



Blinatumomab (again?) The Bs of it...

**Sue Zupanec MN NP Pediatrics
POGO November 1, 2023**



Blinatumomab in Pediatric ALL

- Standard of care for 1st relapse B-ALL based on AALL1331 results
- Under investigation for standard risk B-ALL in AALL1731
- Planned investigation for infant ALL based on highly promising results (babies – another B)
- Planned investigation for Ph+ and Ph-like B-ALL based on highly promising adult clinical trial results for Ph+ ALL
- Often used when toxicity prevents administration of chemotherapy bridging (yet another B)

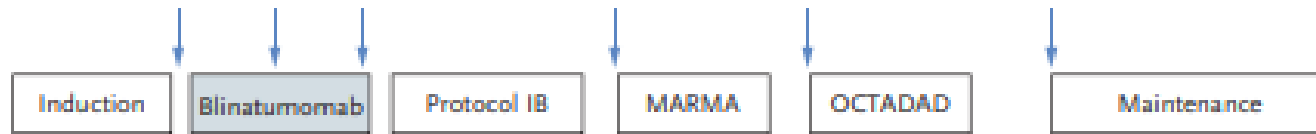
Blinatumomab

- Blinatumomab is complex to deliver, requiring continuous infusion for 28 days per cycle through CVAD, often a PORT
- Typically, 2-3 cycles of blinatumomab
- Can be administered primarily at home – after recommended 2-3 day stay at initiation of each cycle
- Required bag changes – currently every 96 hours (at SickKids)



Babies (Infant B-ALL) - KMT2A (previously called MLL)

- Single arm prospective study, compared to historical outcomes
- N=30
- 2-year disease free survival – 81.6% (blina) versus 49.4%
- 2-year overall survival – 93.3% (blina) versus 65.8%
- Minimal toxicity observed
- Early...

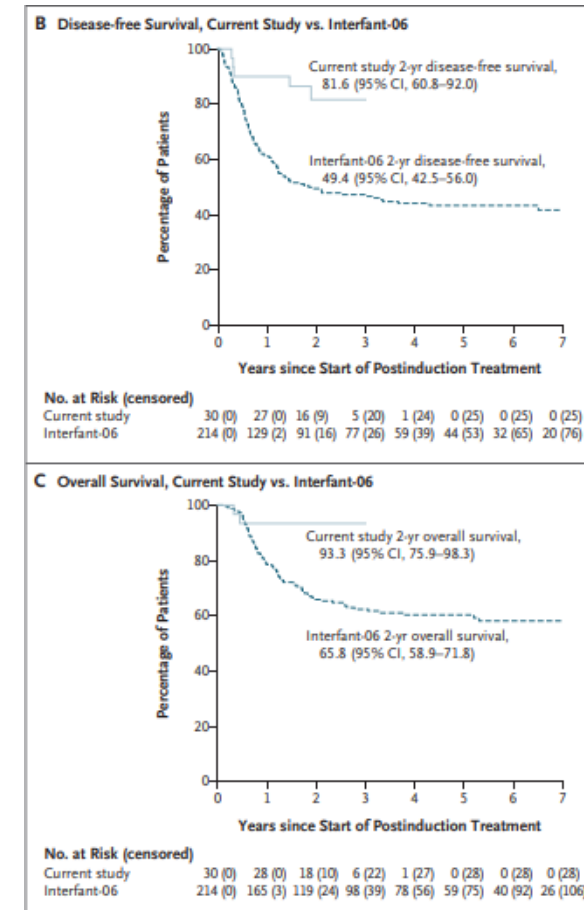


THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Blinatumomab Added to Chemotherapy in Infant Lymphoblastic Leukemia

Inge M. van der Sluis, M.D., Ph.D., Paola de Lorenzo, Ph.D., Rishi S. Kotecha, M.B., Ch.B., Ph.D., Andishe Attarbaschi, M.D., Gabriele Escherich, M.D., Karsten Nysom, M.D., Ph.D., Jan Stary, M.D., Ph.D., Alina Ferster, M.D., Benoit Brethon, M.D., Franco Locatelli, M.D., Ph.D., Martin Schrappe, M.D., Peggy E. Scholte-van Houtem, M.Sc., Maria G. Valsecchi, Ph.D., and Rob Pieters, M.D., Ph.D.



Van der Sluis, NEJM, 2023

Blinatumomab Burden – How can we best understand?



- COG Embedded study AALL1731
- Qualitative Burden Study – Multi-site, led by SickKids (Jibb and Zupanec)
- COG Nursing Survey Results – Quantifying unplanned medical visits

Ongoing work...only the previews (for some)



Burden of Care – Families/Caregivers

- Burden of responsibility for monitoring both the infusion and the child receiving blinatumomab falls on the family caregivers
- How do we best prepare family caregivers for the experience of caring for their child receiving home administered blinatumomab?
- What are the caregiving demands?
 - **Monitoring and managing potential side effects**
 - **How to plan for and navigate anticipated complications**
 - **Recommendations for day-to-day life of the child and family**

Complimentary Embedded Study: COG AALL1731

- Caregiver Burden embedded aim (opt in) (with HMH study)
- Questionnaire based – Quantitative - Caregiving Demands and Caregiver Work Limitations
- Planned enrollment 340 participants - 240 consented

Qualitative Study – SickKids led, Multi-site

Multi-site Qualitative study

- SickKids coordinating site
- CHOP, CHLA, Texas Children's, Children's National
- NP lead identified at each site

- 6 interviews completed to date
- 20 planned or until saturation is reached



Primary Aim: To describe family caregiver's experience (caregiving demands, areas of worry and confidence, impact of family at home, and perceived met and unmet support needs) of caring for their child receiving blinatumomab in the home/outpatient setting

Sneak peek...

“We thought that it would have required a lot more attention than it actually did. After the first day I'd say that ourselves and my son were all kind of used to it. We weren't ever too concerned about it other than maybe the actual tube getting stuck on something, but even then, it didn't ever happen.”

“I've also been told that if there's a kink, then the machine will just keep drawing on air and not drawing on the Blina, so that was also implanted in my head. So, then I'm always constantly checking if it's kinked somewhere, like is there air in the line.”

“At the beginning, it was kind of confusing to figure out how we were going to like manage the multiple pumps and like having like the backpack and everything.”

A few more...

“We had to just make sure that the rough housing and all that action is minimal or at least the items were protected.”

“So, when I got the all the instructions of the different pumps, I took photos of it so I could share it with different people that may look after [child] because if I wasn't around when an error code came up, I wanted them to have the instructions. So, the hospital could maybe have those instructions digitally available so that you can just like e-mail them to somebody.”

A few more...

“The hospital gave us like a **really cool** backpack for the immunotherapy and like whenever he was sitting on the couch, we would take out the cords a little bit. So, he was able to like put the backpack on the ground and like, have it sitting beside him. But then as soon as he wanted to get up and move around, we put like the backpack on him and made sure the cords were really tucked in properly so they wouldn't get caught on anything or anything like that.”

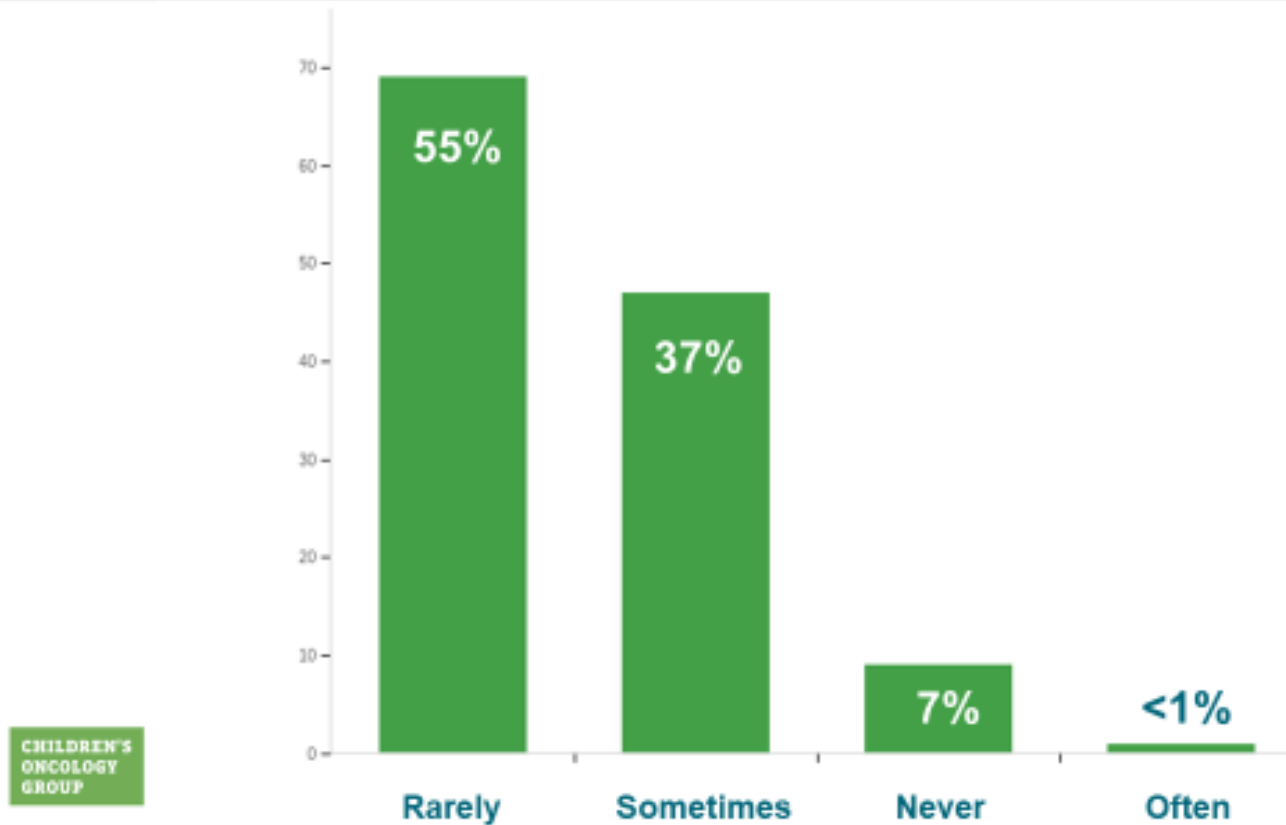


Anticipatory Guidance



COG Nursing Study – Quantitative Results

How often do patients/families experience unplanned clinic or ER visits for blinatumomab pump and infusion related concerns?

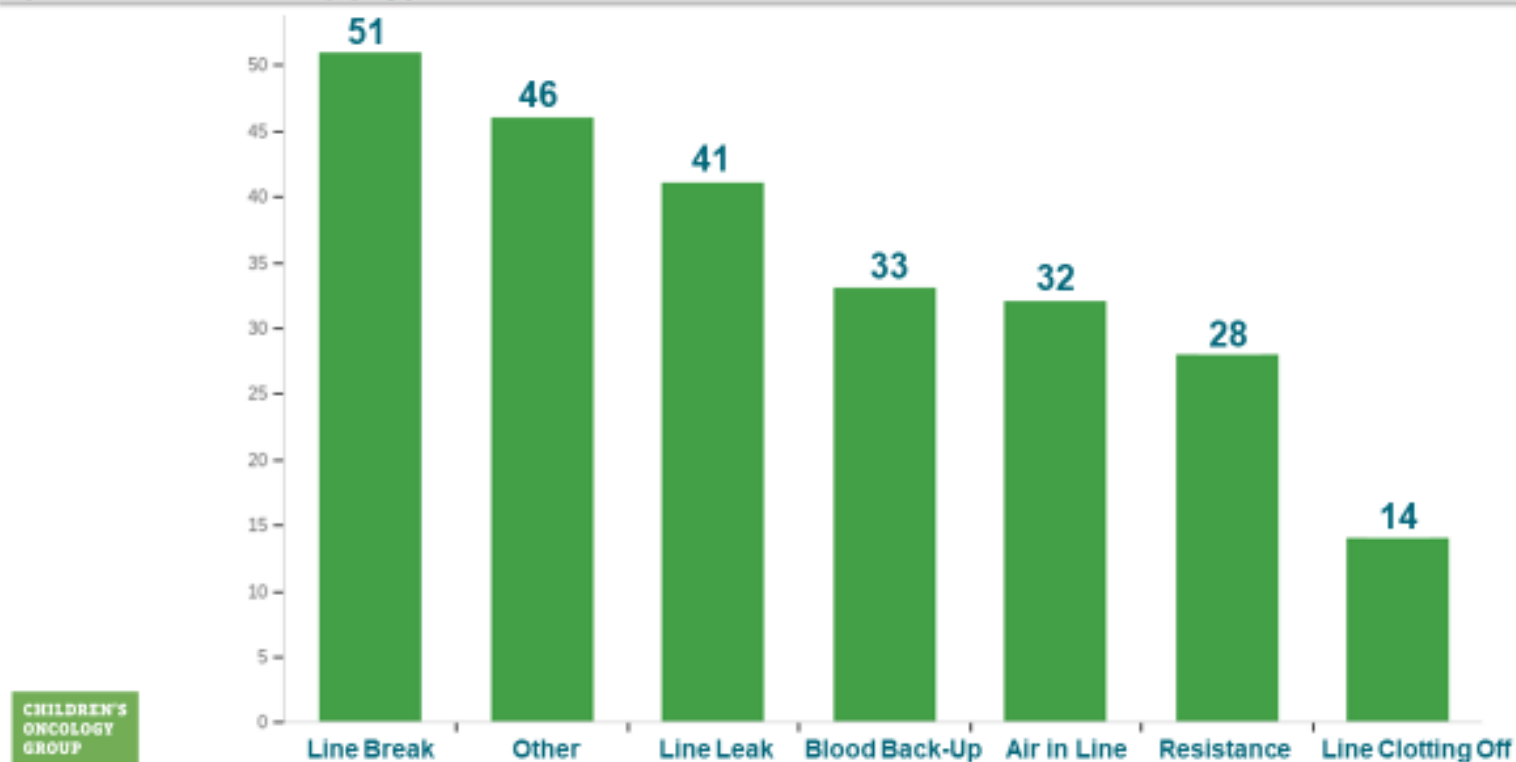


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Withycombe, in press

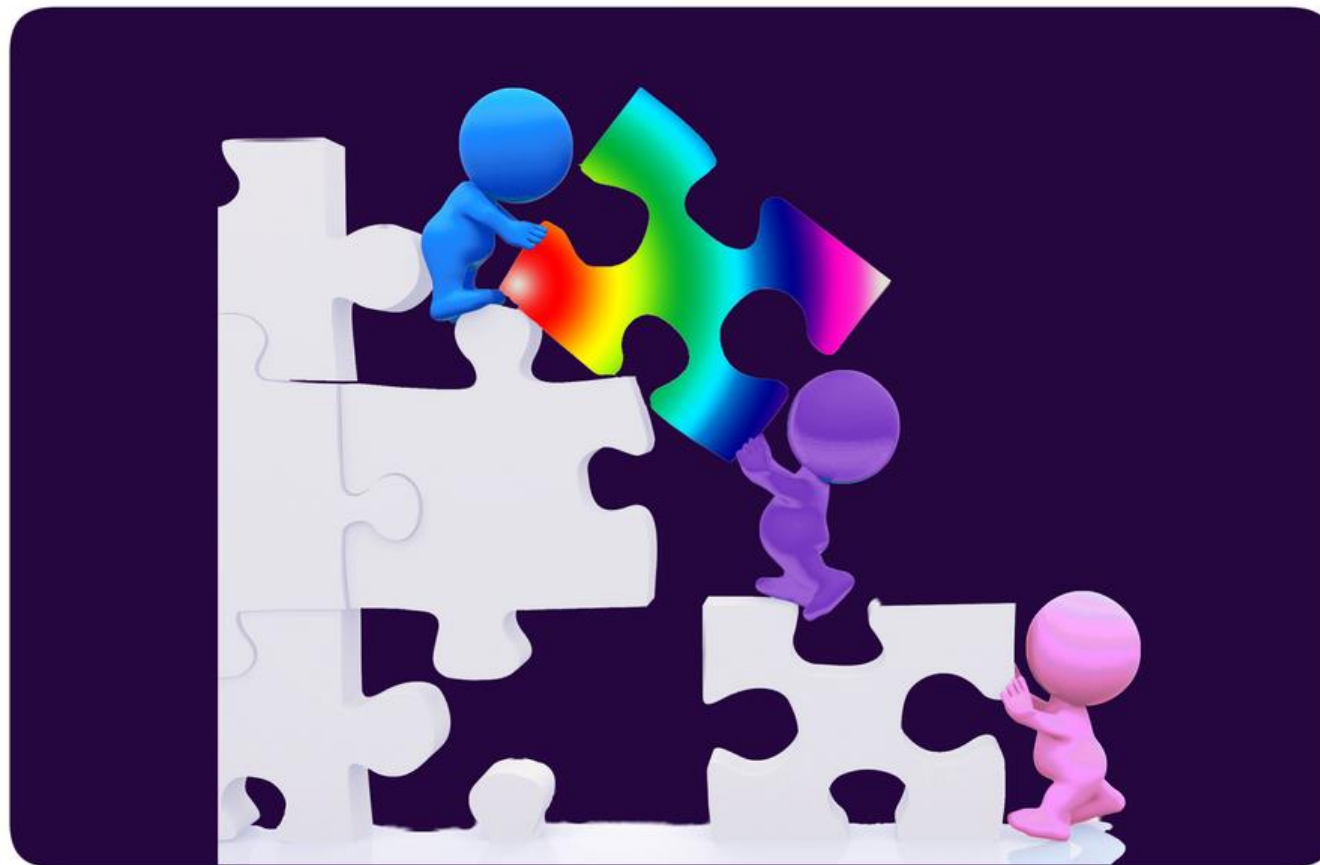
Pump or equipment issues

*Please select any outpatient issues you have had with pump or equipment
(Select all that apply)*

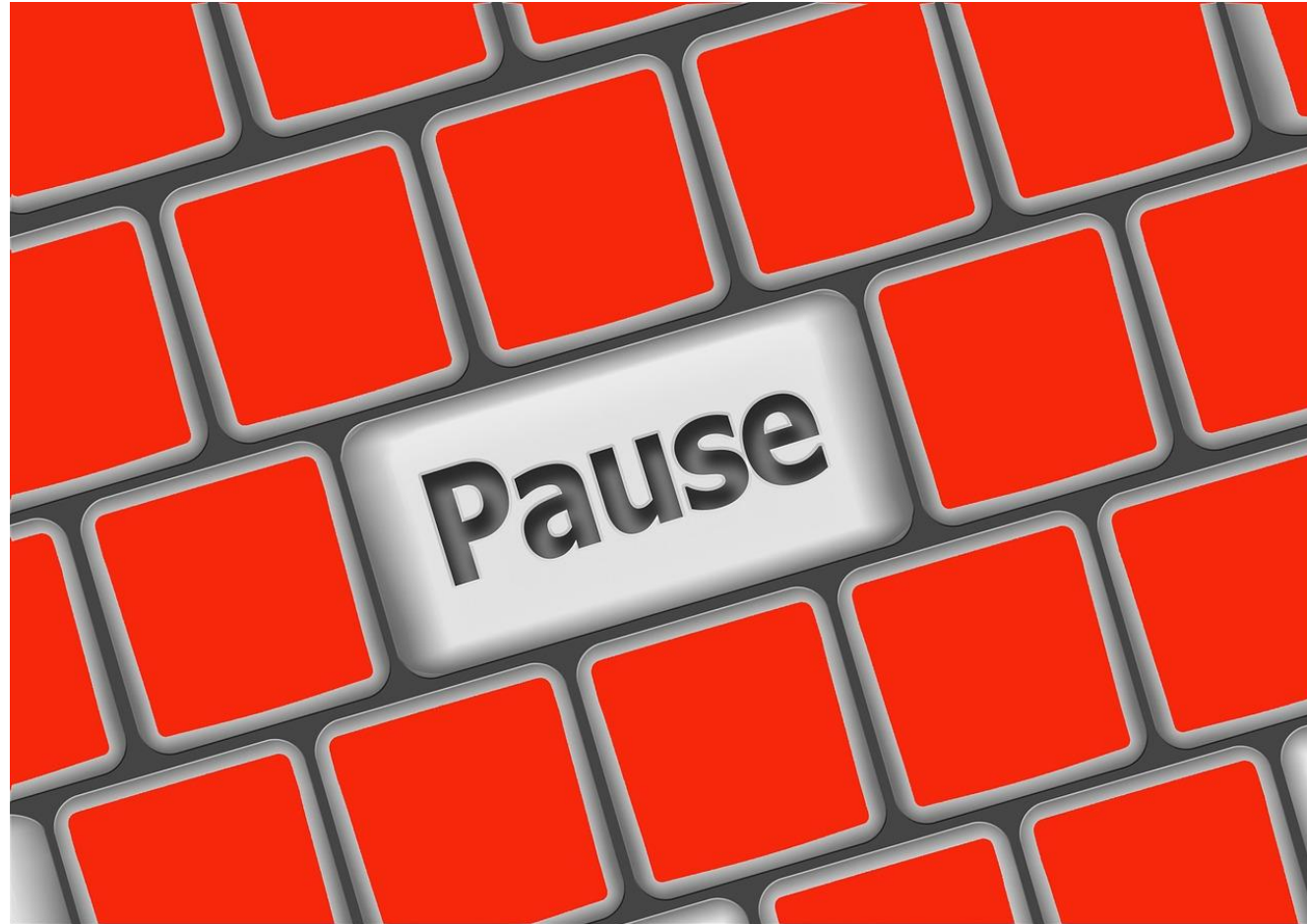


Withycombe, in press

Putting it all together...



Burden shift – now on us...



COG with Blinatumomab studies halted – December 2022 – Bag sizes

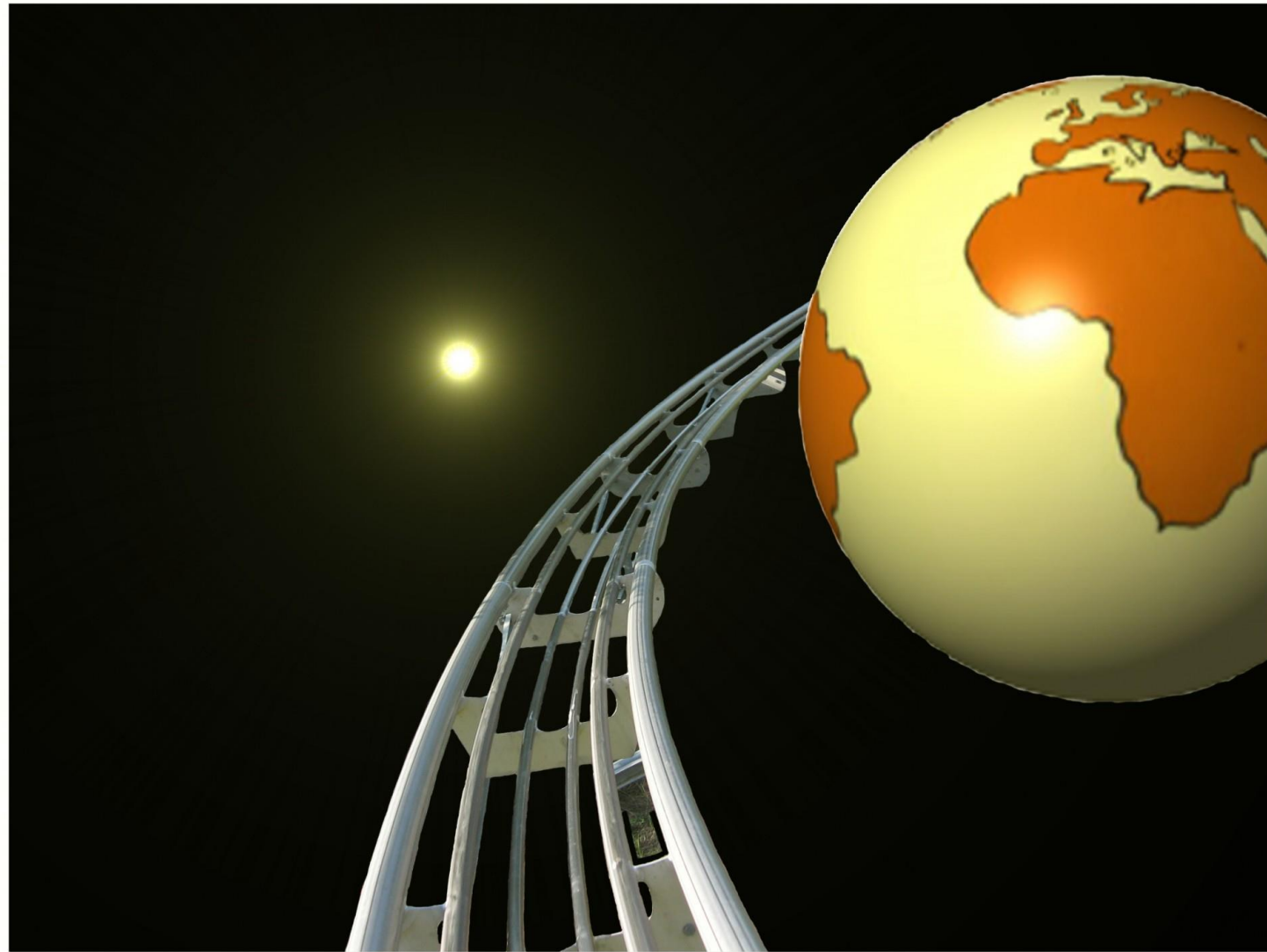
- A new burden – burden of proof...
- 72- and 96-hour bag preparations were not included in the investigator brochure (IB) or the USPI
- Only 24 and 48 hour and 7-day bag preparations listed in the IB
- 7-day bags restricted to over 22kg/48lbs (due to addition of benzyl alcohol)



Burden of Proof

**B U R D E N
O F P R O O F**

A compelling story...



COG Nursing Survey – Bag sizes

150 (78%) COG institutions responded to blinatumomab survey

125 sites answered question about outpatient blinatumomab use:

2 (2%) used only 24-hour bags

5 (4%) used only 48-hour bags

12 (10%) used only 72-hour bags

21 (17%) used only 96-hour bags

10 (8%) used only 168-hour bags

59 (47%) used a combination of bag sizes that included 72 or 96-hour bags

3 (2%) used combinations that did not include 72 or 96-hour bags

13 (10%) reported use of combination bags but did not specify bag size(s)

Overall, 92 (73.6%) used 72- and/or 96-hour bags (or combinations of these sizes)

Withycombe, in press

AALL1331: Blinatumomab blocks are less toxic than chemotherapy blocks as post-induction/pre-transplant therapy for early first relapse B-ALL

Adverse Event	Blinatumomab Cycle 1 N = 102		Chemotherapy Cycle 1 N = 97		Blinatumomab Cycle 2 N = 88		Chemotherapy Cycle 2 N = 62	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Febrile Neutropenia	6 (6%)	5 (5%)	43 (44%)	43 (44%)	0	0	28 (45%)	28 (45%)
Mucositis	4 (4%)	0	44 (45%)	25 (26%)	2 (2%)	1 (1%)	16 (26%)	5 (8%)
Sepsis	1 (1%)	1 (1%)	13 (13%)	13 (13%)	2 (2%)	2 (2%)	14 (23%)	14 (23%)
Typhlitis	0	0	1 (1%)	1 (1%)	0	0	4 (7%)	4 (7%)



★ Advancing Knowledge, Discovery, and Collaboration ★

Risk of Sepsis During Blinatumomab Administration in Children: A Report from the Children's Oncology Group

Joel C. Thompson, MD

On behalf of the AALL1731 study committee

★ MAY 10-13 ★

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AALL1731 Rates of Grade 3+ catheter infection and sepsis in blinatumomab blocks in newly diagnosed NCI SR ALL in CR1

Blinatumomab Block	Patients		Catheter Infection		Sepsis		Catheter Infection + Sepsis	
	N		N	%	N	%	N	%
Block 1	658		5	0.8%	18	2.7%	20	3.0%
Block 2	530		0	0.0%	13	2.5%	13	2.5%
Block 3	71		0	0.0%	2	2.8%	2	2.8%
Total	1259		5	0.4%	33	2.6%	35	2.8%

Thompson, ASH, May 2023

Hot of the press – AALL1731 Reactivated!

- COG studies can open and continue to have 72- and 96-hour bag options
- Lower limit for use of 7-day bags (dropped from 22kg to 5.4kg (12lbs – will we really do this?))
- Is this an opportunity?
- Will this increase access – what supports will families/caregivers need? (especially if they live farther from the treating center)

HOT OFF THE PRESS

Equipment needed for home administration

- CADD pump – weights 2 lbs...then add the blinatumomab bag
- Infusion set (IV tubing) – length 108 inches or 9 feet
- Back up charger/batteries
- Medical carrying bag to make it portable



Concerns with existing medical bag used at SickKids

- Bag length - too short – requires pinching of the Blinatumomab bag
- Poor fit and uncomfortable (heavy on day 1, single strap with no padding or support)
- Single strap limited adjustment to length
 - For younger patients required another person to hold/carry
- Identified as a medical bag (sick stigma)
- Limited padding and protection
 - Families worried about damaging the expensive pump
 - Noise of operating pump
- Created a list of priorities for an improved bag design
- Built a prototype



Design for testing phase

Eligible participants:

Any pediatric patient being treated at SickKids planned to receive blinatumomab for any indication and any cycle and their primary caregiver

8-10 participants, convenience sample

Design:

Random cross-over design (half to start cycle with standard carrying bag, and half to start cycle with innovative backpack)

After 8-12 days participants will switch to the alternate bag (this will align with a planned blinatumomab bag change)

5 families selected for Qualitative interview to occur at completion of the blinatumomab cycle

...and the winner is...

- Overwhelming preference for the backpack prototype
- Some tweaks underway
- Dissemination...more complicated than we anticipated

"the backpack let me be more like a kid"



Conclusions/thoughts

- 7-day bags – is this an opportunity, if yes, what information about the experience would be important to gather?
- Backpacks in our limited testing were preferred by kids and caregivers, and improved overall comfort and function – how can we provide the backpack to all kids planned to receive blinatumomab
- Consolidating the information around burden for kids and families – to developing resources to improve anticipatory guidance, and inform processes

