Best Pharmaceuticals for Children Act (BPCA)
Pediatric Oncology Working Group Conference Call
March 7, 2017
11:00 a.m. – 11:30 a.m. EST

Participants

Peter Adamson, M.D.
Kristin Baird, M.D.
Amy Barone, M.D.
Najat Bouchkouj, M.D.
Diana Bradford, M.D.
Patricia Dinndorf, M.D.
Martha Donoghue, M.D.
Nicole Drezner, M.D.
Steven Dubois, M.D.
Lori Ehrlich, M.D.
Richard Gorlick, M.D.
Katherine Janeway, M.D.
E. Anders Kolb, M.D.
Aviva Krauss, M.D.
Ruby Leong, Pharm.D.
Leigh Marcus, M.D.
Lily Mulugeta, Pharm.D.
Gregory Reaman, M.D.
C. Patrick Reynolds, M.D., Ph.D.
Nicholas Richardson, M.D.
Malcolm Smith, M.D.
Brenda Weigel, M.D., M.Sc.
Carolyn Yancey, M.D.

Purpose

The purpose of this Working Group (WG) conference call was to:

- Introduce new Pediatric Oncology Medical Officers participating in the WG
- Confirm the dates of the next Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (ODAC) meeting
- Update WG members on the status of invitations issued to product developers/sponsors for presentation at the upcoming ODAC meeting
- Recommend/suggest additional presenters

Introduction of Pediatric Oncology Medical Officers

Dr. Reaman began by introducing several new participants in the WG:

- Diana Bradford, M.D.

- Maura O'Leary, M.D.
- Kristin Baird, M.D.
- Najat Bouchkouj, M.D.
- Emily Jen, M.D.

He noted that their participation attests to the increasing expertise in pediatric oncology within the FDA Centers for Drug Evaluation and Research and Biologics Evaluation and Research.

Pediatric Subcommittee of the ODAC

Dr. Reaman confirmed that the next ODAC meeting is scheduled for June 21 and June 22, 2017. He explained that publication of the meeting announcement in the *Federal Register* is pending per official approval of these dates.

Product/Sponsor Invitations Issued and Declined

Dr. Reaman noted that several of the sponsors, whose products had previously interested the WG have been invited to the upcoming meeting. He also explained that unfortunately, the following invitees have declined, and presented a brief update of the status of the development of these products, as well as their responses to the WG invitation:

- **Ipatasertib, Genentech:** This sponsor indicated that it feels that it is somewhat premature to discuss a pediatric development plan for this product despite its potential broad applicability.
- **Quizartinib, Daiichi Sankyo:** The sponsor felt that a presentation was premature given their clinical development.
- **AG-221, Agios:** Some early pediatric investigations are underway; at this time, the sponsor is over-committed with application plans.
- **CPX-351, Celator**: While this developer expressed interest in presenting, it is preparing to submit an application to the Agency; there are ongoing pediatric investigations of this product.
- **CUDC907, Curis:** A pediatric Phase I study is in process. The sponsor indicated that it considers it premature to present at the June meeting but expressed interest in presenting at a later date.
- **Palbociclib, Pfizer:** Currently working on a pediatric plan, this developer declined the invitation for the June meeting, but would like to be invited to the next Subcommittee meeting.
- **Pexidartinib, Plexxicon:** This firm also expressed interest in presenting at the next Subcommittee meeting.
- **Onivyde, Merrimack:** Dr. Reaman explained that the sponsor has been invited to discuss this product for the past 2-½ years. The most recent invitation was declined because Merrimack has sold the product. Dr. Reaman noted that if there is continued interest within the WG, the Agency will extend an invitation to the new owner/licensing entity.

Product/Sponsor Invitations Issued and Accepted

Dr. Reaman provided a brief update on the following sponsors that have accepted invitations to discuss their products at the June 2017 meeting:

- **APX005M, Apexigen:** This sponsor would like to present and discuss this immune-activating agent. Dr. Reaman noted that there has been significant activity in some adult tumors, but he was not aware of pre-clinical work in pediatric tumor systems.
- **Olaratumab, Eli Lilly:** This product has been approved for adult soft tissue sarcomas. The June meeting may be an opportunity to discuss and examine use in pediatric soft tissues sarcomas, as well.
- **Gilteritinib, Astella:** This developer indicated that it is enthused about having an opportunity to come and discuss potential pediatric development.
- **Lurbenectidin, Pharma Mar:** Derived from Mediterranean Ocean sea life, this product induces double-strand DNA breaks. Dr. Reaman noted that is has demonstrated activity in platinum-resistant ovarian cancer. The sponsor is considering development in sarcomas.
- **Prexasertib (LY 2606368), Eli Lilly:** This product, a CHK inhibitor, has been added to the June agenda.
- **Belinostat, (Beleodaq), Spectrum:** Dr. Reaman reported that this sponsor has not yet responded to the Agency's invitation.

Other Products Recommended for Invitation to Present

Dr. Reaman asked WG participants if they had any questions about any presenters/products on the proposed June agenda. He also noted that participants could still recommend other products that would possibly warrant an invitation to present in June. However, he emphasized that WG members should submit their recommendations as soon as possible.

Additional Discussion

Dr. Kolb asked for clarification regarding the process for presenting at the Subcommittee meeting. Dr. Reaman explained that product developers/sponsors accepting invitations to the meeting are asked to present an overview of their product, focusing on pre-clinical background and their clinical experience in adults. Their presentations are followed by discussion with the Advisory Committee regarding what a potential pediatric development program could/should look like. Dr. Reaman pointed out that this information is useful to the Agency in considering whether to issue a Written Request (WR).

Dr. Kolb also asked if there is coordination with European Medicines Agency (EMA) and Pediatric Committee (PDCO) in what they are requesting from these companies. Dr. Reaman noted that invited sponsors are also asked to provide information regarding interaction with EMA or PDCO when they present at Subcommittee meetings. He remarked that discussing and

sharing information is always important when dealing with rare diseases, and especially important when discussing rare diseases in specific pediatric populations.

Dr. Reaman also noted that if the developer is working on a Pediatric Investigational Plan (PIP), it would be a good idea to align the PIP with the same, or at least non- conflicting, development plans in the United States. He agreed that it is important to also consider the opportunity for international trials. Dr. Reaman explained that the FDA's Office of Pediatric Therapeutics coordinates monthly conference calls with its EMA counterparts, as well as with representatives of Health Canada, the Pharmaceuticals and Medical Devices Agency (PMDA), and the Therapeutic Goods Administration (TGA), regarding specific products, often oncology products, during the evaluation of study plans, Proposed Pediatric Study Request (PPSRs), or when considering a WR.

Dr. Smith noted that he had no new recommendations or comments at this time from the National Cancer Institute (NCI) regarding presentations at the upcoming June meeting, but that he would confer with Dr. Reaman in a separate conversation.

Dr. Weigel inquired if any developers of immune therapy inhibitor groups products have presented at these Subcommittee meetings. She noted that many have of these developers have PIPs underway, with a variety to choose from.

Dr. Reaman explained that both Bristol-Myers Squibb (BMS) and Merck have presented at Subcommittee meetings. As a result, a WR has been issued for a number of products that were presented. WRs have been issued for ipilumumab, nivolumab, and atezolizumab. He also pointed out that immuno-oncology drug development has evolved slowly especially in pediatric oncology. Dr. Reaman mentioned that BMS had made a pipeline presentation to the FDA the previous day and that several products in early development that were included in that presentation may be relevant to pediatrics.

Dr. Janeway noted that the Pediatric MATCH project has considerable interest in ATR inhibitors. She explained that Vertex is furthest along in developing ATR inhibitors such as VX970. Dr. Janeway also noted that results from very early Phase 1-B trials and pre-clinical work suggest some vulnerability induced possibly by TP53 mutations or abraxa. She suggested that this drug, as well as other ATR inhibitors, might warrant consideration for presentation at upcoming Subcommittee meetings.

Dr. Reaman agreed, noting that the FDA will definitely track these products, and will include them as possible invitees to future Subcommittee meetings, if and when appropriate. He also explained that to this date Vertex has not responded to two written invitations and a telephone call asking the company to present at the June meeting.

Other Business/Closing Comments

Dr. Reaman pointed out that Dr. Taylor-Zapata and Dr. Zajicek were unable to join the conference call. Therefore, discussion of potential off- patent products for WRs at NIH would be postponed. Dr. Mulugeta agreed, noting that it might be more appropriate to table a discussion of information on the priority list until the next meeting.

Next Scheduled WG Meeting

Dr. Reaman concluded by emphasizing that he would keep WG participants apprised of further developments for the June meeting. He also invited WG members to consider joining the meeting as a consultant or Special Government Employee (SGE).

He again emphasized the need to quickly contact additional presenters/sponsors that the WG would recommend inviting to the June Subcommittee meeting.

The next WG conference call is scheduled for Tuesday, May 2, 2017, at 11:00 a.m. (EDT).