

Novel treatment options in acute lymphocytic leukemia

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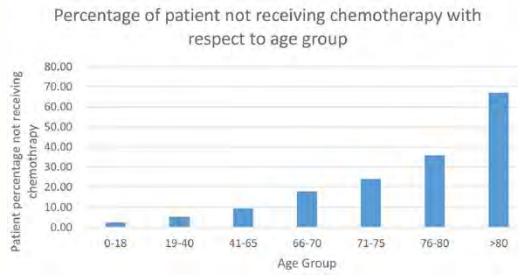
Disclosure

- Safety Monitoring Committee: Protagonist
- Consultant: Abbvie, Servier, Incyte, Genentech
- Research Grant (institutional): Incyte, NMDP, Jazz, Pfizer, Abbvie, Oncoceutics (drug support)
- **Off-label use:** Upfront use of Inotuzumab and Blinatumomab



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Older adults: chemo use in practice vs. survival in trials

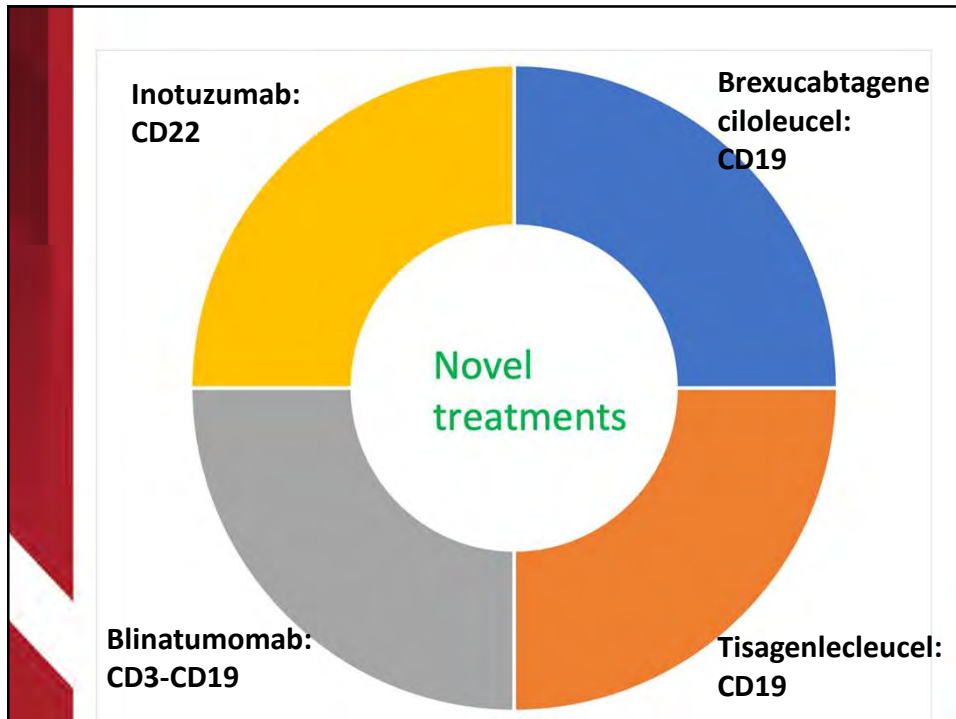


**Survival improved:
3 months -- > 3 years**

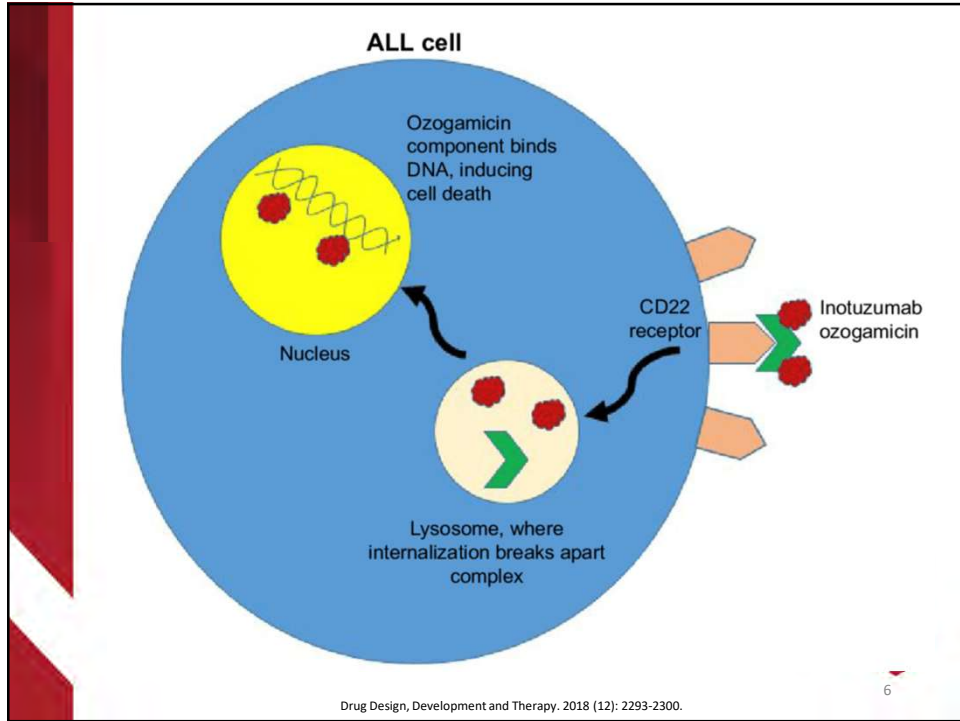


Clin Lymphoma Myeloma Leuk . 2022 Jan 10

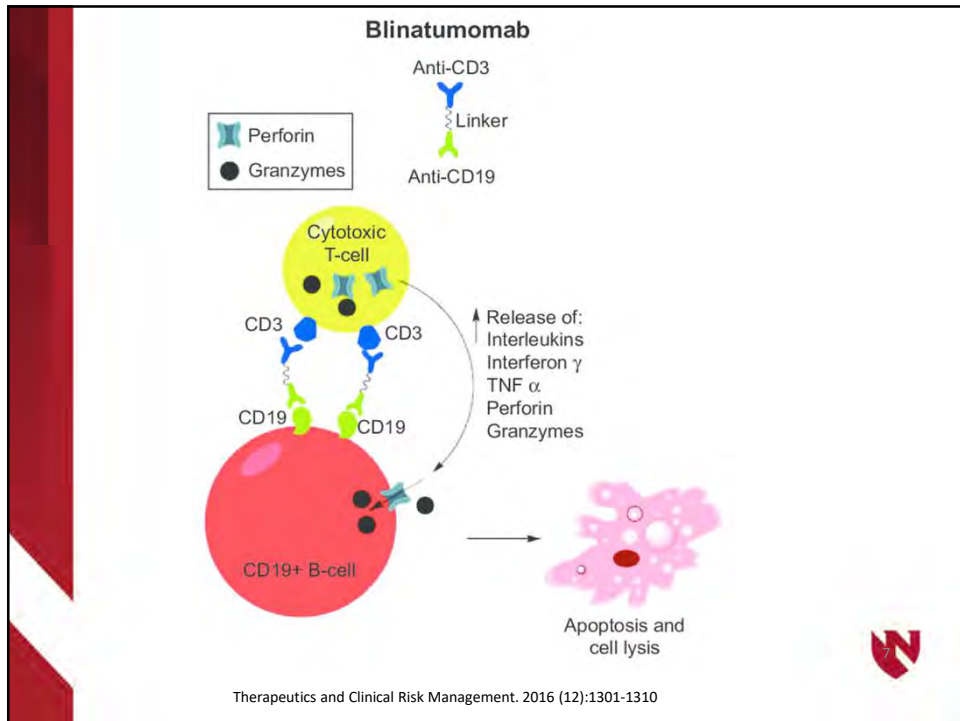
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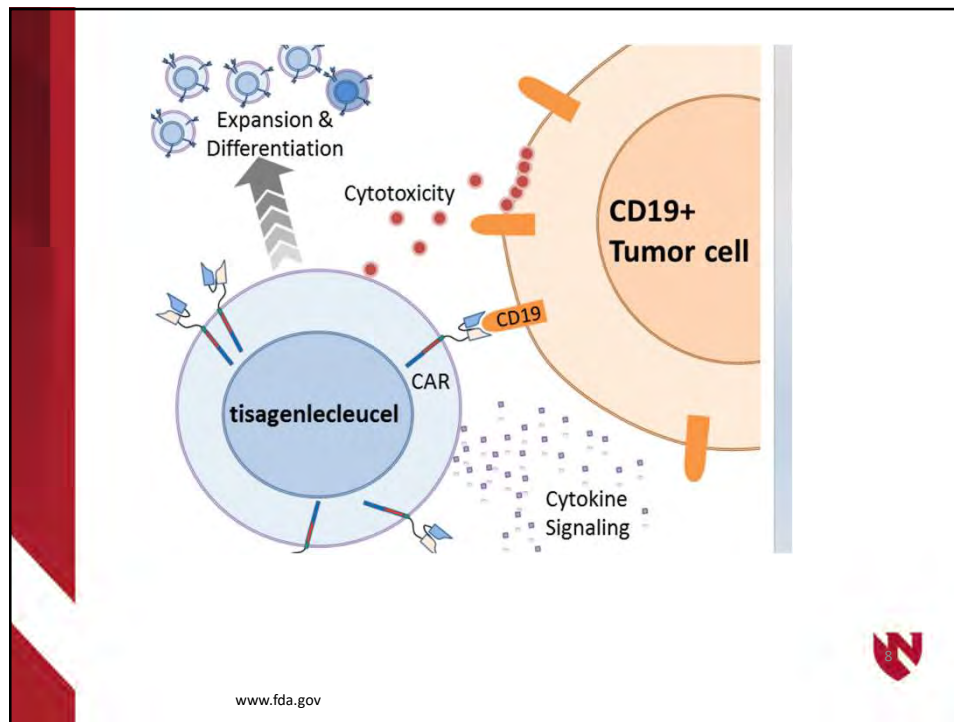
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FDA Approved indications: RR B-cell ALL

Monoclonal Ab

- Inotuzumab: Adults
- Blinatumomab: Adults or **children**

CAR T

- Tisagenlecleucel: **up to 25 years**; refractory or in second or later relapse.
- Brexucabtagene autoleucel: Adults

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FDA Approved indication: MRD positive

Blinatumomab:

- Adults or children
- First or second complete remission MRD greater than or equal to 0.1%



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Management of R/R ALL



- High tumor burden



- Low tumor burden, MRD+ disease, liver disease



- Up to 25 years, \geq second relapses, refractory ALL



- Adults, RR ALL



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Unique Toxicities

Ino

- **VOD risk**

Blin, CAR T cell


- **Neurotoxicity, CRS**



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Principles: management of R/R ALL

1. Outcomes are poor
2. Ino: high responses; blin: more durable
3. Allotransplant recommended



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Principles: management of R/R ALL

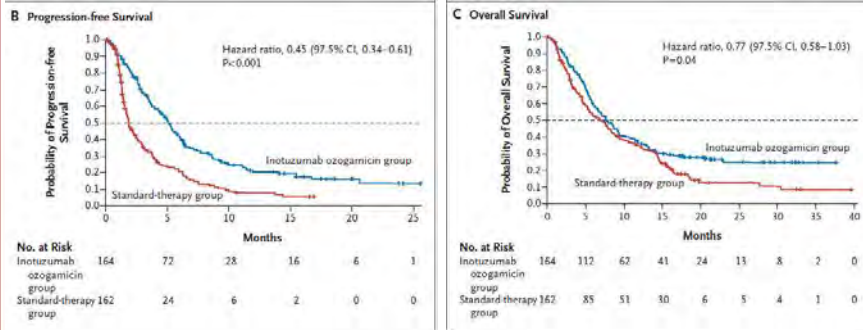
CAR T cell

- high responses even after failure of allo
- issues with manufacturing



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Ino vs SOC ALL



CR 80.7% vs. 29.4%
MRD among CR patients 78.4% vs. 28.1%
OS, Median 7.7 vs. 6.7 m



N Engl J Med 2016;375:740-753

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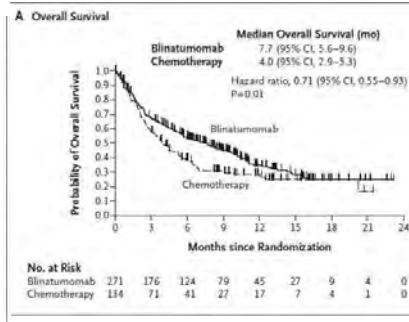
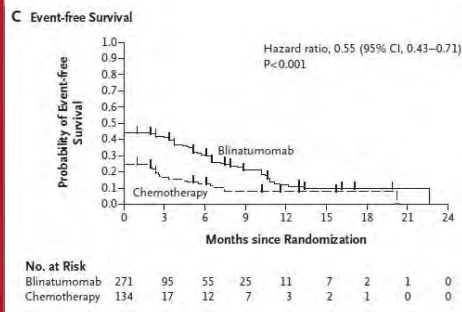
Ino: Risk of VOD

1. Especially post-HCT
2. Mitigation strategies
 - use earlier in therapy
 - limit to 2 cycles (pre-transplant)
 - ursodiol
 - limit azole antifungal
 - avoid dual alkylator during conditioning (e.g. busulfan, cyclophosphamide, melphalan)



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Blin vs SOC ALL



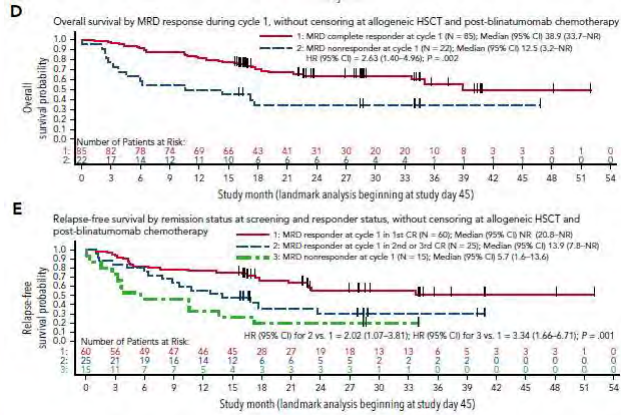
CR/CRi/CR with partial count recovery 44% vs. 25%
MRD among CR/CRi/CR with partial count recovery patients 76% vs. 48%
OS, Median 7.7 vs. 4.0 m



N Engl J Med 2017;376:836-47.

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Blin MRD+ ALL



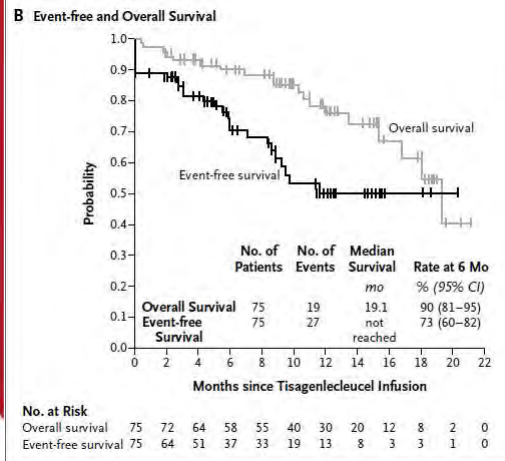
RFS and OS at 18 months 53 and 67%

Blood. 2018;131(14):1522-1531



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Tisagenlecleucel in Children and Young Adults

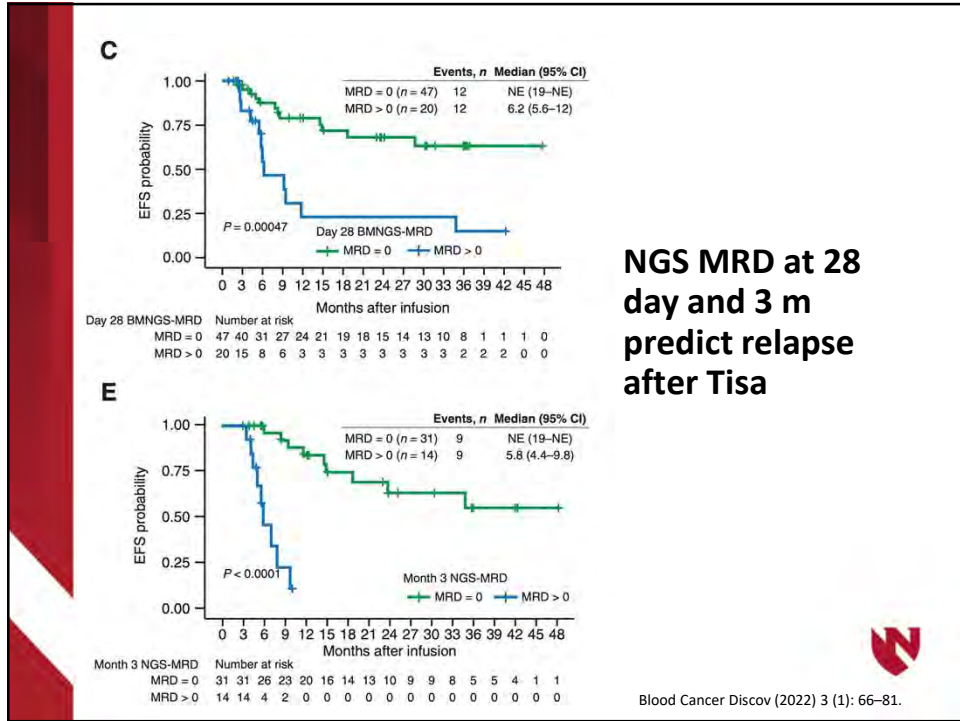


- >10% could not received the product
- ORR 80%, all flow MRD negative
- Effective: Failed Allo

N Engl J Med 2018;378:439-48.



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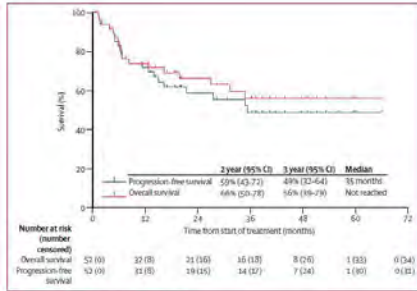


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Novel drugs: upfront incorporation
-ongoing trials
-not approved yet

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Inotuzumab and mini-hyper-CVD



Older Adults

3-year OS 56%
8% VOD

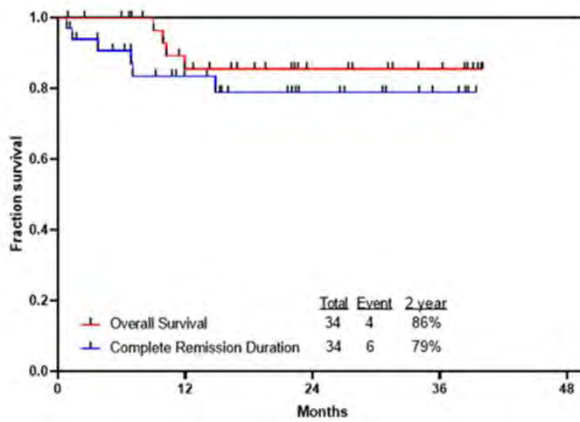
Figure 2: Progression free and overall survival



Lancet Oncol 2018; 19: 240-48

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Hyper-CVAD and Sequential Blinatumomab



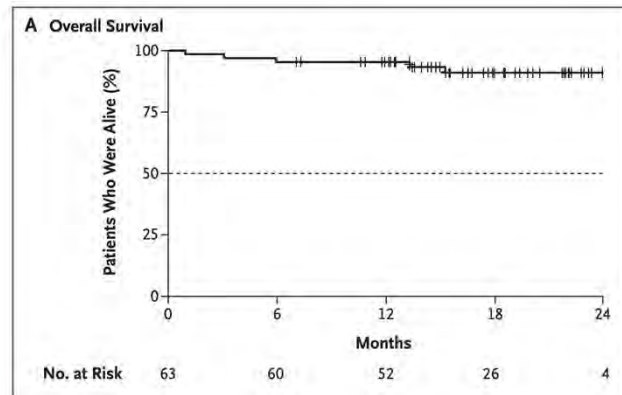
Younger adults



Blood (2020) 136 (Supplement 1): 9-11.

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Dasatinib blinatumomab



Adults

N Engl J Med 2020;383:1613-23



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Conclusions

- **CD19 and CD22-targeted effective treatment options**
- **Inotuzumab: High tumor burden, VOD risk**
- **Blinatumomab: Low tumor burden, MRD+**
- **CAR T cell: highly effective, CRS and neurotoxicities**
- **Allotransplant recommended for RR ALL**
- **Upfront use of novel drugs- exciting results!**



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