Practice Changing Data from 2023: Hematologic Malignancies

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5th Annual LEAD2023 Enriching Experiences for Women in Hematology & Oncology

University of Nebraska Medical Center

Bio Ascend™

Disclosures

- I specialize in lymphoid malignancies.

- Stock ownership: Poseida Therapeutics
- Advisory board: Novartis

Objectives

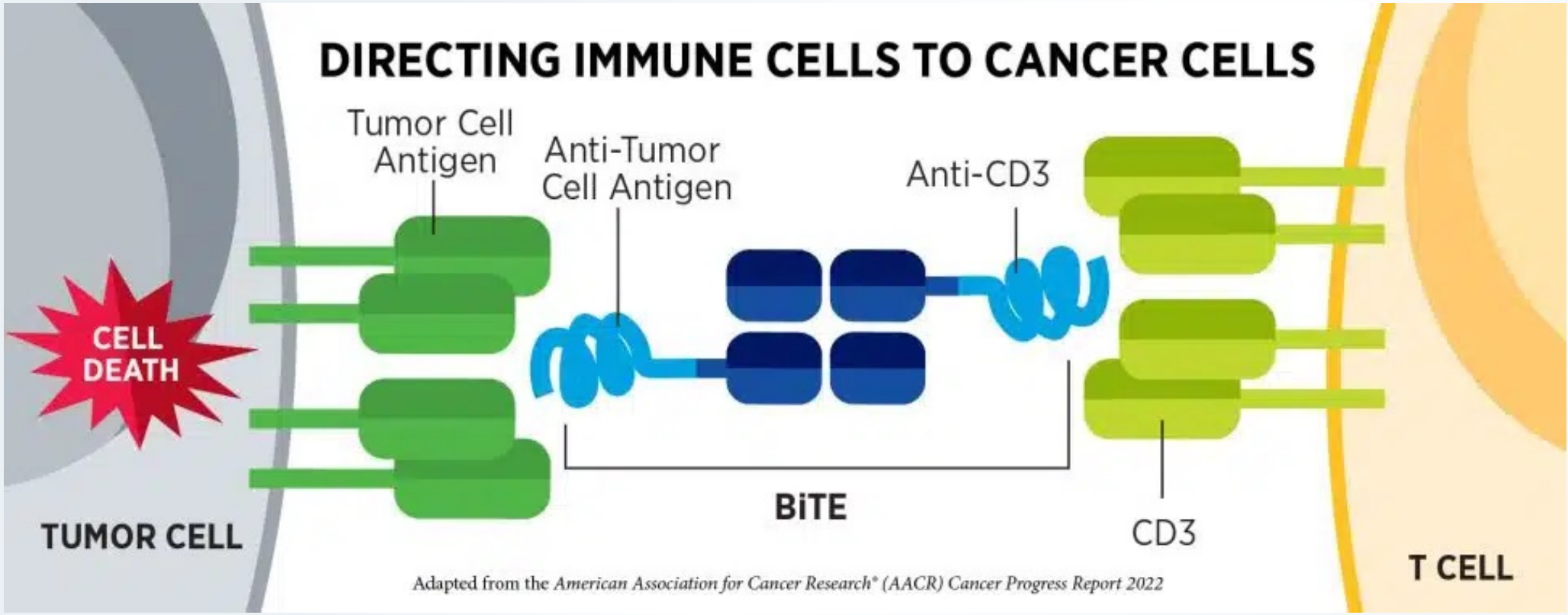
To review the FDA updates and pivotal trials from 2023 for:

1. Lymphoid Malignancies
2. Acute Leukemia
3. Myeloma

Lymphoid Malignancies

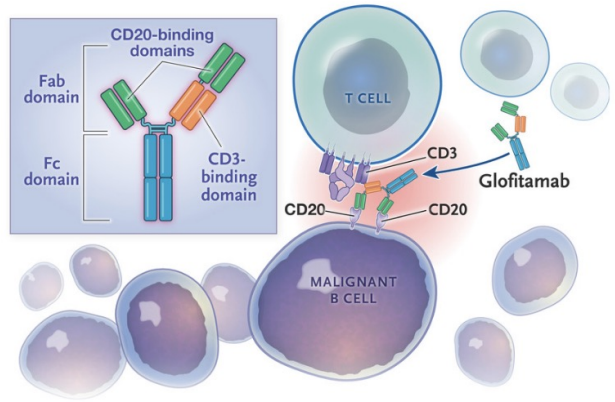
Lymphoma and Chronic Lymphocytic Leukemia

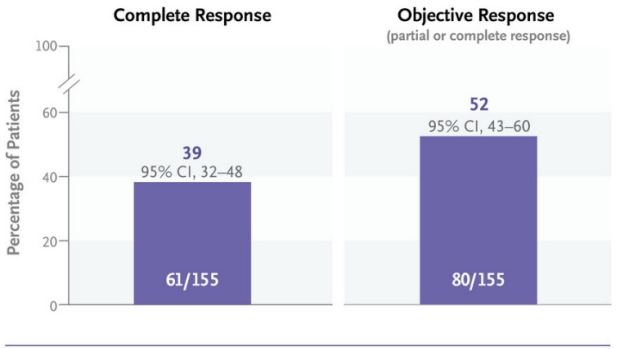
Bispecific T-cell Engagers

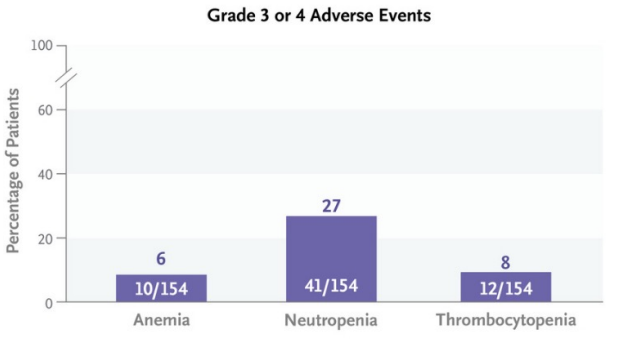


Phase 1/2 Glofitamab for R/R DLBCL (FDA Approved)

- **Population:** R/R DLBCL (after ≥ 2 prior lines), N=154
- **Intervention:** Glofitamab IV
- **Comparison:** None
- **Outcome:** ORR 52%, CR 39%, median time to response was 42 days



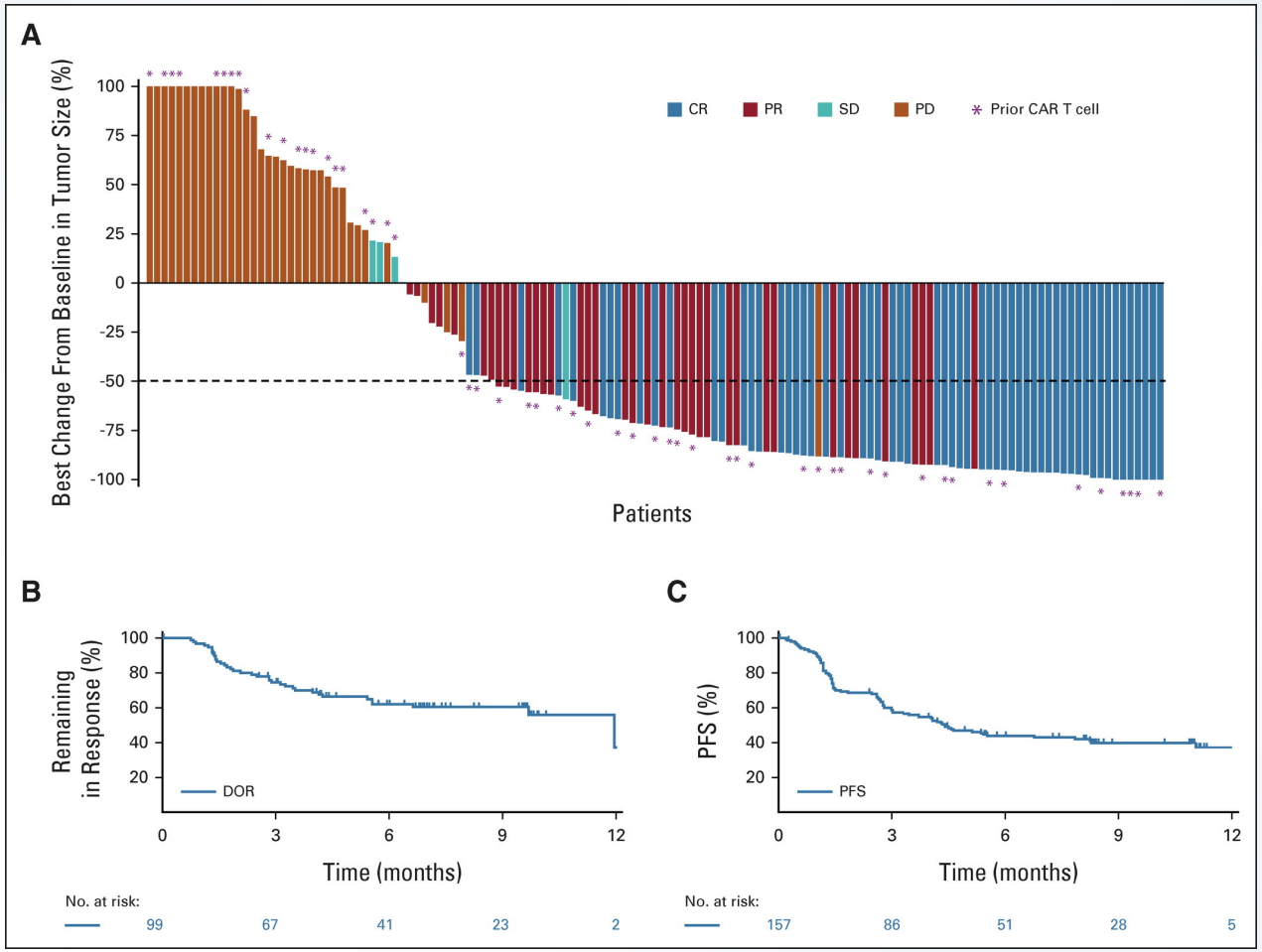




MJ Dickinson et al. N Engl J Med 2022;387:2220-2231

Phase 1/2 EPCORE NHL-1: Epcoritamab in R/R DLBCL (FDA Approved)

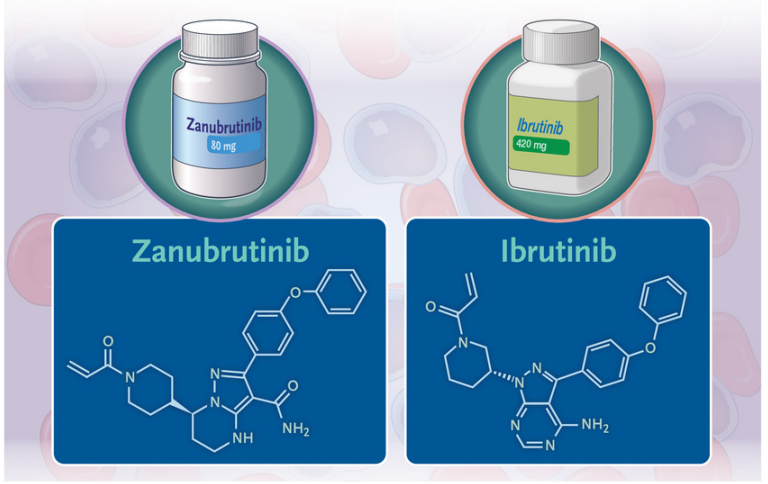
- **Population:** R/R DLBCL (after ≥ 2 prior lines), N=157
- **Intervention:** Epcoritamab SC
- **Comparison:** None
- **Outcome:** ORR 63%, CR 39%, median DOR 12 months, median time to response 1.4 months

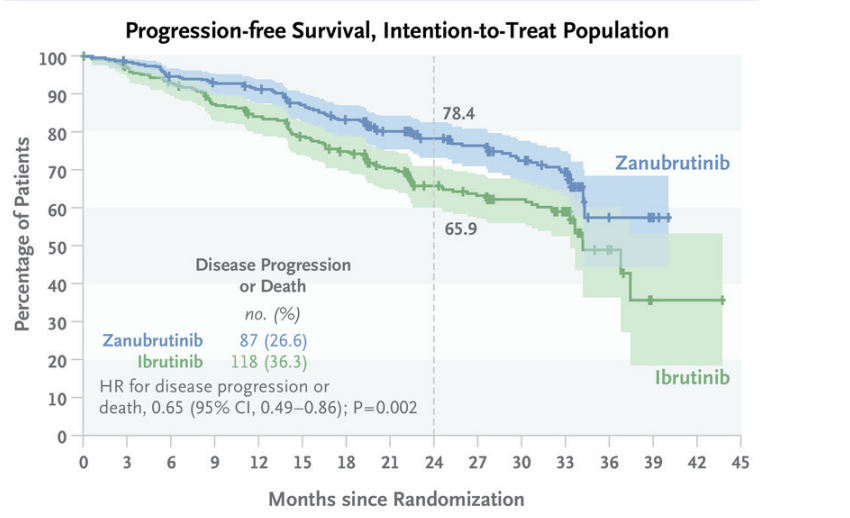


Thieblemont et al. JCO 2023 Apr 20;41(12):2238-2247

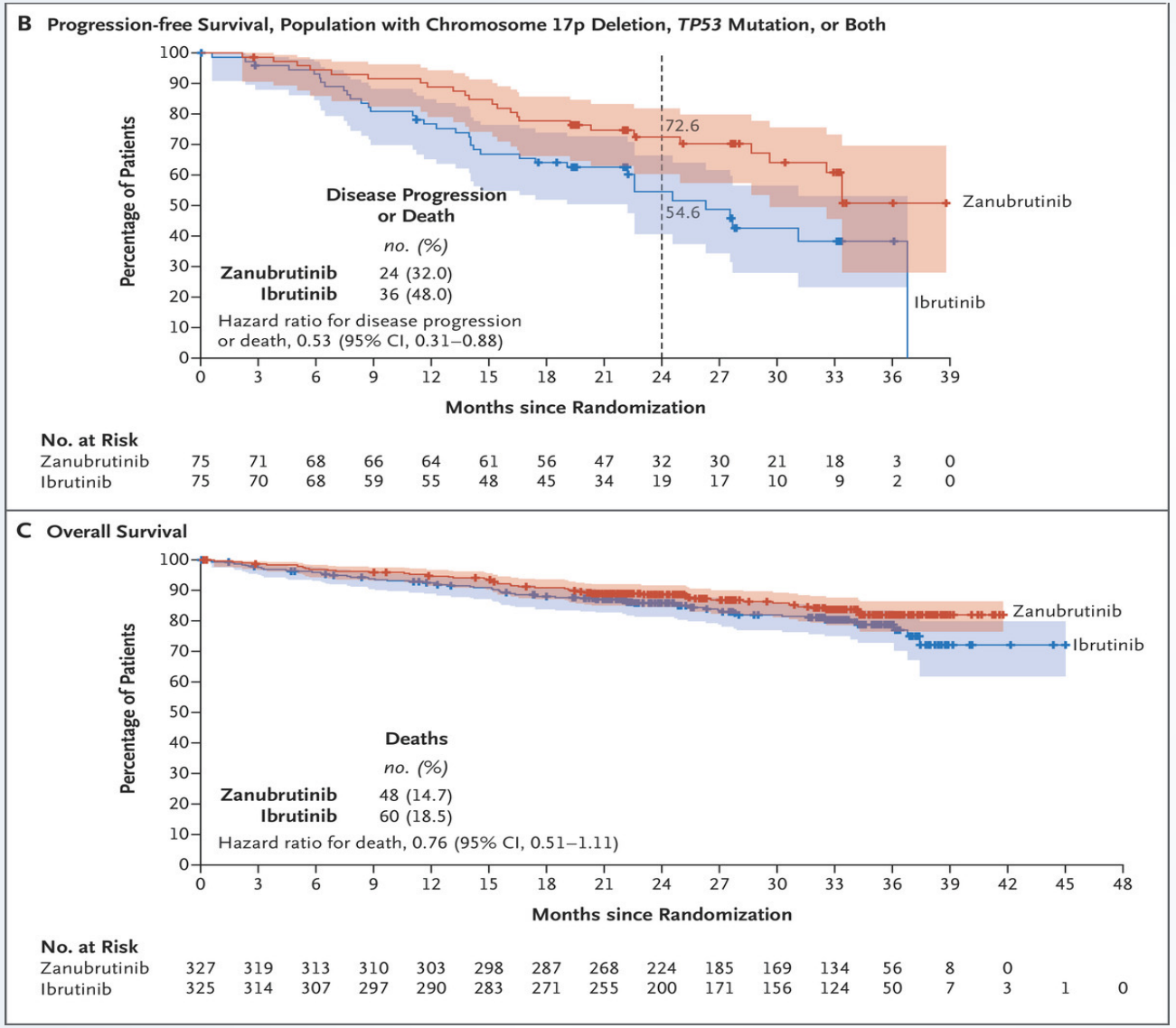
Phase 3 ALPINE: Zanubrutinib for R/R CLL/SLL (FDA Approved)

- **Population:** R/R CLL/SLL
- **Intervention:** Zanubrutinib
- **Comparison:** Ibrutinib (1:1)
- **Outcome:** ORR 83.5% in zanubrutinib vs 74.2% in ibrutinib arm





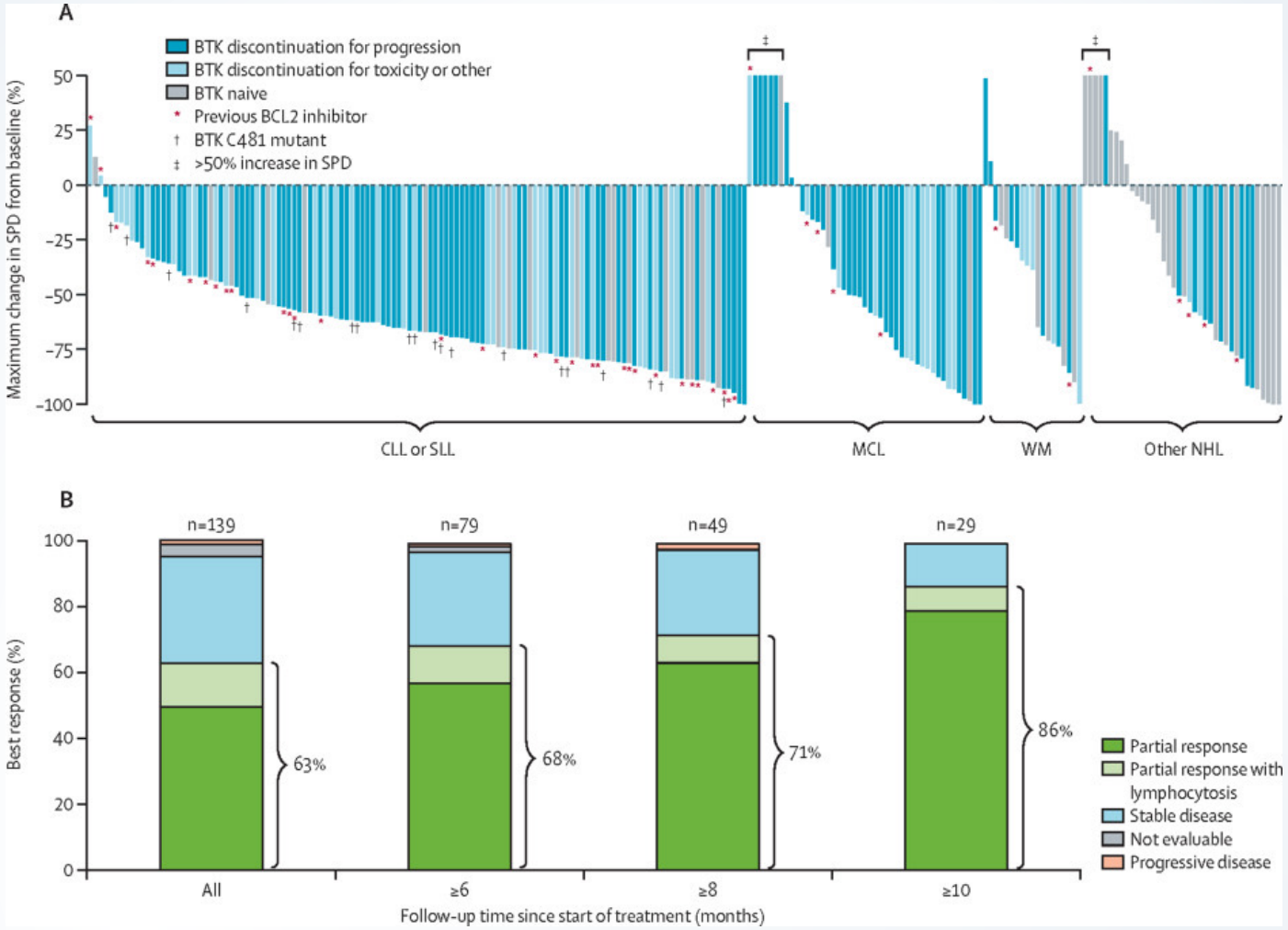
JR Brown et al. N Engl J Med 2023;388:319-332



JR Brown et al. N Engl J Med 2023;388:319-332

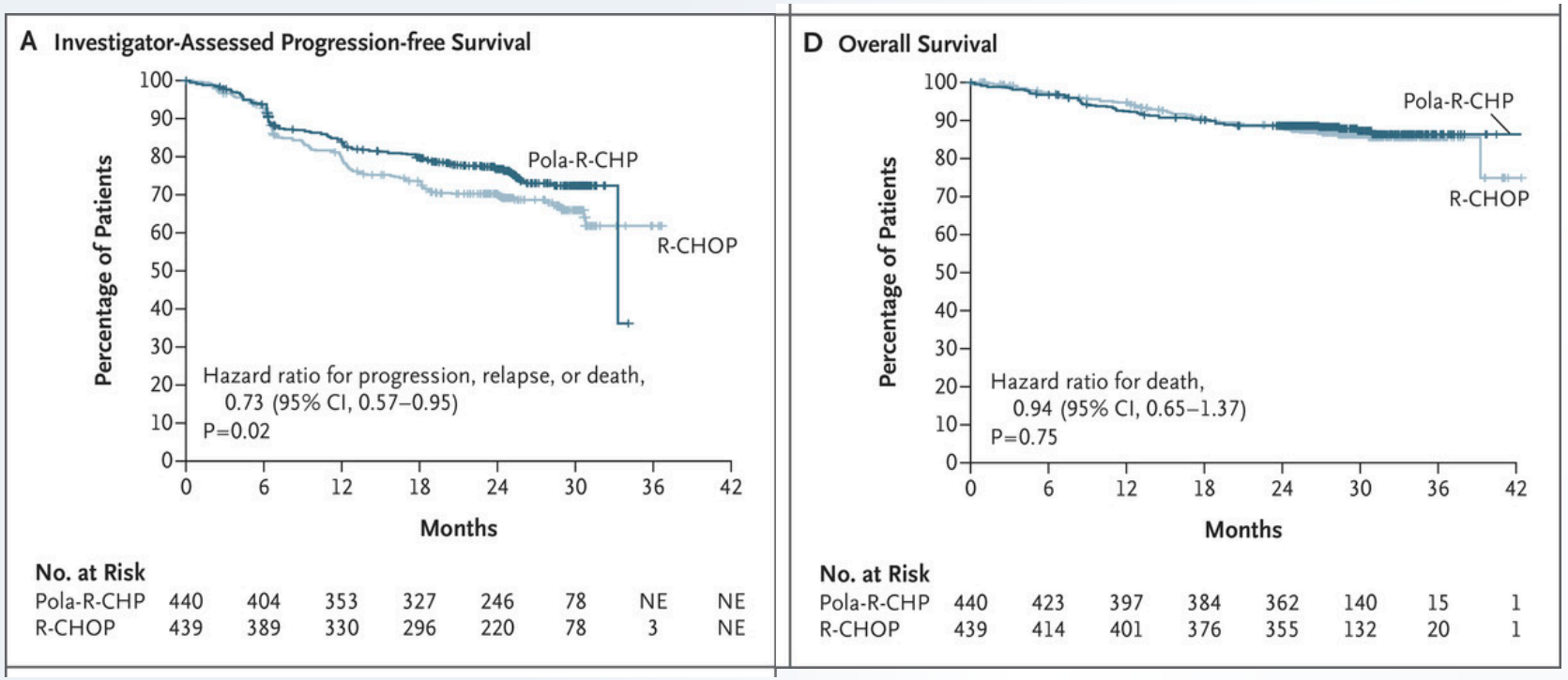
Phase 1/2 BRUIN: Pirtobrutinib in R/R Mantle Cell (FDA Approved)

- **Population:** R/R MCL prior BTKi, N=120 (phase 2)
- **Intervention:** Pirtobrutinib 200 mg daily
- **Comparison:** None
- **Outcome:** ORR 50%, CR 13%, median DOR 8.3 months



Mato et al. Lancet 2021 Mar 6;397(10277): 892-901

Phase 3 POLARIX: Polatuzumab + R-CHP for New DLBCL or HGBL (FDA Approved)

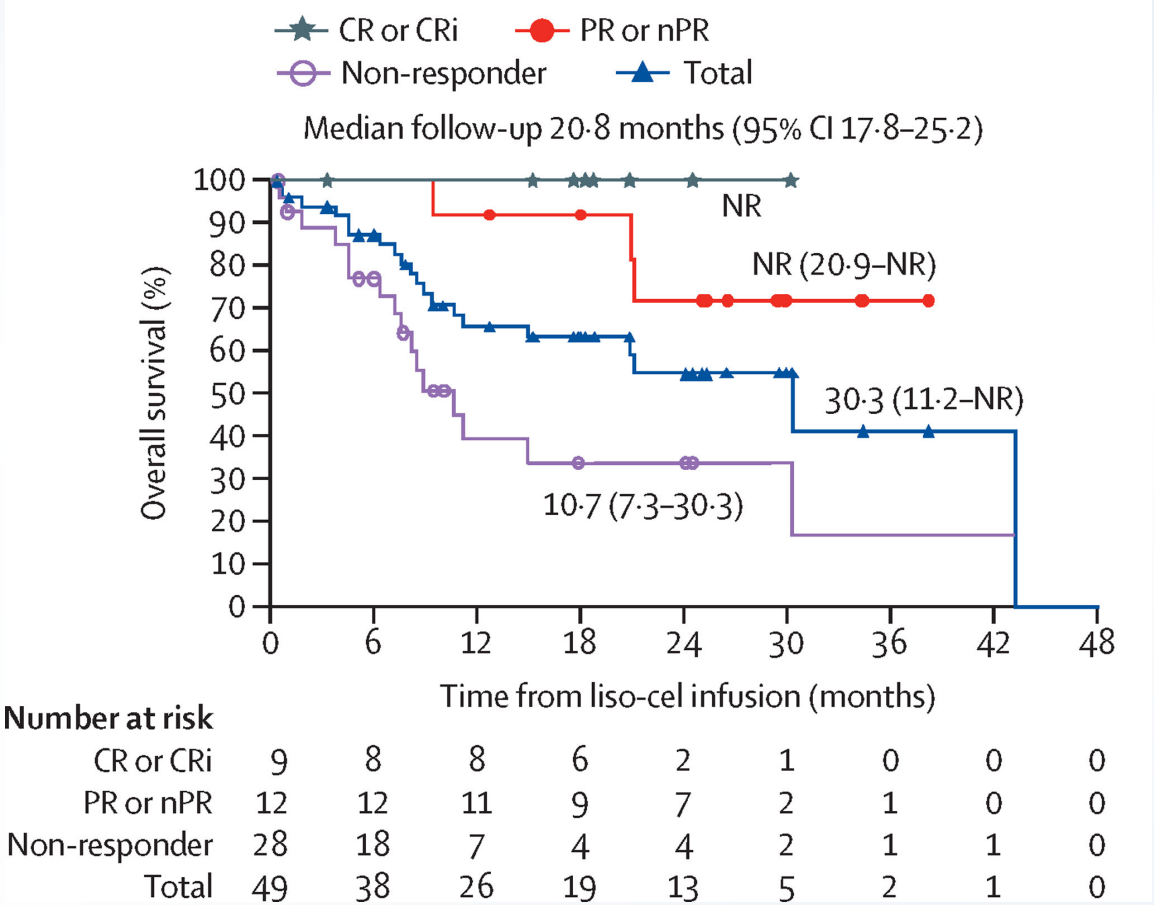


- **Population:** New intermediate- or high-risk DLBCL, N=879
- **Intervention:** Pola-R-CHP
- **Comparison:** 1:1, double-blind, placebo-controlled R-CHOP
- **Outcome:** At 2 years, PFS 76.7% in POLA-R-CHP vs 70.2% in R-CHOP group; no OS difference

H Tilly et al. N Engl J Med 2022;386:351-363

Phase 1/2 TRANSCEND CLL 004: R/R CLL/SLL

- **Population:** R/R CLL/SLL (≥ 2 prior lines), N=117
- **Intervention:** Lisocabtagene maraleucel
- **Comparison:** None
- **Outcome:** CR 18%, ORR 43%, median DOR 35 mo
- **Deaths:** 43/51 after liso-cel infusion



Number at risk									
CR or CRi	9	8	8	6	2	1	0	0	0
PR or nPR	12	12	11	9	7	2	1	0	0
Non-responder	28	18	7	4	4	2	1	1	0
Total	49	38	26	19	13	5	2	1	0

Siddiqi et al. Lancet 2023: 402: 641-54

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Acute Leukemia

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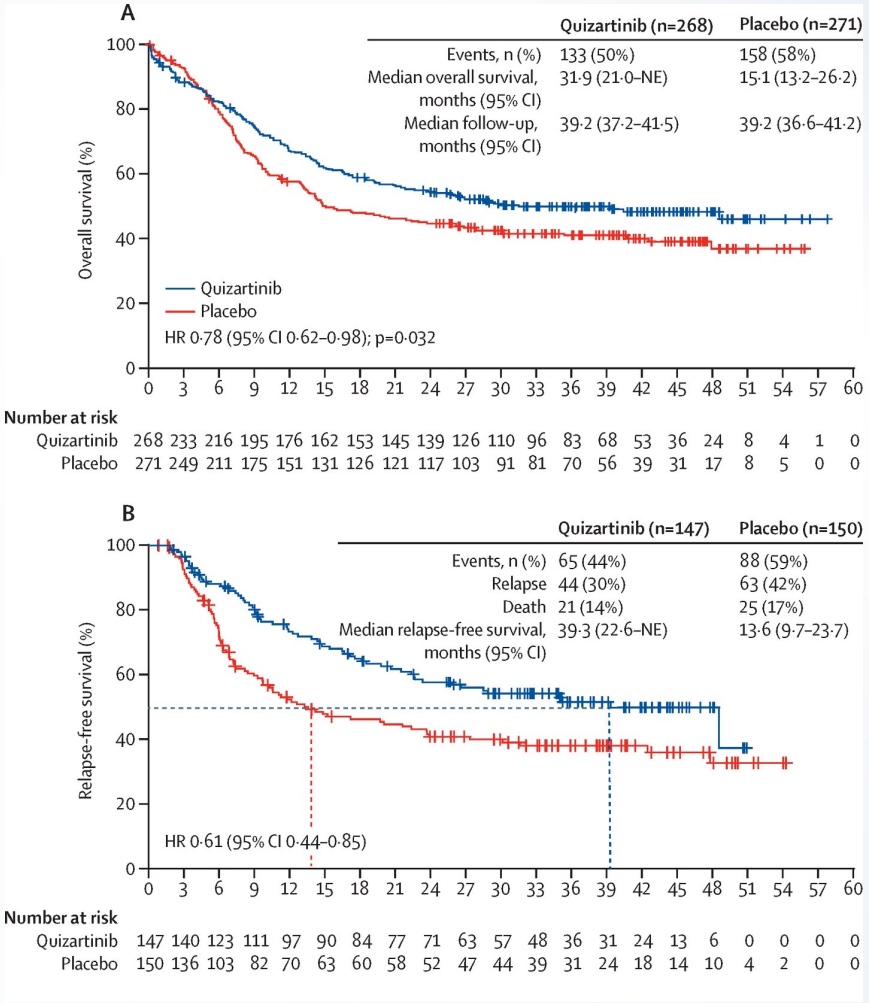
Phase 3 QuANTUM-First: Quizartinib for FLT3-ITD positive AML (FDA Approved)

- Population: Newly diagnosed FLT3-ITD positive AML, N=539
- Intervention: Quizartinib + standard induction and consolidation, and quizartinib as maintenance
- Comparator: 1:1 double-blinded, placebo-controlled trial
- Outcome: Median OS 31.9 mo for quizartinib vs 15.1 mo for placebo

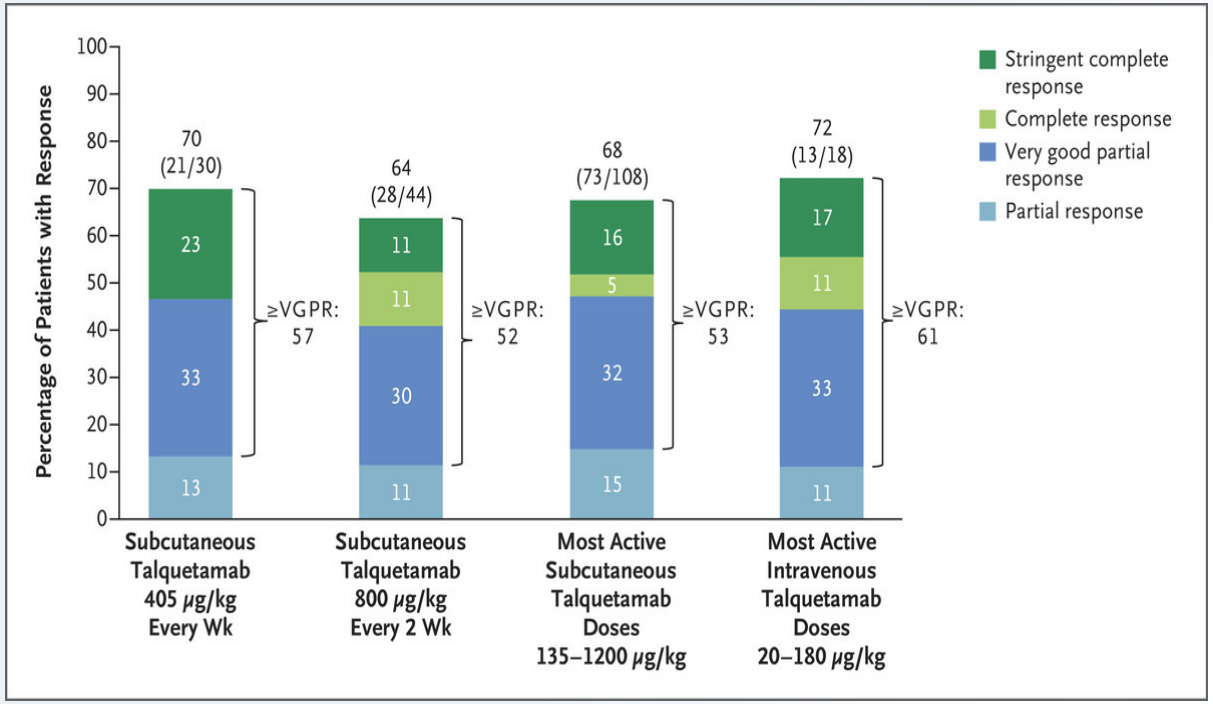


Erba et al. Lancet 2023 May 13;401(10388): 1571-1583

Practice Changing Data from 2023: Hematologic Malignancies

Multiple Myeloma

Phase 1 MonumenTAL-1: Talquetamab (GPRC5D-CD3 T-cell engager) in R/R MM (FDA Approved)

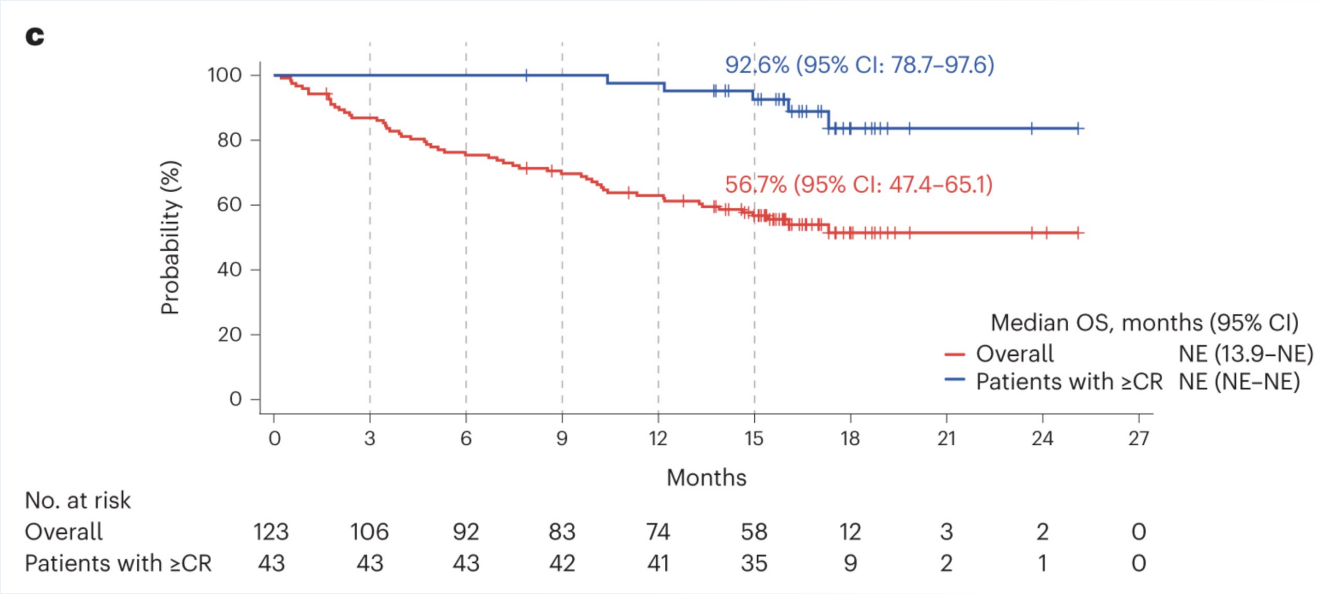


- Population: R/R MM (after >4 prior lines), N=187
- Intervention: Single-arm open label talquetamab 0.4 mg/kg subcutaneous weekly or 0.8 mg/kg subcutaneous every other week
- Comparator: None
- Outcome: For 0.4 mg/kg, ORR 73% with median DOR 9.5 months. For 0.8 mg/kg, ORR 73.6%, median DOR not estimated

A Chari et al. N Engl J Med 2022;387:2232-2244

Phase 2 MagnetisMM-3: Elranatamab in R/R MM (FDA Approved)

Figure: OS in overall cohort (red) and patients with >CR (blue)

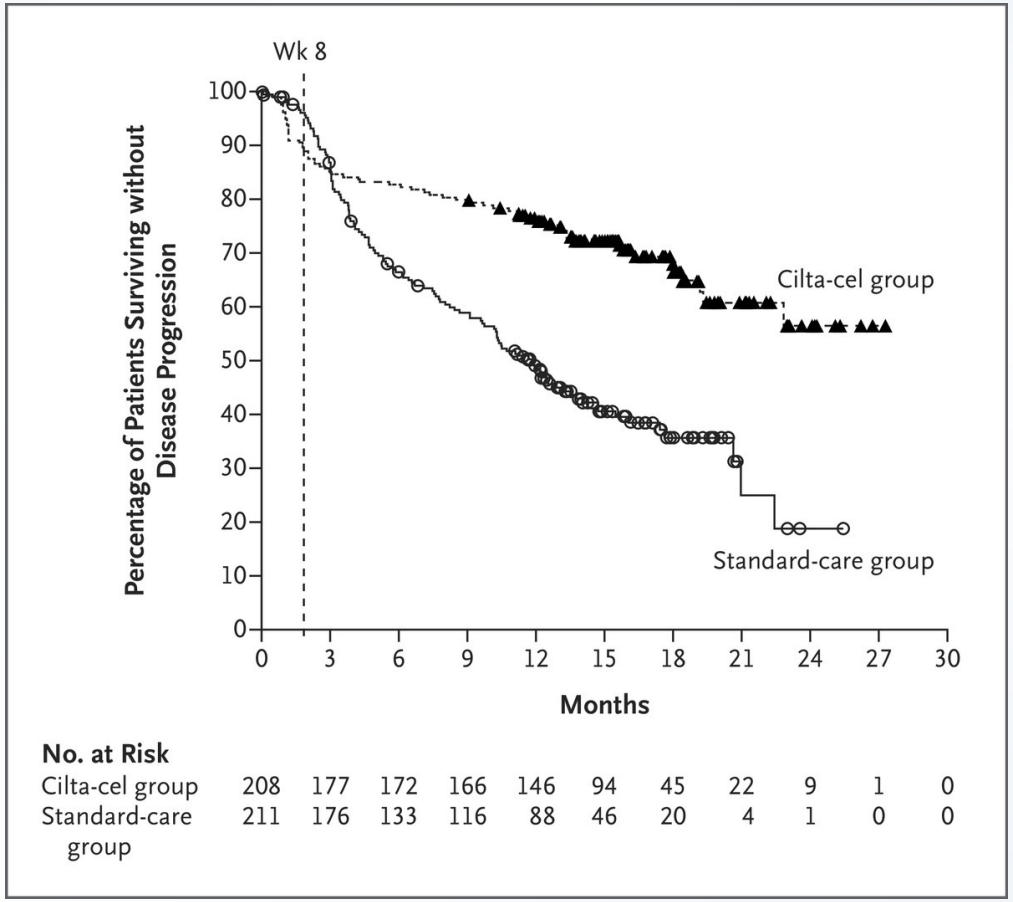


- **Population:** R/R MM (after ≥4 prior lines), N=123
- **Intervention:** Subcutaneous elranatamab weekly after two step-up doses; biweekly if responding
- **Comparator:** None
- **Outcome:** ORR 61%, 35% ≥complete response. Duration of response 90.4% at 6 months and 82.3% at 9 months

Lesokhin et al. Nat Med 29: 2259–2267 (2023)

Phase 3 CARTITUDE-4: Ciltacabtagene Autoleucel in Lenalidomide Refractory MM

- Population: Lenalidomide-refractory MM (after 3 prior lines), N=419
- Intervention: 1:1 randomization single cilta-cel infusion after bridging therapy
- Comparison: SOC (physician's choice PVd or DPd)
- Outcomes: Cilta-cel (median PFS not reached, ORR 84.6%, CR 73.1%) vs. SOC (median PFS 11.8 mo, ORR 67.3%, CR 21.8%)



J San-Miguel et al. N Engl J Med 2023;389:335-347

Thank You, LEAD!