



February 13, 2023

Dr. Robert M. Califf
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Partial clinical hold on AALL1731 and AALL1821

Dear Dr. Califf:

The undersigned childhood cancer organizations are members of the Alliance for Childhood Cancer, consisting of patient advocacy groups, healthcare professionals and scientific organizations, representing Americans who care deeply about childhood cancer. We write to express our concerns about the U.S. Food and Drug Administration's (FDA) notice of a partial clinical hold for trials AALL1731 and AALL1821, both of which include the delivery of blinatumomab.

As you know, each year in the U.S. an estimated 16,000 children are diagnosed with cancer. Approximately 1 in 263 children in the U.S. are diagnosed with cancer before their 20th birthday. Overall, incidence rates from 2010 through 2019 have stabilized in children after increasing since 1975 but continued to rise in adolescents by 1% per year, although trends vary by cancer type. Unfortunately, cancer remains the most common cause of death by disease for children in America.

Together, we have made significant advances to develop better treatments for many forms of childhood cancer. However, for too many children, progress is limited and there is no available cure. Unfortunately, 1 in 5 children diagnosed with cancer in the U.S. will not survive, and for the ones who do, the battle is never over. By the age of 50, more than 99% of survivors have had a chronic health problem, and 96% have experienced a severe or life-threatening condition caused by the toxicity of the treatment that initially saved their life, including brain damage, loss of hearing and sight, heart disease, secondary cancers, learning disabilities, infertility and more.

Childhood cancer research uniquely depends on clinical trials to advance care and treatment for kids facing a cancer diagnosis. In addition to discovering new treatments and cures, children with cancer depend on the research community to unlock safer, less toxic therapies.



In many cases, clinical trials provide kids with cancer the best or only treatment option available and appropriate for their condition.

It has come to our attention that the FDA has disallowed the delivery of 72- and 96-hour IV bags of blinatumomab to newly diagnosed patients enrolling in AALL1731 and AALL1821 due to safety concerns. These are two critical trials that the Children's Oncology Group (COG) is conducting for standard risk and relapsed acute lymphoblastic leukemia (ALL). We agree that the safety of children enrolled in these studies is of the utmost importance, and we are concerned that this decision could lead to new safety risks for children involved in these studies.

In addition, we are concerned that the FDA's hold decision could lead to new safety risks for children involved in these studies by placing an undue burden on families receiving this treatment. In the absence of 72- and 96-hour IV bag options, families choosing to participate in AALL1731 or AALL1821 will either need to be hospitalized for the entirety of the 28-day infusion of blinatumomab or will need to return to the clinic every 1-2 days for an IV bag change, both of which carry their own health and safety risks. The logistics required to return to the clinic every 1-2 days – from time off of work to travel time and lodging requirements to additional childcare needs – could make trial participation no longer possible for a significant portion of children with ALL, particularly those with limited resources. We urge the FDA to work expeditiously with trial sponsors in considering the impact this clinical hold could have on trial participation and accessibility in addition to weighing any safety concerns.

Thank you for your work on behalf of children, adolescents, and young adults with cancer. The Alliance for Childhood Cancer welcomes the opportunity to discuss this matter further and to more fully understand what the FDA is doing to address these concerns. Please contact Sarah Milberg, Co-Chair of the Alliance for Childhood Cancer, at smilberg@allianceforchildhoodcancer.org or Dr. Michael Link, Co-Chair of the Alliance for Childhood Cancer, at mlink@stanford.edu for any additional information.

Sincerely,

The Alliance for Childhood Cancer

American Childhood Cancer Organization

American Society of Pediatric Hematology/Oncology

The Andrew McDonough B+ Foundation

Association of Pediatric Hematology/Oncology Nurses



Association of Pediatric Oncology Social Workers
Children's Brain Tumor Foundation
Children's Cancer Cause
Children's Oncology Group
The Leukemia & Lymphoma Society
Mattie Miracle Cancer Foundation
National Brain Tumor Society
Rally Foundation for Childhood Cancer Research
St. Baldrick's Foundation