

**Best Pharmaceuticals for Children Act (BPCA)
Pediatric Oncology Working Group Conference Call
February 2, 2016
11:00 a.m.–11:40 p.m. ET**

Participants

Peter Adamson, M.D.
Amy Barone, M.D.
Gilbert Burckart, Pharm.D.
Meredith Chuk, M.D.
Martha Donoghue, M.D.
Lori Ehrlich, M.D.
Rachel Ershler, M.D.
Lia Gore, M.D.
Richard Gorlick, M.D.
Mark Kieran, M.D., Ph.D.
Leigh Marcus, M.D.
Kathleen Neville, M.D., M.S.
Gregory Reaman, M.D.
Hari Cheryl Sachs, M.D.
Malcolm Smith, M.D.
Donna Snyder, M.D.
Perdita Taylor-Zapata, M.D.
Ashley Ward, M.D.
Brenda Weigel, M.D., M.Sc.
James Whitlock, M.D.
Anne Zajicek, M.D., Pharm.D.

Purpose

The purpose of this call was to discuss the following items:

- Plans for the 2nd Pediatric Cancer Advocacy Forum and possible topics
 - Current status of BPCA-related activities in the Office of Hematology and Oncology Products (OHOP); number of Written Requests (WRs) issued and timing
 - Patient-Reported Outcomes (PROs) and Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)
 - Update on engineered cell products for pediatric cancer; challenges, prospects, promise
 - Improving the relevance of the Pediatric Research Equity Act (PREA) to oncology product development
 - Expanded access and single-patient Investigational New Drug (IND) applications
- Pediatric subcommittee of the Oncologic Drugs Advisory Committee (ODAC)
- Possible products for discussion

- CUDC-907
 - CBL0137 (Cleveland BioLabs)
 - LOXO-101
 - Venetoclax
 - Liposomal irinotecan
 - MDX-1105/MEDI14736/MPDL 3280A (PDL-1 inhibitors)
- Other products of interest: suggestions from the Working Group

Opening Remarks

Dr. Reaman began the meeting by welcoming several pediatric hematologists-oncologists who had recently joined the U.S. Food and Drug Administration (FDA) as Medical Officers. He asked those staff members who were able to join the call to introduce themselves, noting that 11 pediatric hematologists-oncologists are currently members of the Review Divisions of the Office of Hematology and Oncology Products.

Plans for 2nd Pediatric Cancer Advocacy Forum

Dr. Reaman noted that the 2nd Pediatric Cancer Advocacy Forum is scheduled for April 22, 2016, at the White Oak Campus. He reiterated that this session will be a follow up to the predecessor meeting, structured as “FDA 101”—with likely focus on topics such as:

- Pediatric legislative initiatives
- Status of current BPCA-related activities in OHOP
- Number of WRs issued and the timing of their issuance (attempts to issue WRs earlier in the development timeline rather than waiting for approval of adult indications)
- Pediatric clinical outcome assessments, in particular, the state of the science with PRO-CTCAE
- How pediatrics can join the rest of the FDA in the Agency’s commitment to patient-centered drug development by using PROs (if only as supportive data)
- Update on engineered cell products.

Dr. Reaman mentioned that another likely topic to be included in the Forum will address genetically engineered cell therapy for pediatric cancers—in particular, specific challenges and prospects. Although this issue was not discussed in the previous meeting, Dr. Reaman noted that the significant activity in the Center for Biologics Evaluation and Research (CBER) with respect to cell products likely will warrant discussion. He pointed out that other meeting topics may include the Agency’s approach to expanded access and experience with single-patient IND applications. Finally, the program also will include discussion of opportunities for improving the relevance of PREA (which is indication-based) to oncology product development and addressing the concerns voiced by pediatric cancer advocates that PREA legislation currently has little relevance for cancer drug development for children.

Products for Discussion/Presentation at the Upcoming Pediatric Subcommittee of the ODAC Meeting

Dr. Reaman asked Working Group members for their input regarding considering the following products for discussion at the meeting, planned for late July 2016. He explained that these products have been identified within his office as relevant. He also noted that the sponsors of several of these products have expressed an interest in presenting at the upcoming meeting. For example, Curis, Inc., the developer of CUDC-907, and Epizyme, the Tazemetostat (EZH2-inhibitor) sponsor, already have contacted his office.

- CUDC-907
- CBL0137
- LOXO-101
- Venetoclax
- Liposomal irinotecan
- MDX-1105/MEDI14736/MPDL 3280A
- EZH2-inhibitor

Dr. Reaman briefly reviewed the above products, summarizing their potential relevance for presentation at the Pediatric Subcommittee of ODAC meeting. He reiterated that the intent is to keep discussion as broad as possible, rather than to focus on development of these products for specific diseases.

CUDC-907

This combined PI3 kinase HDAC inhibitor is very early in development for adults. However, its sponsor, Curis, Inc., has indicated an interest in developing this product in pediatrics, as well.

CBL0137

Dr. Reaman noted that this product presents a very interesting mechanism of action. Dr. Reaman also noted that this product has demonstrated significant activity in adult tumor systems and some in vitro evidence of activity in some pediatric cancers. Its developer, Cleveland BioLabs, had hoped to present at a previous subcommittee meeting, but had scheduling conflicts and had to opt out.

LOXO-101

Dr. Reaman next briefly discussed this NTRK inhibitor, which has shown promise in multiple rare tumors, many of which occur in children. This company is interested in presenting as well. Dr. Kieran noted that they already have (or are planning to) run a number of pediatric studies.

Venetoclax

Dr. Reaman explained that this product, a BCL-2 inhibitor, was discussed during the April 2015 conference call. The sponsor, Genentech/AbbVie, was unable to present at the previous meeting, but remains interested in developing this product for use in acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL).

Liposomal irinotecan

The manufacturer of this product, Merrimack, also had to opt out from presenting at the previous meeting. Its application, which was pending at that time, has subsequently been approved, and the company has expressed an interest in presenting at the upcoming meeting.

MDX-1105/MEDI 14736/MPDL 3280A

Dr. Reaman pointed out that while there has been some discussion regarding PD-1 inhibitors, there has been relatively little discussion regarding these three PD-L1 inhibitors. He asked the Working Group for feedback regarding whether any one of these three listed products should have higher priority in being invited to present. He also suggested that it might be possible to have all three developers present their products together. It was mentioned that a pediatric Phase I trial is already in process with MPDL 3280A.

Dr. Gore noted that while the developers of these three products are all major pharmaceutical manufacturers, it may be that not all three products will move forward, and it probably would be best for the Working Group to refrain from selecting presenters too early. However, Dr. Kieran agreed that it would be interesting to have the developers of these three PD-L1 inhibitors present at the same meeting. It was also suggested that having all three developers present at the same meeting could possibly facilitate future combination studies.

While acknowledging that this would be only the second time that the “multiple presenter” approach would be used, Dr. Reaman indicated that he would proceed with moving the Group’s recommendation forward and would keep the Group apprised regarding reaction from the sponsors and their willingness to present within this format. He also emphasized that this is a 2-day meeting. Therefore, the number of products being presented is limited, but that the goal is to present as many products as possible, especially if there are pediatric studies in progress.

Dr. Smith pointed out that if the neo-antigen hypothesis is correct for certain cancers, there may not be much activity to report. Therefore, he asked for the Working Group’s input on how far to go in planning trials for these agents. Dr. Reaman agreed that this issue warrants consideration. Dr. Smith noted that there are some Phase I and Phase II studies in children currently underway.

Other Products of Interest

Dr. Reaman asked Working Group members to suggest other products that they would recommend for presentation.

Dr. Reaman also asked the Working Group to identify any other products that they would like discussed at the next meeting. Dr. Gore offered that organizing this ambitious an agenda could prove challenging, but most importantly, with very interesting presentations.

Given the proposed agenda of presenters, Dr. Gore suggested starting the conflict of interest (COI) process as early as possible. Dr. Reaman explained that the Office is very aware that the COI process is lengthy and OHOP is already starting to identify Special Government Employees (SGEs), but final SGE selections will require knowing what companies are coming and what products are being presented.

Dr. Gore asked if it is within the purview of the Working Group to suggest as part of the PD-L1 discussions that presenters include combination development or ask advisers to suggest combinations as a long-term strategy. She also pointed out that this approach could enrich the conversation, and lay the framework for long-term product development.

Next Scheduled Meeting

The next quarterly Working Group call is scheduled for May 3, 2016, at 11:00 a.m. (ET).

Action Items

- Dr. Reaman will keep Working Group alerted to final dates for the meeting.
- Dr. Reaman also will keep Working Group members posted on what companies are invited to present and scheduling.
- He will also follow up with them regarding incorporation of a “combination” presentation as a long-term strategy.