Drug Safety Module: Summary and Recommendations

The Drug Safety Module Program built on previous OMERACT meetings and ongoing discussions on the development of adverse event (drug safety) forms and the need to establish a longterm database(s) to capture the drug safety issues of the exciting new interventions now being developed in rheumatology.

Thasia Woodworth presented the data forms that had been developed by the Drug Safety Working Party over the last few years. These forms can be accessed through the ILAR website (www.ilar.org), but to date very little feedback has been obtained. Pharmaceutical companies and investigators are encouraged to use these data sheets and to compare them to industry "norms." We continue to encourage investigators to use these forms and to provide feedback to the Working Party to improve them.

Professor Ralph Edwards described the activities of the WHO Collaborating Centre for Drug Evaluation and demonstrated how this could be used to link with other groups. Vibeke Strand and Kent Johnson provided background on the principles to be employed in the development of a longterm database and presented a model of how this might work. Lars Klareskog discussed the database that has been developed in Sweden to collect adverse events on disease modifying agents in rheumatoid arthritis.

Group sessions then took place to tease out various aspects of the issues:

• A group discussed methodology and in particular reviewed the data forms: What data needed to be collected and how these might link in to existing clinical trials without having to provide yet another dataset.

• Logistics were discussed in depth: Who would form the alliances, and how would links between the players be developed and maintained? The other major issue was that of maintaining confidentiality of the datasets.

• Another group discussed links to existing databases: What databanks are available and how links can be established to and across these databanks.

• The 4th workshop focused on the issue of funding: What needs to be funded? and who would pay?

METHODOLOGY

Current methods of capturing drug safety data need to be reevaluated. The challenges are to assure reporting of all untoward events and to try to simplify the process. It was felt that both patients and health professionals should have input into drug reporting through these simplified report forms. There still needed to be considerable education as to what to report. The issues of comorbidities, the cycling of treatments (particularly with new agents) and other medications that patients might be taking needed to be considered.

Issues relating to treatments are to include the amount, duration, and response. In terms of data collection it was felt that emphasis should be placed on: cancer, death, serious infections, hospitalizations, miscarriages, and birth defects.

Resources for data included national registries (United Kingdom), health maintenance organizations (United States), pharmaceutical chains. The database could be established as a simple nested case control study with unidentified data. The challenges in data collection included privacy/confidentiality, the issue of case controls, and the issue of attribution. Groups may wish to look at both short and longterm results. In terms of "controlled" populations, this might be patients who are already in current databases or who were dropouts from treatment. Patient identifiers could be date of birth, sex, and ethnicity, with the treatment being the "index" case. Comorbidities would raise specific concerns that needed to be addressed. The patient should be the focus of contact.

Case report forms should be as simple as possible with an identifier and contact, diagnosis, date of birth, sex, and ethnicity. Duration of disease, treatment (dose and duration), and the event would be entered. Data would be collected at baseline and at annual followup.

ALLIANCES

As a prelude to the establishment of the safety databases, it was felt important to capture significant disease and efficacy data. This might lead to the establishment of a number of arthritis registries (as operate in some countries) that would be very much like the cancer registries in Sweden and Norway. In the Netherlands all diagnoses are collected and in the UK there are regional arthritis registries run through the Arthritis and Rheumatism Council. In the United States the Arthritis, Rheumatism and Aging Medical Information System (ARAMIS) has established a national disease/drug registry; in Canada there is an Arthritis Treatment Registry. Denmark has just established a new treatment data base in the Rheumatoid Arthritis Registry. It was felt that some links could be developed with existing cancer registries or even with the Centers for Disease Control's infectious disease and arthritis link. In a number of countries there was increased interest in the establishment of joint replacement registries (hip and knee). Pharmacoepidemiological approaches might also be used. Data would need to be very carefully collected to ensure records are as complete and accurate as possible.

Record linkage should link drug use and disease; the longterm database should focus on serious adverse drug reactions. Any new system that was established should adopt a minimalist approach but have the ability to support

more sophisticated data collection. In any new database it was felt to be very important to have a patient driven approach.

Ground rules would need to be established for the use of the data and these would include issues such as confidentiality, who has access to the data, publication, the role of the pharmaceutical industry, other partners who might wish to submit data or utilize the database, and the importance of building incentives into the system.

In terms of the development of a new longterm database it was felt that this should be an OMERACT-ILAR-WHO project that would also link with other existing and emerging initiatives including those being developed through EULAR, The American College of Rheumatology (ACR), industry, WHO, and other regulatory groups.

The most important thing was to ensure inclusivity and internationalization for the project. In this regard it was felt useful to consider linking the project to the Bone and Joint Decade project.

In terms of alliances, these were felt to be patients, industry, government, and professional organizations. Industry and regulators were seen as an essential partnership, who would also be expected to provide some funding for the development of the database. Other groups who might be interested in funding parts of the project would include professional organizations, nonprofit patient advocacy organizations, WHO-OMERACT-ILAR-EULAR-ACR, the EEC, medical charities such as the Wellcome Trust or the RW Johnson Foundation, managed care/third party payer organizations, International Federation of Pharmaceutical Manufacturers' Associations and the International Committee on Harmonisation, local community organizations, and insurance companies.

The major outcome of the workshop was to establish a small group to develop a business plan. This would include the issue of funding options — for the establishment of the database, the survey itself, and the ongoing data collection.

Timelines would be developed, and to this end the steering committee hosted a one day workshop after the ACR meeting in Philadelphia in October 2000. The working party will develop an expert group with links to the major organizations and maintain regular contact via E-mail; it would also develop a strategy to involve patients as an integral part of the data collection and evaluation process.

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