meeting was adjourned at 5:00 pm.