

**Best Pharmaceuticals for Children Act (BPCA)
Pediatric Oncology Working Group Conference Call
November 4, 2014
11:00 a.m.–11:50 a.m. ET**

Participants

Amy Barone, M.D.
Meredith Chuk, M.D.
Martha Donoghue, M.D.
Lori Gorski
Mark Keiran, M.D., Ph.D.
Kate Matthay, M.D.
Gregory H. Reaman, M.D.
C. Patrick Reynolds, M.D., Ph.D.
Nita Seibel, M.D.
Malcolm Smith, M.D., Ph.D.
Donna Snyder, M.D.
Perdita Taylor-Zapata, M.D.
Brenda Weigel, M.D., M.Sc.
James Whitlock, M.D.
Erica Wynn, M.D.

Purpose

The purpose of this call was to discuss the following:

- Follow-up of Master Protocol (Pediatric MATCH Study) Workshop
- U.S. Food and Drug Administration (FDA) Outreach to Pediatric Cancer Advocacy Community (November 18)
- Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (ODAC) meeting: products for discussion: ganetespib (Hsp90 inhibitor), etirinotecan pegol, RO5503781 (MDM2 inhibitor)
- Potential products for future consideration: taselisib (P13K inhibitor), SGI-110
- Other suggestions
- Other business.

Master Protocol (Pediatric MATCH Study) Workshop

Dr. Reaman reported that the Master Protocol (Pediatric MATCH Study) Workshop, discussed in the previous call, was conducted in September 2014. This mini-symposium focused on planning a master protocol on pediatric cancer.

Dr. Donoghue explained that the workshop focus was informational, eliciting input from participants regarding the planning and processes implemented in the adult trial currently in progress, from both a study design and device platform perspective. The workshop was also an

opportunity to discuss regulatory requirements that could be expected, as well as a means to elicit feedback from participants, including Dr. Peter Adamson and statisticians, and to discuss ways that the FDA could assist during earlier formative stages. Dr. Donoghue also noted that she found the meeting productive, with valuable and interesting information, including hearing from Dr. Alice Chen of the National Cancer Institute (NCI) about how the adult MATCH study was designed and what they are working towards. Dr. Donoghue concluded that the meeting was a positive first step in opening lines of communication among adult and pediatric stakeholders that will be important as the pediatric master protocol is designed.

Dr. Reaman reiterated that this symposium was an opportunity to exchange information, including what plans might be under way, as well as to offer any regulatory advice to help facilitate moving forward. He also noted that plans are progressing, and that the NCI has made available to the Children's Oncology Group (COG) a set-aside of funds to support the Pediatric MATCH Study. Dr. Reaman explained that this issue was discussed at the January 2014 Rare Disease Workshop in the Pediatric Cancer breakout—specifically that a master protocol likely would expedite and facilitate pediatric drug development. He said that COG is developing several committees/subcommittees, and that their management has committed to assist this process. Dr. Reaman further noted that the study design, endpoints that will be used, and drugs that may be prioritized for inclusion as part of MATCH have been discussed, as well as the technology platform that will be used for sequencing and the need for input and oversight from the devices center at the FDA. Dr. Reaman said there has been interest from the FDA Center for Devices and Radiological Health to assist. He hoped that more updates will follow.

Dr. Matthey asked Dr. Reaman to identify the entity running the protocol and when it is scheduled to be activated. Dr. Reaman explained that this is a COG study, funded by the NCI. The protocol is still in the planning stage, regarding issues such as writing the protocol, defining sequencing strategies and platforms and where it will be performed. He suggested that Dr. Smith or Dr. Seibel could provide more information. Dr. Seibel said that tentative timelines had been established and that a draft protocol is slated for January, although she was unaware of any committee meetings that had taken place.

FDA Outreach to Pediatric Cancer Advocacy Community

The Office of Hematology and Oncology Products (OHOP) and the Office of Health and Constituent Affairs will host an open public forum for the pediatric cancer advocacy community. Scheduled within the next few weeks, this forum follows what FDA does each year at the American Society of Hematology and American Society of Clinical Oncology (ASCO) conferences, providing an opportunity for cancer advocates to meet with the FDA, ask questions, and attend brief FDA presentations on the most current information on new developments, breakthrough designations, expedited approval, pathways, and expanded access. At this past year's ASCO meeting, the forum was attended by international and U.S. advocates. Dr. Reaman said that while informative, these discussions and presentations were not particularly relevant or exclusive to pediatric oncology.

Building on that framework, the FDA has scheduled a 3-hour workshop, with approximately 45 minutes allocated to “FDA 101,” focusing on pediatric legislative initiatives related to drug development, including brief presentations on topics such as an Investigational New Drug (IND) submissions and New Drug and New Biologic Applications. Other presentations and question-and-answer periods are also scheduled. More details on the workshop, including registration information, are available on the FDA Web site. Invitations have been sent to 40–50 groups, and 50–60 registrations already have been received, including several from pharmaceutical companies. Dr. Reaman extended invitations to all members of the Pediatric Oncology Working Group and noted that the workshop will be posted on the FDA Web site and that participants will be able to telephone in their questions, as well. He suggested that this workshop may help clear up common misconceptions about the FDA—what it does/does not do, what it can/cannot do.

Dr. Reaman explained that the FDA sent invitations to advocacy groups it identified and also requested that these groups forward invitations and workshop information to other relevant groups and individuals that may not have been on the FDA distribution list. In addition, the workshop announcement is posted on the FDA public Web site.

Pediatric Subcommittee of the ODAC Meeting: Products for Discussion

The next meeting of the Pediatric Subcommittee of the ODAC is scheduled for December 11, 2014. Three products will be discussed:

- Ganetespib (Hsp90 inhibitor)
- Etirinotecan pegol
- RO5503781 (MDM2 inhibitor).

Sponsors have accepted invitations to attend. In addition to their presentations during the meeting, the sponsors will submit briefing books that will be posted in the *Federal Register* and on the Web site. Subcommittee members also will receive summaries of background information on each of the three products, as well as copies of questions from a panel of advisors who will participate. The meeting also will be webcast, and Dr. Reaman invited group members to participate online, in addition to those group members who are also members of the advisory subcommittee.

Potential Products for Future Discussion

Dr. Reaman listed a number of agents that have been identified through the office as INDs, most before the end of phase 2. He asked that working group members indicate their interest in inviting the sponsors of these agents to discuss these products further at the next Pediatric Subcommittee meeting (May 2015):

- Taselisib (P13K inhibitor): potential relevance in several pediatric tumors, developed by Genitech

- SGI-110: DNA methyltransferase inhibitor; early clinical evaluations in acute myeloid leukemia (AML) in both a relapsed/refractory setting and in elderly patients newly diagnosed with AML indicate impressive activity as a single agent.

Although he is not aware of any immediate plans for pediatric study of these agents, Dr. Reaman presented them to the group members to ascertain their potential interest. He noted that these agents could be open to a pediatric study. If the group expresses interest in these products, agent sponsors can be invited to one of the Pediatric Subcommittee meetings to present and discuss possible pediatric evaluation and the types of studies that could be helpful in formulating a Written Request. Dr. Reaman emphasized that OHOP is open to considering products identified by group members.

Dr. Smith said that taselisib is currently included in the Lung MAPP study, and an agreement is already in place with Genitech. As such, this may facilitate an agreement for future pediatric study.

Dr. Whitlock noted that given the numerous agents, the decision about what agent to study is especially complex and difficult. This issue is a recurring problem.

Dr. Reaman asked working group members for other possible agents to consider for discussion.

- Dr. Whitlock said the resubmission of the Pediatric Investigation Plan for inotuzumab ozogamycin (discussed in a previous call) has been approved and that he will be working with Pfizer to complete a formal investigator-initiated request. When that occurs, Dr. Whitlock said he would present inotuzumab to the group for possible pediatric evaluation.
- Dr. Keiran noted that the company sponsoring Xerecept is reconsidering this agent for possible further study.
- Dr. Reynolds explained that Merrimack Pharmaceuticals' product, MM-398, had promising results in the phase 1 trials. Dr. Reynolds suggested that the group continue to track this agent for possible discussion.

Dr. Reaman closed the meeting, thanking participants for their input.

Action Items:

- Dr. Reaman will send group members the link for the FDA Outreach to Pediatric Cancer Advocacy Community workshop.
- Recurring calls have been set up, and the next meeting will occur in 3 months on February 3, 2015.