AFM-13 in Hodgkin lymphoma

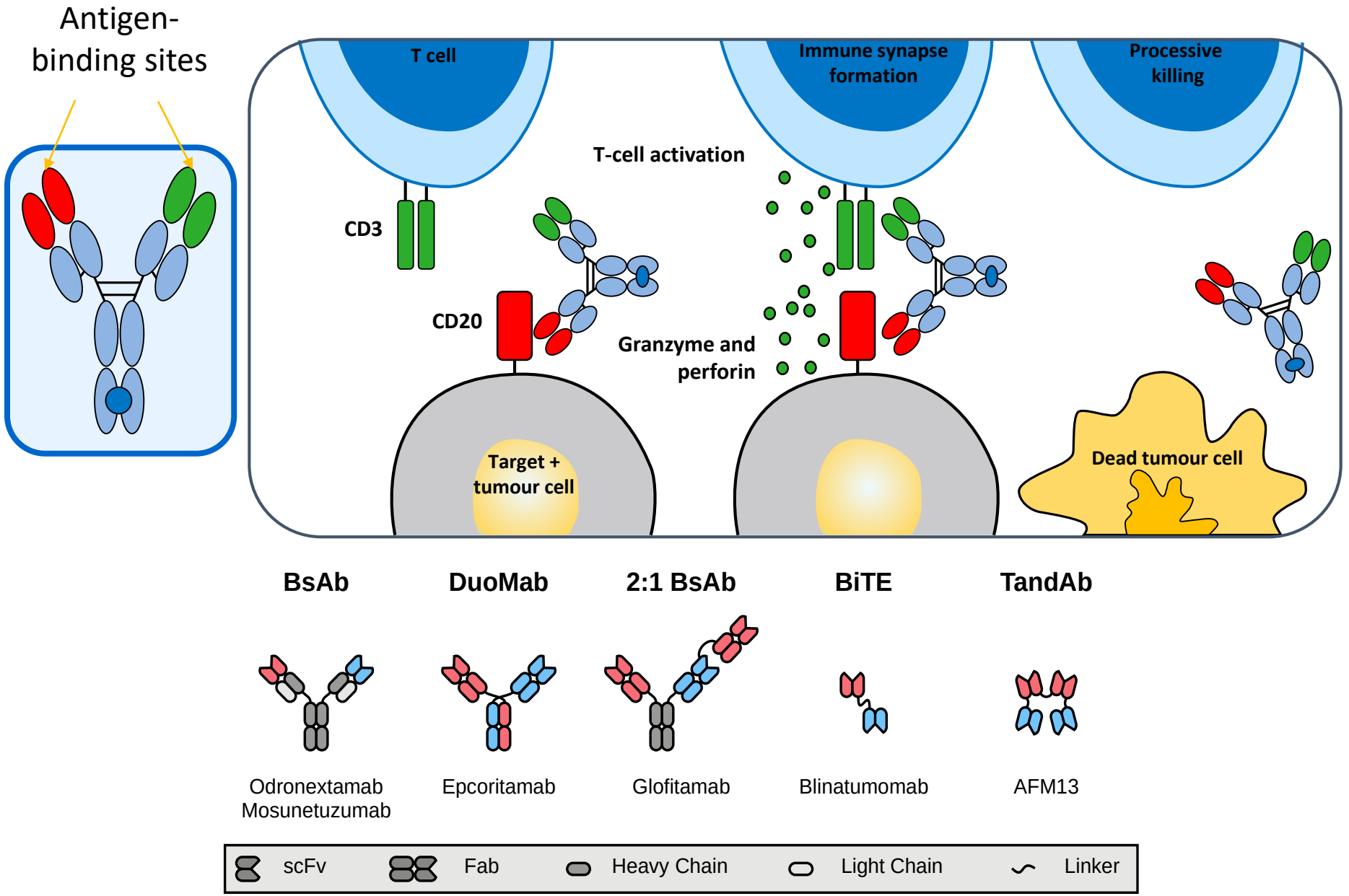
Stephen M. Ansell, MD, PhD

Dorotha W. and Grant L. Sundquist Professor in Hematologic Malignancies Research

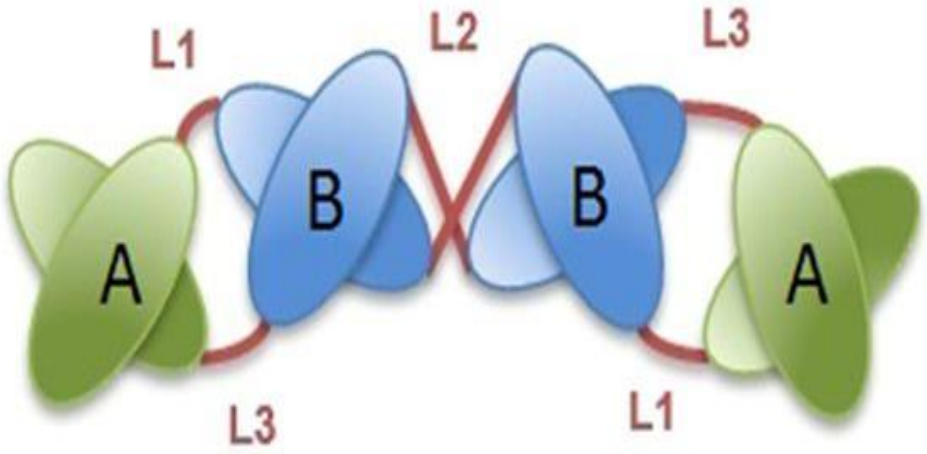
Chair, Lymphoma Group

Mayo Clinic

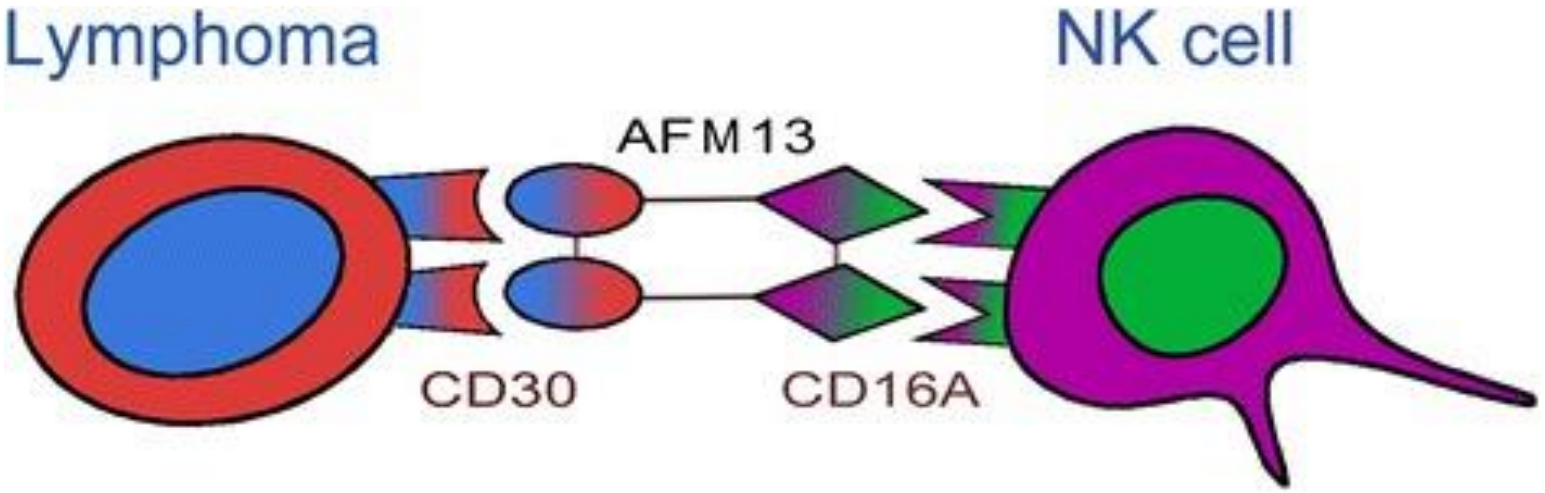
Bispecific antibodies – force T-cell or NK-cell activation



Bispecific antibodies – force NK-cell activation

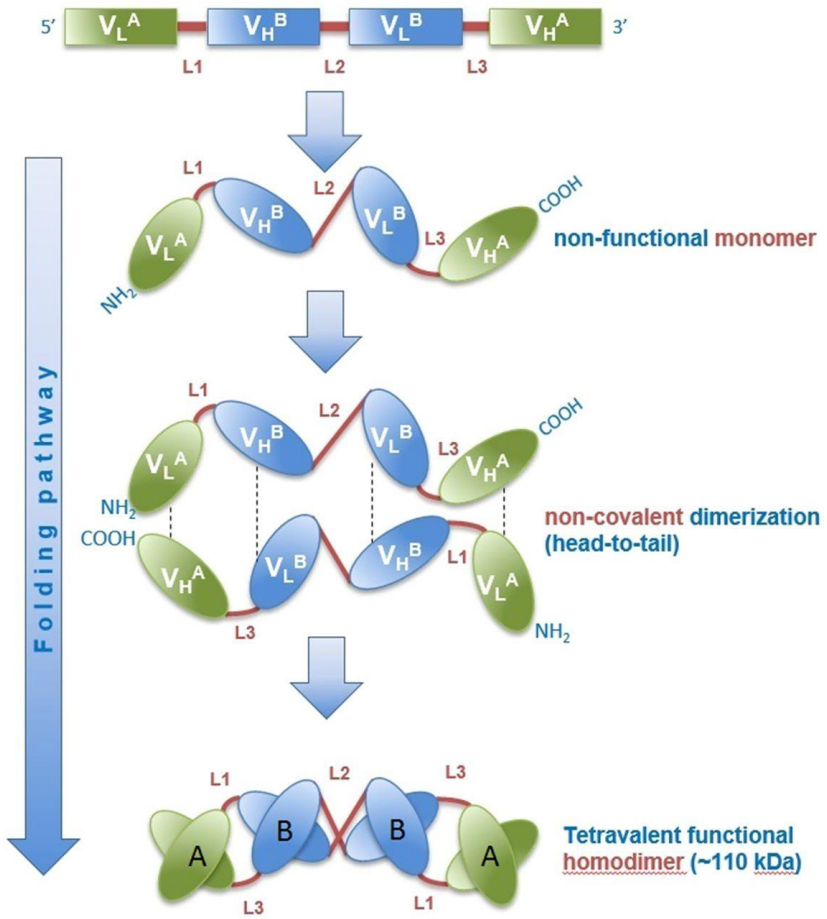


Tetravalent functional homodimer (~110 kDa)



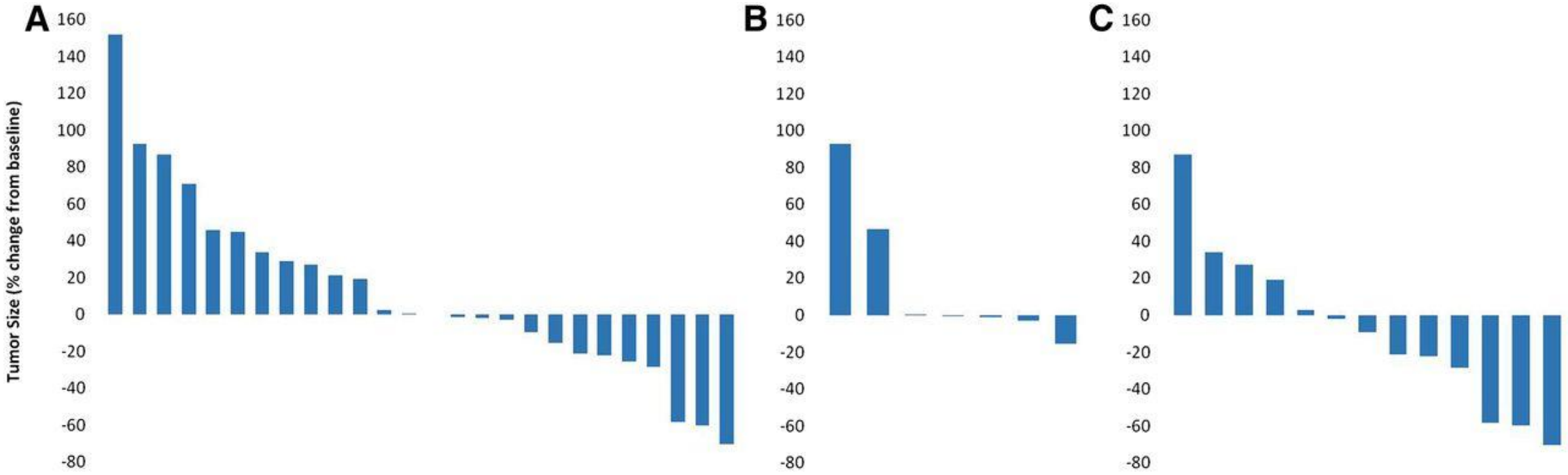
Wu et al. J Hematol Oncol. 2015 Aug 1;8:96.

A phase 1 study of the bispecific anti-CD30/CD16A antibody construct AFM13 in patients with relapsed or refractory Hodgkin lymphoma



Rothe A, et al. Blood. 2015 Jun 25;125(26):4024-31

A phase 1 study of the bispecific anti-CD30/CD16A antibody construct AFM13 in patients with relapsed or refractory Hodgkin lymphoma



3 of 26 patients - PR (11.5%) and 13 patients achieved stable disease (50%).
In 13 patients who received doses of ≥1.5 mg/kg AFM13, the ORR was 23% and the disease control rate was 77%.

Rothe A, et al. Blood. 2015 Jun 25;125(26):4024-31

CD30/CD16A Tetravalent Bispecific Antibody (AFM13) in Relapsed or Refractory CD30-Positive Lymphoma with Cutaneous Presentation

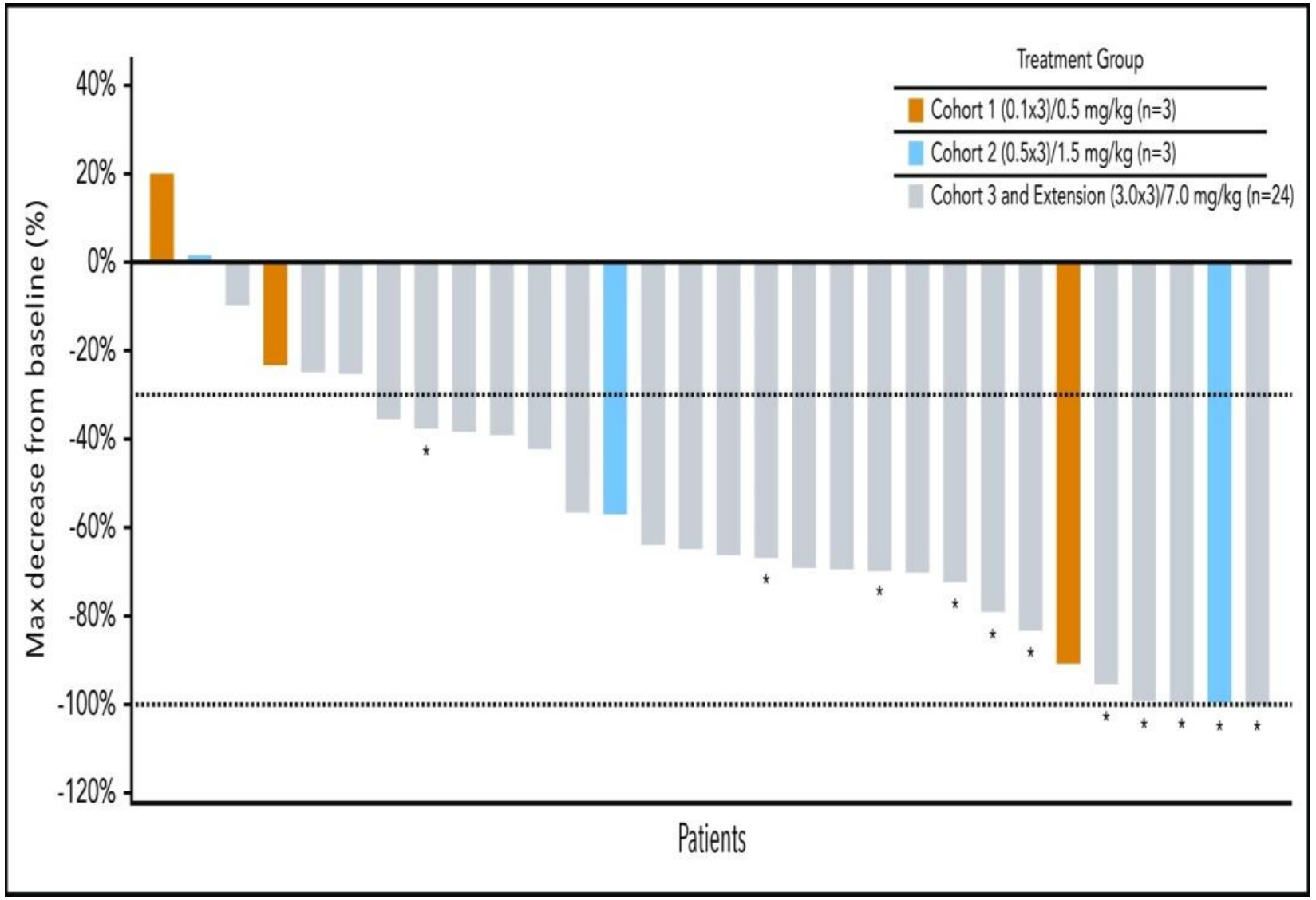
Table 1: Clinical results displayed by cohort, disease, toxicity and response

Cohort	Disease	Toxicity	Response
1.5 mg/kg IV weekly	Systemic Anaplastic Large Cell Lymphoma-ALK negative	No AE	PR
	Transformed Mycosis Fungoides	No AE	POD
	Cutaneous anaplastic large cell lymphoma	Rash (G4) Skin infection (G3)	CR
7 mg/kg IV weekly	Mycosis Fungoides	IRR (G1)	SD
	Transformed Mycosis Fungoides	IRR (G1)	SD
	Transformed Mycosis Fungoides	Skin infection (G3) IRR (G1)	Not assessed
7 mg/kg CIVI over 5 days weekly	Transformed Mycosis Fungoides	No AE	PR
	Systemic Anaplastic Large Cell Lymphoma-ALK negative	No AE	PR
	Mycosis Fungoides	No AE	POD
200 mg weekly	Transformed Mycosis Fungoides	No AE	PR
	Mycosis Fungoides	No AE	SD
	Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS)	No AE	SD
	T-cell-prolymphocytic leukemia (T-PLL)	No AE	SD
	Angioimmunoblastic T-cell lymphoma (AITL)	No AE	POD
	Transformed Mycosis Fungoides	No AE	PR

- AFM13 demonstrated a high ORR of 40% among a population of heavily pretreated subjects with CD30 positive lymphoproliferative T-cell malignancies.
- AFM13 exhibited activity post brentuximab vedotin failure.
- In addition, biological changes in NK infiltration and activation in the PB and tissue biopsy correlated with response.

Sawas A et al. ASH 2020, #2971

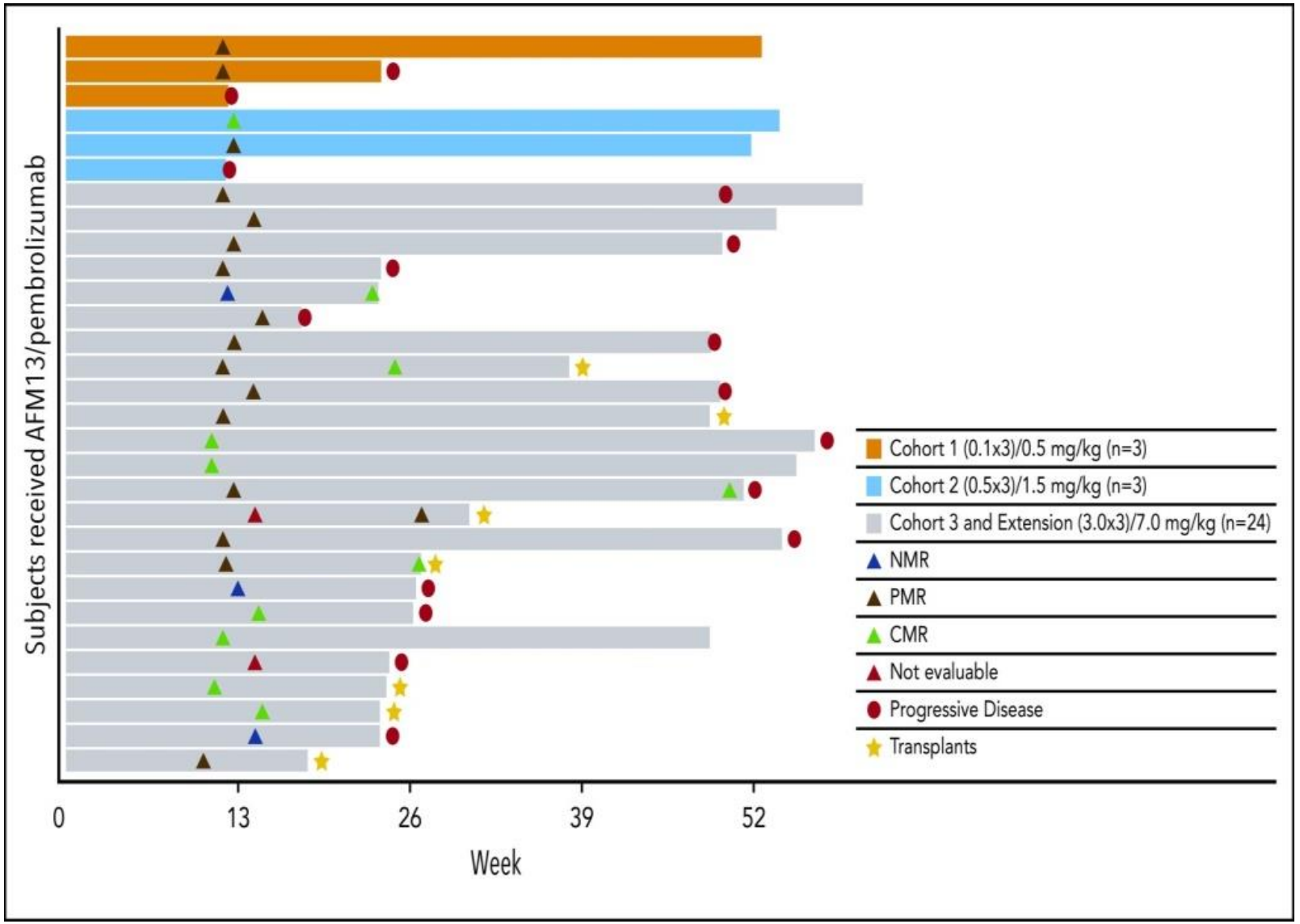
Bispecific antibody AFM13 + Pembrolizumab in cHL



- The combination of AFM13 with pembrolizumab demonstrated an objective response rate of 88% at the highest treatment dose, with an 83% overall response rate for the overall population.
- 37% (11 patients) experienced a CMR and 47% (14 patients) experienced a PMR

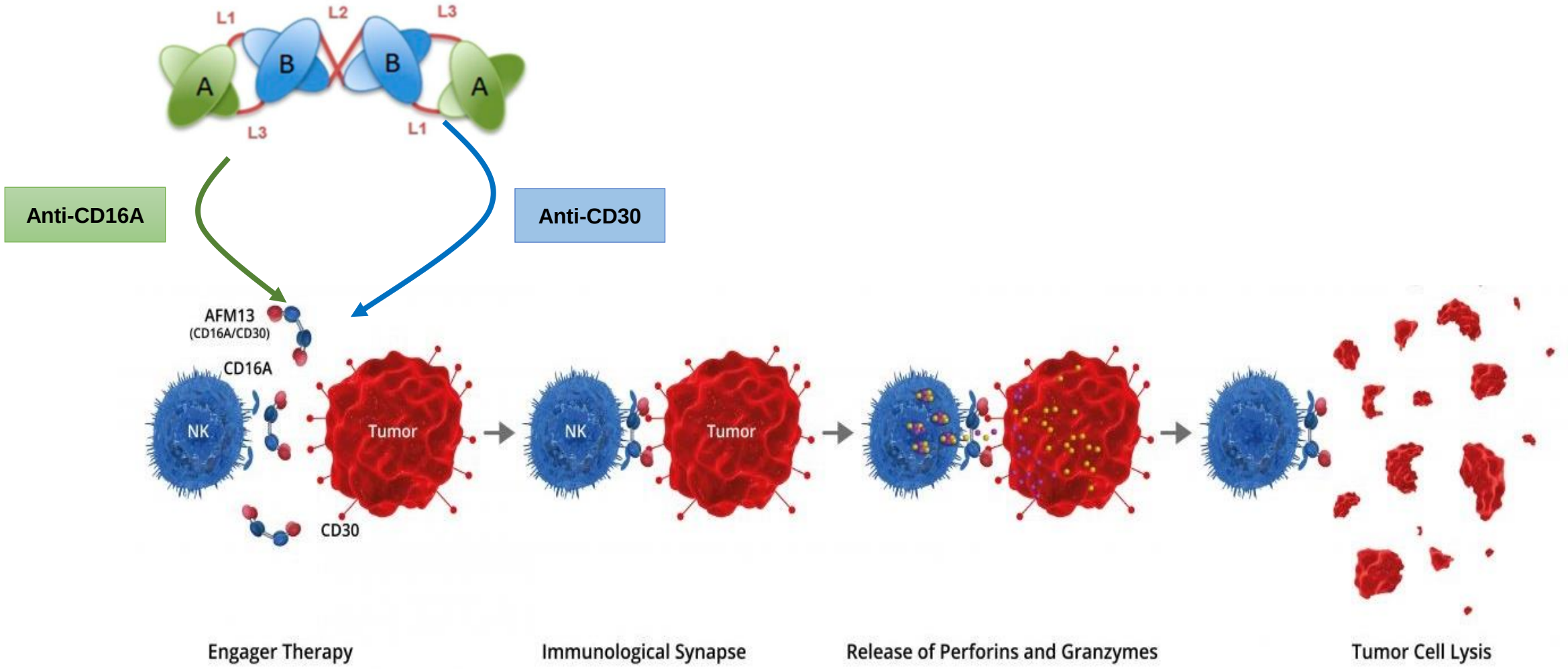
Bartlett NL, et al. Blood. 2020 Nov 19;136(21):2401-2409.

Bispecific antibody AFM13 + Pembrolizumab in cHL

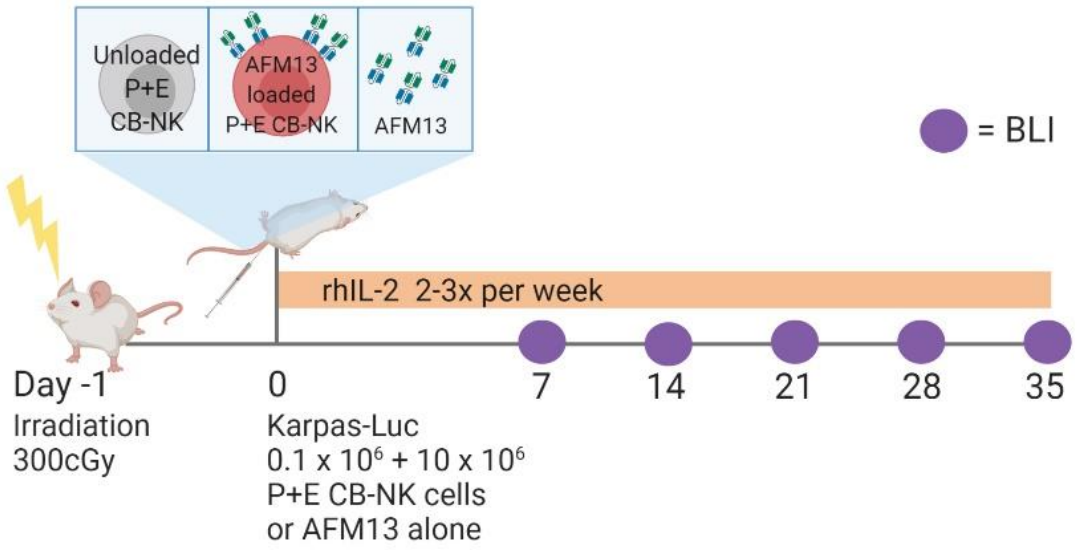


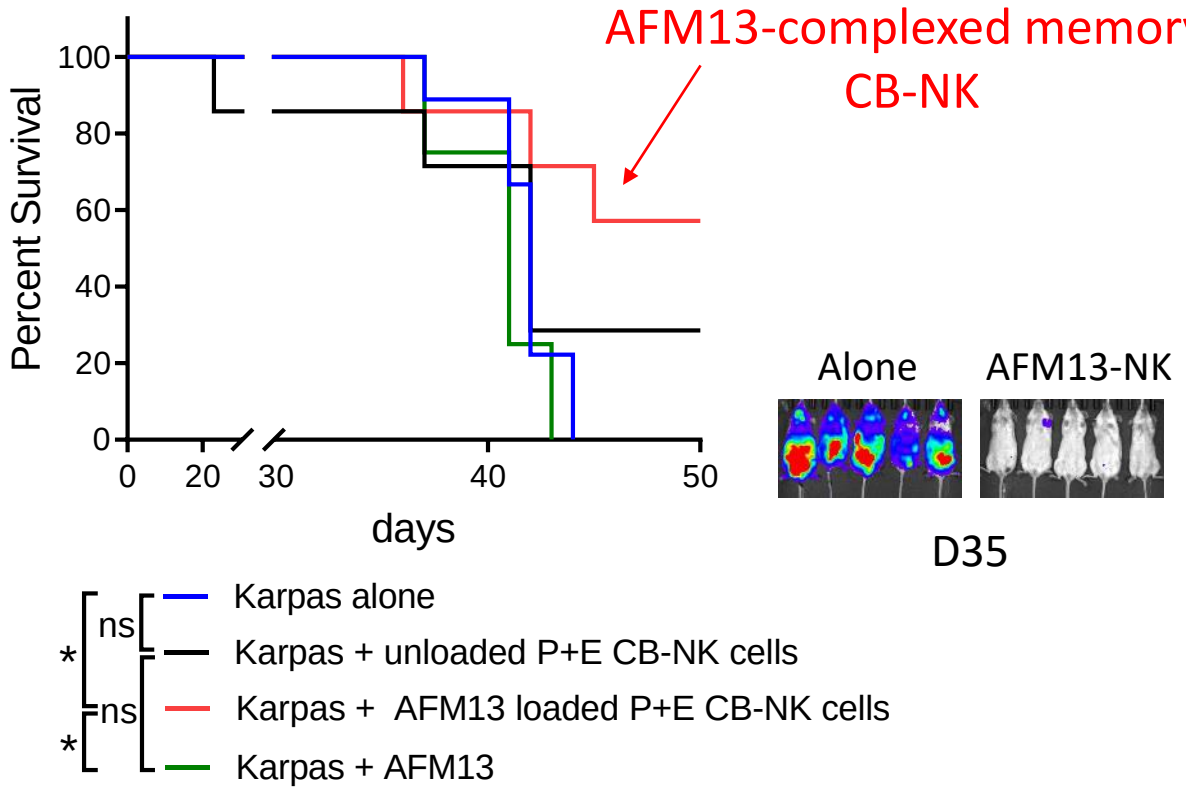
Bartlett NL, et al. Blood. 2020 Nov 19;136(21):2401-2409.

Pre-complexing allogeneic NK cells with bispecific innate cell engager AFM13 increases their cytotoxic capacity



Pre-complexing cord blood-derived NK cells with AFM13 prior to infusion facilitates CAR-like responses in a CD30+ T-NHL mouse xenograft



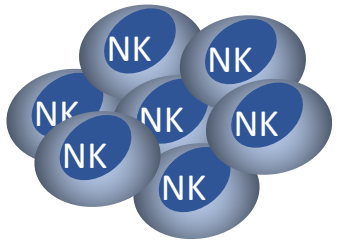


- Persistence of NK cells enhanced by pre-activation with IL-12/IL-15/IL-18 cytokines to induce a **memory phenotype**
- NK cells expanded by >1,000 fold in the presence of uAPC (K562 feeder cells)

Kerbauy et al, Clin Cancer Res 27: 3744-56, 2021

AFM13-complexed CB-Derived NK cells for Refractory/Relapsed CD30+ Lymphoma (NCT04074746)

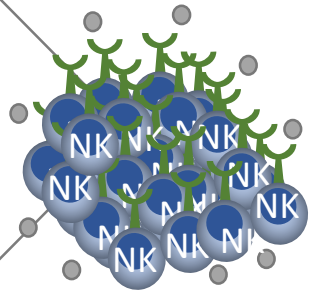
CB-derived NK cells



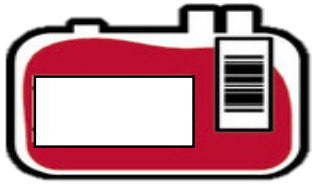
GMP lab

- **Preactivation** (IL-12/IL-15/IL-18)
- **Expansion** with uAPC K562 feeder cells + IL-2
- **Precomplexing** with AFM13 (100 µg/mL)

Infusion of AFM13 CAR-like NK cells



3 dose levels
1 x 10^6/kg
1 x10^7/kg
1x10^8/kg



Banked umbilical cord blood

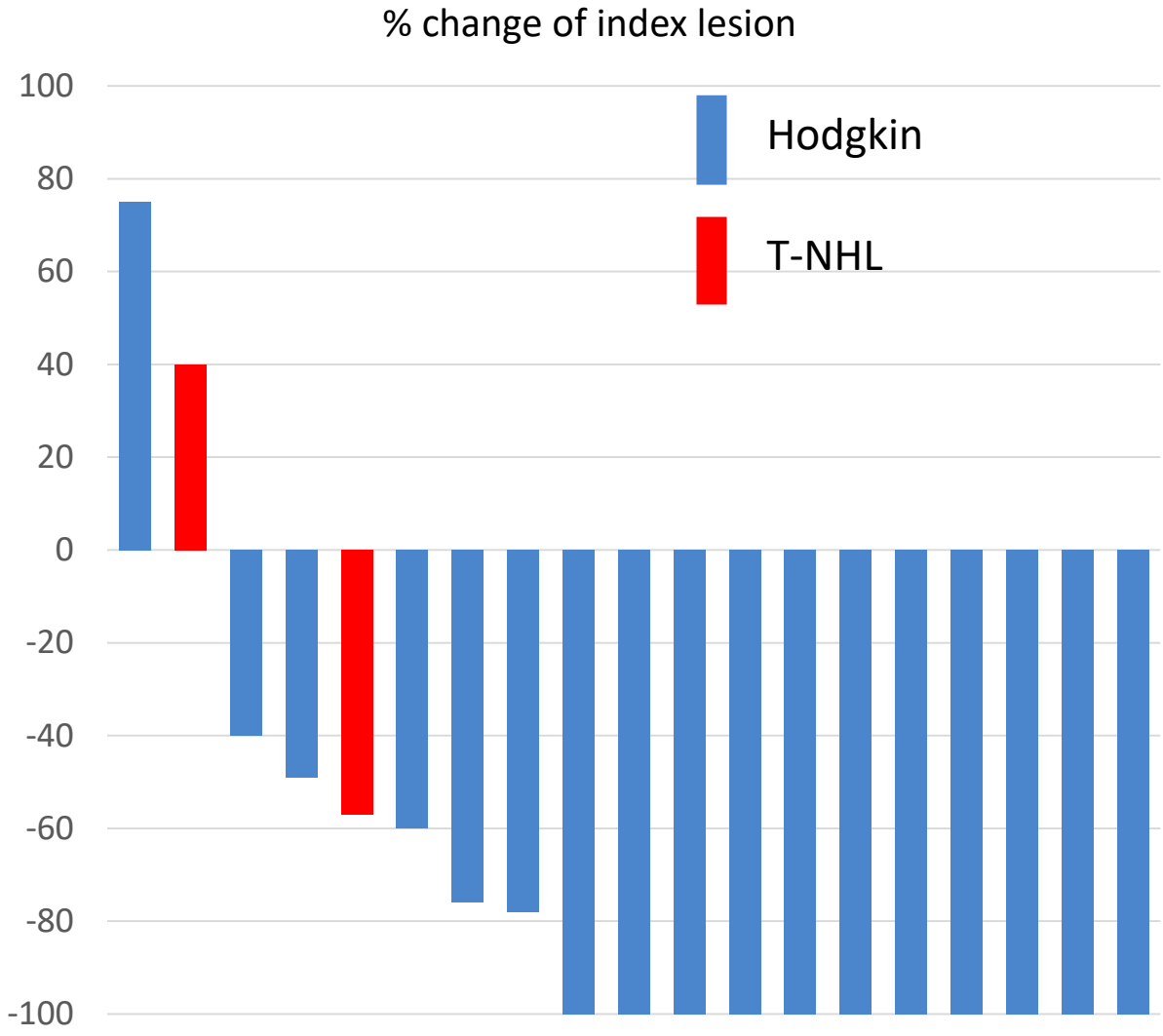
D-15	D-14	D-5	D-4	D-3	D-2	D0	D7	D14	D21	D28
							AFM13 200 mg IV	AFM13 200 mg IV	AFM13 200 mg IV	PET/CT

- Fludarabine 30 mg/m^2/day
- Cyclophosphamide 300 mg/m^2/day

Nieto et al. AACR 2022 CT003

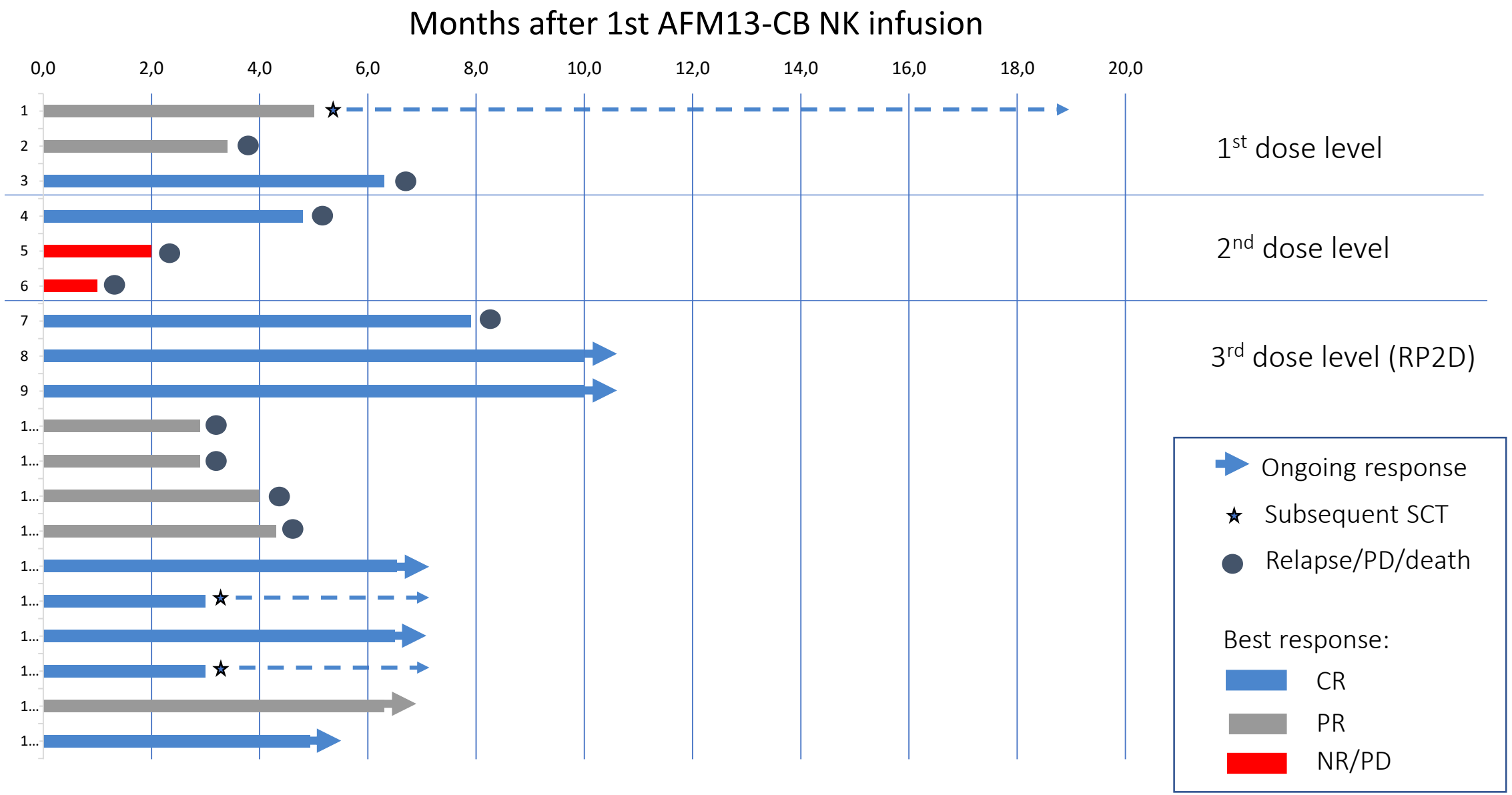
Antitumor Activity

- Responses were evaluated by PET using Lyric criteria on day 28 of each cycle
- 17/19 metabolic responses (ORR 89.5%) (10 CR, 7 PR)
- All 13 patients treated at the RP2D responded (8 CR, 5 PR)
  - 5 CR after C1 → 8 CR after C2

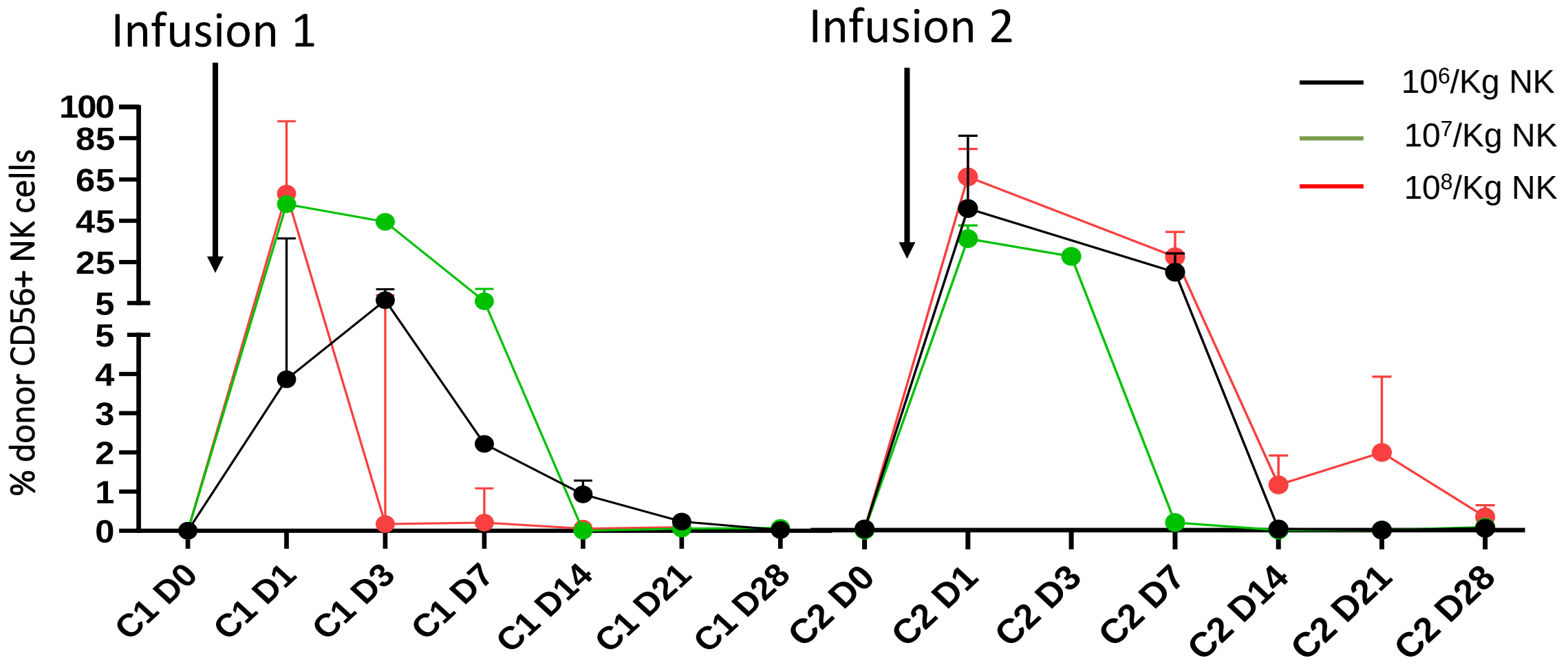


Nieto et al. AACR 2022 CT003

Duration of responses



Donor NK cells are detectable for up to 3 weeks



Nieto et al. AACR 2022 CT003

Conclusions

- AFM13 is a homodimer engaging CD30 and CD16
- AFM13 has modest single agent activity in Hodgkin lymphoma and cutaneous T-cell lymphoma
- In combination with pembrolizumab, responses are high, CR rate seems increased, and responses are durable.
- AFM13-complexed cord blood NK cells persist in the blood, are safe and have clinical activity in relapsed Hodgkin lymphoma