

CART versus allogenic stem cell transplant for Acute B cell lymphoblastic leukemia patients

Great Debate Sea Island 2022

The Debaters

The “CART gunner”



The “Transplant Sage”



“You can't let a young 'un decide for himself. He'll grab at the first flashy thing with shiny ribbons on it, then when he finds out there's a hook in it, it's too late” Andy Griffith, the Andy Griffith Show 1961

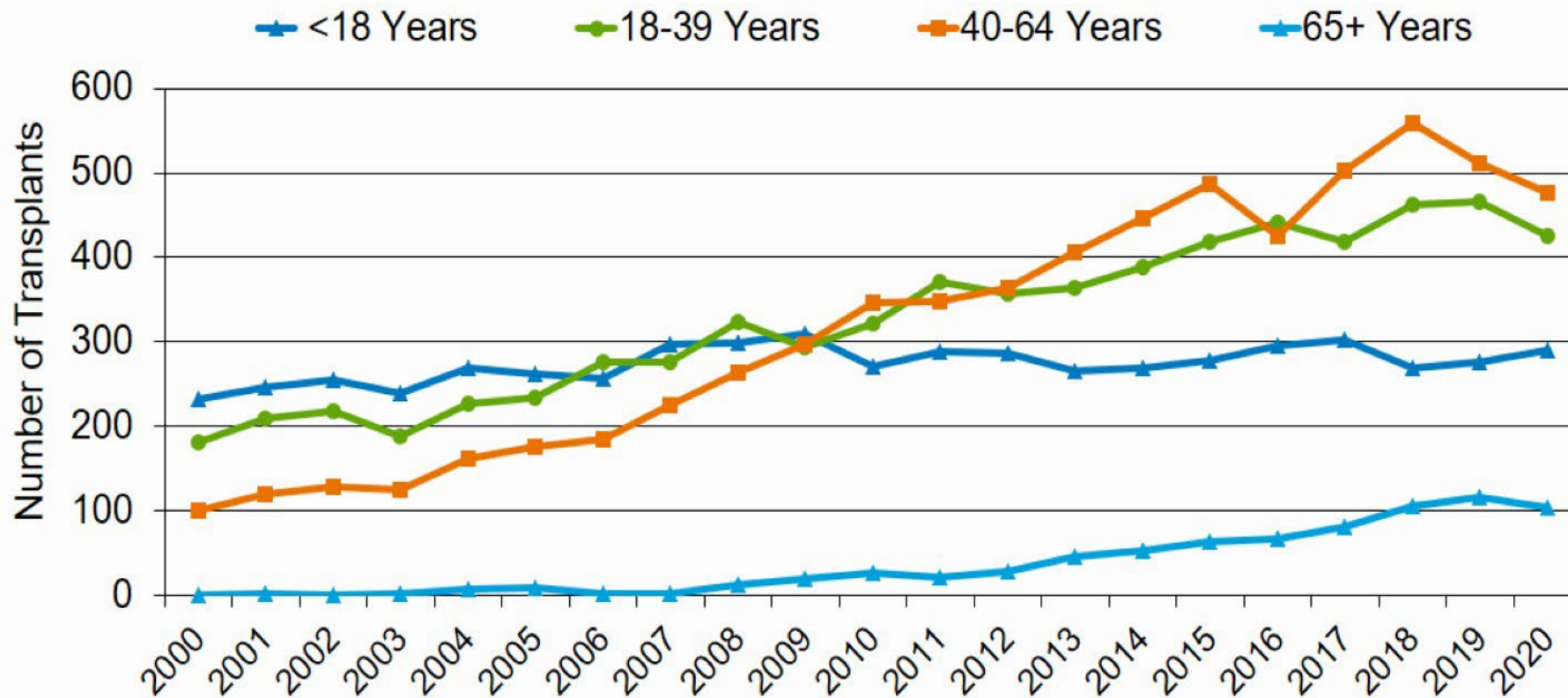
A question of effective versus experimental....

Allogeneic transplant offers superior curative therapy for patients with B cell acute lymphoblastic leukemia compared with anti-CD19 directed CART

What is the clinical experience of
using allogeneic stem cell
transplantation for ALL?

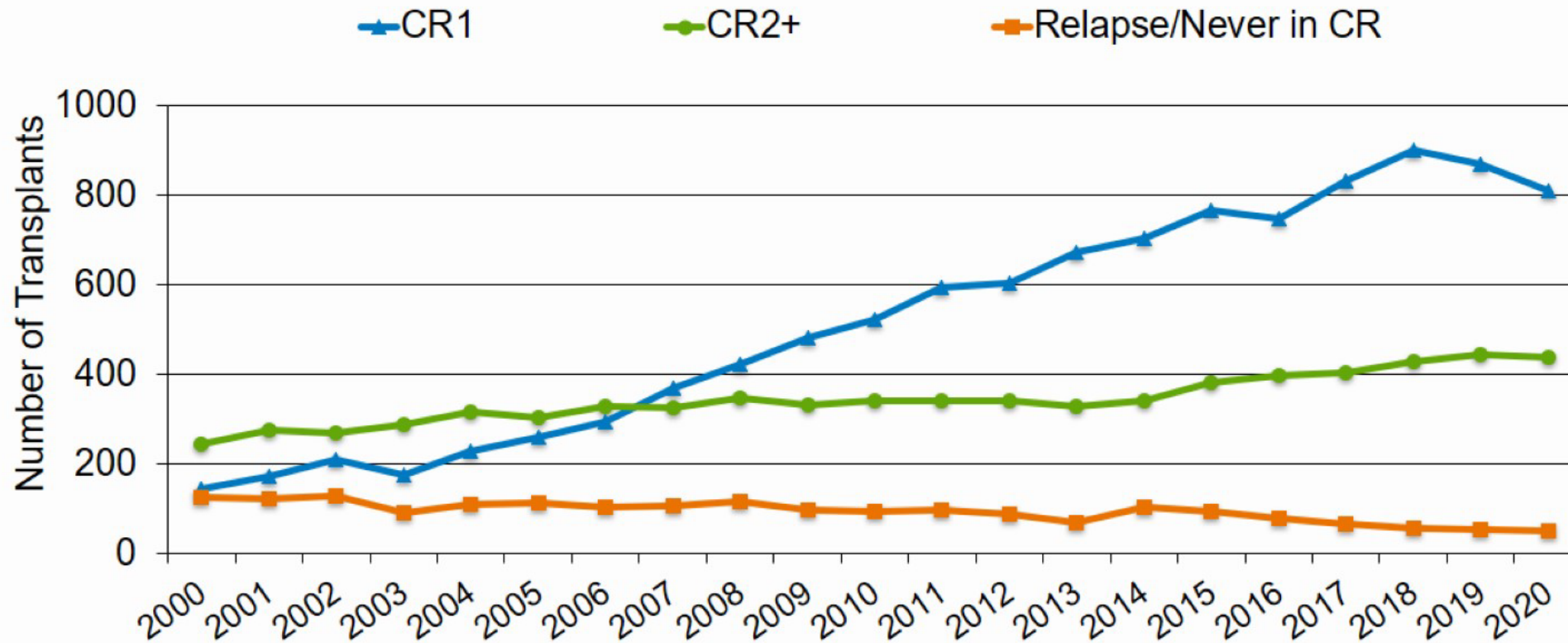
Allo-transplant for adults with ALL is growing over time

Number of Allogeneic HCTs for Acute Lymphoblastic Leukemia (ALL) by Recipient Age (Pediatric category) in the US



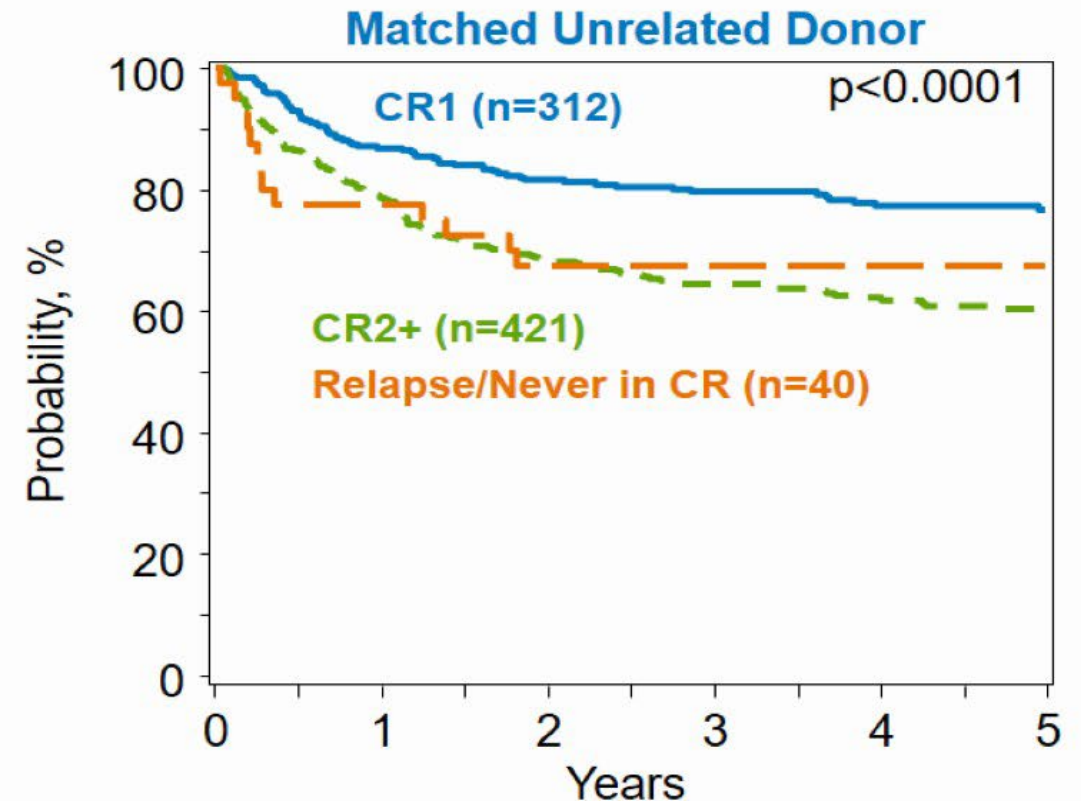
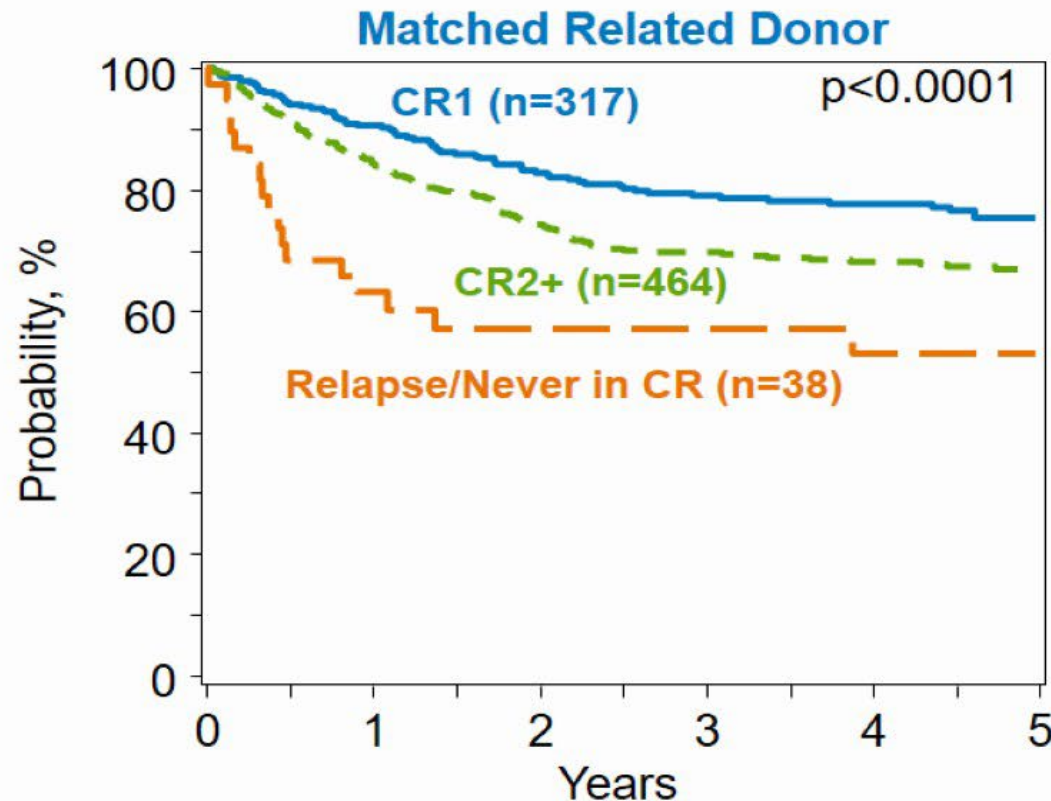
Allo-transplant as consolidation for ALL patients in CR1 or CR2

Number of Allogeneic HCTs for Acute Lymphoblastic Leukemia (ALL) by Disease Status in the US



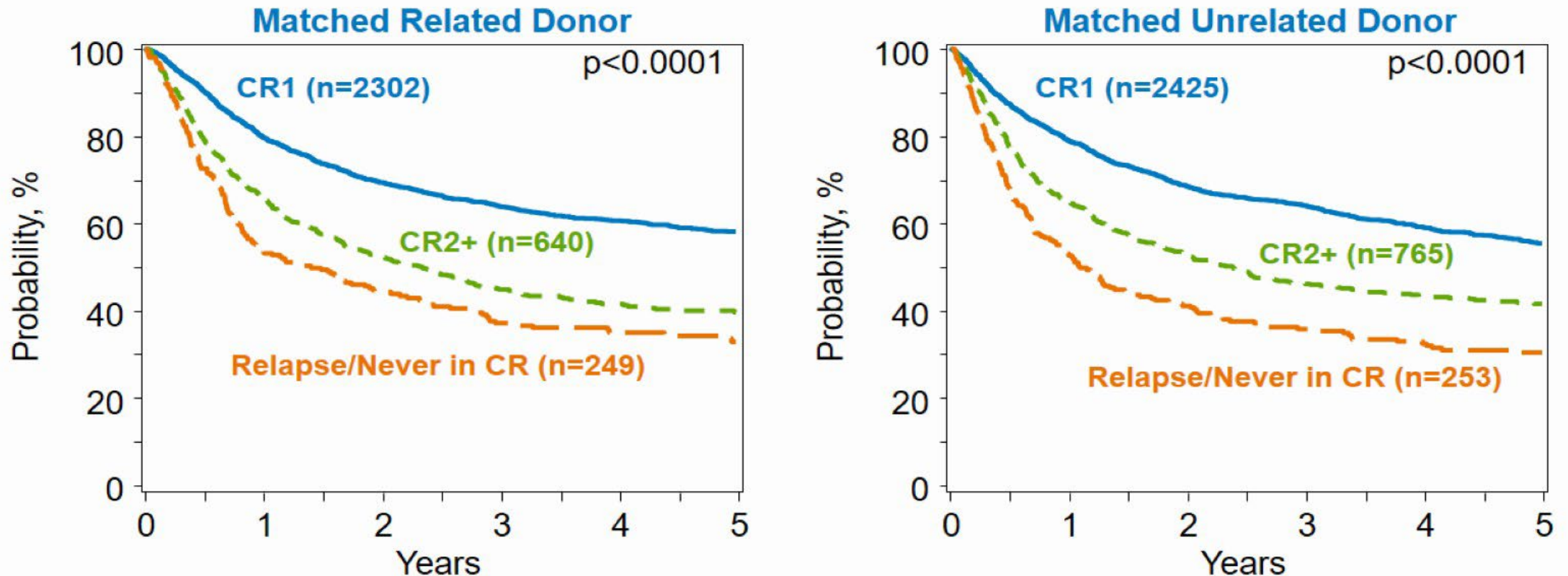
Allo-HSCT from HLA matched donors is curative in >50% of pediatric patients

Survival after Allogeneic HCTs for Acute Lymphoblastic Leukemia (ALL), Using Matched Donors, Age <18 Years, in the US, 2009-2019



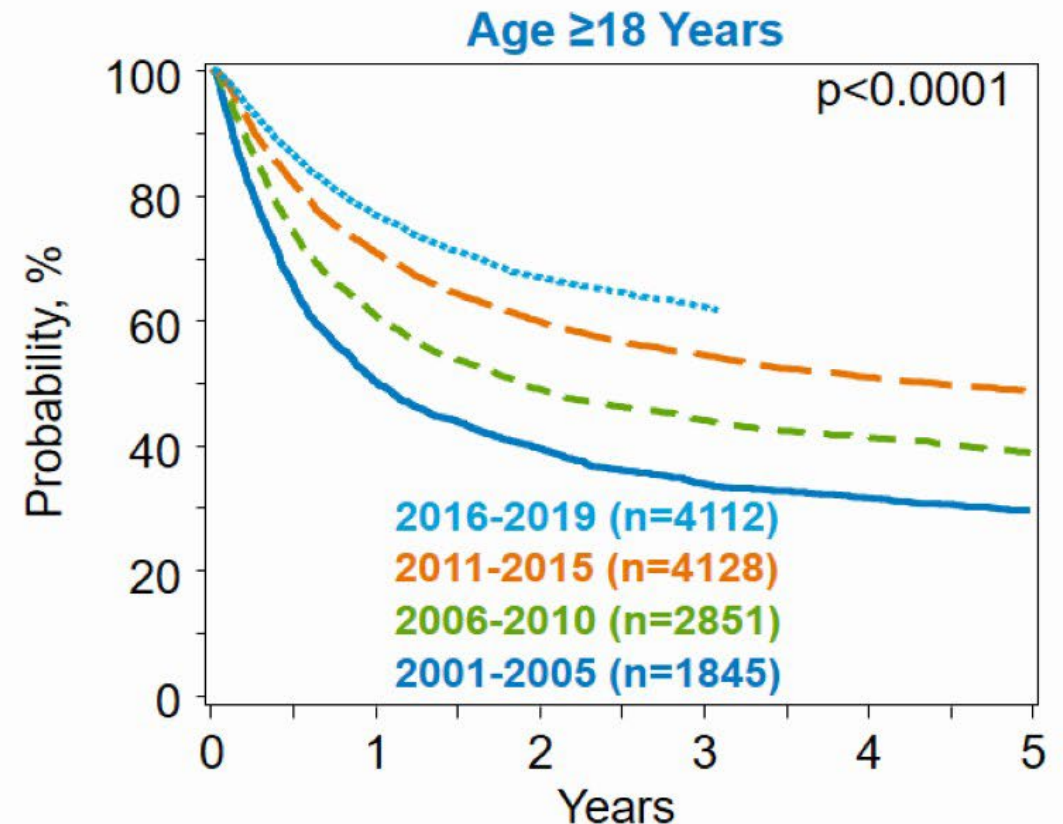
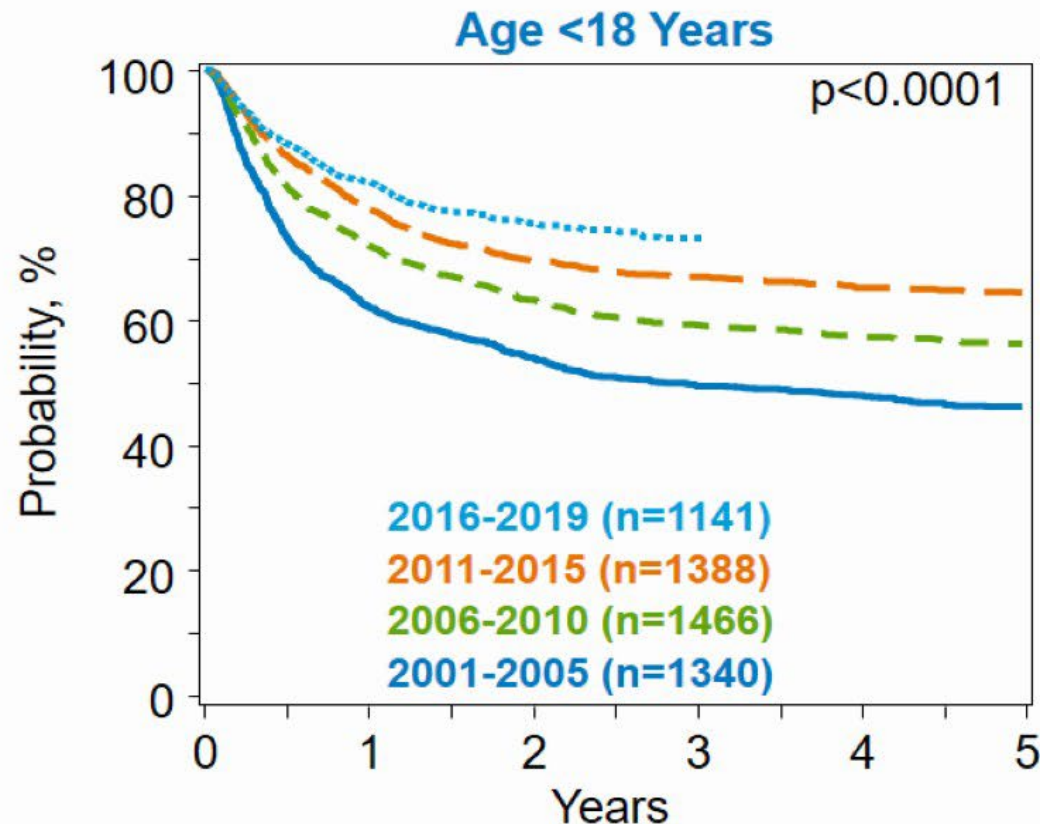
Allo-HSCT from HLA matched donors is curative in >40% adult patients in CR and 30% patients in relapse.

Survival after Allogeneic HCTs for Acute Lymphoblastic Leukemia (ALL), Using Matched Donors, Age ≥ 18 Years, in the US, 2009-2019



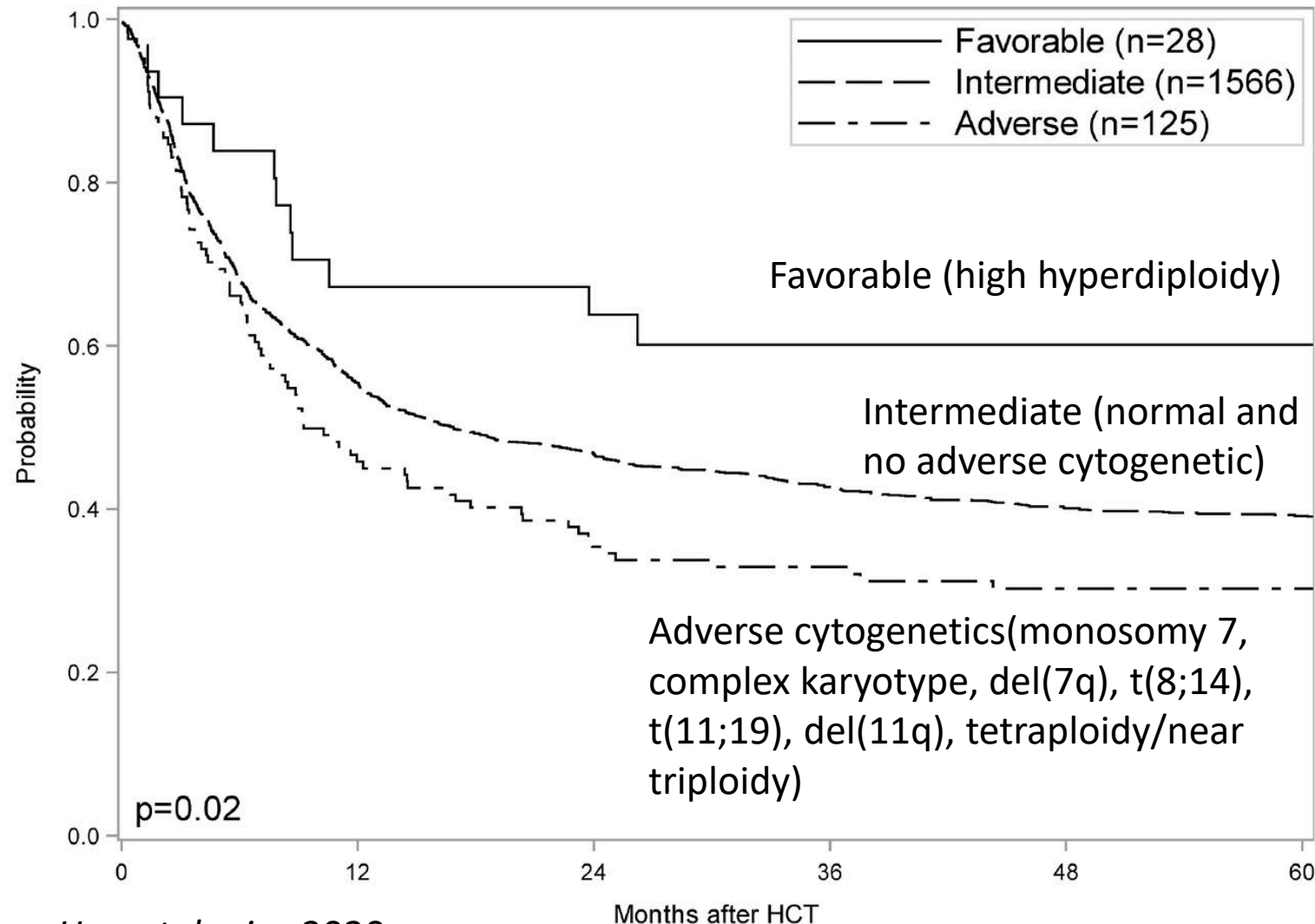
Allo-transplant outcomes for ALL are improving over time

Trends in Survival after Allogeneic HCTs for Acute Lymphoblastic Leukemia (ALL), in the US, 2001-2019



Allo-transplant is effective across different cytogenetic risk groups for Ph(-) ALL

B



57% CR1

43% CR2

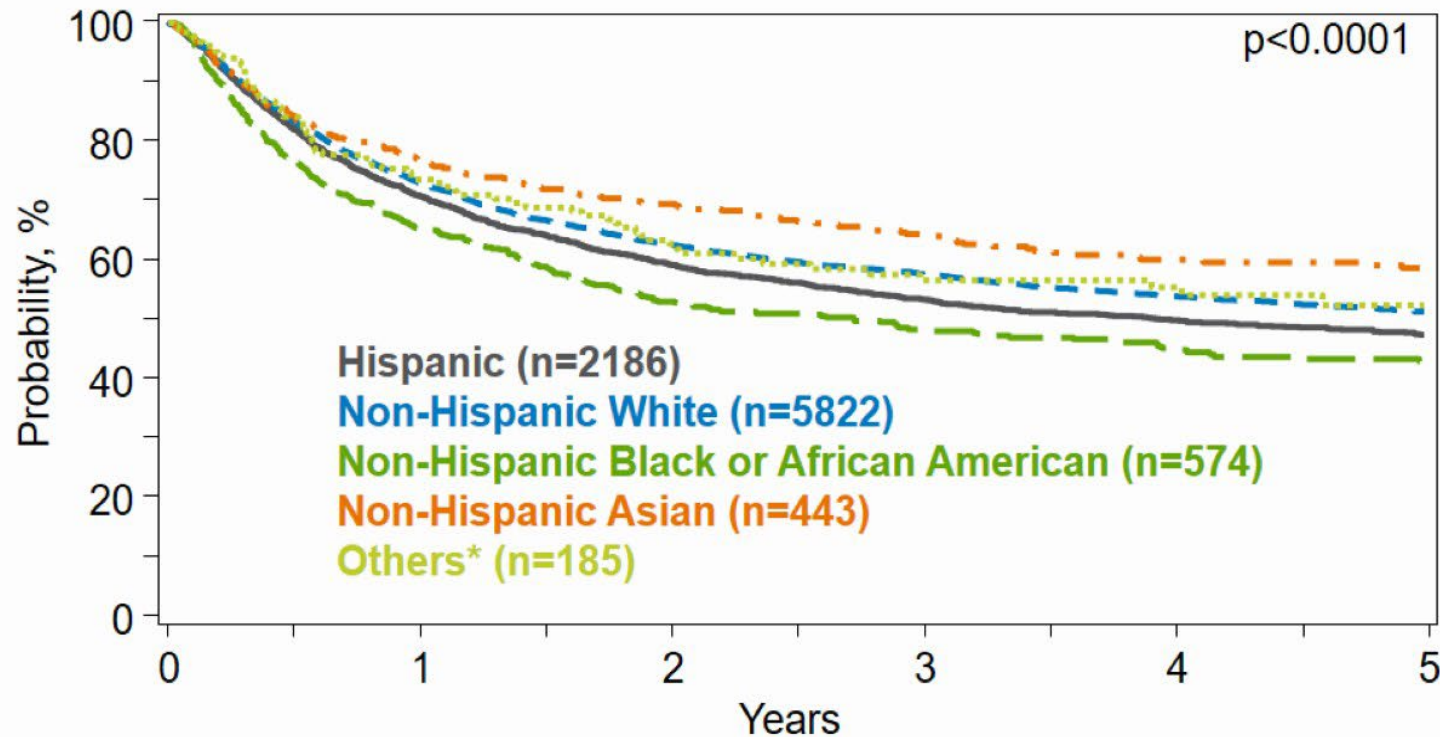
69% B-ALL

23% T-ALL

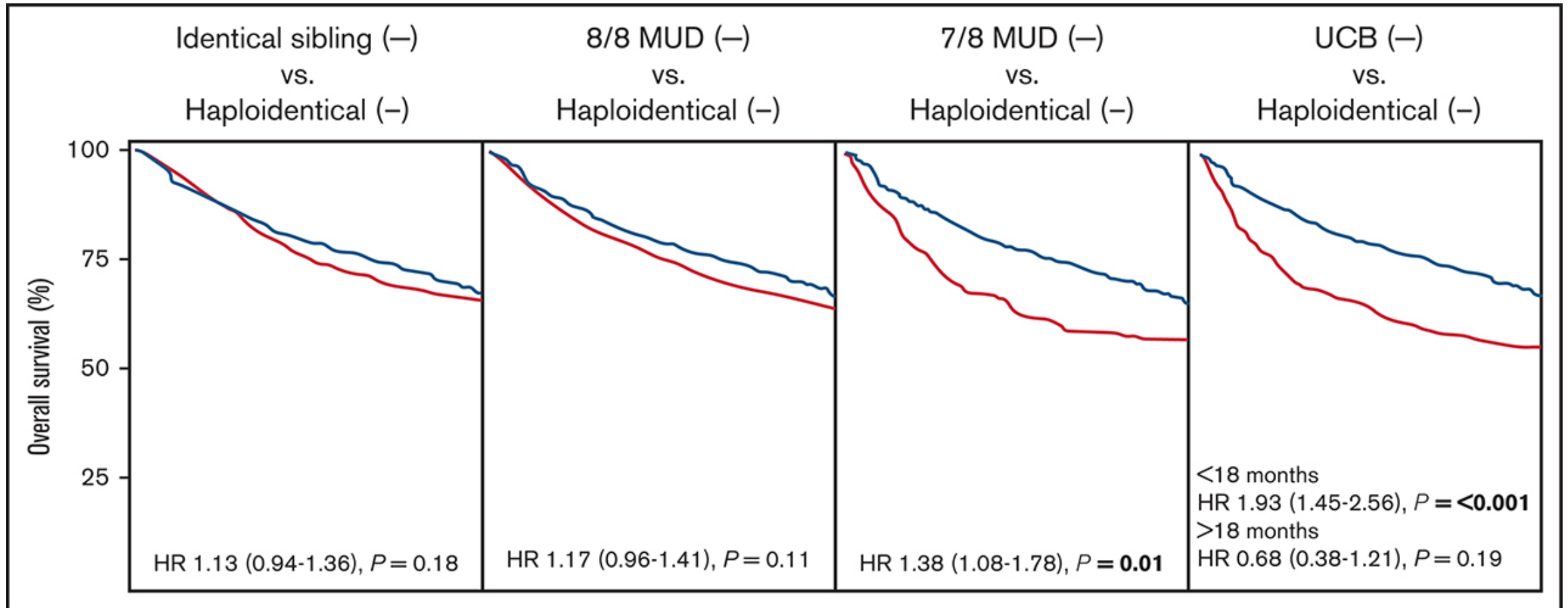
8% unknown

Survival after allo-transplant varies by race, likely as a consequence of different successes in finding HLA matched donors across different racial/ethnic groups

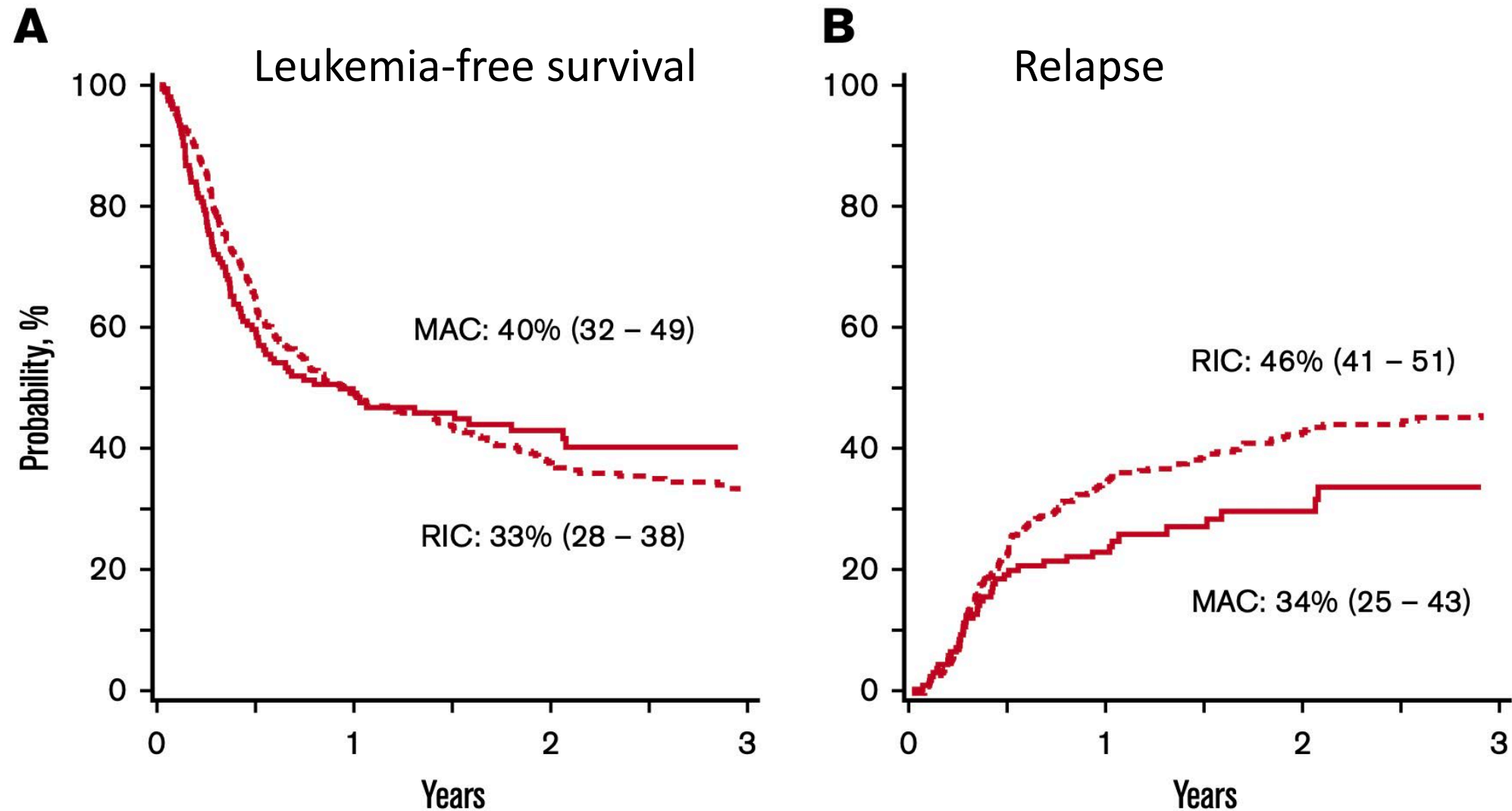
Survival after Allogeneic HCTs for Acute Lymphoblastic Leukemia (ALL), Age ≥ 18 Years, in the US, 2009-2019



Haplo-transplants yield equivalent or better outcomes as other donor sources in ALL patients

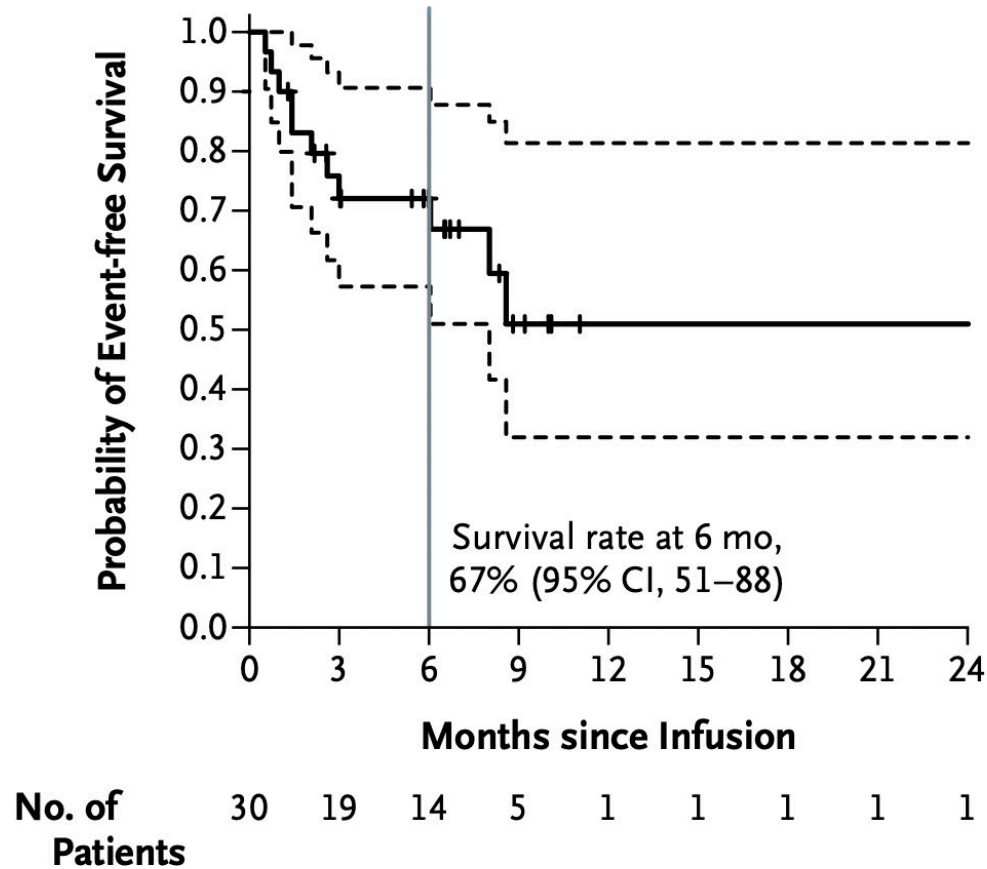


Equivalent LFS in older ALL patients conditioned with MAC or RIC and transplanted with a haplo-identical donor

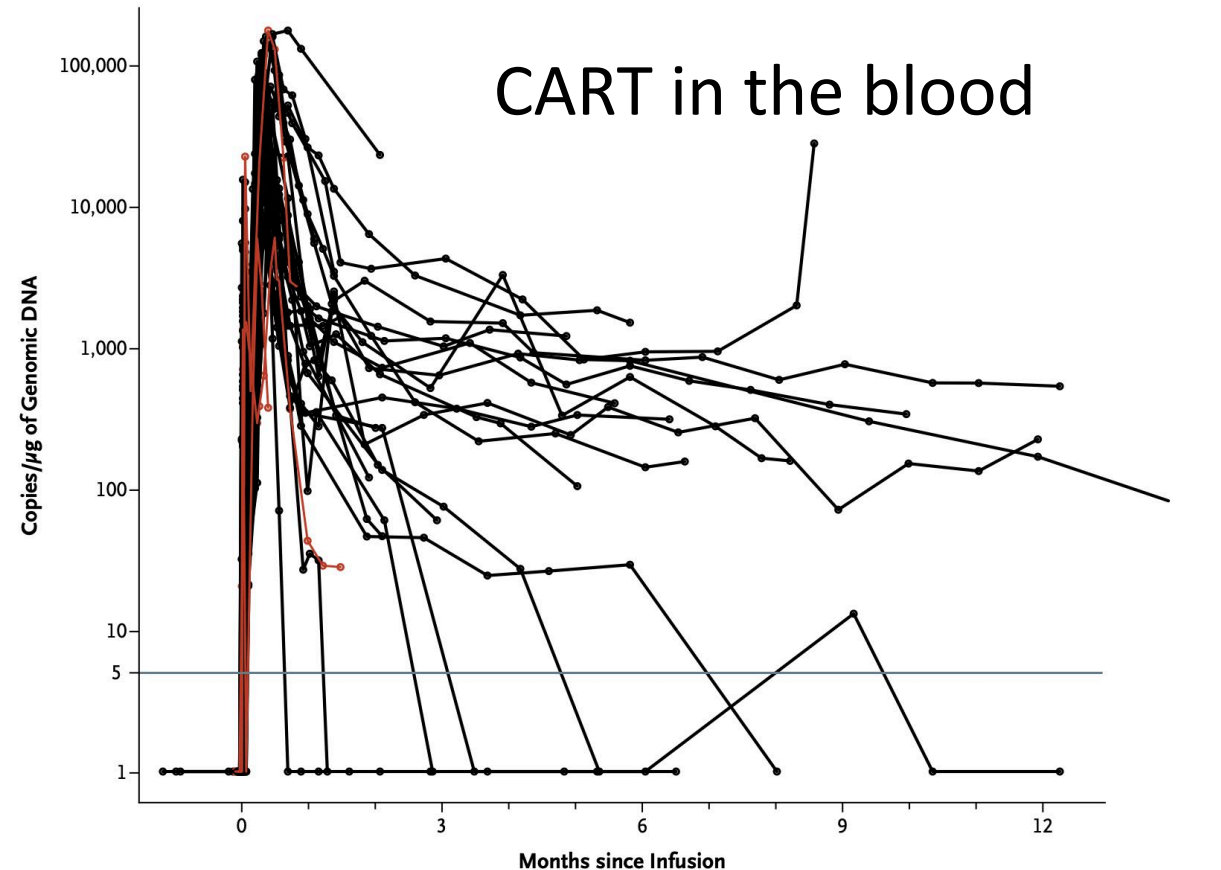


CD19 41BB CART produce durable remissions in pediatric ALL but at the cost of long-term B cell aplasia

A

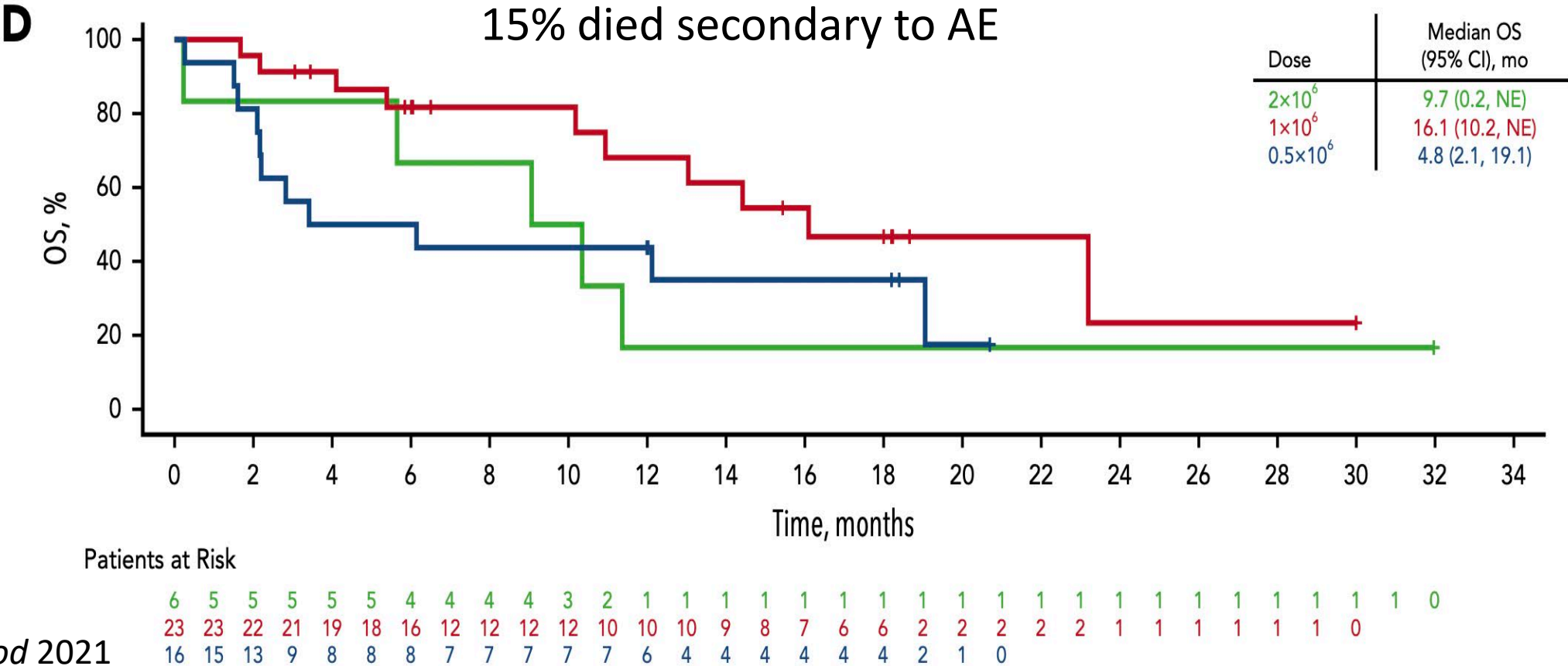


C Levels of CTL019 DNA in Peripheral Blood



FDA approved brexucabtagene autoleucel CART for adults based upon ZUMA-3 phase 1/2 clinical trial

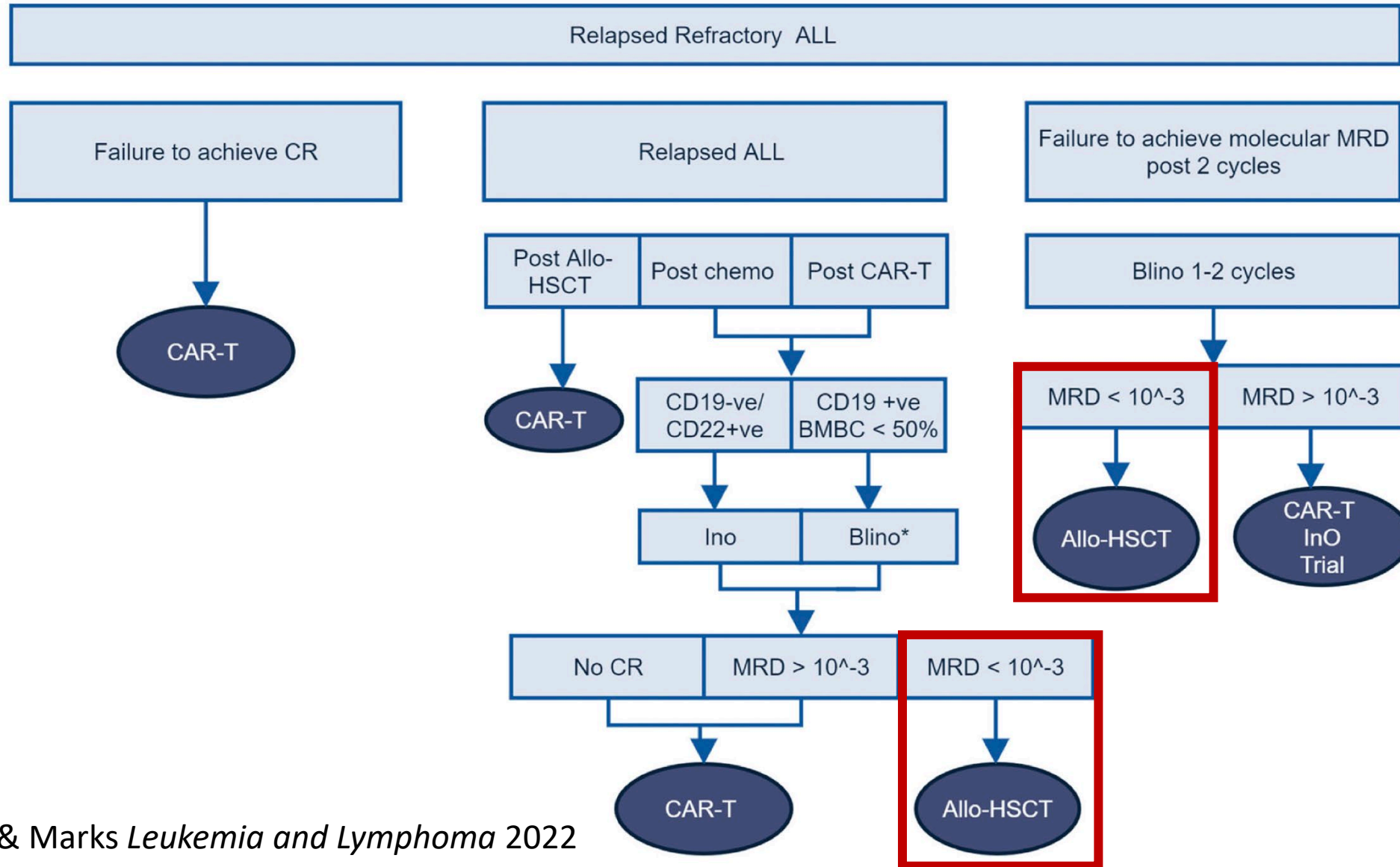
42% died due to disease progression
15% died secondary to AE



Only about ¼ of adult ALL patients have PFS at 1 year with 40% having grade ¾ CRS and/or grade ¾ neurotoxicity

	Complete remission	Minimal residual disease negative	Overall survival at 1 year after anti-CD19 CART-cell infusion	Progression-free survival at 1 year after anti-CD19 CART-cell infusion	Cytokine release syndrome	Grade 3 or 4 cytokine release syndrome	Neurotoxicity	Grade 3 or worse neurotoxicity
Age group								
Adults (N=263)	75.3% (66.9–82.9)	61.0% (45.5–75.7)	48.5% (39–58.1)	28.3% (11.9–47.8)	79.2% (56.2–96.1)	29.1% (11.0–50.8)	15.3% (2.2–34.2)	10.4% (1.8–22.9)
Children (N=346)	80.5% (72.9–87.2)	74% (64.8–82.3)	61.7% (50.9–71.9)	46.3% (37.0–55.7)	86.5% (68.3–98.4)	23.1% (13.7–33.7)	43.0% (31.6–54.6)	14.7% (8.9–21.6)
p value	0.24	0.11	0.069	0.10	0.50	0.52	0.020	0.77

Allo-transplant is recommended treatment for MRD(-) r/r ALL



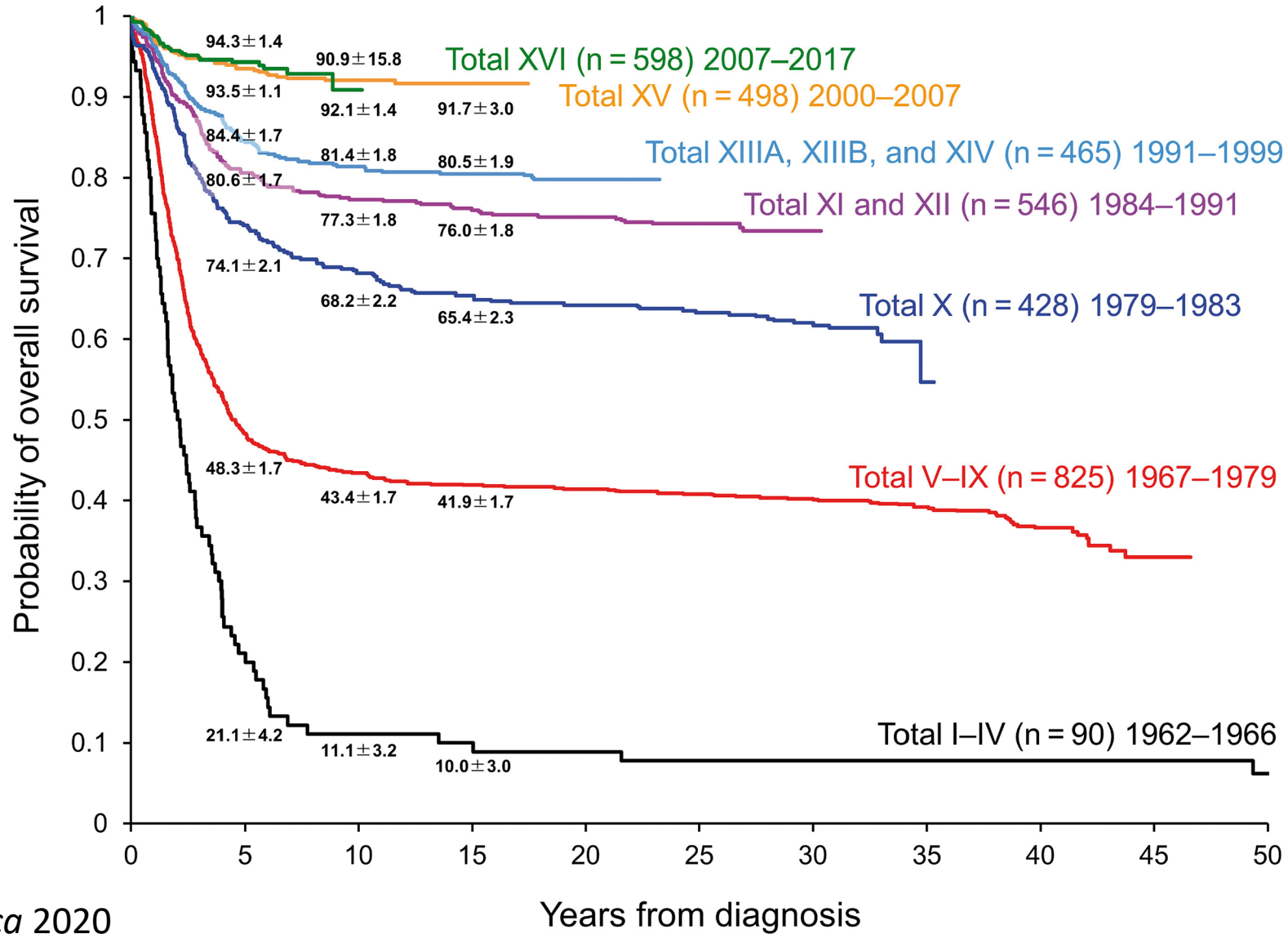
Summary of CART for ALL

- Pediatric ALL versus adult ALL
 - 46% 1-year PFS in r/r pediatric patients treated with CART
 - 28% 1-year PFS in r/r adult patients treated with CART
- CART as a “bridge to transplant”
 - 10% of pediatric Elaina patients in CR received allo-HSCT
 - 18% of adult ZUMA-3 patients in CR received allo-HSCT
- CART versus allo-transplant
 - ZUMA-3 shows 20% 2-year survival in r/r adult patients
 - Allo-transplant yields 30% 5-year survival for patients with r/r disease
 - CART in pediatric patients with r/r ALL yields ~50% long term PFS
 - Allo-HSCT in pediatric patients with r/r ALL results in 5—60% 5-year survival

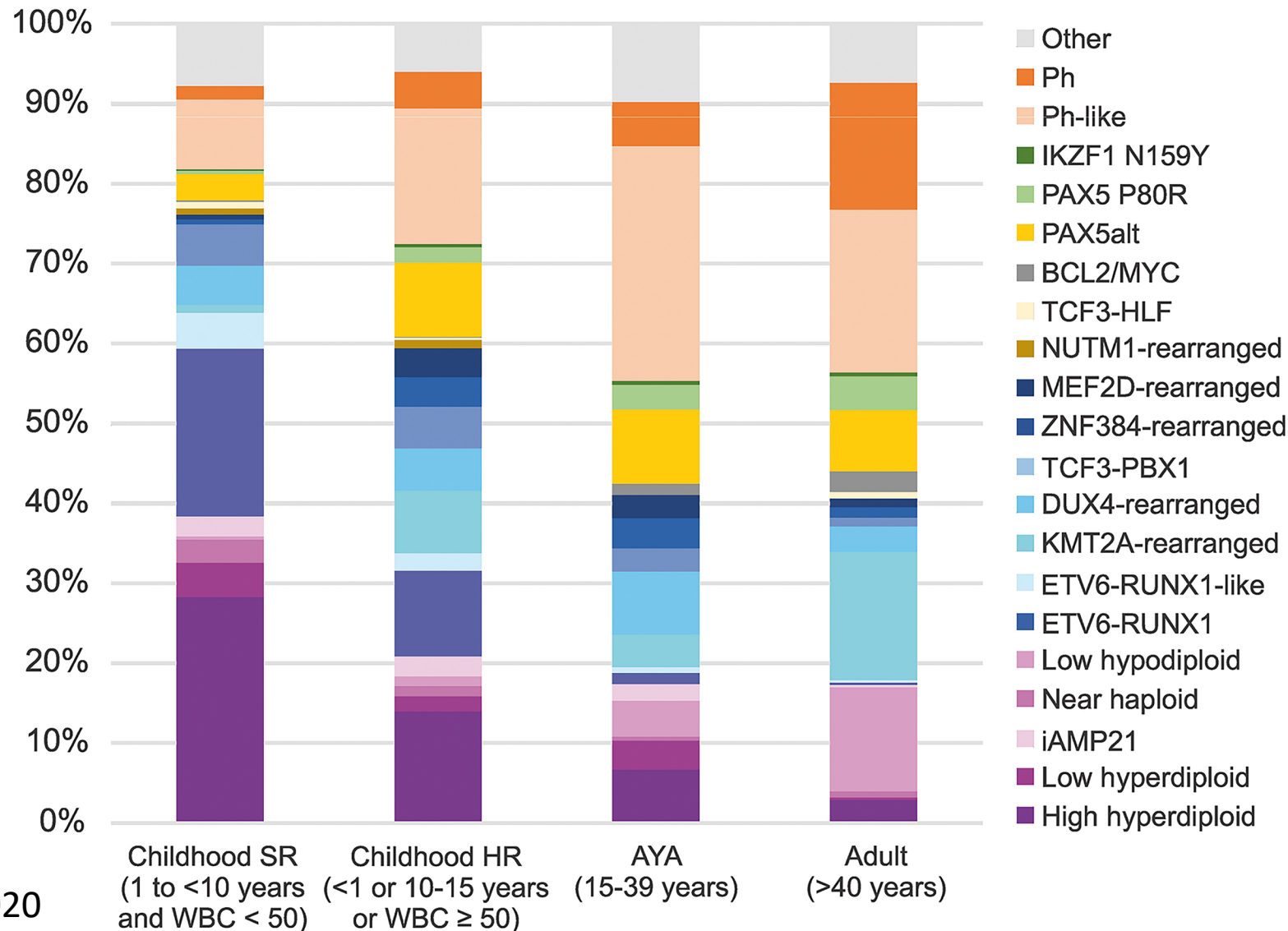
Questions?



Outcomes for pediatric ALL after chemotherapy have improved so much, there is less need for CART or allo-transplant.



Increasing frequency of Ph+ and Ph-like genetic subtypes in older ALL patients



Outcomes for adults with ALL treated with chemotherapy are inferior due, in part, to increased frequency of adverse genetic features in older patients

