

**Best Pharmaceuticals for Children Act (BPCA)
Pediatric Oncology Core Working Group Conference Call
June 26, 2012
1:00 p.m.–1:30 p.m. ET**

Participants

Peter C. Adamson, M.D.
Beth Durmowicz, M.D.
Oluchi Elekwachi, Pharm.D., M.P.H.
Erica Radden, M.D.
Gregory H. Reaman, M.D.
Perdita Taylor-Zapata, M.D.

Purpose

The purposes of this call were to review the May 23 conference call summary, to answer any questions regarding the summary, and to discuss next steps. Because Lisa Mathis, M.D., was traveling and could not participate, Dr. Reaman facilitated the discussion.

Discussion

Dr. Taylor-Zapata asked whether the lists of existing Written Requests (WRs) and Pediatric Investigation Plans (PIPs) for the oncology drugs mentioned in the last call were collected. It was noted that the lists are being compiled by Drs. Durmowicz and Elekwachi. They are checking into what information can be obtained from the European Medicines Agency (EMA). Although some of the EMA information may be proprietary, the EMA does post agreed-upon PIP opinions on its Web site. They will also work with Suzanne Malli and Jean Temeck to obtain more information.

Dr. Reaman noted that although submitted PIPs and WRs are public information, WRs that are not responded to positively by sponsors fall off the list. Thus, the U.S. Food and Drug Administration (FDA) WR list may not be complete. Once the complete lists are compiled and distributed to this working group, it is hoped that the Children's Oncology Group and the clinical investigators' community can be approached to offer early feedback about what agents they have an interest in investigating further. Sponsors can be also be invited to the next FDA Pediatric subcommittee of the Oncologic Drugs Advisory Committee meeting to discuss whether or not they have any pediatric evaluation or investigation plans, and if not, why not. It could also be determined how such plans could be developed and for which specific pediatric populations.

Dr. Taylor-Zapata mentioned that in the last call, investigators said it would be useful for them to receive specific information/questions about the drugs for which their feedback is requested. She asked whether it is possible to give investigators a list of drug categories and to specify what is being looked for, such as safety or pharmacokinetics questions, rather than just giving them a general list of drugs about which to respond. Dr. Reaman said the reason the questions/lists are

general is because the working group is interested in any information about evaluations of these drugs in the pediatric population to determine whether there is any reason to formally investigate these drugs in pediatrics through BPCA. It was hoped that the broader questions would help garner information about which agents may be of interest to the investigator community. If there is interest in a specific agent and if there are in-house applications, recommendations or discussions about developing WRs could occur as early as possible. It was noted that a comment was made in the last call that the United States is behind the European Union (EU) because of PIP timing. Dr. Reaman responded that there are no specifics about when WRs should or can be issued; timing is very flexible, and WRs can be issued at the same time PIPs are being developed if there is actual interest in investigating a particular agent. However, there is no reason to develop a WR if there is no compelling rationale and if interest does not exist within the clinical investigator community. It is important to find out where investigators' interests lie.

Possible Agents for Study

Dr. Reaman said the Review Division came up with some agents that were not discussed in depth during the last call that may be of interest to investigators. These drugs are as follows:

- Sorafenib, an anti-VEGF that could be studied in relation to treating hepatocellular/liver tumors in children.
- TH-302, an alkylating agent whose activity is induced/increased in hypoxic situations. The sponsor is interested in using it to treat soft tissue sarcomas in adults. There are no stated plans for pediatric use, but that could change.
- Ombribulin, a tubulin binder that may be somewhat specific for vascular endothelial cells; it disrupts the formation of new vessels. The agent may have broader implications, and there is a sponsor plan for developing its use for soft tissue sarcomas.
- Trametinib, a new MEK inhibitor being developed for melanoma treatment.
- Volasertib, a new PK-1 inhibitor/checkpoint inhibitor for adults with acute myeloid leukemia; there is already a pre-nondisclosure agreement application with the sponsor and there has been some communication with the EMA. There is interest in developing a pediatric investigator plan in Europe, and there may be interest in the United States.
- Blinatumomab, an anti-CD3/anti-CD19 BiTE humanized monoclonal agent. The new sponsor is Amgen, but currently there is no WR. It may be possible to work with the company and cooperative groups to develop a WR if there is an interest.
- LDE 225, a hedgehog pathway inhibitor developed by Novartis. There is interest in using it for both adults and children with medulloblastoma. Hedgehog activation rates are higher in adults, even though disease incidence rates are higher in children.
- Prochymal, a biologic agent/stem cell product developed by Osiris Therapeutics for treating children with graft-versus-host-disease post transplant. The agent was approved in Canada and is being marketed there. The FDA was not privy to the Canadian discussions, but it is hoped that some information will come out in the next tri-lateral call with the European Union and Health Canada. It is a class of products that could be brought to the subcommittee for discussion. Patients have been calling about getting access to the drug.

Dr. Adamson was asked to share the above list of agents with sponsors to measure their interest. He agreed to circulate the list.

Dr. Reaman said sponsors could be invited to present at future meetings, and that they may be more inclined to attend if they know there is active interest and enthusiasm.

Next Pediatric Subcommittee (PSC) Meeting

The subcommittee meeting originally planned for November has been moved to December 4, 2012, to accommodate the FDA Oncologic Drugs Advisory Committee's (ODAC) presentations at the November PSC meeting.

Reauthorization by Congress

Dr. Reaman said the reauthorization of the BPCA and the Pediatric Research Equity Act (PREA) is still under way. There will likely be permanent reauthorization so such efforts will not need to be made every 5 years. There was a request for future focus on rare diseases, but pediatric cancer was not accepted by the Senate committee as a specific rare disease. There will be a public meeting within a year about BPCA and PREA that will review all that has been done in relation to drug development for rare diseases, including pediatric cancer.

Dr. Reaman stated that there is a commitment to making PSC meetings semiannual, with a focus on bilateral presentations and discussions about agents that can and should be evaluated in children and how to best design those studies and move new drugs forward. He noted that the December meeting announcement will be posted in the *Federal Register*, and that sponsors are invited to present products they may be interested in developing for pediatric studies.

It was noted that the minutes for the call summaries for the Oncology Working Group will eventually be posted online to allow for transparency and immediate input.

Action Items:

- Dr. Reaman will compile and circulate the list of agents discussed during the call along with a brief description of each.
- Dr. Adamson will take the list and make contact with investigators about potential interest.