

# Erfaringer fra CAR-T studier og klinisk praksis maligne lymfomer

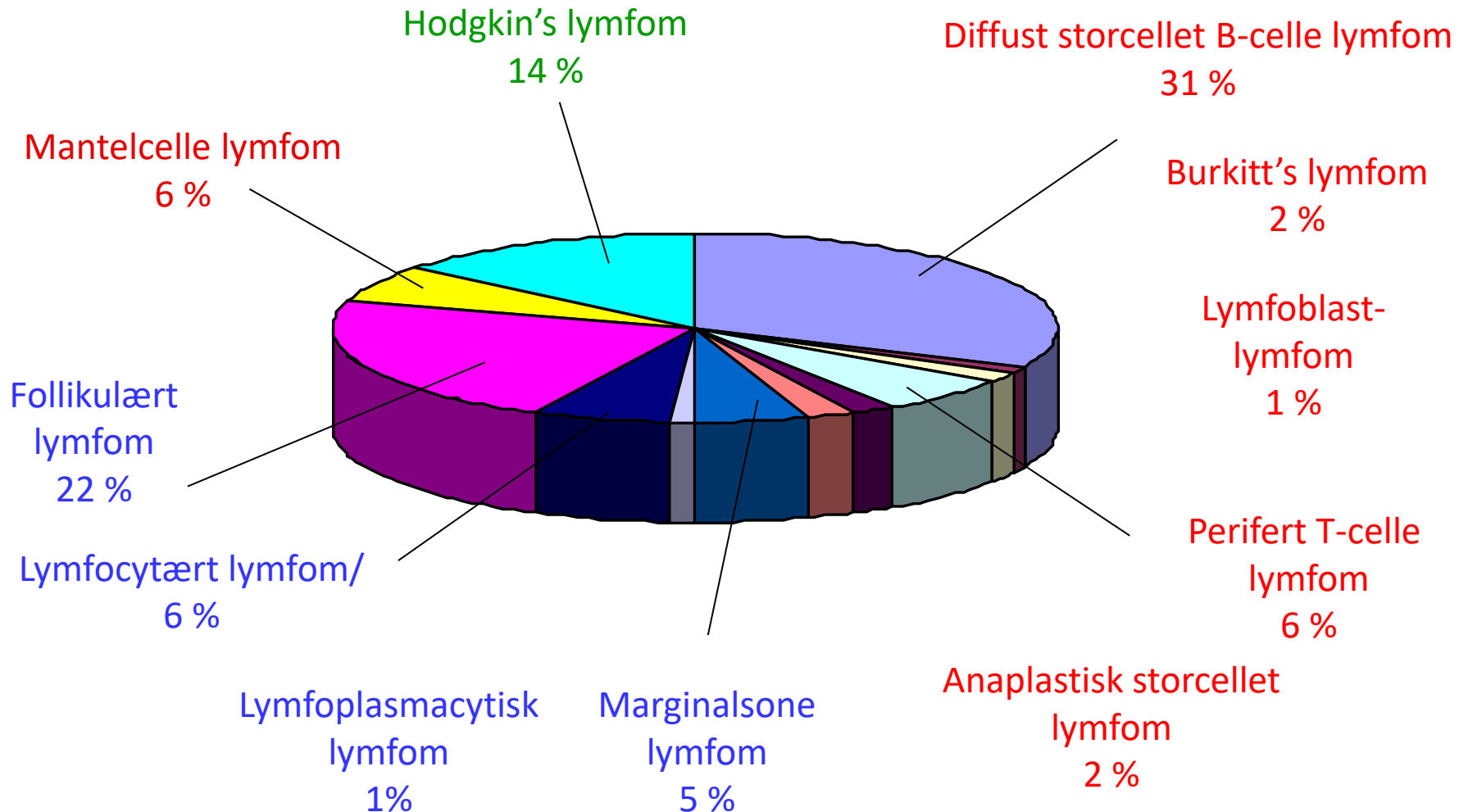
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# Disclosures

J&J	Honoraria
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MSD	Honoraria
BMS	Honoraria
Kyowa Kirin	Honoraria
Kite Gilead	Honoraria
EUSA Pharma	Honoraria and research support

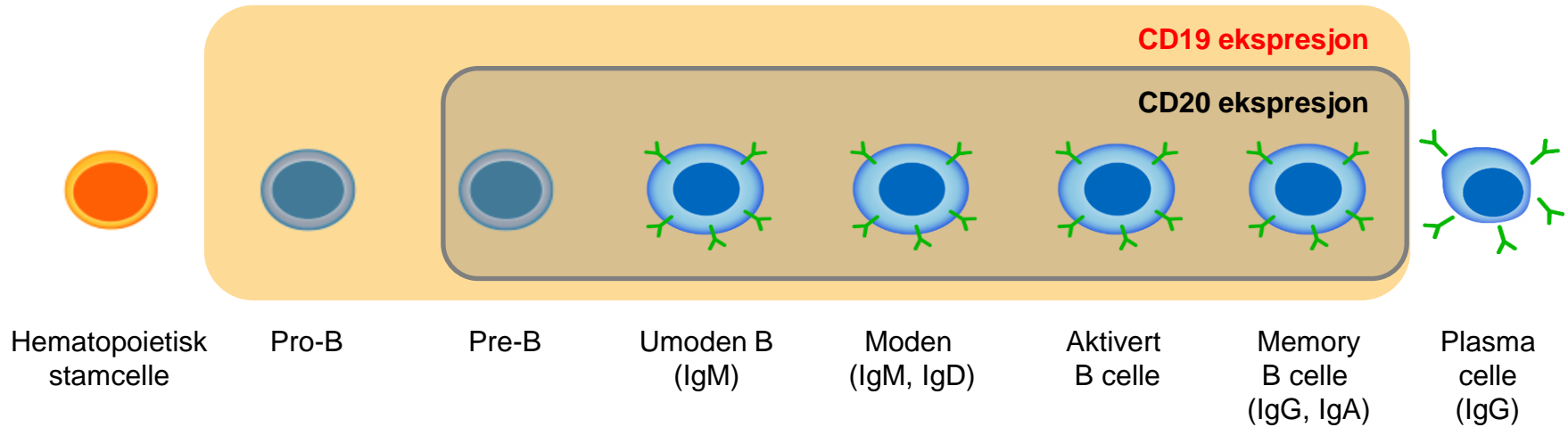


# Lymfomer for dummies...



Adaptert fra Nasjonalt handlingsprogram maligne lymfomer, januar 2019

# CD19 og CD 20: Gode mål for immunterapi ved B-celle neoplasier



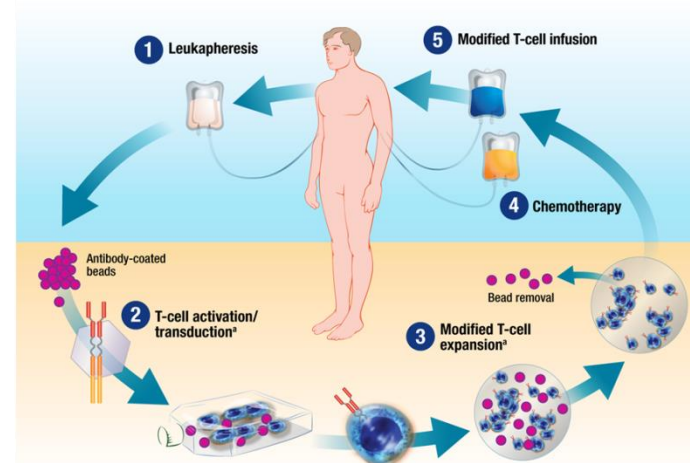
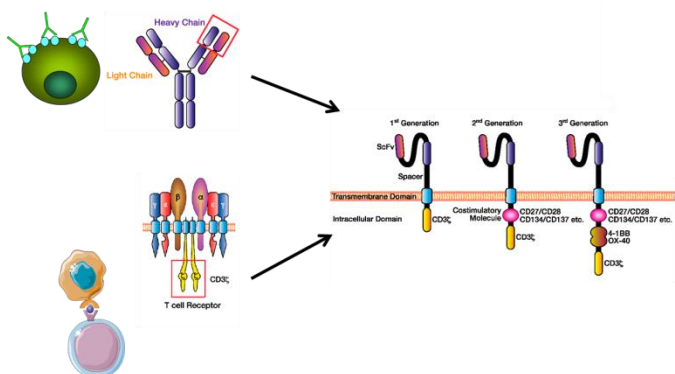
- CD19/CD20 ekspresjon er begrenset til B-celler og B-celle forstadier<sup>1</sup>
  - er ikke uttrykt på hematopoietiske stamceller eller plasmaceller<sup>1</sup>
- CD19/CD 20 er uttrykt på de fleste B-celle neoplasier
  - Kronisk og akutt lymfatisk leukemi, diffust storcellet B-celle lymfom, follikulært lymfom, mantelcelle lymfom...<sup>1</sup>
- Mennesker kan klare seg over tid uten B-celler

1. Scheuermann RH, et al. *Leuk Lymphoma*. 1995;18:385-397

Image adapted from Janeway CA, Travers P, Walport M, et al. *Immunobiology*. 5th ed. New York, NY: Garland Science; 2001:221-293; Scheuermann RH, et al. *Leuk Lymphoma*. 1995;18:385-397; and Feldman M, Marini JC. Cell cooperation in the antibody response. In: Roitt I, Brostoff J, Male D, eds. *Immunology*. 6th ed. Maryland Heights, Missouri: Mosby;2001:131-146.

# CD 19 Kimær antigen reseptor T-celler

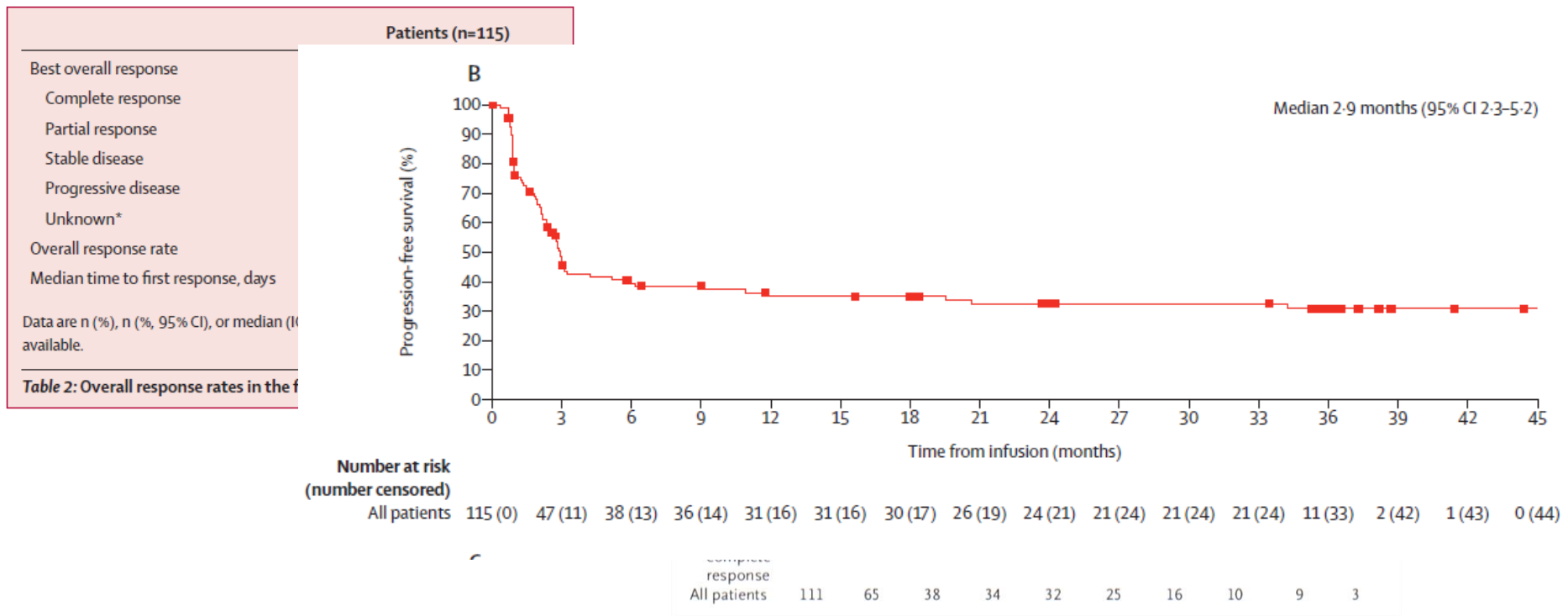
- Tisa-cel: Kymriah - Novartis
- Axi-cel: Yescarta – Kite Gilead
- Liso-cel: Bryanzi - BMS
- Brexu-cel: Tecartus – Kite Gilead



\* Cellular reprogramming and ex vivo expansion are conducted at a cell processing facility.

# JULIET: CAR19 for refraktært/residivert diffust storcellet B-celle lymfom, 3. linje

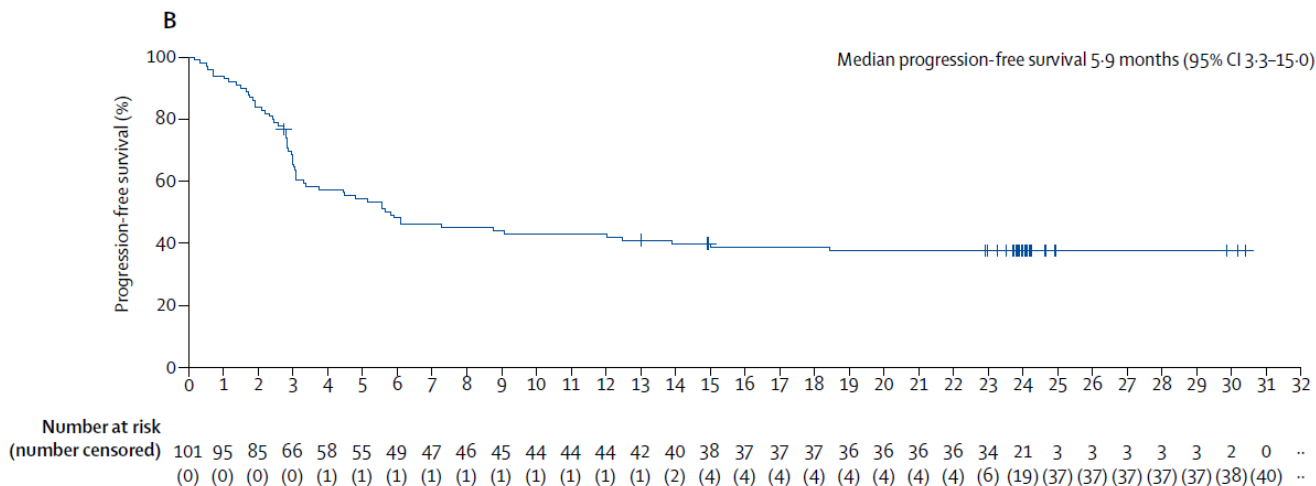
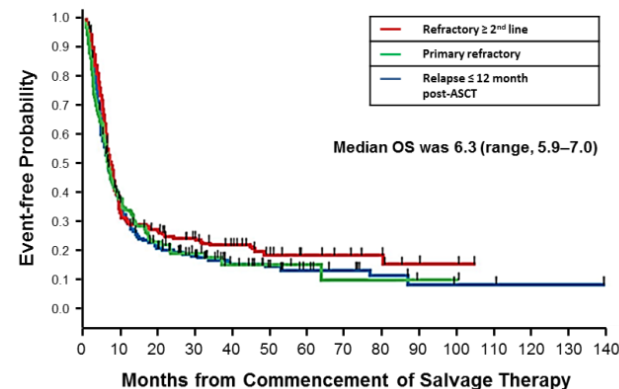
## Objektiv tumor respons



Schuster et al 2019; Schuster et al 2021

# Zuma-1: CAR19 for refraktært/residivert diffust storcellet B-celle lymfom, 3. linje

	Investigator-assessed (n=101)	IRC-assessed (n=101)
Objective response*	84 (83%)	75 (74%)
Complete response†	59 (58%)	55 (54%)
Partial response	25 (25%)	20 (20%)
Ongoing response‡	39 (39%)	36 (36%)
Complete response	37 (37%)	35 (35%)
Partial response	2 (2%)	1 (1%)



Locke et al 2019; Crump et al 2017

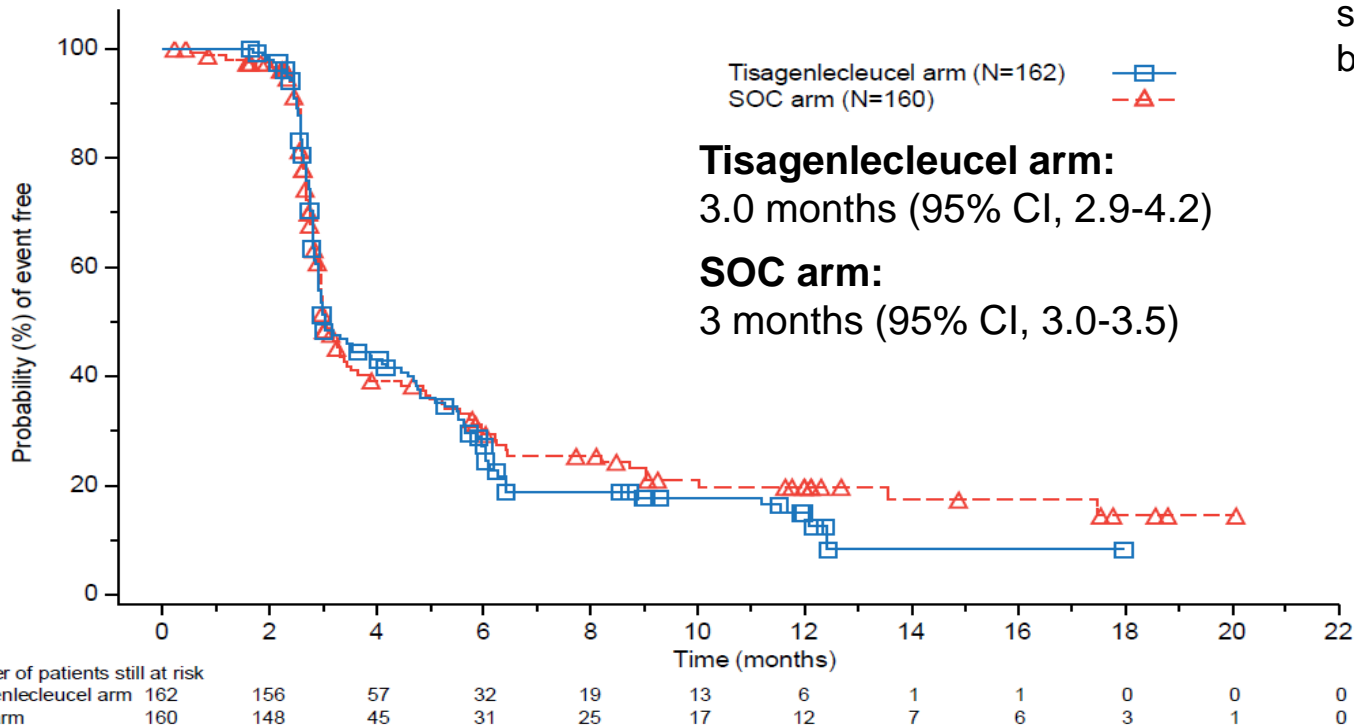
## Real world experience med CAR-T i DLBCL 3. linje

- Kommersielt produkt i de fleste land
- Tatt over for allogen transplantasjon
- Erfaringer om hvilke pasienter som profiterer mest
  - Lite tumorvolum
  - God almentilstand
- Rask utvidelse av kunnskap
  - Pasientseleksjon
  - Forbehandling “bridging therapy”



# BELINDA: CAR19 for refraktært/residivert diffust storcellet B-celle lymfom, 2. linje

## EFS per BIRC in Tisagenlecleucel and SOC Arms



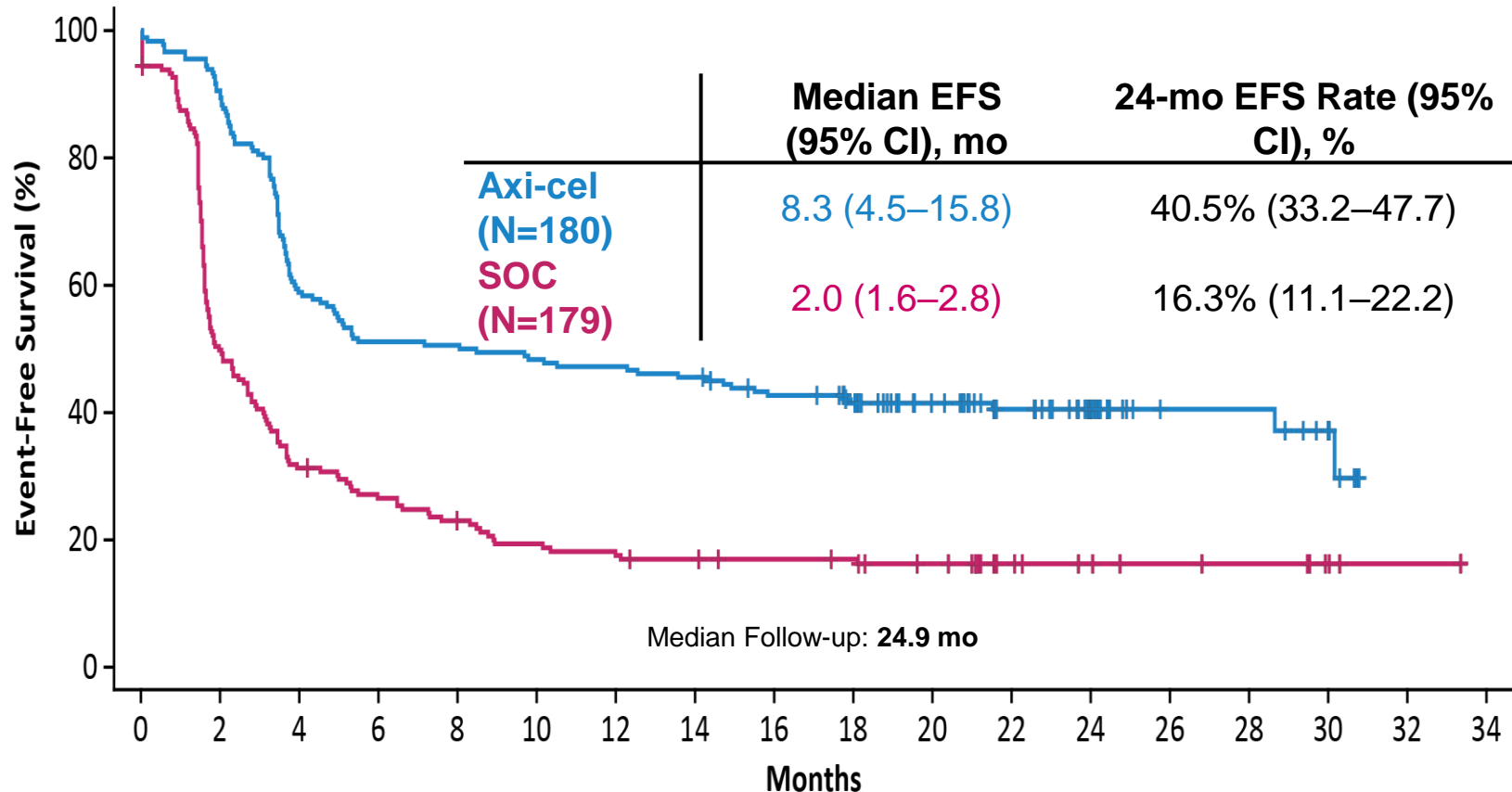
- Median EFS\* was not significantly different between treatment arms
  - Stratified unadjusted HR: 1.07 (95% CI, 0.82-1.40; stratified log-rank P=0.69, 1-sided)
  - Stratified adjusted HR: 0.95 (95% CI, 0.72-1.25)

\*EFS events defined as PD/SD after day 71 or death at any time (EFS at a given timepoint represents the estimated proportion of responders at this timepoint among all randomized patients)  
 BIRC, blinded independent review committee; CI, confidence interval; EFS, event-free survival; HR, hazard ratio; OS, overall survival; PD, progressive disease; SD, stable disease; SOC, standard of care.

Adapted from Bishop et al, ASH 2021

# Zuma-7: CAR19 for refraktært/residivert diffust storcellet B-celle lymfom, 2. linje

HR 0.398 (95% CI, 0.308–0.514);  $P < 0.0001$



No. at Risk

<b>Axi-cel</b>	180	163	106	92	91	87	85	82	74	67	52	40	26	12	12	6		
<b>SOC</b>	179	86	54	45	38	32	29	27	25	24	20	12	9	7	6	3	1	0



# ELARA-Tisa-cel in relapsed/refractory follicular lymphoma

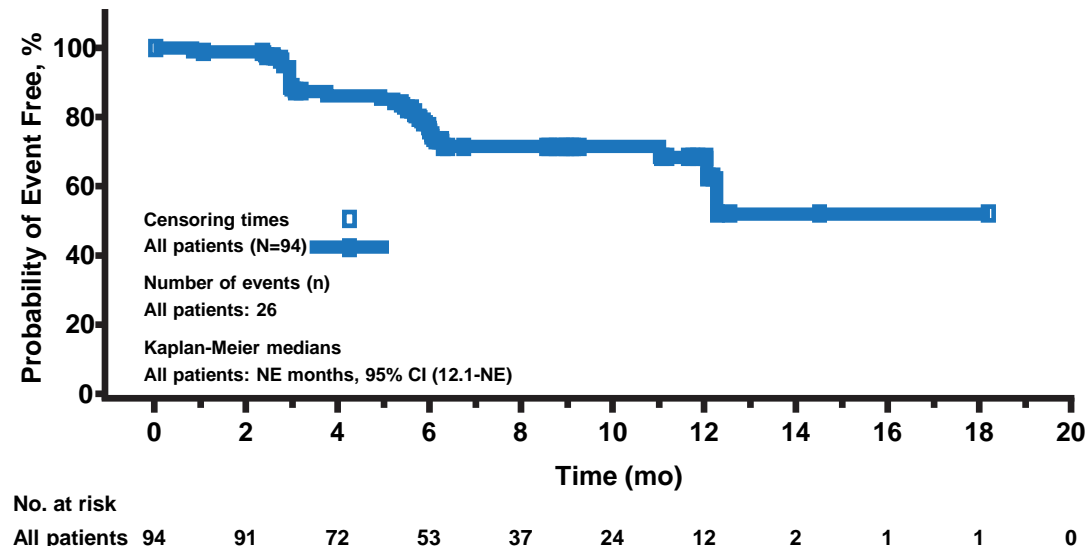
## Best Overall Response Rate

Response Rate, %	Patients Evaluable for Efficacy <sup>b</sup> (n=94)
CR	66.0 <sup>b</sup>
PR	20.2
ORR (CR+PR)	86.2

- Investigator-assessed CRR was 69.1%<sup>c</sup> (ORR 90.4%)
- CRRs/ORRs were comparable among key high-risk subgroups

- Median follow-up for efficacy (n=94): 10.9 (4.3-19.7) months
- Probability for a responding patient to remain in response  $\geq 6$  months was 84.4%
- 12 of 18 PRs (66.6%) converted to CRs; all but 1 occurred between Month 3 and Month 6
- Median time to next antilymphoma treatment was not reached

## Median DOR Was Not Reached at 10.9 Months Median Follow-Up

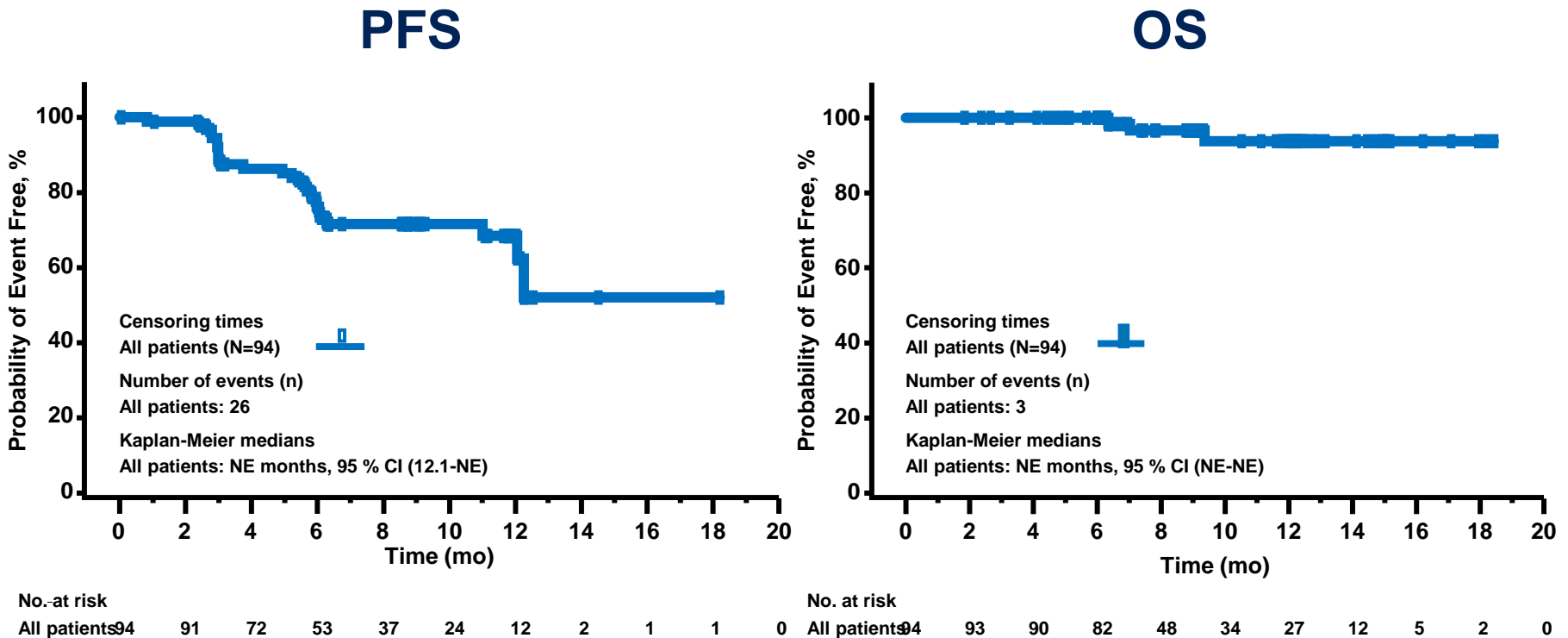


First efficacy assessment conducted at Month 3 (all but 1 responded at Month 3 assessment); probability of remaining in CR > Month 6.

<sup>a</sup>The primary end point was met at interim analysis. <sup>b</sup> $P < 0.0001$ ; indicates statistical significance (1-sided) at the 0.0025 level so that the null hypothesis  $CRR \leq 0.15$  is rejected. <sup>c</sup>95% CI, 52.9-79.7.

CI, confidence interval; CR, complete response; CRR, complete response rate; DOR, duration of response; NE, not estimable; PR, partial response; ORR, overall response rate.

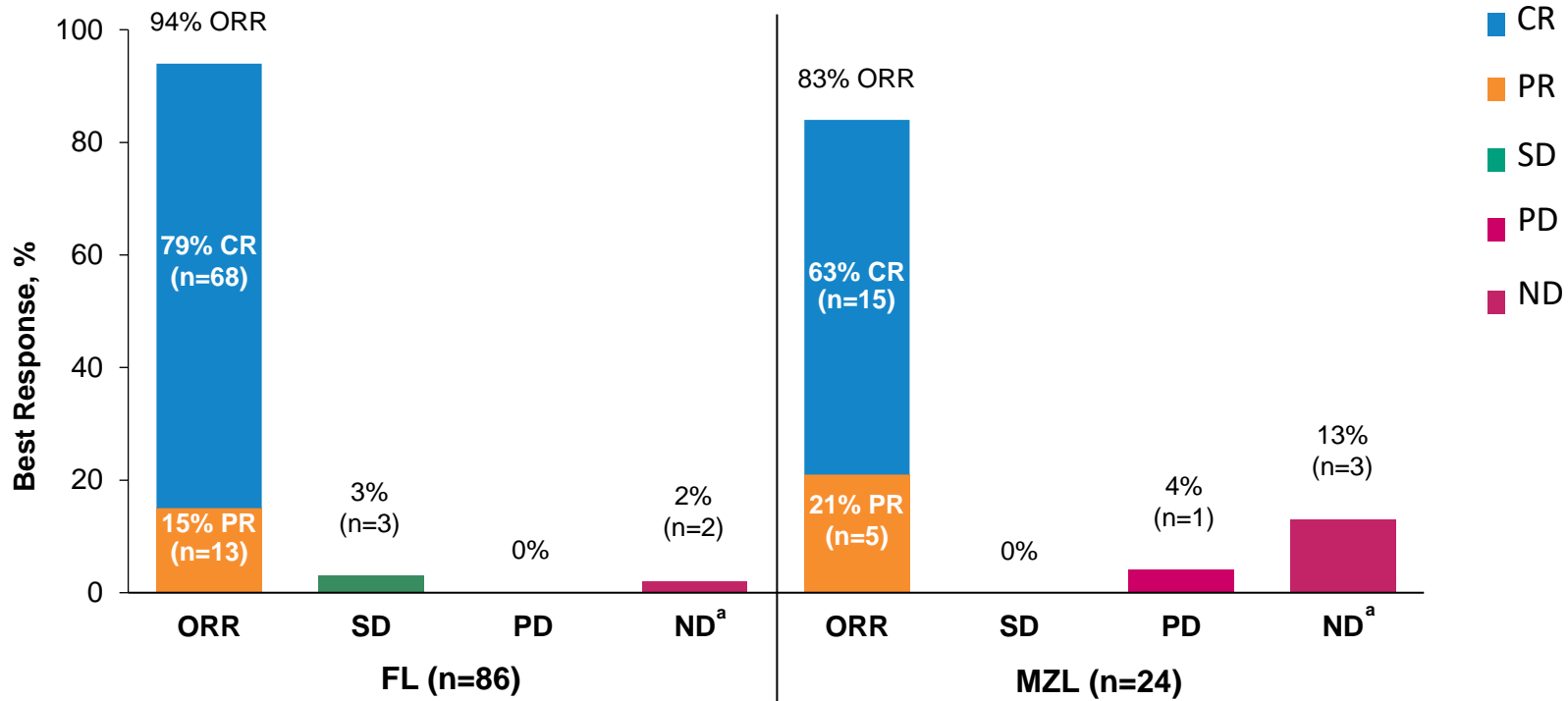
# Median PFS and OS Were Not Reached



- Median PFS (95% CI, 12.1-NE) and OS (95% CI, NE-NE) were not reached
- 6-month PFS was 76% (95% CI, 65-84)

CI, confidence interval; IRC, Independent Review Committee; NE, not estimable; OS, overall survival; PFS, progression-free survival.

# Zuma-5: Axi-cel in relapsed/refractory indolent Non-Hodgkin lymphoma



- Among efficacy-eligible patients with iNHL (n=110), the ORR was 92% (95% CI, 85–96), with a 75% CR rate
- Among all treated patients with iNHL (n=149), the ORR was 92% (95% CI, 86–96), with a 77% CR rate

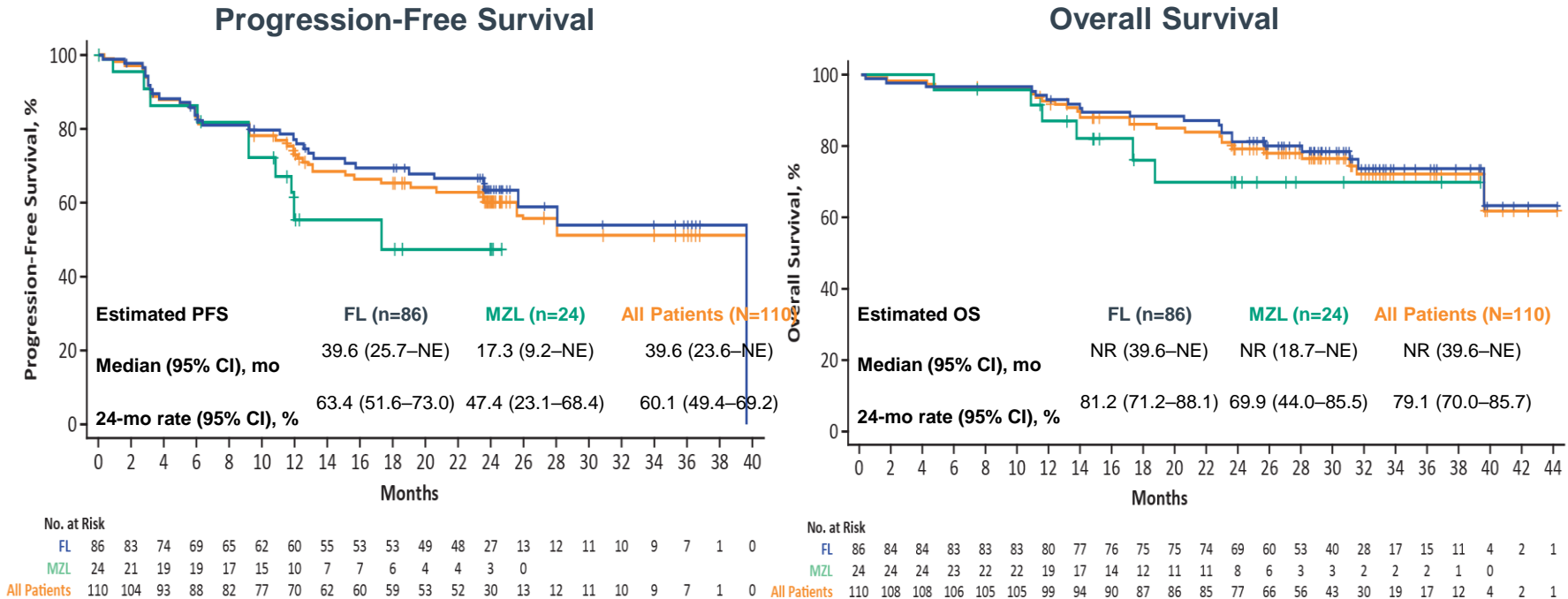
Assessed in efficacy-eligible patients (n=110) by an IRRC according to the Lugano Classification (Cheson BD, et al. *J Clin Oncol.* 2014;32:3059–3068).

<sup>a</sup> Among the 5 patients reported as ND, 4 (1 FL; 3 MZL) had no disease at baseline and post-baseline per IRRC but were considered with disease by the investigator; 1 patient with FL died before the first disease assessment.

CR, complete response; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; IRRC, Independent Radiology Review Committee; MZL, marginal zone lymphoma; ND, not done/undefined; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.



# Zuma-5: Long term outcome – PFS and OS



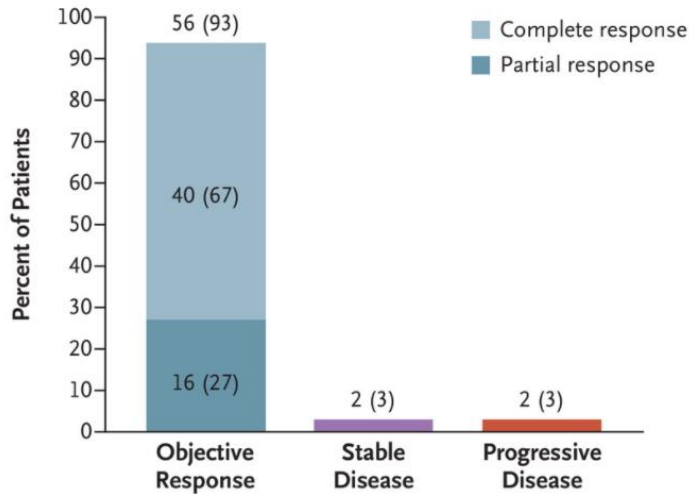
- Median OS was not yet reached in efficacy-eligible patients with FL or MZL
- Among patients with FL, 3 deaths occurred after Month 24<sup>a</sup>; no disease progression events occurred after Month 24

<sup>a</sup> Of the 3 deaths, 2 were from COVID-19 and one was from sepsis.

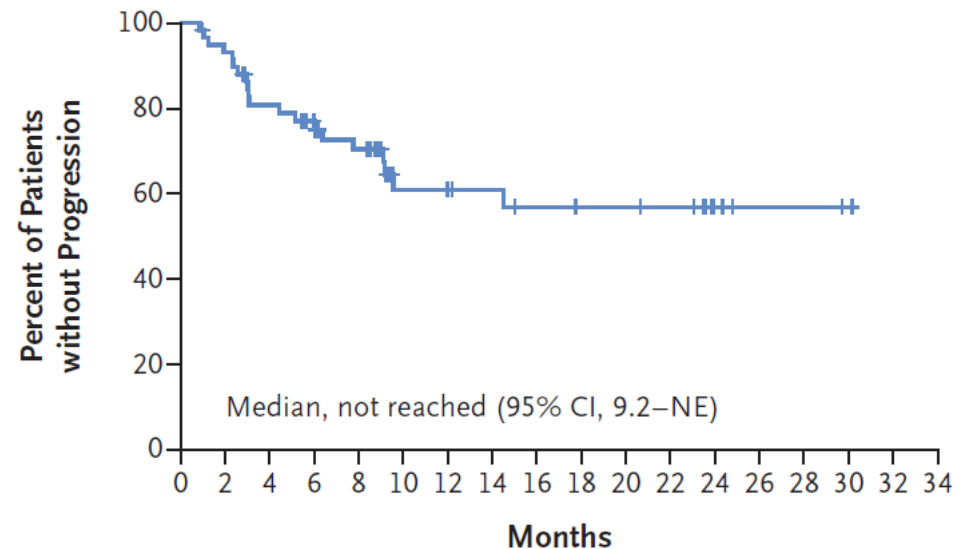
FL, follicular lymphoma; MZL, marginal zone lymphoma; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

# Zuma-2 – Brexu-cel CAR 19 T-celler i mantelcelle lymfomer

**A Best Response**



**C Progression-free Survival**



No. at Risk 60 54 43 38 31 17 16 15 13 12 12 11 4 2 2 1 0

Wang et al 2020

## Noen avsluttende kommentarer

- Reell forbedring for pasienter med forskjellige typer lymfom
- Mye å utvikle videre
  - Produkt, indikasjon, kombinasjon med andre muligheter
  - Studier, vi jobber med saken
- Ikke sikkert dette er den beste løsningen
  - Engangs behandling?
  - Overlevelse og effekt av celle produktet?



