# La rivoluzione terapeutica nel **linfoma** e nel **mieloma**

Napoli, Royal Hotel Continental • 14–15 Maggio 2026

## La terapia del MCL R/R

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## Disclosures

| Company name | Research support | Employee | Consultant | Stockholder | Speakers bureau | Advisory board | Other |
|---|---|---|---|---|---|---|---|
| Abbvie | | | X | | X | X | |
| Astrazeneca | | | | | X | X | |
| Beigene | | | | | X | | |
| Eli-Lilly | | | | | X | | |
| Incyte | | | X | | X | | |
| Jannsen | | | X | | X | | |
| Kite-Gilead | | | | | X | X | |
| Novartis | | | X | | X | X | |
| BMS | | | X | | X | | |
| Roche | | | x | | X | X | |
| Recordati-Rare disease | | | | | X | | |
| Sobi | | | | | X | | |
| Takeda | | | | | X | X | |

# Key Considerations After First-Line Therapy

## Patient Characteristics

- AEs
- Fixed duration vs no limits
- Comorbidity burden

Impact on tolerability and on Fitness status

## Disease Characteristics

- Classic
- Pleomorph
- Blastoid

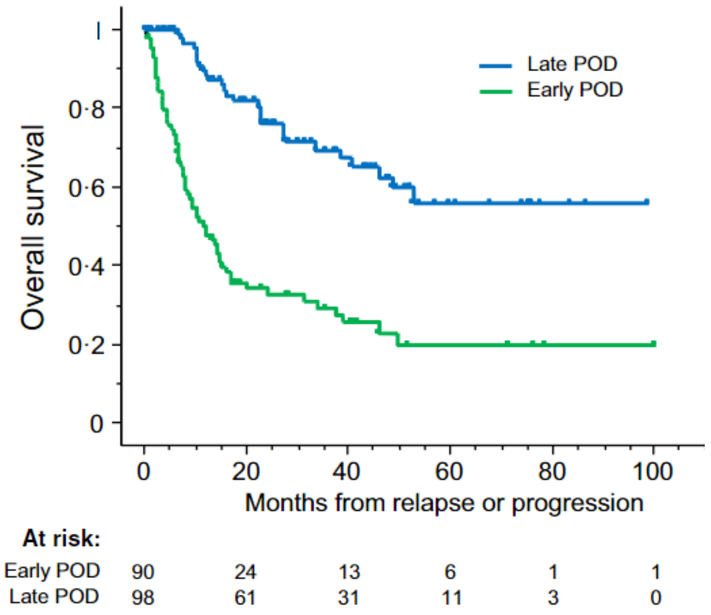
- Ki67 >30%
- Ki67 >50%

- TP53 gene mut

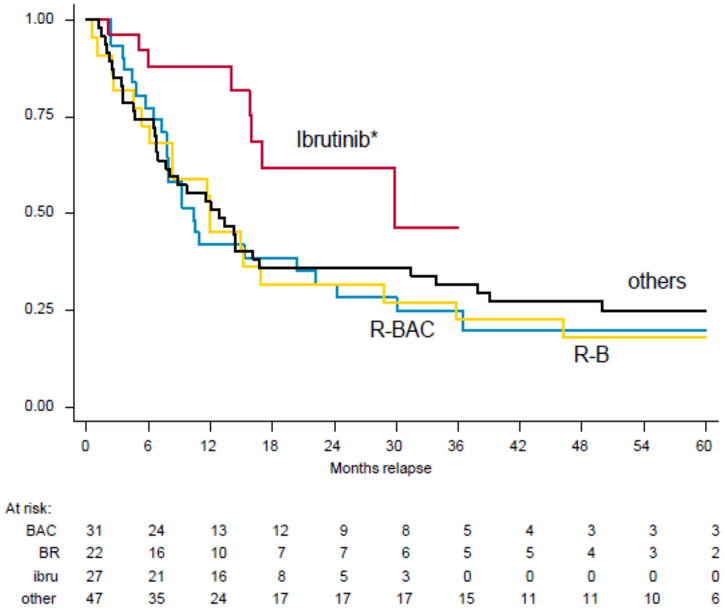
- MIPI

Impact on efficacy and timing of relapse (early vs late POD)

# Timing to Relapse or Progression: Early vs Late POD

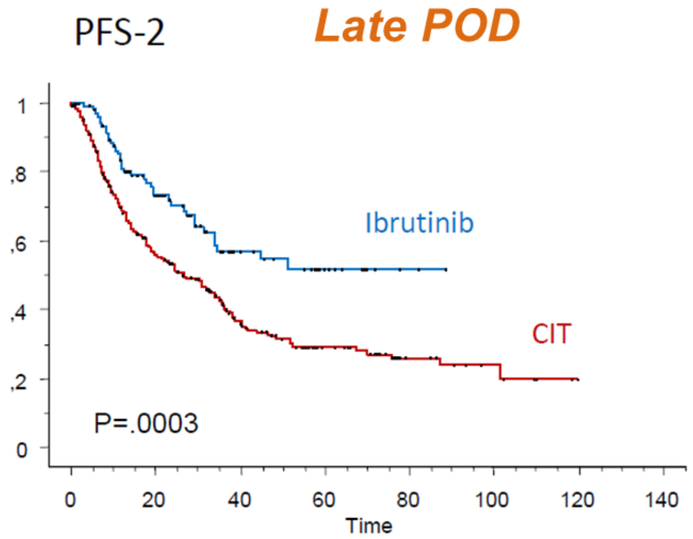



## Early POD




*Ibru vs R-B and R-BAC (P=0.02); vs others (P=0.03)

## Late POD




Median 26 months for CIT;
NR for Ibrutinib

*Visco C et al, BJH 2019; Visco C et al, Leukemia 2020; Malinverni C et al, Blood 2024*

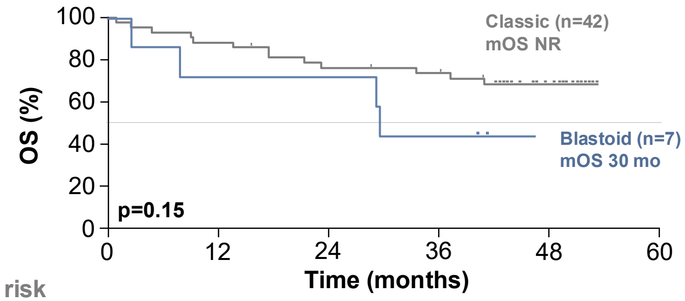
# Outcomes Are Poor in Patients With R/R MCL and High-Risk Features After Treatment With Ibrutinib

## Phase 2 open-label study of ibrutinib plus rituximab *(N=50; median 3 [range 1–6] prior lines of therapy)*

**High-risk feature**

**OS**

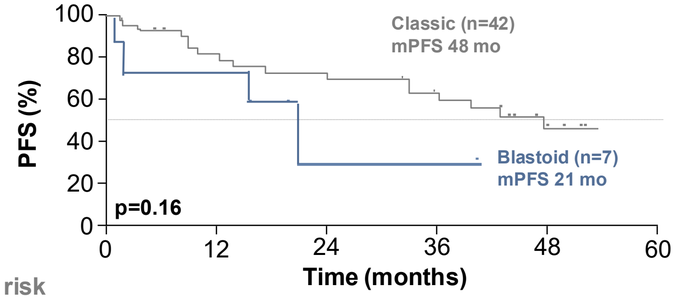
**MCL morphology (classic vs. blastoid)**




| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| Blastoid | 7 | 6 | 5 | 4 | 1 | 0 |
| Classic | 42 | 37 | 32 | 29 | 15 | 0 |

*Adapted from Figure 2D in Ref.* Jain P, *et al. Br J Haematol* 2018

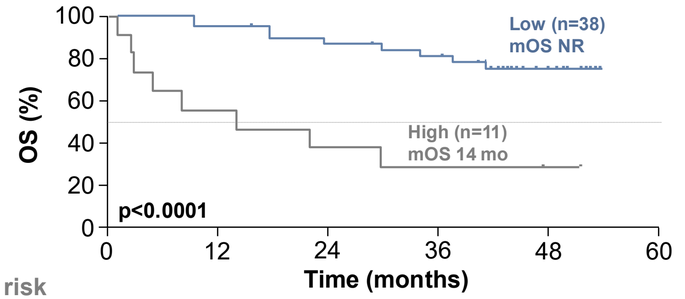
**PFS**




| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| Blastoid | 7 | 6 | 2 | 1 | 1 | 0 |
| Classic | 42 | 27 | 23 | 18 | 8 | 0 |

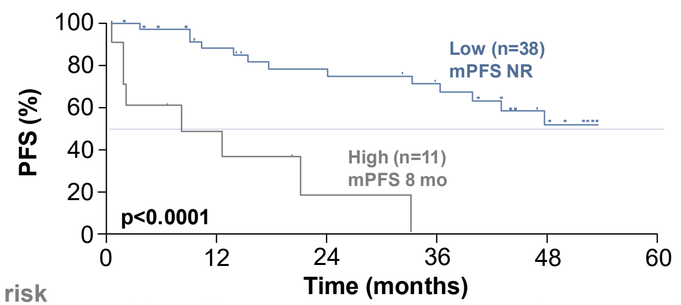
*Adapted from Figure 2A in Ref.* Jain P, *et al. Br J Haematol* 2018

**Ki-67 index (low <50% vs. high ≥50%)**




| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| Low | 38 | 37 | 33 | 29 | 14 | 0 |
| High | 11 | 6 | 5 | 4 | 2 | 0 |

*Adapted from Figure 2F in Ref.* Jain P, *et al. Br J Haematol* 2018




| No. at risk | | | | | | |
|---|---|---|---|---|---|---|
| Low | 38 | 29 | 23 | 18 | 8 | 0 |
| High | 11 | 4 | 2 | 1 | 1 | 0 |

*Adapted from Figure 2C in Ref.* Jain P, *et al. Br J Haematol* 2018

Median OS and PFS were lower in patients with vs. without high-risk features

*Jain P, et al. Br J Haematol 2018; 182:404–411*

# Current Treatment in Mantle Cell Lymphoma

**Preferred First-line Treatment Options**

**Aggressive Chemotherapy**
R-DHAP ( cisplatin, or oxaliplatin)
R-CHOP/R-DHAP (alternating)
NORDIC (maxi-CHOP/R + HD cytarabine)

→ **Consolidation and Maintenance**
HDT + ASCT → R maint for 3 yr

**Less Aggressive Chemotherapy**
BR
R-CHOP
RBAC

→ **Maintenance**
After R-CHOP: R maint until Progression.

**Preferred Second-line Treatment Options**

**BTK inhibitor**
- Ibrutinib
- Pirtobrutinib (if previously treated with Ibrutinib)

**Third-line Treatment**

**Brexucabtagene autoleucel (after chemoimmunotherapy and BTK inhibitor)**

Pirtobrutinib

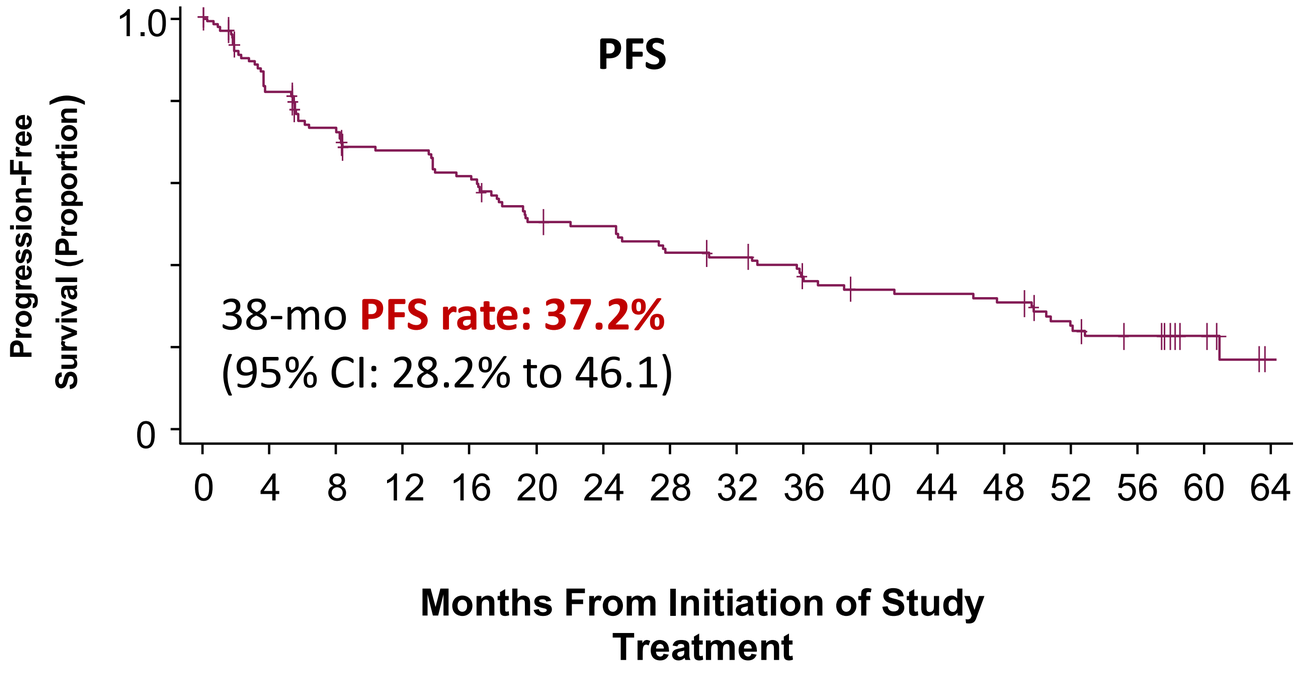
Adattato da NCCN guidelines version 1.0 2024.

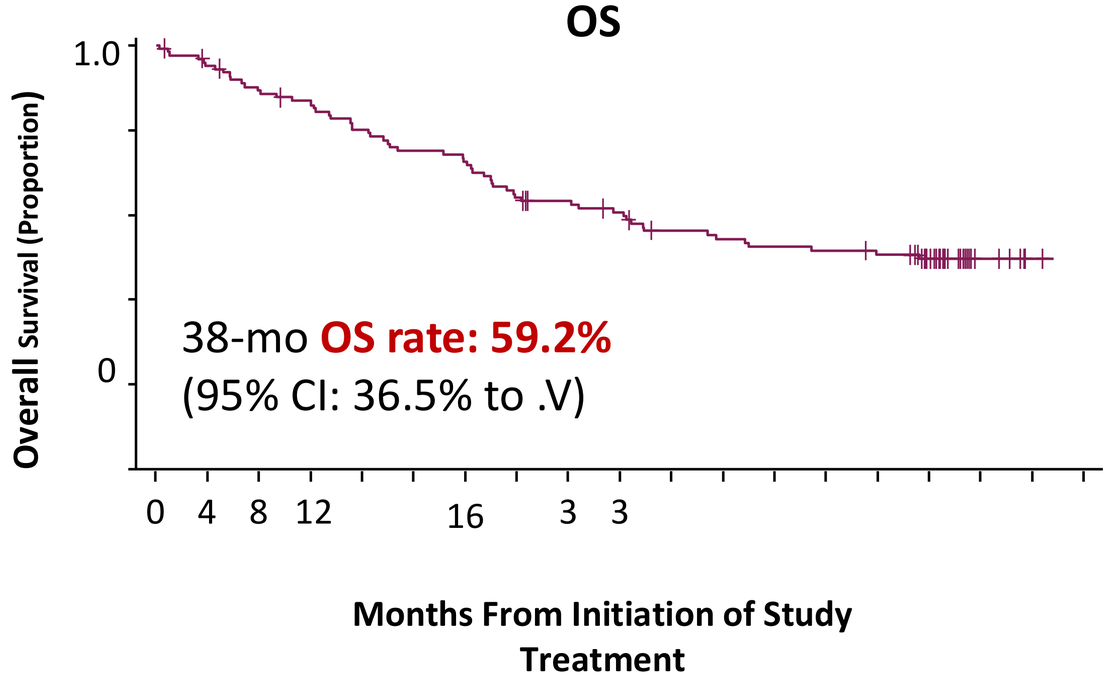
# ACE-LY-004 (38-Month Results): Acalabrutinib in RR-MCL
# PFS and OS

Adult patients with MCL;
1-5 prior lines of tx; ECOG PS 0-2; no notable CVD*; no concurrent use of warfarin/equivalent vitamin K antagonists, no prior BTK inhibitors
**(N = 124)**
**ORR= 81%, CRR = 40%**

**Acalabrutinib** 100 mg PO BID in 28-day cycles

***Until PD***




Le Gouill S et al. *Haematologica*. 2024; 109(1): 343-350

blood® Regular Article

# Zanubrutinib in relapsed/refractory mantle cell lymphoma: long-term efficacy and safety results from a phase 2 study

**Zanubrutinib** 160 mg PO BID

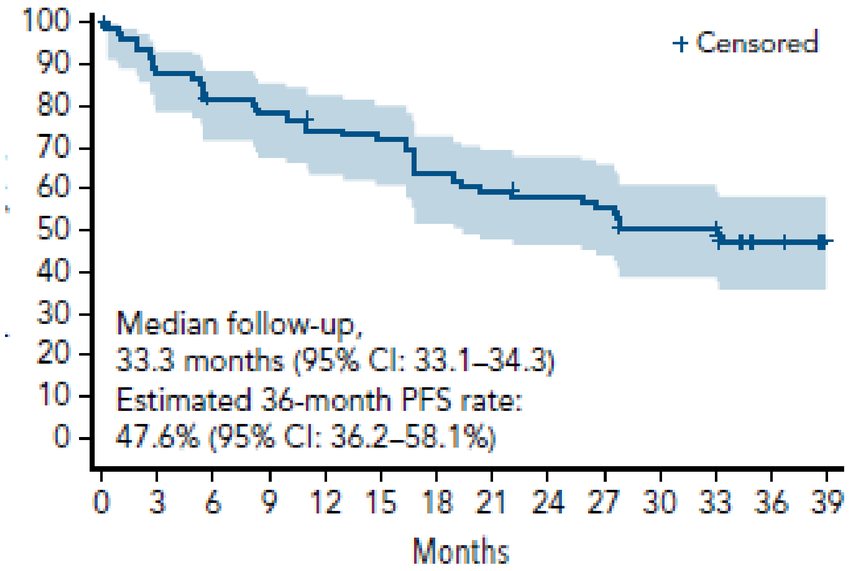
**Zanubrutinib monotherapy demonstrates durable clinical benefit in the long-term follow-up of patients with relapsed/refractory MCL**

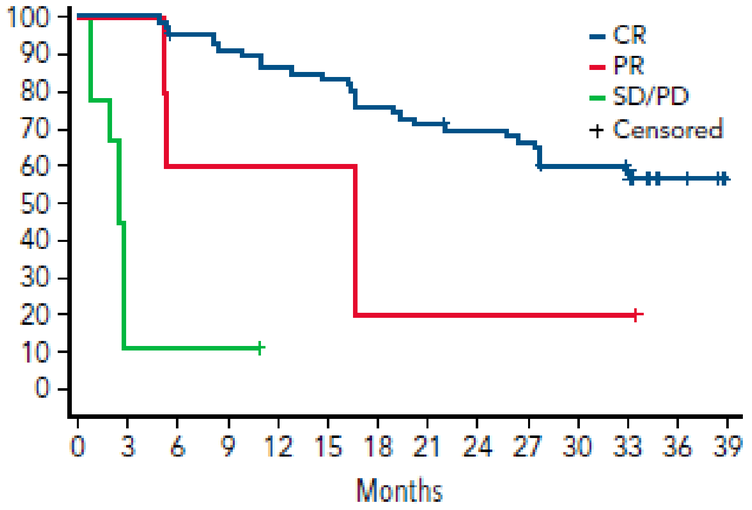
| | Response | PFS 2 years | PFS 3 years |
|---|---|---|---|
| Phase 2<br>86<br>Patients with R/R MCL<br>Median follow-up 35.3 months | ORR 84%<br>CR 78% | 58% | 48% |
| | **Median DOR** | **OS 2 years** | **OS 3 years** |
| | Not reached (95% CI: 24.9 months to NE) | 80% | 75% |

**Zanubrutinib was well tolerated**

- Few discontinuations (9.3%) due to AEs
- Majority of AEs: low-grade severity
- No atrial fibrillation/flutter
- No second primary malignancies

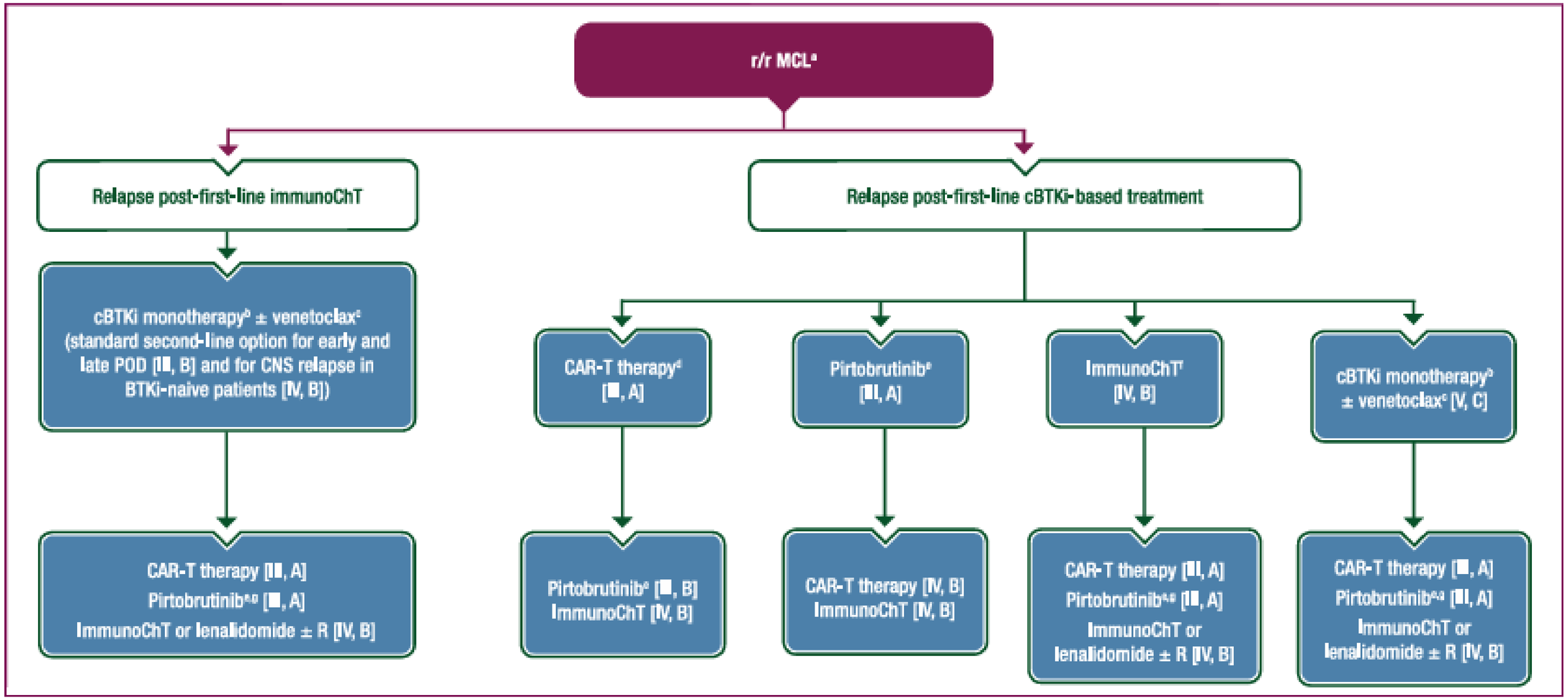
## PFS 36-months follow up




Song Y. et al . Blood . 2022; 139:3149

# Lymphomas: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆




T. A. Eyre et al. ESMO GUIDELINES 2025

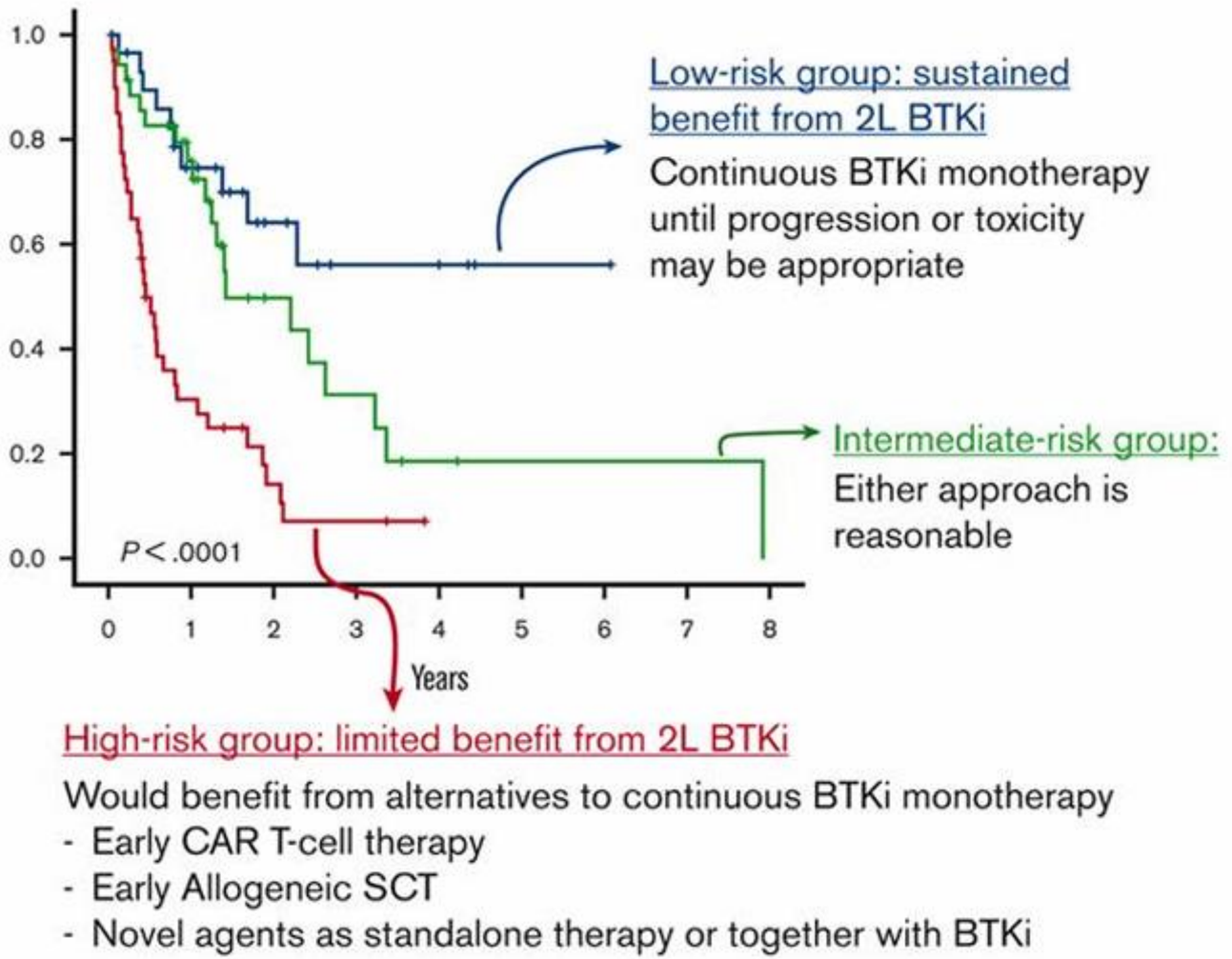
# Time to progression of disease and outcomes with second-line BTK inhibitors in R/R MCL

- Prognostic index: 2L BTKi MIPI

| Variable | | N | Hazard ratio | P |
|---|---|---|---|---|
| POD | POD>24 | 79 | Reference | |
| | POD6–24 | 51 | 2.19 (1.47, 3.28) | <.001 |
| | POD6 | 30 | 4.82 (3.04, 7.65) | <.001 |
| KI67 | <30% | 92 | Reference | |
| | >=30% | 68 | 1.47 (1.11, 1.94) | .007 |
| MIPI | Low | 49 | Reference | |
| | Intermediate or High | 111 | 1.18 (0.81, 1.72) | .384 |

1 2 3 4 5 6 7

The 2L BTKi MIPI identifies patients expected to have **limited disease control with 2L BTKis** and **who may benefit from other therapies**



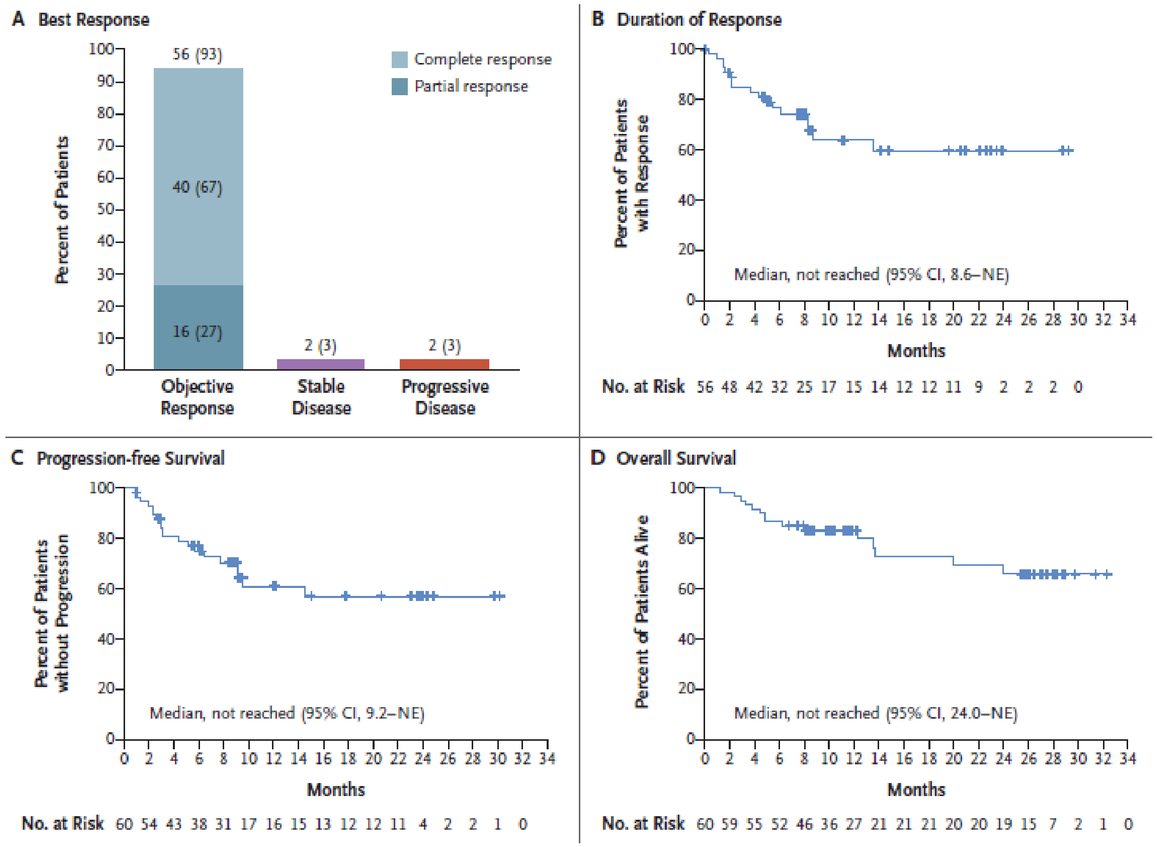

*Villa et al, Blood Advances 2023*

# (KTE-X19) in Relapsed or Refractory Mantle Cell Lymphoma

## ZUMA-2 study

**Table 1. Baseline Characteristics of All 68 Treated Patients.***

| Characteristic | Patients |
|---|---|
| Median age (range) — yr | 65 (38–79) |
| Intermediate or high risk according to Simplified MIPI — no. (%)†‡ | 38 (56) |
| Blastoid or pleomorphic morphologic characteristics of MCL — no. (%) | 21 (31) |
| Ki-67 proliferation index ≥30% — no./total no. (%)‡ | 40/49 (82) |
| *TP53* mutation — no. (%) | 6/36 (17) |
| Positive CD19 status — no./total no. (%) | 47/51 (92) |
| Median no. of previous therapies (range)§ | 3 (1–5) |
| ≥3 Previous lines of therapy — no. (%) | 55 (81) |
| Previous autologous stem-cell transplantation — no. (%) | 29 (43) |
| Previous BTK inhibitor therapy — no. (%)§ | 68 (100) |
| Ibrutinib | 58 (85) |
| Acalabrutinib | 16 (24) |
| Both | 6 (9) |
| Relapsed or refractory disease — no. (%) | |
| Relapse after autologous stem-cell transplantation | 29 (43) |
| Refractory to most recent previous therapy | 27 (40) |
| Relapse after most recent previous therapy | 12 (18) |
| Disease that relapsed or was refractory to BTK inhibitor therapy — no. (%) | 68 (100) |
| Refractory to BTK inhibitor therapy | 42 (62) |
| Relapse during BTK inhibitor therapy | 18 (26) |
| Relapse after BTK inhibitor therapy | 5 (7) |
| Could not take BTKi therapy because of adverse events | 3 (4) |




**Toxicity**

| Event | Any Grade | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|---|
| | *number of patients (percent)* | | | | | |
| Symptom of cytokine release syndrome | | | | | | |
| Any | 62 (91) | 20 (29) | 32 (47) | 8 (12) | 2 (3) | 0 |
| Neurologic event | 43 (63) | 13 (19) | 9 (13) | 15 (22) | 6 (9) | 0 |

Wang M, et al. New Engl J Med (2020) 382:1331-42

# ZUMA-2: has Brexu-cel shown durable responses in R/R MCL?

**ZUMA-2**

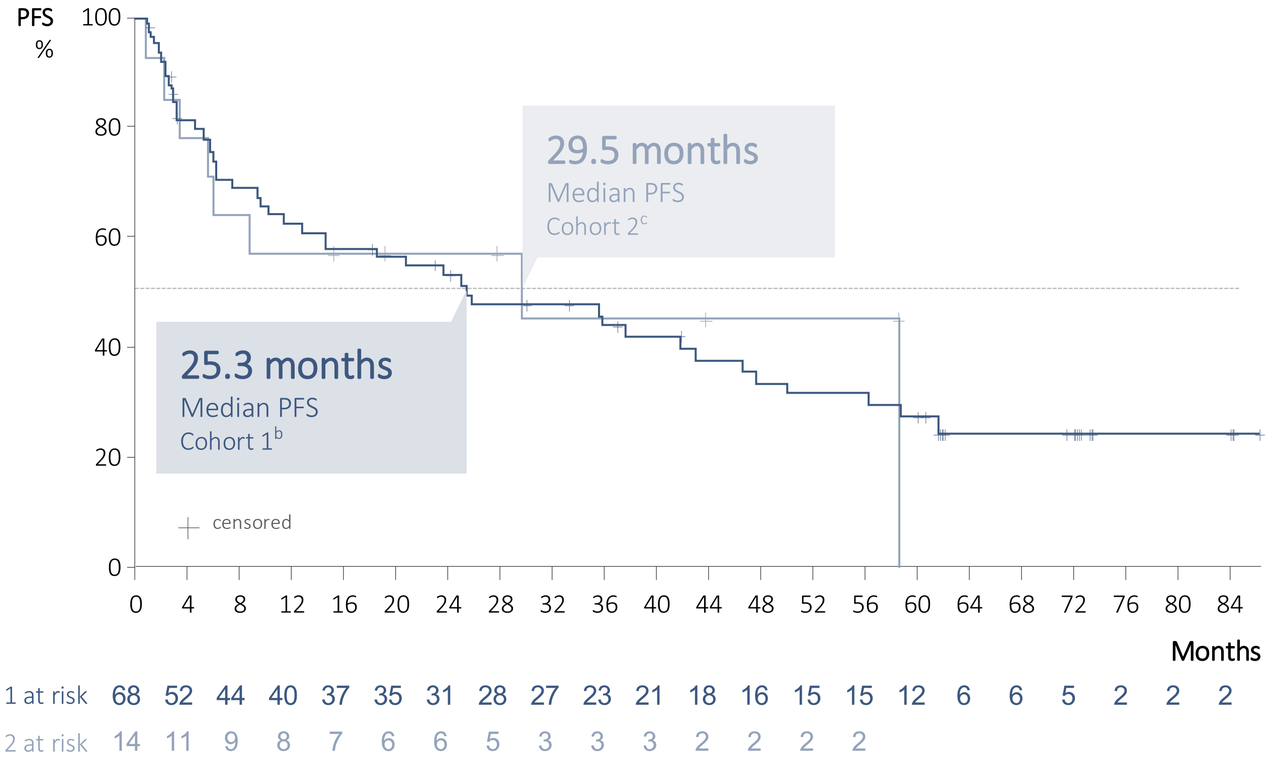
Analysis of patients with R/R 2L+ R/R MCL[a] receiving **brexu-cel**

**ZUMA-2 cohort 1:**[b] N=68
mFU: 67.8 months

**ZUMA-2 cohort 2:**[c] N=14
mFU: 72.3 months

All patients received prior BTKi

**37%** and **50% of patients** received bridging therapy in **cohort 1** and **cohort 2**, respectively




**Median follow-up of 5 years**

**ORR 93%**
**CR rate 64%**

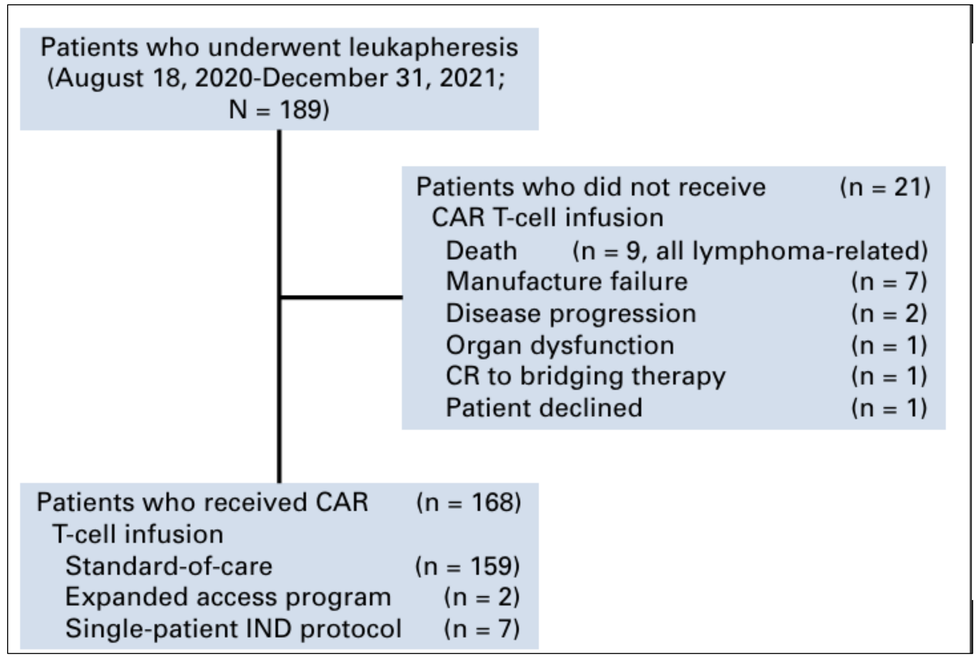
Late-onset toxicities were infrequent; only 3% of treatment-emergent adverse events of interest in ZUMA-2 occurred during this longer follow-up

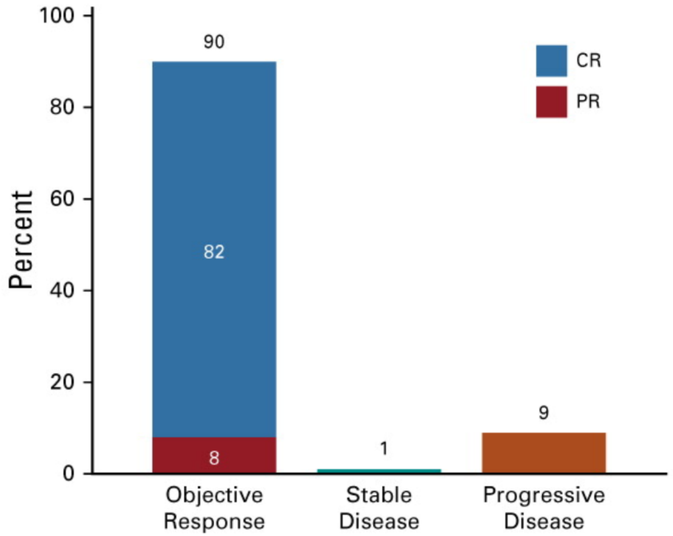
With >5 years of median follow-up, brexu-cel shows **durable responses** in this hard-to-treat population

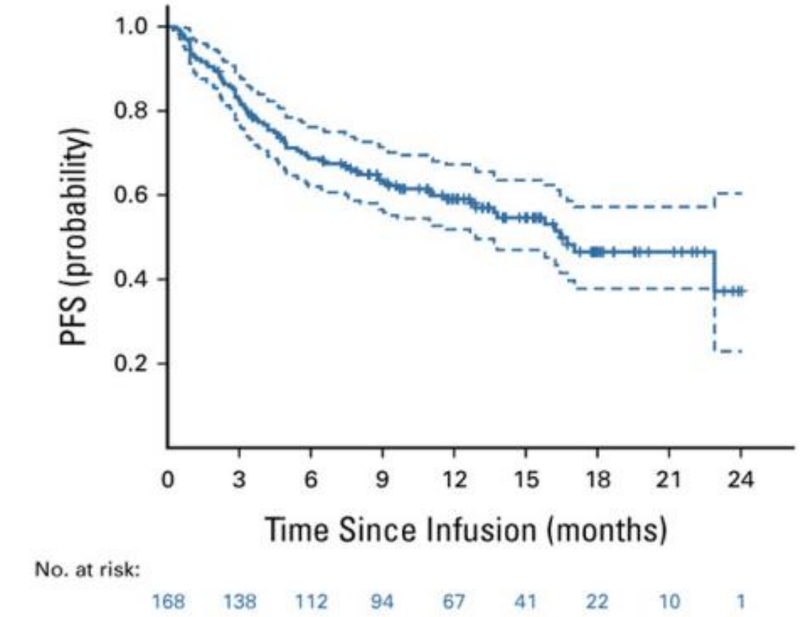
Adapted from Wang M, et al. ASH 2024 (Abstract 4388, poster); 2. https://www.clinicaltrials.gov/study/NCT02601313#participation-criteria as support. (accessed June 2025)

# Brexu-cel for R/R MCL in Standard of Care Practice: results from the US consortium

**US Lymphoma CAR T Consortium: retrospective, multicenter study in patients receiving KTE-X19 (n= 189)**



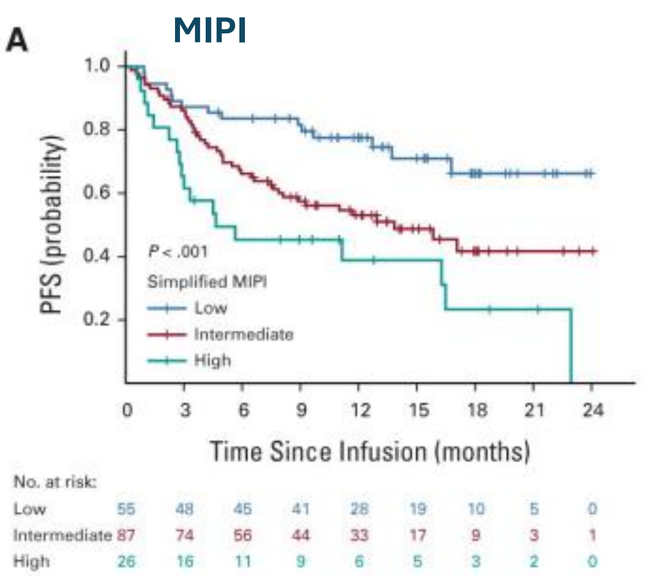



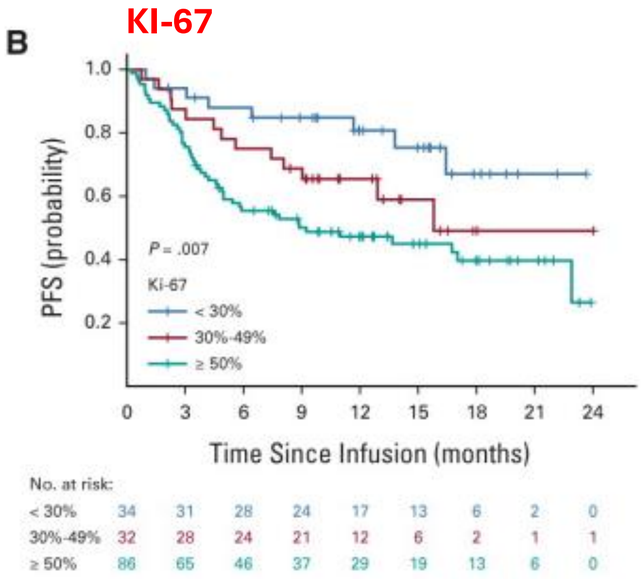



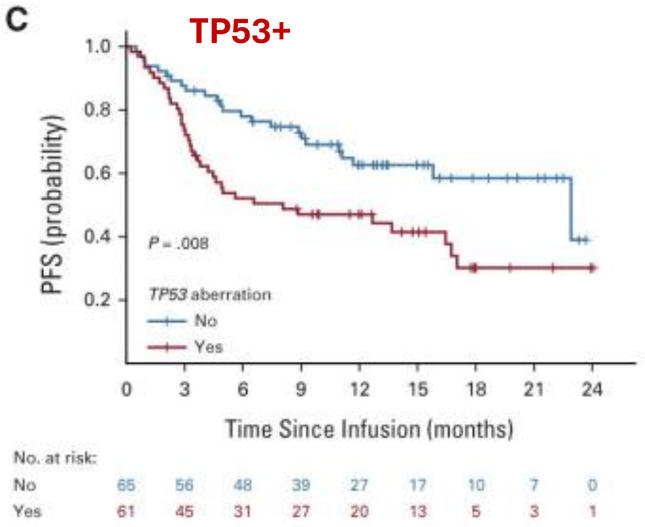

The 12-month estimates for PFS rate appeared to be comparable with those in ZUMA-2

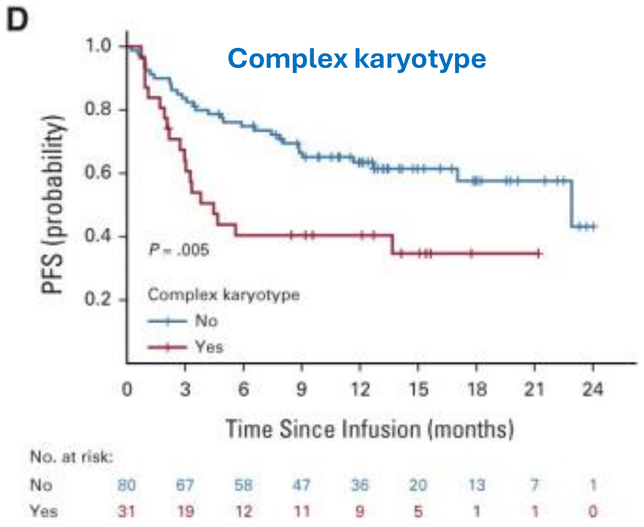
*Wang Y, et al. JCO 2023*

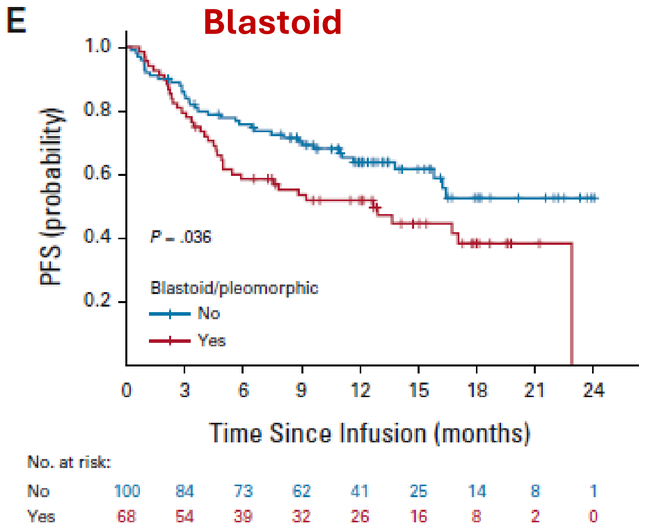
# Brexu-cel for R/R MCL in Standard-of-Care Practice

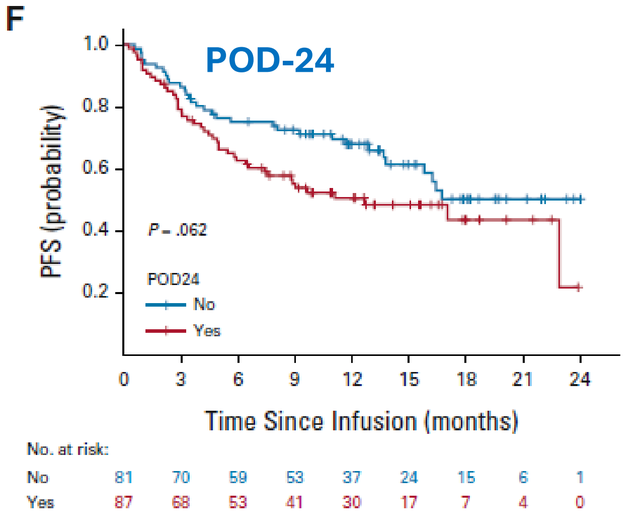


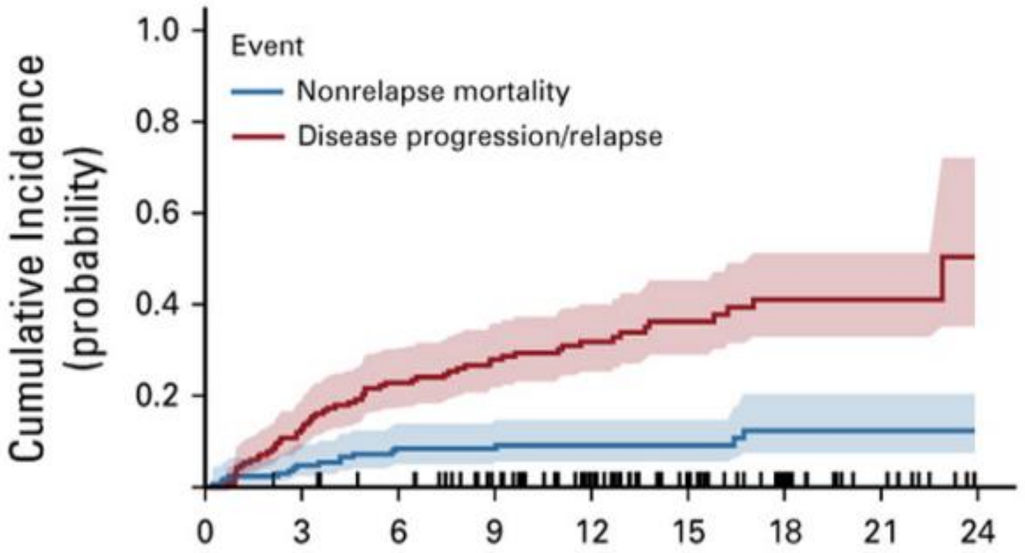

*Wang Y, et al. JCO 2023*

# Short term and long term toxicity

- The incidences of CRS and ICANS were comparable to those reported in ZUMA-2.
- Tocilizumab and corticosteroids use appeared to be more frequent in this Consortium study cohort

| | CRS, n (%) | ICANS, n (%) | ZUMA-2 CRS (%) | ZUMA-2 NE (%) |
|---|---|---|---|---|
| **Total** | 86 (91%) | 57 (60%) | 91% | 63% |
| **Max Grade*** | | | | |
| **1-2** | 78 (82%) | 24 (25%) | 76% | 32% |
| **3-4** | 8 (8%) | 33 (35%) | 15% | 31% |
| **Days to onset** | 4 (0-11) | 6 (1-15) | 2 (1-13) | 7 |
| **Days to max Grade** | 5 (0-7) | 7 (3-15) | - | - |
| **Duration** | 5 (1-33+) | 6 (2-144+) | 11 | 12 |

- **The non relapse mortality was 9.1% at 1 year**, primarily because of infections.

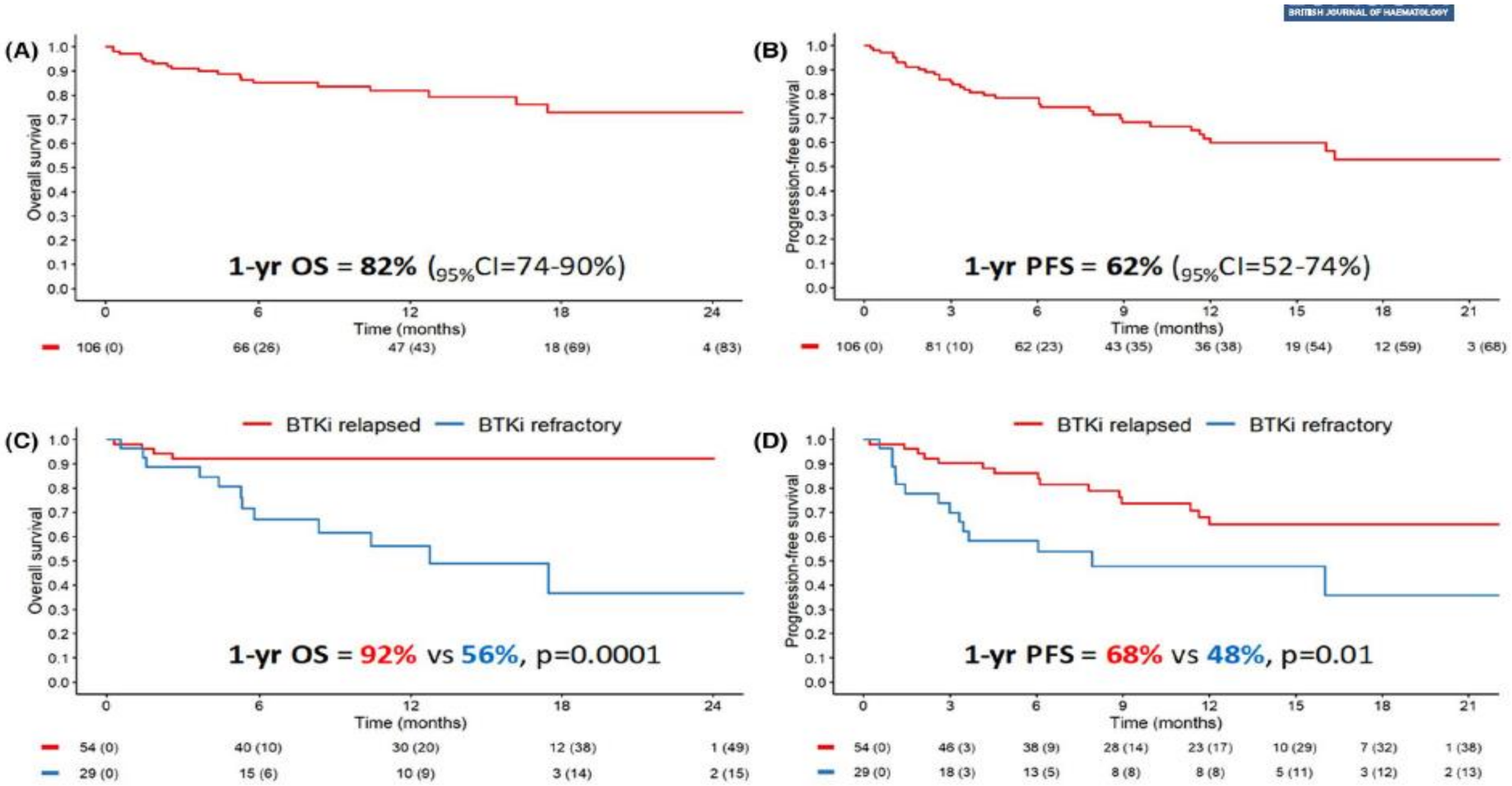



*Wang Y, et al. JCO 2023*

ORIGINAL PAPER
Transplantation and Cellular Therapy

# Brexucabtagene autoleucel in-vivo expansion and BTKi refractoriness have a negative influence on progression-free survival in mantle cell lymphoma: Results from CART-SIE study

# CART-SIE




**Response @ day + 90: ORR 77%, CR 70%**

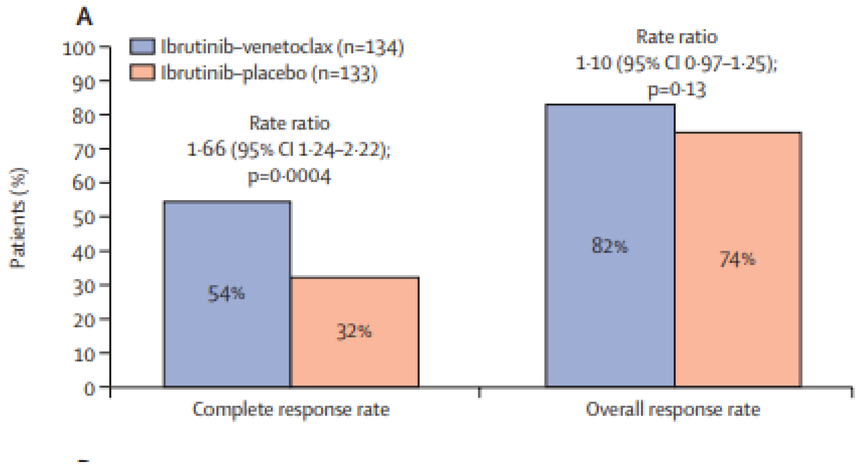
**Median follow-up: 12.07 months (IQR: 5.95, 17.86**

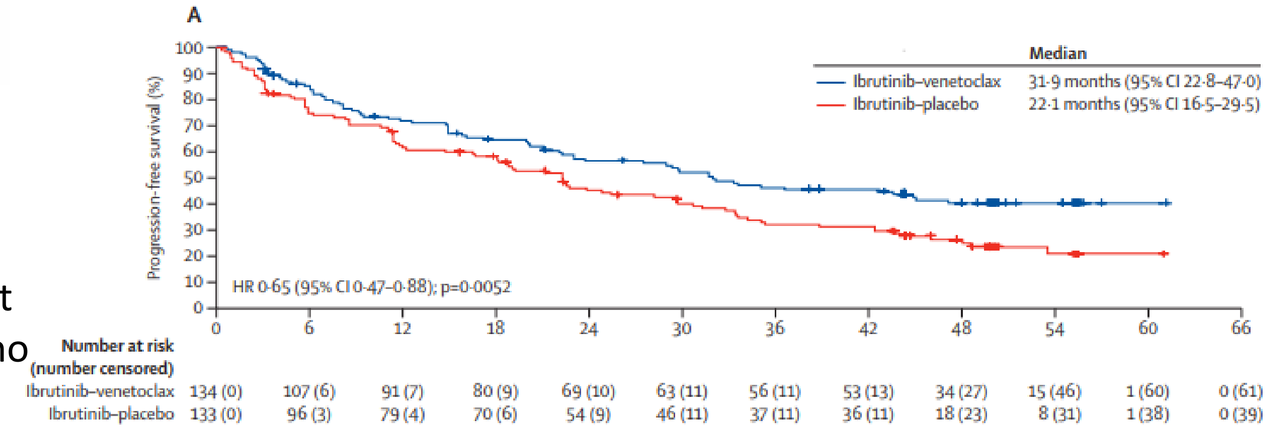
Stella F. et al, B.J.Hematology 2024

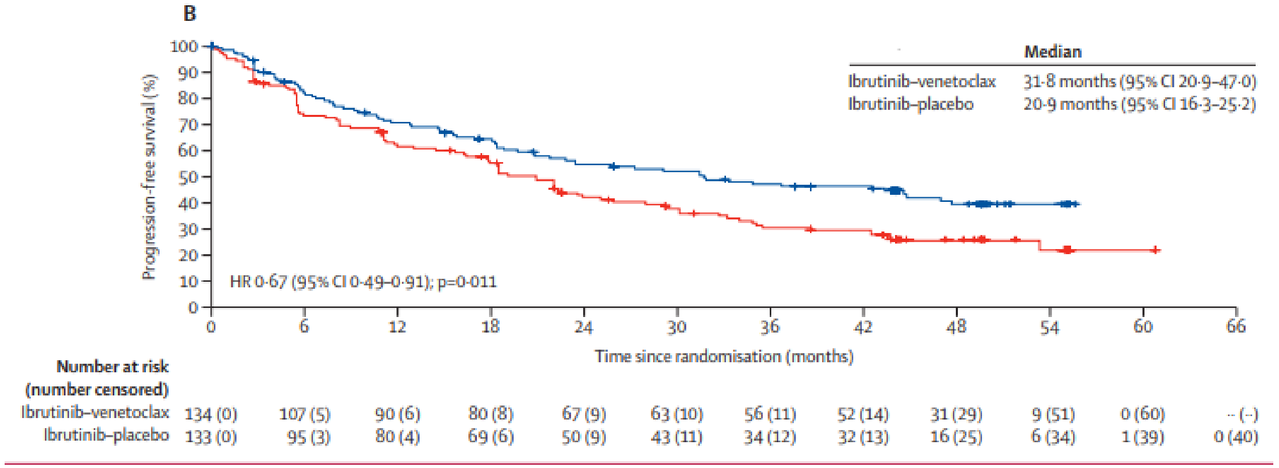
# Ibrutinib plus venetoclax in relapsed or refractory mantle cell lymphoma (SYMPATICO): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study

Michael Wang, Wojciech Jurczak, Marek Trneny, David Belada, Tomasz Wrobel, Nilanjan Ghosh, Mary-Margaret Keating, Tom van Meerten, Ruben Fernandez Alvarez, Gottfried von Keudell, Catherine Thieblemont, Frederic Peyrade, Marc Andre, Marc Hoffmann, Edith Szafer-Glusman, Jennifer Lin, James P Dean, Jutta K Neuenburg, Constantine S Tam

- The addition of venetoclax to ibrutinib in an all-oral regimen improved outcomes compared with ibrutinib alone
- The safety profile of ibrutinib–venetoclax was consistent with known adverse events for each single agent, with no new safety signals observed

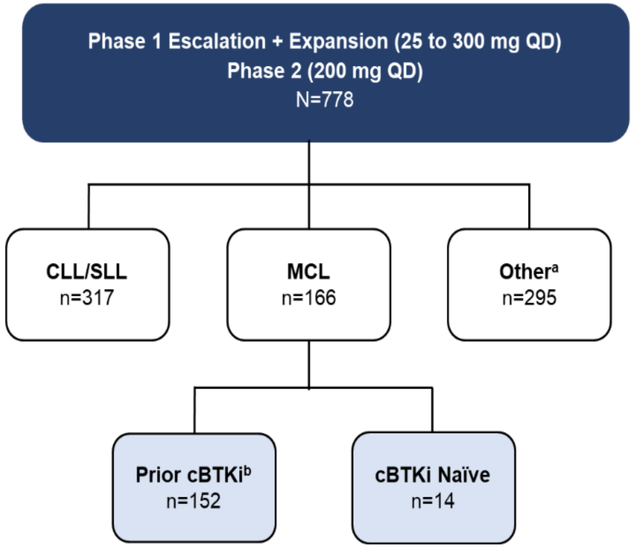



Wang et al. Lancet Oncol 2025

# Pirtobrutinib in Relapsed/Refractory (R/R) Mantle Cell Lymphoma (MCL) Patients with Prior cBTKi: Phase 1/2 BRUIN Study




**Key endpoints**

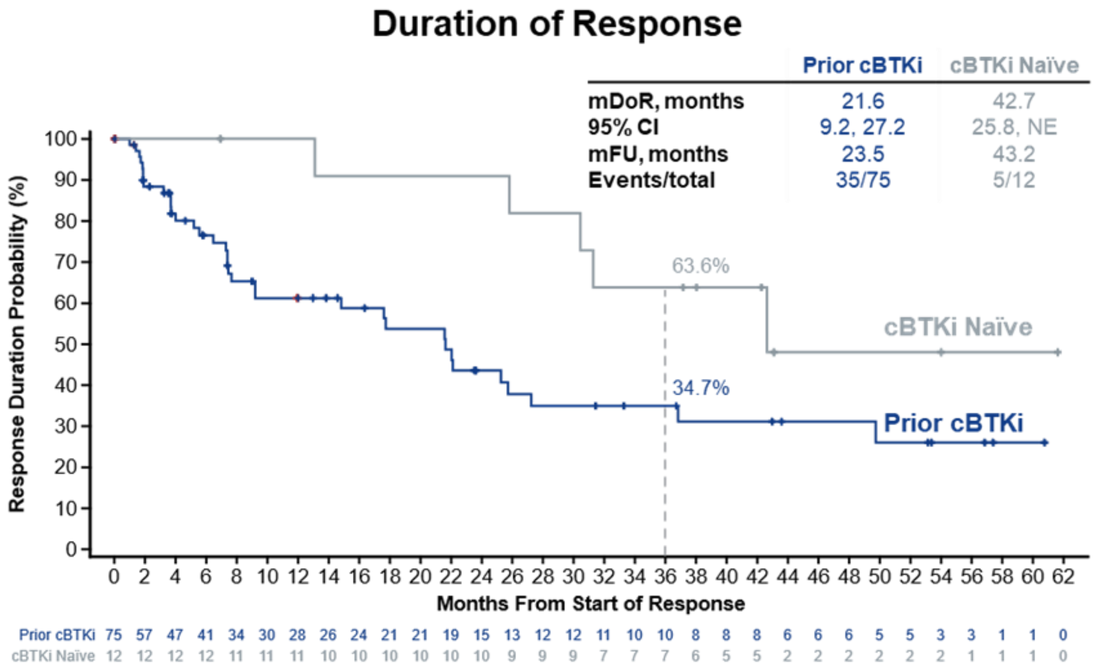
- Safety/tolerability
- Determine MTD and RP2D
- Pharmacokinetics
- Efficacy (ORR according to Lugano criteria, DoR, PFS, and OS)

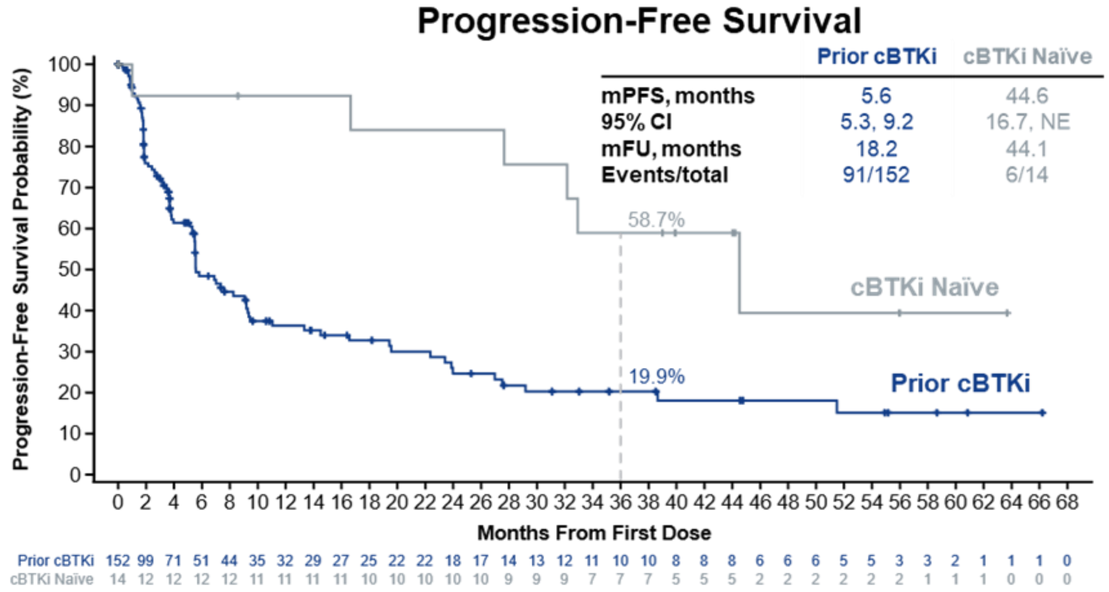
| Characteristics | Prior cBTKi n=152 | cBTKi Naïve n=14 |
|---|---|---|
| **Prior therapy**, n (%) | | |
| BTK inhibitor | 152 (100) | 0 (0) |
| Anti-CD20 antibody | 147 (97) | 14 (100) |
| Chemotherapy | 137 (90) | 14 (100) |
| **Reason discontinued any prior BTKi[a]**, n (%) | | |
| Progressive disease | 128 (84) | - |
| Toxicity / Other | 21 (14) | - |
| Unknown | 3 (2) | - |
| **Ki-67 index**, n (%) | | |
| <30% | 18 (12) | 2 (14) |
| ≥30% | 45 (30) | 6 (43) |
| Missing | 89 (59) | 6 (43) |
| **Histology**, n (%) | | |
| Classic/leukemic | 120 (79) | 11 (79) |
| Pleomorphic/Blastoid | 32 (21) | 3 (21) |
| **sMIPI score**, n (%) | | |
| Low risk (0-3) | 30 (20) | 3 (21) |
| Intermediate risk (4-5) | 79 (52) | 5 (36) |
| High risk (6-11) | 43 (28) | 6 (43) |

| Prior cBTKi | n=152 |
|---|---|
| **ORR[b]** % (95% CI) | 49.3 (41.1-57.6) |
| **Best Response,** n (%) | |
| **CR** | 24 (15.8) |
| **PR** | 51 (33.6) |

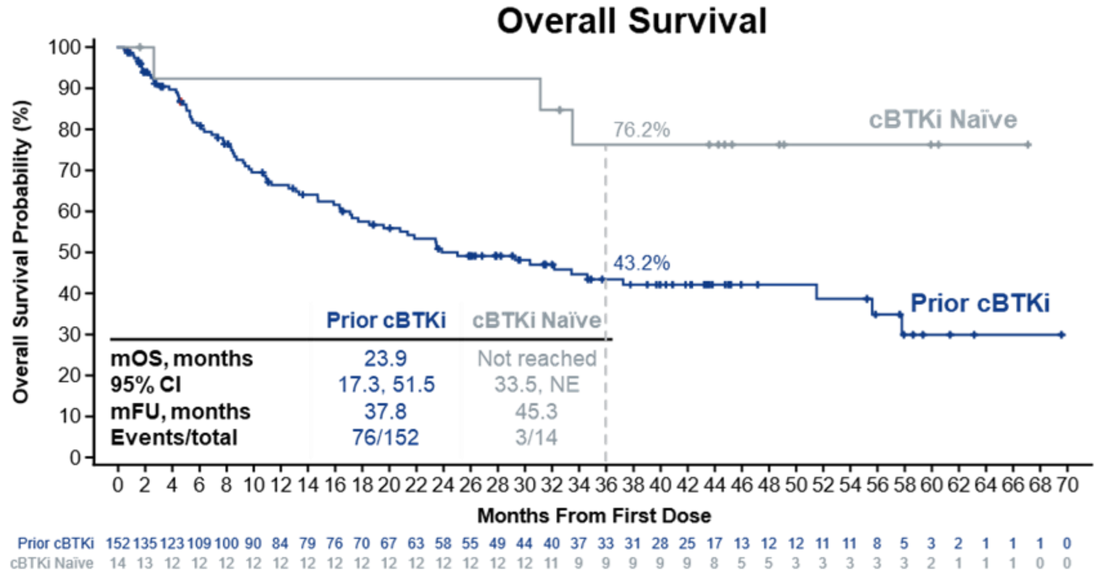
Cohen et al, ASH 2023

# Pirtobrutinib in Relapsed/Refractory (R/R) Mantle Cell Lymphoma (MCL): Final Update From the Phase 1/2 BRUIN Study




| Outcome by Reason of Discontinuation From Prior BTKi | PD | Toxicity/Other |
|---|---|---|
| mDoR, months<br>95% CI | 14.8<br>4.0, 27.2 | 25.3<br>7.5, NE |
| mPFS, months<br>95% CI | 5.5<br>3.8, 7.4 | 27.0<br>9.3, NE |
| mOS, months<br>95% CI | 18.5<br>11.3, 33.5 | 57.8<br>32.2, NE |




*Abbreviations: BTKi, Bruton tyrosine kinase inhibitor; cBTKi, covalent BTKi; CI, confidence interval; MCL, mantle cell lymphoma; mDoR, median duration of response; mFU, median follow-up; mOS, median overall survival; mPFS, median progression-free survival; NE, not estimable; PD, progressive disease.*

*Wang M et al., ASH 2025, Abstract 7068*

# Pirtobrutinib Safety Profile in MCL Patients

>1 LINE and BTK exposed

| | Treatment-Emergent AEs in Patients with MCL (n=166) | | | |
|---|---|---|---|---|
| | All Cause AEs, (≥15%), % | | Treatment-Related AEs, % | |
| **Adverse Event** | **Any Grade** | **Grade ≥3** | **Any Grade** | **Grade ≥3** |
| Fatigue | 31.9 | 3.0 | 21.1 | 2.4 |
| Diarrhea | 22.3 | 0.0 | 12.7 | 0.0 |
| Dyspnea | 17.5 | 1.2 | 9.0 | 0.6 |
| Anemia | 16.9 | 7.8 | 7.2 | 2.4 |
| Platelet Count Decreased | 15.1 | 7.8 | 7.8 | 3.0 |
| **AEs of Interest[a]** | **Any Grade** | **Grade ≥3** | **Any Grade** | **Grade ≥3** |
| Infections[b] | 42.8 | 19.9 | 15.7 | 3.6 |
| Bruising[c] | 16.3 | 0.0 | 11.4 | 0.0 |
| Rash[d] | 14.5 | 0.6 | 9.0 | 0.0 |
| Arthralgia | 9.0 | 1.2 | 2.4 | 0.0 |
| Hemorrhage[e] | 10.2 | 2.4 | 4.2 | 0.6 |
| Hypertension | 4.2 | 0.6 | 1.8 | 0.0 |
| Atrial Fibrillation/Flutter[f,g] | 3.6 | 1.8 | 0.6 | 0.0 |

**Median time on treatment was 5.5 months for the MCL cohort**

**Discontinuations due to TRAEs occurred in 3% (n=5) of patients with MCL**

**Dose reductions due to TRAEs occurred in 5% (n=8) of patients with MCL**

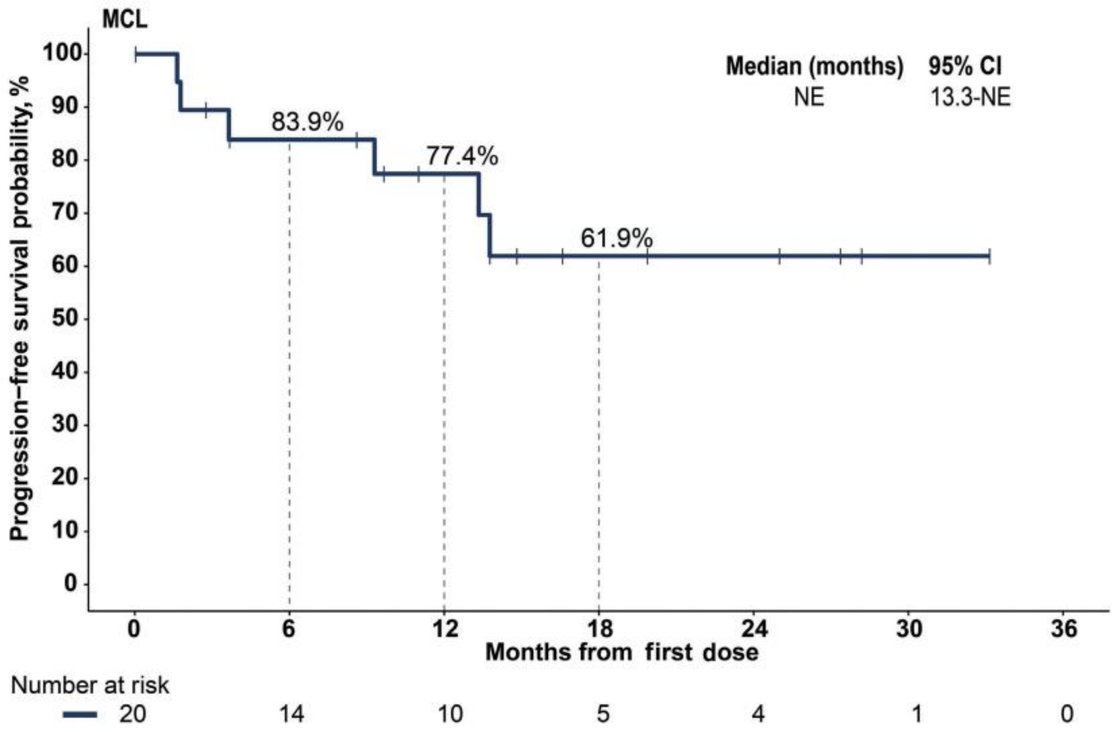
[a]AEs of interest are those that were previously associated with covalent BTK inhibitors. [b]Aggregate of all preferred terms including infection and COVID-19. [c]Aggregate of contusion, bone contusion, ecchymosis, and increased tendency to bruise. [d]Aggregate of all preferred terms including rash. [e]Aggregate of all preferred terms including hemorrhage or hematoma. [f]Aggregate of atrial fibrillation and atrial flutter. [g]Of 6 total atrial fibrillation and atrial flutter TEAEs, 3 occurred in patients with a prior medical history of atrial fibrillation. In the MCL cohort, treatment-related AEs leading to discontinuation included weight decrease/alopecia/fatigue (1), neutropenia (1), platelet count decreased (1), pneumonitis (1), and cholecystitis (1).

# Pirtobrutinib monotherapy in Bruton tyrosine kinase inhibitor-intolerant patients with B-cell malignancies: results of the phase I/II BRUIN trial

>1 LINE and BTK intolerant

| Adverse events | AE by prior BTKi N (%) | | | |
|---|---|---|---|---|
| | Any BTKi N=127 | Ibrutinib N=120 | Acalabrutinib N=9 | Zanubrutinib N=3 |
| Cardiac disorders<br>Atrial fibrillation | 40 (31.5)<br>30 (23.6) | 39 (32.5)<br>30 (25.0) | 1 (11.1)<br>- | -<br>- |
| Infection | 13 (10.2) | 13 (10.8) | - | - |
| Neutropenia[b] | 12 (9.4) | 9 (7.5) | 1 (11.1) | 1 (33.3) |
| Rash | 11 (8.7) | 9 (7.5) | - | - |
| Arthralgias/myalgias | 10 (7.9) | 9 (7.5) | 2 (22.2) | - |
| Bleeding/hemorrhage[c] | 9 (7.1) | 8 (6.7) | 1 (11.1) | - |
| Gastrointestinal disorders<br>Diarrhea | 8 (6.3)<br>6 (4.7) | 7 (5.8)<br>5 (4.2) | 1 (11.1)<br>1 (11.1) | -<br>- |
| Fatigue | 6 (4.7) | 5 (4.2) | - | 1 (33.3) |
| Pain | 6 (4.7) | 6 (5.0) | 1 (11.1) | - |
| Unknown | 5 (3.9) | 3 (2.5) | 1 (11.1) | - |
| Depression | 2 (1.6) | 1 (0.8) | 1 (11.1) | - |
| Headache | 2 (1.6) | - | 1 (11.1) | - |
| Joint effusion | 1 (0.8) | - | - | 1 (33.3) |

| Response | MCL N=21 |
|---|---|
| Overall response rate,[a] % (95% CI) | 81.0 (58.1-94.6) |
| Best response, N (%) | |
| Complete response | 9 (42.9) |
| Partial response | 8 (38.1) |
| Partial response with lymphocytosis | NA |
| Stable disease | 1 (4.8) |
| Progressive disease | 1 (4.8) |
| Not evaluable | 2 (9.5) |

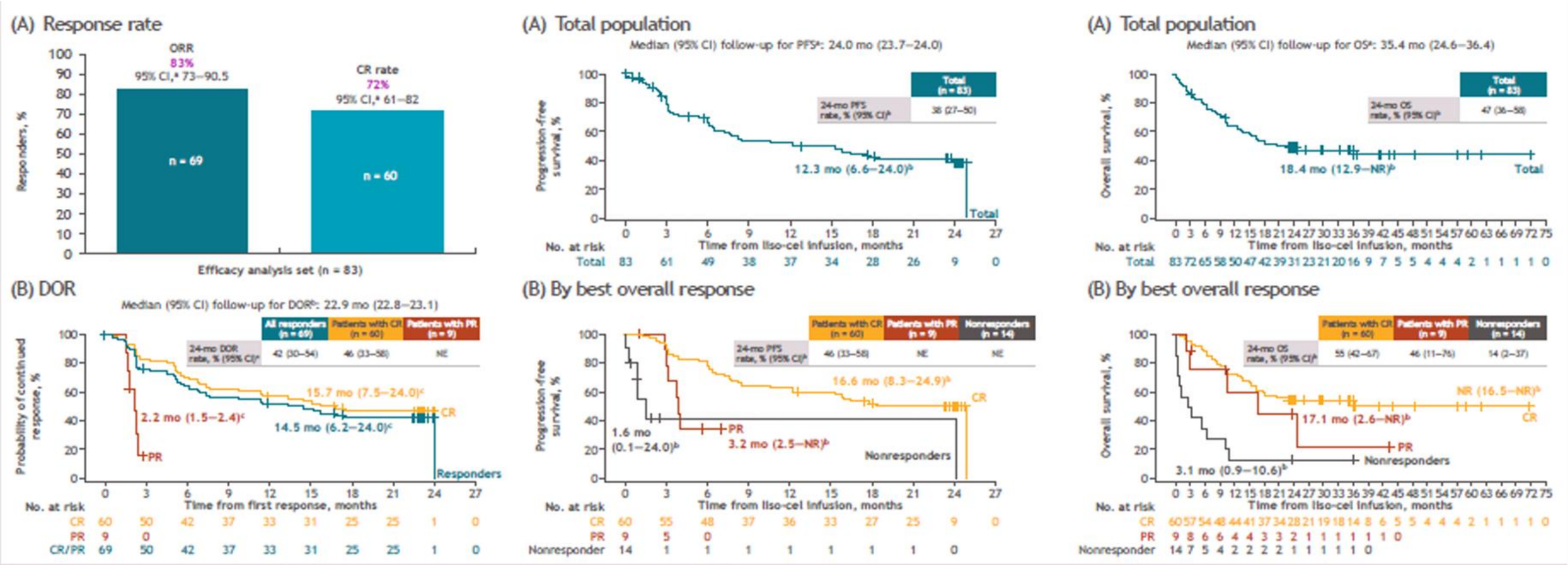



median follow-up was 17.4 months

Shah et al, Haematologica 2025

# Future Prospectives in R/R MCL

# CAR-T: TRANSCEND NHL 001 study, Liso-Cel



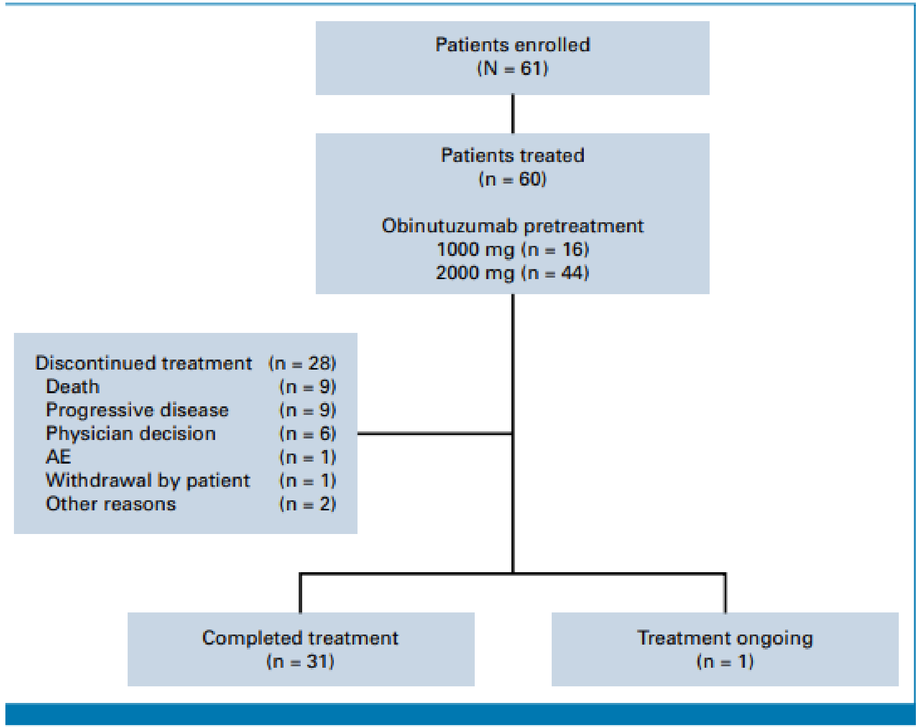

**CRS any grade: 61%**
**CRS grade 3-4: 1%**
**NEs any grade: 31%**
**NEs grade 3-4: 9%**
**No grade 5 CRS or NEs**

*Palomba et al, ASH 2023, abstr 3505; Wang et al, JCO 2024*

ASCO Journal of Clinical Oncology

# Glofitamab in Relapsed/Refractory Mantle Cell Lymphoma: Results From a Phase I/II Study

Tycel Jovelle Phillips, MD[1,2]; Carmelo Carlo-Stella, MD[3]; Franck Morschhauser, MD, PhD[4]; Emmanuel Bachy, MD, PhD[5]; Michael Crump, MD, FRCPC[6]; Marek Trněný, MD[7]; Nancy L. Bartlett, MD[8]; Jan Zaucha, MD, PhD[9]; Tomasz Wrobel, PhD[10]; Fritz Offner, MD, PhD[11]; Kathryn Humphrey, BSc[12]; James Relf, MD[12]; Audrey Filézac de L'Etang, PhD[13]; David J. Carlile, PhD[12]; Ben Byrne, MSc[12]; Naseer Qayum, MBChB, DPhil[12]; Linda Lundberg, PhD[13]; and Michael Dickinson, MBBS, DMedSc[14]




| Efficacy (INV-assessed) | Glofitamab SUD | | All Patients | | |
|---|---|---|---|---|---|
| | 1,000 mg Gpt Cohort (n = 16) | 2,000 mg Gpt Cohort (n = 44) | Previous BTKi (n = 31) | No Previous BTKi (n = 29) | All Patients (N = 60) |
| Complete response rate | | | | | |
| No. (%) | 11 (68.8) | 36 (81.8) | 22 (71.0) | 25 (86.2) | 47 (78.3) |
| 95% CI | 41.3 to 89.0 | 67.3 to 91.8 | 52.0 to 85.8 | 68.3 to 96.1 | 65.8 to 87.9 |
| Partial response rate | | | | | |
| No. (%) | 1 (6.3) | 3 (6.8) | 1 (3.2) | 3 (10.3) | 4 (6.7) |
| 95% CI | 0.2 to 30.2 | 1.4 to 18.7 | 0.1 to 16.7 | 2.2 to 27.4 | 1.9 to 16.2 |
| Overall response rate | | | | | |
| No. (%) | 12 (75.0) | 39 (88.6) | 23 (74.2) | 28 (96.6) | 51 (85.0) |
| 95% CI | 47.6 to 92.7 | 75.4 to 96.2 | 55.4 to 88.1 | 82.2 to 99.9 | 73.4 to 92.9 |

| Efficacy (INV-assessed) | Previous BTKi (n = 32) | All Patients (N = 61) |
|---|---|---|
| Median PFS, months | 8.6 | 16.8 |
| 95% CI | 3.4 to 15.6 | 8.9 to 21.6 |

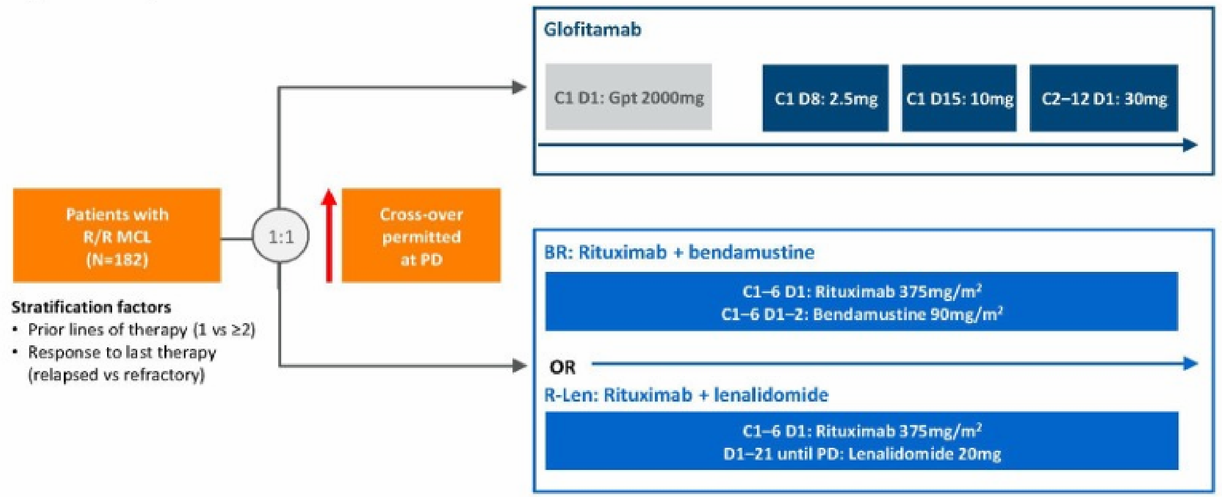
| Efficacy (INV-assessed) | Previous BTKi (n = 22) | All Patients (n = 47) |
|---|---|---|
| Median DoCR, months | 12.6 | 15.4 |
| 95% CI | 5.4 to NE | 12.7 to NE |

| Efficacy (INV-assessed) | Previous BTKi (n = 23) | All Patients (n = 51) |
|---|---|---|
| Median DoR, months | 12.6 | 16.2 |
| 95% CI | 7.4 to NE | 12.6 to NE |

# Future prospectives

## GLOBRYTE: A Phase III, Open-Label, Multicenter, Randomized Trial Evaluating Glofitamab Monotherapy in Patients with Relapsed or Refractory Mantle Cell Lymphoma

**Figure.** Study schema




B, bendamustine; C, cycle; D, day; Gpt, obinutuzumab pretreatment; Len, lenalidomide; MCL, mantle cell lymphoma; PD, progressive disease; R/R, relapsed/refractory; R, rituximab. Relapsed disease is defined as disease progression after the last regimen; refractory disease is defined as failure to achieve a partial response or complete response to the last regimen.

MD01-01_I01_PFIL06

FONDAZIONE ITALIANA LINFOMI

**Clinical Protocol**

**Title**

**A phase II, multicenter study of GlOfitamab in patients with mantle cell Lymphoma and inaDequate response or relapse following CAR T-cell therapy (GOLD)**

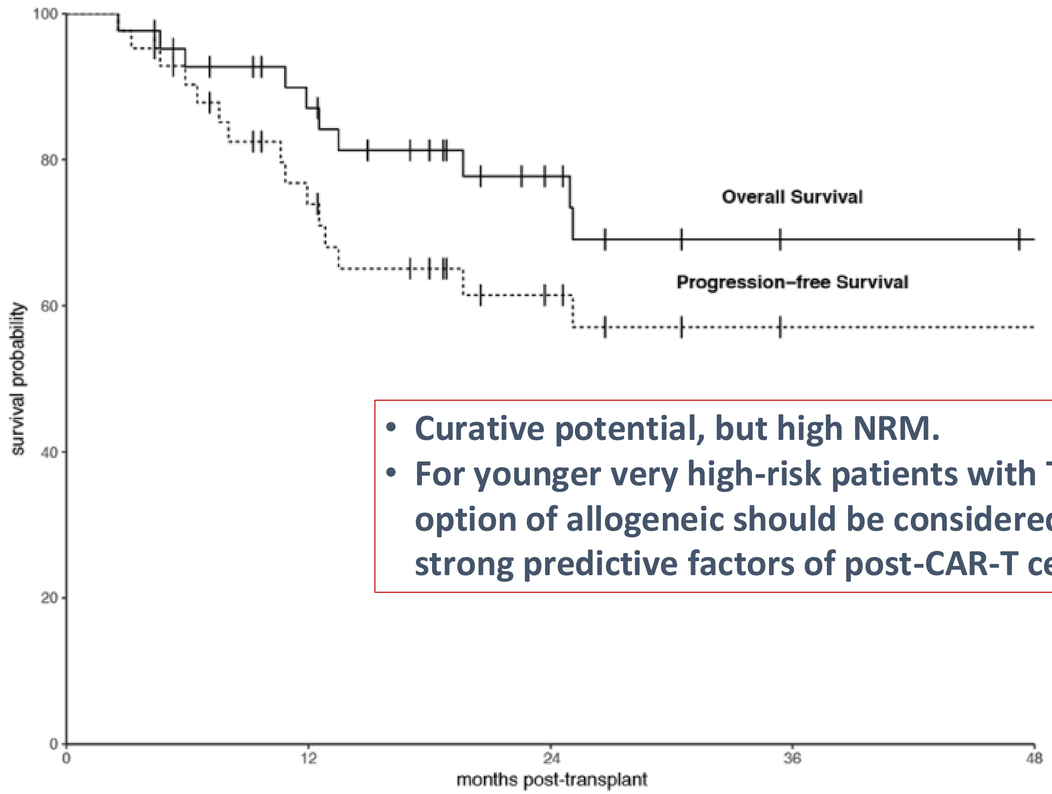
# Sonrotoclax monotherapy in R/R MCL previously treated with a BTK inhibitor: Early results from a phase 1/2 study

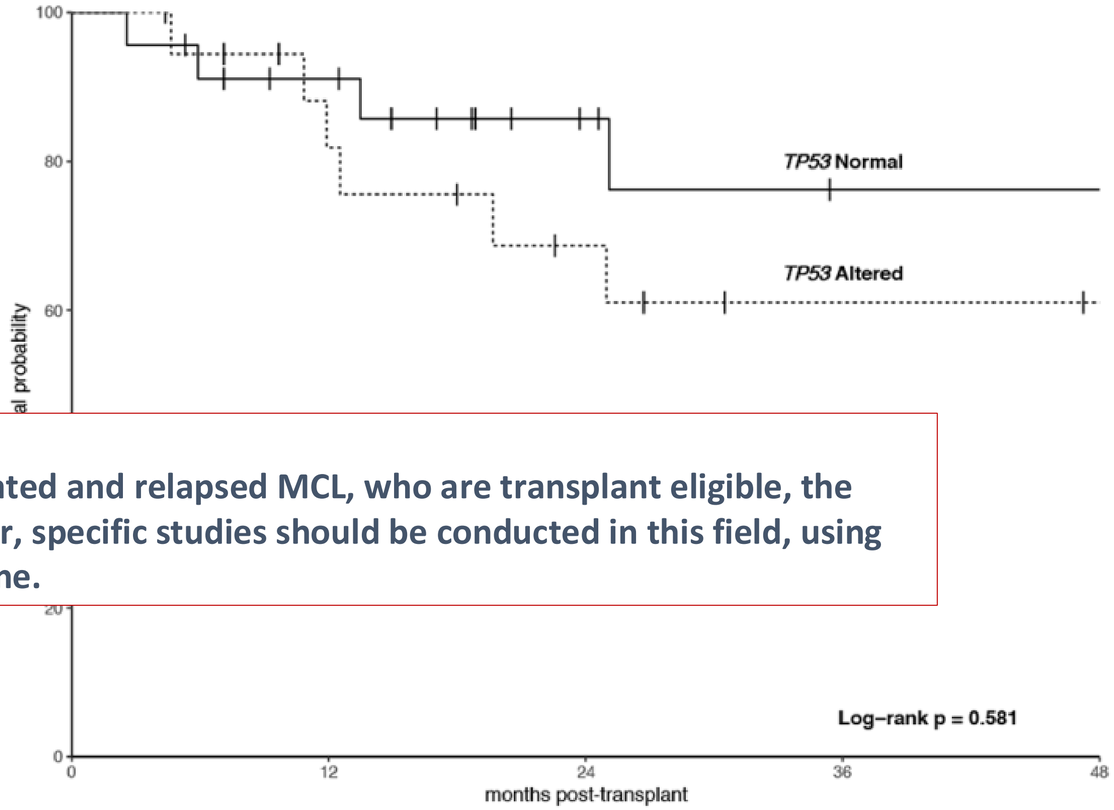
| | Sonrotoclax | Venetoclax | Differences in Design |
|---|---|---|---|
| **Potency ($IC_{50}$)** | 0.014 nM[1] | 0.20 nM[1] | 14-fold more potent, which may potentially lead to deeper target inhibition |
| **Selectivity (vs BCL-xL)** | 2000×[1] | 325×[1] | Improved (6-fold) selectivity |
| **Half-life in humans** | ≈5 hours[2] | 26 hours[3] | Short half-life and no accumulation may potentially result in simplified TLS monitoring during sonrotoclax ramp-up |

*Wang M et al, ASH 2025*

….and Allo????

# Allogeneic Haematopoietic Cell Transplantation Impacts on Outcomes of Mantle Cell Lymphoma with *TP53* Alterations




- **Curative potential, but high NRM.**
- **For younger very high-risk patients with TP53-mutated and relapsed MCL, who are transplant eligible, the option of allogeneic should be considered. However, specific studies should be conducted in this field, using strong predictive factors of post-CAR-T cells outcome.**

- 2-year overall survival and progression-free survival of **78%** (95% confidence interval [CI] 60–88) and **61%** (95% CI 43–75)
- non-relapse mortality was 20%

RJ Lin et al. Br J Haematol. 2019 March

# Scenari di sequencing terapeutico in R/R MCL

**PAST**

Patients mostly relapse after chemo-immunotherapy → cBTKi → CAR-T ncBTKi

**Present**

Patients mostly relapse after cBTKi → ncBTKi cBTKi (+ BCL-2*) → CAR-T**

*Off lable

** consider allo-SCT consolidation if young, high risk


Gruppo per la terapia dei linfomi non Hodgkin
Ematologia Sapienza Roma

# *Grazie!*

## *… a voi tutti per l'attenzione*

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