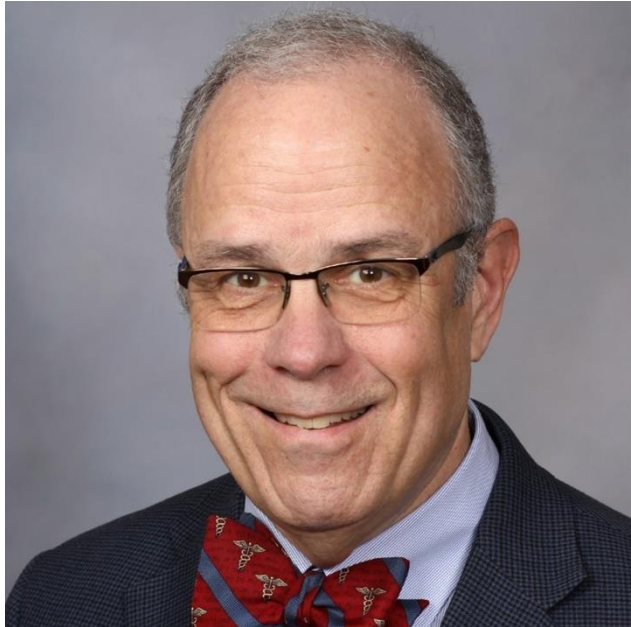


# Practical Management Pearls for Immunotherapy for the Treatment of Acute Leukemia

October 14, 2021

11:30 a.m. – 12:30 p.m. ET

# Webinar faculty



Mark R. Litzow, MD – *Mayo  
Clinic Cancer Center*



Daniel A. Arber, MD – *University  
of Chicago*

# Learning objectives

- Outline practical considerations for diagnostic testing and classification in acute leukemia and the implications for immunotherapy treatment planning
- Appropriately manage challenging and/or uncommon toxicities/irAEs associated with immunotherapy in acute leukemia
- Determine optimal sequencing of immunotherapies in all stages of acute leukemia treatment, including treatment for persistent or relapsed/refractory disease after initial therapy

# Outline

- Guideline development
- Diagnostic testing in AL
  - New data in acute leukemia (new classifications)
- Toxicities associated with immunotherapy for acute leukemia
- Sequencing therapies in acute leukemia

# Guideline development

**Open access**

**Position article and guidelines**

 Journal for  
ImmunoTherapy of Cancer

## **The Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of acute leukemia**

Michael M Boyiadzis,<sup>1</sup> Ivan Aksentijevich,<sup>2</sup> Daniel A Arber,<sup>3</sup> John Barrett,<sup>4</sup> Renier J Brentjens,<sup>5</sup> Jill Brufsky,<sup>1</sup> Jorge Cortes,<sup>6</sup> Marcos De Lima,<sup>7</sup> Stephen J Forman,<sup>8</sup> Ephraim J Fuchs,<sup>9</sup> Linda J Fukas,<sup>10</sup> Steven D Gore,<sup>11</sup> Mark R Litzow,<sup>12</sup> Jeffrey S Miller,<sup>13</sup> John M Pagel,<sup>14</sup> Edmund K Waller,<sup>15</sup> Martin S Tallman<sup>5</sup>

# Guideline development

- *The Institute of Medicine's Standards for Developing Trustworthy Practice Guidelines* used to develop these recommendations
- Panel consisted of 17 participants, including medical oncologists, hematologists, a hematopathologist, a leukemia research nurse, and a patient advocate
- Recommendations come from literature evidence, supplemented with clinical experience of the panel members where necessary
- Consensus defined as  $\geq 75\%$  agreement

# Outline

- Guideline development
- Diagnostic testing in AL
  - New data in acute leukemia (new classifications)
- Toxicities associated with immunotherapy for acute leukemia
- Sequencing therapies in acute leukemia

# Initial Diagnostic Workup of Acute Leukemia

## Guideline From the College of American Pathologists and the American Society of Hematology

Daniel A. Arber, MD; Michael J. Borowitz, MD, PhD; Melissa Cessna, MD; Joan Etzell, MD; Kathryn Foucar, MD; Robert P. Hasserjian, MD; J. Douglas Rizzo, MD; Karl Theil, MD; Sa A. Wang, MD; Anthony T. Smith, MLS; R. Bryan Rumble, MSc; Nicole E. Thomas, MPH, CT(ASCP)<sup>cm</sup>; James W. Vardiman, MD

• **Context.**—A complete diagnosis of acute leukemia requires knowledge of clinical information combined with morphologic evaluation, immunophenotyping and karyotype analysis, and often, molecular genetic testing. Although many aspects of the workup for acute leukemia are well accepted, few guidelines have addressed the different aspects of the diagnostic evaluation of samples from patients suspected to have acute leukemia.

**Objective.**—To develop a guideline for treating physicians and pathologists involved in the diagnostic and prognostic evaluation of new acute leukemia samples, including acute lymphoblastic leukemia, acute myeloid leukemia, and acute leukemias of ambiguous lineage.

**Design.**—The College of American Pathologists and the American Society of Hematology convened a panel of

experts in hematology and hematopathology to develop recommendations. A systematic evidence review was conducted to address 6 key questions. Recommendations were derived from strength of evidence, feedback received during the public comment period, and expert panel consensus.

**Results.**—Twenty-seven guideline statements were established, which ranged from recommendations on what clinical and laboratory information should be available as part of the diagnostic and prognostic evaluation of acute leukemia samples to what types of testing should be performed routinely, with recommendations on where such testing should be performed and how the results should be reported.

**Conclusions.**—The guideline provides a framework for the multiple steps, including laboratory testing, in the evaluation of acute leukemia samples. Some aspects of the guideline, especially molecular genetic testing in acute leukemia, are rapidly changing with new supportive literature, which will require on-going updates for the guideline to remain relevant.

(*Arch Pathol Lab Med.* 2017;141:1342–1393; doi: 10.5858/arpa.2016-0504-CP)

Accepted for publication December 9, 2016.  
Published as an Early Online Release February 22, 2017.  
Supplemental digital content is available for this article at [www.archivesofpathology.org](http://www.archivesofpathology.org) in the October 2017 table of contents.  
From the Department of Pathology, University of Chicago,

asco special article

# Initial Diagnostic Work-Up of Acute Leukemia: ASCO Clinical Practice Guideline Endorsement of the College of American Pathologists and American Society of Hematology Guideline

Valérie de Haas, PhD<sup>1</sup>; Nofisat Ismaila, MD<sup>2</sup>; Anjali Advani, MD<sup>3</sup>; Daniel A. Arber, MD<sup>4</sup>; Raetasha S. Dabney, MD<sup>5</sup>; Dipti Patel-Donnelly, MD<sup>6</sup>; Elizabeth Kitlas, LMSW<sup>7</sup>; Rob Pieters, MD, PhD<sup>1</sup>; Ching-Hon Pui, MD<sup>8</sup>; Kendra Sweet, MD<sup>9</sup>; and Ling Zhang, MD<sup>9</sup>

abstract

**PURPOSE** The College of American Pathologists (CAP) and the American Society of Hematology (ASH) developed an evidence-based guideline on the initial diagnostic work-up of acute leukemia (AL). Because of the relevance of this topic to the ASCO membership, ASCO reviewed the guideline and applied a set of procedures and policies for endorsing clinical practice guidelines that have been developed by other professional organizations.

**METHODS** The CAP-ASH guideline on initial diagnostic work-up of AL was reviewed for developmental rigor by methodologists. Then, an ASCO Endorsement Expert Panel updated the literature search and reviewed the content and recommendations.

**RESULTS** The ASCO Expert Panel determined that the recommendations from the guideline, published in 2016, are clear, thorough, and based on the most relevant scientific evidence. ASCO fully endorsed the CAP-ASH guideline on initial diagnostic work-up of AL and included some discussion points according to clinical practice and updated literature.

**CONCLUSION** Twenty-seven guideline statements were reviewed. Some discussion points were included to better assess CNS involvement in leukemia and to provide novel insights into molecular diagnosis and potential markers for risk stratification and target therapy. These discussions are categorized into four sections: (1) initial diagnosis focusing on basic diagnostics and determination of risk parameters, (2) molecular markers and minimal residual disease detection, (3) context of referral to another institution with expertise in the management of AL, and (4) reporting and record keeping for better outlining and follow-up discussion. Additional information is available at: [www.asco.org/hematologic-malignancies-guidelines](http://www.asco.org/hematologic-malignancies-guidelines).

# CAP/ASH Guideline

Expert Panel	Advisory Panel	CAP/ASH Staff
Daniel Arber, MD, Co-Chair, CAP	Frederick R. Appelbaum, MD	Nicole Thomas, MPH, CT(ASCP), CAP
James Vardiman, MD, Co-Chair, ASH	Clara Bloomfield, MD	Robert Plovnick, MD, ASH
Michael Borowitz, MD, PhD, ASH	William L. Carroll, MD	Robert Kunkle, ASH
Melissa Cessna, MD, CAP	Laura Housley, Patient Advocate	Kendall Alexander, MPH, ASH
Joan Etzell, MD, CAP	Jerry Hussong, MD	R. Bryan Rumble, MSc, methodologist
Kathryn Foucar, MD, ASH	Steven H. Kroft, MD, FASCP	Christina Lacchetti, MHSc, methodologist
Robert Hasserjian, MD, ASH	Michelle Le Beau, PhD	Tony Smith, MLS, CAP, Medical Librarian
J. Douglas Rizzo, MD, ASH	Martin S. Tallman, MD	
Karl Theil, MD, CAP		
Sa Wang, MD, CAP		

# CAP/ASH Guideline

- Developed key questions
- Performed baseline survey of pathologists and hematologists (Arch Pathol Lab Med (2017) 141(8):1101-1106)
- Performed meta-analysis
- Public comment period
- Resulted in 27 guideline statements regarding the initial workup of acute leukemia (Arch Pathol Lab Med (2017) 141(10):1342–1393)

# CAP/ASH Guideline

- Wide variety of recommendations, including
  - Immunophenotyping
  - Genetic and molecular genetic testing
  - Classification

# Immunophenotyping

**Table 2** Recommended immunotherapy-centric diagnostic markers for acute leukemia

Disease type	Marker	Agents for consideration
Acute lymphoblastic leukemia	CD19	Blinatumomab
	CD19	Tisagenlecleucel (patients aged $\leq 25$ years)
	CD22	Inotuzumab ozogamicin
	CD20	Rituximab
Acute myeloid leukemia	CD33	Gemtuzumab ozogamicin

# Immunophenotyping – Baseline Survey

	AML Response Percent	AML Response Count	ALL Response Percent	ALL Response Count
Morphologic assessment	100.0%	234	99.1%	232
Flow cytometric analysis	99.1%	232	98.3%	229
Conventional cytogenetics (karyotype)	96.2%	225	96.6%	225
Molecular testing	78.2%	183	54.9%	128

# Genetic and Molecular Genetic Testing (Karyotype; Mutational studies)

	AML Response Percent	AML Response Count	ALL Response Percent	ALL Response Count
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# Genetic and Molecular Genetic Testing (Karyotype; Mutational studies)

## Statement 15 Other ALL Testing

- B-ALL
  - Mutations panels that may include, but are not limited to
    - *PAX5*, *JAK1*, *JAK2*, and/or *IKZF1* R
  - Expression of CRLF2 R
- T-ALL
  - Mutations panels that may include, but are not limited to
    - *NOTCH1* and/or *FBXW7* R

R, recommendation

# Genetic and Molecular Genetic Testing (Karyotype; Mutational studies)

Statements 16, 17, 19 Adult and Pediatric AML

- *FLT3*-ITD SR – all types
- *NPM1*, *CEBPA*, *RUNX1* SR – most types
- *KIT* SR (adult), R (peds) – Core binding factor AML
- Mutations panels that may include, but are not limited to
  - *IDH1*, *IDH2*, *TET2*, *WT1*, *DNMT3A*, and/or *TP53* R
  - (*ASXL1*)

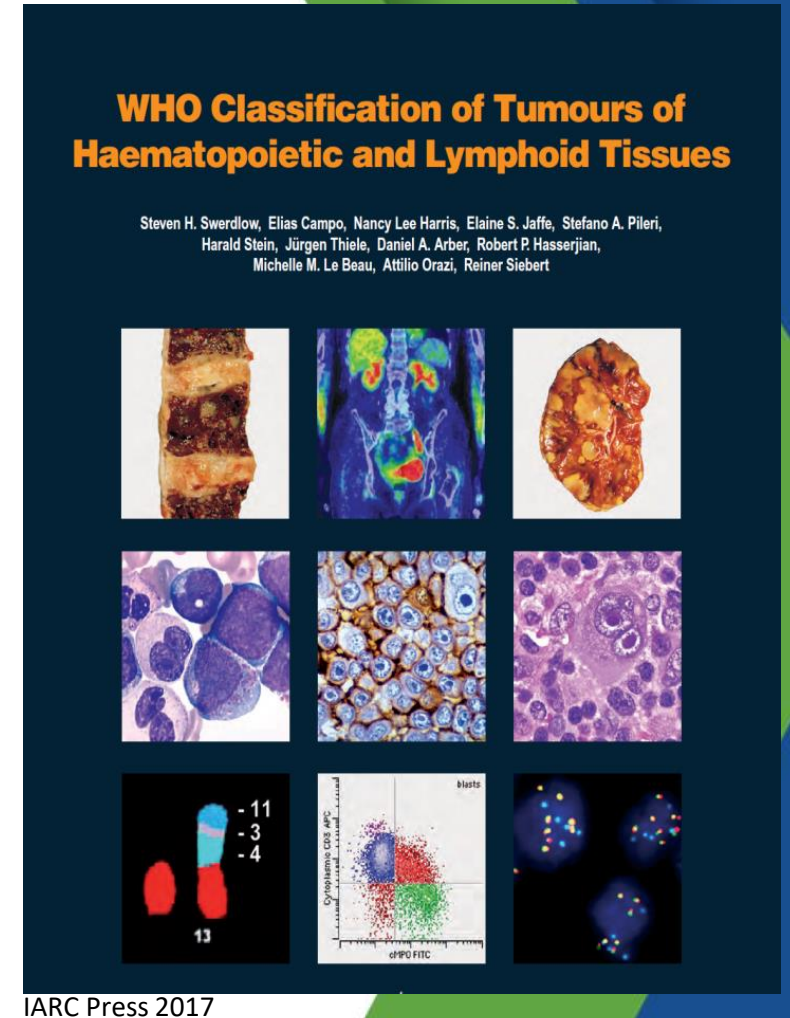
SR, strong recommendation; R, recommendation

# Diagnostic tests for ALL/AML

ASCO/CAP/ASH recommended genetic tests (Adopted by SITC Guideline)	
Acute lymphoblastic leukemia	Acute myeloid leukemia
<i>t(9;22)(q34.1;q11.2); BCR-ABL1</i>	<i>FLT3-ITD</i>
<i>PAX5; CRLF2; JAK1; JAK2</i>	<i>NPM1; CEBPA; RUNX1</i>
CRLF2 overexpression (for B-ALL)	<i>IDH1; IDH2; TET2; WT1; DNMT3A; TP53</i>
<i>KMT2A</i> (MLL); <i>IKZF1</i> (for B-ALL)	<i>KIT</i> (for CBF AML)
<i>NOTCH1</i> and/or <i>FBXW7</i> (for T-ALL)	<i>RUNX1-RUNXT1/CBFB-MYH1</i> (for CBF AML)
	<i>PML-RARA</i> for suspected APL

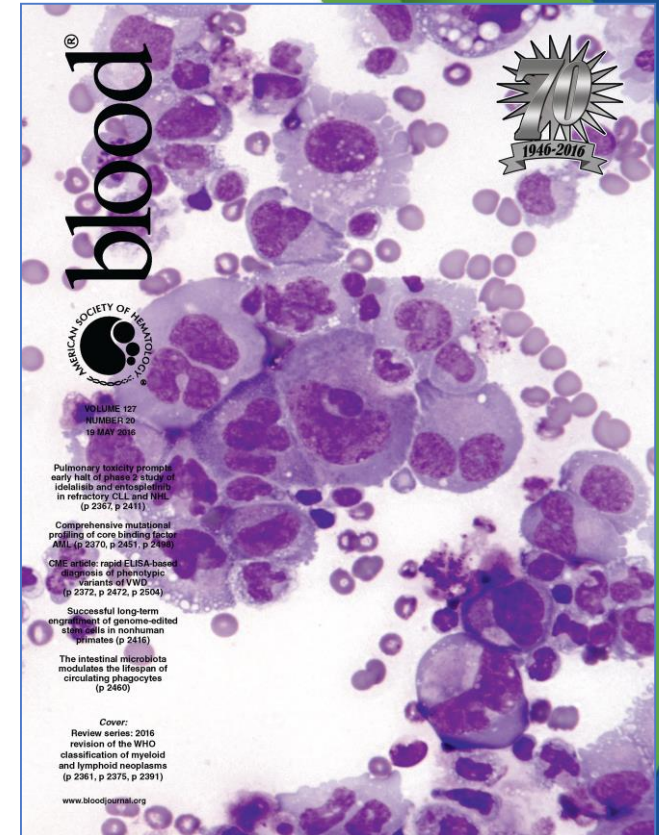
# Classification

- Current Recommendation
  - Use the current WHO classification diagnostic terminology
- Future Direction
  - 5<sup>th</sup> edition WHO classification in the works with IARC
    - Expected publication date of late 2022
    - Have changed their process to not incorporate a clinical advisory committee, to exclude prior editors and to refuse input from hematopathology societies



# Classification

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  - Separate International Consensus Classification of Myeloid and Lymphoid Neoplasms
    - Clinical Advisory Committee meeting held in September 2021
    - Expected publication in 2022
  - Update of CAP/ASH guidelines
    - Planned to occur after new classifications are published

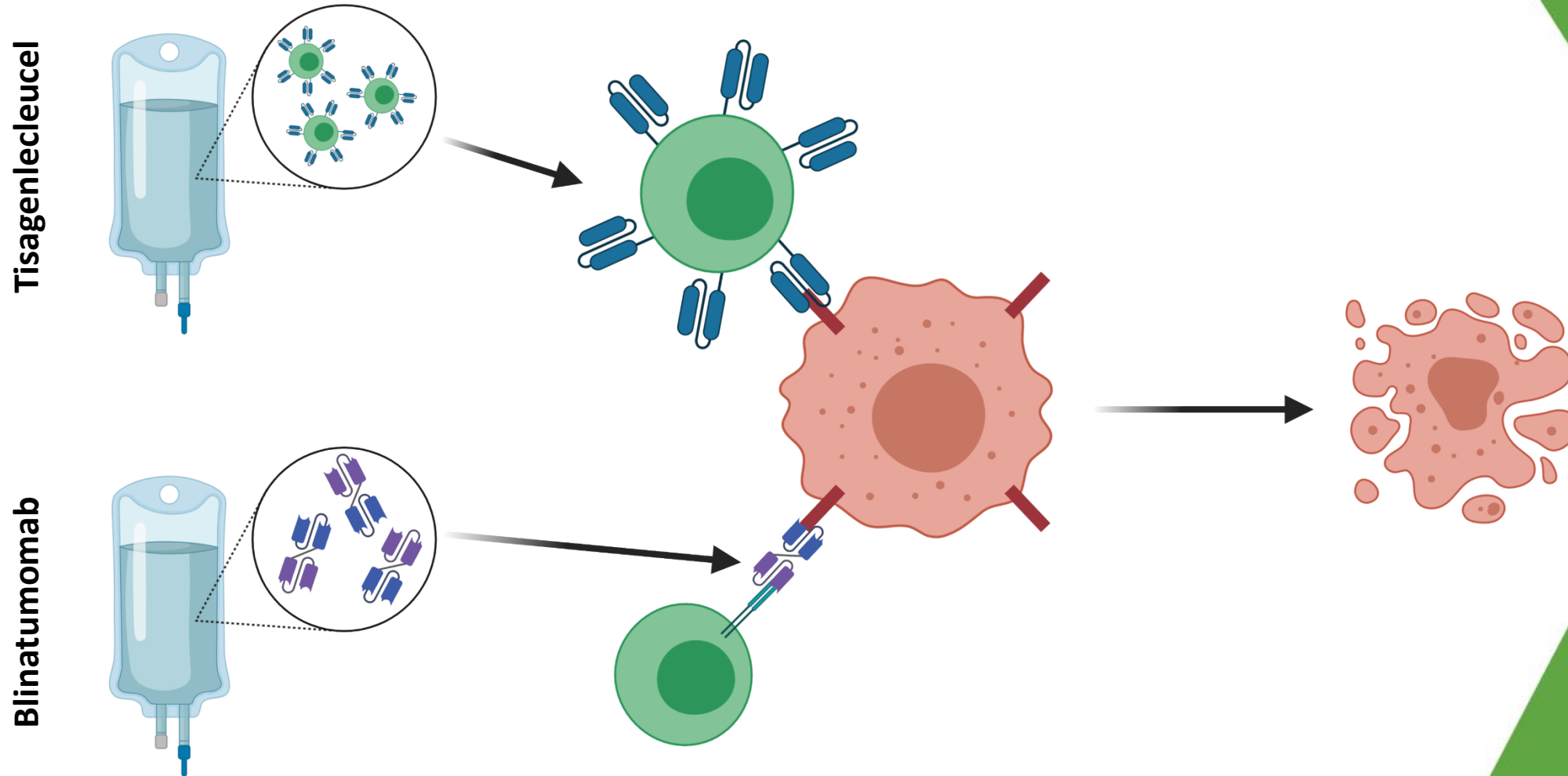


Blood 127:2391, 2016

# Outline

- Diagnostic testing in AL
- Toxicities associated with immunotherapy for acute leukemia
- Sequencing therapies in acute leukemia

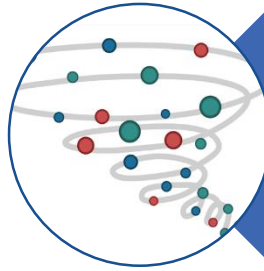
# T cell engagers vs. CAR T therapy



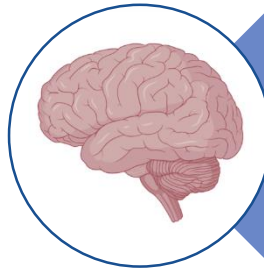
# T cell engagers vs. CAR T therapy

	CAR T cells	T cell engagers
Structure	Synthetic gene construct encoding an scFv against tumor antigen linked to activation/costimulatory motifs	Recombinant protein with two specificities: one for tumor antigen and one for T cell antigen (usually CD3)
Effector cell types	Engineered CD8+ and CD4+ T cells	Endogenous CD8+ and CD4+ T cells
Immune synapse	Atypical	Typical
Serial killing	Yes	Yes
Killing mechanisms	Perforin and granzyme B, Fas-Fas-L, or TNF/TNF-R	Perforin and granzyme B
Trafficking	Active	Passive
Clinical applications	Pre-treatment lymphodepletion followed by a single infusion	No lymphodepletion; repeat administration and continuous infusions
Specificity	Manufactured for each patient	“Off-the-shelf”
Availability	Limited to REMS program facilities	Most cancer centers

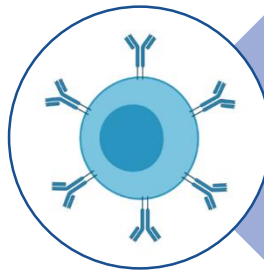
# Common toxicities with tisagenlecleucel and blinatumomab



Cytokine release  
syndrome

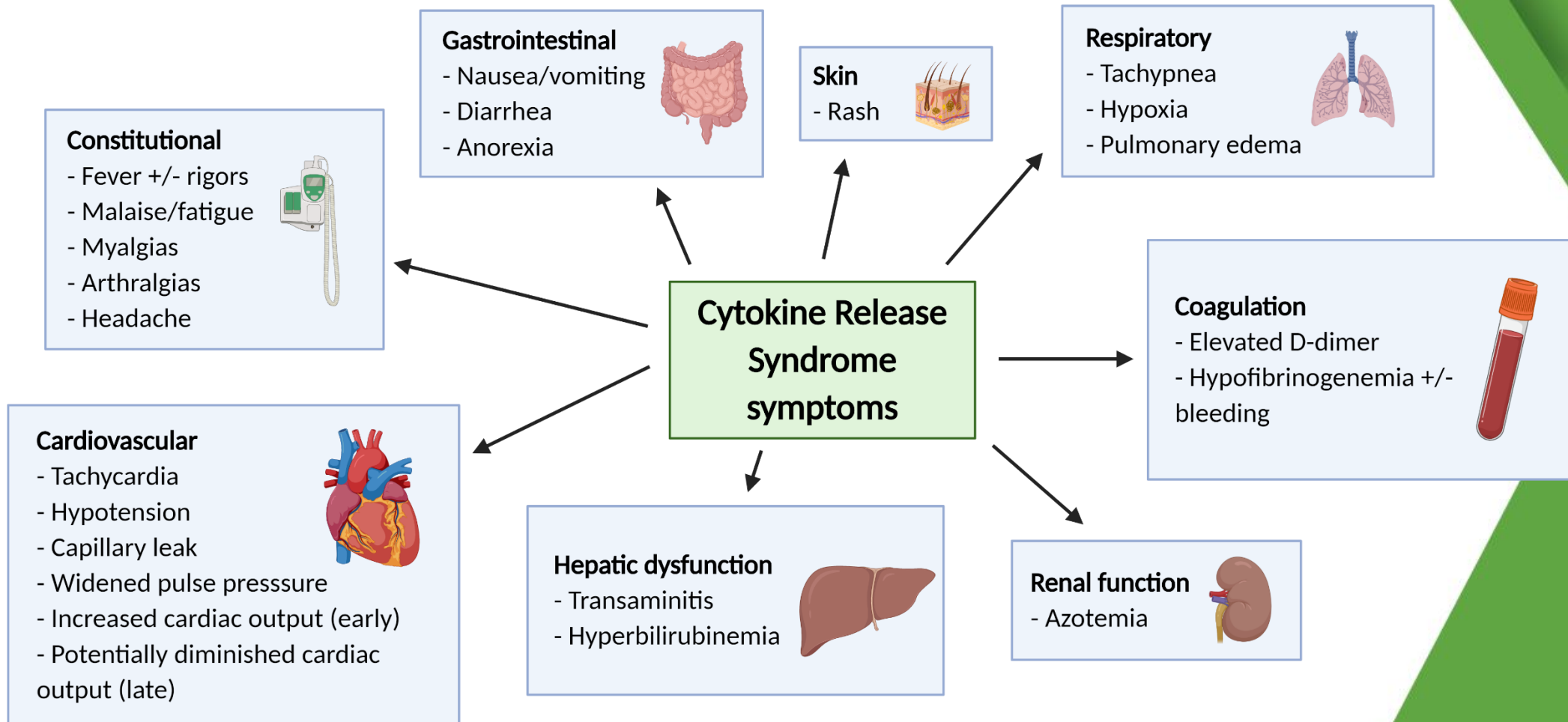


Neurotoxicity



B cell aplasia

# Cytokine release syndrome



# ASTCT CRS grading

CRS parameter	Grade 1	Grade 2	Grade 3	Grade 4
<b>Fever</b>	$\geq 38^{\circ}\text{C}$	$\geq 38^{\circ}\text{C}$	$\geq 38^{\circ}\text{C}$	$\geq 38^{\circ}\text{C}$
with				
<b>Hypotension</b>	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
and/or				
<b>Hypoxia</b>	None	Requiring low-flow nasal cannula or blow-by	Requiring high-flow nasal cannula, face mask, non-rebreather mask or venturi mask	Requiring positive pressure (e.g. CPAP, BiPAP, intubation and mechanical ventilation)

# Monitoring for CRS

- Events requiring physician notification include:
  - Deviations from baseline systolic blood pressure
  - Heart rate >120 or <60 bpm
  - Arrhythmia
  - Respiratory rate >25 or <12 breaths/minute
  - Arterial oxygen saturation <92% on room air
  - Upward trend in blood creatinine or liver function tests
  - Tremors or jerky movements in extremities
  - Altered mental status
  - Temperature  $\geq 38^{\circ}\text{C}$

# Management of CRS with CAR T

Grade 1	Grade 2	Grade 3	Grade 4	Tocilizumab-unresponsive	Tocilizumab + steroids-unresponsive
Close monitoring and supportive care	Consider tocilizumab	Tocilizumab	Tocilizumab + steroids	If CRS does not respond to 1 dose of tocilizumab, combine steroids + tocilizumab	Options include: Anakinra, siltuximab, HD methylprednisone

- For **elderly patients or those with significant co-morbidities**, tocilizumab should be considered earlier in the treatment course.
- If CRS does not improve after tocilizumab + steroids, **infections** should be considered and managed appropriately.
- If steroids are used, a **rapid taper** should be employed once symptoms begin to improve.

# Management of CRS with blinatumomab

CRS grade	Patients weighing 45 kg or more	Patients weighing less than 45 kg
3	<ul style="list-style-type: none"><li>• Interrupt blinatumomab.</li><li>• Administer dexamethasone 8 mg Q8h intravenously or orally for up to 3 days and taper thereafter over 4 days</li><li>• When CRS is resolved, restart blinatumomab at 9 mcg/d, and escalate to 28 mcg/d after 7 days if CRS does not recur.</li></ul>	<ul style="list-style-type: none"><li>• Interrupt blinatumomab.</li><li>• Administer dexamethasone 5 mg/m<sup>2</sup> Q8h intravenously or orally for up to 3 days and taper thereafter over 4 days</li><li>• When CRS is resolved, restart blinatumomab at 5 mcg/m<sup>2</sup>/d, and escalate to 15 mcg/m<sup>2</sup>/d after 7 days if CRS does not recur.</li></ul>
4	Discontinue blinatumomab permanently. Administer dexamethasone as instructed for Grade 3 CRS.	

# ASTCT ICANS grading - adults

*ICANS: Immune cell associated neurotoxicity syndrome*

Neurotoxicity domain	Grade 1	Grade 2	Grade 3	Grade 4
<b>ICE score</b>	7–9	3–6	0–2	0 (patient is unarousable)
<b>Depressed level of consciousness</b>	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse; stupor or coma
<b>Seizure</b>	N/A	N/A	Any clinical seizure focal or generalized that resolves rapidly or non-convulsive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (>5 min), repetitive clinical or electrical seizures without return to baseline in between
<b>Motor findings</b>	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
<b>Elevated ICP/cerebral edema</b>	N/A	N/A	Focal/local edema on neuroimaging	Diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing, cranial nerve VI palsy, papilledema, or Cushing's triad

# ASTCT ICANS grading - pediatric

Neurotoxicity domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score (age ≥12 years)	7–9	3–6	0–2	0 (patient is unarousable)
CAPD score (age <12 years)	1–8	1–8	≥9	Unable to perform CAPD
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Unarousable or requires vigorous or repetitive tactile stimuli to arouse
Seizure (any age)	N/A	N/A	Any clinical seizure focal or generalized that resolves rapidly or non-convulsive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (>5 min), repetitive clinical or electrical seizures without return to baseline in between
Motor weakness (any age)	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
Elevated ICP/cerebral edema (any age)	N/A	N/A	Focal/local edema on neuroimaging	Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing, cranial nerve VI palsy, papilledema, or Cushing's triad

# Immune effector cell-associated encephalopathy (ICE) score

- **Orientation:** Orientation to year, month, city, hospital: 4 points (1 point each)
- **Naming:** Name 3 objects (e.g., clock, pen, button): 3 points (1 point each)
- **Following commands:** (e.g., Show me 2 fingers or close your eyes and stick out your tongue): 1 point
- **Writing:** Ability to write a standard sentence (e.g., Our national bird is the bald eagle): 1 point
- **Attention:** Count backwards from 100 by 10: 1 point
- **Total scale:** 0-10

# Monitoring for ICANS

- Altered mental status defines the onset of ICANS
- Work-up should include:
  - CRP
  - CBC
  - CMP
  - Fibrinogen
  - Prothrombin time test
  - PT/INR
- Head CT, EEG, and brain MRI may be considered

# Management of ICANS with CAR T

- **4-1BB** CAR T agents: consider steroids at grade 2 ICANS; administer steroids for grades 3-4 ICANS
- Management of neurotoxicity **may take precedence** over low-grade CRS, due to possibility of tocilizumab worsening ICANS
  - For example: in the case of a patient with concomitant grade 1 CRS (fever) and grade 2 ICANS, steroids should be given. This does not apply to higher-grade CRS.
- If **steroids** are used, administer at least two doses and employ a fast taper
- **Levetiracetam** is recommended for management of seizures

# Management of ICANS with blinatumomab

ICANS grade	Patients weighing more than 45 kg	Patients weighing less than 45 kg
3	Withhold blinatumomab until no more than Grade 1 and for at least 3 days, then restart blinatumomab at 9 mcg/d. Escalate to 28 mcg/d after 7 days if symptoms do not recur. If ICANS occurred at 9 mcg/d or takes more than 7 days to resolve, discontinue permanently.	Withhold blinatumomab until no more than Grade 1 and for at least 3 days, then restart blinatumomab at 5 mcg/m <sup>2</sup> /d. Escalate to 15 mcg/m <sup>2</sup> /d after 7 days if symptoms do not recur. If ICANS occurred at 5 mcg/m <sup>2</sup> /d or takes more than 7 days to resolve, discontinue permanently.
4	Discontinue blinatumomab permanently.	

# B cell aplasia

- Due to current clinical agents targeting CD19, which is expressed by both normal and neoplastic B cells
- Short- or long-term
- May result in hypogammaglobulinemia
- Increased risk of infection – prophylaxis required
- Managed through administration of intravenous immunoglobulin
- Might indicate persistence of CAR T cells

# Outline

- Diagnostic testing in AL
- Toxicities associated with immunotherapy for acute leukemia
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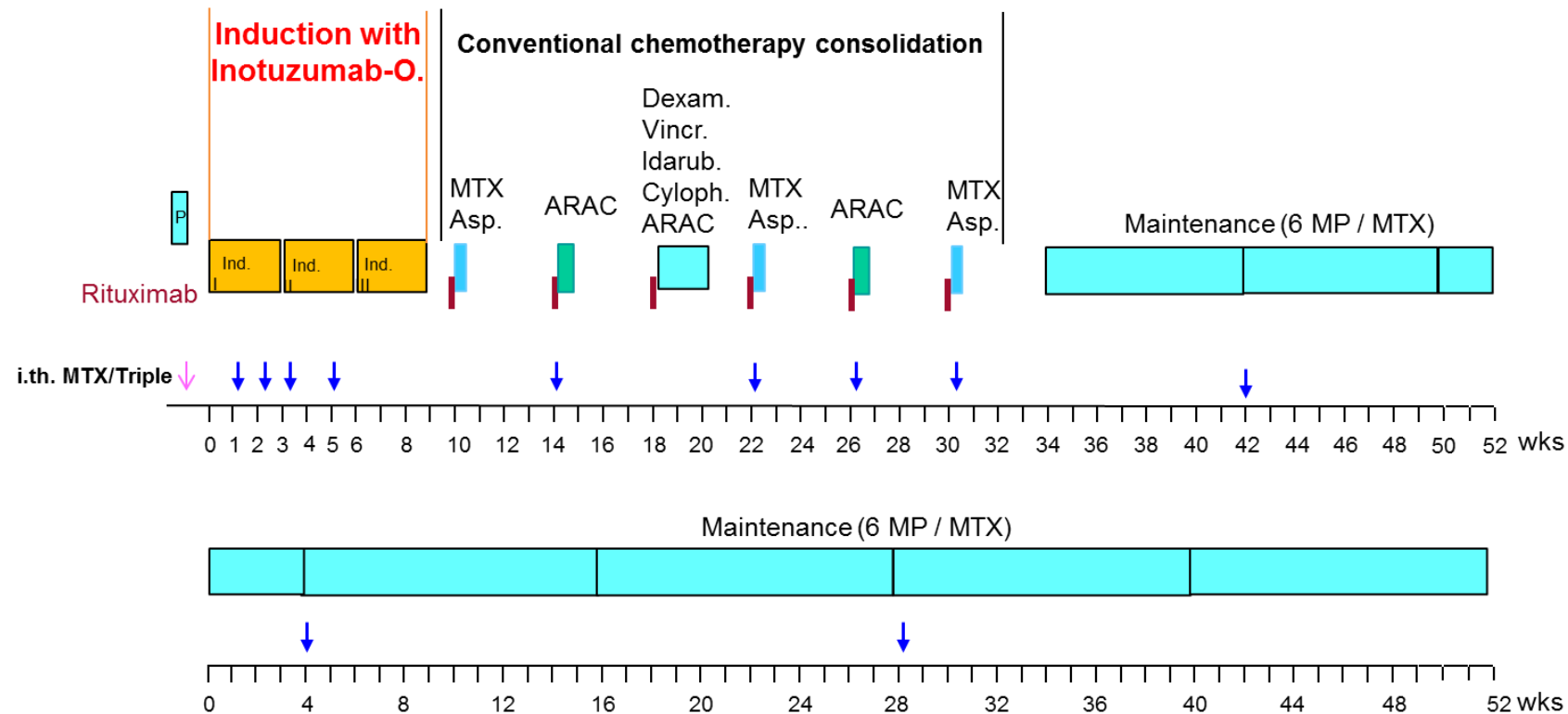
First Results of an Open Label Phase II Study to Evaluate  
the Efficacy and Safety of Inotuzumab Ozogamicin for  
Induction Therapy followed by a Conventional  
Chemotherapy Based Consolidation and Maintenance  
Therapy in Patients Aged 56 Years and Older with Acute  
Lymphoblastic Leukemia (INITIAL-1 trial)

**Matthias Stelljes**

University of Muenster / Germany  
for the GMALL study group

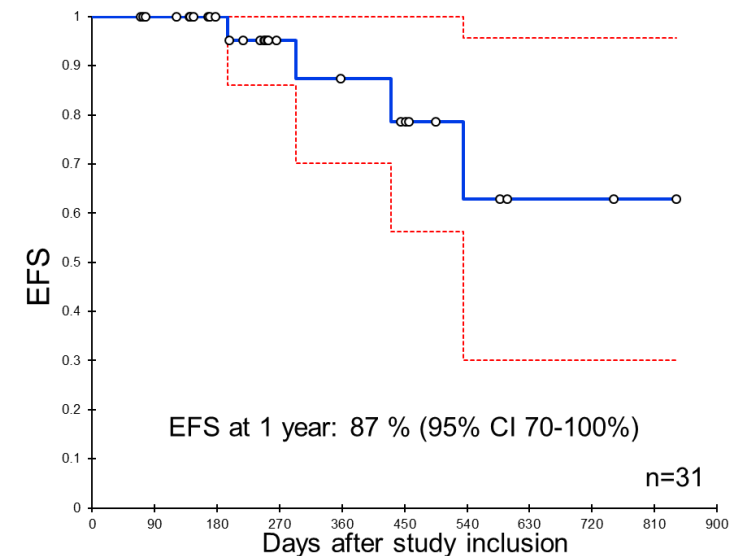
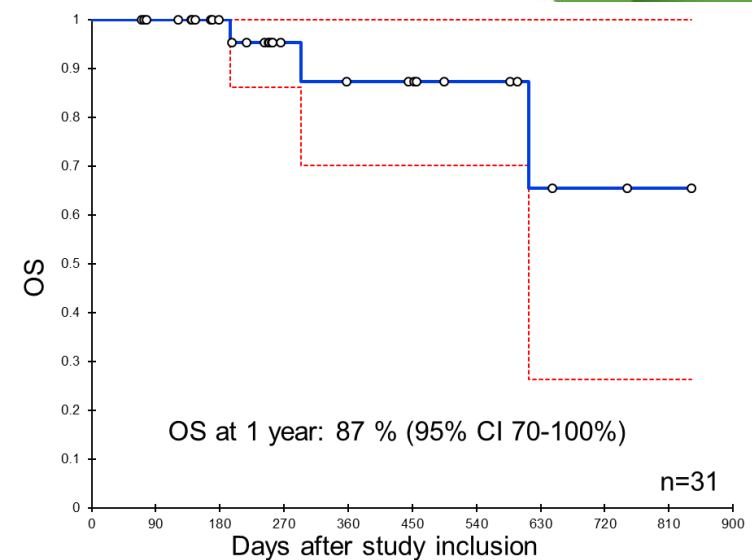
# INITIAL-1 Trial: Treatment Schedule

An open label phase II study to evaluate the efficacy and safety of Inotuzumab Ozogamicin for Induction Therapy followed by a conventional chemotherapy-based consolidation and maintenance therapy In patients aged 55 years and older with Acute Lymphoblastic leukemia (ALL)



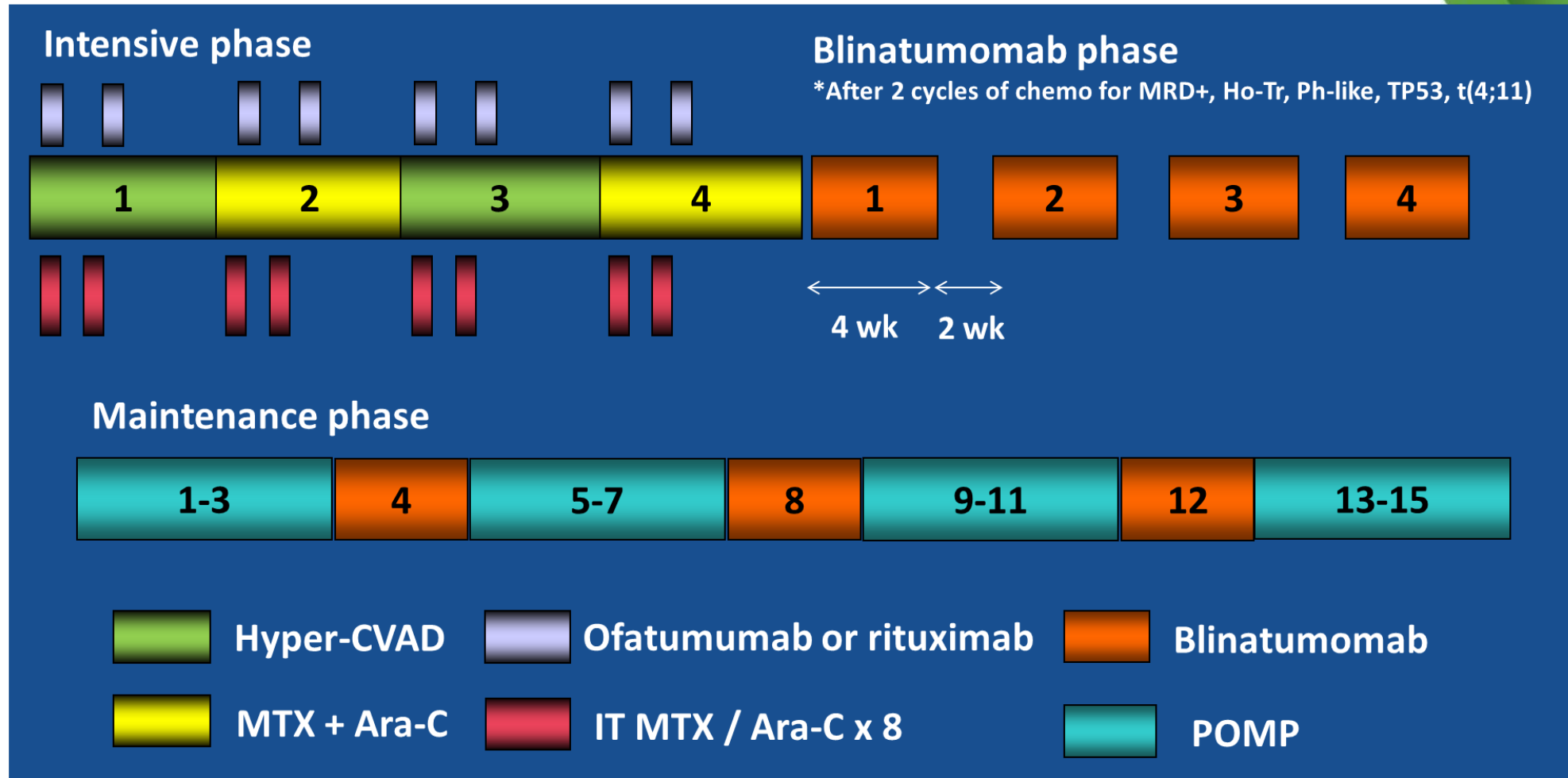
# INITIAL-1 Trial: Results

Evaluable for hematological remission, n=31	
CR / CRi after at least 1 induction	31 pts (100%)
Patients receiving 3 cycles inotuzumab	29 pts (94%)
Early deaths within the first 3 months	0
Evaluable for MRD (by PCR), n=27	
MRD negative remission as best response	21 pts (78%)
Hematological / molecular relapse	2 / 1 pts
Allogeneic HSCT in remission / after relapse	3 / 1 pts



Median FU: 249 (70-842) days

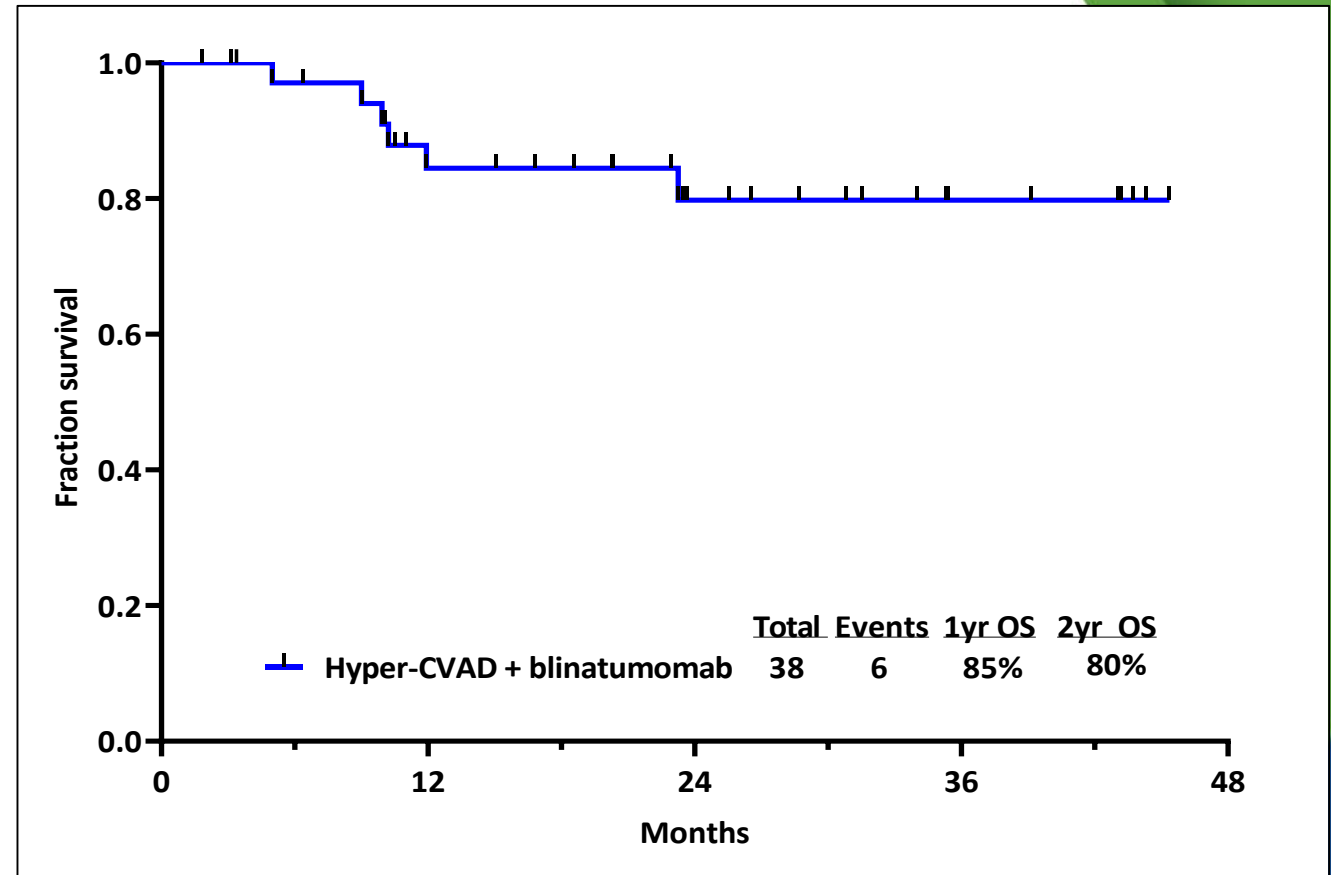
# Hyper-CVAD + blinatumomab in newly-diagnosed B-ALL



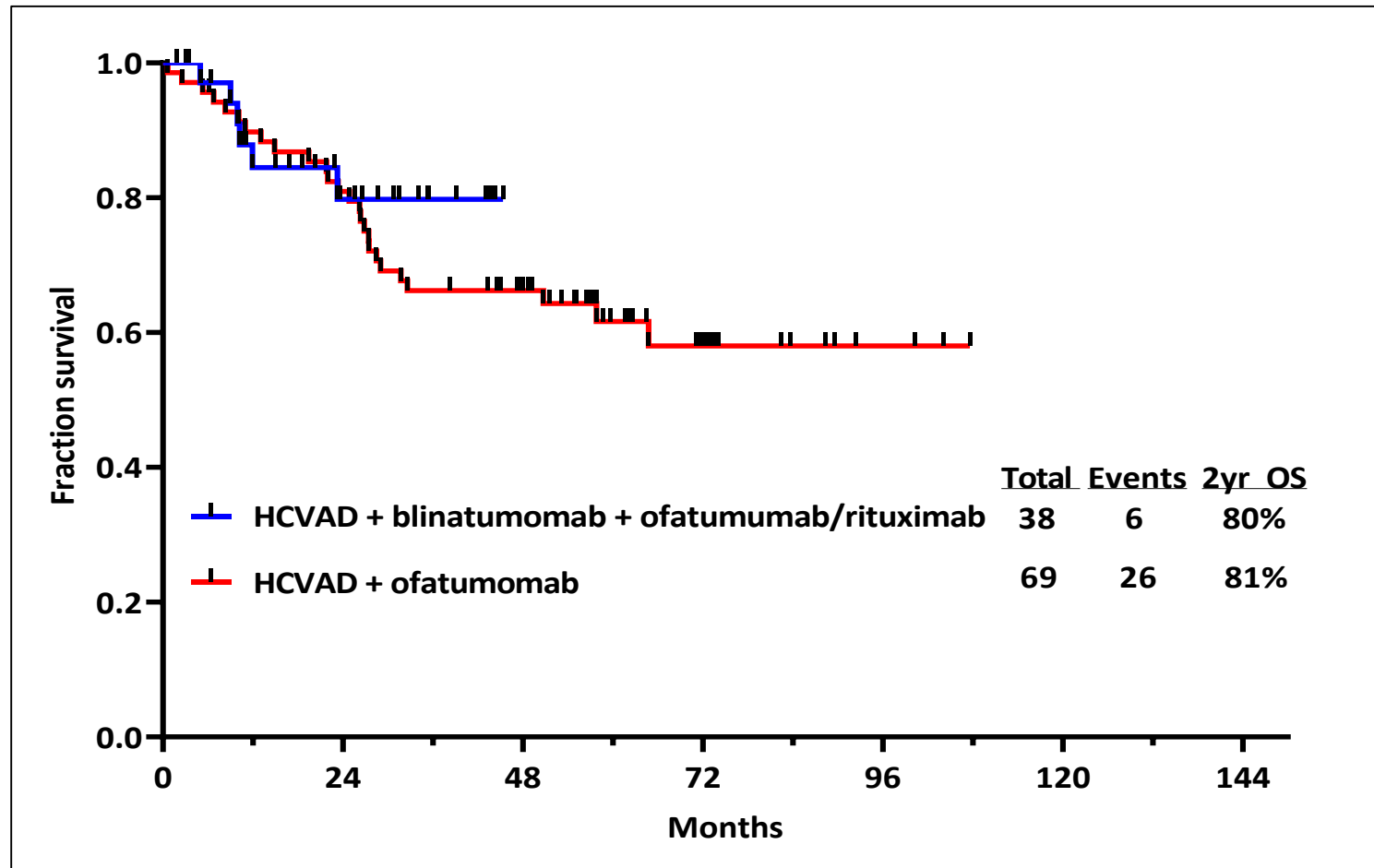
# Hyper-CVAD + blinatumomab in newly-diagnosed B-ALL

Response*	n/N (%)
CR after induction	26/32 (81)
CR at any time	32/32 (100)
MRD negativity after induction	24/34 (71)
MRD negativity at anytime	33/34 (97)
30-day mortality	0

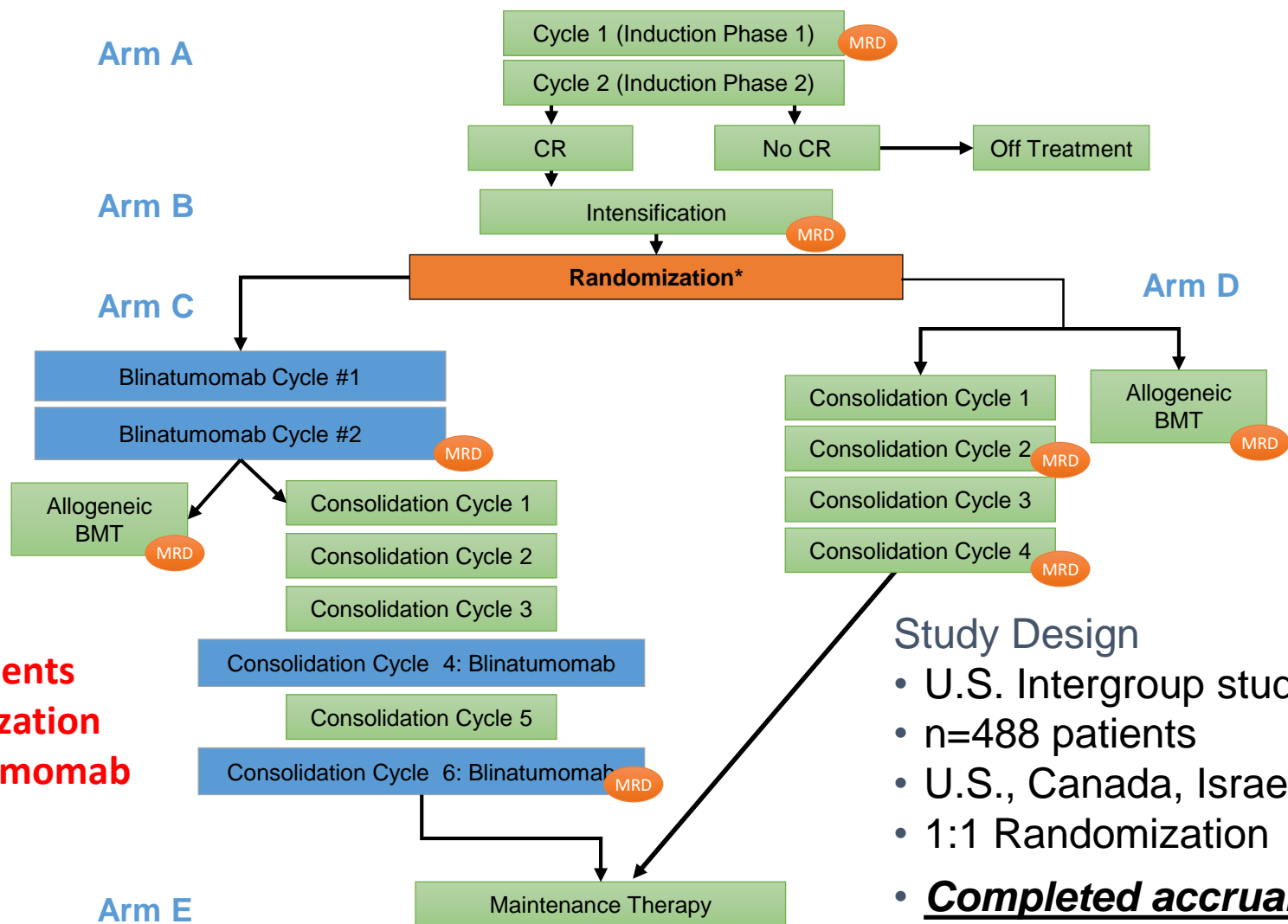
\* 6 pts in CR at start; 4 pts MRD negative at start



# Hyper-CVAD + blinatumomab in B-ALL: Historical comparison



# E1910: Randomized Ph III Adult Frontline ALL



**\*MRD positive patients  
at time of randomization  
assigned to blinatumomab**

## Study Design

- U.S. Intergroup study
- n=488 patients
- U.S., Canada, Israel
- 1:1 Randomization
- **Completed accrual  
October, 2019**

# Approved immunotherapies for ALL

Drug	Type	Mechanism	Approval	Indications
<b>Blinatumomab</b>	Bispecific T cell engager (BiTE)	CD3 x CD19 bispecific	March 2018	Adult and pediatric patients with B-cell precursor ALL in first or second complete remission with MRD $\geq 0.1\%$
			July 2017	Relapsed or refractory B-cell precursor ALL in adults and children
			December 2014	Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL
<b>Inotuzumab ozogamicin</b>	Anti-CD22 antibody–drug conjugate	Antibody-drug conjugate, CD22 antibody + calicheamicin	August 2017	Adults with relapsed or refractory B-cell precursor ALL
<b>Tisagenlecleucel</b>	CAR T cell therapy	CD19 CAR T cells	August 2017	Patients up to 25 years of age with B-cell precursor ALL that is refractory or in second or later relapse

# New CAR-T cell therapy just approved

- Brexucabtagene autoleucel (BA) approved on October 1 for adult patients with relapsed/refractory B cell precursor ALL
- Similar structure to axicabtagene ciloleucel, the approved CAR-T product for NHL (somewhat different manufacturing)
- Retroviral vector vs lentiviral vector for tisagenlecleucel (T)
- Signaling domain CD28z for BA, 41BBz for (T)
- In Zuma-3 phase 2 trial CR rate by 3 months 28/54 (52%); 97% MRD negative
- $\geq$ grade 3 CRS and neurotoxicity 24 and 25%, respectively

# Role of HCT and immunotherapy

- There is some concern of increased GVHD with combination of checkpoint inhibitors and HCT
- ELIANA and TOWER trials treated patients with prior allo-HCT, apparently safely
- In one study of CD19 CAR T treatment:
  - 17 patients with CR after CAR T proceeded to transplantation
  - 5 were alive with a complete remission
  - 6 had a relapse
  - 6 died from transplant-related toxic effects

# Role of immunotherapy post-CAR T

- Patients may relapse after CAR T treatment due to lack or loss of target antigen, or other reasons.
- Potential treatment options include CAR T therapy targeting different antigens, blinatumomab, allo-HCT or salvage chemotherapy.
- Clinical trial enrollment should be strongly considered.

Thank you!

Learn more and register at:  
<https://www.sitcancer.org/CPG-webinars>

## **Case Studies in Immunotherapy for the Treatment of Acute Leukemia**

November 15, 2021, 11:30 a.m. – 12:30 p.m. ET

## **Immunotherapy for the Treatment of Breast Cancer**

October 29, 2021, 1 – 2 p.m. ET

## **Case Studies in Immunotherapy for the Treatment of Urothelial Cancer**

November 5, 2021, 5:30 – 6:30 p.m. ET

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# Thank you for attending the webinar!

Questions or comments: [connectED@sitcancer.org](mailto:connectED@sitcancer.org)