



SINTOMA'24

PARCERIA **soho**
society of hematologic oncology

APOIO
INSTITUCIONAL

bp Educação
e Pesquisa

To 2L and Beyond: Treatment options in R/R MCL

Tycel J. Phillips, MD

Associate Professor of Medicine

Department of Hematology and Bone Marrow Transplantation

City of Hope National Medical Center

Duarte, CA 91010

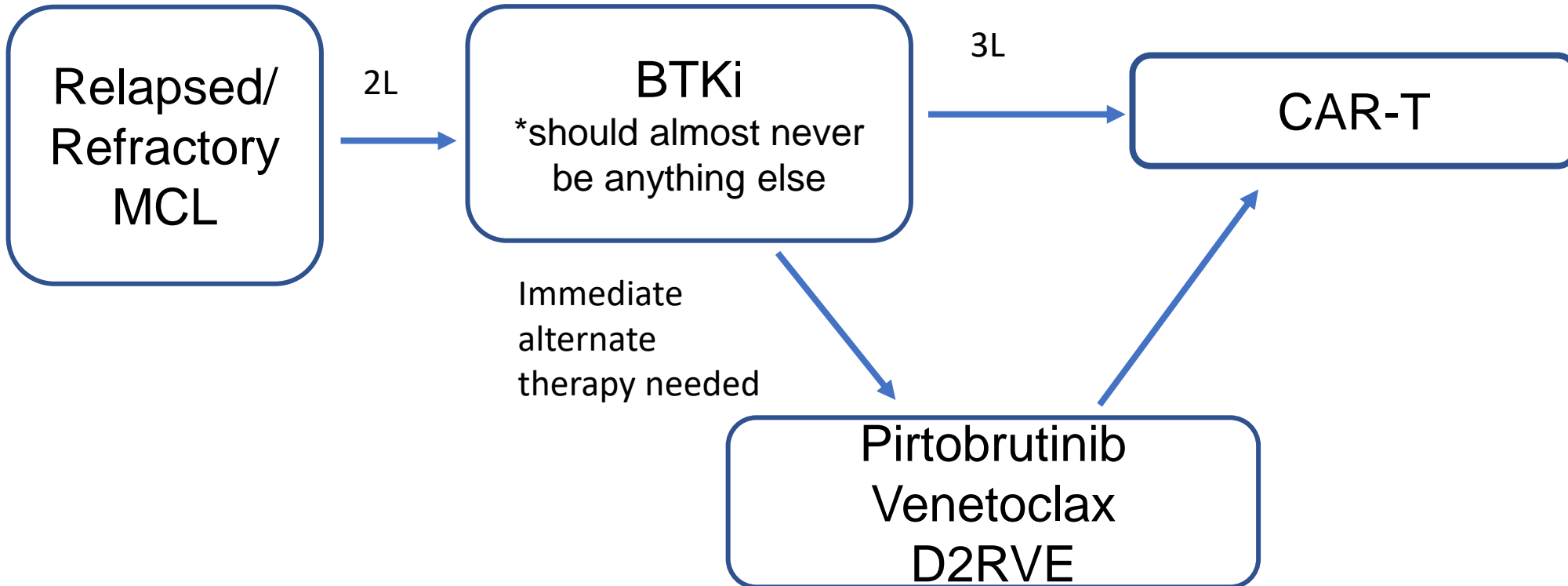
Tphillips@coh.org



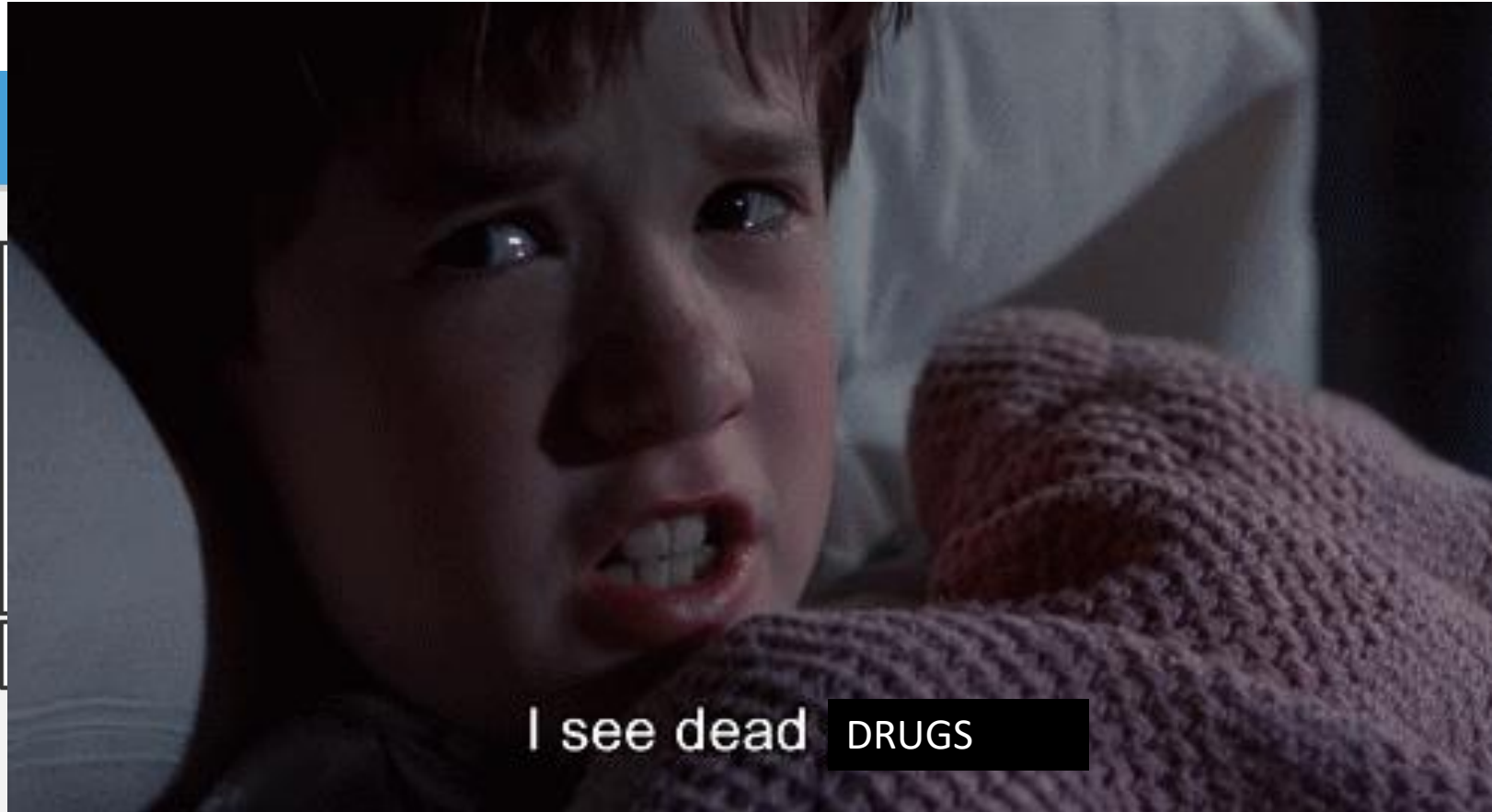
- MCL remains a difficult disease to treat mainly due to the variability in patient presentations/outcomes with current therapy
 - 1L therapy remains in flux
 - BTKi continue to attempt to move into the 1L setting
 - How does this (1L BTKi) either continuous or intermittent impact 2L space as this isn't going to cure patients
 - Potentially moves up other agents and accentuates the need for novel treatments in MCL

R/R MCL

- My current view



Sixth Sense.....



Induction: **Bendamustine** 90 mg/m² Days 1 and 2, **Rituximab** 375 mg/m² Day 1, Q4W. A cycle is defined as 28 days.

CR, complete response; ITT, intent-to-treat; MIPI, Mantle Cell Lymphoma International Prognostic Index; PD, progressive disease; PFS, progression-free survival; PR, partial response.



FDA



Ibrutinib





- In the US we have 2 cBTKi left on the market
 - Acalabrutinib and Zanubrutinib
 - No major issues to distinguish between the two drugs
 - Acalabrutinib 100 mg BID
 - Harder to dose reduce
 - Zanubrutinib
 - More neutropenia
 - Ultimately choice of agent is subjective

• Can we do better?

Acalabrutinib

ORR using the 2014 Lugano Classification

| | N=124 | |
|---------------|-----------------------|--------------|
| | Investigator assessed | IRC assessed |
| | n (%) | n (%) |
| ORR (CR + PR) | 100 (81) | 99 (80) |
| Best response | | |
| CR | 49 (40) | 49 (40) |
| PR | 51 (41) | 50 (40) |
| SD | 11 (9) | 9 (7) |
| PD | 10 (8) | 11 (9) |
| Not evaluable | 3 (2) | 5 (4) |

- Wang M, et al. Acabrutinib in relapsed or refractory mantle cell lymphoma (ACE-LY-004): a single-arm, multicentre, phase 2 trial. *Lancet* 2018;391(10121):659-667
- Constantine S. Tam, et al., Zanubrutinib for the treatment of relapsed or refractory mantle cell lymphoma, *Blood Adv*, 2021,

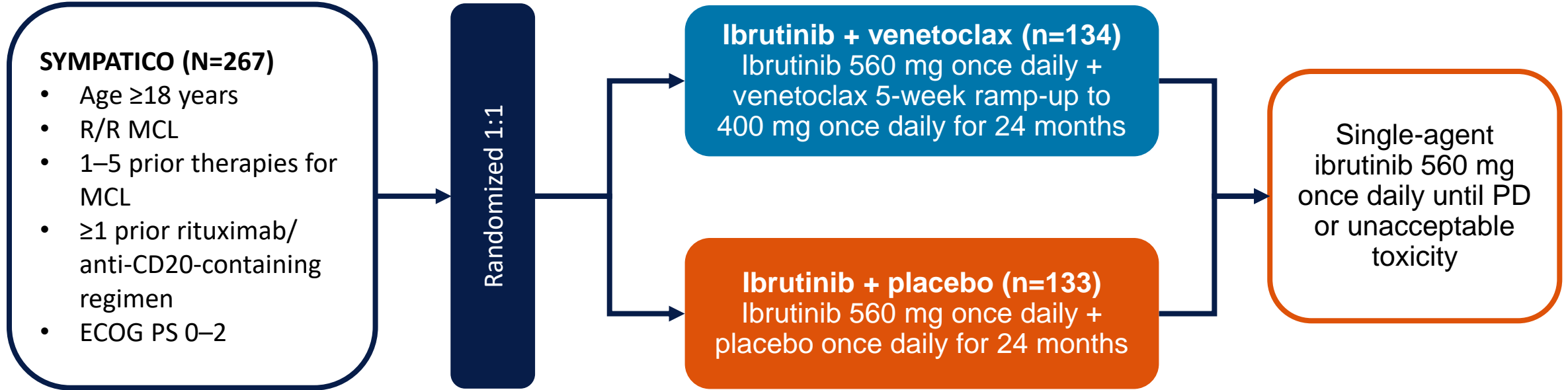
Zanubrutinib

| Response assessment | Investigator-assessed response (N = 32) | IRC-assessed response (N = 32) |
|----------------------|---|--------------------------------|
| ORR 95% CI* | 29 (90.6) (75.0-9x8.0) | 27 (84.4) (67.2-94.7) |
| Best response | | |
| CR | 10 (31.3) | 8 (25.0) |
| PR | 19 (59.4) | 19 (59.4) |
| Stable disease | 1 (3.1) | 2 (6.3) |
| PD | 2 (6.3) | 2 (6.3) |
| Unknown† | 0 | 1 (3.1) |



SYMPATICO Study Design

- SYMPATICO (NCT03112174) is multinational, randomized, double-blind, placebo-controlled, phase 3 study



Stratification: ECOG PS, prior lines of therapy, TLS risk^a

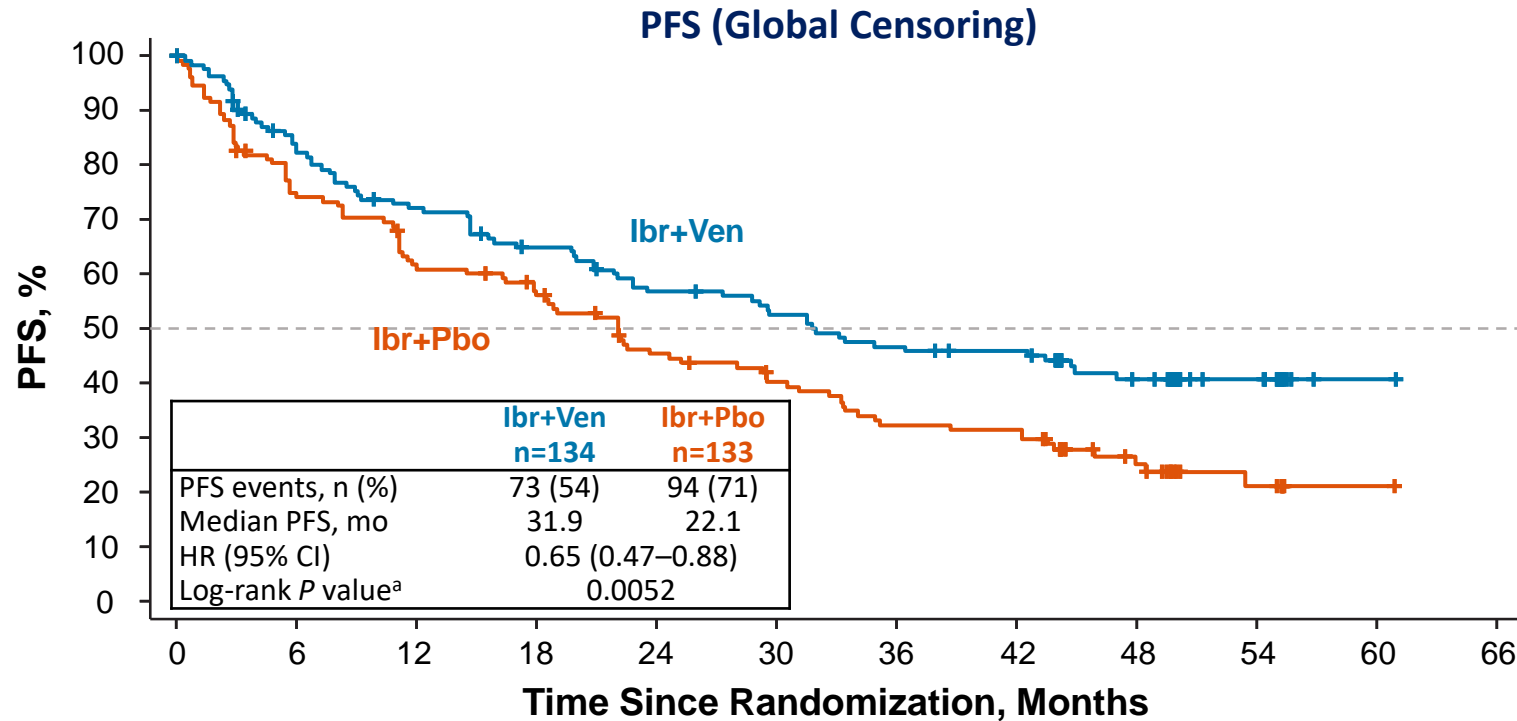
- **Primary endpoint:**
 - PFS by investigator assessment using Lugano criteria
- **Secondary endpoints (tested hierarchically in the following order):**
 - CR rate by investigator assessment
 - TTNT^b
 - OS (interim analysis)
 - ORR by investigator assessment

CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; PD, progressive disease; PFS, progression-free survival; ORR, overall response rate; OS, overall survival; TLS, tumor lysis syndrome; TTNT, time to next treatment.

^aIncreased TLS risk was defined as at least 1 lesion >10 cm, or at least 1 lesion >5 cm with circulating lymphocytes >25,000 cells/mm³, and/or creatinine clearance <60 mL/min. ^bFor hierarchical testing per US FDA censoring, TTNT was tested after OS.



Primary Endpoint: Investigator-Assessed PFS Was Significantly Improved With Ibrutinib + Venetoclax Versus Ibrutinib + Placebo



Patients at risk:

| | | | | | | | | | | | | |
|---------|-----|-----|----|----|----|----|----|----|----|----|---|---|
| Ibr+Ven | 134 | 107 | 91 | 80 | 69 | 63 | 56 | 53 | 34 | 15 | 1 | 0 |
| Ibr+Pbo | 133 | 96 | 79 | 70 | 54 | 46 | 37 | 36 | 18 | 8 | 1 | 0 |

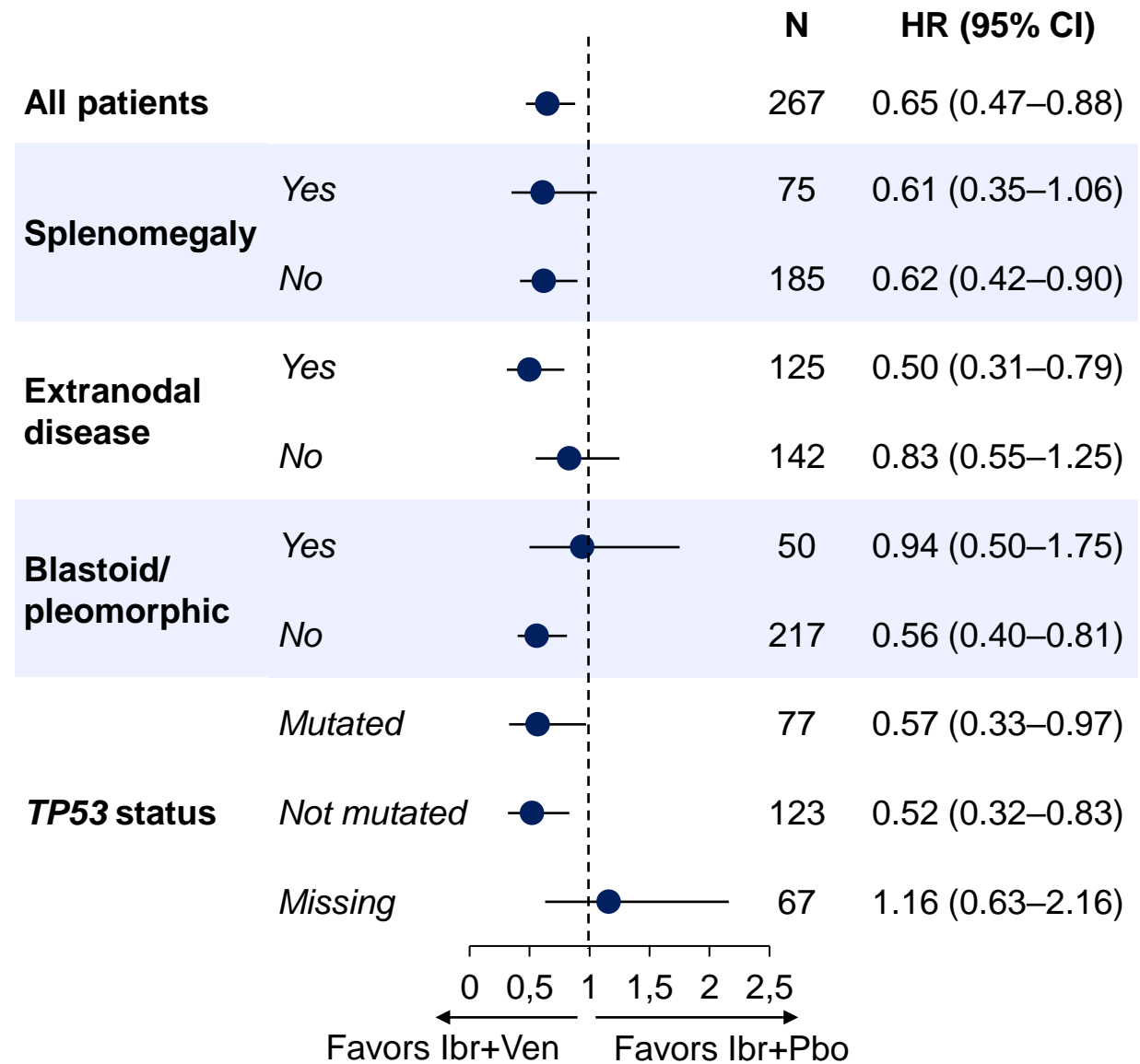
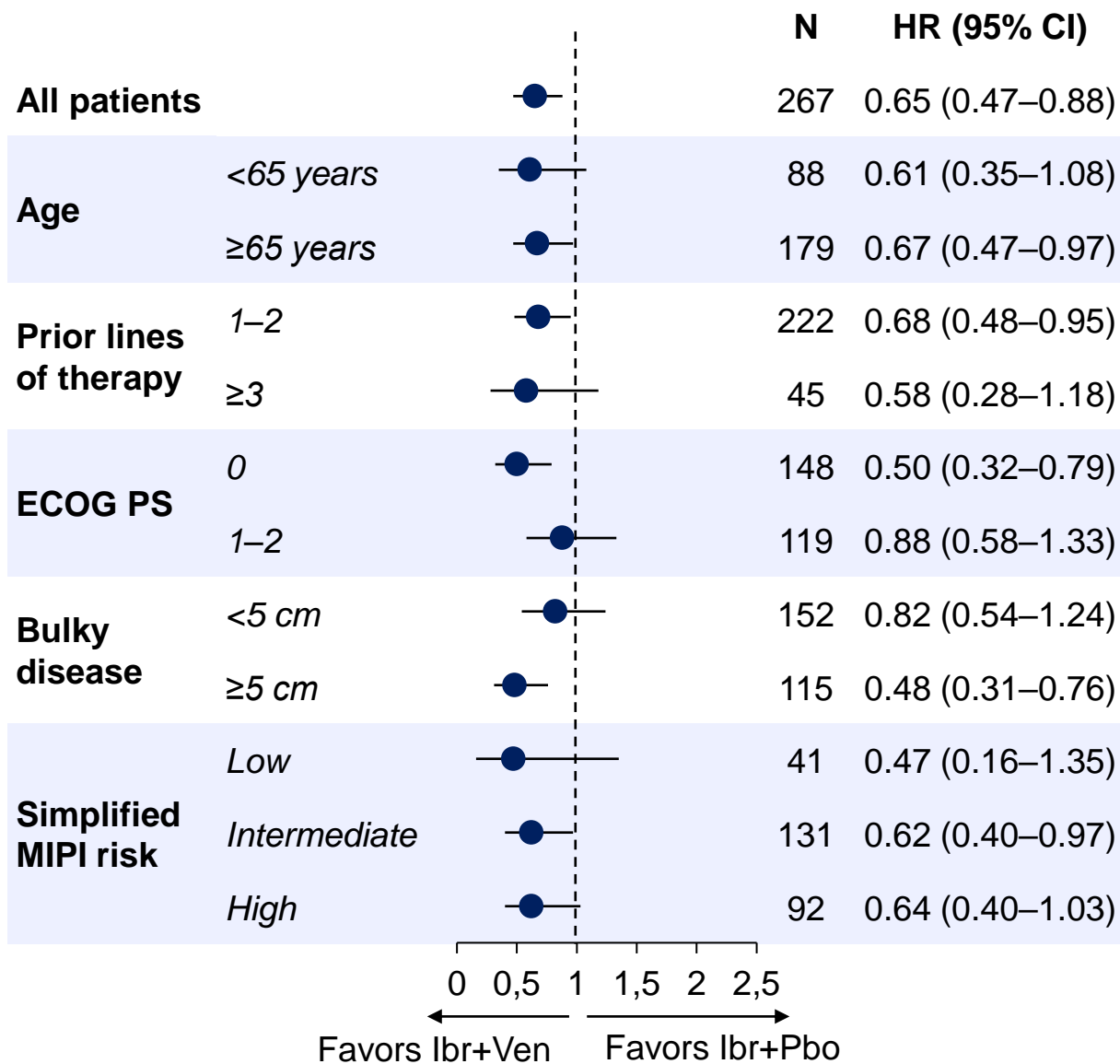
| Median PFS, mo | Global Censoring ^b | | | | US FDA Censoring ^c | | | |
|--------------------------------|-------------------------------|------------------|------------------|---|-------------------------------|------------------|------------------|---|
| | Ibr+Ven n=134 | Ibr+Pbo n=133 | HR (95% CI) | Log-rank <i>P</i> value ^a | Ibr+Ven n=134 | Ibr+Pbo n=133 | HR (95% CI) | Log-rank <i>P</i> value ^a |
| Investigator assessment | 31.9 | 22.1 | 0.65 (0.47–0.88) | 0.0052 | 42.6 | 22.1 | 0.60 (0.44–0.83) | 0.0021 |
| IRC assessment | 31.8 | 20.9 | 0.67 (0.49–0.91) | 0.0108 | 43.5 | 22.1 | 0.63 (0.45–0.87) | 0.0057 |

HR, hazard ratio; Ibr, ibrutinib; Pbo, placebo; Ven, venetoclax.

^a*P* values were determined by stratified log-rank test (stratification factors: prior lines of therapy [1–2 vs ≥3] and TLS risk category [low vs increased risk]). ^bCensoring at last non-PD assessment for patients without PD or death. ^cPatients were censored at last non-PD assessment before start of subsequent anticancer therapy or missing ≥2 consecutive visits prior to a PFS event, whichever occurred first.



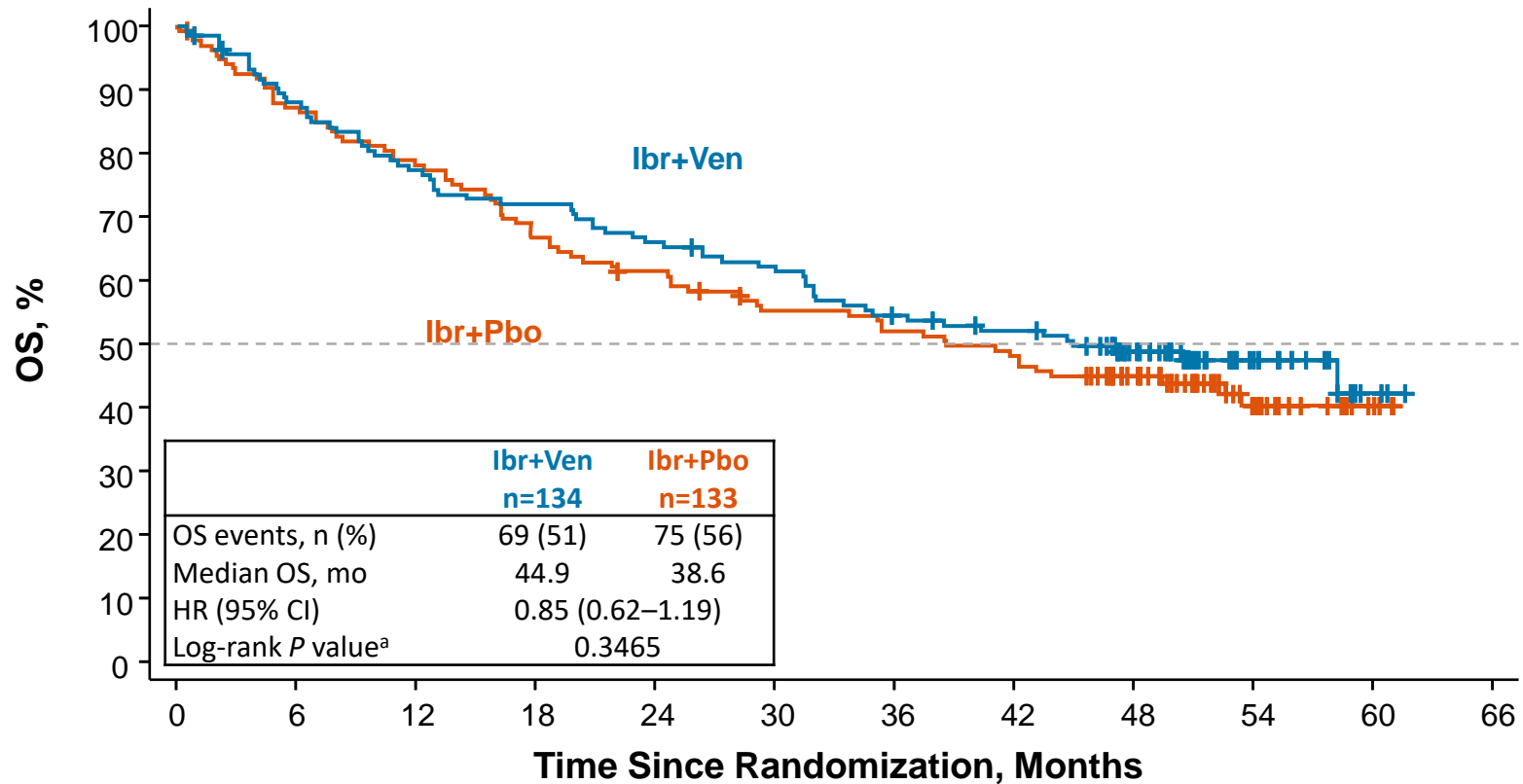
PFS Benefit^a Was Generally Consistent Across Prespecified Subgroups



^aGlobal censoring (censoring at last non-PD assessment for patients without PD or death).



OS Was Numerically Improved At This Interim Analysis



Patients at risk:

| | | | | | | | | | | | | |
|---------|-----|-----|-----|----|----|----|----|----|----|----|---|---|
| Ibr+Ven | 134 | 116 | 102 | 95 | 87 | 81 | 70 | 65 | 48 | 20 | 3 | 0 |
| Ibr+Pbo | 133 | 115 | 103 | 88 | 80 | 70 | 66 | 61 | 46 | 20 | 4 | 0 |

^aP values were determined by stratified log-rank test (stratification factors: prior lines of therapy [1–2 vs ≥3] and TLS risk category [low vs increased risk]).



Safety Was Consistent With Known AEs of Each Single Agent

- Median overall treatment duration:
 - Ibrutinib + venetoclax, 22.2 months (range, 0.5–60.4)
 - Ibrutinib + placebo, 17.7 months (range, 0.1–58.9)

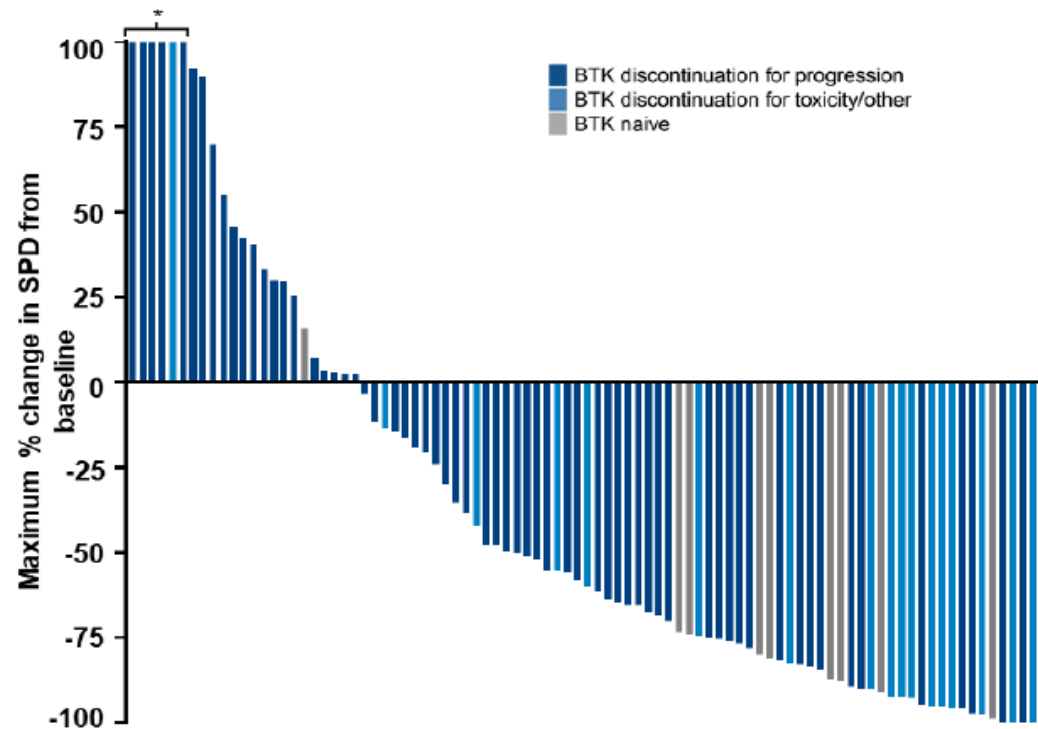
| AE, n (%) | Ibrutinib + venetoclax n=134 | Ibrutinib + placebo n=132 |
|---|------------------------------------|---------------------------------|
| Grade ≥3 AEs | 112 (84) | 100 (76) |
| Serious AEs | 81 (60) | 79 (60) |
| AEs leading to discontinuation | 41 (31) | 48 (36) |
| <i>Ibrutinib only</i> | 11 (8) | 10 (8) |
| <i>Venetoclax/placebo only</i> | 2 (1) | 7 (5) |
| <i>Both</i> | 28 (21) | 31 (23) |
| AEs leading to dose reduction | 48 (36) | 29 (22) |
| <i>Ibrutinib only</i> | 17 (13) | 14 (11) |
| <i>Venetoclax/placebo only</i> | 14 (10) | 7 (5) |
| <i>Both</i> | 17 (13) | 8 (6) |
| AEs leading to death | 22 (16) | 18 (14) |
| <i>Ibrutinib-related^a</i> | 3 (2) | 2 (2) |
| <i>Venetoclax/placebo-related^a</i> | 0 | 1 (1) |
| Tumor lysis syndrome | | |
| <i>Laboratory</i> | 7 (5) | 3 (2) |
| <i>Clinical</i> | 0 | 0 |

| AE, n (%) | Ibrutinib + venetoclax n=134 | Ibrutinib + placebo n=132 |
|--|------------------------------------|---------------------------------|
| Most frequent any-grade AEs^b | | |
| <i>Diarrhea</i> | 87 (65) | 45 (34) |
| <i>Neutropenia</i> | 46 (34) | 19 (14) |
| <i>Nausea</i> | 42 (31) | 22 (17) |
| <i>Fatigue</i> | 39 (29) | 36 (27) |
| <i>Anemia</i> | 30 (22) | 16 (12) |
| <i>Pyrexia</i> | 28 (21) | 26 (20) |
| <i>Cough</i> | 27 (20) | 36 (27) |
| <i>Muscle spasms</i> | 11 (8) | 32 (24) |
| Most frequent grade ≥3 AEs^c | | |
| <i>Neutropenia</i> | 42 (31) | 14 (11) |
| <i>Pneumonia</i> | 17 (13) | 14 (11) |
| <i>Thrombocytopenia</i> | 17 (13) | 10 (8) |
| <i>Anemia</i> | 13 (10) | 4 (3) |
| <i>Diarrhea</i> | 11 (8) | 3 (2) |
| <i>Leukopenia</i> | 10 (7) | 0 |
| <i>MCL^d</i> | 9 (7) | 16 (12) |
| <i>Atrial fibrillation</i> | 7 (5) | 7 (5) |
| <i>COVID-19</i> | 7 (5) | 1 (1) |
| <i>Hypertension</i> | 6 (4) | 12 (9) |

^aPer investigator opinion. ^bOccurring in ≥20% of patients in either arm. ^cOccurring in ≥5% of patients in either arm. ^dWorsening of MCL without meeting criteria for PD.

Pirtobrutinib (Post BTKi Outcomes)

Pirtobrutinib Efficacy in Mantle Cell Lymphoma



| BTK Pre-Treated MCL Patients^a | | n=100 |
|--|---------|--------------------|
| Overall Response Rate^b, % (95% CI) | | 51% (41-61) |
| Best Response | | |
| CR, n (%) | 25 (25) | |
| PR, n (%) | 26 (26) | |
| SD, n (%) | 16 (16) | |
| BTK Naive MCL Patients^a | | n=11 |
| Overall Response Rate^b, % (95% CI) | | 82% (48-98) |
| Best Response | | |
| CR, n (%) | 2 (18) | |
| PR, n (%) | 7 (64) | |
| SD, n (%) | 1 (9) | |

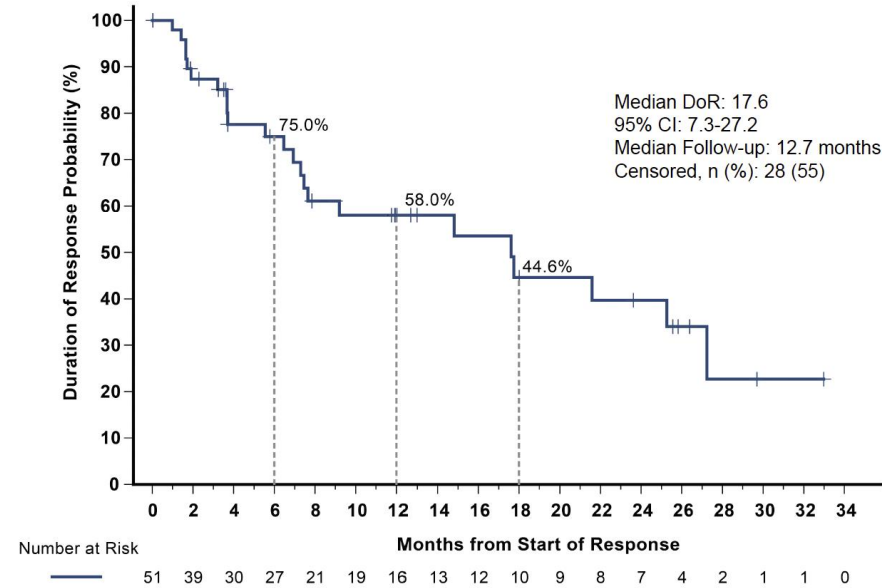
Efficacy also seen in patients with prior:

- Stem cell transplant (n=28): ORR 64% (95% CI: 44-81)
- CAR-T therapy (n=6): ORR 50% (95% CI: 12-88)

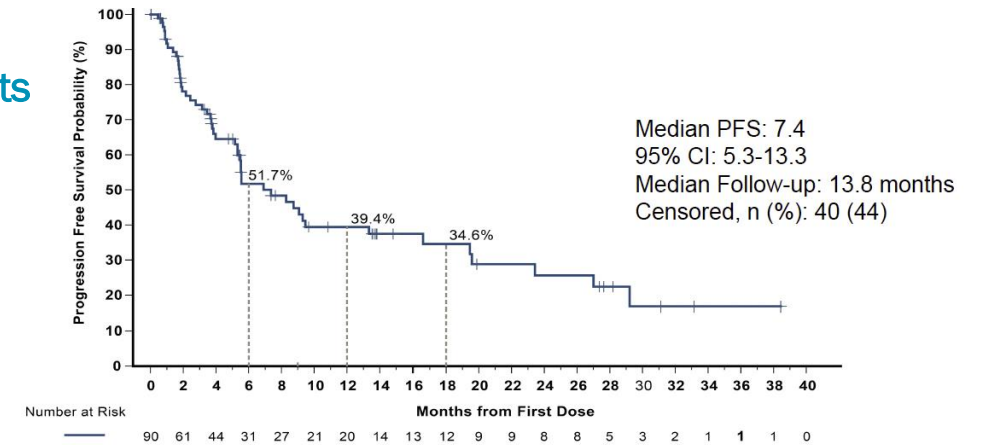
Data cutoff date of 16 July 2021. Data for 20 MCL patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. *Indicates patients with >100% increase in SPD. ^aEfficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. ^bORR includes patients with a best response of CR and PR. Response status per Lugano 2014 criteria based on investigator assessment. Total % may be different than the sum of the individual components due to rounding.

Updated Results and Subgroup Analysis From the BRUIN Phase 1/2 Study of Pirtobrutinib in Patients With R/R MCL: DOR, PFS, and OS

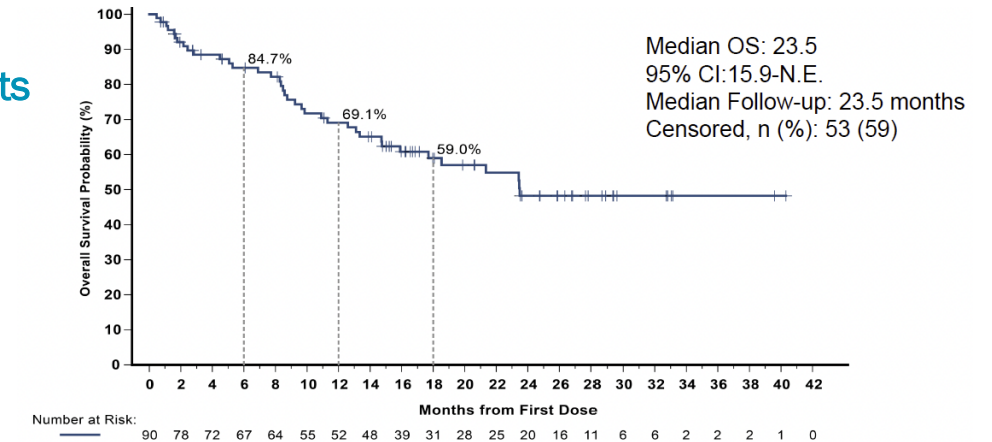
DOR in Prior cBTKi Patients



PFS in Prior cBTKi Patients

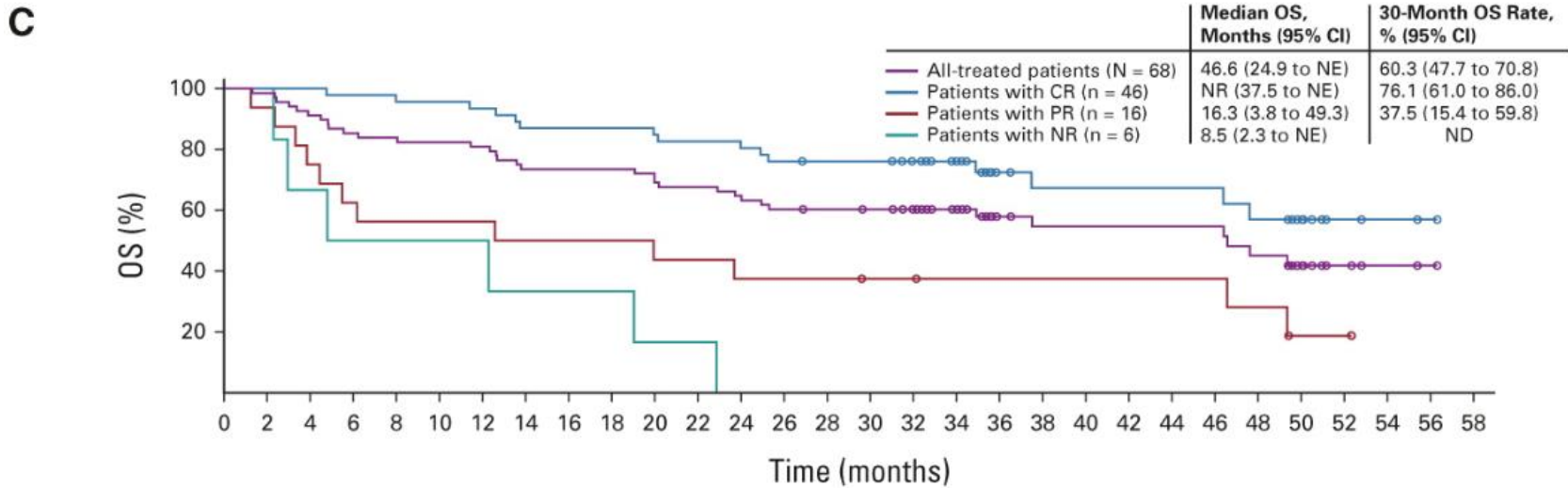
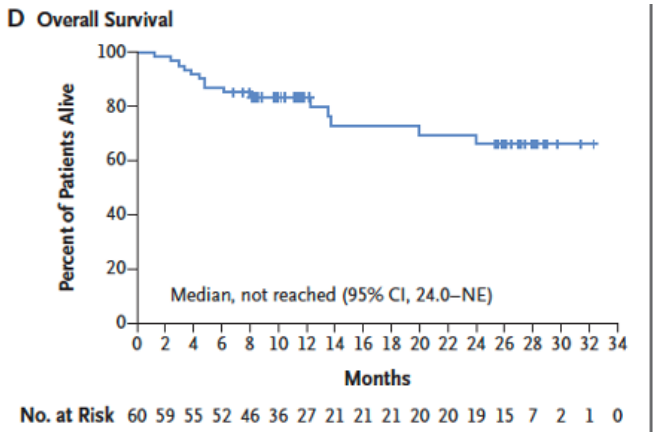
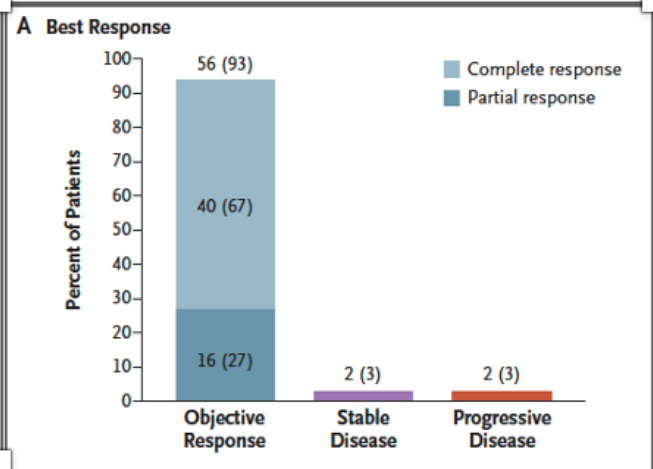


OS in Prior cBTKi Patients



- Median DOR, PFS, and OS were not reached in the cBTKi-naïve cohort
- 18-month rates (95% CI)
 - DOR: 100% (100)
 - PFS: 92.3% (56.6-98.9)
 - OS: 92.3% (56.6-98.9)

Brexucabtagene autoleucel



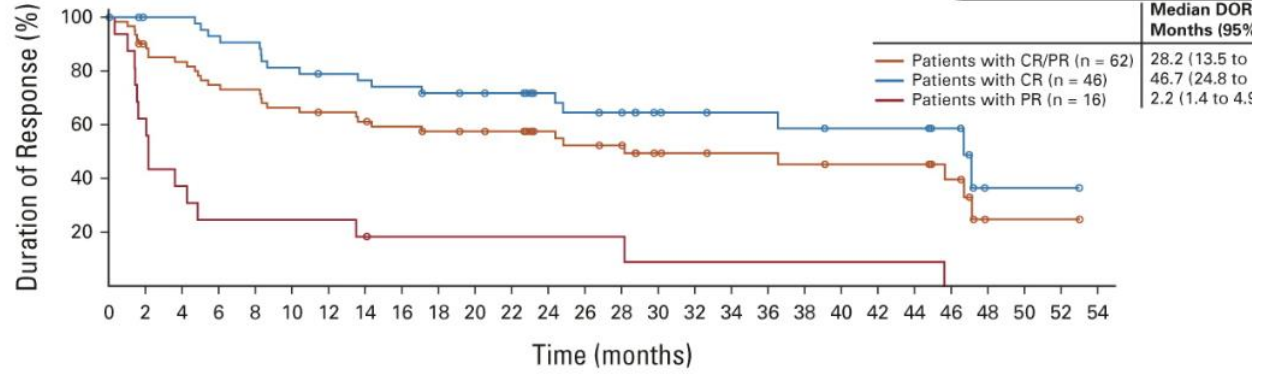
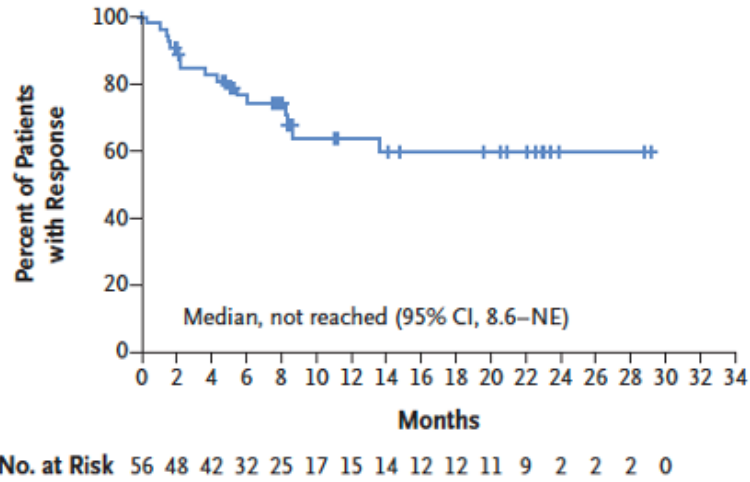
No. at risk:

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|---|---|---|
| All-treated patients | 68 | 67 | 62 | 58 | 56 | 56 | 55 | 50 | 50 | 50 | 47 | 46 | 43 | 41 | 40 | 39 | 35 | 28 | 19 | 17 | 17 | 17 | 17 | 17 | 14 | 9 | 4 | 2 | 1 | 0 | |
| Patients with CR | 46 | 46 | 46 | 45 | 44 | 44 | 43 | 40 | 40 | 40 | 39 | 38 | 37 | 35 | 34 | 34 | 30 | 24 | 15 | 13 | 13 | 13 | 13 | 13 | 11 | 8 | 3 | 2 | 1 | 0 | |
| Patients with PR | 16 | 15 | 12 | 10 | 9 | 9 | 9 | 8 | 8 | 8 | 7 | 7 | 6 | 6 | 6 | 5 | 5 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 3 | 1 | 1 | 0 | 0 | 0 |
| Patients with NR | 6 | 6 | 4 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Wang M et al, KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med. 2020 Apr 2;382(14):1331-1342. doi: 10.1056/NEJMoa1914347. PMID: 32242358; PMCID: PMC7731441.

Then vs. Now

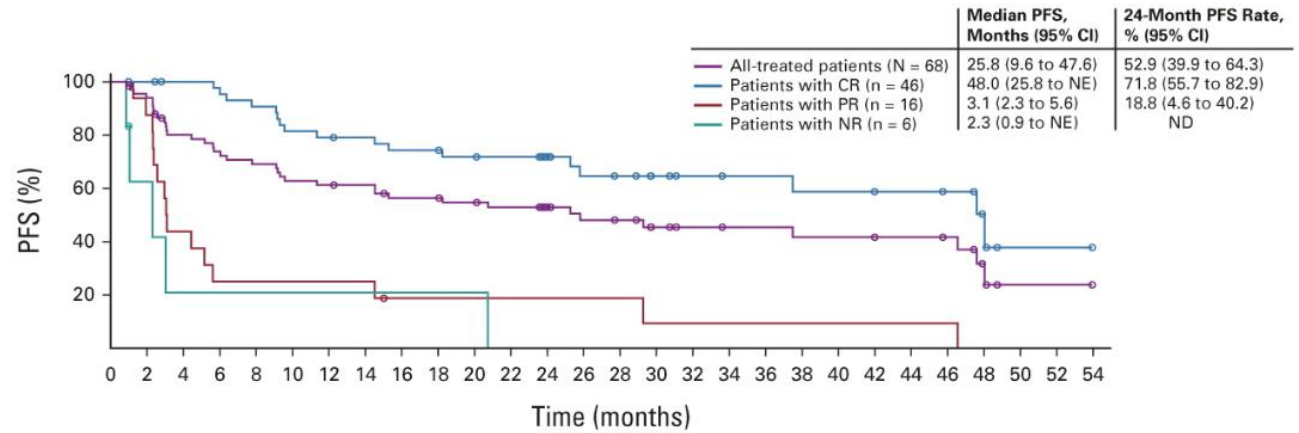
B Duration of Response



No. at risk:

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|---|---|
| Patients with CR/PR | 62 | 53 | 49 | 44 | 43 | 39 | 37 | 35 | 33 | 31 | 30 | 29 | 22 | 20 | 19 | 14 | 13 | 12 | 12 | 11 | 10 | 10 | 10 | 7 | 1 | 1 | 1 | 0 |
| Patients with CR | 46 | 43 | 43 | 40 | 39 | 35 | 33 | 32 | 31 | 29 | 28 | 27 | 20 | 18 | 17 | 13 | 12 | 11 | 11 | 10 | 9 | 9 | 9 | 7 | 1 | 1 | 1 | 0 |
| Patients with PR | 16 | 10 | 6 | 4 | 4 | 4 | 4 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |

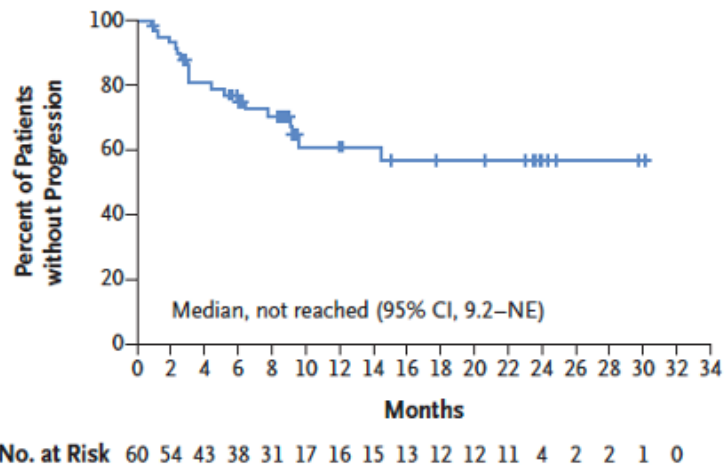
B



No. at risk:

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|----------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|---|---|
| All-treated patients | 68 | 62 | 51 | 47 | 44 | 40 | 39 | 38 | 34 | 34 | 32 | 30 | 24 | 20 | 19 | 15 | 13 | 12 | 12 | 11 | 11 | 10 | 10 | 9 | 4 | 1 | 1 | 0 |
| Patients with CR | 46 | 45 | 43 | 42 | 39 | 35 | 34 | 33 | 31 | 31 | 29 | 28 | 22 | 18 | 17 | 14 | 12 | 11 | 11 | 10 | 10 | 9 | 9 | 8 | 4 | 1 | 1 | 0 |
| Patients with PR | 16 | 14 | 7 | 4 | 4 | 4 | 4 | 4 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Patients with NR | 6 | 3 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

C Progression-free Survival



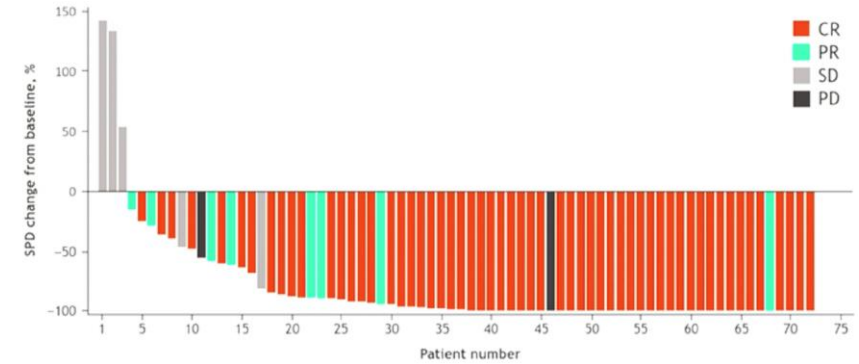
Results From the TRANSCEND-NHL-001 Study of Liso-cel in Patients With R/R MCL: Response and Analysis DOR

| Best Response | Primary Analysis Set (n=74) |
|-----------------|--------------------------------|
| ORR, % (95% CI) | 86.5 (76.5-93.3); $P < 0.0001$ |
| CR, % (95% CI) | 74.3 (62.8-83.8); $P < 0.0001$ |
| PR, % | 12.2 |
| SD, % | 6.8 |
| PD, % | 0 |
| NE, % | 6.8 |

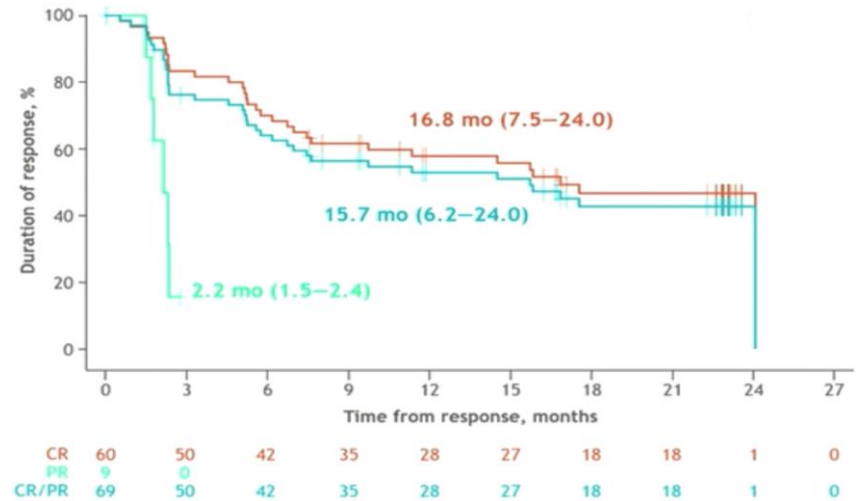
| Response | Efficacy Analysis Set (n=83) |
|--------------------------------------|------------------------------|
| ORR, % (95% CI) | 83.1 (73.3-90.5) |
| CR, % (95% CI) | 72.3 (61.4-81.6) |
| Median months to first CR/PR (range) | 0.95 (0.7-3.0) |

| DOR Per IRC | Responders (n=69) | Patients with CR (n=60) |
|-----------------------------------|-------------------|-------------------------|
| Median, months (95% CI) | 15.7 (6.2-24.0) | 16.8 (7.5-24.0) |
| Rate, % (95% CI) | | |
| 12-month | 52.9 (40.1-64.2) | 57.8 (44.2-69.2) |
| 18-month | 42.7 (29.9-54.9) | 46.7 (32.8-59.4) |
| Median follow-up, months (95% CI) | 22.8 (16.7-23.0) | |

Change in SPD and Response Status per IRC (Efficacy Analysis Set, n=83)



DOR per IRC (Efficacy Analysis Set, n=83)



Cytokine Release Syndrome/Neurotoxicity

Brexucabtagene

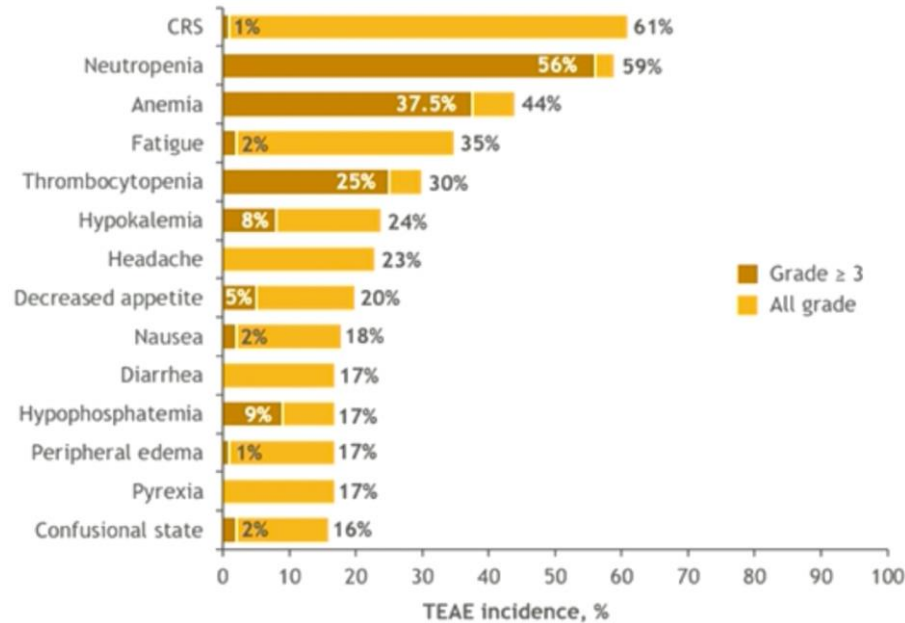
- No Grade 5 CRS occurred

| Parameter | N = 68 |
|--|-------------|
| CRS, n (%) ^a | |
| Any grade | 62 (91) |
| Grade ≥ 3 | 10 (15) |
| Most common any grade symptoms of CRS, n (%) | |
| Pyrexia | 62 (91) |
| Hypotension | 35 (51) |
| Hypoxia | 23 (34) |
| AE management, n (%) | |
| Tocilizumab | 40 (59) |
| Corticosteroids | 15 (22) |
| Median time to onset (range), days | 2 (1 – 13) |
| Median duration of events, days | 11 |
| Patients with resolved events, n (%) | 62/62 (100) |

| Parameter | N = 68 |
|---------------------------------------|-------------------------|
| Neurologic events, n (%) ^a | |
| Any grade | 43 (63) |
| Grade ≥ 3 | 21 (31) |
| Most common any grade symptoms, n (%) | |
| Tremor | 24 (35) |
| Encephalopathy | 21 (31) |
| Confusional state | 14 (21) |
| AE management, n (%) | |
| Tocilizumab | 18 (26) |
| Corticosteroids | 26 (38) |
| Median time to onset (range), days | 7 (1 – 32) |
| Median duration of events, days | 12 |
| Patients with resolved events, n (%) | 37/43 (86) ^b |

Primary Analysis Results From the TRANSCEND-NHL-001 Study of Liso-cel in Patients With R/R MCL: Safety

TEAEs (Liso-cel-Treated Set, n=88)

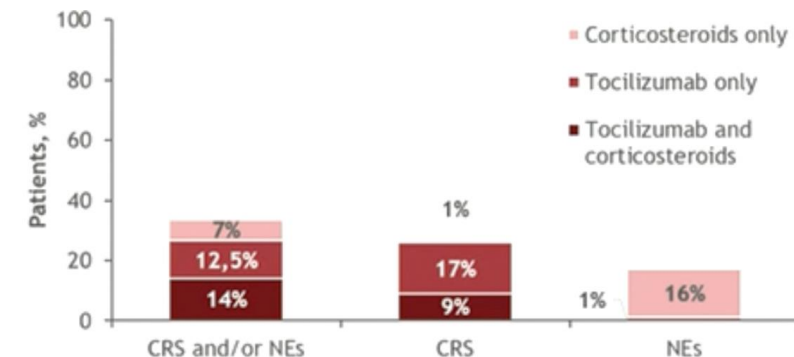


- MTD was not reached; 2 patients with a DLT among 31 DLT-evaluable patients (both at DL2)
 - Grade 5 TLS in a patient with high tumor burden
 - Grade 3 neutropenia/grade 4 thrombocytopenia
- Grade 5 TEAEs in 4 (4.5%) patients
 - 3 were considered related to liso-cel
 - 1 was considered unrelated

| CRS and NEs (Liso-cel-Treated Set, n=88) | CRS | NEs |
|--|------------|------------|
| Any grade, n (%) | 54 (61) | 27 (31) |
| Grade 1/2 | 53 (60) | 19 (22) |
| Grade 3 | 0 | 7 (8) |
| Grade 4 | 1 (1) | 1 (1) |
| Grade 5 | 0 | 0 |
| Median time to: Onset | 4.0 (1-10) | 8.0 (1-25) |
| (range), days Resolution | 4.0 (1-14) | 5.0 (1-45) |

| Other AEs of Special Interest, n (%) | Liso-cel-Treated Set (n=88) |
|--------------------------------------|-----------------------------|
| Prolonged cytopenias | 35 (40) |
| Grade ≥3 infections | 13 (15) |
| Hypogammaglobulinemia | 6 (7) |

Treatment for CRS and NEs



CRS – Cytokine Release Syndrome
 DLT – Dose limiting Toxicity
 MTD – Maximum Tolerated Dose, NE – Neurological Event

Glofitamab

Glofitamab dosing schedules

Phase I dose escalation in R/R MCL

Glofitamab IV administration

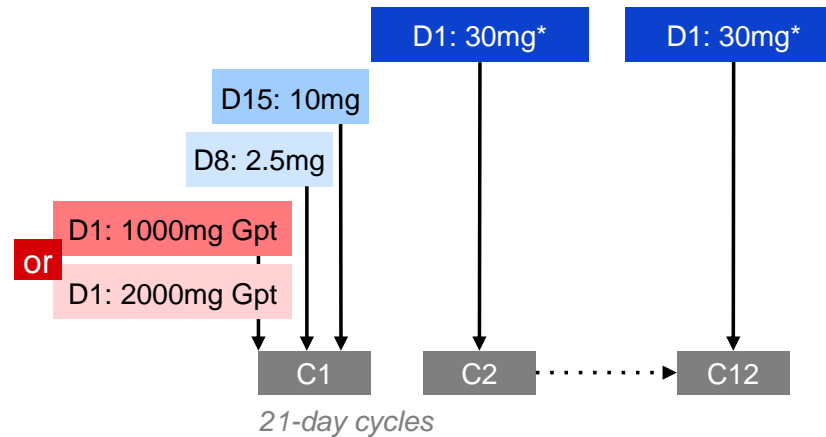
- Fixed-duration treatment: maximum 12 cycles

CRS mitigation

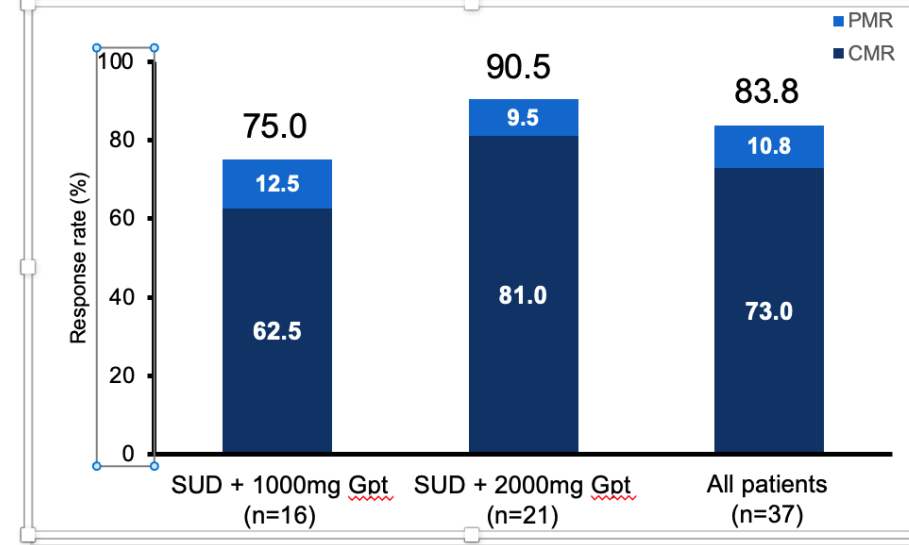
- Obinituzumab pretreatment (1 x 1000mg or 1 x 2000mg)
- C1 step-up dosing
- Monitoring after first dose (2.5mg)

Population characteristics:

- Age ≥ 18 years
- ≥ 1 prior systemic therapy
- ECOG PS ≤ 1



All patients*



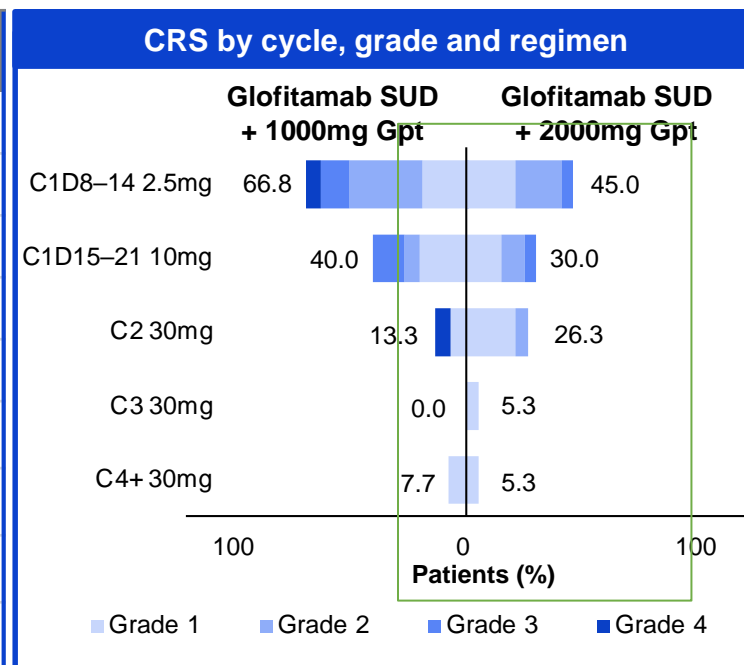
Clinical cut-off date: March 14, 2022; *In the glofitamab SUD + 1000mg Gpt cohort, two patients had 16mg glofitamab as their target dose.

Updated data will be presented at ASCO and EHA

Adverse Events

Cytokine release syndrome*

| n (%) of patients with ≥1 AE unless stated | Glofitamab SUD + 1000mg Gpt (n=16) | Glofitamab SUD + 2000mg Gpt (n=21) | All patients (N=37) |
|--|------------------------------------|------------------------------------|---------------------|
| Any CRS | 14 (87.5) | 14 (66.7) | 28 (75.7) |
| Grade 1 | 4 (25.0) | 7 (33.0) | 11 (29.7) |
| Grade 2 | 6 (37.5) | 5 (23.8) | 11 (29.7) |
| Grade 3 | 2 (12.5) | 2 (9.5) | 4 (10.8) |
| Grade 4 | 2 (12.5) | 0 (0.0) | 2 (5.4) |
| Serious AE of CRS (any grade) | 10 (62.5) | 5 (23.8) | 15 (40.5) |
| Median time to CRS onset, hours (range) | 7.55 (4.4–14.0) | 9.77 (5.0–20.8) | 9.31 (4.4–20.8) |
| Tocilizumab for CRS management | 11 (68.8) | 6 (28.6) | 17 (45.9) |
| Corticosteroid for CRS management | 8 (50.0) | 6 (28.6) | 14 (37.8) |



Higher Gpt (2000mg) was associated with a lower rate of CRS, with no Grade 4 events reported in this group

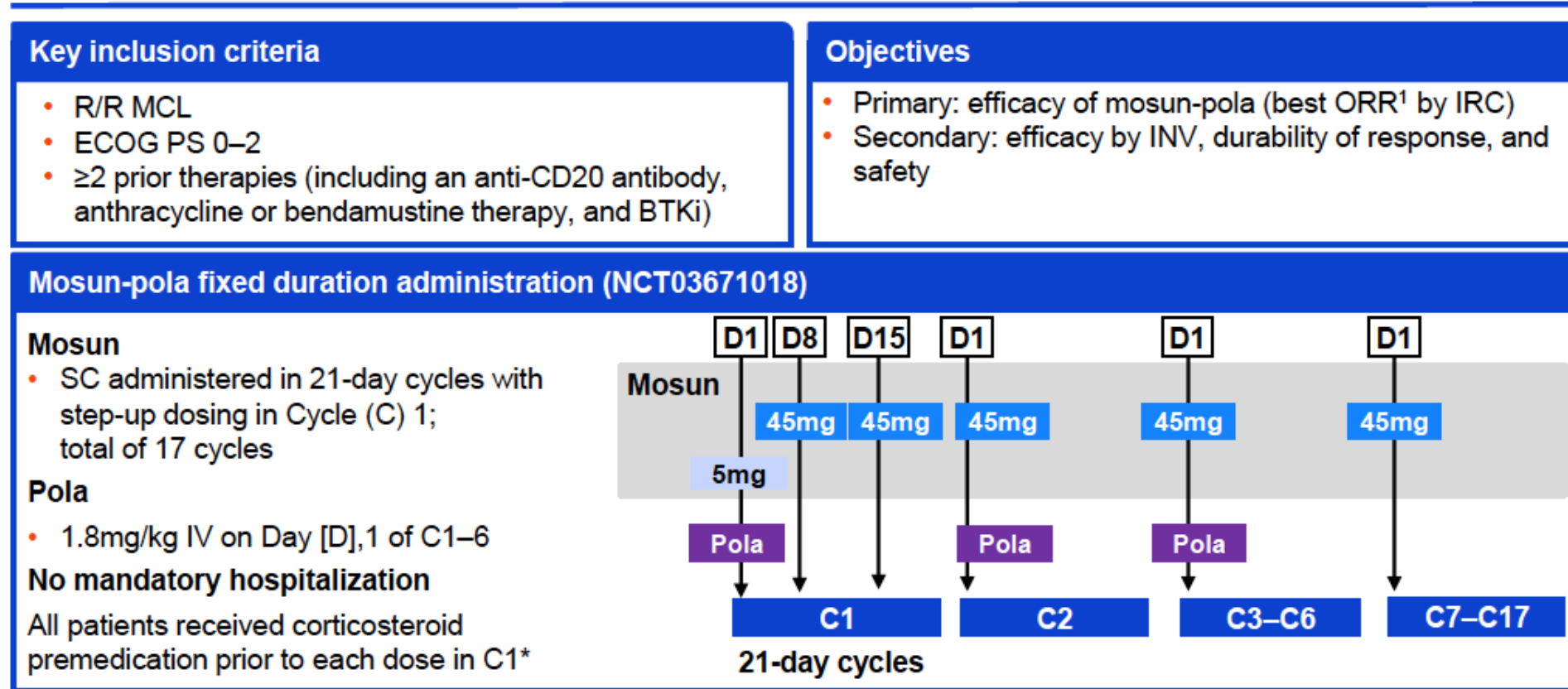
| AE, n (%) | All grades (N=37) | Grade ≥3 (N=37) |
|------------------------------|-----------------------|----------------------|
| ICANS (derived) [†] | 5 (13.5) [‡] | 0 (0.0) [‡] |

Mosunetuzumab

- All original bispecific studies enrolled MCL patients
 - Thus far only two products have published results
 - We have already discussed Glofitamab
 - Published data from Mosunetuzumab Budde et al.
 - 13 enrolled patients
 - ORR 30.8% (CR 23.1%)

Study design: Phase II dose expansion (MCL)

Study design: Phase II dose expansion



*From C2 and beyond, premedication was optional for patients who did not experience CRS in the previous cycle; corticosteroid premedication consisted of 20mg of dexamethasone or 80mg of methylprednisolone, either IV or orally.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

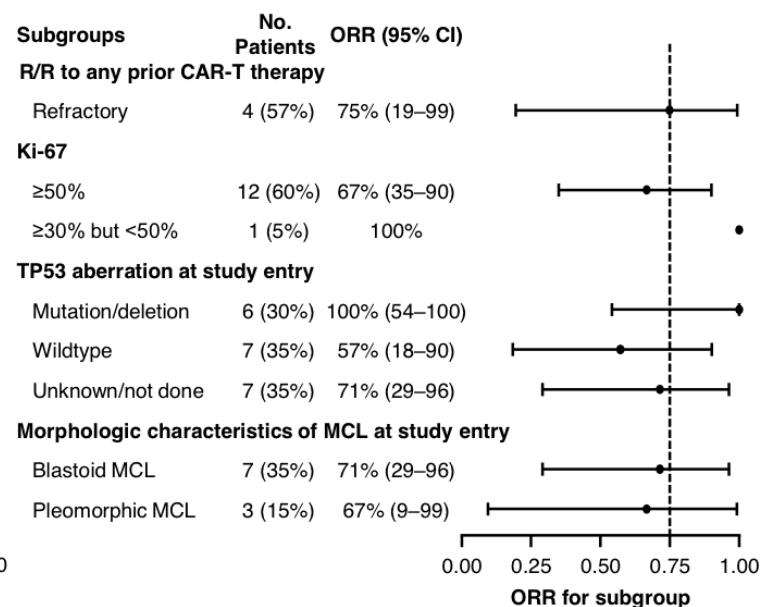
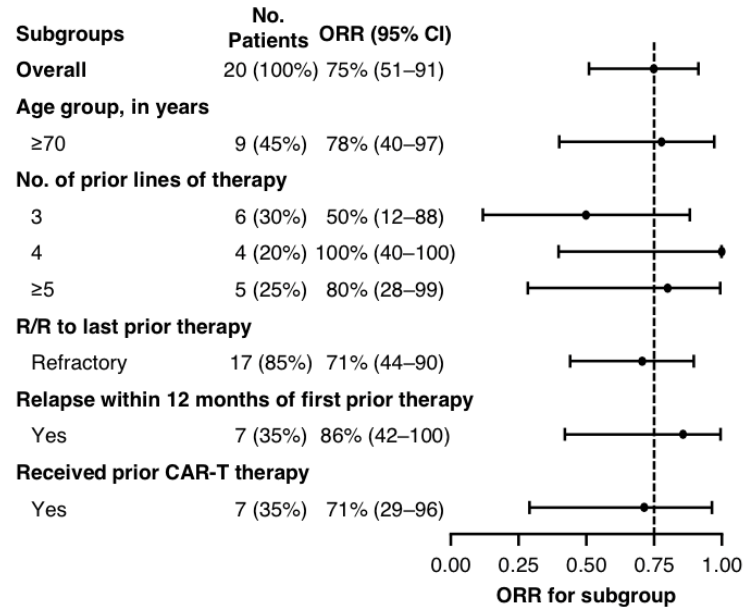
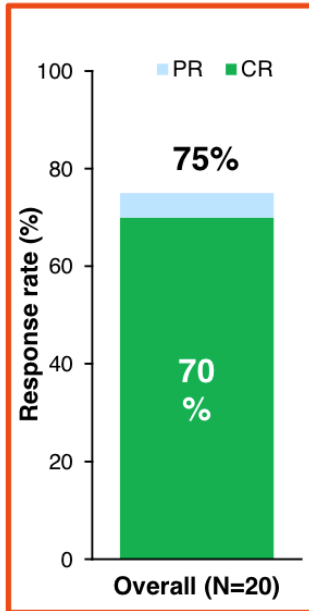
*From C2 and beyond, premedication was optional for patients who did not experience CRS in the previous cycle; corticosteroid premedication consisted of 20mg of dexamethasone or 80mg of methylprednisolone, either IV or orally.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

Response

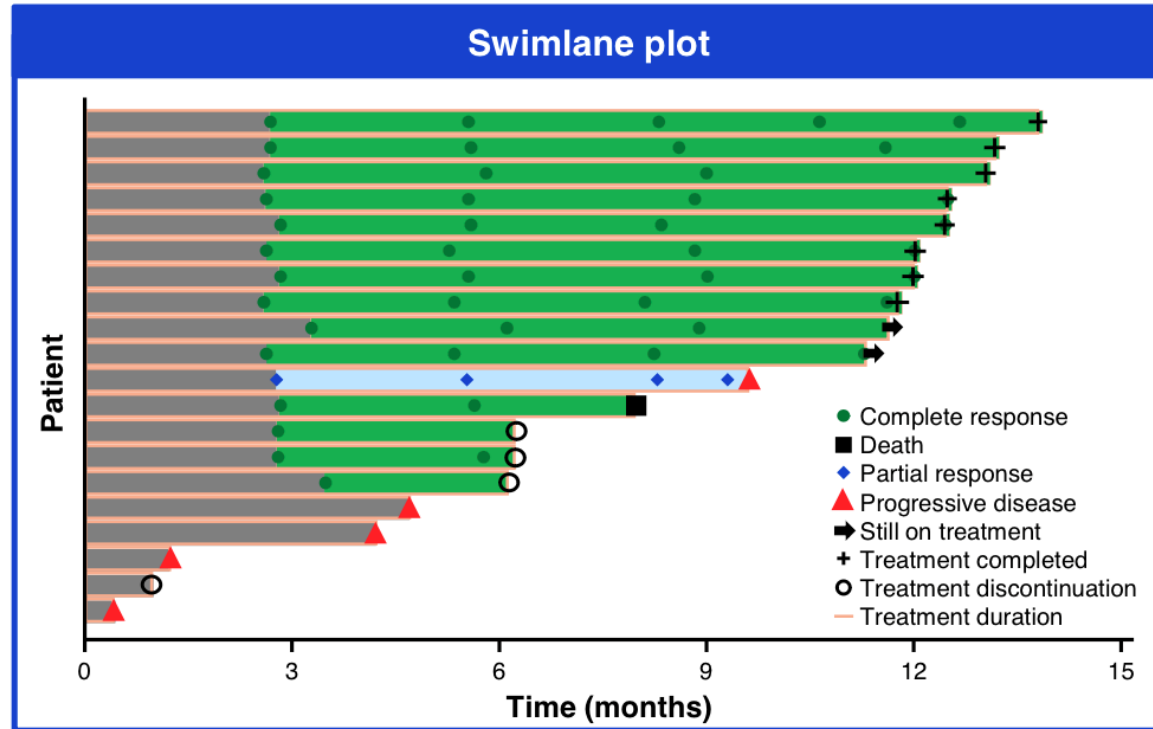
INV-assessed best ORR

ORR and CR rates in the overall population were 75% and 70%, respectively



Best ORR rates were generally consistent across high-risk MCL subgroups

Durability of response



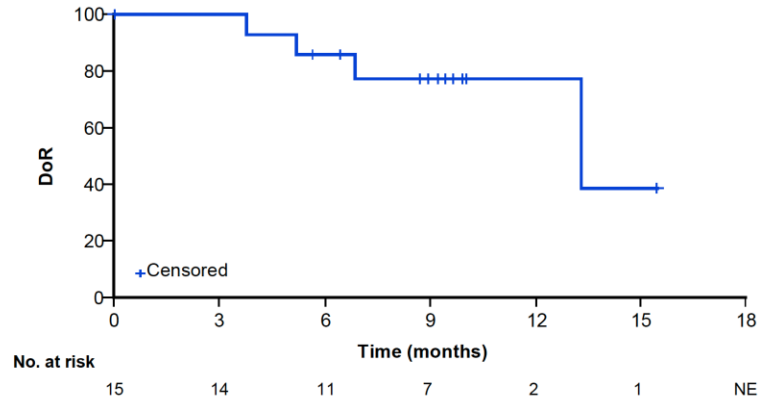
- Median follow-up: 15.8 months (range: 0–25)
- Median time to first response: 2.8 months (range: 2.6–3.4)
- Of 14 patients with CR, 11 remain in remission*

Complete remission was achieved early and remained durable

K/M Curves

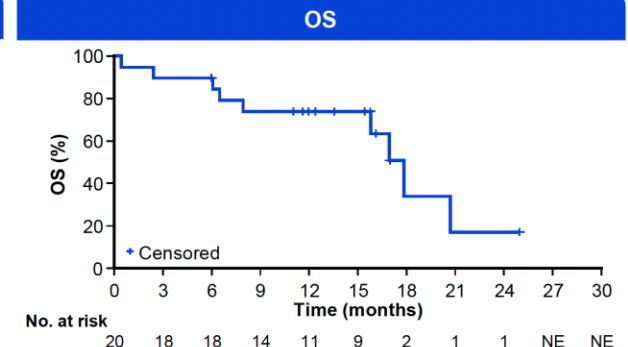
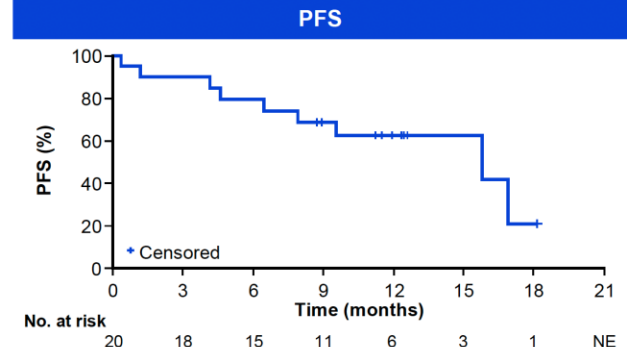
Duration of response (DoR)

Median DoR: 13.3 months (95% CI: 13.3–NE)



PFS and OS

Median follow-up: 15.8 months (95% CI: 12.4–NE)

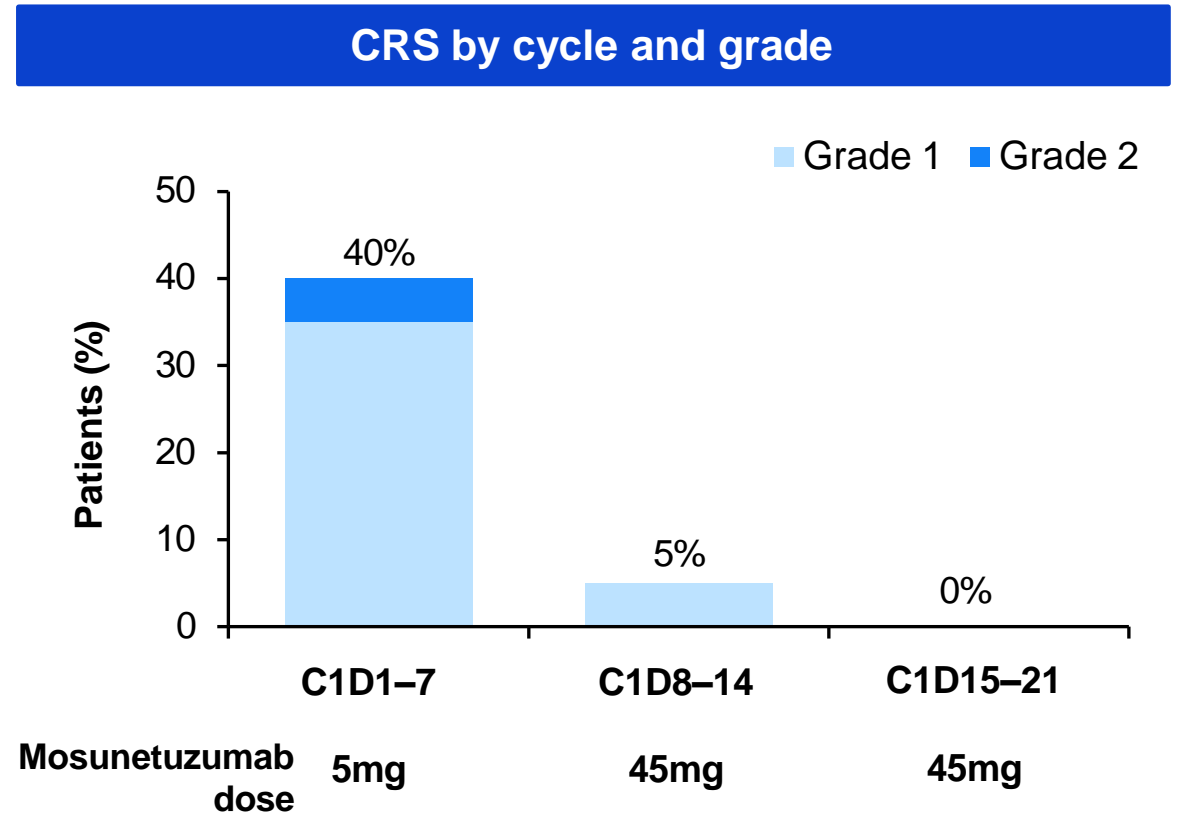


| N=20 | |
|-------------------------------------|-------------------|
| Median PFS, months (95% CI) | 15.8 (8.0–NE) |
| 9-month event-free rate, % (95% CI) | 68.8% (48.1–89.6) |

| N=20 | |
|-------------------------------------|-------------------|
| Median OS, months (95% CI) | 17.9 (15.8–20.7) |
| 9-month event-free rate, % (95% CI) | 74.1% (54.5–93.7) |

CRS summary

| CRS by ASTCT criteria ¹ | N=20 |
|--|---------|
| Any grade, n (%) | 9 (45) |
| Grade 1 | 8 (40) |
| Grade 2* | 1 (5) |
| Grade 3+ | 0 |
| Median time to first CRS onset relative to last dose, days (range) | 1 (0–2) |
| Median CRS duration, days (range) | 3 (1–9) |
| CRS management, n (%) | |
| Corticosteroids | 1 (5) |
| Tocilizumab | 1 (5) |
| Low-flow oxygen | 1 (5) |



All CRS events were low grade and resolved within C1

Clinical cut-off date: July 6, 2023. *This patient experienced Grade 2 fever, confusion, and hypoxia on D3; management included tocilizumab, low-flow oxygen, acetaminophen, and broad-spectrum antibiotics.
 ASTCT, American Society for Transplantation and Cellular Therapy

ICANS/Neuropathy

Other adverse events of interest

| AE summary, n (%) | | N=20 | AE summary, n (%) | | N=20 |
|------------------------------|--|----------|----------------------------|--|----------|
| ICANS* | | | Serious infections | | |
| Any grade | | 4 (20) | Any grade | | 8 (40.0) |
| Grade 3–4 | | 0 | Grade 3–4 | | 3 (15.0) |
| | | | Grade 5 [†] | | 3 (15.0) |
| Peripheral neuropathy | | | Neutropenia | | |
| Any grade | | 2 (10.0) | Any grade | | 4 (20.0) |
| Grade 3–4 | | 0 | Grade 3–4 | | 3 (15.0) |
| Tumor flare | | | Febrile Neutropenia | | |
| Any grade | | 2 (10.0) | | | 1 (5.0) |
| Grade 3–4 | | 0 | | | |

Mosun-pola demonstrated a manageable safety profile consistent with that of the individual agents in patients with R/R MCL, including those with high-risk features

Clinical cut-off date: July 6, 2023. *Treatment-related neurologic AEs potentially consistent with ICANS; patient cases included two cases of memory impairment (Grade 1 and Grade 2), amnesia (Grade 2), agitation (Grade 1), confusional state (Grade 1).

[†]Grade 5 infections included 2 cases of COVID-19 pneumonia and 1 case of COVID-19.

Conclusion

- Based on SYMPATICO should BTKi combo with venetoclax be considered SOC in 2L?
 - acalabrutinib, zanubrutinib since ibrutinib is no longer approved in R/R MCL (issue in US only)
- Where will pirtobrutinib fit?
 - Will results of BRUIN 302 bump up the agent
 - What does that mean for the cBTKi??
- T-cell therapies
 - CAR-T only one approved option (now) – high toxicity (brexucabtegene)
 - Liso-cel likely approved soon
 - Better option in older/frail patients?
 - Where will bispecifics fit in?
- Other agents/targets
 - Nemtabrutinib, Zilovertamab, Golcadomide, BAFF-R



Thank you!

Enter your name

Enter your position, contacts (e-mail) and other related information