La terapia cellulare CAR-T è più efficace del trapianto autologo nella terapia di seconda linea dei linfomi B a grandi cellule ricaduti precocemente?

Le ragioni del no

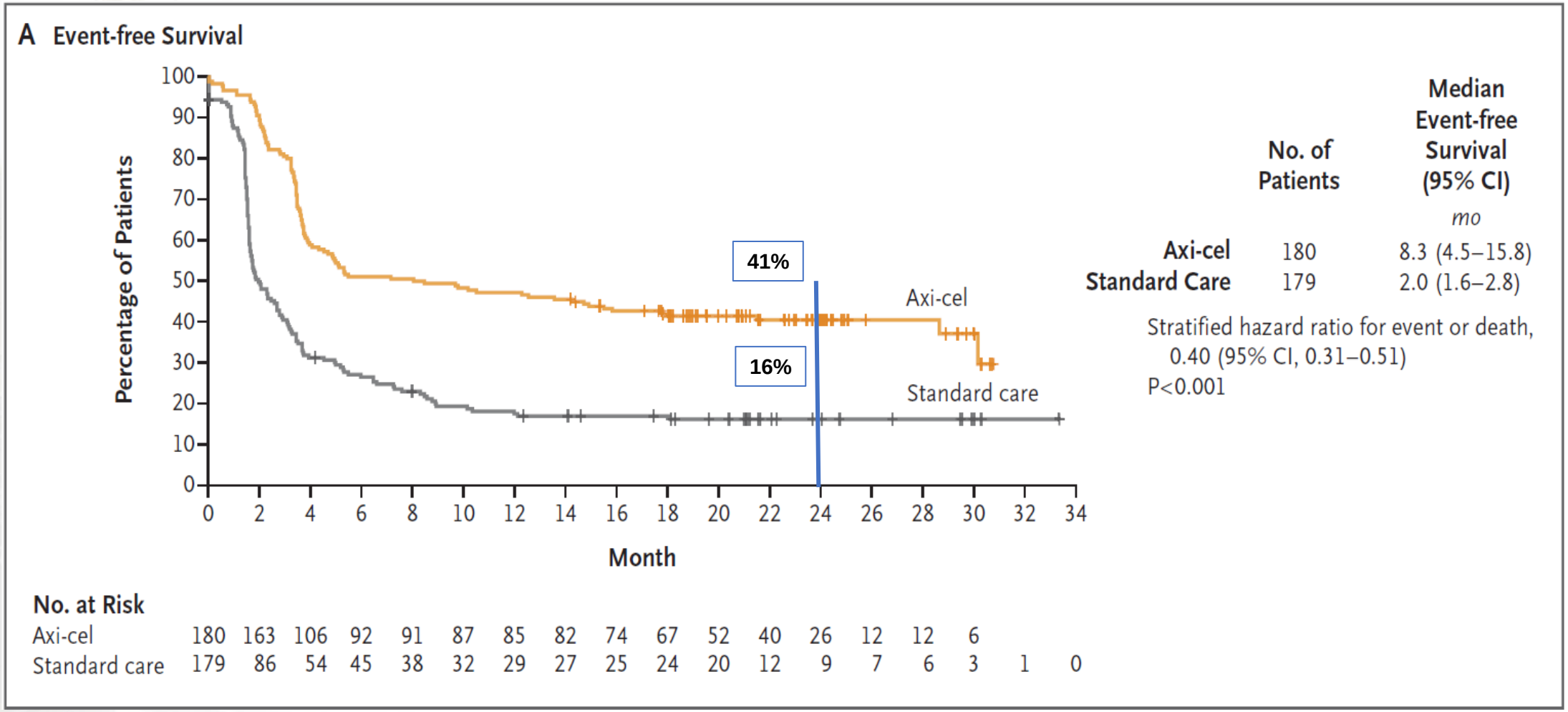
Luca Castagna, MD

Ospedale Cervello, Palermo

NOME COMMERCIALE	INN*	INDICAZIONE	SOMMINISTRAZIONE E VETTORE	AZIENDA	APPROVAZIONE EUROPEA	AIC* IN EUROPA	AIC* IN ITALIA
Kymriah®	tisagenlecleucel	**leucemia linfoblastica acuta a cellule B** e **linfoma diffuso a grandi cellule B**	**ex vivo** lentivirus	Novartis Europharm Limited	**agosto 2018** farmaco orfano	✓	✓ Classe H* **agosto 2019**
		linfoma follicolare recidivante o refrattario			**maggio 2022**	✓	✓
Yescarta®	axicabtagene ciloleucel	**linfoma diffuso a grandi cellule B** e **linfoma primitivo del mediastino a grandi cellule B refrattari o recidivanti**	**ex vivo** retrovirus	Kite Pharma EU	**agosto 2018** farmaco orfano	✓	✓ Classe H* **novembre 2019**
		linfoma follicolare recidivante o refrattario			**giugno 2022**	✓	✗
		linfoma diffuso a grandi cellule B e **linfoma a cellule B di alto grado** con ricaduta entro 12 mesi o refrattari			**ottobre 2022**	✓	✗
Tecartus™	brexucabtagene autoleucel	**linfoma a cellule mantellari** recidivante o refrattario	**ex vivo** retrovirus	Kite Pharma EU	**dicembre 2020** farmaco orfano	✓	✓ Classe H* **marzo 2022**
		leucemia linfoblastica acuta da precursori delle cellule B recidivante o refrattaria			**settembre 2022**	✓	✗
Breyanzi®	lisocabtagene maraleucel	**DLBCL, linfoma primitivo del mediastino a grandi cellule B** e **linfoma follicolare**	**ex vivo** lentivirus	Bristol-Myers Squibb / Celgene	**aprile 2022**	✓	✗
		linfoma a grandi cellule B refrattario o recidivante			**luglio 2023**	✓	✗

Dati OTA, settembre 2023

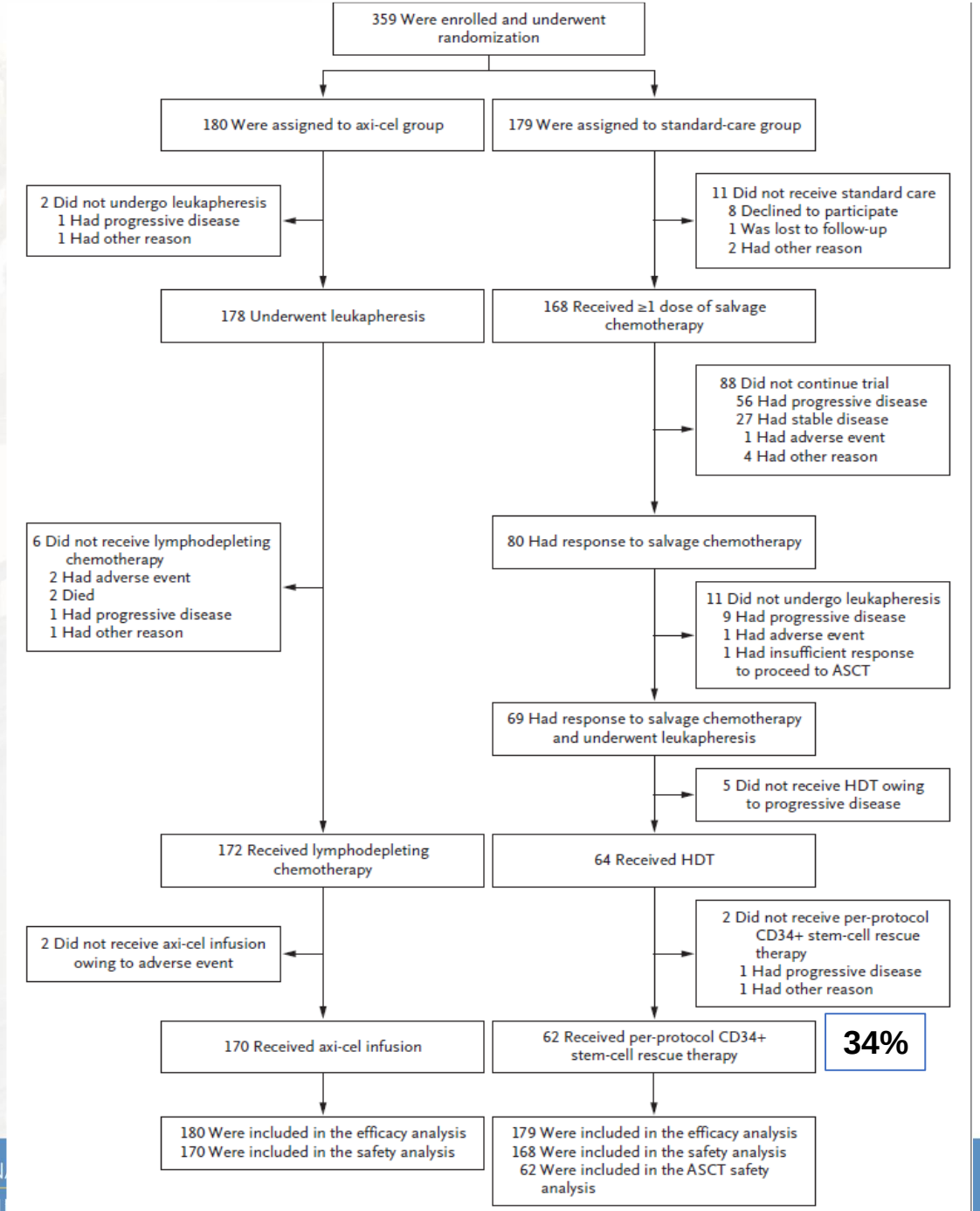
ZUMA7



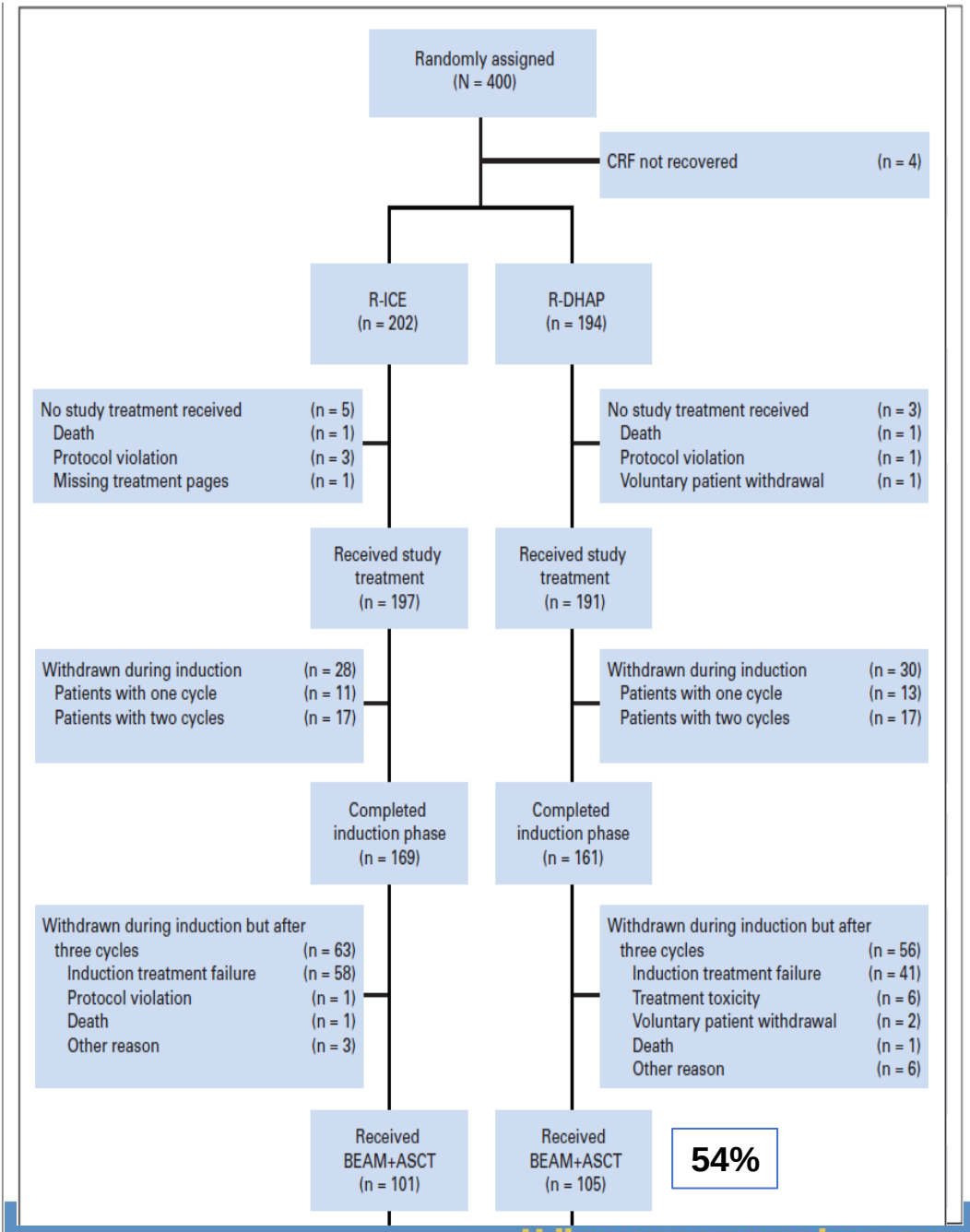
Locke, NEJM 2021

ZUMA7

13 days

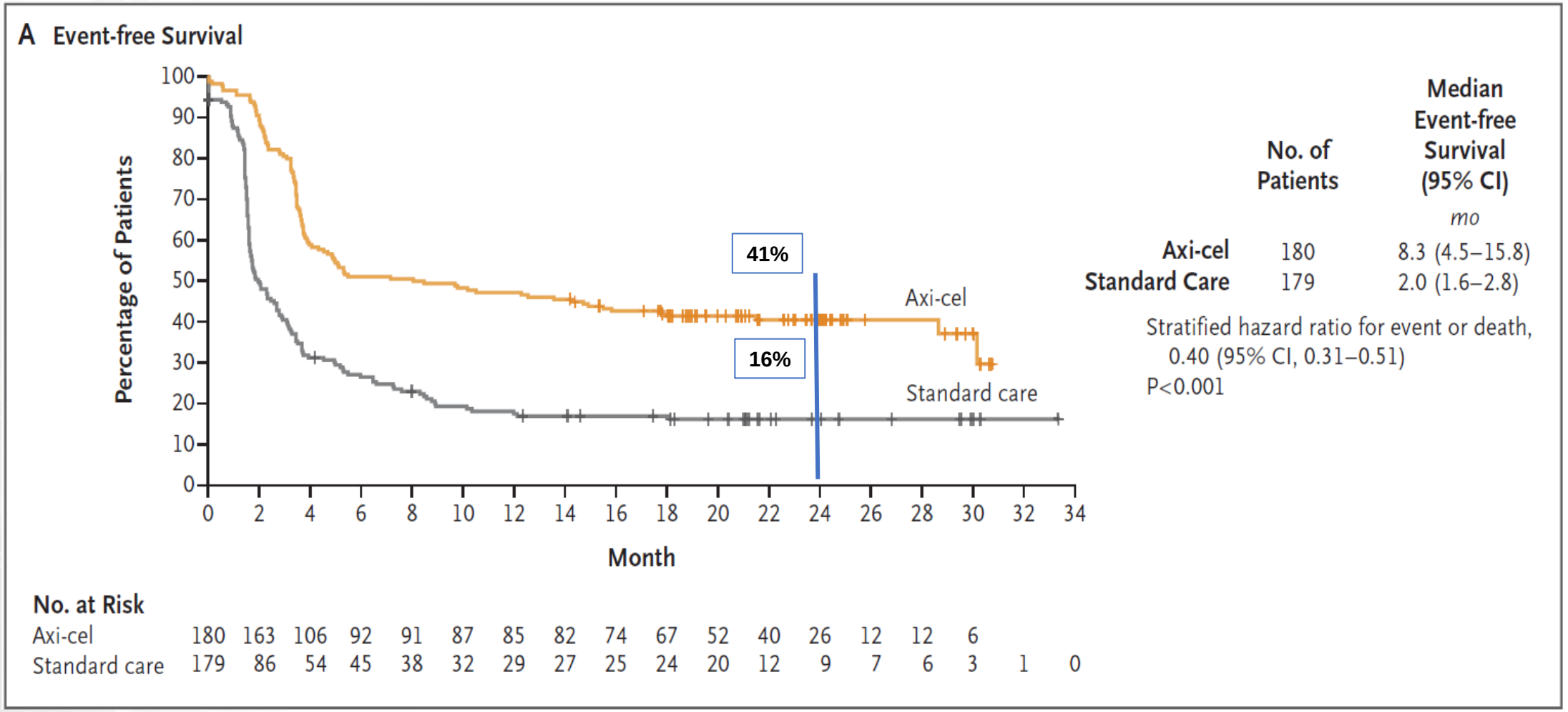


Locke, NEJM 2021



Gisselbrecht, JCO 2010
Crump, JCO 2014

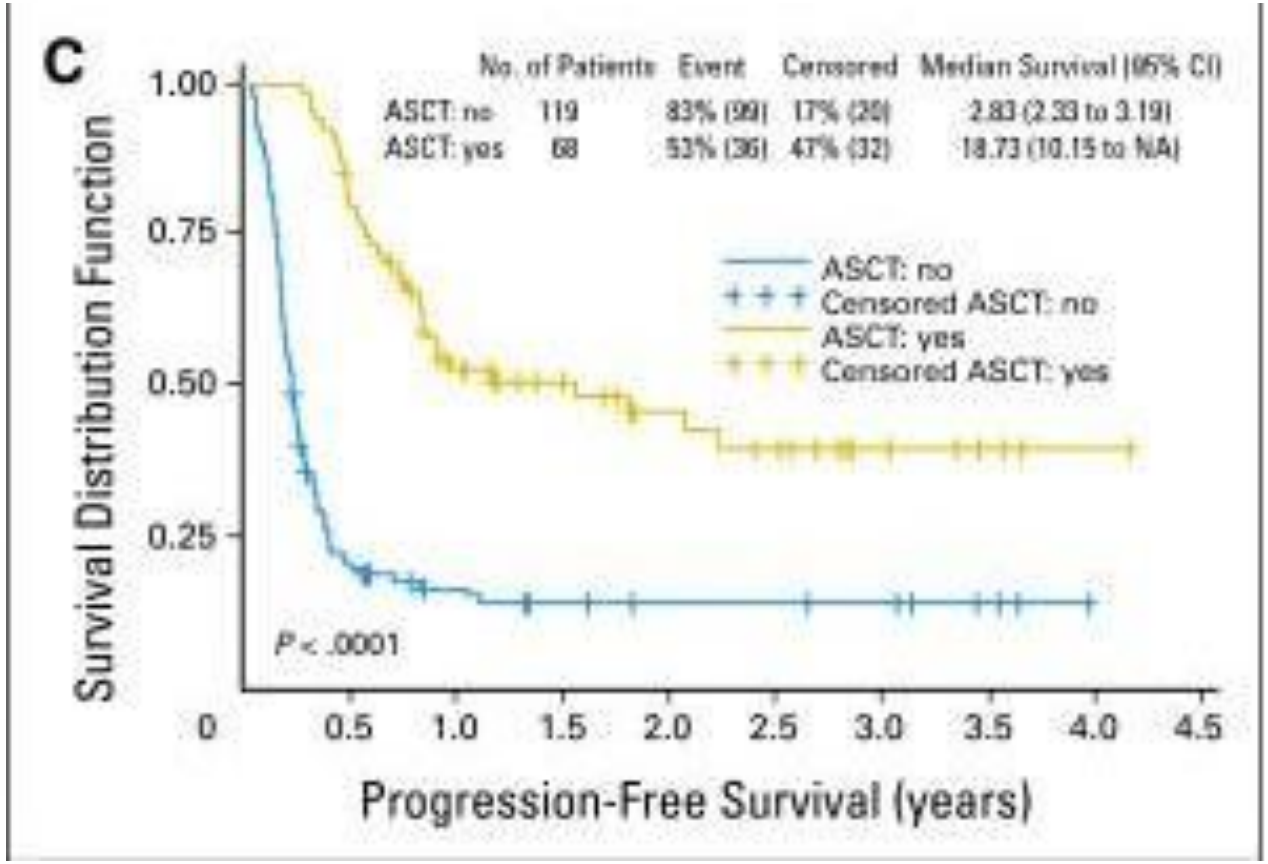
ZUMA7



Locke, NEJM 2021

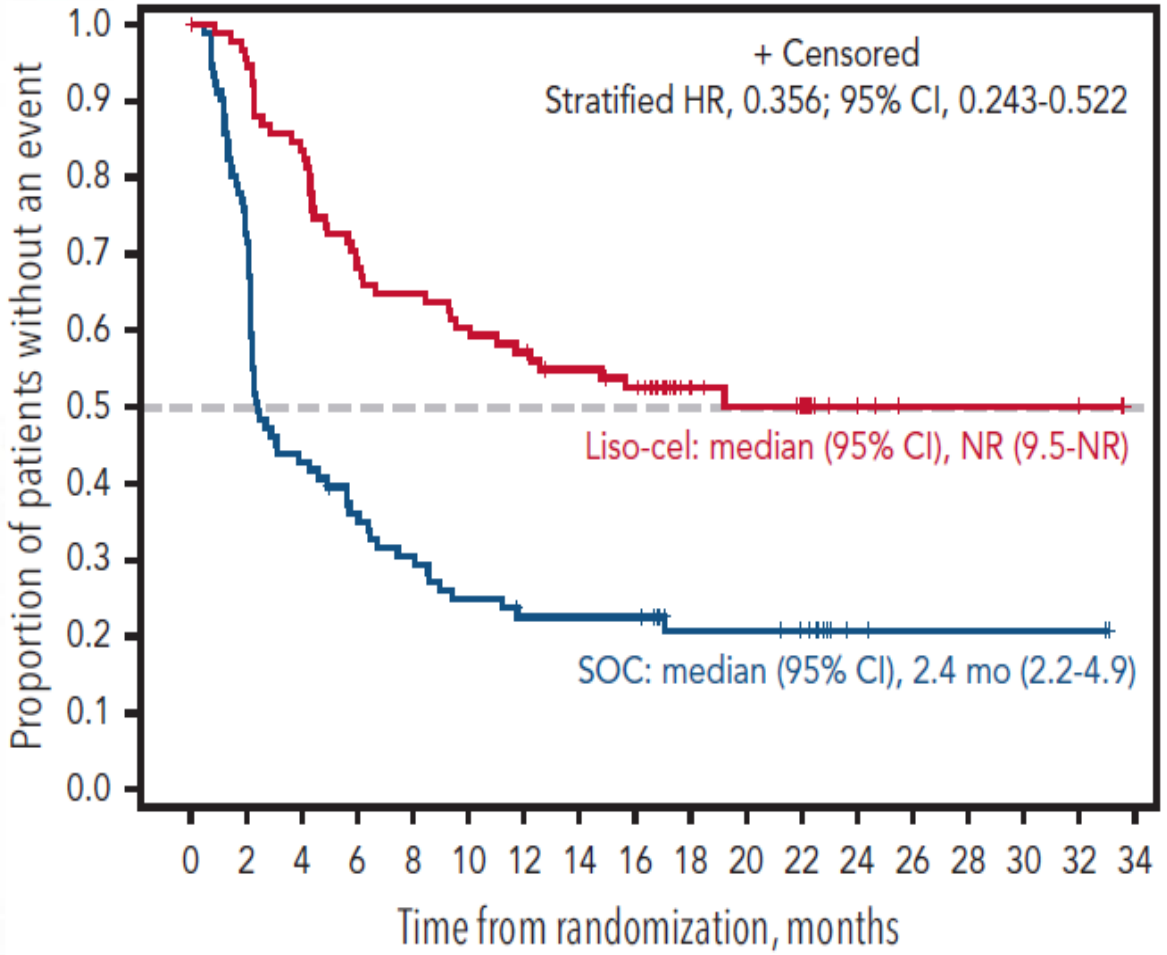
CORAL study: HDC in poor prognosis DLBCL

Patients in CR/PR after salvage CT



Gisselbrecht, JCO 2010

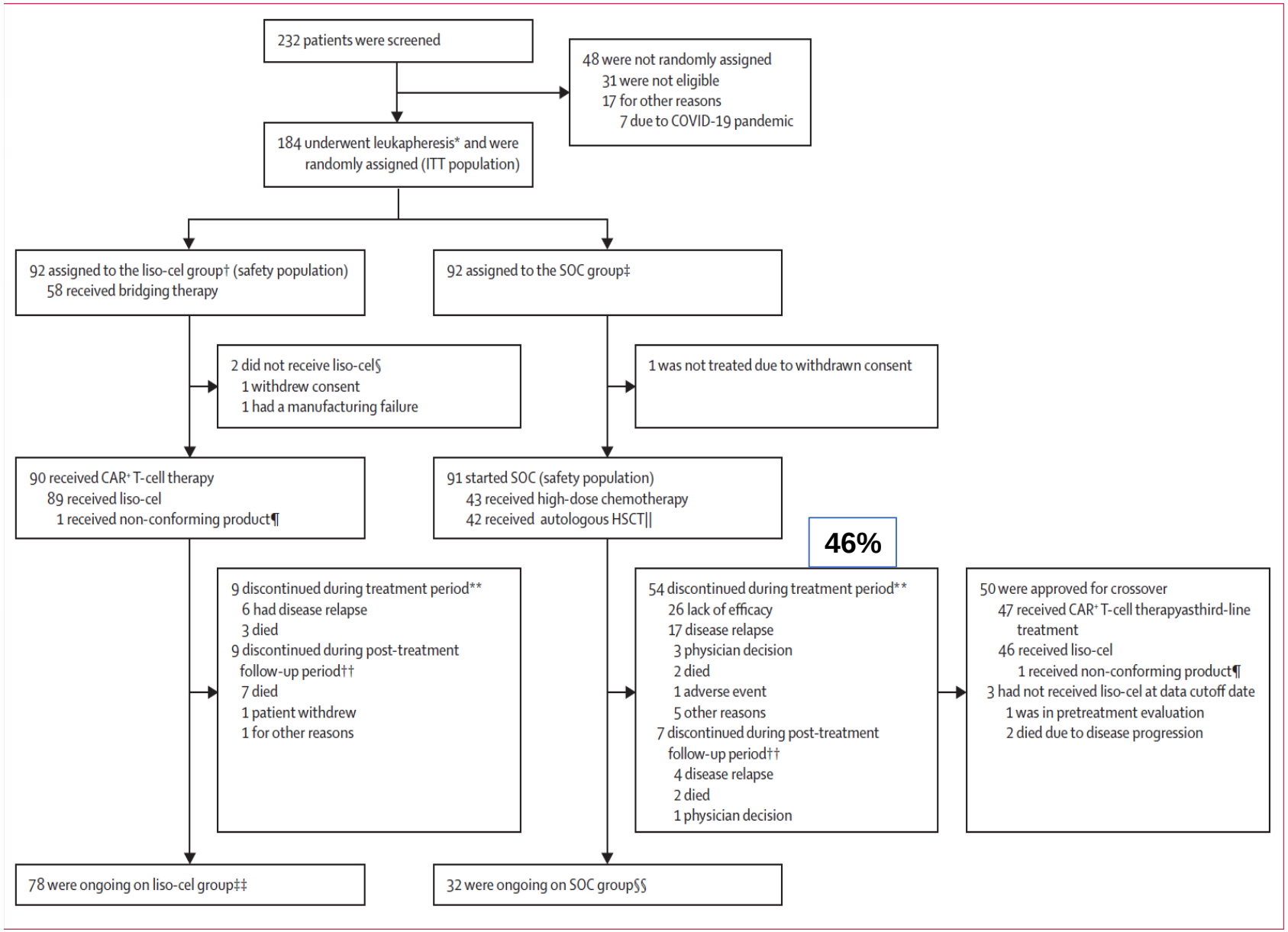
TRANSFORM



Abramson, Blood 2023

TRANSFORM

36 days



Kamdar, Lancet Haematol 2022

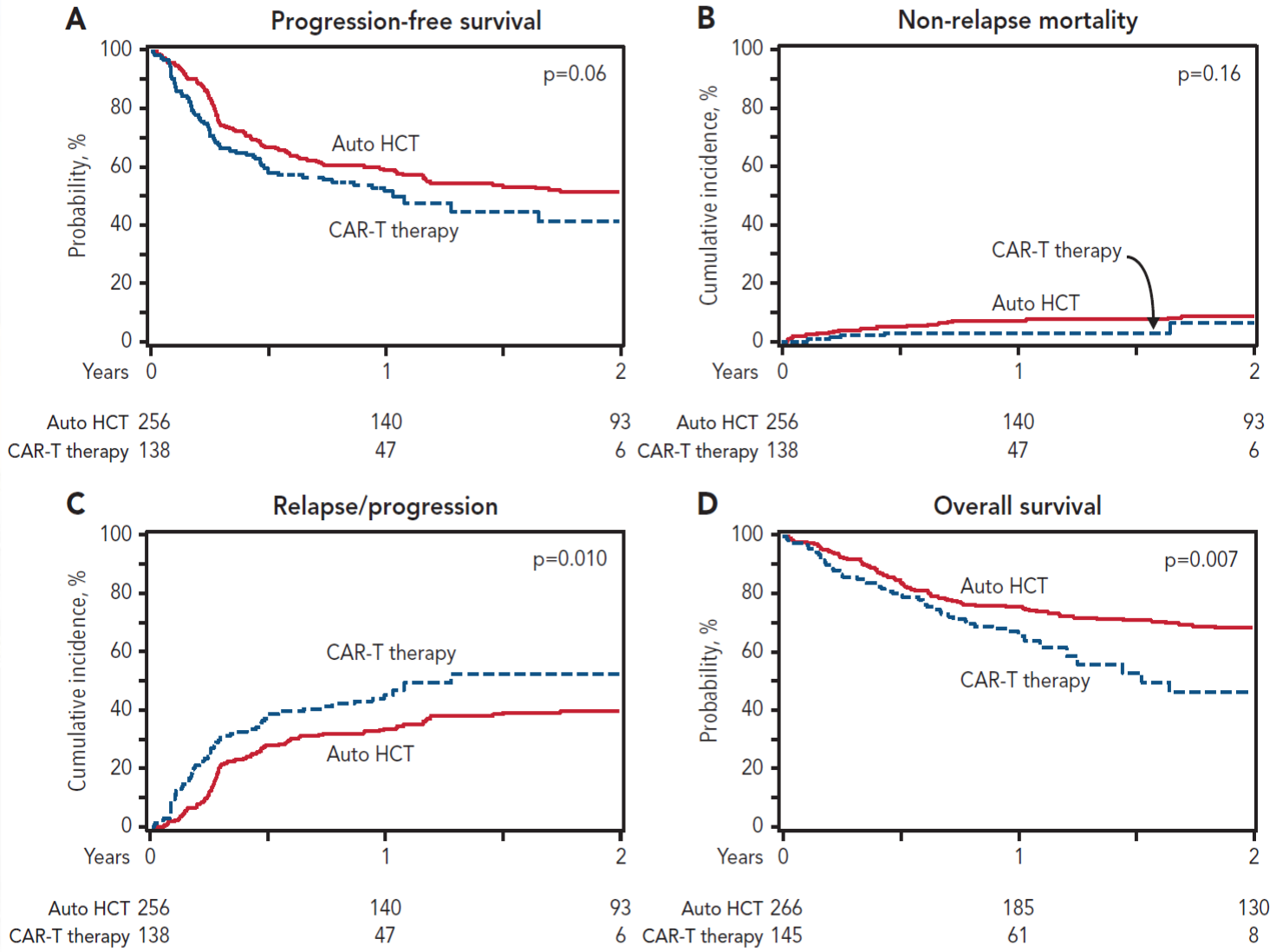
TRANSFORM

	Liso-cel group (n=92)	Standard-of-care group (n=92)	Stratified HR (95% CI)*	p value
Duration of response for patients who achieved a complete response				
Number of patients with events	14 (15%)	12 (13%)	..	
Duration (95% CI), months	NR (6·8–NR)	14·5 (4·7–NR)	0·65 (0·30–1·43)	
6-month duration (95% CI‡)	71·0% (56·1–86·0)	65·9% (47·2–84·5)	..	
12-month duration (95% CI‡)	62·1% (44·6–79·6)	54·7% (33·7–75·7)	..	

Kamdar, Lancet Haematol 2022

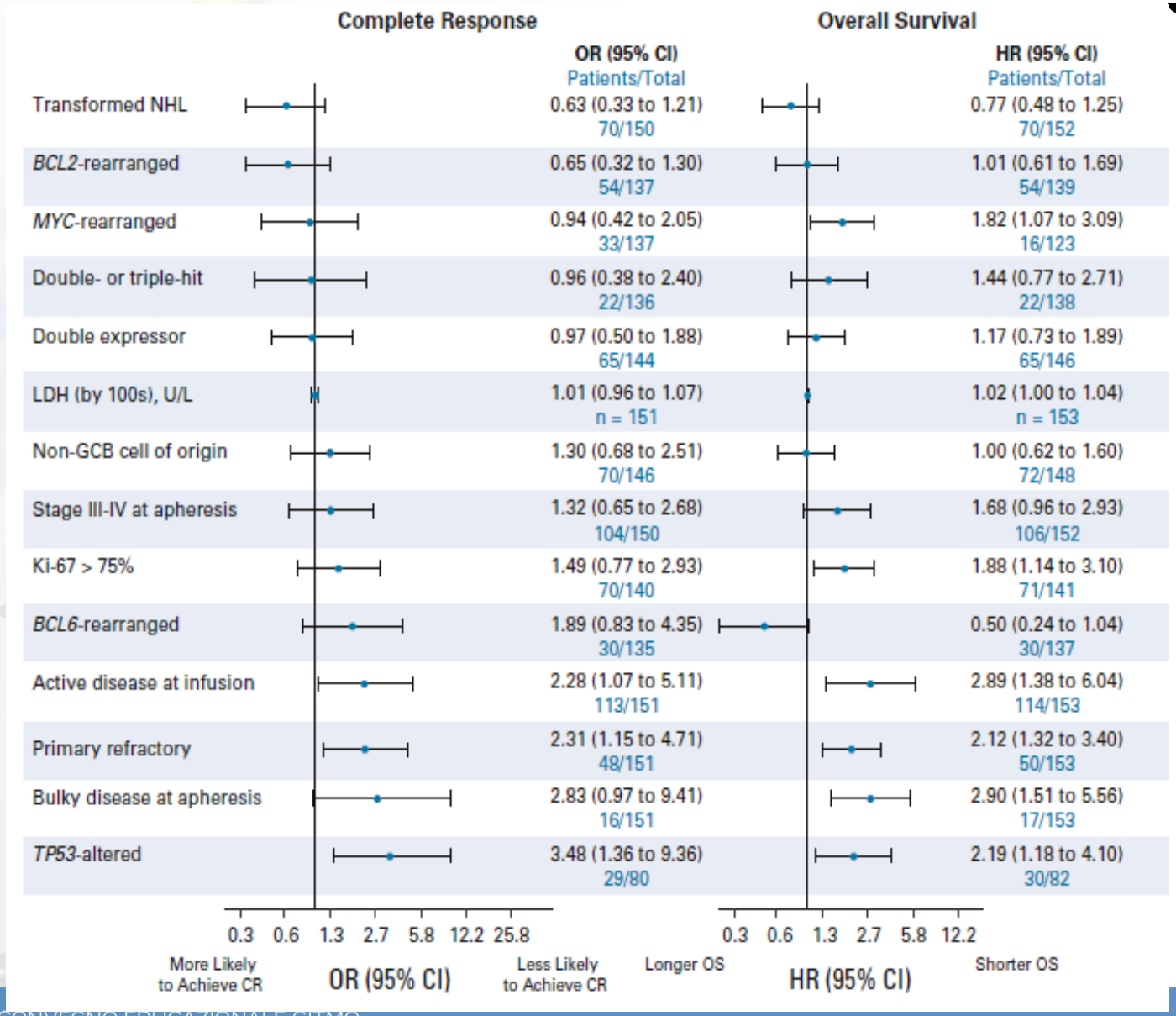
Disease status

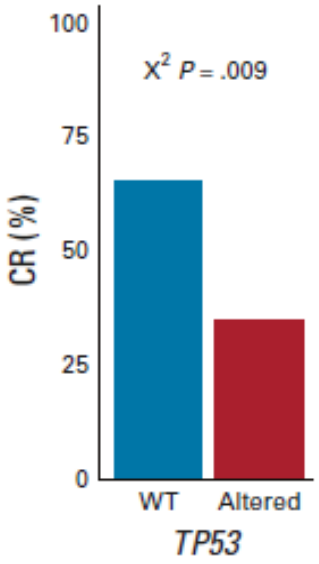
DLBCL in PR before HDC or CART (Axi-cel)

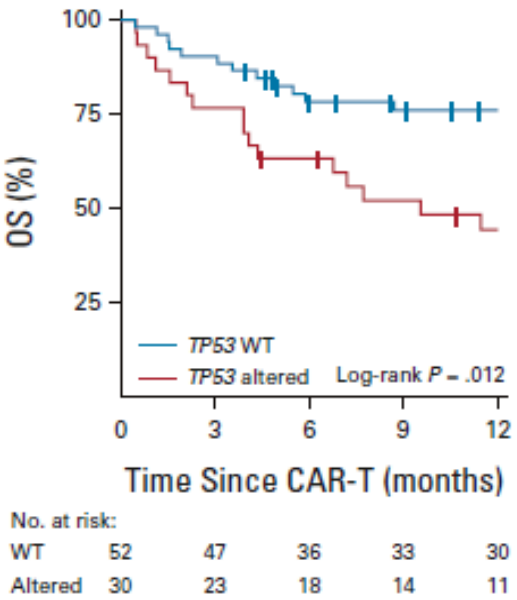


Shadman, Blood 2022

Disease heterogeneity







Shouval, JCO 2022

Conclusions 1

Patients RR LBCL achieving CR/PR after salvage CT can be offered HDC

More effective salvage CT can improve the proportion of responding patients

Subgroups of patients can be less susceptible to CART

However,

Conclusions 2

Disease	Disease status	MSD allo	MUD allo	MMAD allo	Auto	CAR-T
Haematological malignancies						
LBCL	CR1 (intermediate/high IPI at diagnosis)	GNR/III	GNR/III	GNR/III	CO/I	GNR/III
	Untested relapse	GNR	GNR	GNR	GNR	S/I
	Chemosensitive early relapse, ≥CR2	CO/II	CO/II	D/III	CO/I	S/II
	Chemosensitive late relapse, ≥CR2	CO/II	CO/II	D/III	S/II	CO/II
	Chemosensitive relapse after auto-HSCT failure	CO/II	CO/II	CO/III	GNR/III	S/II
	Refractory disease	CO/II	CO/II	CO/III	GNR/I	S/I
	Primary CNS lymphoma	GNR/III	GNR/III	GNR/III	S/II	D/III

Snowden, BMT 2022