

Minutes

SIOP Europe Clinical Trials Meeting held at SIOP Geneva Tuesday 19th September 2006

Chairs: Andrea Biondi (Italy) & Kathy Pritchard-Jones (UK)

See end of document for list of attendees.

The meeting was opened by Andrea Biondi who welcomed everyone and explained the purpose of the meeting. He summarised that SIOP Europe has previously organised two meetings of clinical trial groups and national groups, to discuss common issues in relation to running clinical trials in paediatric haemato-oncology in Europe. These meetings had led to the drafting of a Position Paper by SIOP Europe in which it was proposed to create a much stronger structure for SIOP Europe that could support the Groups in their endeavours in clinical research (the Position Paper is attached to these Minutes for further information). He explained the current situation with FECS (Federation of European Cancer Societies) now that ESMO (European Society of Medical Oncology) had set up as an independent group. SIOP Europe was aiming to be part of this reorganised structure in Brussels but if this were not possible, then a long term location for a SIOP Europe Office would need to be considered.

Kathy Pritchard-Jones (SIOPE Board) described how SIOP Europe had represented the views of the paediatric haemato-oncology community at discussions with EORTC, DG Research, EMEA, the TEDDY Network and various meetings with Pharma in relation to early drug development.

Heribert Jurgens (Euro-Ewings) agreed with the views expressed in the Position Paper and the previous discussion. The main question was how to achieve these aims. He supported the view that setting up a SIOP Europe Office would be a good way forward but questioned how this would be affordable.

Eva Koscielniak (CWS) stated that a very important issue was how to influence the national variation in implementation of the EU Clinical Trials Directive.

Agnes Saint Raymond (EMEA) then stated that this was the right time to be organising ourselves as a childhood cancer community. The paediatric regulation was due to come into force within the next few months and the Paediatric Committee of the EMEA would be established within six months. It was recognised that paediatric oncology was very important within paediatric clinical research. She informed the meeting that it is possible that discussions may be reopened on the EU Clinical Trials Directive at the Commission level. This was the right time to lobby for this.

Andy Pearson (SIOPEN) said that the SIOPEN group were very supportive of this initiative. They had two key areas with which they were struggling: finding appropriate sponsorship was impeding timely opening of trials and funding was very difficult. He emphasised the need for clear aims.

Jan Inge Henter (Rare Tumour.Net) stated that the definition of a rare disease was one which occurred in <1 patient per 2000 inhabitants. On this basis, all childhood cancers could be

defined as rare diseases. He informed us the Framework 7 (FP 7) will support rare diseases and that he is part of an international society for rare diseases that involves the NIH, FDA, EMEA etc. They were currently working on the best way to recruit patients into clinical research in rare diseases and also improvements in statistical approaches.

Jeremy Whelan (EURAMOS) wanted to share the experience of how the EURAMOS collaborative clinical trial had become established. He emphasised that it had achieved its funding from the European Science Foundation because it was successful in achieving a strong collaboration, rather than the other way around, ie. they had achieved a lot through getting agreement and not inviting competition and this had led to a strong consortium for bidding for funding.

Stefan Bielack (EURAMOS) emphasised the need for one overall sponsor and one institution that took overall responsibility for a trial. There was an absolute need for a functioning safety desk and clear definition of responsibilities of all of the involved partners. He emphasised the need for the partners to address issues together and for them to accept responsibilities in a collective fashion and to assume these responsibilities in a timely and full fashion. He again emphasised that EURAMOS had been successful in obtaining funding because it was well set up from the outset by the participating groups.

Maria Valsecchi (Interfant trial and Statistics) described the new pan-European Interfant trial whose central sponsor will be the Dutch Children's Leukaemia and Oncology Group (DCLOG). She described how it had been a learning experience in setting up a trial under the current EU CTD when they implemented Interfant. She will be able to provide a summary of their practical experiences in submitting the trial to so many national regulators by the end of 2006 and she will be happy to share these experiences with the Group.

Ruth Ladenstein (SIOPEN) again emphasised the need for clear delegation of trial responsibilities and the need for oversight of the whole trial by a single entity.

Modesto Carli (EpSSG) highlighted the absurdity of the current different interpretations of sponsor requirements in different countries. He hoped that this could be resolved in the very near future.

Marianne Naafs-Wilstra (representing Parents organisations) stated that the parent organisations were very supportive of this initiative and wanted to do everything they could to help facilitate clinical research in childhood cancer in Europe. She also introduced her colleague, Anita Kienesberg, who will replace her as the Parent's Representative in these endeavours.

Bruce Morland (UKCCSG) proposed an important action was that SIOP Europe should collate the differences in implementation of the EU CTD that they had identified in their survey of the clinical trial and national groups. This should be presented to relevant bodies in Brussels asking for a generic solution to the problem. He emphasised that it was important for there to be a single point of reference and contact for these ongoing communications and supported that this should be done through SIOP Europe.

Gilles Vassal (ITCC) reminded the Group that Italy seems to have solved the problem for academic trials by implementing a new law applicable to clinical trials intended to "enhance clinical practice as an integral part of health and medical care and not for industrial purposes". Such trials must have an academic or charitable promoter (sponsor) and be "not for profit" and

the trial data and its results must belong to the promoter. This law defines certain exceptions to the EU CTD for such trials, for example, the provision of funded drugs from National Health Services or charitable sources, an obligation on drug companies to provide pharmacovigilance data and relevant product dossiers for communication with ethics committees and the Italian Drugs Agency (an English translation is attached to these Minutes). He also informed the Group that Ireland had published data showing a 30% decrease in clinical trials since the implementation of the EU CTD. He supported that SIOP Europe should be a single voice for paediatric haematology/oncology in this area.

Joachim Boos (ITCC and GPOH) emphasised that there is now more uniformity in Europe than perhaps we feel. The sponsor issue can be solved if a single sponsor can be identified and there is clear delegation of the roles. This should involve standardised procedures and we need to learn from one trial to another, building on experience rather than duplicating it. He stated that there was an urgent need to define the current accepted "standard of care" for the common childhood cancers. This might facilitate obtaining an exemption from inclusion as an IMP of the drugs commonly used off-label in childhood cancer. Currently, the product could only be exempted from being defined as an IMP if it was used within its licensed indications. If "standards of care" could be defined and accepted, this would facilitate removing many products in our clinical trials from the need for urgent safety reporting. There was also a need for better risk management programmes. He felt the way forward would be to identify a few centres that were resourced and experienced in pharmacovigilance and explore ways to resource them to take on more pan-European studies.

Paolo Paolucci (TEDDY Network) introduced himself as the Chair of the Therapeutic Evaluation Subgroup in Oncology, which was part of Work Package 4 in this FP6 funded network of excellence. The first "result" from the TEDDY network was planned to be to define the off-licensed use of oncology drugs that were currently accepted as "standard of care". They have established a list of 39 drugs with indication for use and current accepted age ranges. There was a need to get detailed information from the various clinical trial groups to facilitate this work. He welcomed interaction between TEDDY and SIOP Europe and the Groups it represented. He also stated that TEDDY would be in a position to support almost completely any planned website development, should this be requested by SIOP Europe.

Andrea Biondi and Kathy Pritchard-Jones then summarised the meeting and defined the action points needed to move forwards.

1. SIOP Europe would continue lobbying for harmonisation of EU CTD implementation. This will involve producing a summary of the results of the questionnaire, providing an overview to the common issues and remaining obstacles. SIOP Europe would lobby at the European level but will circulate this summary and encourage all the groups to use it to lobby at national level.
2. SIOP Europe will establish a website for facilitating communication and a resource for information on current trials and training. This will be linked to existing resources where relevant to avoid duplication.
3. Coordinate a meeting to bring together groups interested in bidding for funding under FP7 to evaluate off-licensed use of out of patent drugs under the MICE programme to ensure that at least one oncology project is chosen.

Attachments:

1. Copy of the slides presented in Geneva
2. SIOP Europe Position Paper No. 2
3. English translation of the new Italian legislation for non-commercial trials
4. Summary of the SIOP E Questionnaire on the EU CTD (February 2006)
5. Copy of letter submitted to consultation process on guidance on 'specific modalities' of the EU CTD and the definition of IMPs and Non-IMPs, 03.11.06
6. Consultation documents from the European Commission website:
<http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/new.htm>

Attendees:

| Name | Representing and Country of Residence |
|-----------------------|---|
| Ablett, Sue | UKCCSG Data Centre, UK |
| Attina, Giorgio | Italian New Agents (representing Dr Riccardo Riccardi), Italy |
| Banikova, Karen | Slovakia |
| Beieschi, Martin | National Paediatric Haemato-Onc Study Groups, Austria |
| Bielack, Stephan | EURAMOS, Germany |
| Biondi, Andrea | Chair of Meeting and also representing IBFM Leukaemia, Non-Hodgkin's lymphoma, Italy |
| Boos, Joachim | GPOH New Drugs, Germany |
| Breatnach, Fin | Ireland |
| Brugier, Laurence | SFCE, France |
| Carli, Mondesto | EpSSG (Paediatric Soft Tissue Sarcomas), Italy |
| de Lidpa, Dokmanair | Italian New Agents (representing Dr Riccardo Riccardi), Italy |
| Eckschlager, Tomas | Czech Republic and Chairman Solid Tumour Working Group |
| Gaze, Mark | Paediatric Oncology Radiotherapy, UK |
| Graz Benesch, Martin | Representing Austrian National Pediatric Groups |
| Henter, Jan Inge | Histiocyte Society and Rare Disease Network (ICORD), Sweden |
| Henze, Guenter | SIOP Europe Board, Germany |
| Jurgens, Heribert | Euro-Ewings, Germany |
| Kamps, Willem A | DCOG and SIOP Europe Board, The Netherland |
| Kebudi, Rejin | TPOG, Turkey |
| Kienesberg, Anita | SIOP Parents representative, |
| Kogner, Per | NOPHO and SIOPEN, Sweden |
| Konstantinov, D | Bulgaria |
| Koscielniak, Eva | CWS |
| Kovacs, Gabor | Hungary in place of Pal Kajtar (retired) |
| Kowalczyk, Jerzy R | Poland |
| Ladenstein, Ruth | SIOPEN and Euro-Ewings, Austria |
| Morland, Bruce | UKCCSG and the UK |

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| Moschovi, Maria | Greece |
| Naafs-Wilstra, Marianne | SIOP Parents Organisations, Netherlands |
| Oberlin, Odile | EpSSG (Paediatric Soft Tissue Sarcomas) and Euro-Ewings, France |
| Paolucci, Paolo | TEDDY Network, Italy |
| Papadakis, Vassilios | Greece |
| Patte, Catherine | Non-Hodgkin's, France |
| Paulussen, Michael | Euro-Ewings, Switzerland |
| Pearson, Andy | SIOPEN, UK |
| Perilongo, Giorgio | SIOPEL and SIOP Board, Italy |
| Plantaz, Dominique | SIOPEN, France |
| Pritchard-Jones, Kathy | Chair of meeting and SIOP Wilms tumour, UK |
| Roselen, Angelo | Non-Hodgkin's lymphoma, Italy |
| Saint-Raymond, Agnes | EMEA, UK |
| Schmiegelow, Kjeld | SIOP Europe Board, Denmark |
| Schrapppe, Martin | IBFM Leukaemia, Non-Hodgkin's lymphoma, Germany |
| Serban, M | Romania |
| Sary, Jan | EWOG-MDS, SIOP Europe Board, Czech Republic |
| Uyttebroeck, Anne | BSPHO, Belgium |
| Valsecchi, M Grazia | IBFM Leukaemia, Non-Hodgkin's lymphoma and Statistics, Italy |
| Vassal, Gilles | ITCC, France |
| Vermeylen, Christiane | BSPHO, Belgium |
| Voute, PA | Ped Onc EKZ/HOIC, Netherlands |
| Wagner, HP | HGG Infant Study Group, Switzerland |
| Wallace, Hamish | Hodgkin's lymphoma, UK |