Applications for Community Oncology

ASH 2025 Data Review

February 19, 2026

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

Plenary Scientific Session

Is azacitidine with venetoclax a beneficial treatment option for fit patients with newly diagnosed acute myeloid leukemia (AML) compared to conventional induction chemotherapy?

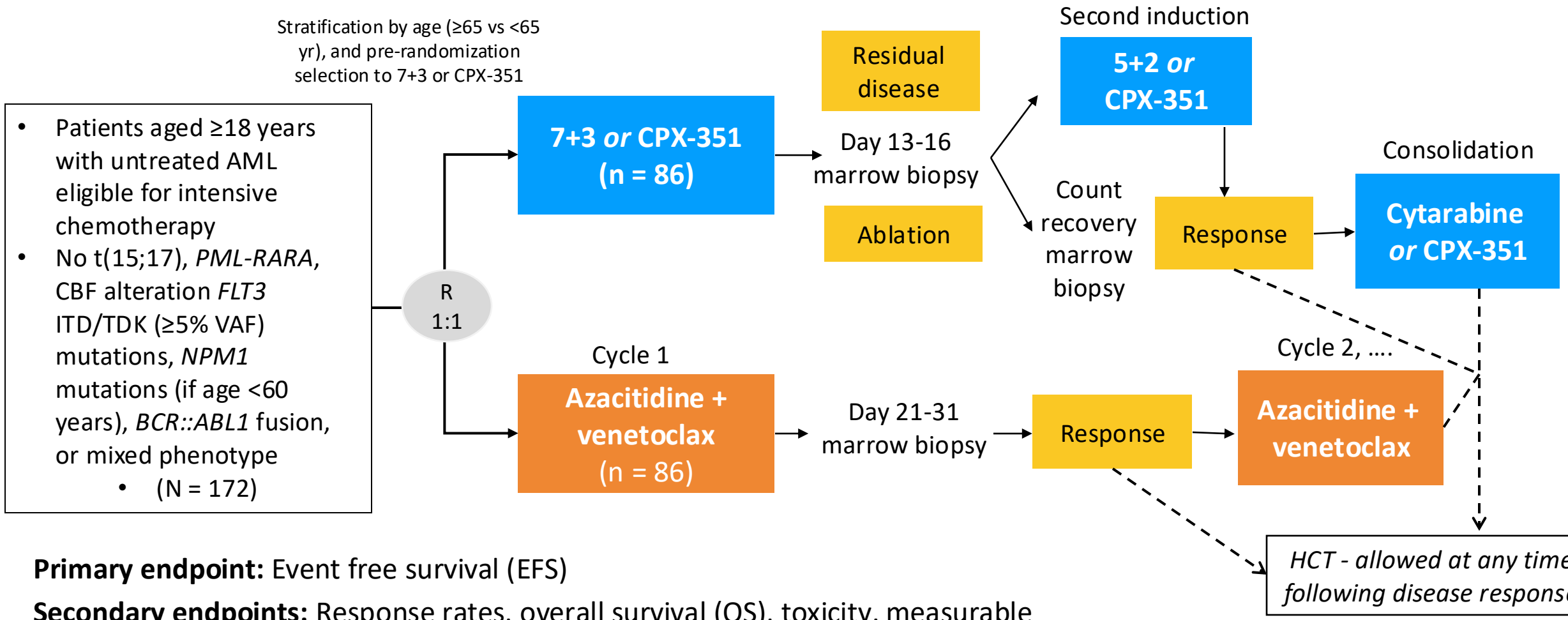
Phase 2 study

*Reminder: On **November 21, 2018**, the FDA granted accelerated approval to venetoclax (VENCLEXTA, AbbVie Inc. and Genentech Inc.) in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed AML in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy based on Study M14-358 and Study M14-387*

KEY DATA

PARADIGM: 1L Azacitidine + venetoclax vs Chemo in AML

Study Design: Randomized, multicenter phase II trial



Primary endpoint: Event free survival (EFS)

Secondary endpoints: Response rates, overall survival (OS), toxicity, measurable residual disease (MRD), hospitalization metrics, quality of life (QoL), and cost analyses

Data cutoff: October 17, 2025
Median follow-up: 21.9 mo

KEY DATA

PARADIGM: 1L Azacitidine + venetoclax vs Chemo in AML

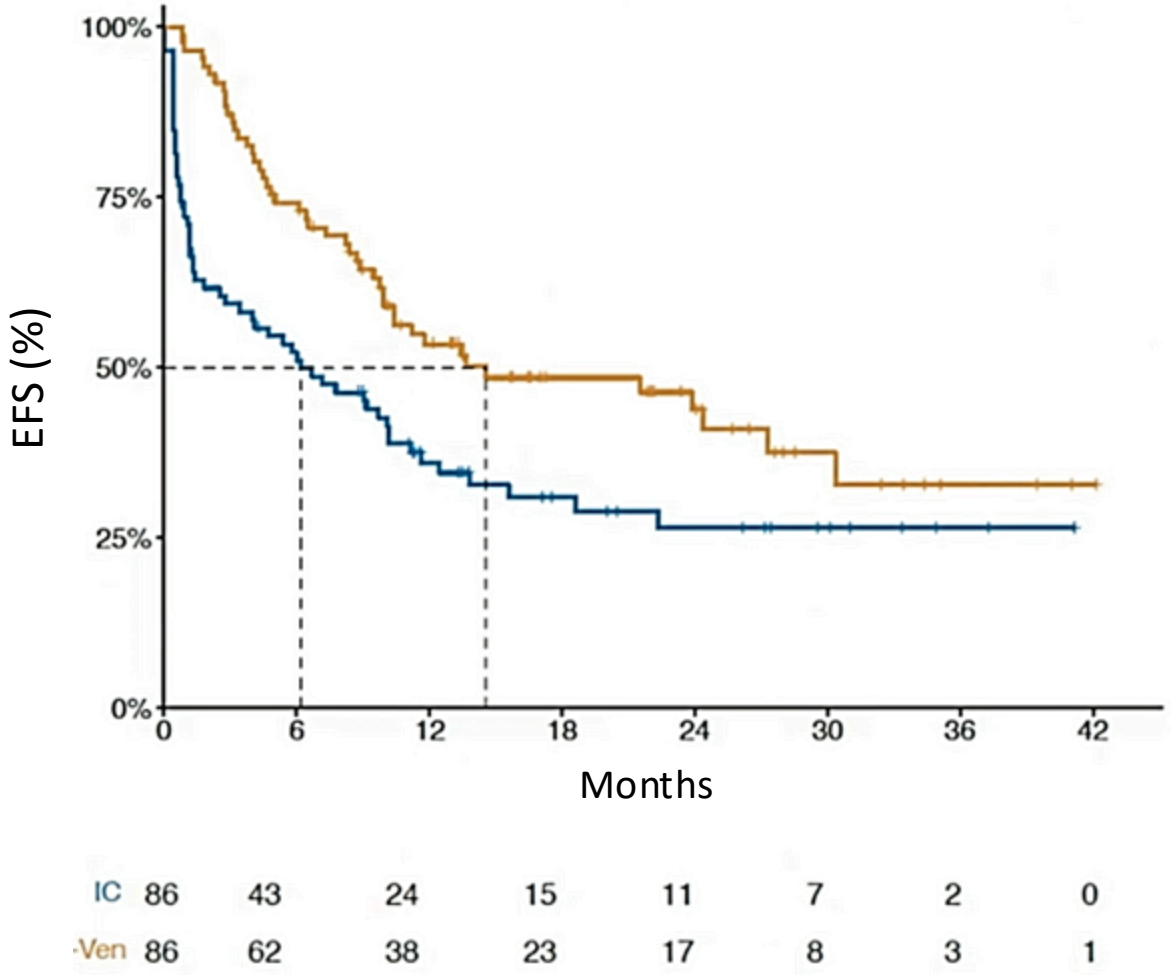
Baseline Characteristics, n (%)

	Ven/Aza (n = 86)	Induction Chemotherapy (IC) (n = 86)
Median age, yr (range)	65 (23-79)	64 (28-79)
Age ≤65 yr	43 (50.0)	44 (51.2)
Male	55 (64.0)	60 (69.8)
Race		
• White	65 (75.6)	69 (80.2)
• Black	5 (5.8)	5 (5.8)
• Hispanic	6 (7.0)	7 (8.1)
• Asian	10 (11.6)	5 (5.8)
ECOG PS		
• 0/1	79 (91.9)	82 (95.4)
• 2	7 (8.1)	3 (3.5)
ELN 2022 risk		
• Favorable	13 (15.1)	9 (10.5)
• Intermediate	15 (17.4)	11 (12.8)
• Adverse	58 (67.4)	66 (76.7)
Mutations		
• *NPM1*	11 (12.8)	5 (5.8)
• *IDH1*	8 (9.3)	7 (8.1)
• *IDH2*	19 (22.1)	9 (10.5)
• *TP53*	9 (10.5)	16 (18.6)
• *RUNX1*	14 (16.3)	18 (20.9)
• *KRAS/NRAS*	17 (19.8)	15 (17.5)

KEY DATA

PARADIGM: 1L Azacitidine + venetoclax vs Chemo in AML

Primary Endpoint: Event Free Survival (EFS)



	Aza/Ven (n = 86)	IC (n = 86)
Median EFS, mo	**14.6**	6.15
1-yr EFS, %	**53.4**	36.0
HR (p-value)	0.57 (0.0022)	

In a multivariate analysis, adjusted HR for EFS with Aza/Ven vs IC

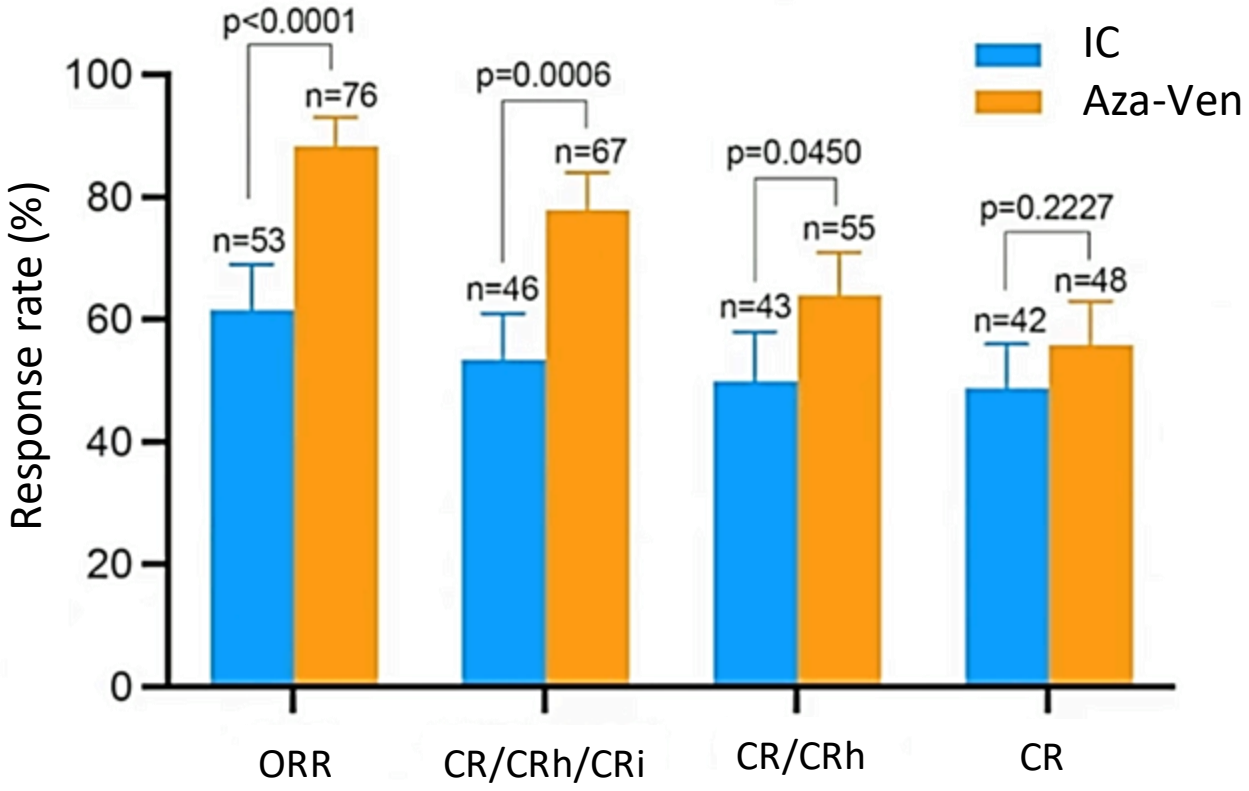
- HR: 0.66; *P* = 0.0231

IC: induction chemotherapy

KEY DATA

PARADIGM: 1L Azacitidine + venetoclax vs Chemo in AML

Secondary Endpoint: Response rates



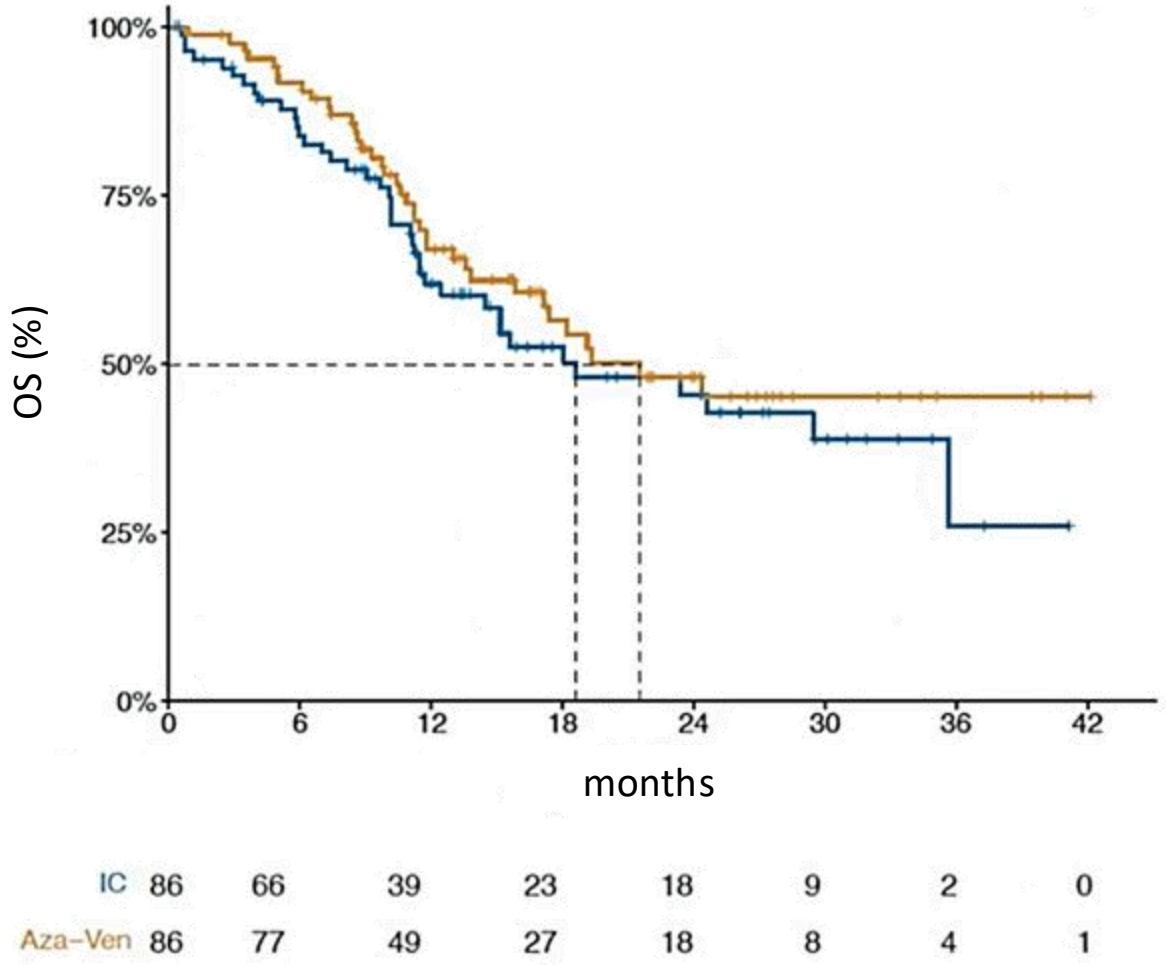
Best response, %	Aza/Ven (n = 86)	IC (n = 86)
CR	**55.8**	48.8
CRh	**8.1**	1.2
CRi	**14.0**	3.5
MLFS	**8.1**	4.7
PR	**2.3**	3.5
Refractory	**10.5**	27.9
Not evaluable	**1.2**	10.5

IC: induction chemotherapy

KEY DATA

PARADIGM: 1L Azacitidine + venetoclax vs Chemo in AML

Secondary Endpoint: Overall survival (OS)



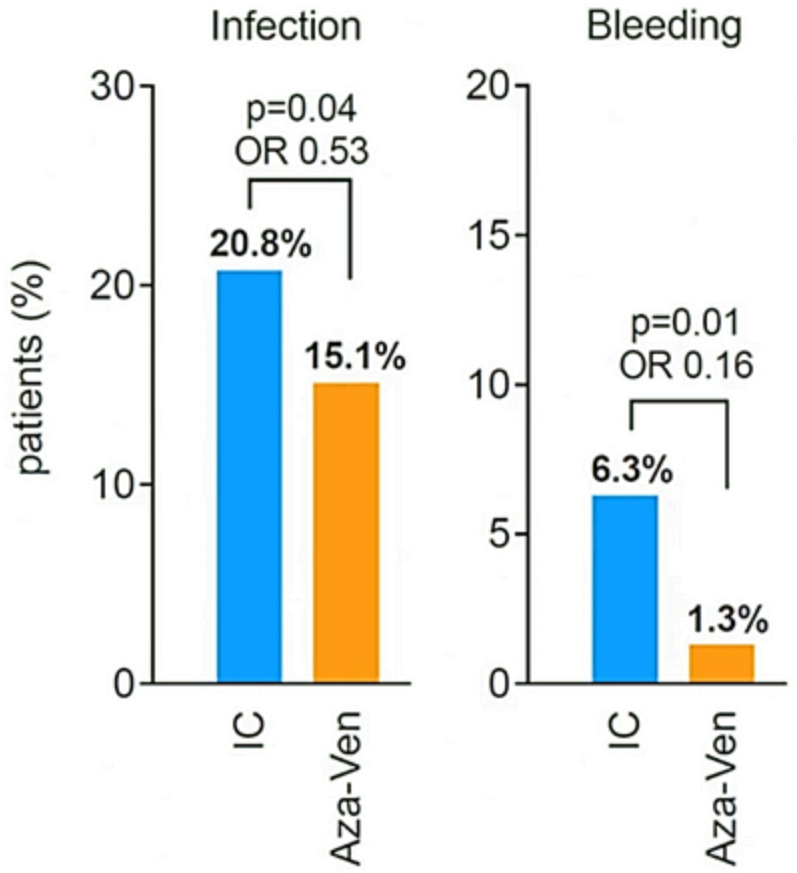
	Aza/Ven (n = 86)	IC (n = 86)
Median OS, mo	**21.5**	18.6
	Log rank, P = 0.1873	

KEY DATA

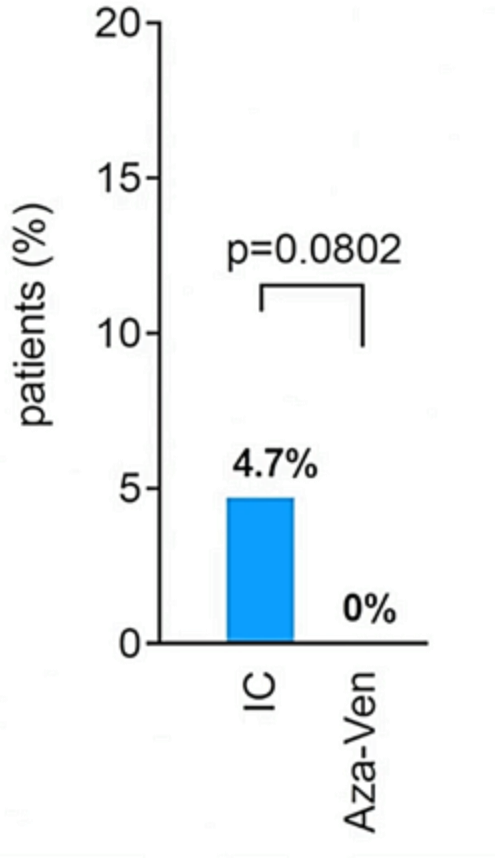
PARADIGM: 1L Azacitidine + venetoclax vs Chemo in AML

Secondary Endpoint: Safety and Tolerability

Treatment emergent adverse events (≥ grade 3)



60-day mortality



IC: induction chemotherapy

KEY DATA

PARADIGM: 1L Azacitidine + venetoclax vs Chemo in AML

Safety Summary

Grade ≥3 AEs in ≥10% of Patients

n (%)	Aza/Ven (n = 86)			IC (n = 86)		
	Grade 3	Grade 4	Grade 5	Grade 3	Grade 4	Grade 5
Febrile neutropenia	46 (53.5)	3 (3.5)	0	51 (62.2)	1 (1.2)	0
Platelet count decreased	8 (9.3)	38 (44.2)	0	3 (3.7)	47 (57.3)	0
Anemia	34 (39.5)	1 (1.2)	0	35 (40.7)	3 (3.5)	0
Neutrophil count decreased	1 (1.2)	48 (55.8)	0	1 (1.2)	39 (47.6)	0
WBC decreased	2 (2.3)	24 (27.9)	0	0	20 (24.4)	0
Lymphocyte count decreased	11 (12.8)	6 (7.0)	0	9 (11.0)	8 (9.8)	0
Lung infection	12 (14.0)	0	0	11 (15.6)	2 (2.4)	2 (2.4)
Sepsis	5 (5.8)	1 (1.2)	0	10 (12.2)	2 (2.4)	0
Anorexia	4 (4.7)	0	0	12 (14.6)	0	0
Hypoxia	4 (4.7)	0	0	7 (8.5)	2 (2.4)	0

SUMMARY

PARADIGM

IMPACT

- Azacitidine + venetoclax improved EFS vs induction chemotherapy (IC) in fit, newly diagnosed adults with AML
  - 14.6 months with Aza/Ven vs 6.15 months with IC
- Azacitidine + venetoclax induced deeper and more frequent responses than IC (ORR: 88% vs 62%) and allowed a significantly higher proportion of patients to successfully bridge to allogeneic HSCT
- Azacitidine + venetoclax reduced toxicity burden compared to traditional induction therapy

Azacitidine + venetoclax should be considered a potential new standard of care for fit patients with newly diagnosed intermediate-risk or adverse-ri FLT3-wild type acute myeloi leukemia

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2025 ASH Key Studies

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(AML, ALL, CML & myelodysplastic syndrome)

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ASC2ESCALATE

Does asciminib benefit patients with chronic myeloid leukemia (CML) who have received 1 prior tyrosine kinase inhibitor (TKI)?

Positive primary results of phase 2 trial

KEY DATA

ASC2ESCALATE: Asciminib in 2L CML-CP

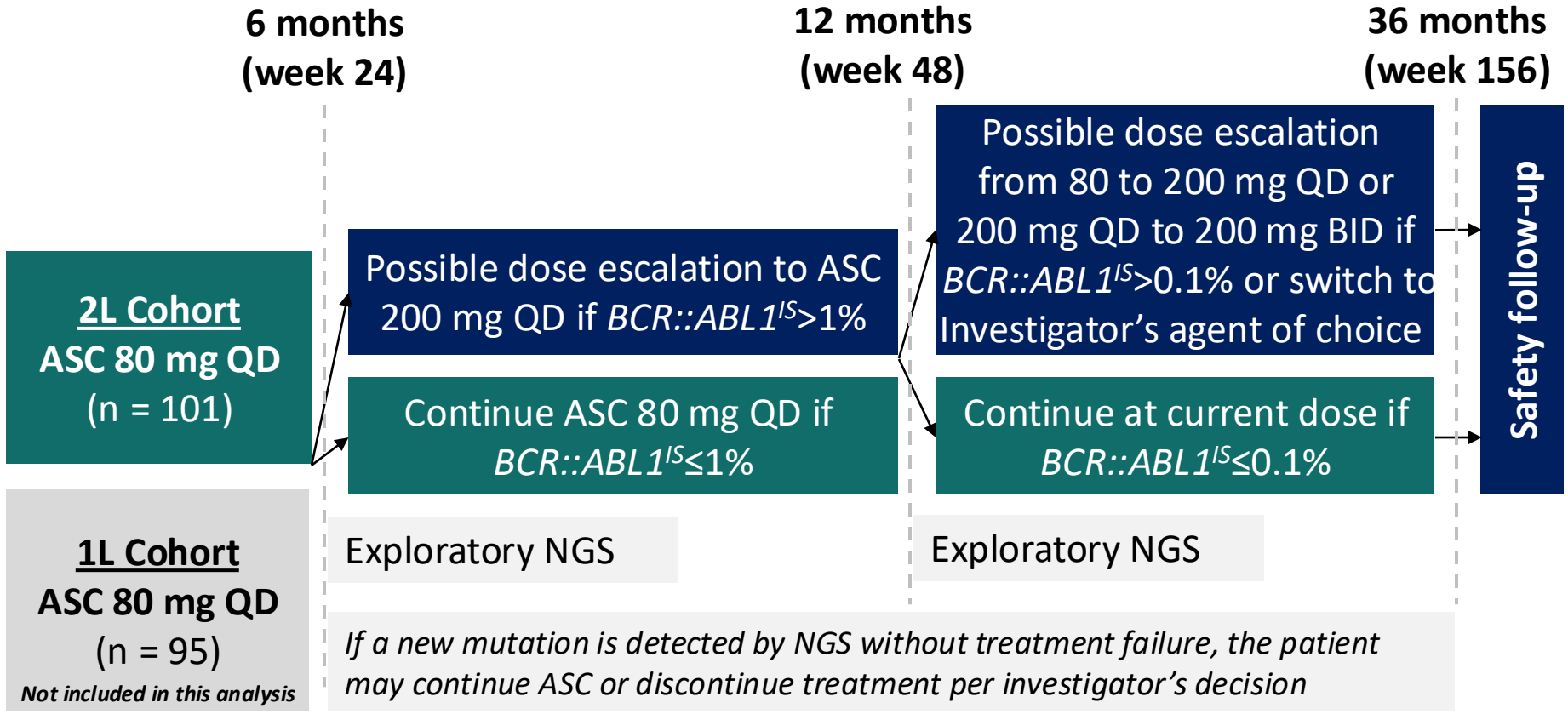
Study Design: First prospective, *US-only* trial of asciminib in 2L CML-CP

For both cohorts
- Aged ≥18 years
- CML-CP (no previous AP or BC)
- No T315I mutation

AND

For 2L cohort
- Warning or failure (per ELN 2020) or first TKI at the time of screening

OR
- Intolerance of first TKI and *BCR::ABL1*^{IS} >0.1% at screening



ELN: European LeukemiaNet

Primary endpoint: Major Molecular Response (MMR) at 12 months in the 2L cohort

Data cutoff: August 13, 2025

KEY DATA

ASC2ESCALATE: Asciminib in 2L CML-CP

Baseline Characteristics

n (%)	All Patients (n = 101)
Median age, yr (range)	50.0 (18-89)
Sex	
• Female	44 (43.6)
• Male	57 (56.4)
Race	
• American Indian or Alaska Native	1 (1.0)
• Asian	4 (4.0)
• Black	9 (8.9)
• White	83 (82.2)
• Unknown	4 (4.0)
Ethnicity	
• Hispanic or Latino/a	12 (11.9)
• Not Hispanic or Latino/a	88 (87.1)
• Unknown	1 (1.0)
ECOG PS	
• 0	73 (72.3)
• 1	26 (25.7)
• 2	2 (2.0)
≥1 mutation detected at baseline	
• E450Q/M244V	1 (1.0)
• E459G	1 (1.0)
• V299L	1 (1.0)

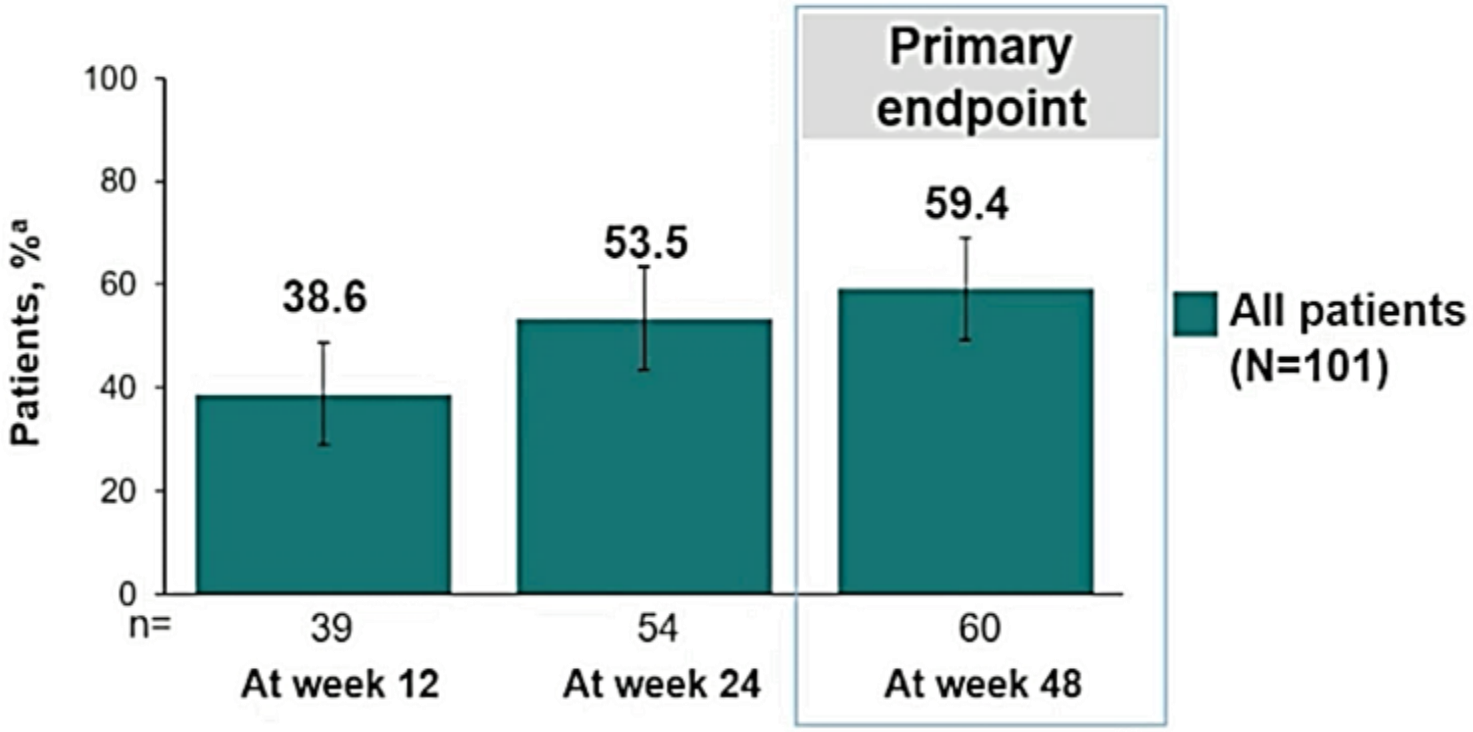
Disposition, n (%)	All Patients (n = 101)
Treated	101 (100)
Treatment ongoing	83 (82.2)
Discontinued from treatment	18 (17.8)
• AEs	8 (7.9)
• Patient decision	4 (4.0)
• Loss to follow-up	2 (2.0)
• Physician decision	2 (2.0)
• Unsatisfactory therapeutic effect	2 (2.0)

- Median duration of exposure: 63.4 weeks (range 6-139)
- Median asciminib dose intensity was 80.0 mg/day (range 28-225 mg/day), and the median relative dose intensity was 100% (range, 29%-100%)
- Dose escalation from 80 to 200 mg QD occurred in 18 patients (4 at week 24 and 14 at week 48)
  - Of 4 patients with dose escalation at week 24, three had had dose escalations from 200 mg QD to 200 mg BID at week 48

KEY DATA

ASC2ESCALATE: Asciminib in 2L CML-CP

Primary Endpoint: Major Molecular Response (MMR)



- MMR rate at week 48 was 59.4% and a 95% CI lower bound of 49.2% that was greater than the prespecified threshold of 30%
  - Of 41 patients without MMR at week 48, a total of 22 had *BCR::ABL1*^{IS} ≤1%
- By data cuff off: 71 patients (70.3%) achieved MMR, and none lost this responses

KEY DATA

ASC2ESCALATE: Asciminib in 2L CML-CP

BCR::ABL1^{IS} Response

	All Patients (N=101)		
	Wk 12	Wk 24	Wk 48
***BCR::ABL1*^{IS} ≤1%**			
All patients (N=101)	80.2	82.2	81.2
Patients without this response at baseline (n = 61)	67.2	73.8	72.1
MMR rate (%)			
Overall MMR rate	38.6	53.5	59.4
MMR rate by reason for discontinuation of prior TKI (%)			
• Lack of efficacy (n = 57)	36.8	45.6	56.1
• Lack of tolerability (n = 44)	40.9	63.6	63.6
MR^4 (%)	9.9	26.7	29.7
MR$^{4.5}$ (%)	2.0	10.9	14.9

MR4: *BCR::ABL1*^{IS} ≤0.01%; MR4.5: *BCR::ABL1*^{IS} ≤0.0032%

ASC2ESCALATE: Asciminib in 2L CML-CP

Response shift from baseline at week 48

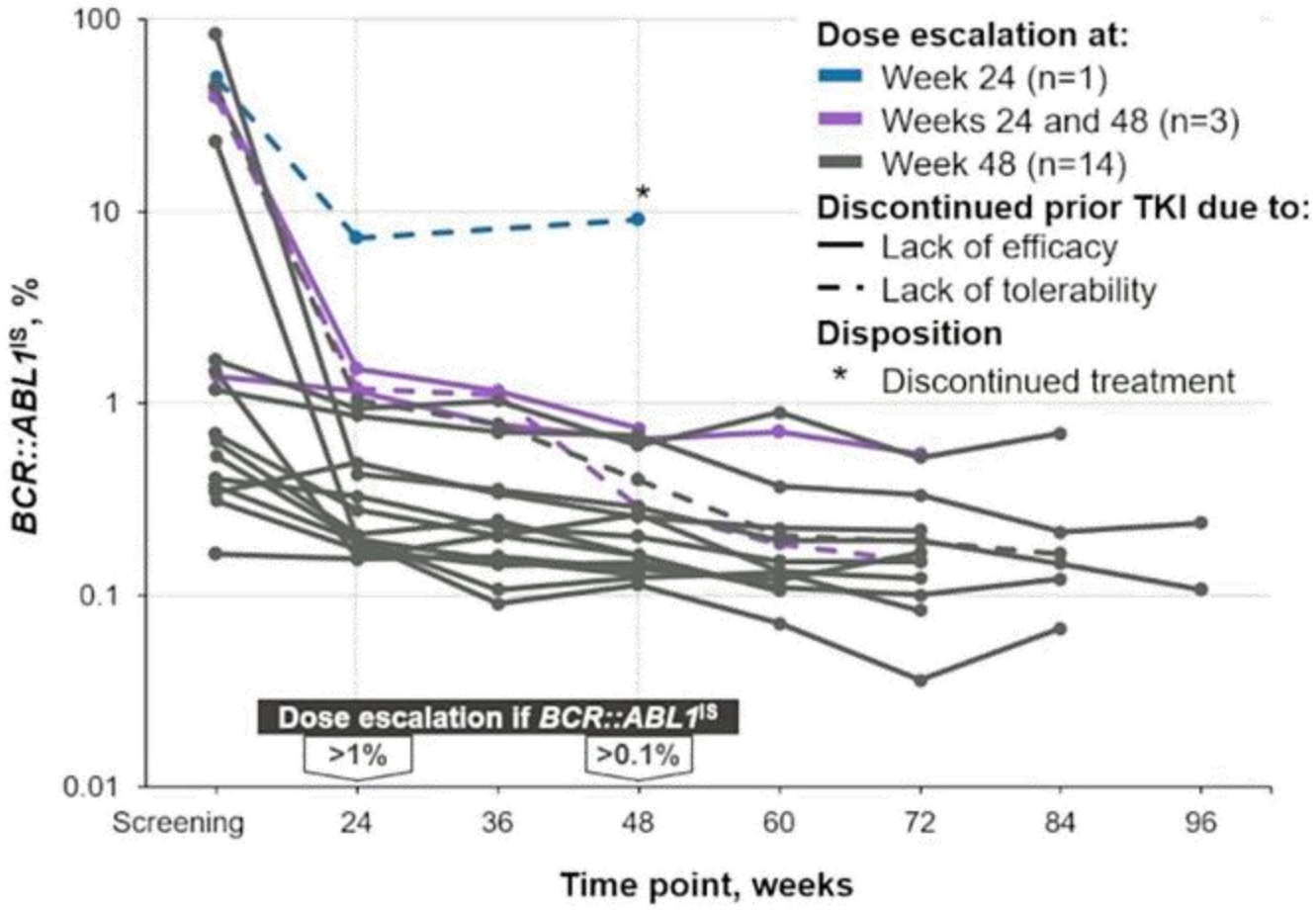
Molecular response at week 48, n (%)	Baseline *BCR::ABL1*^{IS} Level			
	>0.1% to ≤1% (n = 40)	>1% to ≤10% (n = 31)	>10% (n = 30)	All Patients (N = 101)
• ≤0.1%	**25 (62.5)**	**22 (71.0)**	**13 (43.3)**	60 (59.4)
• >0.1% to ≤1%	13 (32.5)	**4 (12.9)**	**5 (16.7)**	22 (21.8)
• >1% to ≤10%	0	0	**2 (6.7)**	2 (2.0)
• >10%	0	0	0	0
Missing assessment	2 (5.0)	5 (16.1)	10 (33.3)	17 (16.8)

Compared with baseline, *BCR::ABL1*^{IS} level category at week 48: Improved Did not change Worsened

ASC2ESCALATE: Asciminib in 2L CML-CP

First analysis of molecular response in patients with dose escalation

BCR::ABL1^{IS} level at time point in patients with dose escalation (n=18)



- Dose escalation from 80 to 200 mg QD occurred in 18 patients (17.8%) per response level at weeks 24 (n=4) and 48 (n=14)
  - 3 of 4 patients with dose escalation to 200 mg QD at week 24 escalated to 200 mg BID at week 48
- Most patients with dose escalation had:
  - Discontinued their prior TKI due to lack of efficacy (n=15) vs lack of tolerability (n=3)
  - Received prior dasatinib (n=12), with fewer having received prior imatinib (n=6)
  - Remained on treatment at the data cutoff (n=17)

ASC2ESCALATE: Asciminib in 2L CML-CP

Safety Summary

AEs, n (%)	All Patients (N = 101)
All-grade AEs	99 (98.0)
Grade ≥3 AEs	42 (41.6)
All-grade SAEs	13 (12.9)
All grade AEs leading to dose adjustment and/or interruption	40 (39.6)
AEs leading to dose reduction	7 (6.9)
AEs leading to dose interruption	38 (37.6)
AEs leading to treatment discontinuation	8 (7.9)*

SAE: serious adverse event

- *AEs leading to discontinuation occurred in 8 patients and included grade 1 and 2 dyspepsia (n=1), tremor (n=1), weight decrease (n=1), and grade ≥3 thrombocytopenia (n=2), vomiting and nausea (n=1), lipase increased (n=1), and neutropenia (n=1)
- No deaths during treatment or within 30 days after the last asciminib dose were reported
- After dose escalation most AEs were grade 1 / grade 2; 2 were grade ≥3

SUMMARY

ASC2ESCALATE

- Second-line Asciminib achieved MMR at 12 months in patients after not achieving optimal response milestones by ELN 2020 (at 6 and 12 mo)
  - MMR at week 48: 59.4%; deep molecular responses (MR^4) were also observed over time, including 29.7% at week 48
- Dose-escalation per protocol led to asciminib dose increase in 17.8% (n = 18) of patients; post-baseline mutations were uncommon
- Asciminib maintained a favorable safety profile, with few discontinuations due to AEs (n = 8), consistent with prior frontline and later-line experience

IMPACT

Asciminib is an effective 2L treatment option for patients with CML after receiving 1 prior tyrosine kinase inhibitor

October 29, 2024: FDA granted accelera approval for newly diagnosed Philadelp chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP) evaluated in ASC4FIRST

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Polling question

Based on the ASC2ESCALATE phase 2 trial, how likely are you to consider dose escalation of asciminib for patients in 2L CML-CP not achieving optimal response milestones?

1. Very likely
2. Somewhat likely
3. Not likely
4. Very unlikely

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KOMET-007

Does ziftomenib in combination with venetoclax and azacitidine benefit patients with newly diagnosed *NPM1*-m acute myeloid leukemia?

Phase 1b Results

*On **November 13, 2025**, the FDA approved **ziftomenib** (Komzifti, Kura Oncology, Inc.), a menin inhibitor, for adults with R/R AML with a susceptible nucleophosmin 1 (NPM1) mutation who have no satisfactory alternative treatment options evaluated in KOMET-001.*

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KEY DATA

KOMET-007: 1L Ziftomenib plus Ven/Aza in *NPM1-m* AML

Study Design: Global, ongoing phase I study

- Adults with newly diagnosed NPM1-mutated AML
- Not eligible for intensive chemotherapy
- ECOG 0-2

(N = 40)

→ **Ziftomenib 600 mg PO QD starting on C1 D8 + Venetoclax/Azacytidine***

→ *Validated recommended phase 2 dose*

*Venetoclax administered per label in 28-day cycles; dosing and cycle length adjusted based on blast clearance in Cycle 1 bone marrow biopsy performed between Days 14 and 28. Azacytidine administered on cycle 1 day 1-7.

Primary endpoints: Complete Response (CR), Adverse Events (AEs)

Secondary endpoints: Composite Complete Remission (CRc), Duration of Response (DOR), Objective Response Rate (ORR), Measurable Residual Disease (MRD)

KEY DATA

KOMET-007: 1L Ziftomenib plus Ven/Aza in *NPM1-m* AML

Efficacy endpoints

Clinical Activity

n (%)	Ziftomenib + Ven/Aza (n = 37)[a]
CRc	**32 (86)**
• Median time to first CRc, week (range)	3.4 (2.4-9.6)
ORR	**33 (89)**
• **CR**	**27 (73)**
• CRh	2 (5)
• CRi	3 (8)
• MLFS	1 (3)
• PR	0 (0)
No Response	1 (3)
Not evaluable[b]	3 (8)

CR/CRh rates by co-mutated status were consistent with overall CR/CRh response rates: 77% (10/13) for *FLT3* and 89% (8/9) for *IDG1/2*
MLFS: morphologic leukemia-free state

Molecular Measurable Residual Disease (MRD) Negativity in CRc Responders

n/N (%)	Central MRD (Threshold ≤0.1%)	Central MRD (Threshold≤0.01%)
MRD negative rate[c]	17/25 (68)	11/25 (44)
• Median time to first MRD negativity, week (range)	9.4 (4.9-22.9)	9.6 (8.4-22.9)
Timing of MRD negativity[d]		
• By cycle 1	1/17 (6)	0
• By cycle 2	12/17 (71)	7/11 (64)
• By cycle 3	16/17 (94)	10/11 (91)
• By cycle 4[e]	17/17 (100)	11/11 (100)

Median follow-up was 26.1 weeks (range 1.6–54.1):
- Median duration of CR not reached
- Median OS not reached

Data cutoff: September 24, 2025

[a]In patients with ≥1 response assessment or had died. [b]Post-baseline response assessment not done (n=3) at time of data cutoff. [c]NPM1 MRd was performed among tested CRc responders by central next-generation sequencing with 0.0005% sensitivity; protocol-defined threshold ≤0.01% was considered meaningful. [d]Among CRc responders who achieved MRD-negativity. [e]Four patients who received less than 4 cycles of therapy were just above the 0.01% MRD threshold at time of analysis.

KEY DATA

KOMET-007: 1L Ziftomenib plus Ven/Aza in *NPM1-m* AML

Safety

TEAEs in ≥25% of patients

n (%)	All TEAEs (n=40)	Ziftomenib-Related TEAEs (n=40)
Any Grade	**40 (100)**	**25 (63)**
Nausea	16 (40)	9 (23)
Vomiting	16 (40)	4 (10)
Diarrhea	16 (40)	5 (13)
Fatigue	16 (40)	8 (20)
Thrombocytopenia	15 (38)	8 (20)
Neutropenia	15 (38)	9 (23)
Leukopenia	12 (30)	5 (13)
Constipation	12 (30)	2 (5)
Peripheral edema	11 (28)	2 (5)
Anemia	10 (25)	5 (13)
AST increased	10 (25)	7 (18)
Decreased appetite	10 (25)	6 (15)

Grade in ≥3 TEAEs in ≥10% of patients

n (%)	All Grade ≥3 TEAEs (n=40)	Grade ≥3 Ziftomenib-Related TEAEs (n=40)
Grade ≥3	**34 (85)**	**16 (40)**
Neutropenia	15 (38)	8 (20)
Thrombocytopenia	11 (28)	7 (18)
Leukopenia	10 (25)	4 (10)
Anemia	8 (20)	5 (13)
Febrile neutropenia	5 (13)	1 (3)
Sepsis	5 (13)	1 (3)
Lymphocytopenia	4 (10)	1 (3)
Pneumonia	4 (10)	0 (0)

- Ziftomenib-related AEs of interest:
  - 1 patient (3%) with grade 2 differentiation syndrome; resolved with protocol-specified mitigation; patient resumed ziftomenib
  - 1 patient (3%) with grade 3 QTc prolongation in context of concomitant significant electrolyte abnormalities; resolved with electrolyte repletion; patient successfully resumed ziftomenib

SUMMARY

KOMET-007

- The combination of ziftomenib with venetoclax and azacitidine demonstrated high rates of durable CRs and MRD negativity
  - 86% CRc (73% CR), with 68% molecular CRc MRD-negativity
- Median duration of response and median overall survival were not reached as of the data cutoff
- Safety profile comparable to reports with venetoclax and azacitidine alone; management of nausea and neutropenia required

IMPACT

Ziftomenib with venetoclax and azacitidine is a potential treatment option for patients with newly diagnosed NPM1-m acute myeloid leukemia

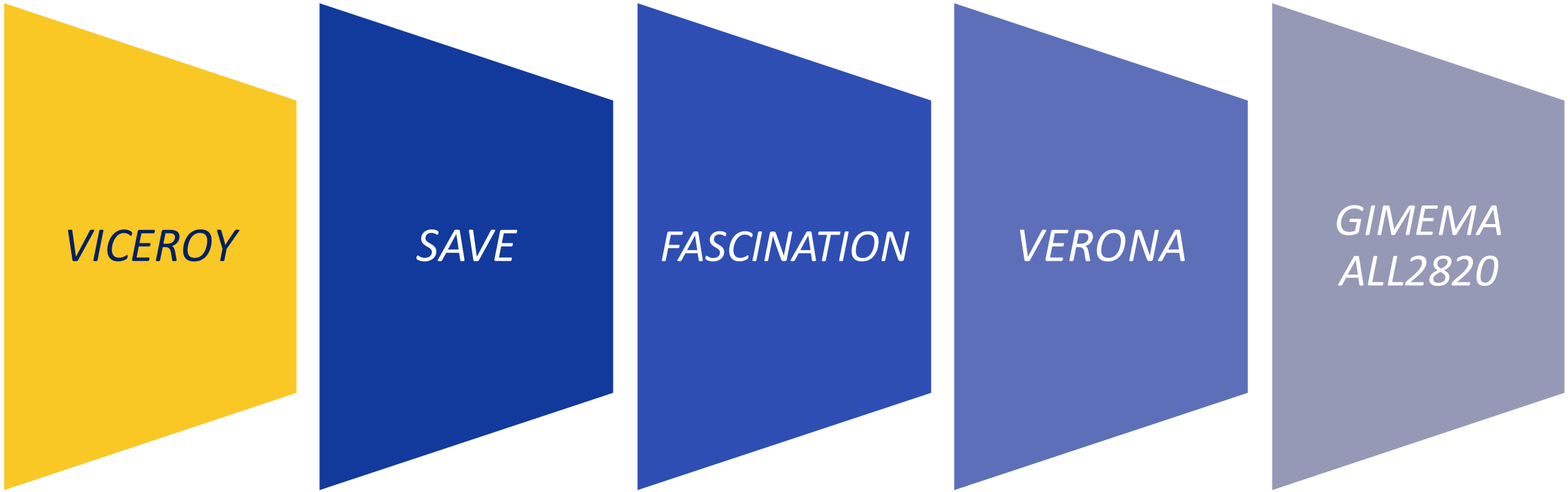
Triplet combination not yet approved

Polling question

Based on the KOMET-007 data, with ziftomenib added to standard AML backbone, how likely are you to incorporate menin inhibition into frontline treatment for patients with NPM1-mutant or KMT2A-rearranged AML if approved?

1. Very likely — this would change my frontline practice
2. Likely — for select molecularly defined patients
3. Unlikely — prefer current standard regimens
4. Unsure — need further data; safety/complexity concerns

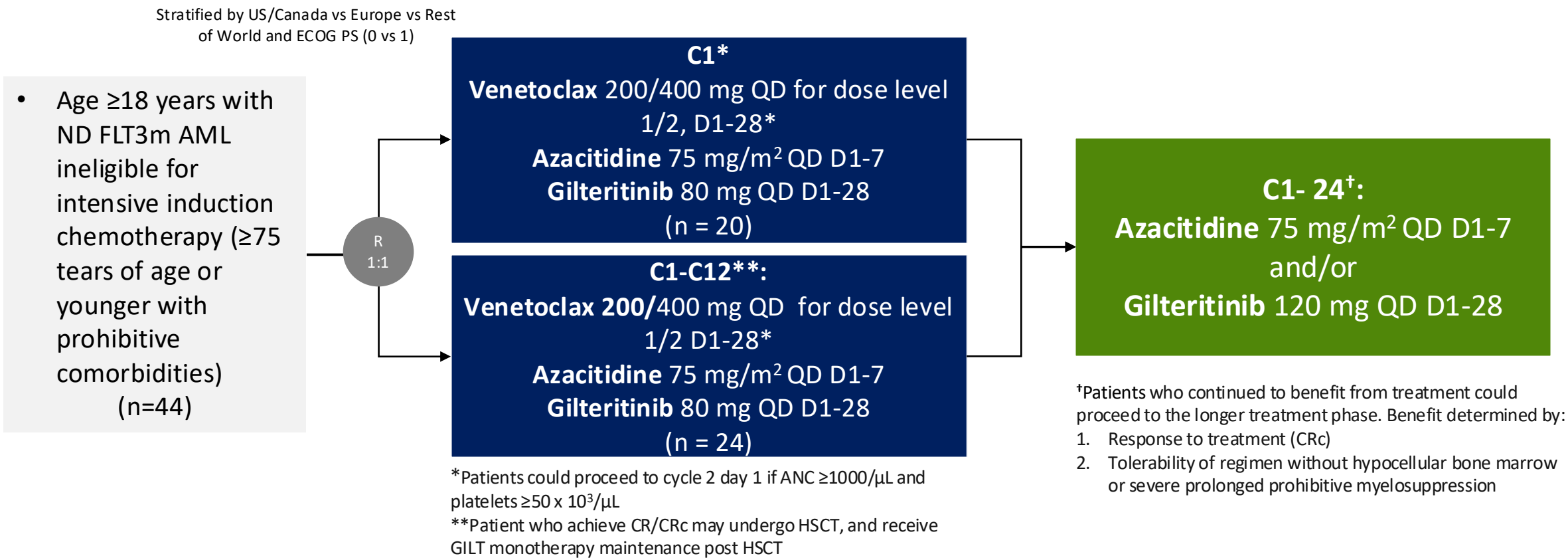
ASH 2025: RAPID REVIEWS



KEY DATA

VICEROY: 1L VEN/AZA/GILT for newly diagnosed *FLT3^{mut+}* AML

Study Design: Randomized, multicenter, open-label, dose-ranging/expansion phase I/II study



*Patients could proceed to cycle 2 day 1 if ANC ≥1000/µL and platelets ≥50 x 10^3/µL

**Patient who achieve CR/CRc may undergo HSCT, and receive GILT monotherapy maintenance post HSCT

†Patients who continued to benefit from treatment could proceed to the longer treatment phase. Benefit determined by:

1. Response to treatment (CRc)
2. Tolerability of regimen without hypocellular bone marrow or severe prolonged prohibitive myelosuppression

Primary endpoint: Dose limiting toxicity (DLT), safety events, complete response (CR) rate, pharmacokinetics (PK)

Secondary endpoints: CRc, composite complete remission rate (CR + CRp + CRi), OS, MRD (measurable residual disease)

CRp: CR with incomplete platelet recovery; CRi: CR with incomplete hematologic recovery

KEY DATA

VICEROY: 1L VEN/AZA/GILT for newly diagnosed *FLT3^{mut+}* AML

Efficacy Endpoints

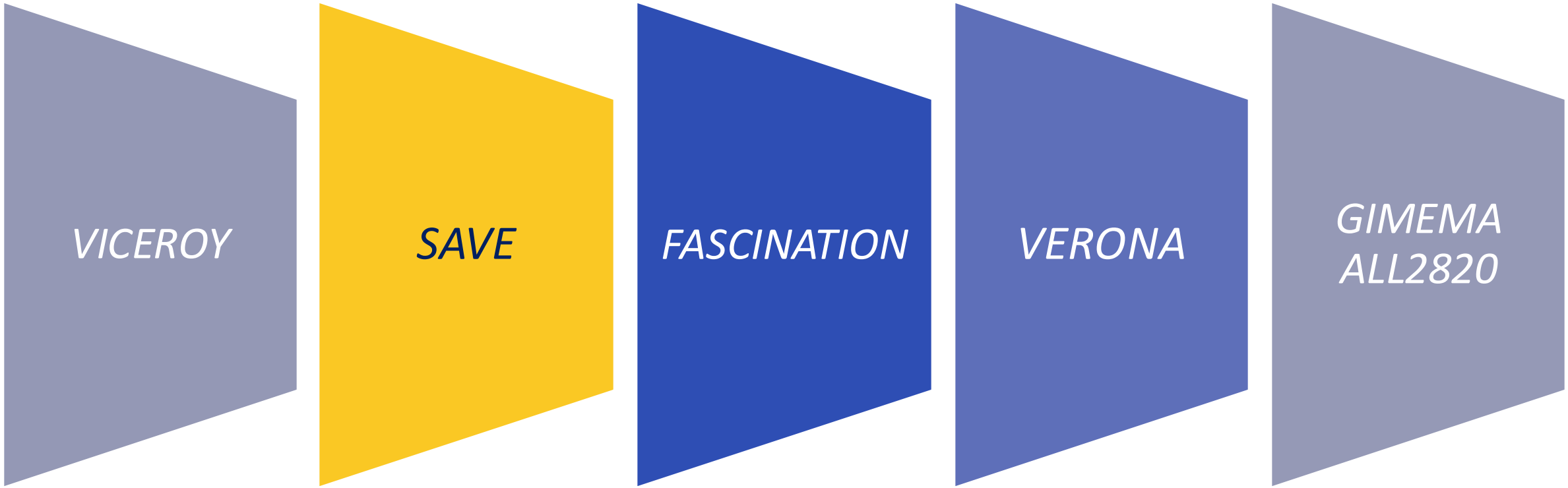
	Ven 200 mg (n = 20)	Ven 400 mg (n = 24)
Composite CR (CR + CRp +CRi)	90%	91%
Complete Remission (CR)	70%	70%
CRp	0%	17%
CRi	20%	4%
Median time to CR, mo (range)	1 (1-8)	1 (1-7)
Median time to CRc, mo (range)	0.6 (0.4-2.0)	1 (0.4-6.0)
Median duration of CR, mo (95% CI)	13 (4-NE)	15 (8-NE)
Median duration of CRc, mo (95% CI)	8 (3-NE)	15 (8-NE)
Median OS, mo (95% CI)	23 (7-NE)	22 (17-NE)

Triplet regimen (VEN/AZA/GILT) for newly diagnosed FLT3^{mut+} AML is a potential new option for patient's ineligible for intensive induction chemotherapy…more to come

Safety summary

n (%)	Ven 200 mg (n = 20)	Ven 400 mg (n = 24)
All-cause TEAEs	20 (100)	23 (96)
All-cause serious TEAEs	17 (85)	19 (79)
Common all-cause serious TEAE (≥6 patients)		
• Febrile neutropenia	10 (50)	7 (29)
• Pneumonia	2 (10)	4 (17)
• Sepsis	3 (15)	4 (17)
• Hypokalemia	2 (10)	3 (13)
• Pyrexia	4 (20)	2 (8)
All-cause TEAEs leading to withdrawal of any treatment, n/N (%)	5 (25)	2 (8)
Any drug-related TEAEs	19 (95)	18 (75)
Serious drug-related TEAE	10 (50)	9 (38)
Common drug-related serious TEAEs (≥6 patients)		
• Febrile neutropenia	5 (25)	3 (13)
Drug-related TEAEs leading to discontinuation of any treatment	2 (10)	1 (4)
• Pericardial effusion	1 (5)	0
• Colitis	1 (5)	0
• Neutropenic sepsis	0	1 (4)

ASH 2025: RAPID REVIEWS



KEY DATA

SAVE: 1L Revumenib with decitabine/cedazuridine and Venetoclax in newly diagnosed AML

Study Design: Open-label phase I/II study

- Aged ≥12 years
- AML or myeloid MPAL with *NPM1mt, KMT2Ar,* or *NUP98r*
- Not eligible for frontline high-intensity chemotherapy; R/R
- ECOG PS ≤2

(Target n = 43)

Revumenib (DL 1) 270 mg without strong CYP3Ai or 160 mg with strong CYP3Ai PO Q12h D1-28*†
+
Decitabine/cedazuridine (35 mg/100 mg)PO QD D1-5†
+
Venetoclax (400 mg, target dose with ramp up) PO QD D1-14†

Maintenance revumenib post SCT for 1 yr

*DL 0: Revumenib 160 mg without strong CYP3Ai or 110 mg with strong CYP3Ai PO Q12h D1-28.
†All patients underwent bone marrow assessment on C1D14, in addition to end of cycle assessment; revumenib held after D21 if bone marrow blasts were <5%.

Primary endpoints: Phase I in R/R (3+3 design): safety, MTD, RP2D; Phase II (frontline and R/R): efficacy
Secondary endpoints: Phase II: Overall survival (OS), RFS, CRD, MRD
Exploratory endpoints: MRD at 10^{-5}, resistance

Select Baseline Characteristics

n, (%)	All (N = 21)	NPM1mt (n = 14)	KMT2Ar (n = 7)
Median age, yr (range)	70 (60-83)	73 (66-83)	64 (60-77)
≥ 70-years	11 (52)	10 (71)	1 (14)
Female	15 (71)	9 (64)	6 (86)
Secondary AML	5 (24)	2 (14)	3 (43)
• Diploid Cytogenetics	9 (43)	9 (64)	0
• Adverse Cytogenetics	7 (33)	1 (7)	6 (86)
Co-mutations			
• NRAS/KRAS	4 (19)	2 (14)	2 (29)
• FLT3	4 (19)	4 (28)	0
• ITD*	1 (5)	1 (7)	0
• TKD	3 (14)	3 (21)	0
• IDH1/2	4 (19)	3 (21)	1 (14)
• MDS associated#	9 (43)	6 (43)	3 (43)

*FLT3-ITD detected with a frequency of 0.03.
#MDS-associated mutations in the following genes: ASXL1, BCOR, EZH2, SF3B1, SRSF2, STAG2, U2AF1, ZRSR2, and/or RUNX1

KEY DATA

SAVE: 1L Revumenib with decitabine/cedazuridine and Venetoclax in newly diagnosed AML

Secondary Endpoints: Duration of Response (DOR)

Best Response, n (%)	All (N = 21)	*NPM1mt* (n = 14)	*KMT2Ar* (n = 7)
ORR	18 (86)	12 (86)	6 (86)
• **CR/CRh**	**17 (81)**	11 (79)	6 (86)
– **CR**	**16 (76)**	10 (71)	6 (86)
– CRh	1 (5)	1 (7)	0
• CRp	1 (5)	1 (7)	0
• MLFS	0	0	0
Early death (30 day)	2 (10)	2 (10)	0
Not evaluable	1 (5)	0	1 (14)
MRD neg by MFC (10^{-4})	18 (86)	12 (86)	6 (86)
• Within responders	18 (100)	12 (100)	6 (100)

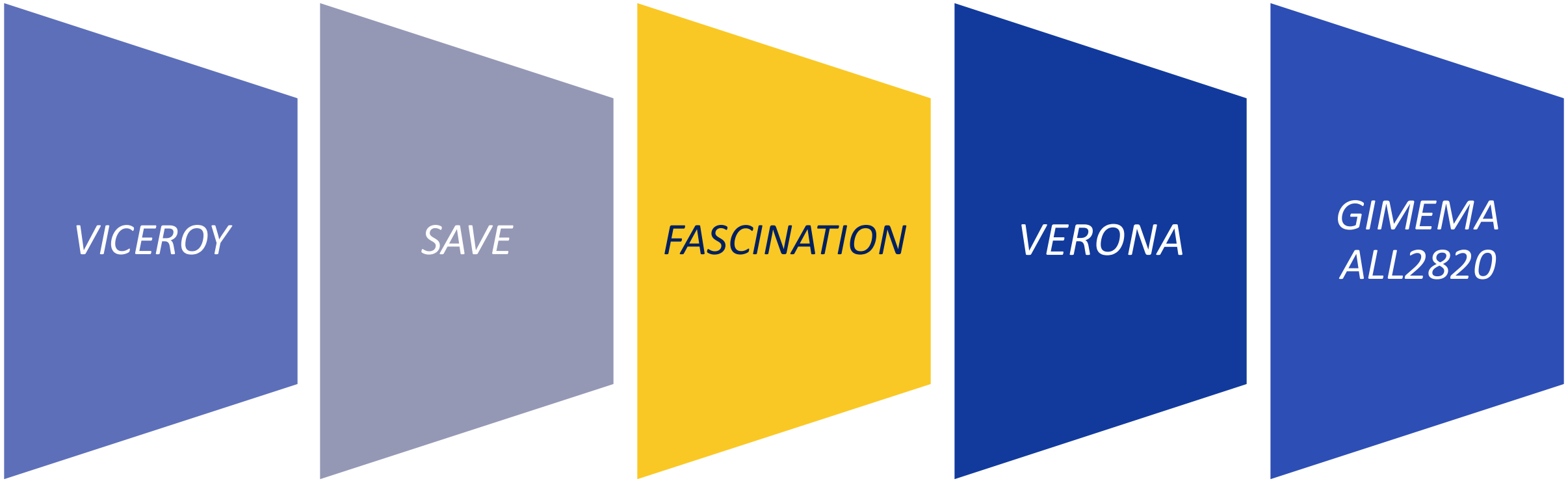
Note: Median DoR, OS and EFS not reached

TEAEs (Any Grade, >30%), n (%)	All (N = 21)
Vomiting	14 (67)
Elevated AST/ALT	13 (62)
Increased potassium	13 (62)
Nausea	12 (57)
Increased phosphorus	11 (52)
Hyponatremia	11 (52)
Febrile neutropenia	10 (48)
Constipation	10 (48)
QTc prolonged*	9 (43)
Thrombocytopenia	8 (38)
Headache	7 (33)
Differentiation syndrome	4 (19)

*No Grade ≥3 QT prolongation

SAVE regimen shows promising activity in older patients with newly diagnosed NPM1mt or KMT2Ar AML not eligible for intensive chemotherapy; confirmation in larger cohorts with longer follow-up is needed

ASH 2025: RAPID REVIEWS



KEY DATA

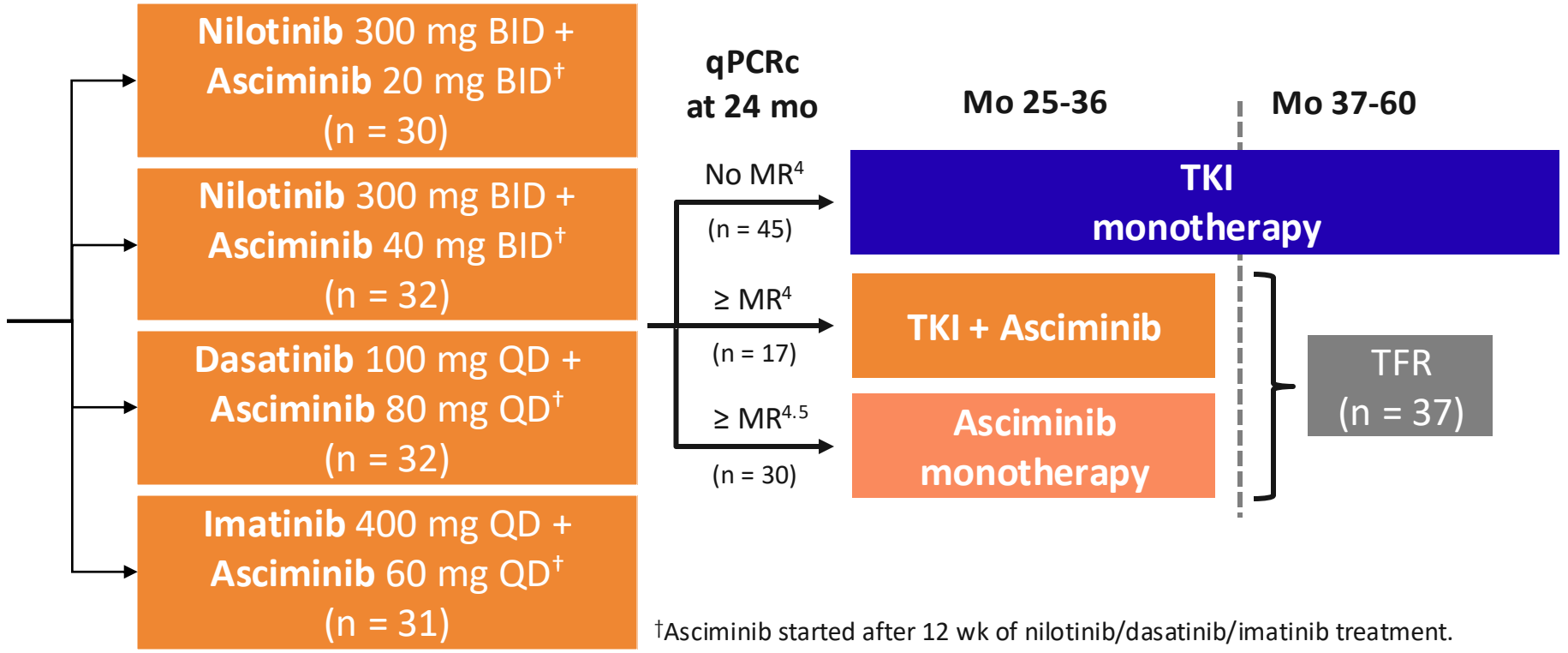
FASCINATION: 1L Asciminib in combination with conventional ATP-competing *BCR::ABL1* inhibitors in newly diagnosed CML → 3-yr update

Study Design: Multicenter, prospective, open-label, international (German), interventional phase II trial

- Adults with newly diagnosed Ph+ CP-CML*
- adequate organ function
- ECOG PS ≤2

(N = 125)

*Ph-negative cases or participants with variant translocations who are *BCR::ABL1* positive also considered.



†Asciminib started after 12 wk of nilotinib/dasatinib/imatinib treatment.

Primary endpoints: MR rate at month 12

Secondary endpoints: MR rate at month 24 and 25, MR maintenance during asciminib monotherapy in months 24 and 36, achievement and duration of TFR in month 37 to 60, incidence of adverse events grade 1-5, quality of life, progression free survival, and overall survival

Treatment-free remission (TFR)

KEY DATA

FASCINATION: 1L Asciminib combination with conventional ATP-competing *BCR::ABL1* inhibitors in newly diagnosed CML → 3-yr update

Primary Endpoint: Molecular responses

n (%)	At months 12 (total eligible for evaluation N =114)	At month 24 (total eligible for evaluation N =110)	At month 36 (total eligible for evaluation N =101)
MMR	77 (68)	95 (86)	92 (91)
MR^4	**43 (38)**	54 (49)	66 (65)
$MR^{4.5}$	25 (22)	37 (34)	45 (45)
MR^5	9 (8)	26 (24)	27 (27)
$MR^{5.5}$	3 (3)	19 (17)	20 (20)

n (%)	*ASXL1* Mutation (n = 8)	No Mutation (n = 103)	Other Mutations (n = 14)	All Patients (N = 125)
MR^4 at 12 mo	6 (75)	33 (32)	4 (29)	43 (34)

- Significantly higher MR^4 rate in patients with *ASXL1* mutation vs without any mutation ($P = 0.0215$)

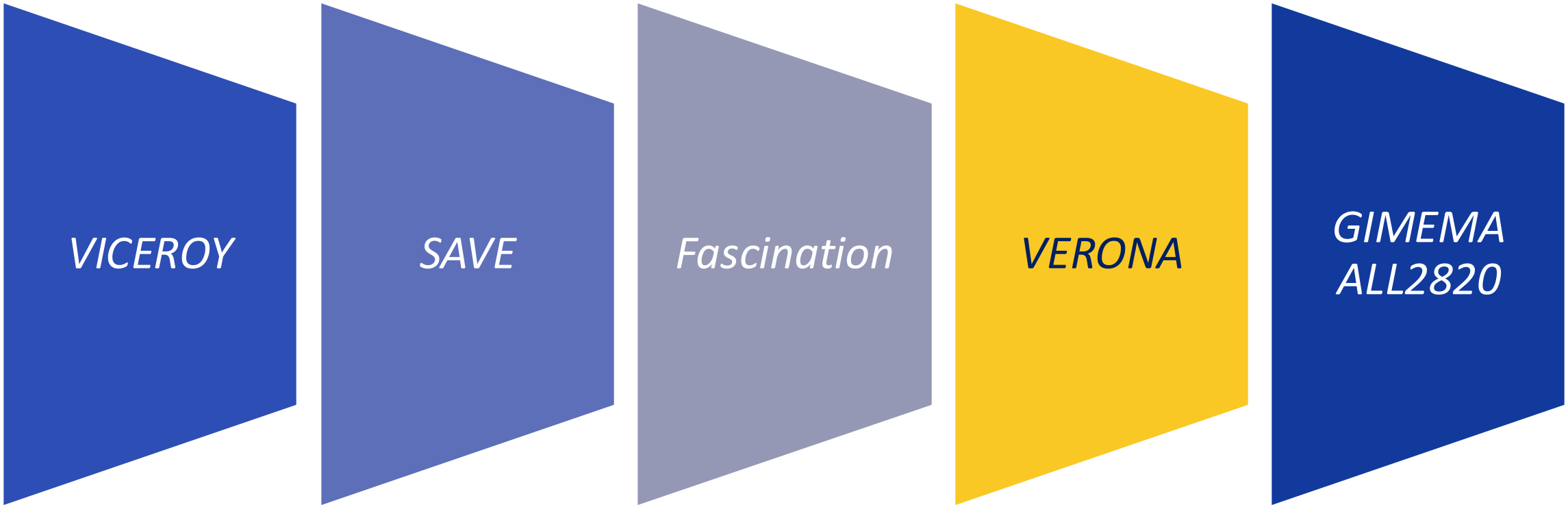
Safety

Select Grade 3-4 Adverse Events

Grade 3/4 AEs, %	All Patients (N = 125)
Investigations (eg, lipase increase)	30.5
Metabolism and nutrition disorders	19.8
Blood and lymphatic system disorders	9.6
Infections and infestations	5.4
Cardiac disorders	4.8
Skin/subcutaneous tissue disorders	4.2
Vascular disorders	4.2

Front-line asciminib combination therapies may be a treatment option for newly diagnosed CML

ASH 2025: RAPID REVIEWS



KEY DATA

VERONA: 1L Venetoclax + Azacitidine in treatment-naïve higher-risk myelodysplastic syndrome

Study Design: Randomized phase III study

Stratified by geographic factors, HSCT (eligible vs ineligible), and IPSS-R

- Aged ≥18 years
- Newly diagnosed MDS per WHO 2016 classification
- IPSS-R score >3
- HSCT eligible without prearranged HSCT (up to 19% of patients) or HSCT ineligible
- ECOG PS 0-2
- No prior therapy with any HMA, CT, or HSCT

(N = 509, R 1:1)

Venetoclax (Ven)
(400 mg PO QD) Days 1-14
+ Azacitidine (Aza)
(75 mg/m² IV or SC) 7 days

Placebo (Pbo)
Days 1-14
+ Azacitidine (Aza)
(75 mg/m² IV or SC) 7 days

Treatment until relapse, PD, HSCT, or unacceptable toxicity

Primary endpoint: Overall survival (OS)

Secondary endpoints: mOR (CR + PR + mCR), overall hematologic improvement (erythroid, neutrophil, or platelet), CR, RBC and platelet transfusion independence, PROs, OR (CR + PR), safety

Select Baseline Characteristics

~65% male, ~ 75% white, ~ 45% European

n (%)	Ven + Aza (n = 256)	Pbo + Aza (n = 253)
Median age, yr (range)	72 (31-86)	72 (25-92)
ECOG PS		
• 0	97 (37.9)	101 (39.9)
• 1	140 (54.7)	132 (52.2)
• 2	19 (7.4)	20 (7.9)
IPSS-R prognostic risk*		
• Intermediate	70 (27.3)	71 (28.1)
• High	96 (37.5)	99 (39.1)
• Very high	90 (35.2)	83 (32.8)
HSCT eligible at baseline	50 (19.5)	47 (18.6)
Bone marrow blast count,		
• < 5%	48 (18.8)	48 (19.0)
• ≥5% to <10%	83 (32.4)	93 (36.8)
• ≥10 to <20%	125 (48.8)	108 (42.7)
• ≥20%	0	4 (1.6)
Baseline mutations detected†		
• ASXL1	60 (30)	68 (33.5)
• RUNX1	49 (24.5)	38 (18.7)
• EZH2	29 (14.5)	49 (24.1)
	5 (2.5)	13 (6.4)

*Data omitted from 1 missing patient in placebo arm
†Based on available samples

Data cutoff: April 10, 2025

KEY DATA

VERONA: 1L Venetoclax + Azacitidine in treatment-naïve higher-risk myelodysplastic syndrome

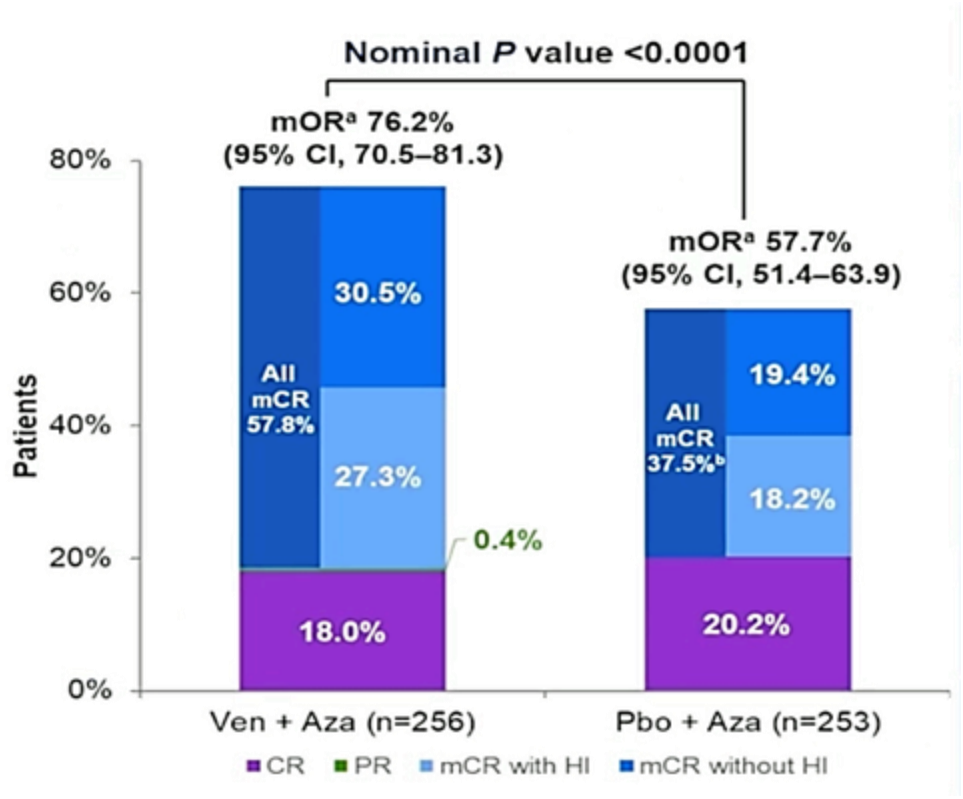
Primary Endpoint: Overall Survival

Median follow-up: 41.2 mos	Ven + Aza (n = 256)	Pbo + Aza (n = 253)
Median duration of treatment, mo (range)	5.9 (0.4-54.0)	6.9 (0.4-48.2)
Median OS, mo (95% CI)	**22.2** (17.3-27.3)	**21.7** (17.8-23.8)
HR (95% CI) Stratified log-rank, nominal *P* value	0.908 (0.733-1.126) 0.38	

Hematological improvement (HI)	Ven + Aza (n = 256)	Pbo + Aza (n = 253)
Overall HI (95% CI)	49.4 (43.0-55.8)	41.2 (35.0-47.6)
Nominal *P* value	0.0723	

Key Secondary Endpoints: Response Rates

Modified Overall Response (mOR)	Ven + Aza (n = 195)	Pbo + Aza (n = 146)
Median duration, mo (95% CI)	15.3 (12.3-20.7)	14.8 (12.4-16.7)



Median number of cycles: 6

KEY DATA

VERONA: 1L Venetoclax + Azacitidine in treatment-naïve higher-risk myelodysplastic syndrome

Secondary Endpoints: Subsequent treatment with HSCT and other regimens

n (%)	Ven + Aza (n = 256)	Pbo + Aza (n = 253)
Overall HSCT	43 (16.8)	33 (13.0)
• HSCT without intervening therapy	39 (15.2)	23 (9.1)
• Post-study treatment prior to HSCT	4 (9.3)	10 (30.3)
• Post-study venetoclax prior to HSCT	0	5 (15.2)
Median time to HSCT, mo (range)	5.6 (2.9-18.1)	6.7 (2.2-33.9)
Best response on study treatment prior to HSCT		
• CR	11 (25.6)	9 (27.3)
• mCR	26 (60.5)	11 (33.3)
• SD	6 (14.0)	13 (39.4)
Subsequent therapy after study treatment		
• All	**73 (28.5)**	**98 (38.7)**
• Venetoclax	27 (10.5)	53 (20.9)

HSCT: Hematopietic Stem Cell Transplant

Safety Summary

n (%)	Ven + Aza (n = 255)	Pbo + Aza (n = 246)
Serious AE	167 (65.5)	135 (54.9)
AEs leading to death*		
• Any	18 (7.1)	20 (8.1)
• Disease progression	4 (1.6)	2 (0.8)
• Septic shock	3 (1.2)	2 (0.8)
• Sepsis	1 (0.4)	2 (0.8)
• AML transformation	1 (0.4)	2 (0.8)
• Cardiac arrest	1 (0.4)	3 (1.2)
• Multiple organ dysfunction syndrome	1 (0.4)	2 (0.8)
Deaths		
• Any cause	167 (65.5)	169 (68.6)
• Most common causes:		
• Disease progression	100 (39.2)	100 (40.7)
• AEs	27 (10.6)	28 (11.4)
• At ≤30 days after last dose	19 (7.5)	21 (8.5)
• At >30 days after last dose	147 (57.6)	147 (59.8)

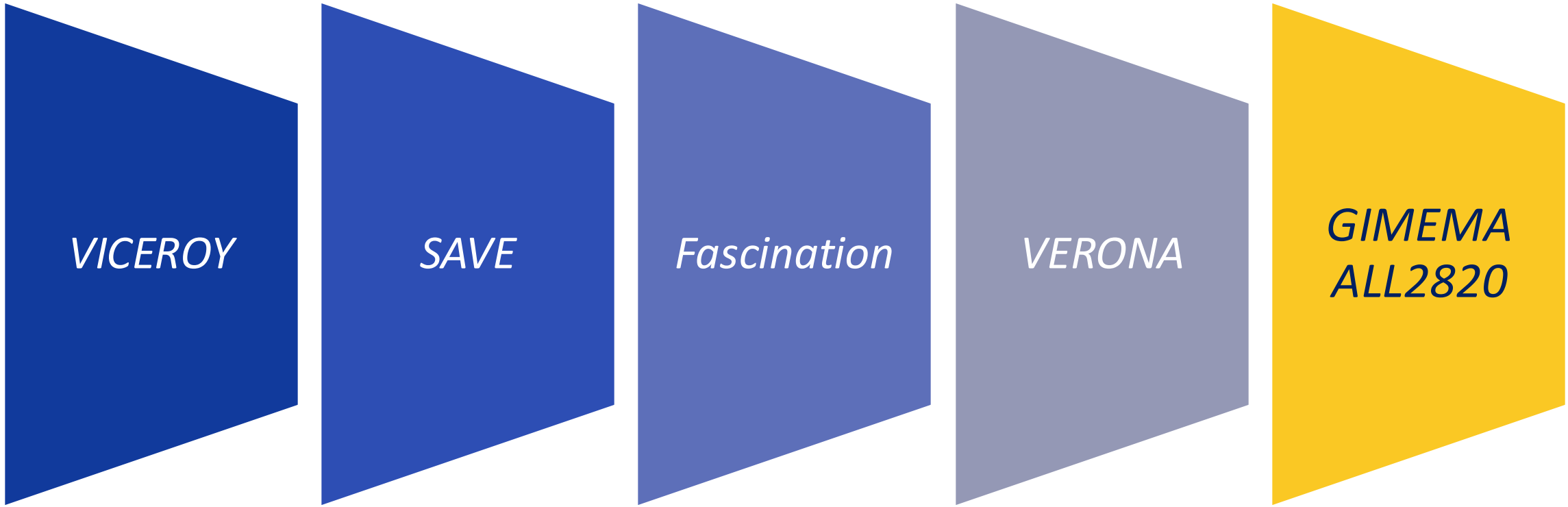
No overall survival improvement with venetoclax plus azacitidine compared to azacitidine alone in high-risk myelodysplastic syndromes; better response rates may help patients reach transplant

Polling question

Given that the VERONA trial did not demonstrate an overall survival benefit but showed higher response rates and subgroup trends, if approved how likely are you to use venetoclax-azacitidine in higher-risk MDS patients?

1. Very likely
2. Somewhat likely – for select patients
3. Not likely

ASH 2025: RAPID REVIEWS



KEY DATA

GIMMA ALL2820 – first results of ponatinib + blinatumomab in newly diagnosed Ph+ ALL

Study Design: Randomized phase III study

- Newly diagnosed adults with Ph+ ALL
- No prior or current CNS
- No HIV, HBV, and HCV infection
- WHO PS ≤2

R: 2:1 (N = 225)

	Induction	Consolidation
→	**Ponatinib** age 18-65 yr, 45 mg for 22 days, then 30 mg to Day 70; If age >65 yr, 30 mg to Day 70 (n = 151)	**Blinatumomab*** **(+ ponatinib)** for 2-5 cycles
→	**Chemotherapy** (mild for patients aged >65 yr) **+ Imatinib** for 3 cycles until Day 70 (n = 74)	**Imatinib†** for cycles4-6 (only for cycle 4 for patients >65 yr)

→ *Stratified for ASCT‡*

*Those without CHR after 2 cycles taken off-study. †Cross over to blinatumomab (+ ponatinib) allowed if no CHR/MRD+. ‡Patients aged 18-65 yr stratified for ASCT: if MRD+ ± *ABL1* mutation or PNQ by q-RT PCR + additional genomic lesions, to receive ASCT; if CMR or PNQ by q-RT PCR without additional genomic lesions, to receive 3 additional blinatumomab + ponatinib cycles (MRD monitored).

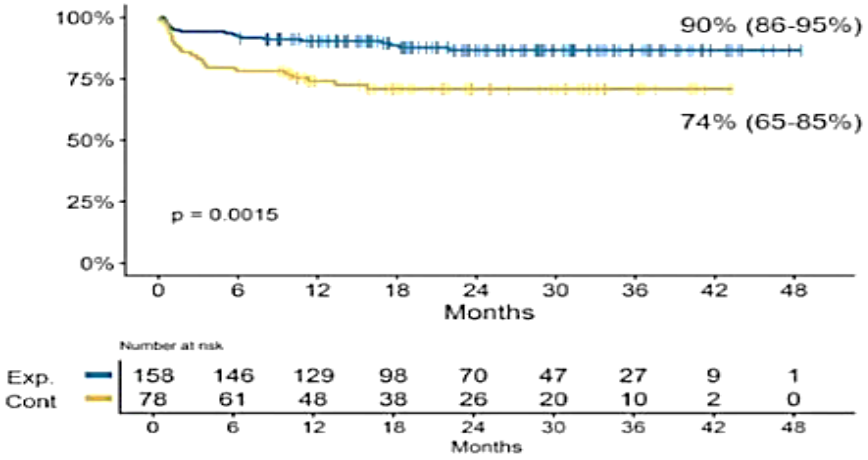
Primary endpoint: Event Free Survival (EFS)

Key secondary endpoints: Hematologic and molecular response, OS, DFS, safety

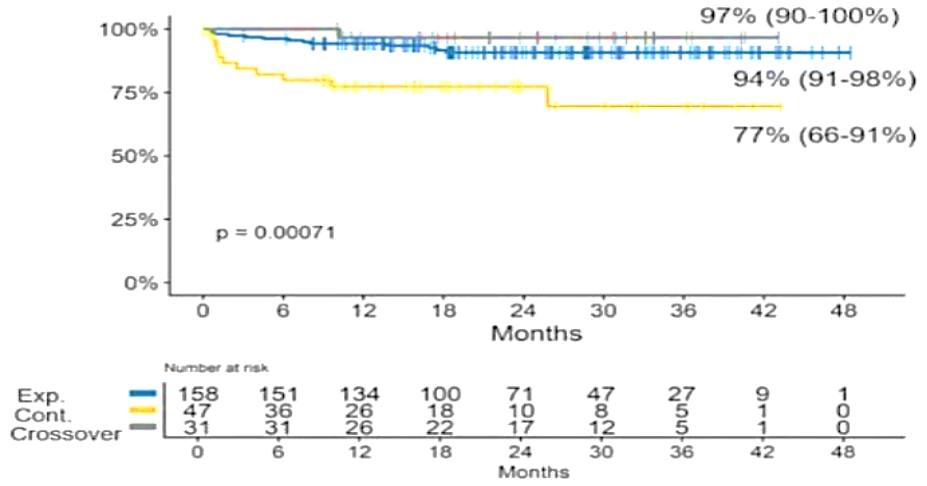
Median follow up: 23.4 months

Key Endpoints

Event Free Survival (EFS)



Overall Survival (OS)



Ponatinib plus blinatumomab (chemo-free approach) may be a new potential standard of care for adult Ph+ ALL
Combination not yet approved…

ASH 2025:

Leukemia

Key Takeaways

Q&A

@PankitVachhaniMD

PARADIGM: Frontline Azacitidine with venetoclax demonstrated deep and more frequent response than induction chemotherapy (ORR: 88% vs 62%) in newly diagnosed intermediate or adverse-risk FLT3-wild type acute myeloid leukemia – *FDA approved November 2018*

ASC2ESCALATE: In chronic myeloid leukemia previously treated with one TKI, asciminib achieved major molecular response of 59.4% at week 48, supporting its potential as a standard of care in the second line setting – *FDA granted accelerated approved October 2024*

KOMET-007: Ziftomenib with venetoclax in the first-line setting provided complete response with an overall response rate of 89% in newly diagnosed *NPM1*-mutated acute myeloid leukemia – *not yet approved in this curative setting*

VICEROY: In the frontline treatment setting for newly diagnosed *FLT3*-mutated acute myeloid leukemia ineligible for intensive induction chemotherapy, venetoclax and azacitidine plus gilteritinib produced high response rates with manageable toxicity – *not yet FDA approved*

SAVE: Frontline revumenib with decitabine/cedazuridine and venetoclax all-oral combination demonstrated early efficacy and high overall response (86%) in a small cohort for newly diagnosed acute myeloid leukemia – *not yet FDA approved*

FASCINATION: In newly diagnosed chronic myeloid leukemia first-line setting, asciminib-based combination therapies improved long-term tolerability while maintaining deep molecular responses – *FDA approved October 2024*

VERONA: For first-line treatment-naïve intermediate- and higher-risk myelodysplastic syndrome, venetoclax plus azacitidine improved response rates but did not achieve an overall survival benefit versus azacitidine alone – *not yet FDA approved*

GIMEMA ALL2820: In newly diagnosed Ph+ acute lymphoblastic leukemia front-line setting, ponatinib plus blinatumomab improved event-free survival (90% vs 74%) and overall survival (94% vs 77%) compared with imatinib plus chemotherapy – *not yet FDA approved*

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

MajesTEC-3

Does teclistamab plus daratumumab benefit patients with relapsed / refractory multiple myeloma (RRMM) compared to investigators choice treatment?

Initial pre-planned analysis

Teclistamab is a T cell engaging bispecific antibody that targets BCMA and CD3, while daratumumab is an anti-CD38 antibody that targets monoclonal antibody

*On **December 15th 2025**, the FDA awarded a **national priority voucher** to teclistamab in combination with daratumumab for relapsed/refractory multiple myeloma.*

cornerstone specialty network™

KEY DATA

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy for RRMM

Study Design: Randomized phase III study

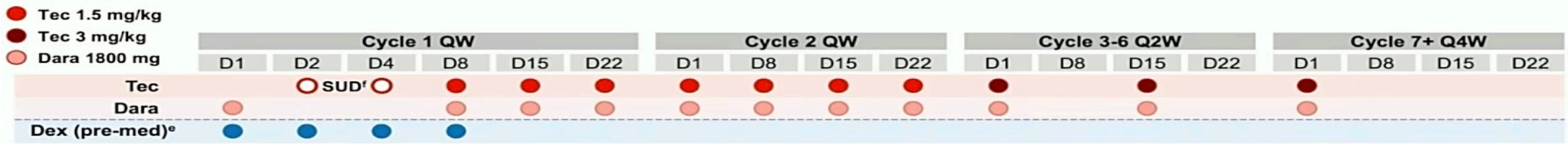
- Relapse refractory multiple myeloma (RRMM)
- 1-3 prior lines of therapy including a PI and lenalidomide
    - Patients with only 1 prior line of therapy must have been lenalidomide refractory per IMWG criteria
- ECOG PS 0 – 2
- No prior BCMA-directed therapy
- No refractory to anti-CD38 mAbs

(N = 587)

R 1:1

Teclistamab + Daratumumab
SC dosing following Dara schedule
(n = 291)

DPd/DVd
by investigator's choice
(n = 296; 91% DPd)



Primary endpoint: Progression-free survival by independent review committee

Key secondary endpoints: Complete response (CR) and overall response rate (ORR), Minimal residual disease (MRD) negativity, overall survival (OS), and MySIm-Q Total symptom score

Other secondary endpoints: Safety, pharmacokinetics and immunogenicity

KEY DATA

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy for RRMM

Baseline Characteristics

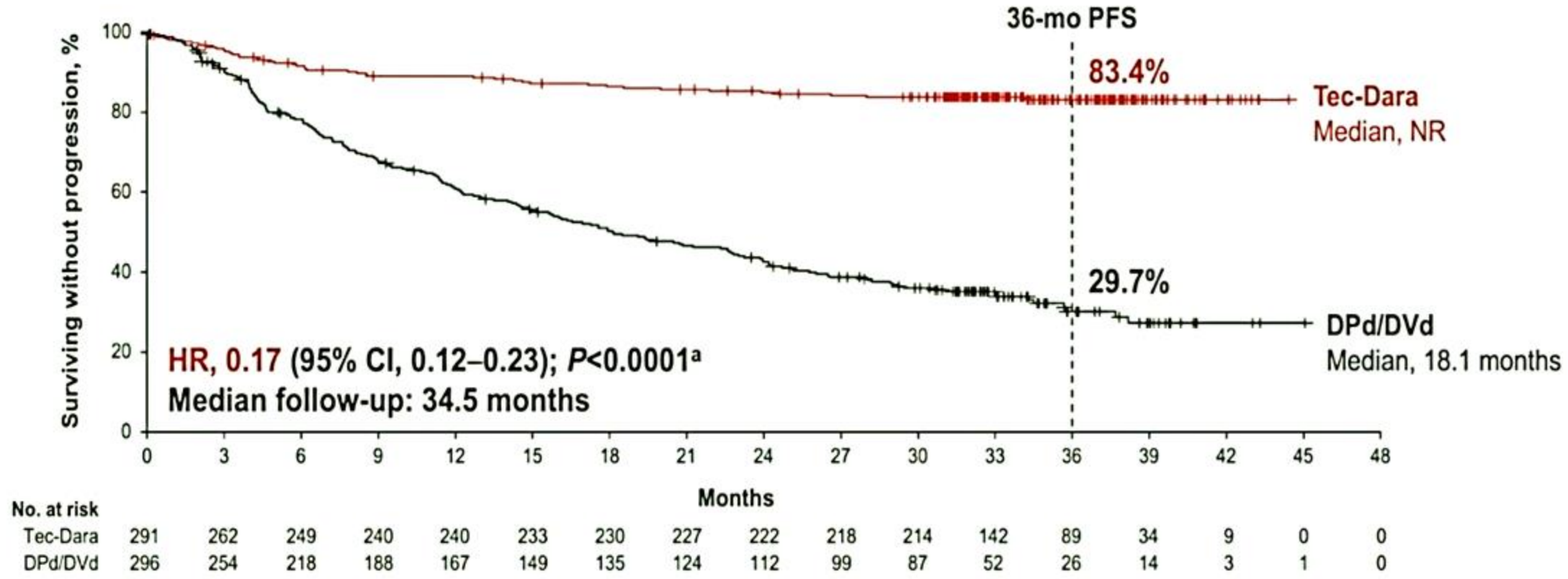
n (%)	Tec-Dara (n = 291)	DPd/DVd (n = 296)
Median age, yr (range)	64 (36-88)	63 (25-84)
• ≥75 yr	31 (10.7)	25 (8.4)
Female	135 (46.4)	127 (42.9)
Race		
• White	190 (65.3)	194 (65.5)
• Asian	68 (23.4)	63 (21.3)
• Black	13 (4.5)	20 (6.8)
• Other	20 (6.9)	19 (6.4)
ECOG PS		
• 0	167 (57.4)	160 (54.1)
• 1	108 (37.1)	127 (42.9)
• 2	16 (5.5)	9 (3.0)
ISS stage		
• I	182 (62.5)	185 (62.5)
• II	85 (29.2)	88 (29.7)
• III	24 (8.2)	23 (7.8)
BMPCs ≥60%, n/N (%)	28/286 (9.8)	24/293 (8.2)
High-risk cytogenetics, n/N (%)	104/285 (36.5)	104/294 (35.4)

n (%)	Tec-Dara (n = 291)	DPd/DVd (n = 296)
Soft-tissue plasmacytomas	41 (14.1)	41 (13.9)
• Extramedullary plasmacytomas	14 (4.8)	17 (5.7)
• Paraskeletal plasmacytomas	32 (11.0)	31 (10.5)
Median prior LOT, n (range)	2 (1-3)	2 (1-3)
• 1	108 (37.1)	114 (38.5)
• 2	134 (46.0)	134 (45.3)
• 3	49 (16.8)	48 (16.2)
Prior transplantation	210 (72.2)	226 (76.4)
Prior therapy		
• PI	290 (99.7)	296 (100)
• IMiD	291 (100)	296 (100)
• Anti-CD38	15 (5.2)	16 (5.4)
Refractory status		
• To last prior LOT	250 (85.9)	251 (84.8)
• Any PI	117 (40.2)	104 (35.1)
• Any IMiD	247 (84.9)	253 (85.5)
• Lenalidomide	240 (82.5)	251 (84.8)
• Double (PI and IMiD)	99 (34.0)	88 (29.7)

KEY DATA

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy for RRMM

Primary Endpoint: Progression-free survival (PFS)

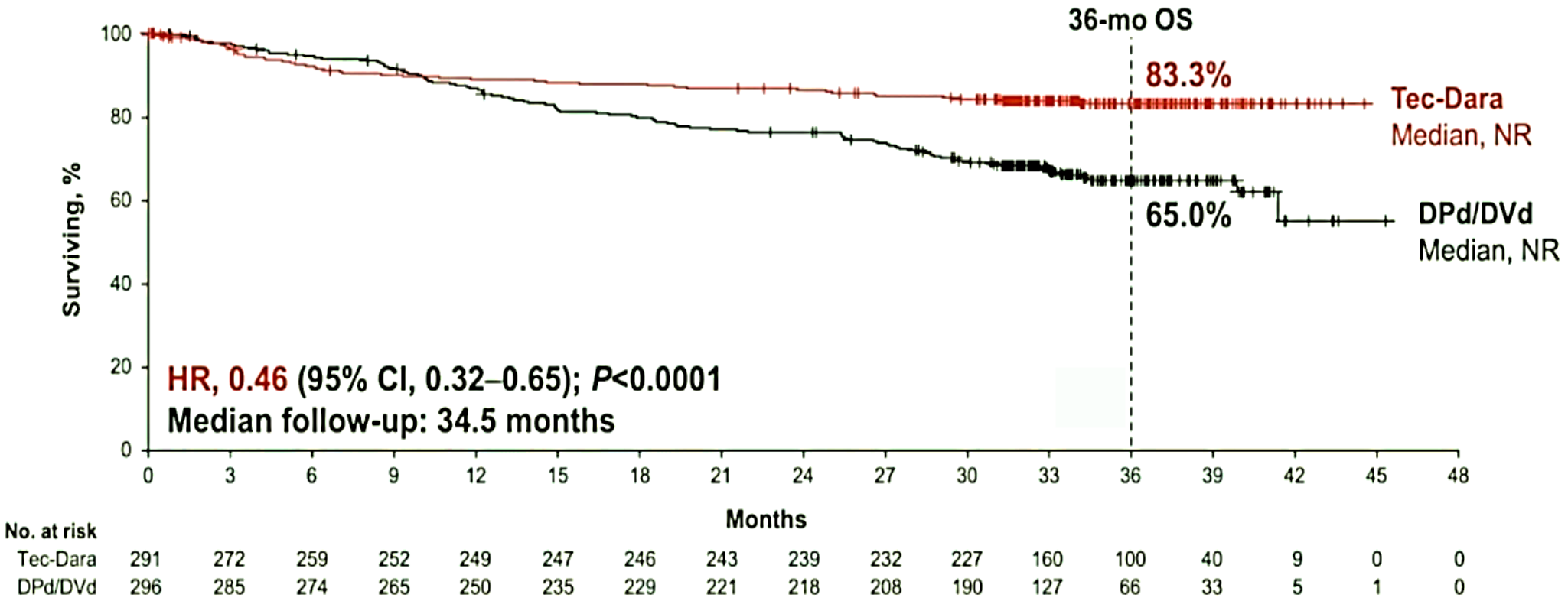


Superior PFS across all prespecified subgroups

KEY DATA

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy for RRMM

Secondary Endpoint: Overall survival (OS)

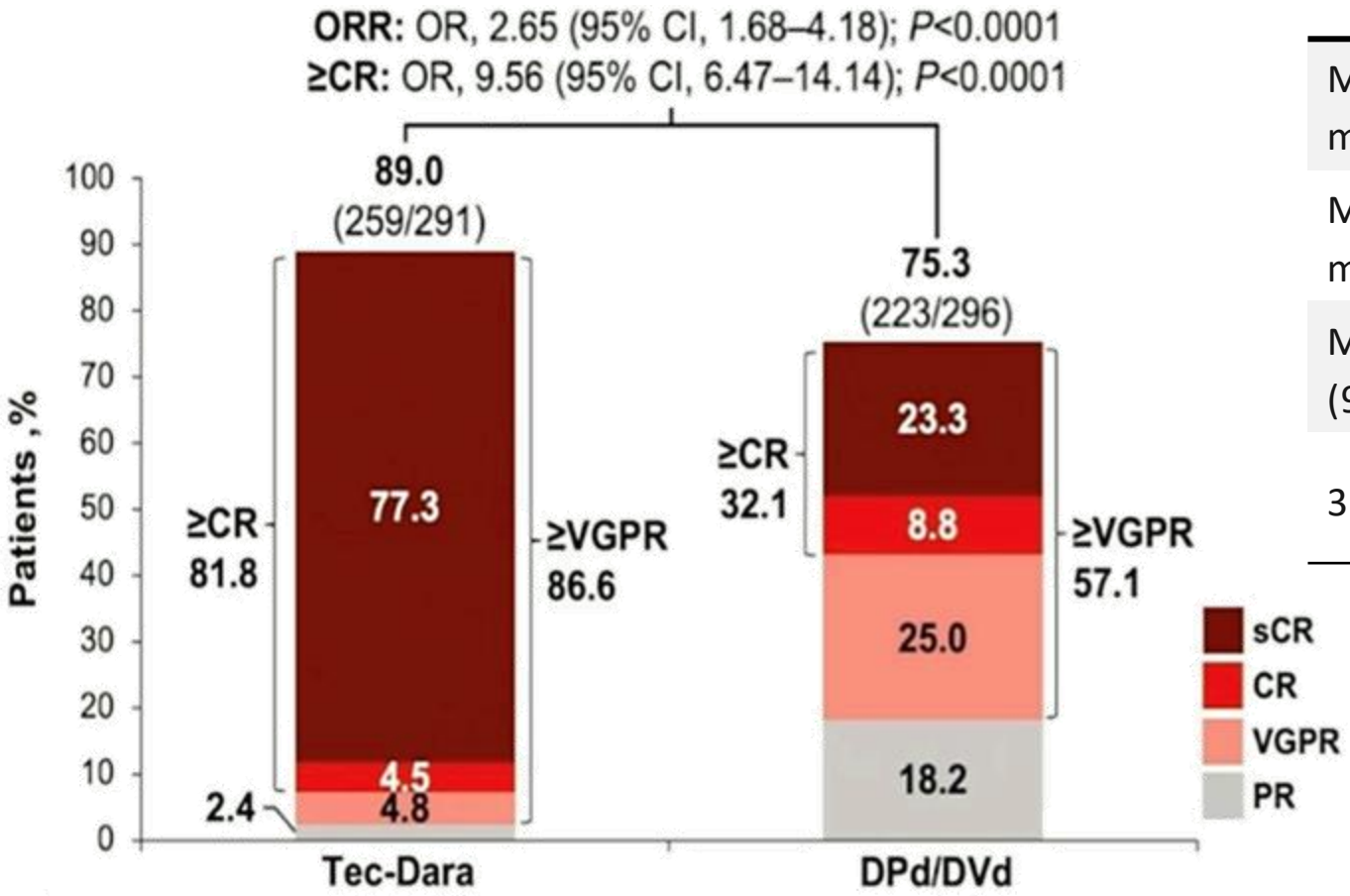


Superior OS across all prespecified subgroups

KEY DATA

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy for RRMM

Secondary Endpoint: Response

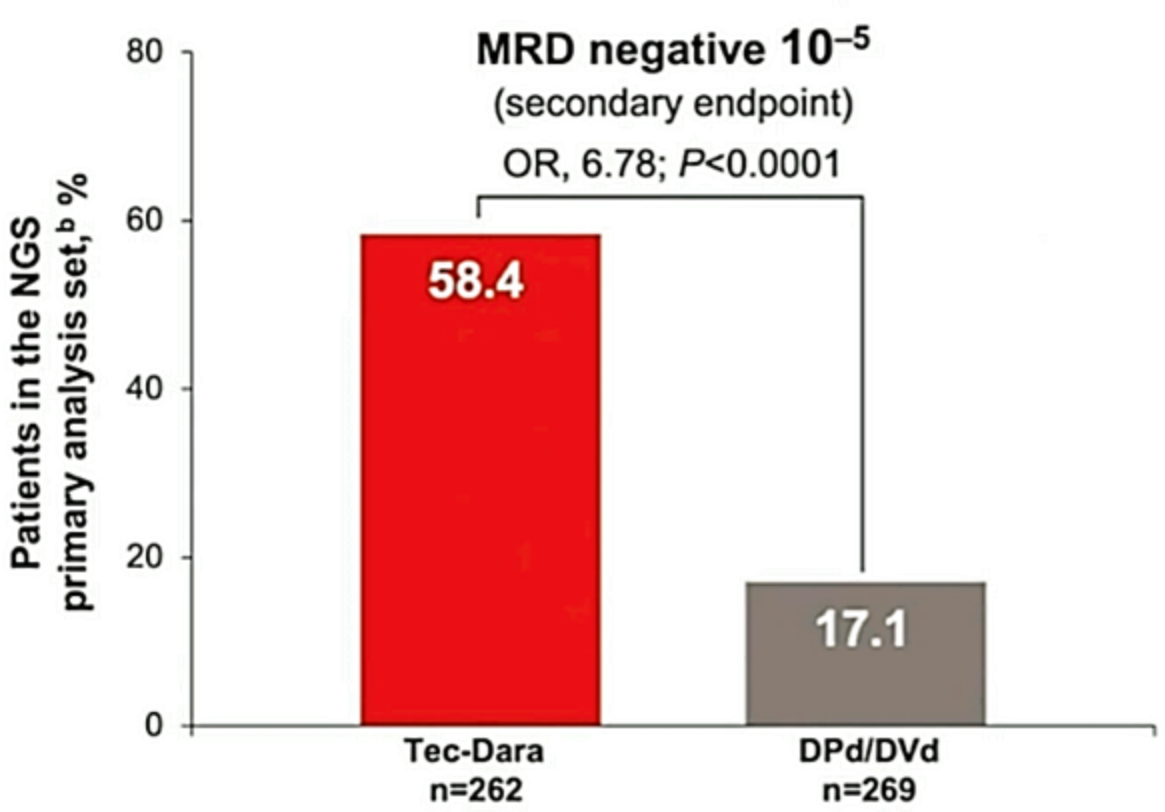


	Tec-Dara (n = 259)	DPd/DVd (n = 223)
Median time to first response, months (range)	1.2 (0.9-25.0)	1.2 (0.7-6.3)
Median time to first response, months (range)	6.9 (1.0-34.5)	6.9 (1.5-18.8)
Median DOR, months (95% CI)	NE (NE-NE)	23.5 (19.8-29.9)
36-months DOR, % (95% CI)	88.5 (83.7-92.0)	36.4 (28.9-43.9)

KEY DATA

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy for RRMM

Secondary Endpoint: Minimal residual disease (MRD) negativity



	Tec-Dara (n = 262)	DPd/DVd (n = 269)
MRD negative ≥CR 10^{-5}		
• Primary NGS	57.6	17.1
• Evaluable	89.3	63.0
MRD negative ≥CR 10^{-6}		
• Primary NGS	53.8	10.4
• Evaluable	87.5	41.8

[a]MRD was assessed in the bone marrow by NGS in accordance with IMWG guidelines. [b]The MRD NGS primary analysis set was defined as all randomized patients in the study except those recruited in China (due to China instead utilizing NGF for MRD assessment; Tec-Dara, n=262; DPd/DVd, n=269). [c]The MRD NGS evaluable set was defined as patients who achieved ≥CR, had a successful baseline calibration, and had ≥1 post-baseline MRD sample with a positive or negative result (per NGS) at the indicated threshold (10^{-5}: Tec-Dara, n=168; DPd/DVd, n=73; 10^{-6}: Tec-Dara, n=160; DPd/DVd, n=67).

KEY DATA

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy for RRMM

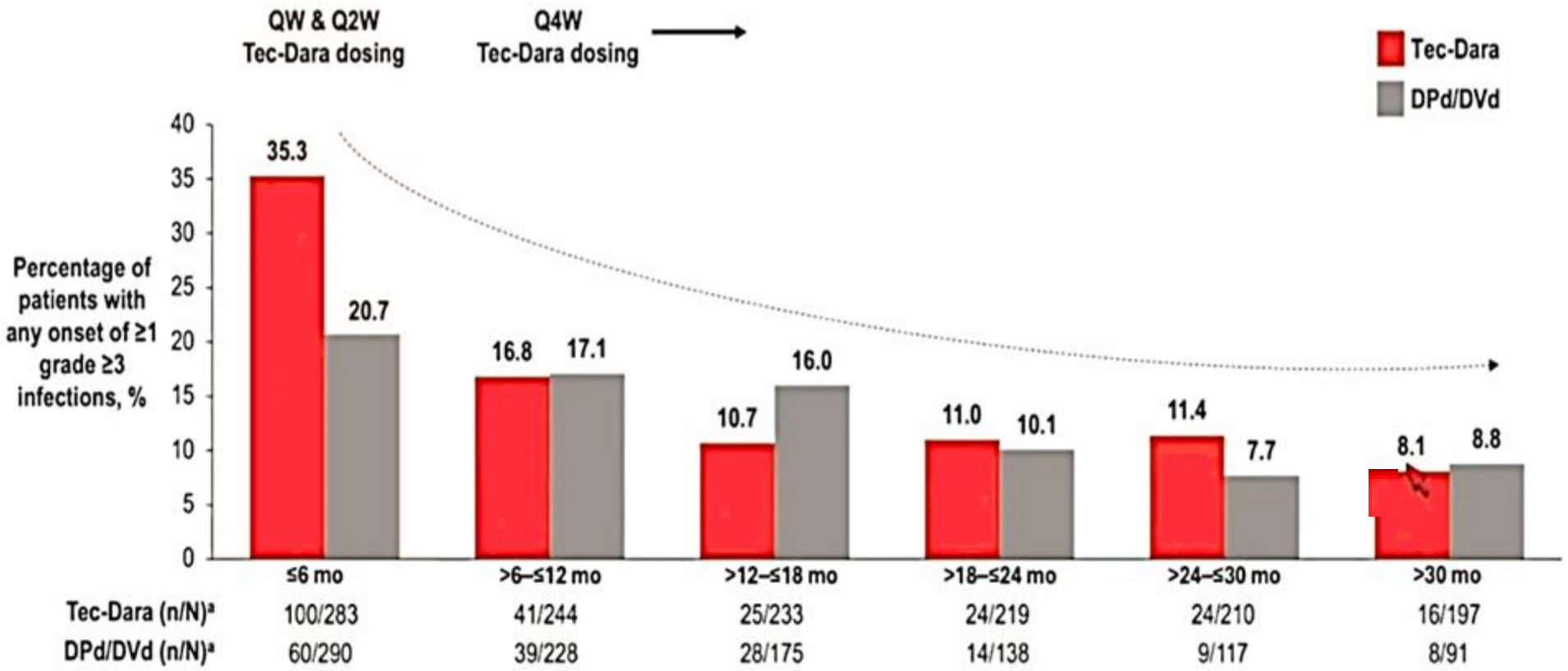
Safety

TEAE, n (%)	Tec-Dara (n = 283)		DPd/DVd (n = 290)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Any	283 (100)	269 (95.1)	290 (100)	280 (96.6)
Hematologic				
• Neutropenia	222 (78.4)	214 (75.6)	240 (82.8)	228 (78.6)
• Anemia	111 (39.2)	58 (20.5)	103 (35.5)	50 (17.2)
• Thrombocytopenia	103 (36.4)	55 (19.4)	126 (43.4)	68 (23.4)
• Lymphopenia	63 (22.3)	59 (20.8)	50 (17.2)	32 (11.0)
• Leukopenia	51 (18.0)	30 (10.6)	61 (21.0)	46 (15.9)
Nonhematologic				
• CRS	**170 (60.1)**	0	-	-
• Diarrhea	147 (51.9)	10 (3.5)	89 (30.7)	7 (2.4)
• Cough	136 (48.1)	1 (0.4)	66 (22.8)	0
• Pyrexia	104 (36.7)	4 (1.4)	55 (19.0)	1 (0.3)

KEY DATA

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy for RRMM

Safety: Grade ≥3 Infections Over Time



SUMMARY

MajesTEC-3

- Tec-Dara demonstrated the strong progression free survival benefit (HR: 0.17)
- 83.4% of patients remained progression-free at 3 years, including those with high-risk features
- Overall survival favored Tec-Dara: HR of 0.46
- Grade ≥3 infections peaked during the initial 6-month period and subsequently declined; optimal management includes prophylaxis, monitoring, and appropriate immunoglobulin replacement therapy application

IMPACT

Teclistamab plus daratumumab may be a potential new treatment option for patients with relapsed refractor multiple myeloma

Not yet FDA approved in combination for earlier line setting

cornerstone specialty network™

Polling question

Does your practice currently prescribe T cell engagers?

1. Yes, we do – both step up and maintenance
2. Yes – but we only do maintenance
3. No, we have not yet – but are planning on doing this in the next 6 months
4. No – and we do not have plans to do so in the near future

Polling question

Based on the MajesTEC-3 clinical trial and if approved, how likely are you adopt teclistamab + daratumumab combination as a preferred second-line treatment option in your practice?

1. Very likely – already administer teclistamab in practice based on later line approval (MajesTEC-1)
2. Somewhat likely – I already use Dara in first line and not sure how many of my patients will be Dara exposed and no refractory
3. Will not change my current practice
4. Unsure

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

CLINICAL QUESTION

COBRA

Does carfilzomib, lenalidomide, and dexamethasone (KRd) benefit patients with newly diagnosed multiple myeloma?

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

Study Design: Multicenter, randomized, open label, phase III study

Stratification by standard vs high-risk cytogenetics t(4:14) or del17p and TE vs TNE

- Newly diagnosed multiple myeloma
- IMWG Frailty Score <2

(N = 250)

KRd - 28-day cycles x 24
Carfilzomib 56 mg/m (20mg CIDI)
DI 8 and 15 – cycle 1-12
DI and 15 – cycles 13-24
Lenalidomide
25 mgDI-21 – cycle 1-24
Dexamethasone
40 mg DI, 8, 15, 22 cycles 1-12 and 20 mg DI, 8, 15, 22 cycles 13-24

R Until progression

VRd 21-day cycle x8
Bortezomib 13mg/m
DI, 4, 8, 11
Lenalidomide 25 mg
DI-14
Dexamethasone 20 mg
DI, 2, 5, 8, 9, 11, 12

RD 28-day cycle x18
Lenalidomide 25 mg
DI-14
Dexamethasone 20 mg
DI, 2, 5, 8, 9, 11, 12

R Until progression

Co-primary endpoint:

Complete response (CR) + Minimal Residual Disease (MRD) negativity 10^{-5} at 12 months and PFS

Secondary endpoints:

MRD negativity, static MRD negativity, ORR, OS, and safety

KRd: carfilzomib, lenalidomide, dexamethasone
VRd: bortezomib, lenalidomide, dexamethasone
RD: lenalidomide, dexamethasone
R: lenalidomide

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

Baseline Characteristics

n (%)	KRd (n = 126)	VRd (n = 124)
Median age, yr (range)	66 (33-78)	67 (31-80)
Sex		
• Female	70 (56)	73 (59)
• Male	56 (44)	51 (41)
Race		
• White	117 (93)	120 (97)
• Black	3 (2)	3 (2)
• Asian	2 (2)	0
• Other	4 (3)	1 (1)
Transplant-eligible (TE)	65 (59)	65 (59)
Transplant non-eligible (TNE)	40 (41)	40 (41)

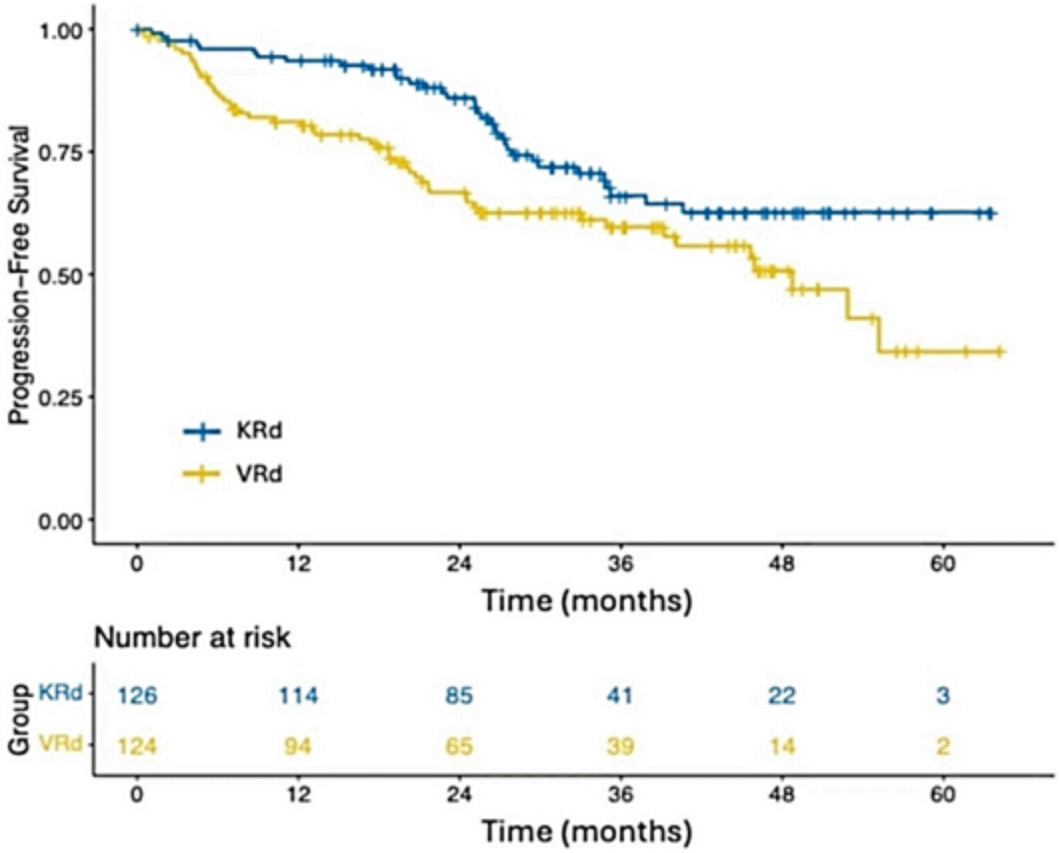
n (%)	KRd (n = 126)	VRd (n = 124)
ECOG		
• 0	31 (25)	31 (25)
• 1	89 (70)	91 (74)
• 2	6 (5)	2 (1)
Standard risk	97 (77)	96 (77)
High-risk	29 (23)	28 (23)
• del17p	14 (48)	15 (53)
• t(4:14)	15 (51)	11 (39)
• t(14:16)	8 (27)	4 (14)
• More than 1	8 (27)	2 (7)

KRd: carfilzomib, lenalidomide, dexamethasone
VRd: bortezomib, lenalidomide, dexamethasone

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

Primary Endpoint: Progression-free survival (PFS)



	KRd (n = 126)	VRd (n = 124)
Progression or death	35 (28%)	51 (41%)
Median PFS, mo	**NR**	48.8
HR	**0.57** (95% CI: 0.37-0.88) p=0.0095	

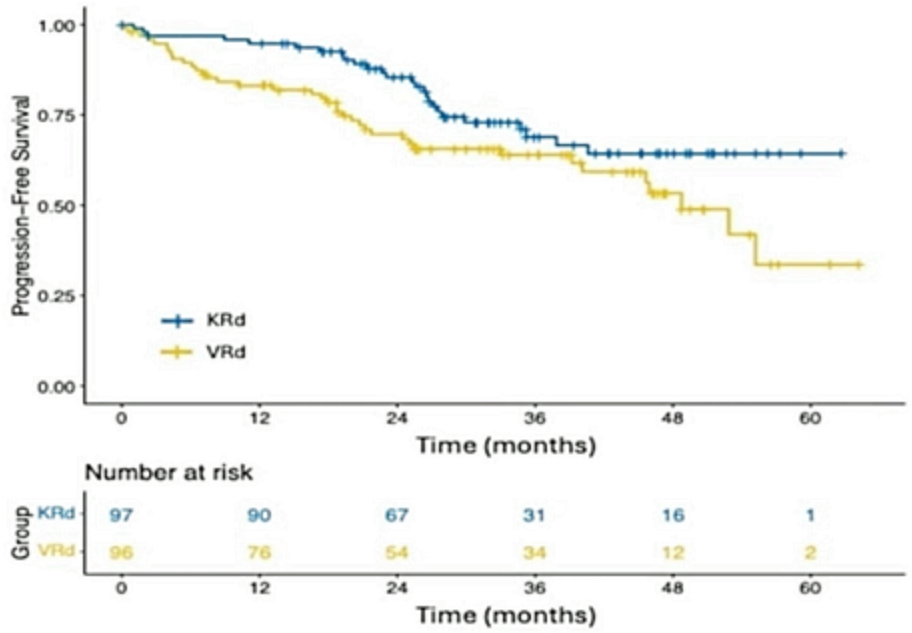
KRd: carfilzomib, lenalidomide, dexamethasone
VRd: bortezomib, lenalidomide, dexamethasone

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

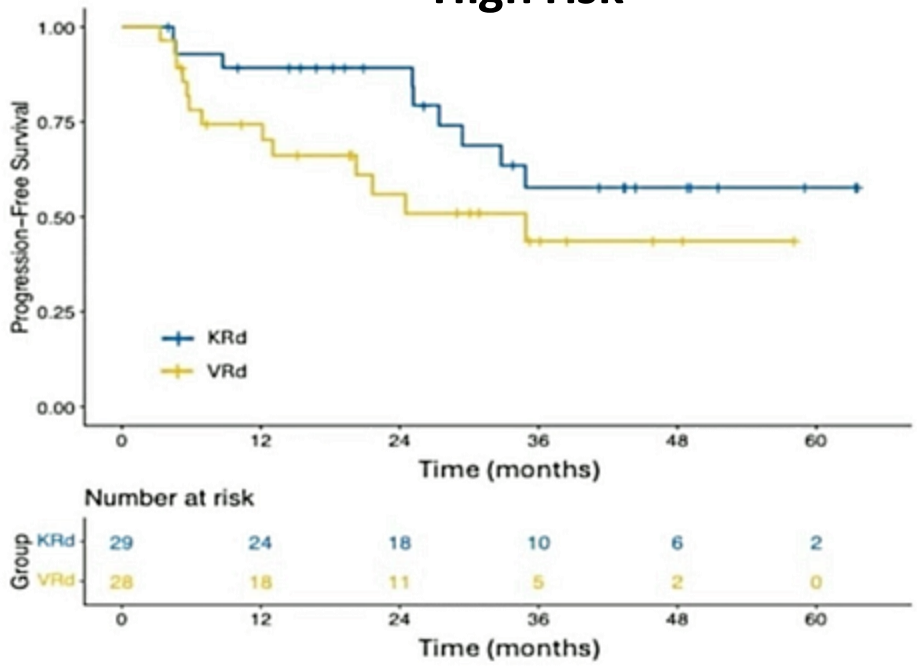
Progression-free survival (PFS) by risk subgroups

Standard risk



	KRd (n = 97)	VRd (n = 96)
Progression or death	26 (27%)	38 (40%)
Median PFS, mo	**NR**	**48.8**
HR	**0.59** (95% CI: 0.36-0.98) p=0.04	

High risk



	KRd (n = 29)	VRd (n = 28)
Progression or death	9 (31%)	13 (31%)
Median PFS, mo	**NR**	**34.9**
HR	**0.52** (95% CI: 0.22-1.22) p=0.12	

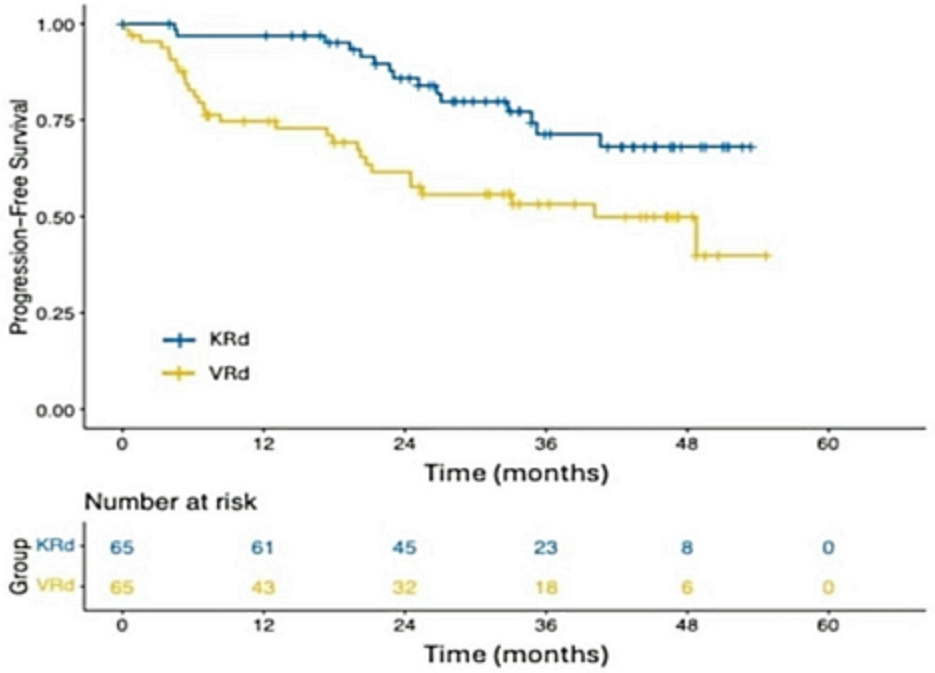
KRd: carfilzomib, lenalidomide, dexamethasone
VRd: bortezomib, lenalidomide, dexamethasone

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

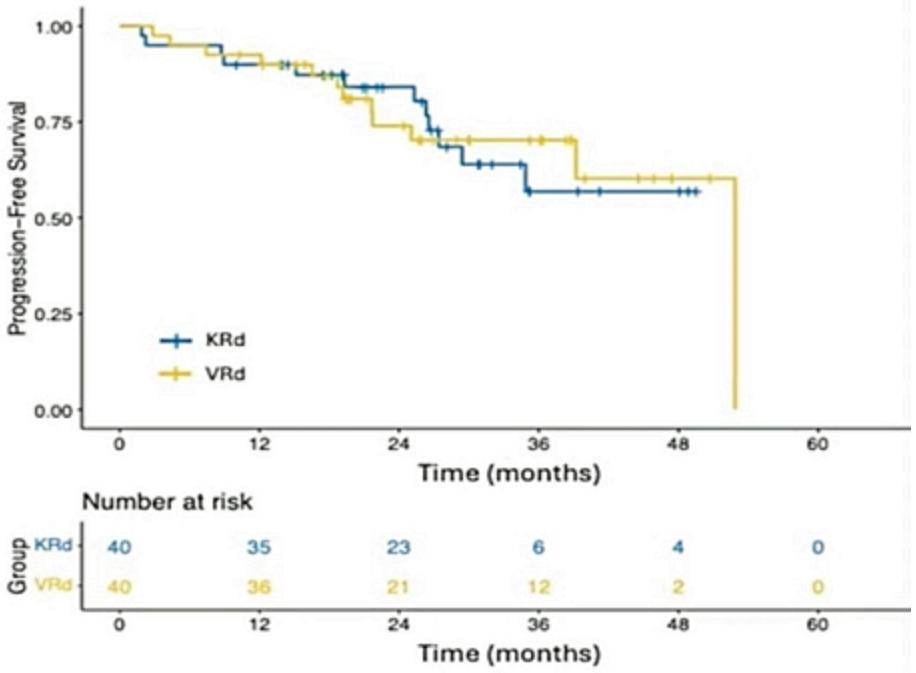
Progression-Free Survival (PFS) by transplant subgroups

Transplant-eligible



	KRd (n = 65)	VRd (n = 65)
Progression or death	15 (23%)	29 (45%)
Median PFS, mo	**NR**	**40.1**
HR	**0.40** (95% CI: 0.21-0.75) p=0.003	

Transplant non-eligible



	KRd (n = 40)	VRd (n = 40)
Progression or death	12 (30%)	12 (30%)
Median PFS, mo	**NR**	**52.9**
HR	**1.06** (95% CI: 0.21-0.75) p=0.87	

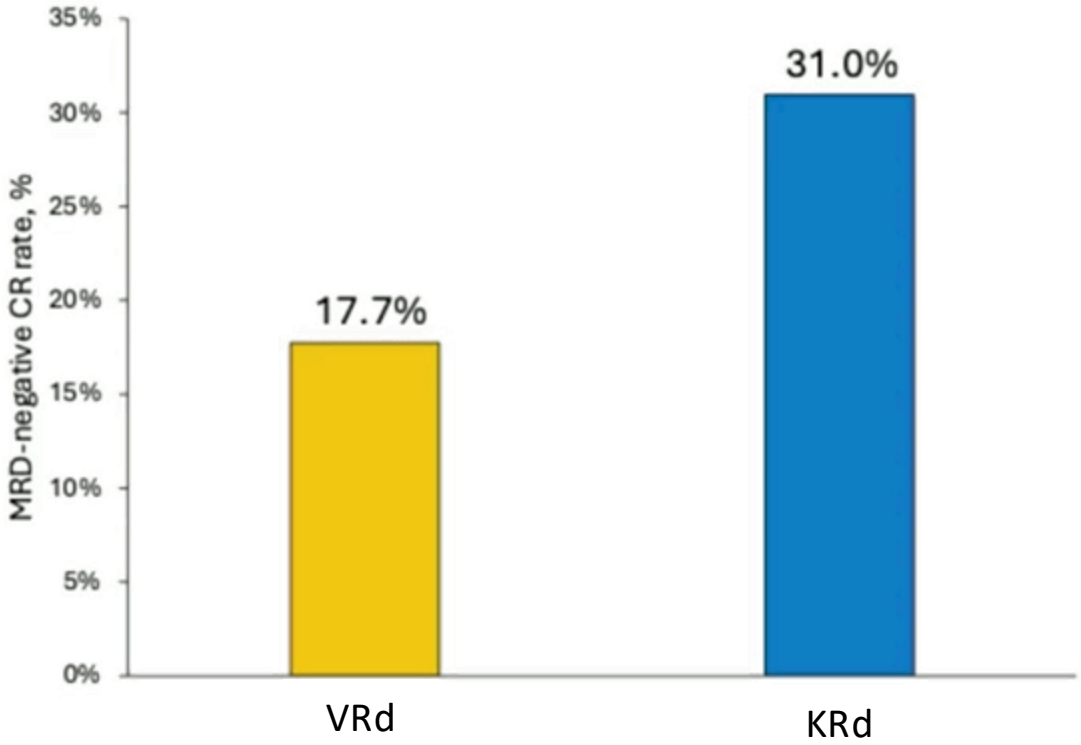
KRd: carfilzomib, lenalidomide, dexamethasone
VRd: bortezomib, lenalidomide, dexamethasone

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

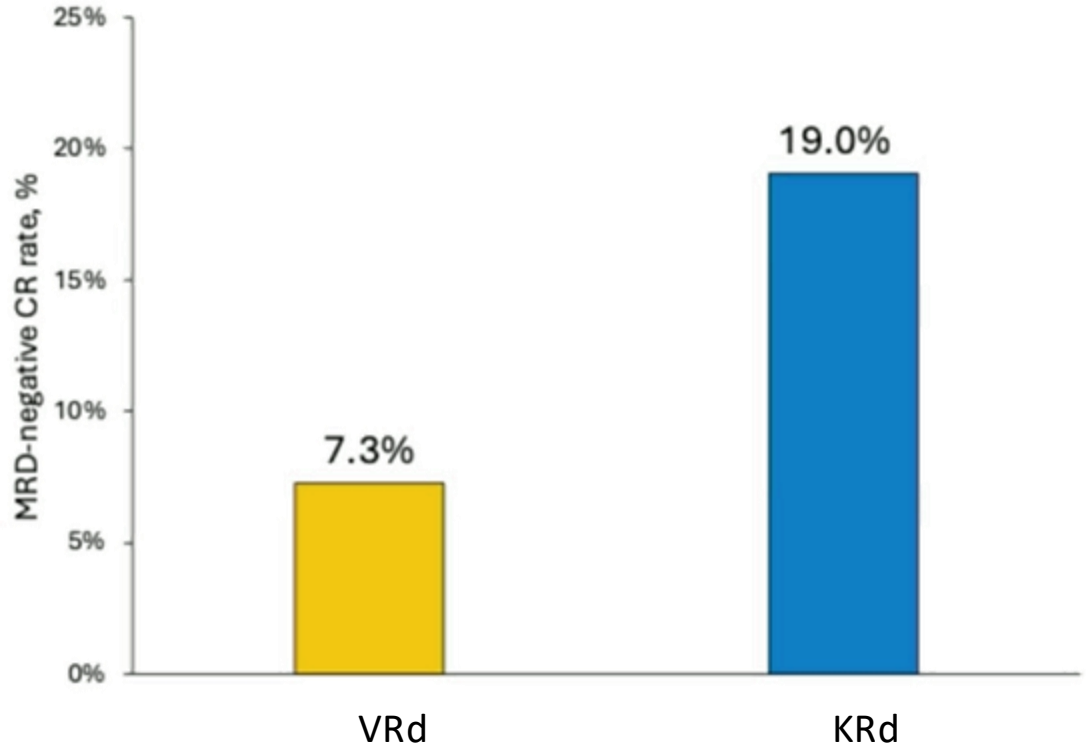
Primary Endpoint: Minimal Residual Disease (MRD)

MRD – 10^{-5}



Odds Ratio = 2.08
95% CI: 1.15-3.77; p=0.016

MRD – 10^{-6}



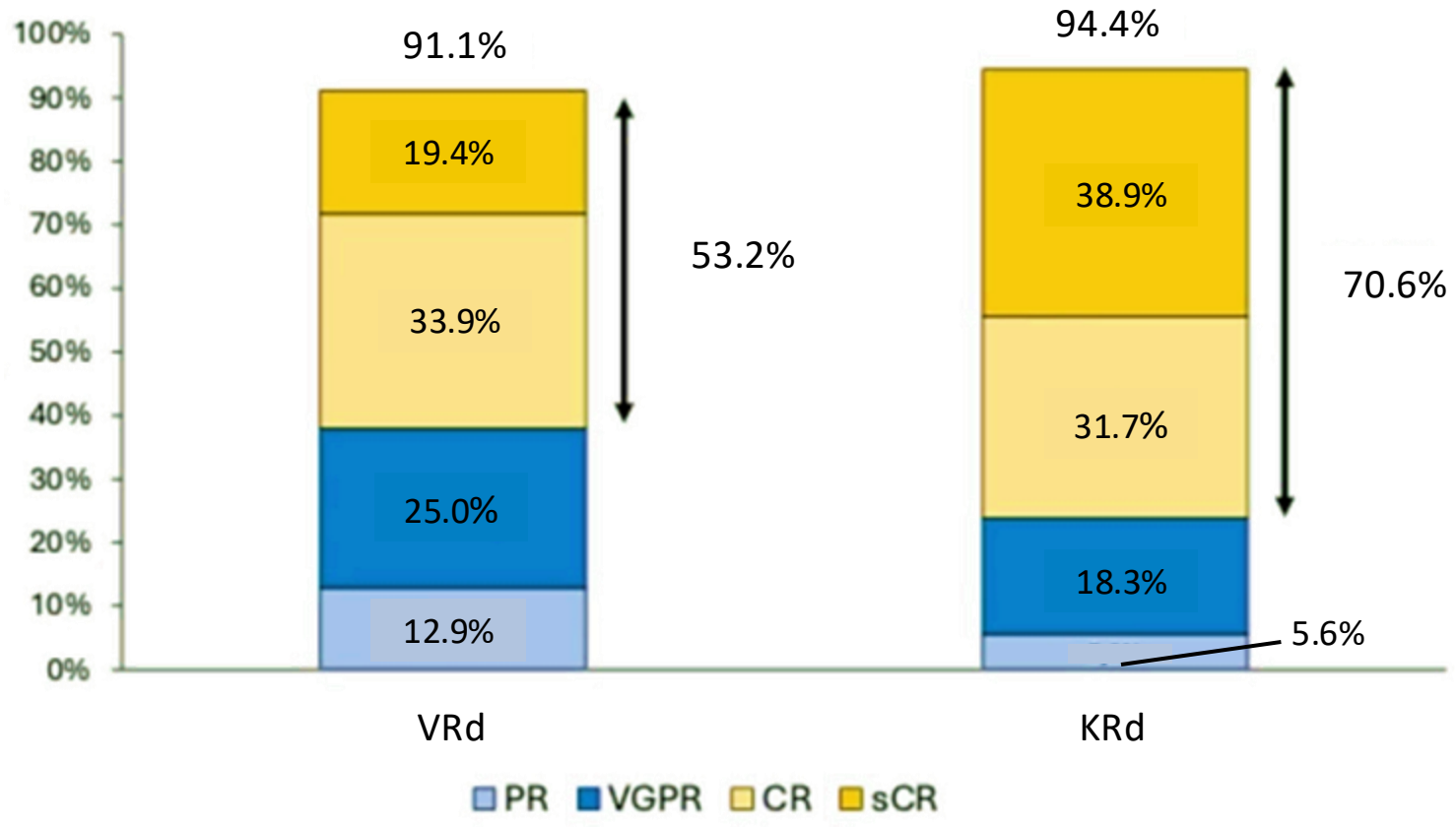
Odds Ratio = 3.01
95% CI: 1.34-6.77; p=0.008

KRd: carfilzomib, lenalidomide, dexamethasone
VRd: bortezomib, lenalidomide, dexamethasone

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

Secondary Endpoint: Overall Response Rate (ORR)



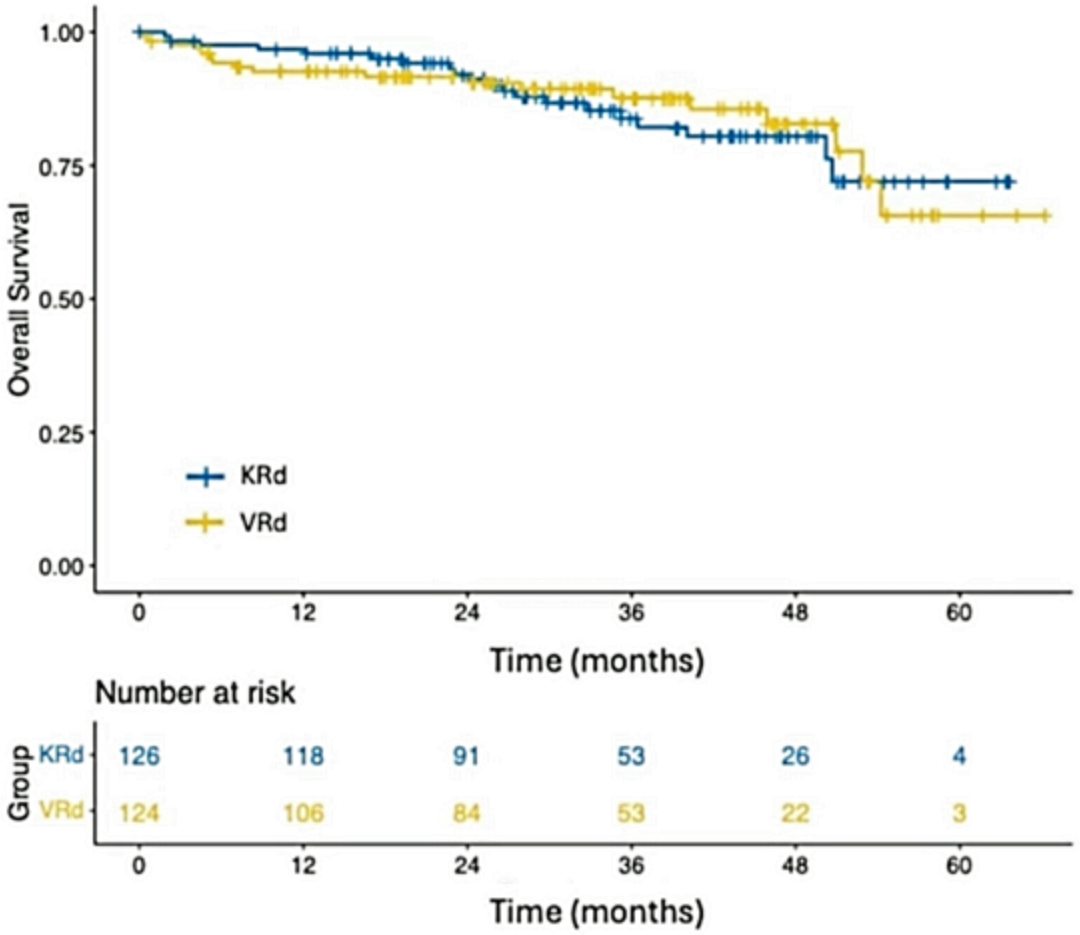
CR%
Odds Ratio = 2.11
95% CI: 1.26-3.56; p=0.005

KRd: carfilzomib, lenalidomide, dexamethasone
VRd: bortezomib, lenalidomide, dexamethasone

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

Secondary Endpoint: Overall Survival (OS)



	KRd (n = 126)	VRd (n = 124)
Progression or death	20 (16%)	18 (15%)
Median PFS, mo	**NR**	**NR**
HR	1.05 (95% CI: 0.56-2.00) p=0.87	

Median follow up: 53 months

KRd: carfilzomib, lenalidomide, dexamethasone
VRd: bortezomib, lenalidomide, dexamethasone

KEY DATA

COBRA: 1L KRd in newly diagnosed multiple myeloma

Safety

	KRd (n = 126)	VRd (n = 124)
Any	96%	94%
Grade ≥3	73%	62%
Any AEs leading to treatment discontinuation	11%	8%
Any AEs Grade 5*	5 (4%)	7 (6%)
Neutropenia any grade	**29%**	**17%**
• Grade ≥3	**21%**	**11%**
Neuropathy any grade	**17%**	**56%**
• Grade ≥3	2%	2%
Cardiac any grade	**18%**	**10%**
• Grade ≥3	**6%**	**2%**
Infection any grade	**75%**	**60%**
• Grade ≥3	25%	23%

*KRd: 1 x COVID, 1 x stroke, 1 x pneumonia, 1 x sepsis, 1 x acute kidney failure
VRd – 3 x COVID, 1 x pneumonia, 1 x respiratory failure, 2 x unknown

SUMMARY

COBRA

- Carfilzomib, lenalidomide, and dexamethasone (KRd) in newly diagnosed MM, met both co-primary endpoints of MRD-negativity CR at 12 months and progression-free survival
- At 12 months, the rate of MRD-negative CR at the 10^{-5} threshold was higher among those treated with KRd than with VRd
  - 31% vs. 18%, respectively; odds ratio [OR] = 2.08; p=0.016
- The PFS benefit of KRd (carfilzomib, lenalidomide, dexamethasone) was observed regardless of cytogenetic risk
- KRd demonstrated anticipated toxicity profiles with higher rates of neutropenia and cardiac events, but less neuropathy

IMPACT

Carfilzomib, lenalidomide, and dexamethasone may be a new potential treatment option for patients with newly diagnosed multiple myeloma

Not yet FDA approved

cornerstone specialty network™

Polling question

Based on the COBRA clinical trial and if FDA approved, how likely are you move KRd into the front-line setting for patients with newly diagnosed MM in your practice?

1. I use QUADS and will only use for those that cannot get an anti-CD38 ab
2. Occasionally – will preferentially use KRd if approved in the frontline
3. Will not change my current practice of VRd
4. Unsure – concerned about toxicities, need more evidence

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

AQUILA

Does daratumumab monotherapy benefit patients with high-risk smoldering multiple myeloma compared to active monitoring?

Outcomes Based on Mayo 2018/IMWG 2020 Risk Stratification, IMWG Scoring, and Age – post hoc analyses

*On **November 6, 2025**, the Food and Drug Administration approved **daratumumab** and hyaluronidase-fihj (Darzalex Faspro, Janssen Biotech, Inc.) for adults with **high-risk smoldering multiple myeloma** (SMM) evaluated in **AQUILA.***

cornerstone specialty network™

KEY DATA

AQUILA: Daratumumab monotherapy for high-risk smoldering multiple myeloma

Study Design: International, open-label, randomized phase III study

- Adults with confirmed smoldering multiple myeloma (sMM) for ≤5 yr
- Clonal bone marrow plasma cells (BMPCs) ≥10% and ≥1 other risk factor for progression to MM (serum M-protein ≥30 g/L, IgA SMM, immunoparesis with reduction of 2 uninvolved Ig isotypes, serum involved:uninvolved free light chain ratio ≥8 and <100, and clonal BMPCs >50% to <60%)

(N = 390)

Daratumumab (DARA)
1800 mg SC QW C1-2 → Q2W C3-6 → Q4W for up to 39 cycles or 36 mo* in 28-d cycles
(n = 194)

Active Monitoring
No disease-specific tx + AE monitoring for up to 36 mo*
(n = 196)

Efficacy follow-up until PD by IMWG SLiM-CRAB criteria
(efficacy tests Q12W by central lab, imaging Q1Y by central review, BM eval at least Q2Y); survival follow-up Q6M

*Or confirmed PD, whichever happens first.
†PFS defined as time from randomization to first documented PD to active MM or death from any cause (whichever happens first).

For this post hoc analysis, outcomes were assessed by IMWG 2020 validated risk stratification, IMWG scoring system, and age (<65 years, 65 to <75 years, ≥75 years)

Primary endpoint: Progression Free Survival (PFS) by IRC using IMWG SLiM-CRAB criteria†

Key secondary endpoints: Time to first-line treatment for MM, Overall survival (OS)

† The International Myeloma Working Group (IMWG) defined SLiM-CRAB criteria as ≥60% clonal plasma cells in bone marrow, involved/ uninvolved free light chain ratio ≥100 or more with involved light chain is ≥ 100mg/L, magnetic resonance image with >1 focal marrow lesion, hypercalcemia renal insufficiency, anemia, bone lesions.

Data cutoff: May 1, 2024

KEY DATA

AQUILA: Daratumumab monotherapy for high-risk smoldering multiple myeloma

IMWG 2020 and IMWG scoring system

The **IMWG 2020 risk stratification is the current, standard validated system** (Mayo 2018 or 20-2-20) – comprises three risk factors:

- BMPC >20%, monoclonal spike >2 g/dL, serum I/U FLC ratio >20

IMWG 2020 risk stratification category	Number of risk factors	2-year progression risk	5-year progression risk
Low risk	0	6%	23%
Intermediate risk	1	18%	47%
High risk	≥2	44%	82%

The **IMWG scoring system incorporating cytogenetics are not yet validated**; this comprises:

- Serum FLC ratio: 0–10, 0 points; 10–25, 2 points; 25–40, 3 points; >40, 5 points
- Monoclonal spike g/dL: 0–1.5, 0 points; 1.5–3, 3 points; >3, 4 points
- Percentage of BMPCs: 0–15, 0 points; 15–20, 2 points; 20–30, 3 points; 30–40, 5 points; >40, 6 points
- FISH abnormalities[a]: No, 0 points; Yes, 2 points

IMWG scoring System category	Score	Corresponding IMWG 2020 risk stratification category based on 2-year progression risk	2-year progression risk	5-year progression risk
Low risk	0 - 4	Low risk	4%	20%
Low-intermediate risk	5 - 8	Low-intermediate risk	26%	55%
Intermediate risk	9 - 12	**High risk**	51%	70%
High risk	>12	**High risk**	73%	85%

[a] Comprising t(4;14), t(14;16) , +1q, and/or del13q/monosomy 13

KEY DATA

AQUILA: Daratumumab monotherapy for high-risk smoldering multiple myeloma

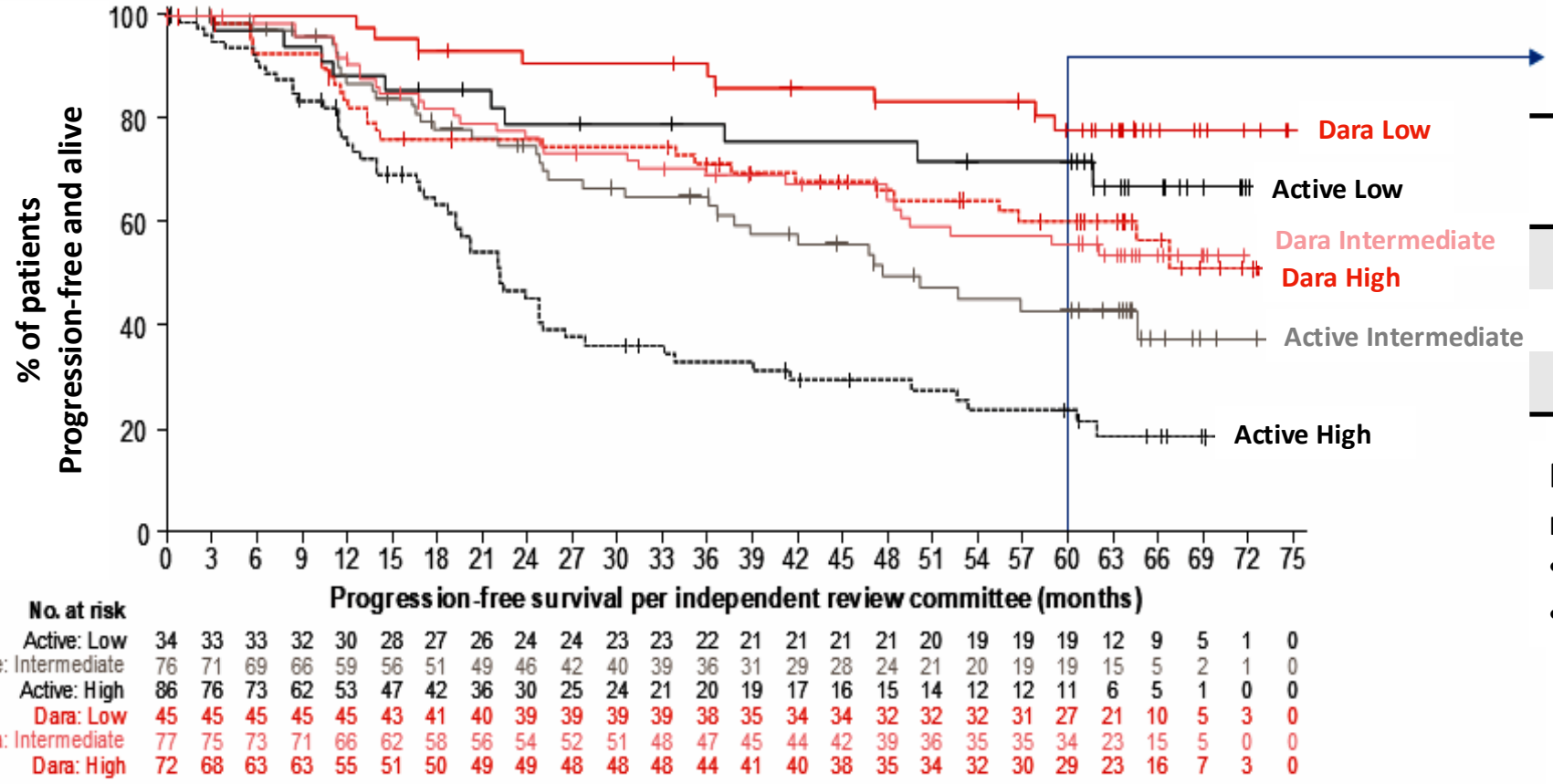
Baseline Characteristics

IMWG 2020 risk category, n (%)	DARA			Active Monitoring		
	Low risk n=45	Intermediate risk n=77	High risk n=72	Low risk n=34	Intermediate risk n=76	High risk n=86
Age, median (range)	61.0 (35-83)	64.0 (34-86)	64.0 (31-79)	65.0 (36-81)	63.0 (38-81)	65.0 (37-83)
Female	20 (44.4)	43 (55.8)	36 (50.0)	19 (55.9)	39 (51.3)	45 (52.3)
Race						
• White	37 (82.2)	64 (83.1)	60 (83.3)	30 (88.2)	65 (85.5)	67 (77.9)
• Black or African American	1 (2.2)	1 (1.3)	2 (2.8)	0	1 (1.3)	6 (7.0)
• Asian	3 (6.7)	8 (10.4)	7 (9.7)	0	5 (6.6)	8 (9.3)
• American Indian or Alaska Native, Native Hawaiian or Pacific Islander	0	0	0	1 (2.9)	2 (2.6)	2 (2.3)
• Multiple/ not reported	4 (8.9)	4 (5.2)	3 (4.2)	3 (8.8)	3 (3.9)	3 (3.5)
ECOG PS, n (%)						
• 0	39 (86.7)	65 (84.4)	61 (84.7)	28 (82.4)	66 (86.8)	66 (76.7)
• 1	6 (13.3)	12 (15.6)	11 (15.3)	6 (17.6)	10 (13.2)	20 (23.3)
ISS stating, N	45	76	70	34	73	85
• I	41 (91.1)	61 (80.3)	52 (74.3)	28 (82.4)	62 (84.9)	65 (76.5)
• II	3 (6.7)	13 (17.1)	17 (24.3)	5 (14.7)	10 (13.7)	18 (21.2)
• III	1 (2.2)	2 (2.6)	1 (1.4)	1 (2.9)	1 (1.4)	2 (2.4)

KEY DATA

AQUILA: Daratumumab monotherapy for high-risk smoldering multiple myeloma

Primary Endpoint: Progression Free Survival (PFS) – IMWG 2020 subgroups



60-month PFS rates, %:

IMWG 2020 Risk group, %	DARA	Active Monitoring
Low	78.2%	71.6%
Intermediate	56.2%	42.9%
High	60.4%	23.6%

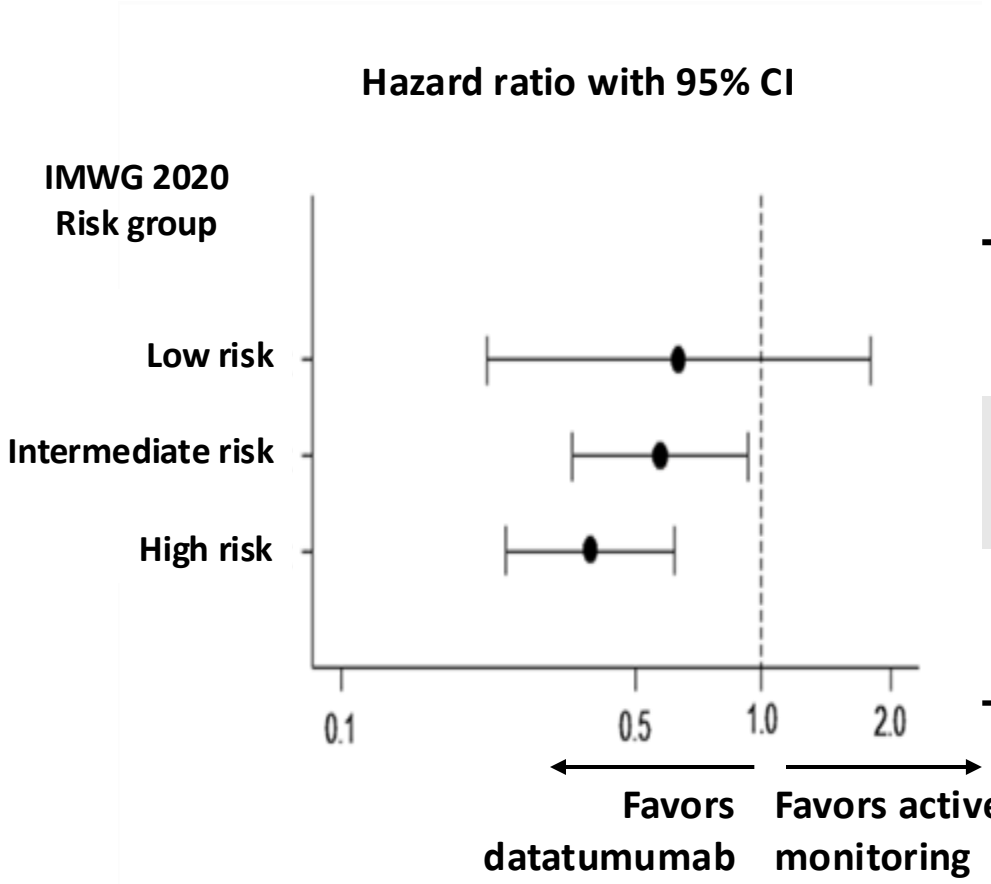
PFS active monitoring vs daratumumab monotherapy, high-risk group:

- 62.8% vs 37.5% events
- **HR 0.36** (95% CI: 0.23, 0.58)

KEY DATA

AQUILA: Daratumumab monotherapy for high-risk smoldering multiple myeloma

Secondary Endpoint: Time to initial Multiple Myeloma Treatment

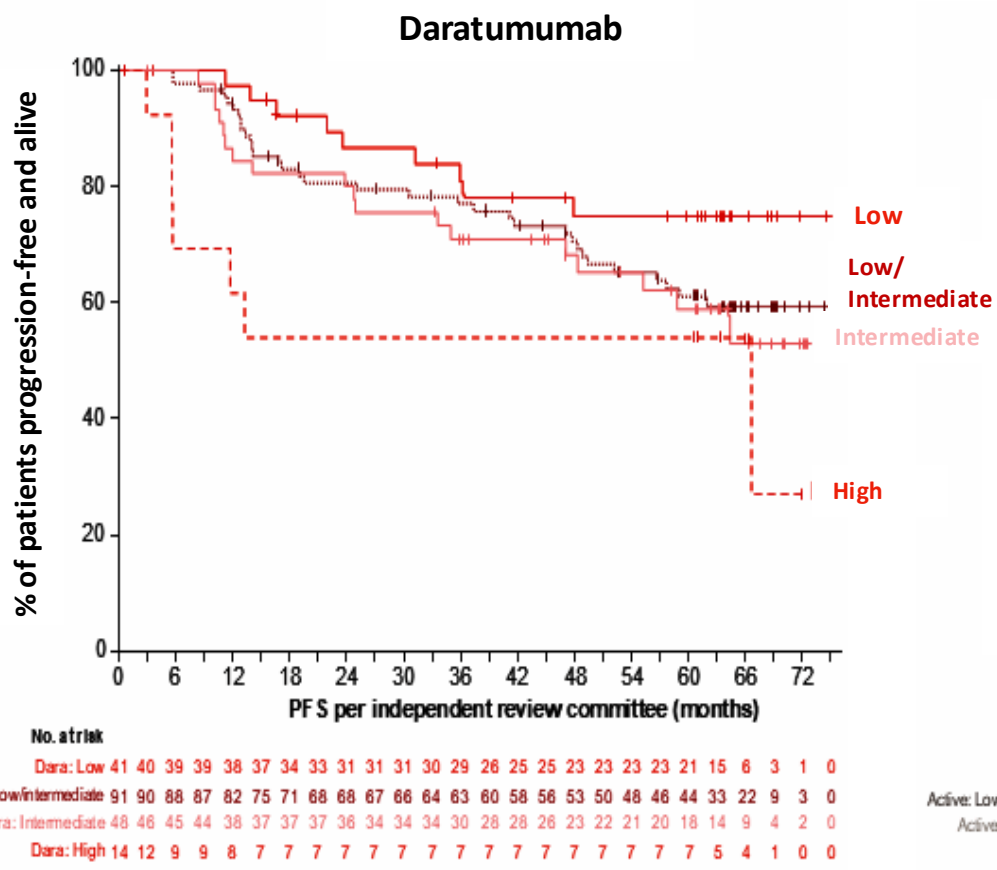


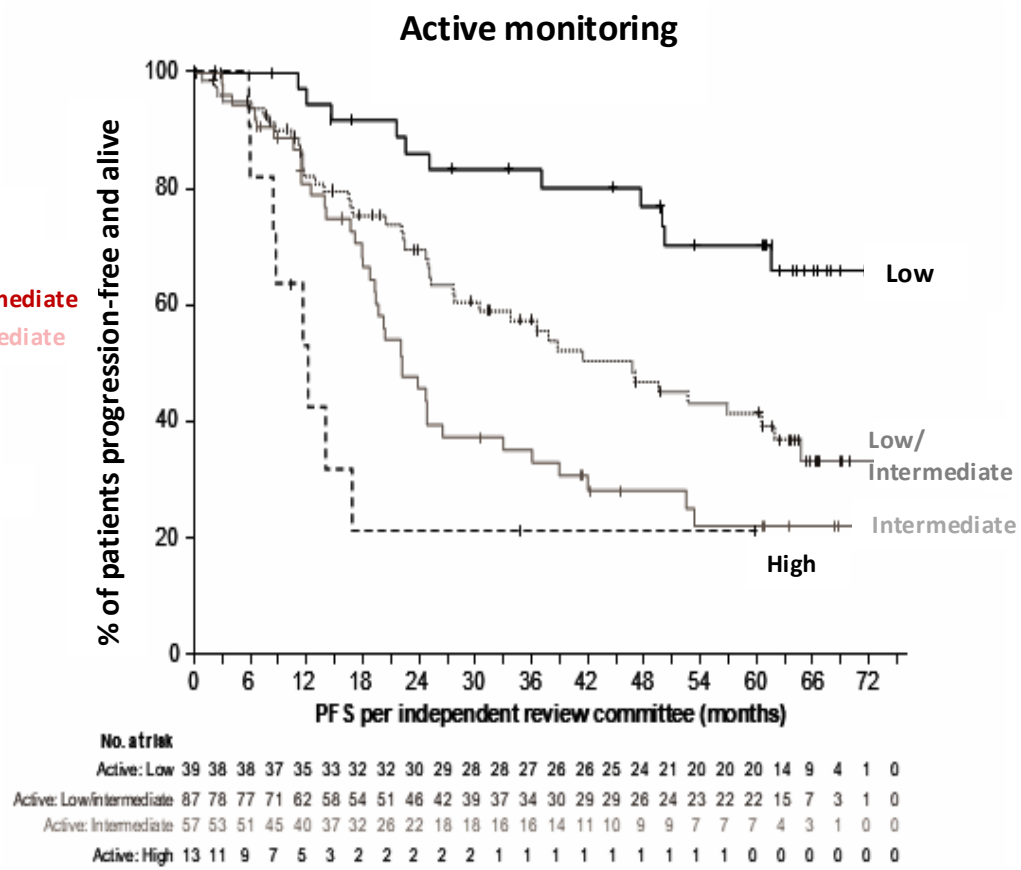
IMWG 2020 Risk group	DARA Event/N	DARA Median (95% CI)	Active Monitoring Event/ N	Active Monitoring Median (95% CI)	HR (95% CI)
Low risk	7/45	NE (NE, NE)	7/34	NE (NE, NE)	**0.63** (0.22, 1.80)
Intermediate risk	29/77	NE (60.6, NE)	40/76	51.8 (37.8, NE)	**0.57** (0.35-0.92)
High risk	28/72	NE (63.1, NE)	55/86	28.0 (21.2, 44.0)	**0.39** (0.25-0.62)

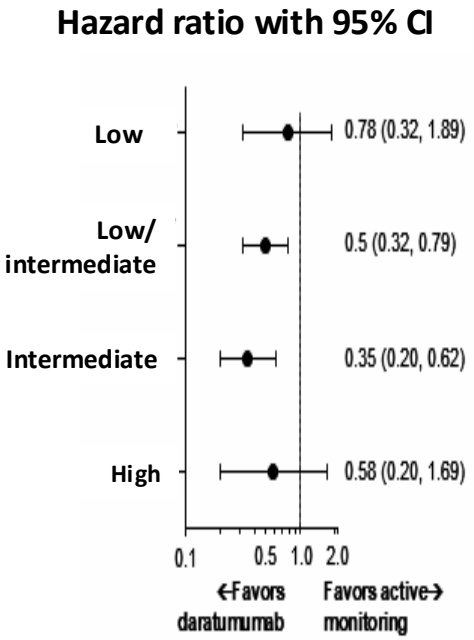
KEY DATA

AQUILA: Daratumumab monotherapy for high-risk smoldering multiple myeloma

Primary Endpoint: Progression Free Survival (PFS) – IMWG Scoring System subgroups



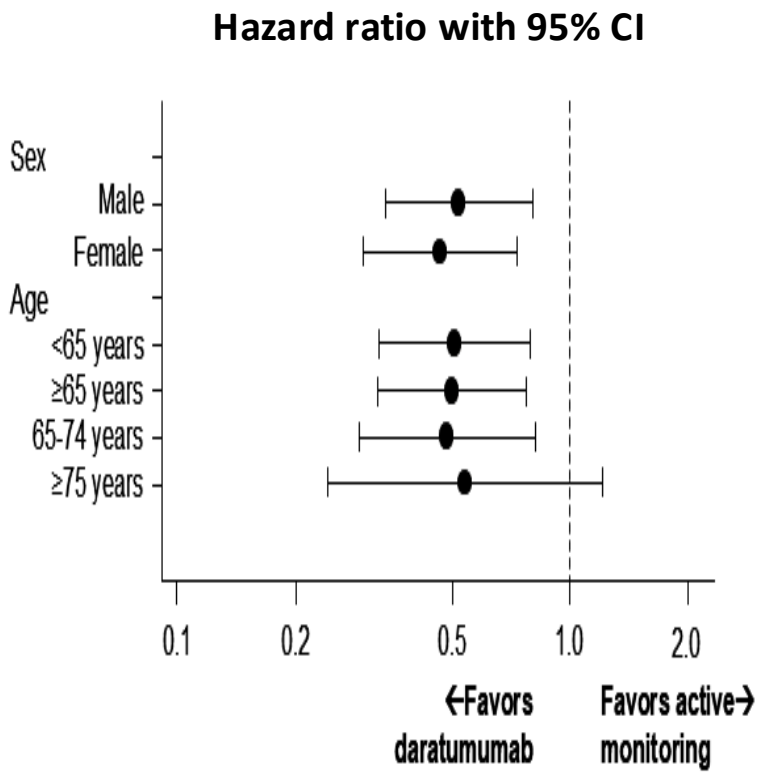




KEY DATA

AQUILA: Daratumumab monotherapy for high-risk smoldering multiple myeloma

Secondary Endpoint: Progression-free survival (PFS) – Gender and Age subgroup



	DARA		Active Monitoring		
	Event/N	Median (95% CI)	Event/N	Median (95% CI)	HR (95% CI)
Sex					
• Male	37/95	NE (57.8, NE)	48/93	41.5 (23.8, 53.3)	**0.52** (0.34, 0.80)
• Female	30/99	NE (66.7, NE)	51/103	38.9 (25, 61.9)	**0.47** (0.30 0.74)
Age					
• <65 years	34/106	NE (66.7, NE)	45/98	NE (25, NE)	**0.51** (0.32, 0.79)
• ≥65 years	33/88	NE (57.8, NE)	54/98	38.8 (22, 52.7)	**0.50** (0.32-0.77)
• 65-74 years	23/67	NE (62, NE)	38/74	50.2 (22, 64.7)	**0.49** (0.29-0.82)
• ≥75 years	10/21	49.5 (14.2, NE)	16/24	22.4 (17.8, 47)	**0.54** (0.24-1.21)

KEY DATA

AQUILA: Daratumumab monotherapy for high-risk smoldering multiple myeloma

Safety Summary

n (%)	DARA <65 years n=104	DARA 65 to <75 years n=67	DARA ≥75 years n=21	Active Monitoring <65 years n=98	Active Monitoring 65 to <75 years n=74	Active Monitoring ≥75 years n=24
Any TEAE	101 (96.2)	66 (98.5)	20 (95.2)	81 (82.7)	60 (81.1)	21 (87.5)
• Infections and infestations SOC, any grade	86 (81.9)	57 (85.1)	11 (52.4)	49 (50.0)	29 (39.2)	10 (41.7)
• Infections and infestations SOC, grade ≥3	10 (9.5)	18 (26.9)	3 (14.3)	3 (3.1)	3 (4.1)	3 (12.5)
Any serious TEAE						
• Serious TEAEs occurring in ≥5% of patients of any group:	26 (24.8)	24 (35.8)	6 (28.6)	12 (12.2)	14 (18.9)	12 (50.0)
Pneumonia	1 (1.0)	6 (9.0)	0	0	1 (1.4)	0
TEAE leading to discontinuation	2 (1.9)	6 (9.0)	3 (14.3)	-	-	-
TEAE leading to dose modification	35 (33.3)	44 (65.7)	11 (52.4)	-	-	-

SUMMARY

AQUILA

IMPACT

- For patients with high-risk smoldering MM, up to 36 mo of daratumumab monotherapy significantly prolonged PFS across IMWG 2020 intermediate and high-risk subgroups compared with active monitoring
  - Prolonged progression to active multiple myeloma or death by 61% for high-risk smoldering multiple myeloma
  - PFS by high-risk group: 62.8% vs 37.5% events (**HR 0.36**; 95% CI: 0.23, 0.58)
  - Provided PFS benefit regardless of age
- Favorable safety profile with maintained patient report health-related QoL

Daratumumab monotherapy may be a new standard of care for patients with high-risk smoldering multiple myeloma, challenging watch and wait practice

FDA approved November 6, 2025

cornerstone specialty network™

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

JCOG1911/B-DASH

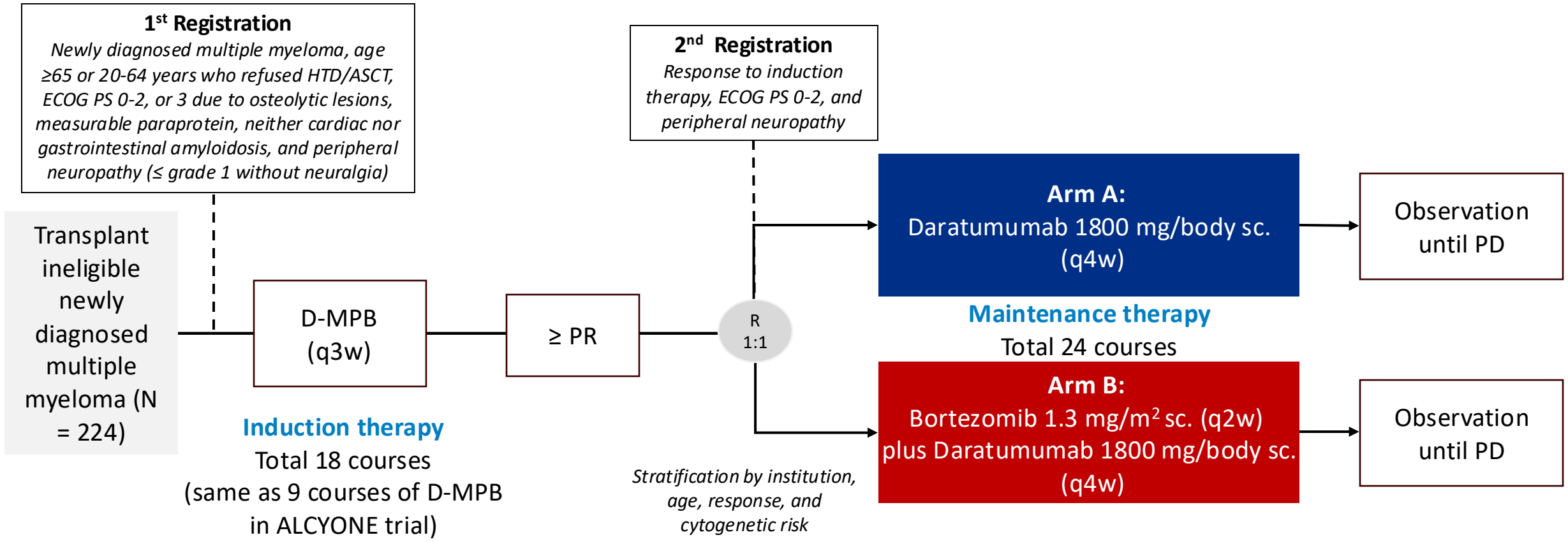
Does adding bortezomib to maintenance daratumumab improve outcomes for transplant-ineligible newly diagnosed multiple myeloma?

Interim analysis

KEY DATA

JCOG1911/B-DASH: Bortezomib plus Daratumumab maintenance therapy for transplant-ineligible newly diagnosed multiple myeloma

Study Design: Multicenter, randomized phase III study



Primary endpoint: Progression-free survival (PFS) from 2nd registration

Key secondary endpoints: Overall survival form 1st/2ndregistration, progression free survival from 1st registration, adverse events, completion of maintenance therapy, time to next treatment from 1st/2ndregistration, response rate of induction therapy, completion of induction therapy

D-MPB: Daratumumab, melphalan, prednisolone, bortezomib

KEY DATA

JCOG1911/B-DASH: Bortezomib plus Daratumumab maintenance therapy for transplant-ineligible newly diagnosed multiple myeloma

Baseline Characteristics

1st Registration	Arm A (n = 73)	Arm B (n = 70)
Median age, yr (range)	74 (65-85)	73 (64-86)
• ≥75 years	37.0%	34.3%
Male	56.2%	42.9%
M protein type		
• IgG	68.5%	67.1%
• IgA	19.2%	22.6%
• BJP	12.3%	10.0%
ISS		
• I	27.4%	15.7%
• II	56.2%	58.6%
• III	16.4%	25.7%
Cytogenetic high risk	19.2%	22.9%

2nd Registration	Arm A (n = 73)	Arm B (n = 70)
Response to D-MPB		
• PR	21.9%	21.4%
• VGPR	27.4%	22.9%
• CR or better	50.7%	55.7%
MRD negative during induction therapy	34.2%	34.3%
IMWG frailty		
• Fit	64.4%	52.9%
• Intermediate	24.7%	24.3%
• Frail	11.0%	22.9%

Adjustment factors

MRD was assessed by multiparameter FCM of bone marrow samples, using a sensitivity threshold of 10^{-5}

KEY DATA

JCOG1911/B-DASH: Bortezomib plus Daratumumab maintenance therapy for transplant-ineligible newly diagnosed multiple myeloma

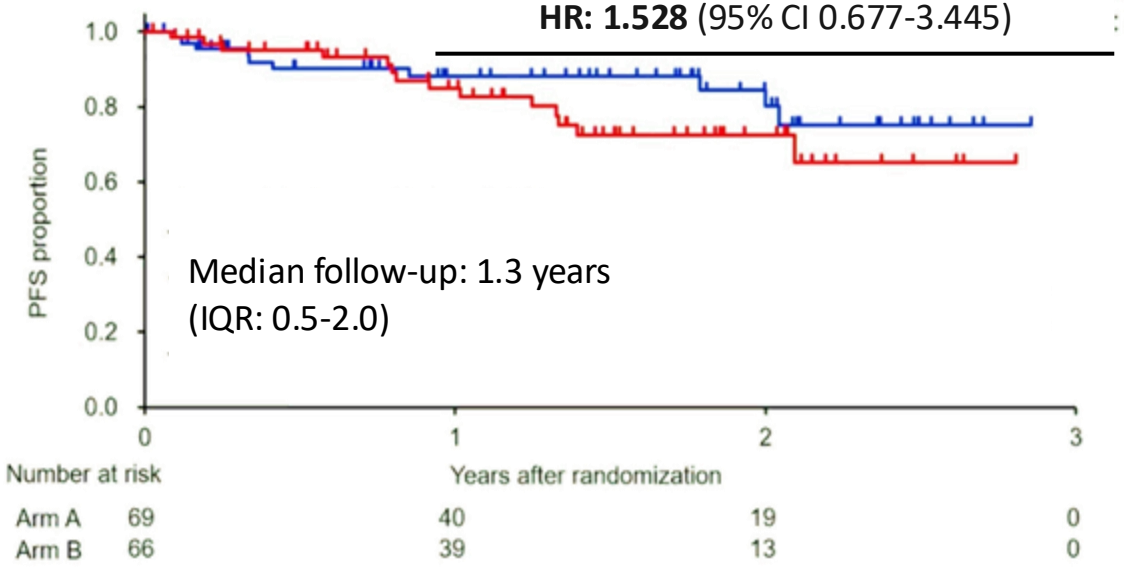
Primary Endpoint: Progression Free Survival (PFS)

Interim analysis

Data cutoff: Nov 2024

	Arm A (n = 69)	Arm B (n = 69)
2-year PFS (95% CI)	**80.2%** (63.2-89.9)	**72.5%** (56.9-83.2)

HR: 1.528 (95% CI 0.677-3.445)

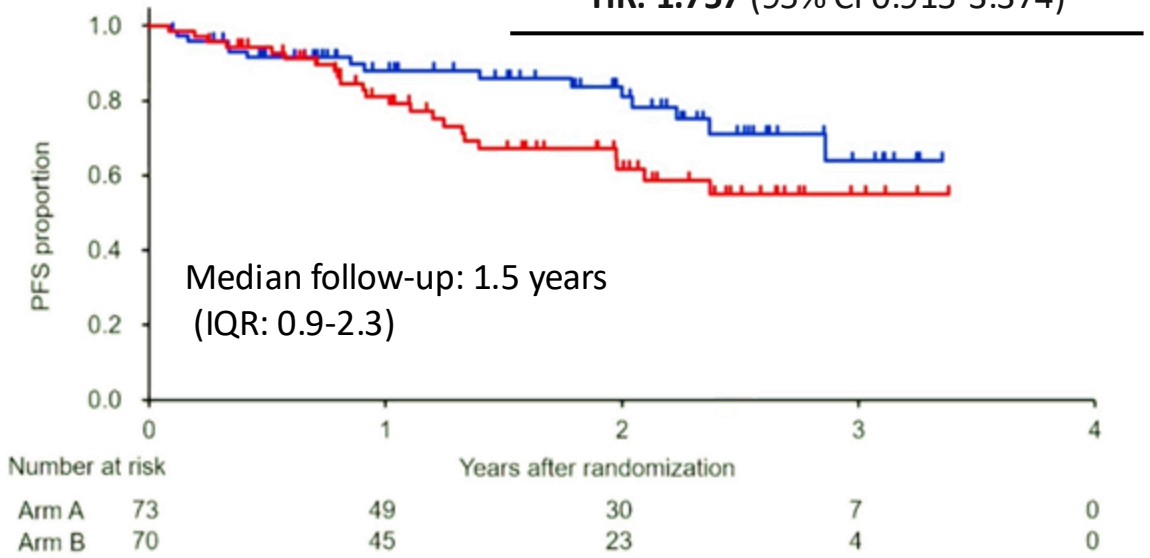


Updated analysis

Data cutoff: Jun 2025

	Arm A (n = 73)	Arm B (n = 70)
2-year PFS (95% CI)	**81.0%** (67.6-89.3)	**61.7%** (46.9-73.6)

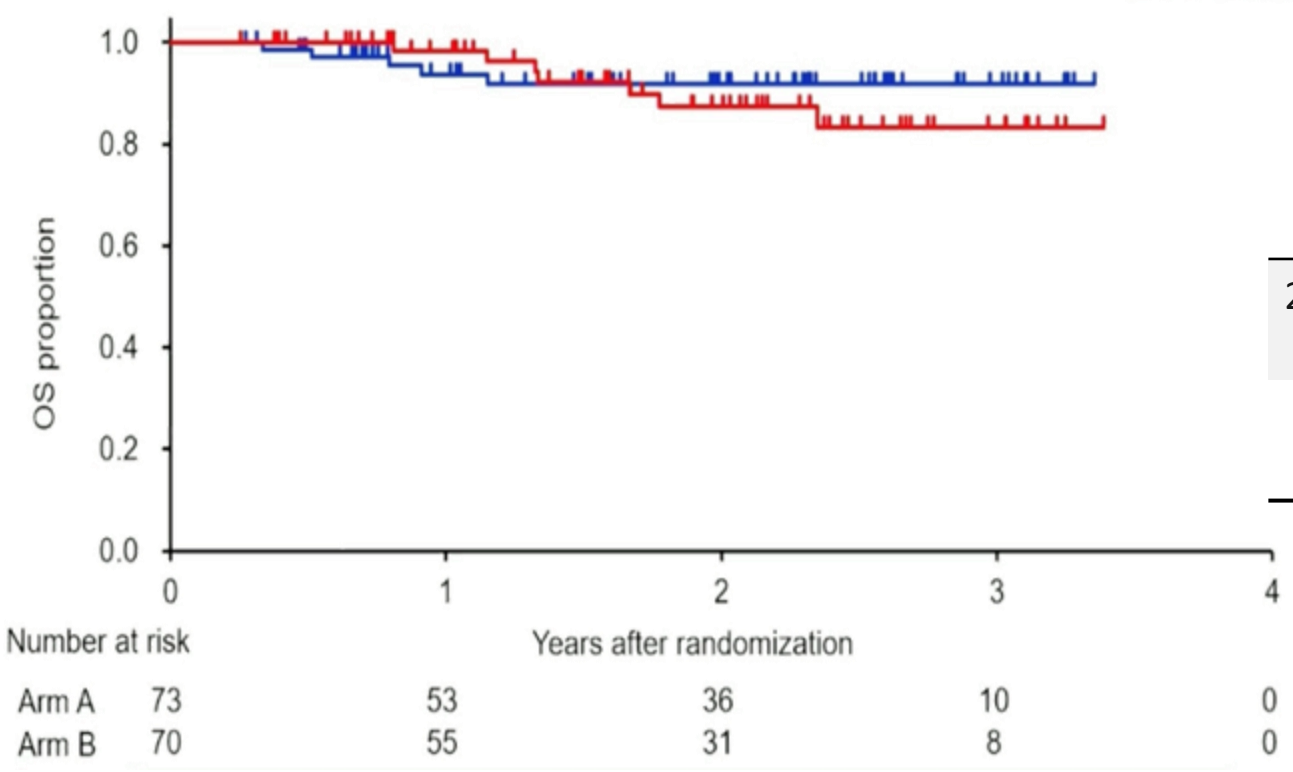
HR: 1.757 (95% CI 0.915-3.374)



KEY DATA

JCOG1911/B-DASH: Bortezomib plus Daratumumab maintenance therapy for transplant-ineligible newly diagnosed multiple myeloma

Secondary Endpoint: Overall survival (updated analysis)



	Arm A (n = 73)	Arm B (n = 70)
2-year OS (95% CI)	**91.8%** (81.3-96.5)	**87.3%** (73.6-94.2)

HR: **1.419** (95% CI 0.450-4.472)

Data cutoff: Jun 2025

KEY DATA

JCOG1911/B-DASH: Bortezomib plus Daratumumab maintenance therapy for transplant-ineligible newly diagnosed multiple myeloma

Safety Summary

n (%)	Arm A (n = 73)	Arm B (n = 70)
Maintenance therapy status[a]		
• Median number of courses (IQR)	19 (6-24)	12 (7-21)
Treatment discontinuation		
• Due to AEs	4 (5.5)	3 (4.3)
• Due to patient refusal	0	9 (12.9)[b]
Any treatment emergent AEs[c]		
• Grade ≥2	29 (41.4)	40 (60.0)
• Grade ≥3	6 (8.6)	8 (12.3)

Common Adverse Events

	Arm A (n = 70)		Arm B (n = 65)	
	Grade ≥2	Grade ≥3	Grade ≥2	Grade ≥3
Hematological				
• Neutropenia	11.4%	0%	15.4%	3.1%
• Lymphocytopenia	27.1%	15.7%	38.5%	12.3%
• Thrombocytopenia	2.9%	1.4%	3.1%	3.1%
Non-hematological				
• Lung or upper respiratory infection	10.0%	2.9%	10.8%	3.1%
• Peripheral neuropathy (sensory or motor)	8.6%	0%	18.5%	0%
• Nausea or appetite loss	1.4%	0%	9.2%	3.1%
• Diarrhea	0%	0%	6.2%	0%

[a]Data cutoff: March 2025
[b]All were considered to be associated with treatment emergent AEs.
[c]Information of safety population (n=70 and 65 in Arm A and Arm B, respectively).

SUMMARY

JCOG1911/B-DASH

- Adding bortezomib to daratumumab maintenance therapy did not improve progression-free survival (PFS) in patients with transplant-ineligible, newly diagnosed multiple myeloma compared to daratumumab maintenance alone
- OS was similar between both arms, with a 2-year OS rate of 91.8% *vs* 87.3% in arm A and B, respectively (HR[95%CI]: 1.42 [0.45–4.47])
- The combination arm (Arm B) had higher rates of adverse events (AEs) and more frequent treatment discontinuations compared to daratumumab maintenance alone

IMPACT

Adding bortezomib to daratumumab maintenance therapy for patients with transplant-ineligible, newly diagnosed multiple myeloma d not provide additional bene

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
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- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

CLINICAL QUESTION

CEPHEUS

Does adding subcutaneous daratumumab to bortezomib, lenalidomide, and dexamethasone (VRd) improve outcomes in patients with newly diagnosed multiple myeloma who are either transplant-ineligible or have had their transplant deferred?

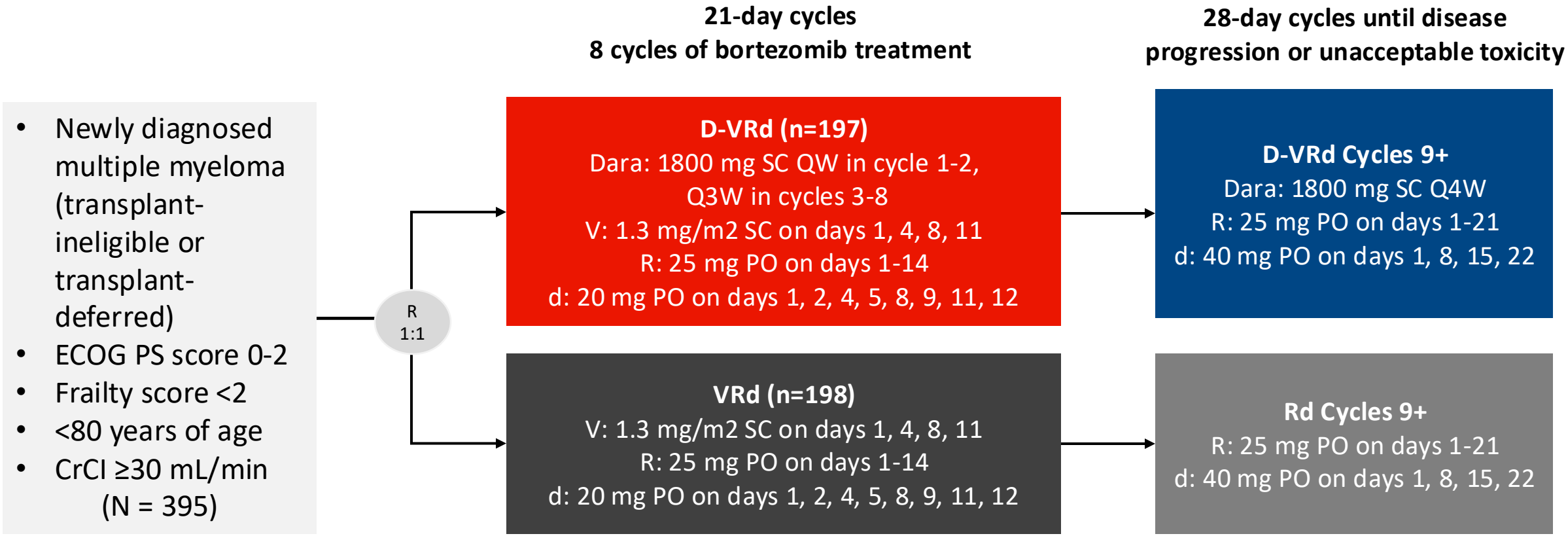
*On **January 27, 2026**, the Food and Drug Administration approved **daratumumab** and hyaluronidase-fihj (Darzalex Faspro, Janssen Biotech, Inc.) in combination with bortezomib, lenalidomide, and dexamethasone (VRd) for adults with **newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant** (ASCT) evaluated in **CEPHEUS** trial.*

cornerstone specialty network™

KEY DATA

CEPHEUS: 1L triplet VRd and quadruplet D-VRd in patients with newly diagnosed MM

Study Design: Open-label, multicenter, randomized, phase 3 trial



Primary endpoint: Overall MRD-negativity ≥CR

Secondary endpoints: Progression-free survival, sustained (≥12 months) MRD-negativity ≥CR, ≥CR rate, overall survival

Nat Med 31, 1195–1202 (2025).
https://doi.org/10.1038/s41591-024-03485-7

KEY DATA

CEPHEUS: 1L triplet VRd and quadruplet D-VRd in patients with NDMM

Baseline Characteristics

n (%)	D-VRd (n = 197)	VRd (n = 198)
Median age (range), years	70 (42-79)	70 (31-80)
Male	87 (44.2)	111 (56.1)
Race		
• White	163 (82.2)	156 (78.8)
• Black	10 (5.1)	9 (4.5)
• Asian	11 (5.6)	14 (7.1)
• Native Hawaiian or other pacific islander	0	1(0.5)
• Other	1 (0.5)	2 (1)
• Not reported	12 (6.6)	16 (8.1)
ECOG		
• 0	71 (36.0)	84 (42.4)
• 1	103 (52.3)	100 (50.5)
• 2	23 (11.7)	14 (7.1)
Frailty score		
• 0 (fit)	124 (62.9)	132 (66.7)
• 1 (intermediate fitness)	73 (37.1)	66 (33.3)

n (%)	D-VRd (n = 197)	VRd (n = 198)
Type of measurable disease		
• Detected in serum only	120 (60.9)	108 (54.5)
• IgG	89 (45.2)	76 (38.4)
• IgA	27 (12.7)	31 (15.7)
• Other	4 (2)	1 (0.5)
• Detected in serum and urine	41 (20.8)	45 (22.7)
• Detected in urine only	20 (10.2)	24 (12.1)
• Detected in serum FLCs only	16 (8.1)	21 (10.6)
ISS disease stage		
• I	68 (34.5)	68 (34.3)
• II	73 (37.1)	75 (37.9)
• III	56 (28.4)	55 (27.8)
Cytogenetic risk profile		
• Standard risk	149 (75.6)	149 (75.3)
• High risk	25 (12.7)	27 (13.6)
• Indeterminate	23 (11.7)	22 (11.1)
Median time since diagnosis of MM (range), months	1.2 (0,4-5.8)	1.3 (0.3-8)

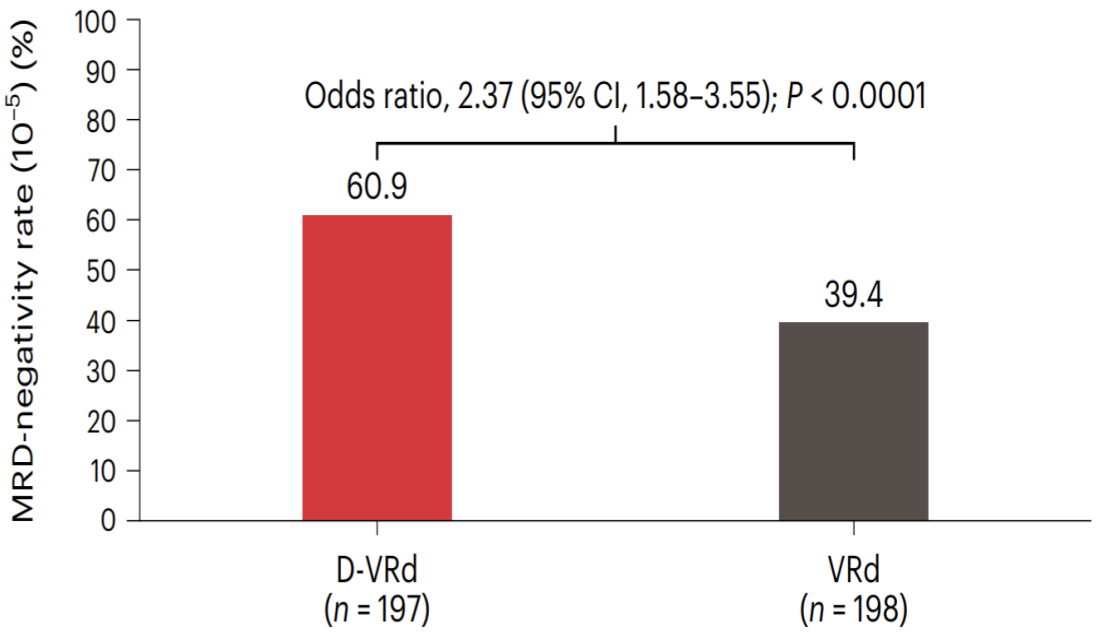
Nat Med 31, 1195–1202 (2025).
https://doi.org/10.1038/s41591-024-03485-7

KEY DATA

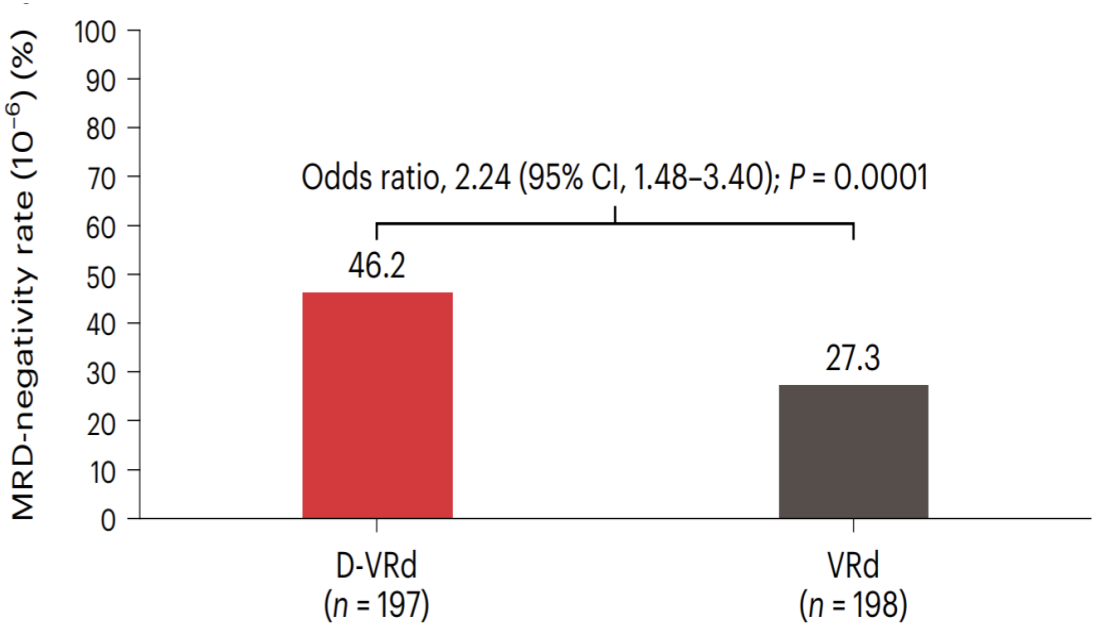
CEPHEUS: 1L triplet VRd and quadruplet D-VRd in patients with NDMM

Primary Endpoint: Overall minimal residual disease (MRD) negativity

Overall MRD-negativity rate (10^{-5})



Overall MRD-negativity rate (10^{-6})



Nat Med 31, 1195–1202 (2025).
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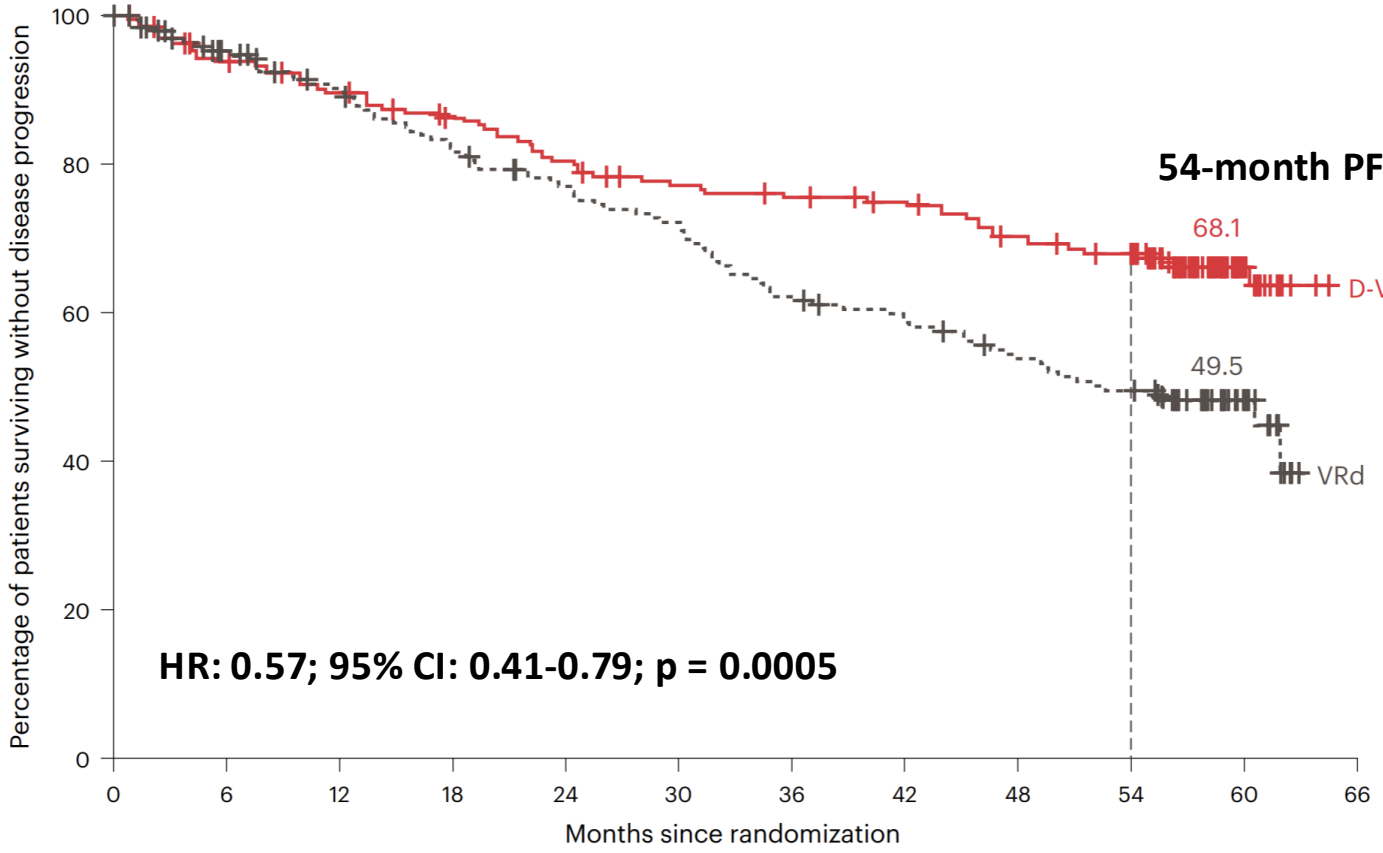
KEY DATA

CEPHEUS: 1L triplet VRd and quadruplet D-VRd in patients with NDMM

Key Secondary Endpoint: Progression Free Survival (PFS) – ITT population



Median: not reached

Median: 52.6 months

No. at risk												
D-VRd	197	180	170	160	149	140	136	132	122	115	33	0
VRd	198	174	157	143	131	123	105	98	88	81	21	0

Median follow-up: 58.7 months

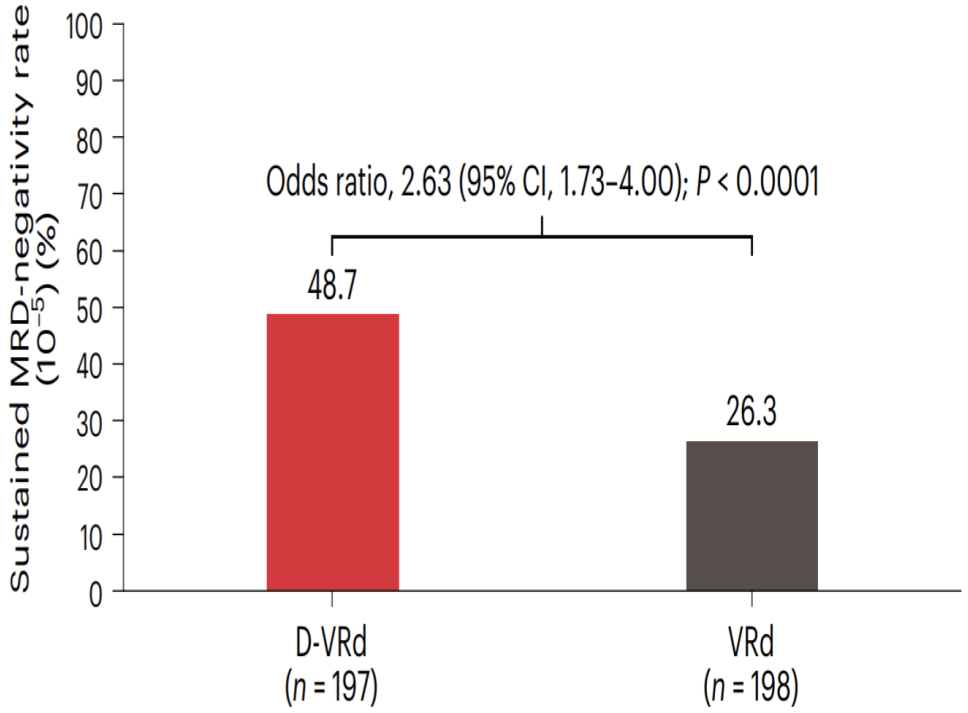
Nat Med 31, 1195–1202 (2025).
https://doi.org/10.1038/s41591-024-03485-7

KEY DATA

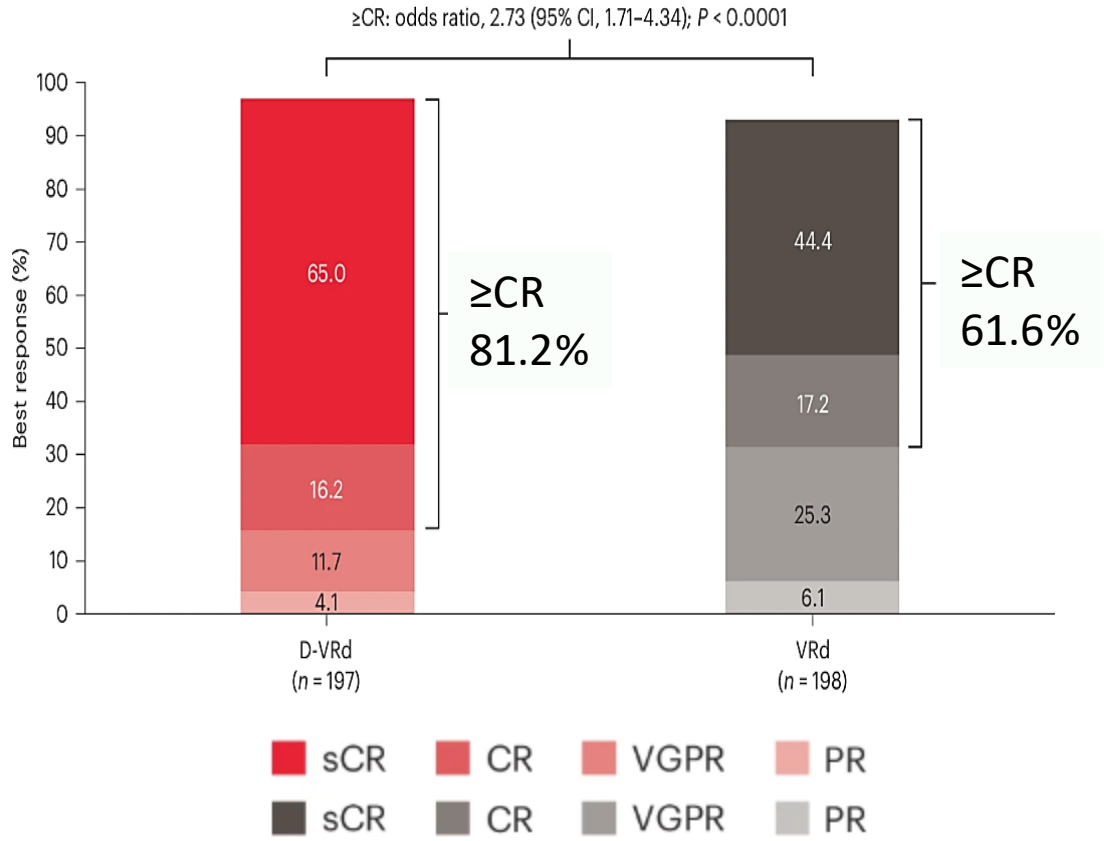
CEPHEUS: 1L triplet VRd and quadruplet D-VRd in patients with NDMM

Key secondary Endpoints:

Sustained MRD-negativity rate (10^{-5})



≥CR rate



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KEY DATA

CEPHEUS: 1L triplet VRd and quadruplet D-VRd in patients with NDMM

Safety Summary

Any grade, n (%)	D-VRd (n = 197)	VRd (n = 198)
Hematological adverse events		
• Neutropenia	110 (55.8)	76 (39.0)
• Thrombocytopenia	92 (46.7)	66 (33.8)
• Anemia	73 (37.1)	62 (31.8)
• Lymphopenia	36 (18.3)	34 (17.4)
Nonhematological adverse events		
• Diarrhea	112 (56.9)	115 (59.0)
• Peripheral sensory neuropathy	110 (55.8)	119 (61.0)
• Peripheral edema	83 (42.1)	76 (39.0)
• Constipation	75 (38.1)	82 (42.1)
• Insomnia	63 (32.0)	63 (32.3)
• Fatigue	63 (32.0)	60 (30.8)
• Hypokalemia	58 (29.4)	25 (12.8)
• Cataract	55 (27.9)	51 (26.2)
• Back pain	55 (27.9)	43 (22.1)
• Cough	53 926.9)	38 (19.5)

Any grade, n (%)	D-VRd (n = 197)	VRd (n = 198)
Nonhematological adverse events		
• Asthenia	51 (25.9)	40 (20.5)
• Rash	50 (25.4)	48 (24.6)
• Nausea	49 (24.9)	48 (24.6)
• Pyrexia	46 (23.4)	30 (15.4)
• Arthralgia	45 (22.8)	39 (20.0)
• Decreased appetite	42 (21.3)	39 (20.0)
• Dizziness	41 (20.8)	41 (21.0)
• Infection	181 (91.9)	167 (85.6)
• Upper respiratory tract infection	78 (39.6)	64 (32.8)
• COVID-19	75 (38.1)	48 (24.6)
• Pneumonia	84 (24.4)	39 (20.0)
• Urinary tract infection	41 (20.8)	29 (14.9)
Second primary malignancy	15 (5.6)	18 (9.2)
Any infection-related reaction	7 (3.6)	N/A

N/A: Not applicable

Nat Med 31, 1195–1202 (2025).
https://doi.org/10.1038/s41591-024-03485-7

SUMMARY

CEPHEUS

- Adding subcutaneous daratumumab (D-VRd) to bortezomib, lenalidomide, and dexamethasone (VRd) increased the rate of undetectable measurable residual disease (MRD-negativity)
  - 60.9% versus 39.3% in the control group
  - Sustained MRD negativity was higher in the D-VRd group (48.7%) compared to the VRd group (26.3%)
- D-VRd also showed superior complete response (81.2% vs. 61.4%) and significantly improved progression-free survival (54-month PFS rate was 69.0% vs 48.0%)
- D-VRd showed a manageable safety profile consistent with known effects, though it included higher rates of neutropenia and thrombocytopenia compared to the triplet regimen

IMPACT

Daratumumab added to bortezomib, lenalidomide, and dexamethasone is an effective standard of care for transplant-ineligible/deferred patients new diagnosed with multiple myelo

FDA approved January 27, 2026

Polling question

Based on the CEPHEUS clinical trial and recent FDA approval, how likely are you to adopt quadruplet therapy as a frontline treatment for eligible patients?

1. I already have incorporated Quad therapy into this patient sub-set
2. Very likely to adopt as frontline standard of care
3. Somewhat likely, but will consider patient-specific factors
4. Will not change my current practice
5. Unsure — will wait for additional long-term data

ASH 2025:

Myeloma

Key Takeaways

Q&A

@EricSchaeferMD

MajesTEC-3: Teclistamab plus daratumumab after 1-3 prior lines of therapy demonstrated strong progression free survival (HR:0.17) and overall survival (HR:0.46) for relapse-refractory multiple myeloma compared to investigators choice treatment – *Not yet FDA approved*

COBRA: In newly diagnosed multiple myeloma first-line setting, carfilzomib, lenalidomide and dexamethasone at 12 months demonstrated a higher MRD-negative CR rate at the 10^{-5} threshold among those treated with KRd than with VRd (31% vs. 18%, respectively), and PFS benefit of KRd was observed regardless of cytogenetic risk – *Not yet FDA approved*

AQUILA: Daratumumab monotherapy in patients with high-risk smoldering multiple myeloma reduced the risk of progression to active multiple myeloma or death by 51% compared to active monitoring for high-risk smoldering multiple myeloma (HR-SMM) – *FDA approved November 2025*

JCOG1911/B-DASH: In patients with transplant-ineligible newly diagnosed multiple myeloma, adding bortezomib to daratumumab maintenance therapy did not improve progression-free survival compared to daratumumab alone, primarily due to higher rates of adverse events with the combination – *Not yet FDA approved*

CEPHEUS: Daratumumab with bortezomib, lenalidomide, and dexamethasone (D-VRd) in the first-line setting provided higher complete response rates compared to VRd alone (81.2% vs. 61.6%) and improved progression-free survival (69.0% vs 48.0% at 54 months) for patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT) – *FDA approved January 2026*

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

CLINICAL QUESTION

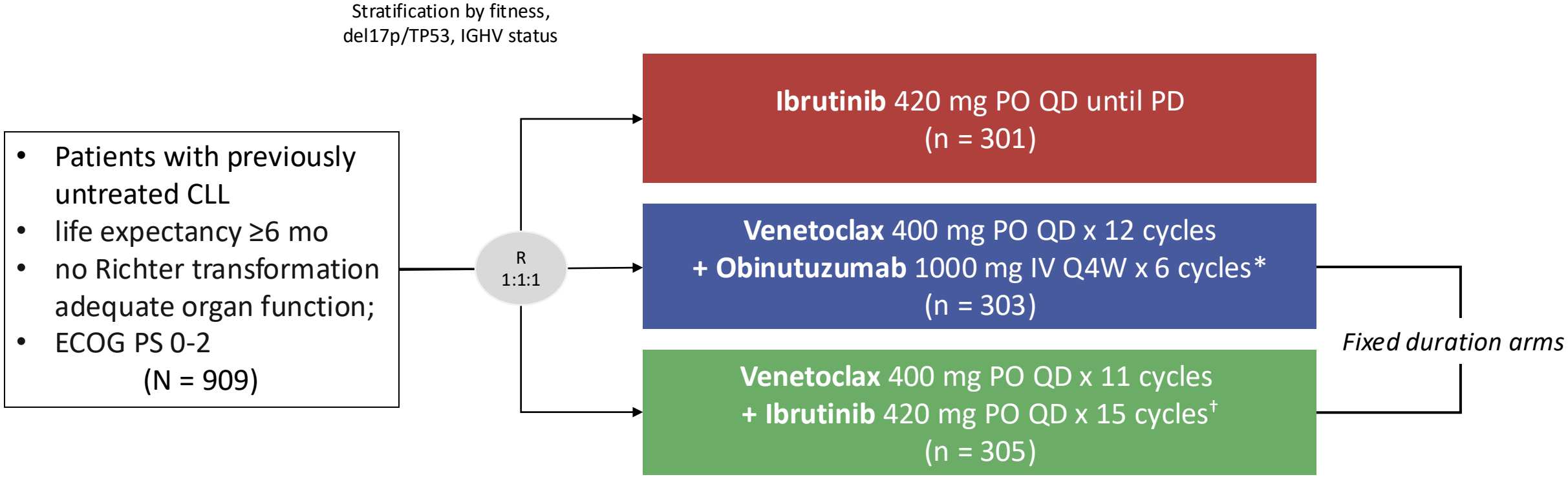
CLL17

Does fixed-duration, time-limited targeted therapy venetoclax-based combinations, compared to ibrutinib, benefit previously untreated chronic lymphocytic leukemia?

KEY DATA

CLL17: 1L venetoclax combinations for previously untreated CLL

Study Design: Randomized, multicenter phase II trial



*Venetoclax: 400 mg C1D22-C12. Obinutuzumab: 1000 mg C1D1 or 100 mg C1D1 and 900 mg C1D2; 1000 mg C1D8 and C1D15; 1000 mg on D1 of C2-6.
†Venetoclax 20 mg C4D1-7; 50 mg C4D8-14; 100 mg C4D15-21; 200 mg C4D22-28; 400 mg QD C5-15.

Primary endpoint: Progression Free Survival (PFS) non-inferiority of fixed duration venetoclax-obinutzumab vs continuous ibrutinib and fixed duration venetoclax-ibrutinib vs continuous ibrutinib

Secondary endpoints: Minimal residual disease (MRD), response, overall survival, and safety

Median follow-up was 34.2 months

ASH 2025. Abstr 1
N Engl J Med . 2025 Dec 6. doi: 10.1056/NEJMoa2515458.

KEY DATA

CLL17: 1L venetoclax combinations for previously untreated CLL

Baseline Characteristics

	Characteristic, n (%)	Ven + Obin (n = 303)	Ven + Ibr (n = 305)	Ibrutinib (n = 301)
Demographics	Male	216 (71.3)	204 (66.9)	196 (65.1)
	Median age, yr (range)	66 (40-90)	66 (37-83)	65 (34-85)
	Age >65 yr	155 (51.2)	158 (51.8)	146 (48.5)
	Median CIRS, n (range)	3 (0-17)	3 (0-18)	3 (1-15)
	GFR <70	101 (33.6)	109 (35.7)	95 (31.7)
	Unfit*	134 (44.5)	136 (44.6)	130 (43.2)
Risk factors	High TLS risk (by ALC and LN)	76 (25.7)	70 (23.0)	67 (22.6)
	Unmutated IGHV status	171 (56.4)	172 (56.4)	171 (56.8)
	*TP53*mut/del(17p)	23 (7.6)	25 (8.2)	21 (7.0)
	High/very high CLL-IPI	176 (61.5)	172 (59.3)	172 (59.9)
	Binet B/C	232 (76.6)	213 (69.8)	225 (75.0)
	Complex karyotype ≥3	42 (15.8)	53 (20.0)	58 (21.9)

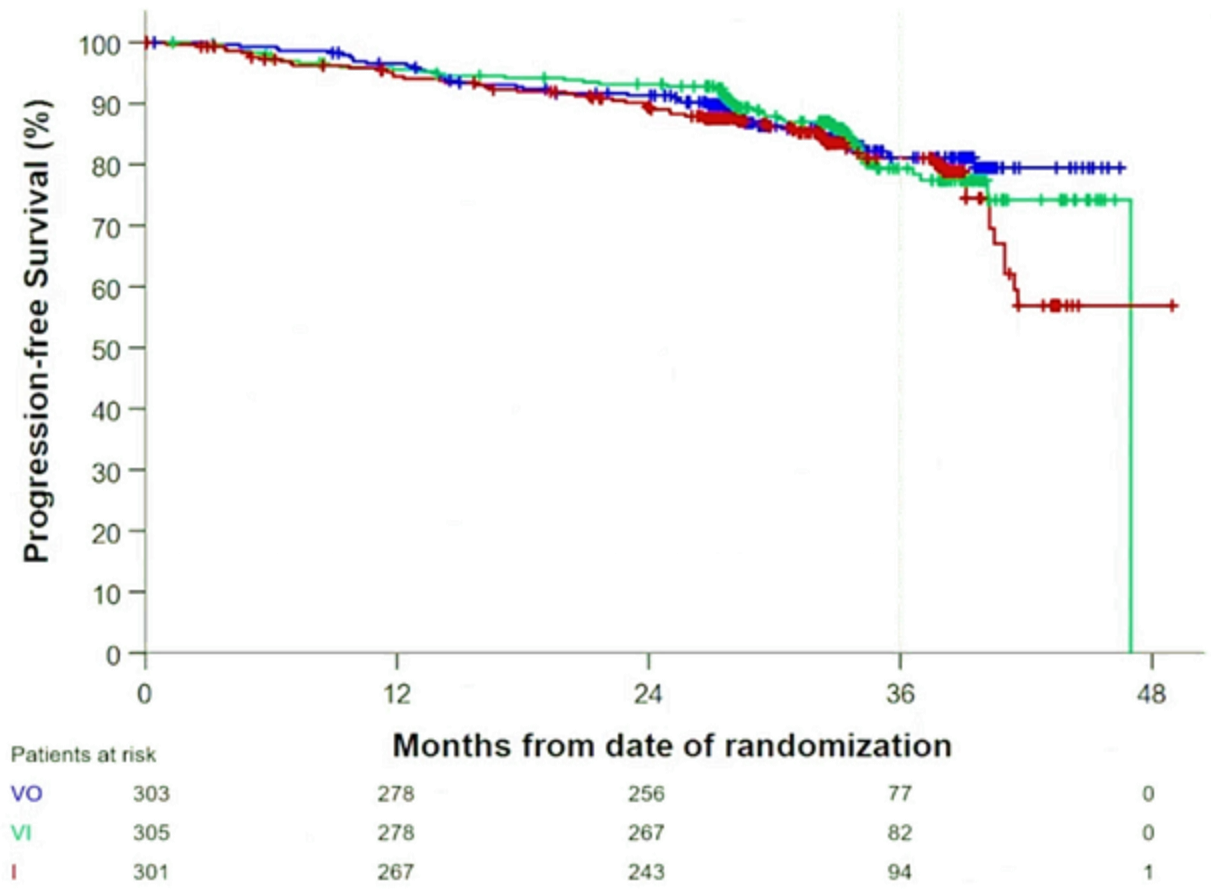
*Unfit: Defined by cumulative illness rating scale >6 and/or GFR <70 ml/min (German CLL study group)

ASH 2025. Abstr 1
N Engl J Med . 2025 Dec 6. doi: 10.1056/NEJMoa2515458.

KEY DATA

CLL17: 1L venetoclax combinations for previously untreated CLL

Primary Endpoint: Progression Free Survival (PFS)



Outcome	Ven + Obin (n = 303)	Ven + Ibr (n = 305)	Ibrutinib (n = 301)
3-yr PFS rate	81.1%	79.4%	81.0%
PD, n	25	37	46
Death, n	21	13	11

Hazard ratio for disease progression or death:

- Venetoclax obinutuzumab versus ibrutinib
  0.87 (98.3% CI 0.54 - 1.41)
- Venetoclax ibrutinib versus ibrutinib
  0.84 (98.0% CI, 0.53 – 1.32)

ASH 2025. Abstr 1
N Engl J Med . 2025 Dec 6. doi: 10.1056/NEJMoa2515458.

KEY DATA

CLL17: 1L venetoclax combinations for previously untreated CLL

Progression Free Survival (PFS) by subgroup

Outcome by IGHV Status	Ven + Obin		Ven + Ibr		Ibrutinib	
	uIGHV (n = 171)	mIGHV (n = 129)	uIGHV (n = 172)	mIGHV (n = 129)	uIGHV (n = 171)	mIGHV (n = 126)
• **3-yr PFS rate**	**75.8%**	**87.6%**	**78.9%**	**80.0%**	**79.7%**	**83.5%**
• HR (95% CI)	VO vs I: 0.98 (0.61-1.59) VI vs I: 0.81 (0.49-1.32)					

Outcome by *TP53*/del17p Status	*TP53*del/mut (n = 23)	*TP53*-WT (n = 280)	*TP53*del/mut (n = 25)	*TP53*-WT (n = 279)	*TP53*del/mut (n = 21)	*TP53*-WT (n = 279)
• **3-yr PFS rate**	**62.0%**	**82.7%**	**69.0%**	**80.1%**	**79.4%**	**81.0%**
• HR (95% CI)	VO vs I: 1.20 (0.40-3.59) VI vs I: 0.70 (0.22-2.16)					

Outcome by Fitness*	Unfit (n = 134)	Fit (n = 167)	Unfit (n = 136)	Fit (n = 169)	Unfit (n = 130)	Fit (n = 171)
• **3-yr PFS rate**	**79.6%**	**82.1%**	**74.9%**	**82.7%**	**70.4%**	**88.7%**
• HR (95% CI)	VO vs I: 0.58 (0.34-0.99) VI vs I: 0.66 (0.40-1.11)					

*Defined by cumulative illness rating scale >6 and/or GFR <70 ml/min (German CLL study group)

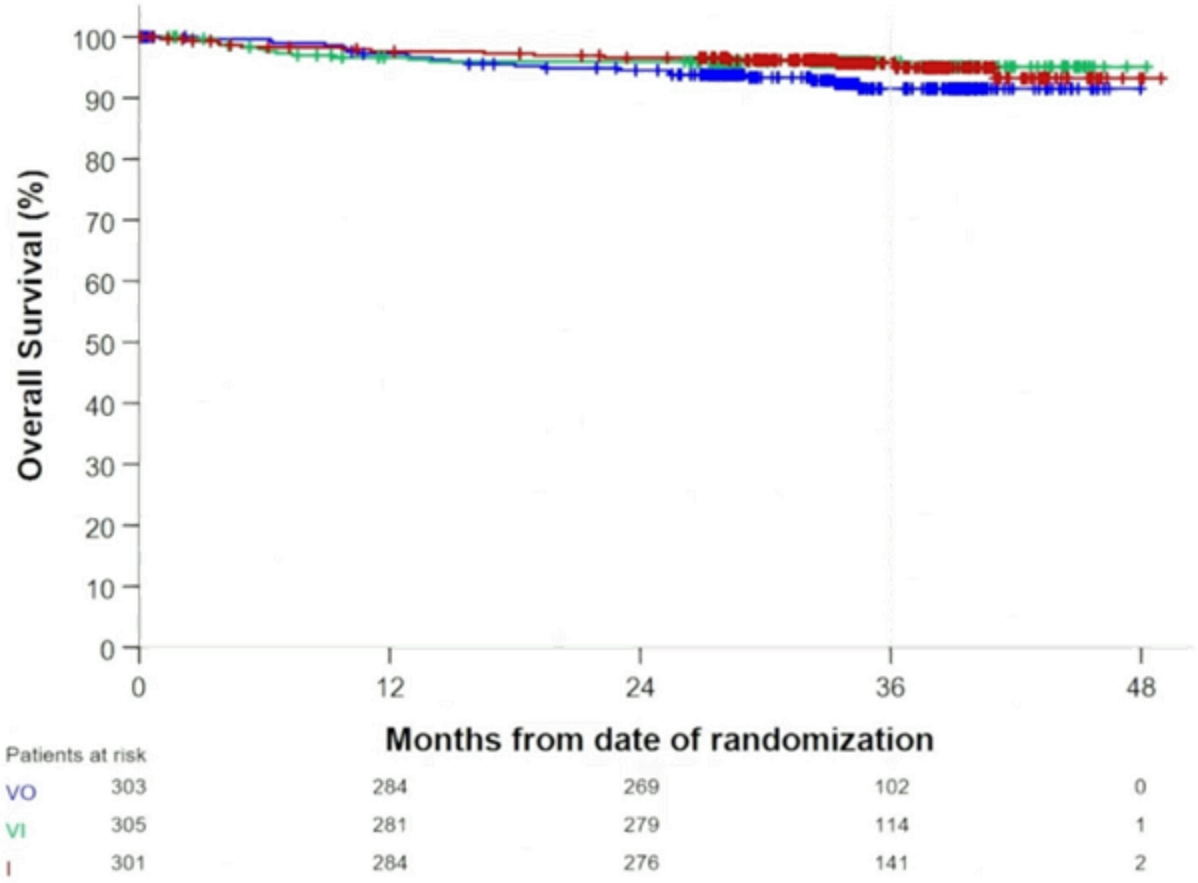
ASH 2025. Abstr 1
N Engl J Med . 2025 Dec 6. doi: 10.1056/NEJMoa2515458.

KEY DATA

CLL17: 1L venetoclax combinations for previously untreated CLL

Key secondary endpoint: Overall survival (OS)

Interim data



OS	Ven + Obin (n = 303)	Ven + Ibr (n = 305)	Ibrutinib (n = 301)
3-yr OS rate	91.5%	96.0%	95.7%
HR (95% CI)	VO vs I: 1.67 (0.86-3.28)	VI vs I: 0.96 (0.45-2.05)	

Cause of Death, n	Ven + Obin (n = 303)	Ven + Ibr (n = 305)	Ibrutinib (n = 301)
All causes	22	13	14
Infection	12	7	3
• COVID-19	7	2	-
Cardiovascular	5	3	5
PD/RT	1	0	0
SPM	4	2	2
Other	0	1	4

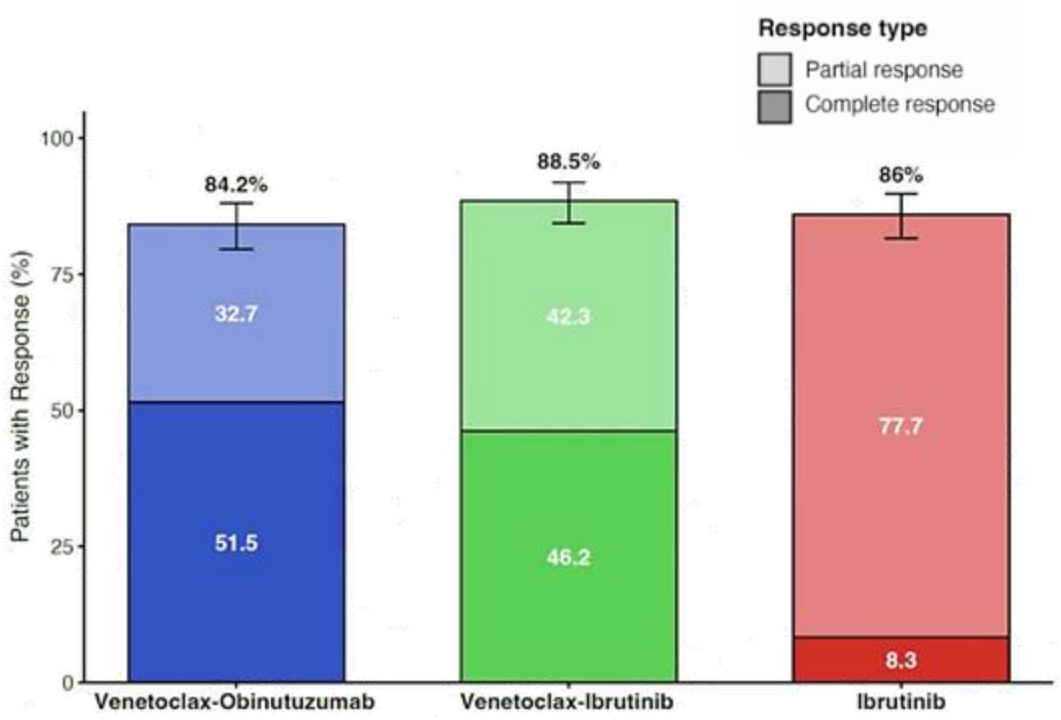
ASH 2025. Abstr 1
N Engl J Med . 2025 Dec 6. doi: 10.1056/NEJMoa2515458.

KEY DATA

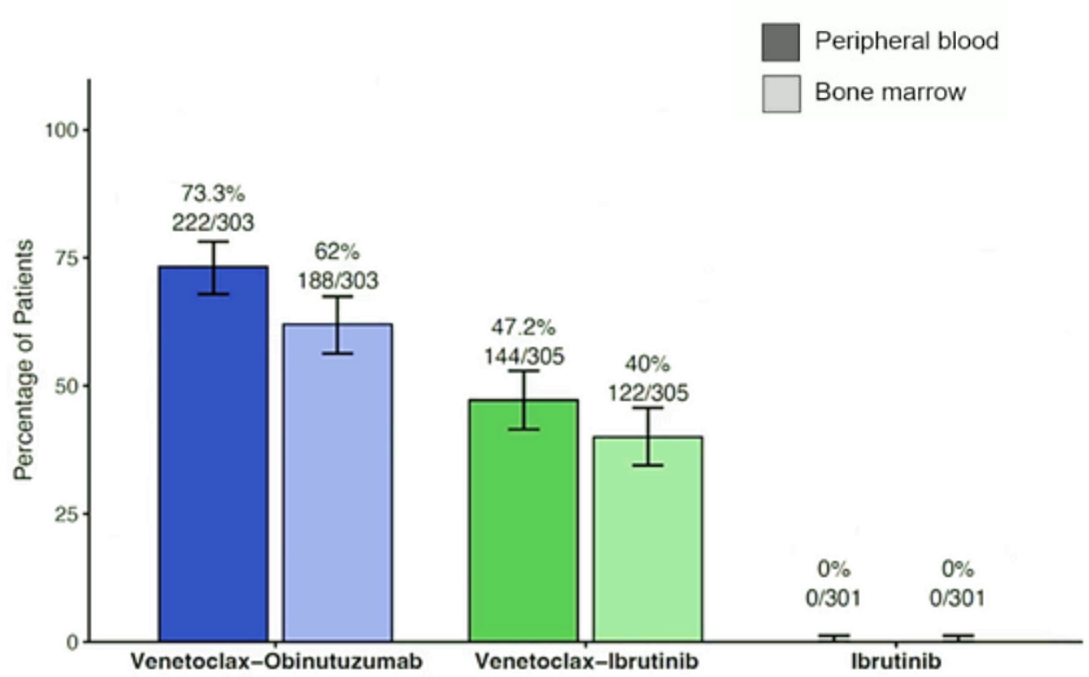
CLL17: 1L venetoclax combinations for previously untreated CLL

Response to treatment

IwCLL response at final restaging (C18D1)



uMRD <10^{-4} in peripheral bone and blood marrow, by flow cytometry, at final restaging



IwCLL: International Workshop on CLL
uMRD: Undetectable Minimal Residual Disease below a threshold of 10^{-4} (or 0.01%) in CLL

ASH 2025. Abstr 1
N Engl J Med . 2025 Dec 6. doi: 10.1056/NEJMoa2515458.

KEY DATA

CLL17: 1L venetoclax combinations for previously untreated CLL

Safety Summary

Selected AEs of Interest (Any Grade), n (%)	Ven + Obin (n = 295)	Ven + Ibr (n = 303)	Ibrutinib (n = 298)
Blood and lymphatic system disorders	174 (59.0)	130 (42.9)	85 (28.5)
• Febrile neutropenia	14 (4.7)	7 (2.3)	0 (0)
• Neutropenia	155 (52.5)	110 (36.3)	49 (16.4)
Cardiac disorders	41 (13.9)	72 (23.8)	103 (34.6)
• Atrial fibrillation	11 (3.7)	38 (12.5)	50 (16.8)
GI disorders	176 (59.7)	225 (74.3)	189 (63.4)
• Diarrhea	80 (27.1)	143 (47.2)	104 (34.9)
Infections and infestations	225 (76.3)	243 (80.2)	238 (79.9)
• COVID-19	113 (38.3)	128 (42.2)	117 (39.3)
• Pneumonia	41 (13.9)	28 (9.2)	40 (13.4)
Metabolism and nutrition disorders	90 (30.5)	75 (24.8)	72 (24.2)
• Tumor lysis syndrome	12 (4.1)	4 (1.3)	1 (0.3)
Benign, malignant, and unspecified neoplasms	35 (11.9)	35 (11.6)	55 (18.5)
• Richter transformation	4 (1.4)	1 (0.3)	4 (1.3)
Vascular disorders	60 (20.3)	102 (33.7)	124 (41.6)
• Hypertension	34 (11.5)	51 (16.8)	72 (24.2)

Grade 3-5 Infections	Ven + Obin (n = 295)	Ven + Ibr (n = 303)	Ibrutinib (n = 298)
Infections and infestations	103 (34.9)	76 (25.1)	74 (24.8)
• COVID-19	47 (15.9)	26 (8.6)	20 (6.7)
• Pneumonia	29 (9.8)	22 (7.3)	22 (7.4)

ASH 2025. Abstr 1
N Engl J Med . 2025 Dec 6. doi: 10.1056/NEJMoa2515458.

SUMMARY

CLL17

- Fixed-duration venetoclax-obinutuzumab and venetoclax-ibrutinib achieved non-inferiority in progression-free survival vs continuous ibrutinib
  - 3-yr PFS rate:
    - Ven + Ibr 79.4%; Ven + Obin 81.1%; Ibr 81.0%
    - Ven + Ibr vs Ibr: HR 0.84 (98.0% CI: 0.53-1.32)
    - Ven + Obin vs Ibr: HR 0.87 (98.3% CI: 0.54-1.41)
- Safety findings consistent with known toxicity profiles of these agents
  - Infection is a significant concern across all CLL therapies and is particularly pronounced with anti-CD20 antibodies
- *Benefit to patients: treatment-free intervals and lower rates of treatment-related toxic effects in the long-term*

IMPACT

Venetoclax-obinutuzumab or venetoclax-ibrutinib are effective frontline options in patients with previously untreated chronic lymphocytic leukemia – potential shift towards fixed-duration therapy

Venetoclax + Obinutuzumab: Approved by the FDA in May 2019 as a 12-month fixed-duration regimen for untreated CLL based on CLL14

Venetoclax + Ibrutinib: Not yet FDA approved

Polling question

Based on the CLL17 results (if approved), how do you anticipate changing your frontline treatment approach for fit patients with treatment-naïve CLL (without TP53 aberration)?

1. I will preferentially use time-limited venetoclax-obinutuzumab
2. I will preferentially use fixed-duration ibrutinib-venetoclax
3. I will continue using single-agent BTK inhibitor therapy
4. Unsure

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

CLINICAL QUESTION

BRUIN CLL-314

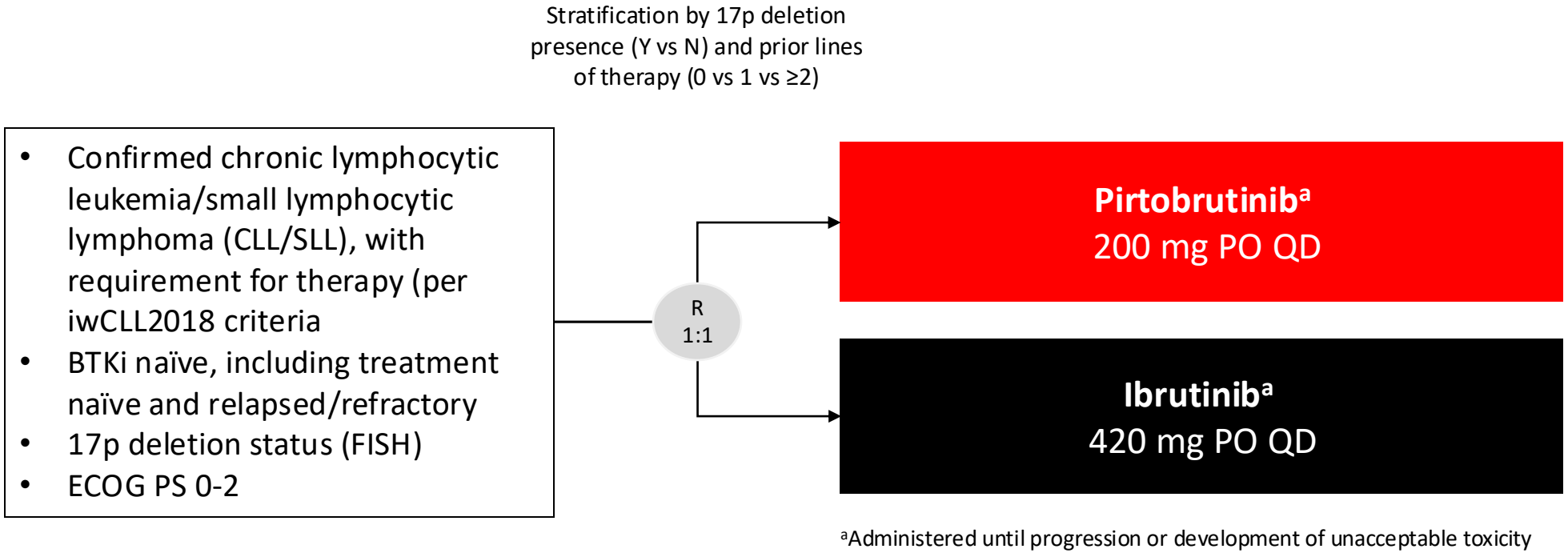
Does pirtobrutinib (a selective, non-covalent BTKi) benefit patients with treatment naïve and relapse/refractory chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/SLL) compared to ibrutinib?

***Reminder**: On **December 3, 2025**, the FDA granted traditional approval (accelerated approval 2023) to **pirtobrutinib** (Jaypirca, Eli Lilly and Company) for adults with **relapsed or refractory** chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have **previously been treated** with a covalent BTK inhibitor evaluated in BRUIN-CLL-321.*

KEY DATA

BRUIN CLL-314: 1L Pirtobrutinib vs ibrutinib in patients with BTKi-naïve R/R CLL/SLL

Study Design: Randomized phase 3 trial



[a]Administered until progression or development of unacceptable toxicity

Primary endpoint: Non–inferiority of overall response rate (ORR) per iwCLL 2018 criteria in ITT population or relapse/refractory population
Key secondary endpoint: Superiority of progression-free survival (PFS) per iwCLL 2018 criteria in ITT population or relapse/refractory population
Exploratory endpoint: Analyses of endpoints in the treatment naïve population

KEY DATA

BRUIN CLL-314: 1L Pirtobrutinib vs ibrutinib in patients with BTKi-naïve R/R CLL/SLL

Baseline Characteristics

Characteristic in ITT Population, n (%)	Pirtobrutinib (n = 331)	Ibrutinib (n = 331)
Median age, yr (range)	67 (39-90)	67 (34-86)
Male	213 (64.4)	215 (65.0)
Region		
• North America	26 (7.9)	21 (6.3)
• Europe	174 (52.6)	171 (51.7)
• South America	61 (18.4)	64 (19.3)
• Asia	42 (12.7)	51 (15.4)
• Other	28 (8.5)	24 (7.3)
Histology		
• CLL	306 (92.4)	294 (88.8)
• SLL	25 (7.6)	37 (11.2)
ECOG PS		
• 0-1	319 (96.4)	321 (97.0)
• 2	12 (3.6)	10 (3.0)
Rai stage		
• 0-II	168 (54.9)	171 (58.2)
• III/IV	135 (44.1)	119 (40.5)
Median duration of disease, yr (Q1-Q3)	5.62 (2.20-8.91)	5.26 (1.88-9.73)

Characteristic in ITT Population, n (%)	Pirtobrutinib (n = 331)	Ibrutinib (n = 331)
Bulky disease	107 (32.3)	116 (35.0)
High-risk molecular features, n/N (%)		
• IGHV unmutated	199/293 (67.9)	183/277 (66.1)
• del(17p) present	50/331 (15.1)	52/331 (15.7)
• *TP53* mutation	92/284 (32.4)	78/273 (28.6)
• Complex karyotype	104/259 (40.2)	78/227 (34.4)

Characteristic in R/R Population, n (%)	Pirtobrutinib (n = 219)	Ibrutinib (n = 218)
Median lines of prior systemic therapy, n (range)	1.0 (1-9)	1.0 (1-8)
Prior therapy		
• BCL2 inhibitor	22 (10.0)	17 (7.8)
• Chemotherapy	201 (91.8)	208 (95.4)
• Anti-CD20 antibody	158 (72.1)	166 (76.1)
• PI3K inhibitor	6 (2.7)	6 (2.8)
• IMiD	1 (0.5)	1 (0.5)
• Autologous/allogeneic SCT	2 (0.9)	2 (0.9)
Reason for d/c of most recent tx		
• Disease progression	31 (14.2)	35 (16.1)
• Toxicity	23 (10.5)	25 (11.5)
• Finished course	148 (67.6)	141 (64.7)
• Other	16 (7.3)	16 (7.3)

KEY DATA

BRUIN CLL-314: 1L Pirtobrutinib vs ibrutinib in patients with BTKi-naïve R/R CLL/SLL

Primary Endpoint: Overall Response Rate

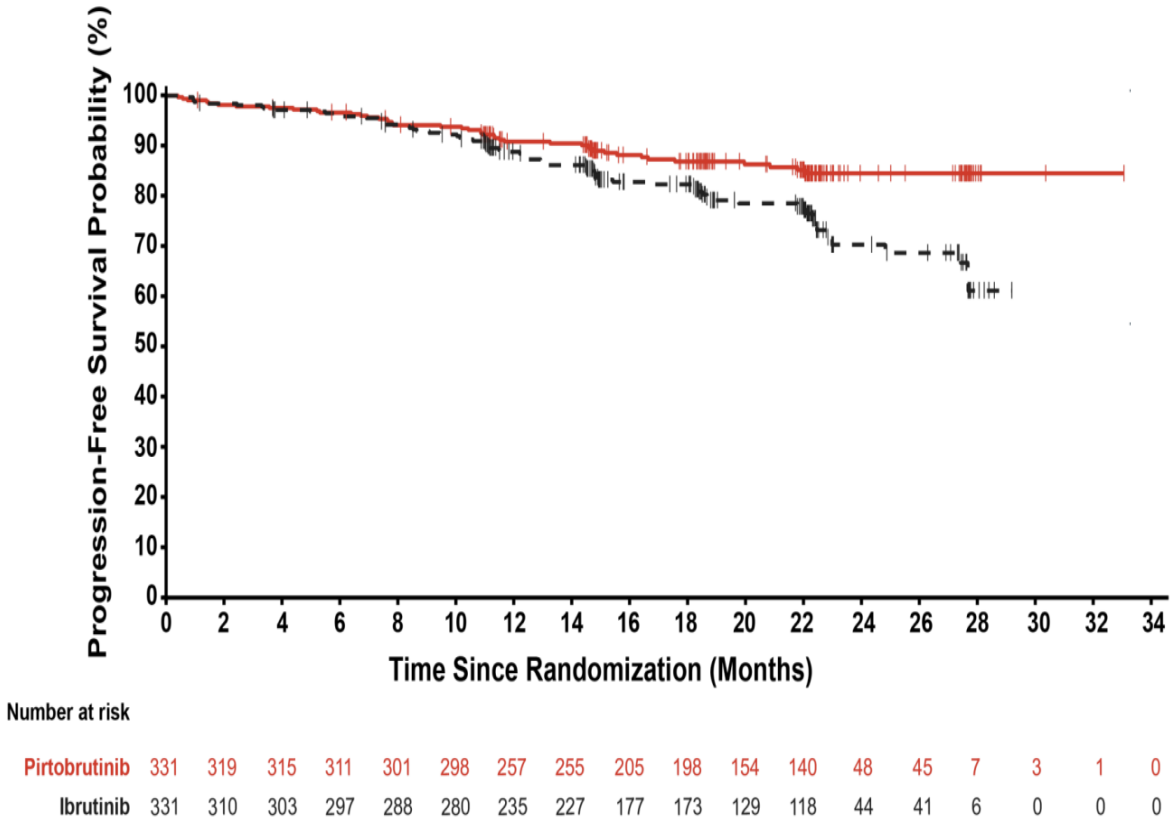
	ITT Population		TN Population		R/R Population	
	Pirtobrutinib (n = 331)	Ibrutinib (n = 331)	Pirtobrutinib (n = 112)	Ibrutinib (n = 113)	Pirtobrutinib (n = 219)	Ibrutinib (n = 218)
ORR (PR or better), %	**87.0**	**78.5**	**92.9**	**85.8**	**84.0**	**74.8**
• 95% CI	82.90-90.44	73.73-82.85	86.41-96.87	78.03-91.68	78.48-88.61	68.46-80.39
• Nominal P value	0.0034		0.0886		0.0175	
ORR ratio						
• ORR ratio (95% CI)	1.1080 (1.034-1.187)		1.0797 (0.989-1.179)		1.1233 (1.020-1.237)	
• P value for NI*	<0.0001		--		<0.0001	
Best overall response, %						
• CR or CRi	4.8	2.4	7.1	3.5	3.7	1.8
• PR or nPR	82.2	76.1	85.7	82.3	80.4	72.9
• PR-L	2.4	3.9	0.9	2.7	3.2	4.6
• SD	5.4	10.9	2.7	4.4	6.8	14.2
• PD	1.5	1.2	0	0	2.3	1.8
ORR including PR-L, %	89.4	82.5	93.8	88.5	87.2	79.4
• 95% CI	85.60-92.52	77.95-86.42	87.55-97.45	81.13-93.73	82.05-91.33	73.37-84.53
• Nominal P value	0.0093		0.1692		0.0286	

CR, complete remission, CRi, CR with incomplete hematologic recovery; ITT, intent-to-treat; NI, non-inferiority; nPR, nodular partial remission; ORR, overall response rate; PD, progressive disease; PR, partial remission; PR-L, partial remission with lymphocytosis; R/R, relapsed/refractory; SD, stable disease; TN, treatment-naïve

KEY DATA

BRUIN CLL-314: 1L Pirtobrutinib vs ibrutinib in patients with BTKi-naïve R/R CLL/SLL

Key Secondary Endpoint: Progression Free Survival (PFS) ITT population



	Pirtobrutinib (n = 331)	Ibrutinib (n = 331)
No. of events, n (%)	43 (13.0)	69 (20.8)
18-mo PFS rate, % (95% CI)	**86.9** (82.4-90.3)	**82.3** (77.3-86.3)
Median follow-up, mo	22.0	19.7
HR (95% CI)	**0.569 (0.388-0.834)**	
P value	0.0034	

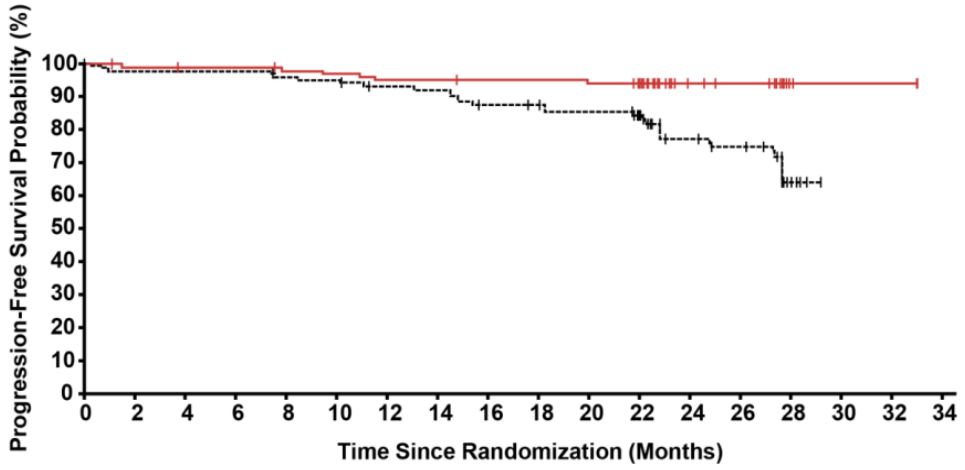
The PFS results presented at INV-assessed

KEY DATA

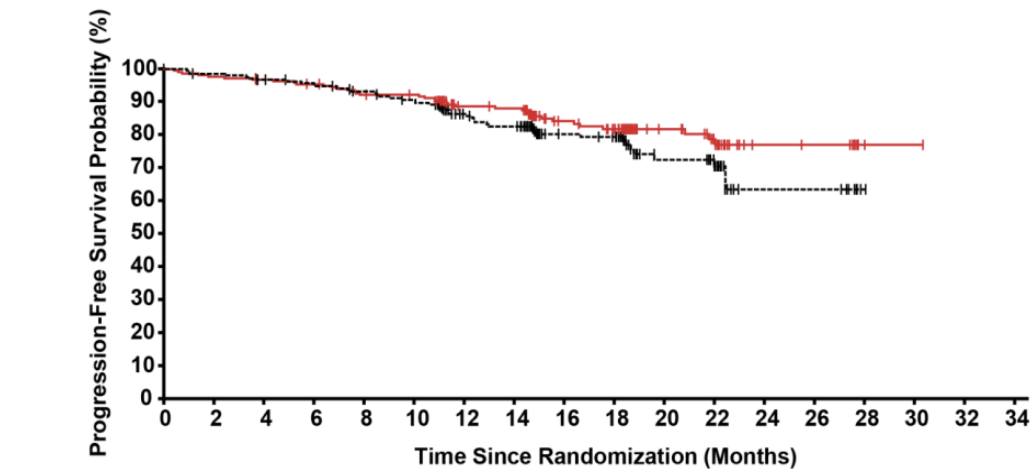
BRUIN CLL-314: 1L Pirtobrutinib vs ibrutinib in patients with BTKi-naïve R/R CLL/SLL

Key Secondary Endpoint: Investigator-assessed Progression Free Survival (PFS) by Prior Treatment Status

Treatment Naïve Population by INV	Pirtobrutinib (n = 112)	Ibrutinib (n = 113)
No. of events, n (%)	6 (5.4)	24 (21.2)
18-mo PFS rate, % (95% CI)	**95.3** (89.1-98.0)	**87.6** (79.7-92.6)
Median follow-up, mo	22.5	22.4
HR (95% CI)	**0.239 (0.098-0.586)**	
P value	0.0007	



Relapsed/ Refractory Population by INV	Pirtobrutinib (n = 219)	Ibrutinib (n = 218)
No. of events, n	37 (16.9)	45 (20.6)
18-mo PFS rate, % (95% CI)	**81.7** (75.1-86.7)	**79.2** (72.3-84.6)
Median follow-up, mo	18.4	15.8
HR (95% CI)	**0.729 (0.471-1.128)**	
P value	0.1563	



KEY DATA

BRUIN CLL-314: 1L Pirtobrutinib vs ibrutinib in patients with BTKi-naïve R/R CLL/SLL

Safety Summary

TEAEs Occurring in ≥10% of Patients

n (%)	Pirtobrutinib (n = 330)		Ibrutinib (n = 325)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TEAE	320 (97.0)	181 (54.8)	318 (97.8)	174 (53.5)
Upper respiratory tract infection	59 (17.9)	2 (0.6)	63 (19.4)	0
Pneumonia	45 (13.6)	21 (6.4)	49 (15.1)	28 (8.6)
Diarrhea	**44 (13.3)**	**1 (0.3)**	**62 (19.1)**	**4 (1.2)**
COVID-19	40 (12.1)	4 (1.2)	33 (10.2)	5 (1.5)
Contusion	33 (10.0)	0	30 (9.2)	0
Arthralgia	**26 (7.9)**	0	**41 (12.6)**	0
Urinary tract infection	26 (7.9)	3 (0.9)	40 (12.3)	3 (0.9)
Leading to treatment discontinuation	31 (9.4)		35 (10.8)	
Leading to dose reduction	**26 (7.9)**		**59 (18.2)**	

AEs of Special Interest Occurring in ≥10% of Patients

n (%)	Pirtobrutinib (n = 330)		Ibrutinib (n = 325)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE of special interest	288 (87.3)	127 (38.5)	288 (88.6)	117 (36.0)
Infection	226 (68.5)	56 (17.0)	241 (74.2)	54 (16.6)
• Infection without COVID-19	214 (64.8)	53 (16.1)	234 (72.0)	49 (15.1)
Bleeding	115 (34.8)	11 (3.3)	118 (36.3)	9 (2.8)
• Hemorrhage	78 (23.6)	11 (3.3)	81 (24.9)	9 (2.8)
• Brusing	45 (13.6)	0	39 (12.0)	0
• Petechiae and purpura	17 (5.2)	0	25 (7.7)	0
Neutropenia	**103 (31.2)**	**83 (25.2)**	**76 (23.4)**	**57 (17.5)**
Anemia	51 (15.5)	**20 (6.1)**	51 (15.7)	**12 (3.7)**
Thrombocytopenia	39 (11.8)	12 (3.6)	57 (17.5)	13 (4.0)
Atrial fibrillation /flutter	**8 (2.4)**	**3 (0.9)**	**44 (13.5)**	**13 (4.0)**
• ≥75 yr of age	**3 (4.5)**	**1 (1.5)**	**15 (21.4)**	**5 (7.1)**

BRUIN CLL-314

SUMMARY

- Among patients with treatment-naive and BTKi-naive CLL/SLL, pirtobrutinib demonstrated noninferior ORR vs ibrutinib in the ITT and R/R populations
  - ITT: 87.0% vs 78.5%; P = 0.0035
  - R/R: 84.0% vs 74.8%; P = 0.0175
- Pirtobrutinib demonstrated to be associated with increased PFS in ITT, treatment- naive, and R/R populations in early analysis
- Pirtobrutinib was effective in treatment-naive patients, with an ORR of 92.9% vs 85.8%; PFS benefit vs ibrutinib: HR 0.239 (95% CI: 0.098-0.586); P = 0.0007
- Lower rates of discontinuation and atrial fibrillation/flutter relative to ibrutinib, particularly in patients ≥75 years old

IMPACT

Pirtobrutinib may become a new treatment option for patients with treatment-naive and BTKi-naive CLL/SLL

Not yet FDA approved in this settin

FDA approved for R/R CLL/SLL previou treated with a covalent BTK inhibitor (accelerated approval 2023 → expanded, traditional approval Dec 2025)

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2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

CLINICAL QUESTION

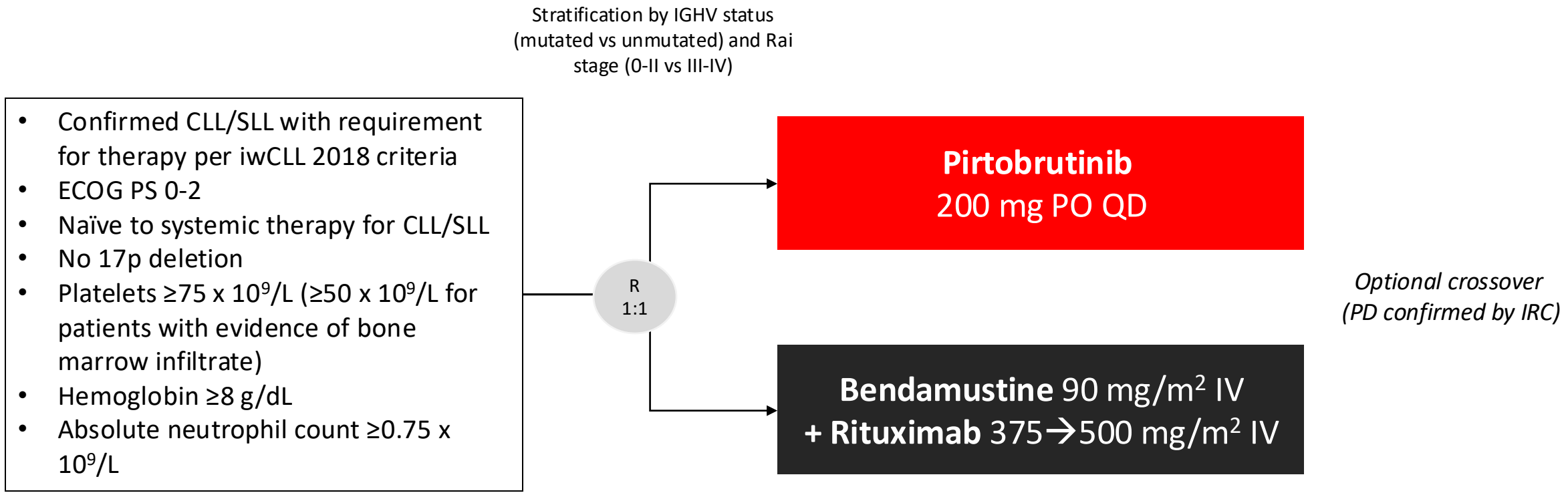
BRUIN CLL-313

Does pirtobrutinib benefit untreated patients with chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/SLL) compared to BR (bendamustine/rituximab)?

KEY DATA

BRUIN CLL-313: Pirtobrutinib in treatment naïve CLL/SLL

Study Design: Randomized, open-label, global phase 3 trial



Primary endpoint: Progression-free survival (PFS) per iwCLL 2018 criteria
Key secondary endpoint: Overall survival (OS)
Secondary endpoint: Overall response rate (ORR) per iwCLL 2018 criteria and safety measures

KEY DATA

BRUIN CLL-313: Pirtobrutinib in treatment naïve CLL/SLL

Baseline Characteristics

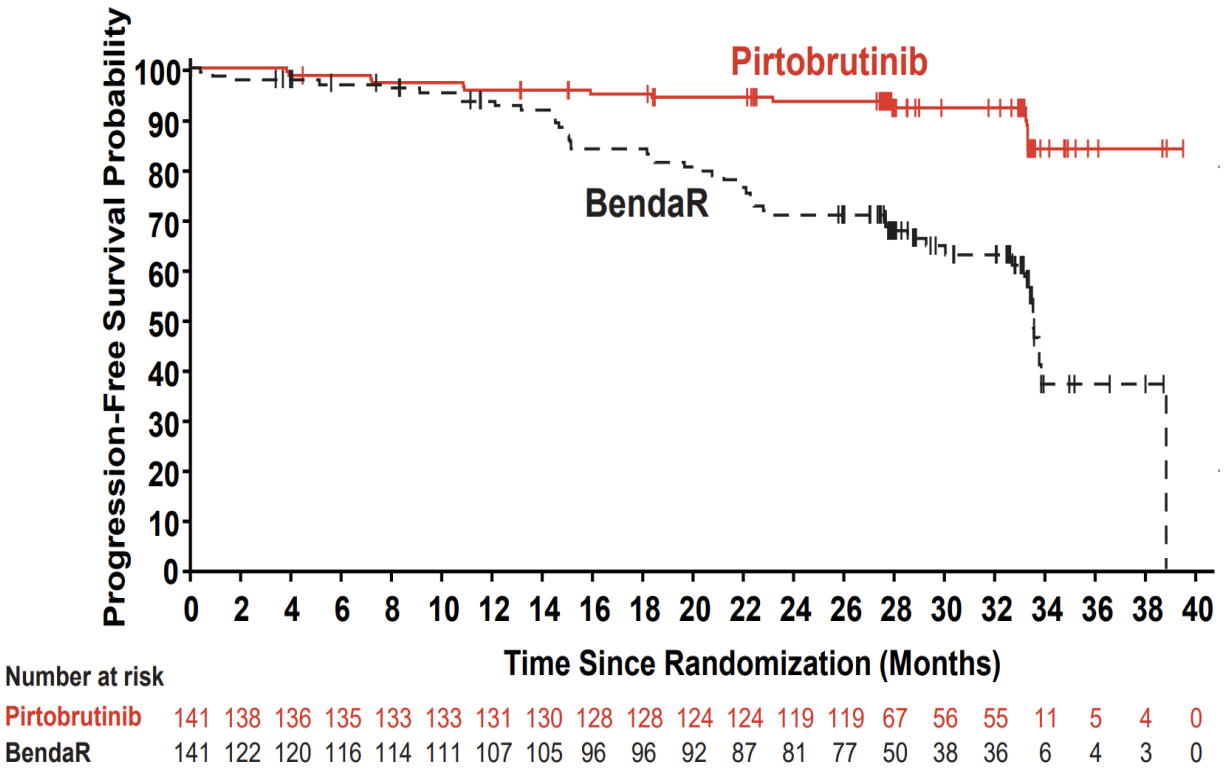
n (%)	Pirtobrutinib (n =141)	BendaR (n = 141)
Median age, yr (range)	65 (29-84)	66 (35-88)
Male	83 (58.9)	90 (63.8)
Region		
• North America	2 (1.4)	5 (3.5)
• Europe	85 (60.3)	85 (60.3)
• Asia	32 (22.7)	31 (22.0)
• South America	9 (6.4)	13 (9.2)
• Australia/New Zealand	13 (9.2)	7 (5.0)
Histology		
• CLL	131 (92.9)	129 (91.5)
• SLL	10 (7.1)	12 (8.5)
Rai stage		
• 0-II	82 (62.6)	81 (62.8)
• III/IV	49 (37.4)	48 (37.2)
ECOG PS		
• 0	68 (48.2)	55 (39.0)
• 1	66 (46.8)	77 (54.6)
• 2	7 (5.0)	9 (6.4)

n (%)	Pirtobrutinib (n =141)	BendaR (n = 141)
Median duration of disease, yr (Q1-Q3)	2.5 (0.8-4.9)	2.0 (0.3-4.7)
Bulky disease	39 (27.7)	35 (24.8)
del(11q)		
• Yes	11 (7.8)	15 (10.6)
• No	97 (68.8)	93 (66.0)
• Missing/unknown	33 (23.4)	33 (23.4)
IGHV mutation status		
• Mutated	61 (43.3)	61 (43.3)
• Unmutated	80 (56.7)	80 (56.7)
TP53 mutation status		
• Present	10 (7.1)	12 (8.5)
• Absent	115 (81.6)	107 (75.9)
• Missing	16 (11.3)	22 (15.6)
Complex karyotype		
• Yes	16 (11.3)	11 (7.8)
• No	75 (53.2)	72 (51.1)
• Missing	50 (35.5)	58 (41.1)

KEY DATA

BRUIN CLL-313: Pirtobrutinib in treatment naïve CLL/SLL

Primary Endpoint: Progression-free survival (PFS)



	Pirtobrutinib (n = 141)	BendaR (n = 141)
PFS events, n (%)	13 (9.2)	48 (34.0)
24-mo PFS, % (95% CI)	**93.4** (87.6-96.5)	**70.7** (61.5-78.1)
Median follow-up, mo	28.1	28.3
HR (95% CI)	**0.20 (0.11-0.37)**	
P value	<0.0001	

The PFS results presented are IRC assessed

KEY DATA

BRUIN CLL-313: Pirtobrutinib in treatment naïve CLL/SLL

Key Secondary Endpoint: Overall Response Rate (ORR)

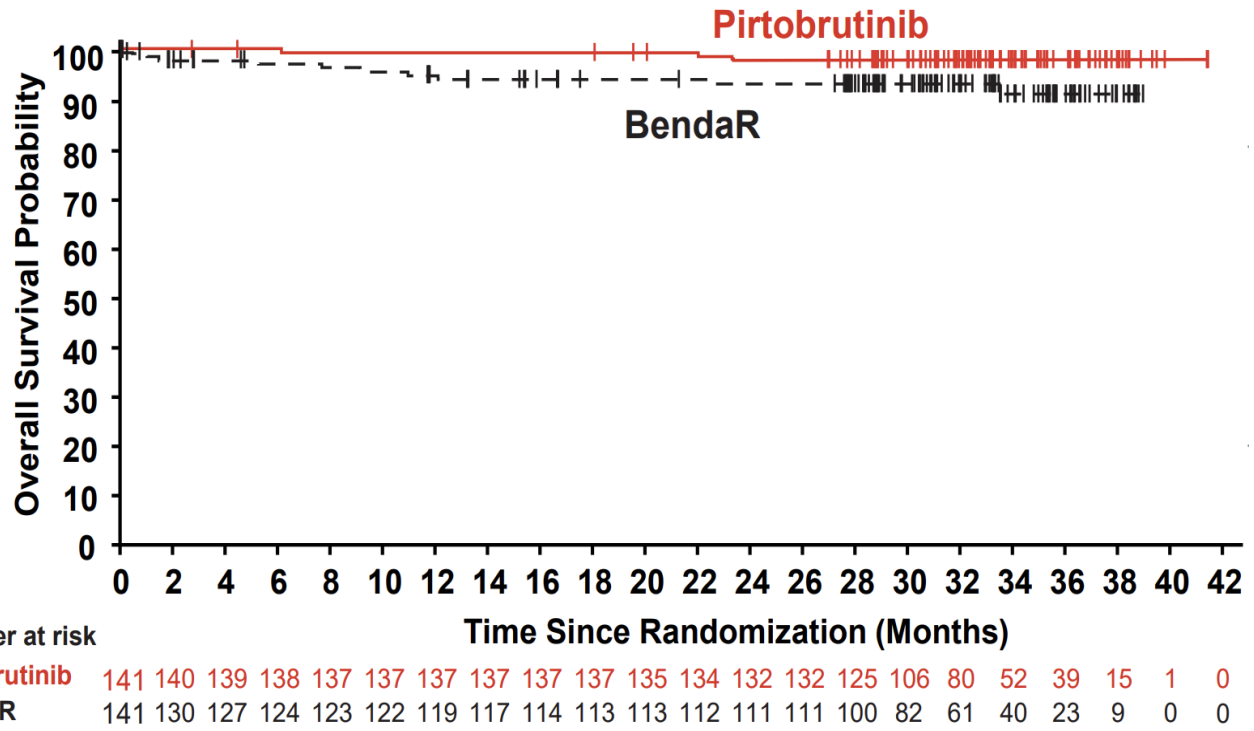
n (%)	IRC-Assessed ORR		INV-Assessed ORR	
	Pirtobrutinib (n =141)	BendaR (n = 141)	Pirtobrutinib (n =141)	BendaR (n = 141)
ORR (PR or better)	133 (**94.3**)	114 (**80.9**)	133 (**94.3**)	116 (**82.3**)
• 95% CI	89.1-97.5	73.4-87.0	89.1-97.5	75.0-88.2
Best overall response				
• CR/CRi	**19 (13.5)**	**29 (20.6)**	**8 (5.7)**	**29 (20.6)**
• PR/nPR	**114 (80.9)**	**85 (60.3)**	**125 (88.7)**	**87 (61.7)**
• PR-L	0	0	2 (1.4)	0
• SD	3 (2.1)	10 (7.1)	1 (0.7)	6 (4.3)
• PD	2 (1.4)	1 (0.7)	2 (1.4)	3 (2.1)
• Unknown/NA	3 (2.1)	16 (11.3)	3 (2.1)	16 (11.3)

KEY DATA

BRUIN CLL-313: Pirtobrutinib in treatment naïve CLL/SLL

Key Secondary Endpoint: Overall survival (OS)

Interim data



	Pirtobrutinib (n =141)	BendaR (n = 141)
OS events, n (%)	3 (2.1)	10 (7.1)
24-mo OS, % (95% CI)	**97.8** (93.3-99.3)	**93.0** (87.0-96.3)
Median follow-up, mo	32.7	31.7
HR (95% CI)	**0.26 (0.07-0.93)**	
P value	0.0261	

Effective crossover rate[a]: 52.9% (18/34)

[a]Uses the number of patients with investigator-assessed PD as the denominator; eligible patients receiving BendaR could crossover to receive pirtobrutinib monotherapy upon confirmation of PD by IRC per protocol.

KEY DATA

BRUIN CLL-313: pirtobrutinib in treatment naïve CLL/SLL

Safety Summary

TEAEs in ≥15% of Patients in Either Arm

n (%)	Pirtobrutinib (n = 140)		BendaR (n = 132)		EAIR per 100 Person-Yr (Any Grade), %		EAIR Ratio (95% CI)
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Pirtobrutinib	BendaR	
Any	131 (93.6)	56 (40.0)	117 (88.6)	89 (67.4)	196.7	844.6	0.23 (0.18-0.30)
Neutropenia	17 (12.1)	10 (7.1)	51 (38.6)	46 (34.8)	5.2	110.0	0.05 (0.03-0.08)
COVID-19	30 (21.4)	1 (0.7)	12 (9.1)	2 (1.5)	9.9	20.9	0.47 (0.24-0.92)
Pyrexia	12 (8.6)	0	25 (18.9)	0	3.5	49.1	0.07 (0.04-0.14)
URTI	25 (17.9)	1 (0.7)	9 (6.8)	0	7.7	15.7	0.49 (0.23-1.05)
Anemia	13 (9.3)	6 (4.3)	21 (15.9)	10 (7.6)	3.8	37.7	0.10 (0.05-0.20)
Nausea	3 (2.1)	0	31 (23.5)	1 (0.8)	0.8	65.1	0.01 (0-0.04)
IRR	0	0	20 (15.2)	4 (3.0)	0	39.0	NA

- Median time on treatment:
  - Pirtobrutinib **32.3** months
  - BendaR 5.6 months
- Richter's transformation reported in 1 patient receiving BendaR
- Discontinuation rate due to TEAEs, including death
  - Pirtobrutinib **4.3**%
  - BendaR 15.4%
- Dose reductions occurred less frequently with
  - pirtobrutinib **3.6**%
  - BendaR 31.1%

EAIR: exposure-adjusted incidence rate

SUMMARY

BRUIN CLL-313

- Pirtobrutinib demonstrated PFS improvement over BendaR in patients with treatment-naive CLL/SLL
  - 80% reduction in risk of progressive disease or death with pirtobrutinib vs BendaR
- OS trend toward pirtobrutinib despite 52.9% crossover rate
- Pirtobrutinib demonstrated favorable tolerability and low rates of discontinuation and atrial fibrillation/flutter

IMPACT

Pirtobrutinib is a potential new standard of care in the first line setting for patients with treatmen naive CLL/SLL

Not yet FDA approved in this setting

cornerstone specialty network™

Polling question

Which strategy for frontline therapy in treatment-naïve CLL/SLL do you believe will be most commonly adopted in community practice over the next year?

1. Pirtobrutinib monotherapy (based on BRUIN CLL-313 or BRUIN CLL-314)
2. Continue using established covalent BTK inhibitors (ibrutinib/acalabrutinib/Zanubrutinib
3. Use fixed-duration regimens as first choice
4. Unsure

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

CLINICAL QUESTION

EPCORE-FL-1

Does adding epcoritamab to rituximab + lenalidomide (R^2) improve outcomes for patients with relapsed/refractory follicular lymphoma?

Epcoritamab is a T-cell engaging bispecific antibody that targets CD3/CD20

On **November 18, 2025**, the FDA approved **epcoritamab-bysp** (Epkinly, Genmab US, Inc.) **with lenalidomide and rituximab** for relapsed or refractory follicular lymphoma (FL).
The FDA also granted traditional approval to **epcoritamab-bysp as monotherapy** for relapsed or refractory FL after two or more lines of systemic therapy (epcoritamab-bysp was granted accelerated approval for this indication in 2024).

KEY DATA

EPCORE-FL-1: 2L+ Epcoritamab + R^2 in R/R FL

Study Design: Global, randomized phase 3 study

- Histologically confirmed FL and CD20+
- Grade 1-3a, Stage II-IV
- ≥ 1 prior treatment (anti-CD20 mAb plus chemotherapy
- Met ≥ 1 GELF criterion

(n=488)

R 1:1

Epcoritamab (48 mg) plus R^2

Epcoritamab (3-SUD cycle 1: QW; cycles 2-3, QW; cycles 4-12, Q4W)
Rituximab (375 mg/m^2), 5 cycles (cycle 1, QW; cycles 2-5, Q4W)
Lenalidomide (20 mg), 12 cycles (cycle 1-12, QD)
(n = 243)

3-SUD: 3-Step Up Dosing schedule

R^2

Rituximab (375 mg/m^2), 5 cycles (cycle 1, QW; cycles 2-5, Q4W)
Lenalidomide (20 mg), 12 cycles (cycle 1-12, QD)
(n = 245)

Dual Primary endpoints: Overall response rate (ORR) and progression-free survival (PFS)
Secondary endpoints: CR rate, overall survival (OS), and minimal residual disease (MRD)
Additional secondary endpoints: DOR, DOCR, TTNLT, safety and PRO assessments

Median follow-up: 14.8 months
Enrollment period: October 2022 – January 2025

ASH 2025. Abstr 466
Lancet. 2026 Jan 10;407(10524):161-173.

KEY DATA

EPCORE-FL-1: 2L+ Epcoritamab + R^2 in R/R FL

Baseline Characteristics

n (%)	Epcoritamab + R^2 (n = 243)	R^2 (n=245)
Median age, years (range)	60 (30-84)	63 (24-89)
ECOG		
• 0	166 (68)	170 (69)
• 1-2	77 (32)	75 (31)
Ann Arbor stage		
• II	37 (51)	44 (18)
• III-VI	206 (85)	201 (82)
FLIPI score		
• 0-1	63 (26)	56 (23)
• 2	79 (33)	76 (31)
• 3-5	100 (41)	113 (46)

n (%)	Epcoritamab + R^2 (n = 243)	R^2 (n=245)
Bulky disease (≥ 7 cm)	47 (19)	61 (25)
Number of prior lines of therapy, median (range)	1 (1-7)	1 (1-6)
• 1	**145 (60)**	**141 (58)**
Prior anti-CD20 antibody	243 (100)	245 (100)
POD24	106 (44)	93 (38)
Refractory to 1L therapy	86 (35)	81 (33)
Double refractory	91 (37)	91 (37)

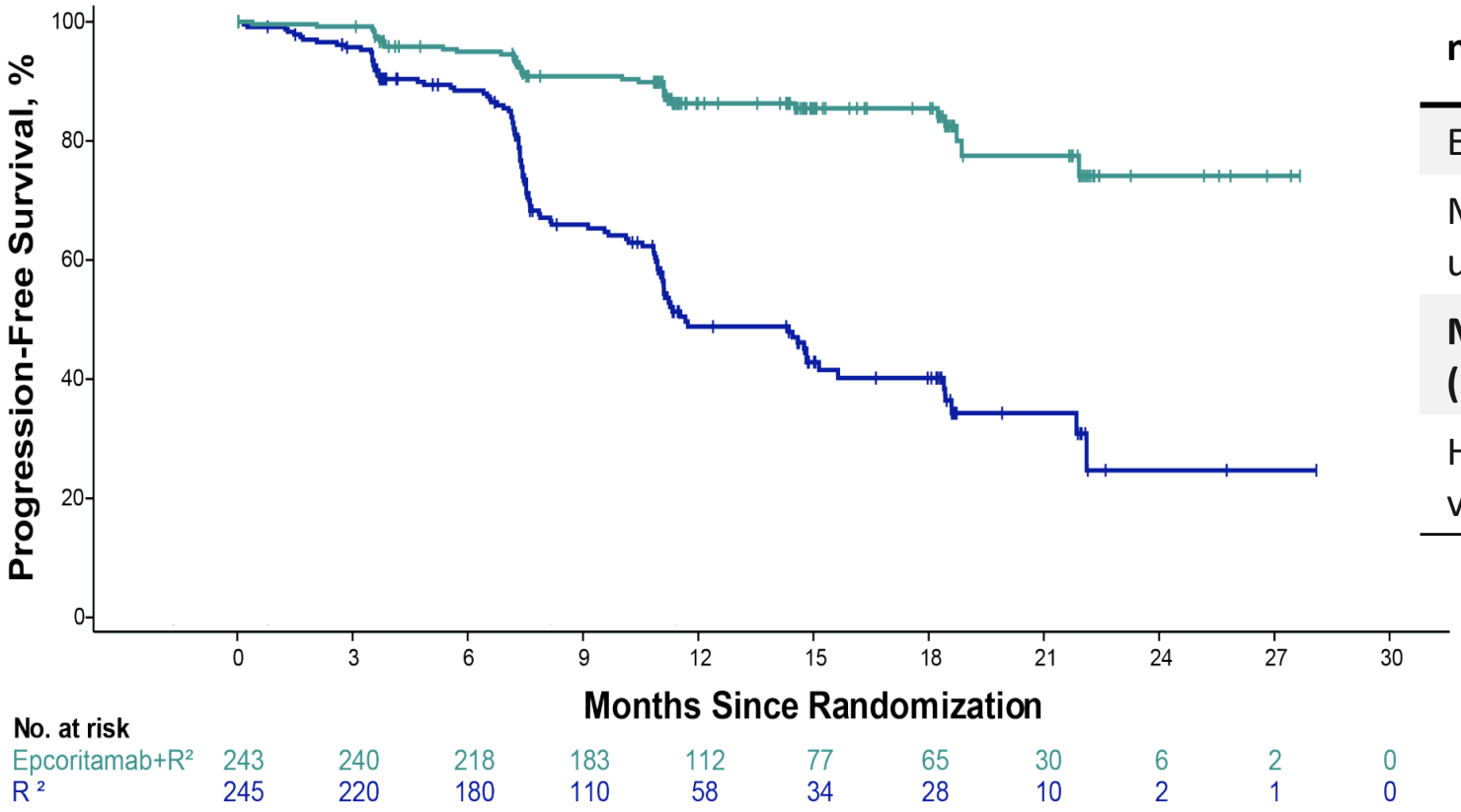
FLIPI: Follicular Lymphoma International Prognostic Index

ASH 2025. Abstr 466
Lancet. 2026 Jan 10;407(10524):161-173.

KEY DATA

EPCORE-FL-1: 2L+ Epcoritamab + R² in R/R FL

Dual Primary Endpoint: Progression-free survival (PFS)



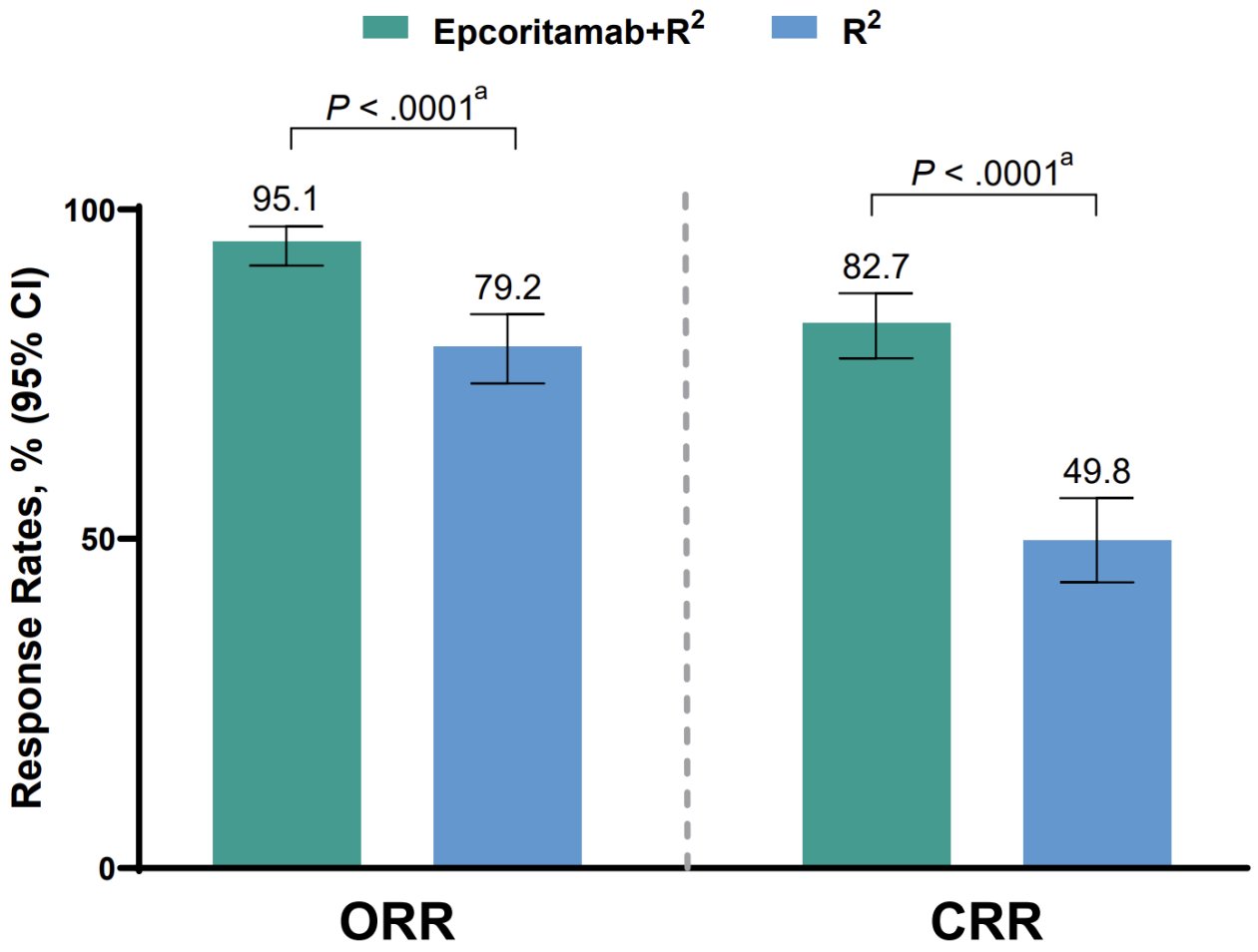
n (%)	Epcoritamab + R² (n = 243)	R² (n=245)
Events	35	106
Median follow-up, mo	14.4	11.5
Median (95% CI), mo	**NE** (NE-NE)	**11.7** (11.1-15.1)
HR (95% CI), P value	**0.21** (0.14-0.31), P < 0.0001	

ASH 2025. Abstr 466
Lancet. 2026 Jan 10;407(10524):161-173.

KEY DATA

EPCORE-FL-1: 2L+ Epcoritamab + R^2 in R/R FL

Dual Primary endpoint: Overall response rates (ORR)



n (%)	Epcoritamab + R^2 (n = 243)	R^2 (n=245)
ORR	**95%**	**79%**
CRR	83%	50%
PR	12%	29%
SD/PD	3%	13%
NE	2%	7%

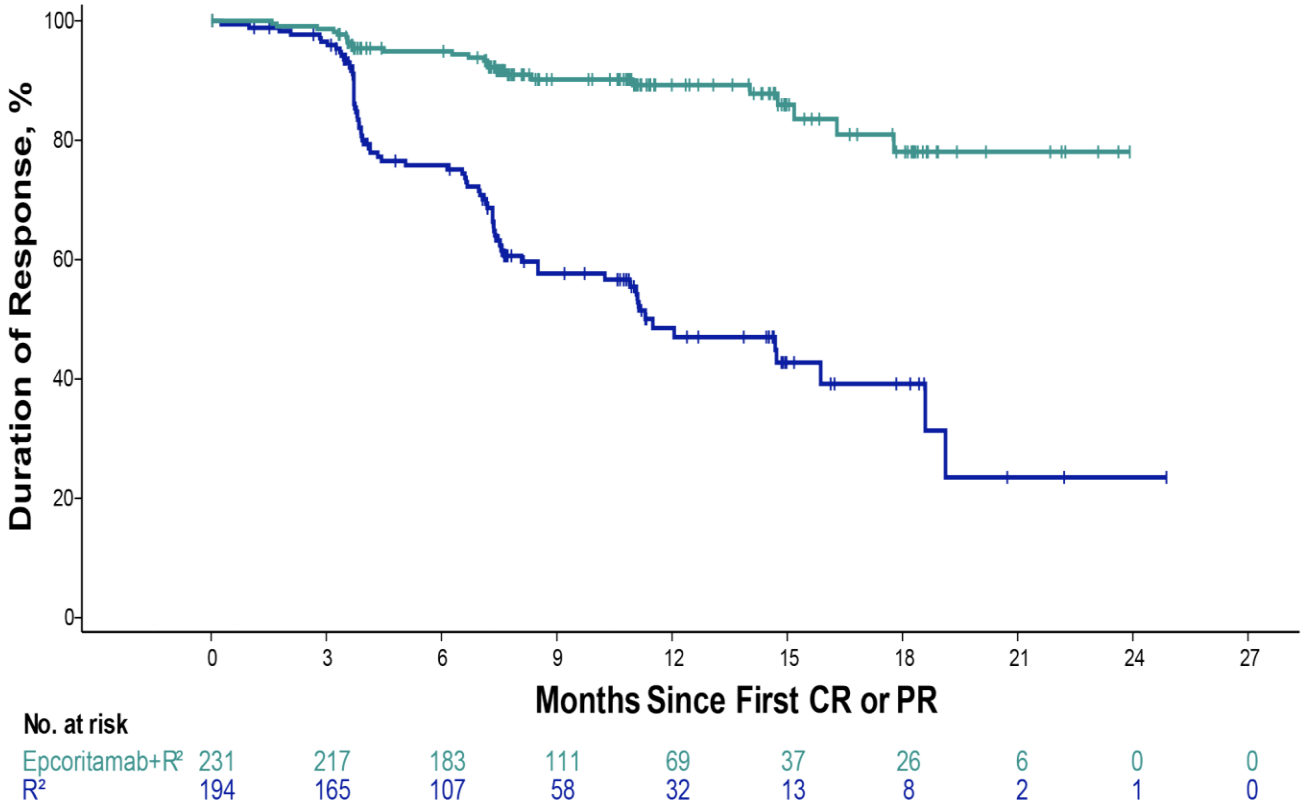
Complete Response Rate (CRR)
Partial Response (PR)
Stable Disease/Progressive Disease (SD/PD)
Not evaluable (NE)

ASH 2025. Abstr 466
Lancet. 2026 Jan 10;407(10524):161-173.

KEY DATA

EPCORE-FL-1: 2L+ Epcoritamab + R^2 in R/R FL

Secondary Endpoint: Duration of response (DoR)



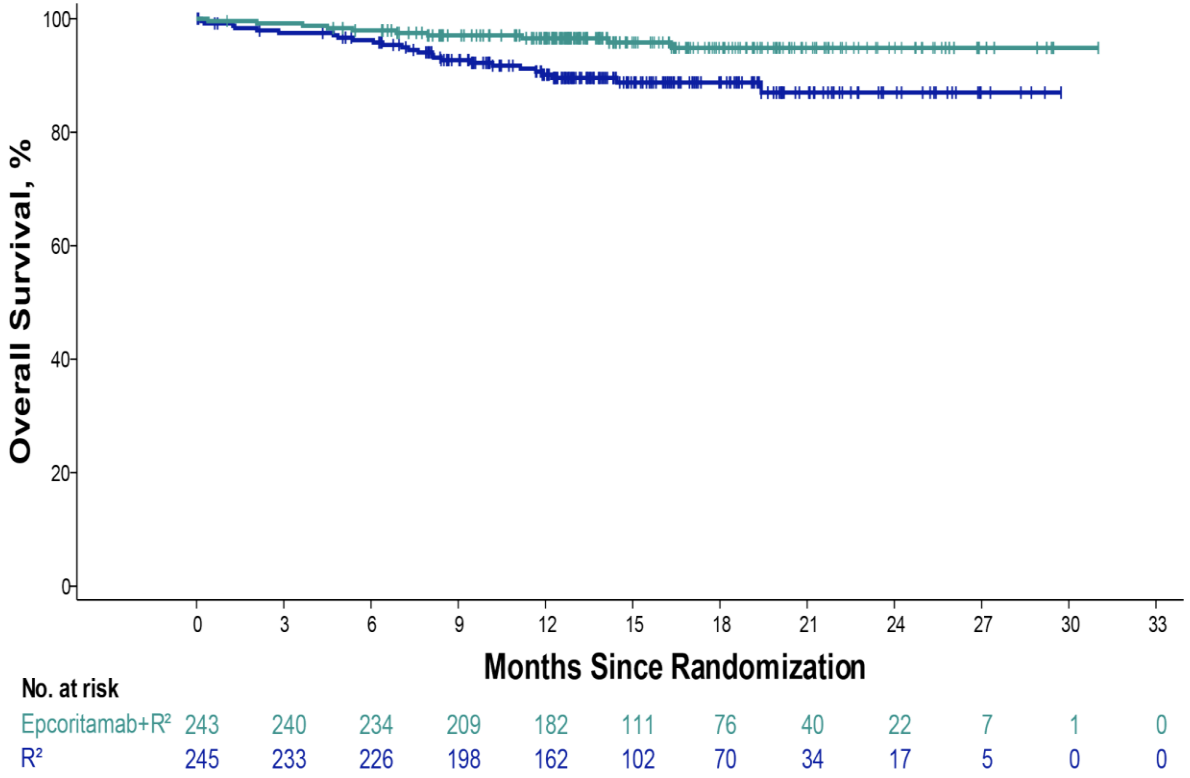
n (%)	Epcoritamab + R^2 (n = 231)	R^2 (n=194)
Events	25	74
Median follow-up, mo	10.6	10.6
Median (95% CI), mo	**NE** (NE-NE)	**11.5** (8.5-18.6)
HR (95% CI), P value	**0.19** (0.12-0.30), P < 0.0001	

ASH 2025. Abstr 466
Lancet. 2026 Jan 10;407(10524):161-173.

KEY DATA

EPCORE-FL-1: 2L+ Epcoritamab + R^2 in R/R FL

Secondary Endpoint: Overall survival (OS)



n (%)	Epcoritamab + R^2 (n = 243)	R^2 (n=245)
Events	10	25
Median follow-up, mo	14.8	14.6
Median (95% CI), mo	**NE** (NE-NE)	**NE** (NE-NE)
HR (95% CI), P value	**0.38** (0.18-0.80), P = 0.0039	

The 16-month estimates for OS was 95.8% with epcoritamab + R^2 and 88.8% with R^2

ASH 2025. Abstr 466
Lancet. 2026 Jan 10;407(10524):161-173.

KEY DATA

EPCORE-FL-1: 2L+ Epcoritamab + R^2 in R/R FL

Safety Summary

n (%)	Epcoritamab + R^2 (n = 243)		R^2 (n=238)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any adverse event	242 (100)	**219 (90)**	235 (99)	**161 (68)**
Serious adverse event	135 (56)	-	69 (29)	-
Adverse event leading to treatment discontinuation	46 (19)	-	29 (12)	-
• Epcoritamab	21 (9)	-	-	-
• Rituximab	7(3)	-	12 (5)	-
• Lenalidomide	45 (19)	-	29 (12)	-
Adverse event of clinical interest >20%				
• **Infections**	**188 (77)**	**81 (33)**	**125 (53)**	**37 (16)**
• **Neutropenia**	**180 (74)**	**167 (69)**	**123 (52)**	**100 (42)**
• **Cytokine release syndrome**	**85 (35)**	-	**1 (< 1)**	-
• Anemia	68 (28)	19 (8)	41 (17)	11 (5)
• Thrombocytopenia	67 (28)	23 (9)	44 (18)	15 (6)
• Pyrexia	58 (24)	1 (< 1)	33 (14)	3 (1)
• Rash	58 (24)	19 (8)	53 (22)	9 (4)
• COVID-19	54 (22)	7 (3)	32 (13)	4 (2)

Fatal adverse events were low:

- Epcoritamab + R^2: 1.6%
- R^2: 3.8%

Median relative dose intensity ≥90% for Epcoritamab + R^2

ASH 2025. Abstr 466
Lancet. 2026 Jan 10;407(10524):161-173.

KEY DATA

EPCORE-FL-1: 2L+ Epcoritamab + R^2 in R/R FL

Select Safety - CRS

3-step up dosage schedule for FL

Cycle[a]	Day	Dose of EPKINLY	
Cycle 1	1	Step-up dose 1	0.16 mg
	8	Step-up dose 2	0.8 mg
	15	Step-up dose 3	3 mg
	22	First full dose	48 mg
Cycle 2 and 3	1, 8, 15, and 22	48 mg	
Cycle 4 to 12	1	48mg	

[a]Cycle = 28 days

- ICANS occurred in 0.8% (1/131) of patients with FL receiving epcoritamab at the recommended 3-step up dosage schedule in combination with R2
- The single ICANS events was reported as Grade 1

n (%)	Epcoritamab + R^2		
	2-SUD (n=110)	3-SUD (n=133)	Overall (n=243)
CRS-n	**50 (45)**	**35 (26)**	**85 (35)**
CRS grade-n			
• 1	40 (36)	28 (21)	68 (28)
• 2	10 (9)	7 (5)	17 (7)
CRS signs and symptoms			
• Fever	49 (98)	33 (94)	82 (96)
• Hypotension	9 (18)	6 (17)	15 (18)
• Hypoxia	1(2)	2 (6)	3 (4)
Time to CRS from first full dose-hour-median (IQR)	n=39; 23.7 (18.5-45.8)	n=25; 34.9 (20.2-100.1)	n=64; 29.5 (19.8-79.4)
Time to CRS resolution from first full dose-hour-median (IQR)	n=39; 27.6 (19.3-84.7)	n=25; 24.0 (11.3-72)	n=64; 26.5 (12.5-72)
CRS intervention-n			
• Treated with Tocilizumab	12 (24)	9 (26)	21 (25)
• Treated with Corticosteroid	23 (46)	13 (37)	36 (42)
ICANs-n	0	1 (1)	1 (<1)
ICANs grade-n			
• 1	0	1 (1)	1 (<1)

The Lancet: Supplementary Material
CRS: Cytokine Release Syndrome

ASH 2025. Abstr 466
Lancet. 2026 Jan 10;407(10524):161-173.

SUMMARY

EPCORE-FL-1

- Fixed duration epcoritamab + R^2 showed a 79% reduction in the risk of progression or death (HR 0.21) compared to R^2 alone
  - The estimated 16-month PFS was 85.5% with the triplet vs. 40.2% with R^2 alone
- Demonstrated significantly higher ORR (95% vs 79%) and CRR (83% vs 50%) with the triplet compared to R^2 respectively
- Median DoR was significantly improved with the triplet, with high rates of deep, sustained remission
- Epcoritamab + R2 can be administered outpatient with 3-step up dosing schedule; monitor for CRS

IMPACT

Epcoritamab plus rituximab and lenalidomide may be a new standard of care for patients with relapsed/refractory follicular lymph

FDA approved November 18, 2025

cornerstone specialty network™

Polling question

In patients with relapsed/refractory follicular lymphoma eligible for R² therapy, how will the EPCORE-FL-1 results and recent FDA approval influence your choice of second-line treatment?

1. I will preferentially use epcoritamab + rituximab + lenalidomide (R²) based on superior response rates and PFS data
2. I will continue to use rituximab + lenalidomide (R²) alone in selected patients
3. I will favor other therapies (e.g., PI3K inhibitors, CAR-T) over R² combinations in most patients

2025 ASH Key Studies

Leukemias
(AML, ALL, CML & myelodysplastic syndrome)

- PARADIGM
- ASC2ESCALATE
  - *Polling Question*
- KOMET-007
  - *Polling Question*
- ***Rapid Reviews***
  - ***VICEROY***
  - ***SAVE***
  - ***FASCINATION***
  - ***VERONA***
  - ***GIMEMA ALL2820***

Myeloma

- MajesTEC-3
  - *Polling Question*
  - *Polling Question*
- COBRA
  - *Polling Question*
- AQUILA
- JCOG1911/B-DASH
- CEPHEUS
  - *Polling Question*

Lymphomas
(including CLL)

- CLL17
  - *Polling Question*
- BRUIN CLL 314
- BRUIN CLL 313
  - *Polling Question*
- EPCORE-FL-1
  - *Polling Question*
- TRANSCEND FL
- ***Rapid Reviews***
  - ***SEQUOIA***
  - ***BGB-11417-201***

TRANSCEND FL

Does Lisocabtagene maraleucel provide long-term efficacy and safety in patient with third-line or later follicular lymphoma?

Lisocabtagene maraleucel is a T-cell engaging CD19-directed, autologous CAR T-cell that targets CD19

3-year follow up

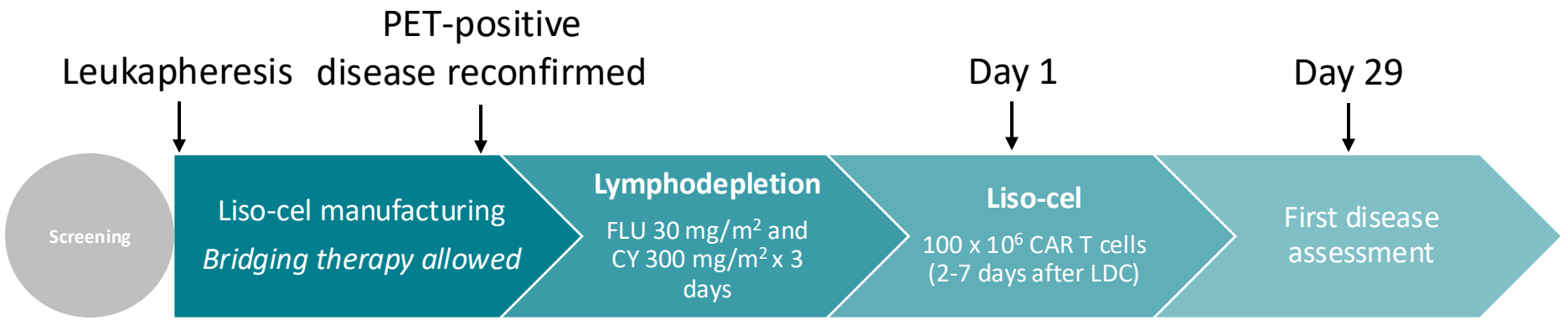
KEY DATA

TRANSCEND FL: Lisocabtagene maraleucel in 3L+ FL

Study Design: Open-label, multicenter, multicohort, phase 2 study

- Age ≥ 18 years
- R/R FL
- FL historically confirmed ≤6 months before screening with PET-positive and measurable disease
- Received combination of an anti-CD20 antibody and an alkylator
- ECOG PS ≤1
- Adequate organ function

(N = 107)



Follow-up
On-study: 5 years
Long term: up to 15 years after liso-cel infusion

Primary endpoint: Overall Response Rate (ORR) (BOR of CR or PR) per IRC by PET/ CT per Lungano 2014 criteria
Secondary endpoints: CR rate, DOR, and PFS per IRC by PET/CT per Lugano 2014, and OS and safety
Post hoc analyses: TTNT, efficacy subgroup analyses by POD24, bulky disease, double-refractory disease and prior bendamustine treatment, longitudinal safety analyses of infection, key laboratory parameters and supportive treatments

KEY DATA

TRANSCEND FL: Lisocabtagene maraleucel in 3L+ FL

Baseline Characteristics

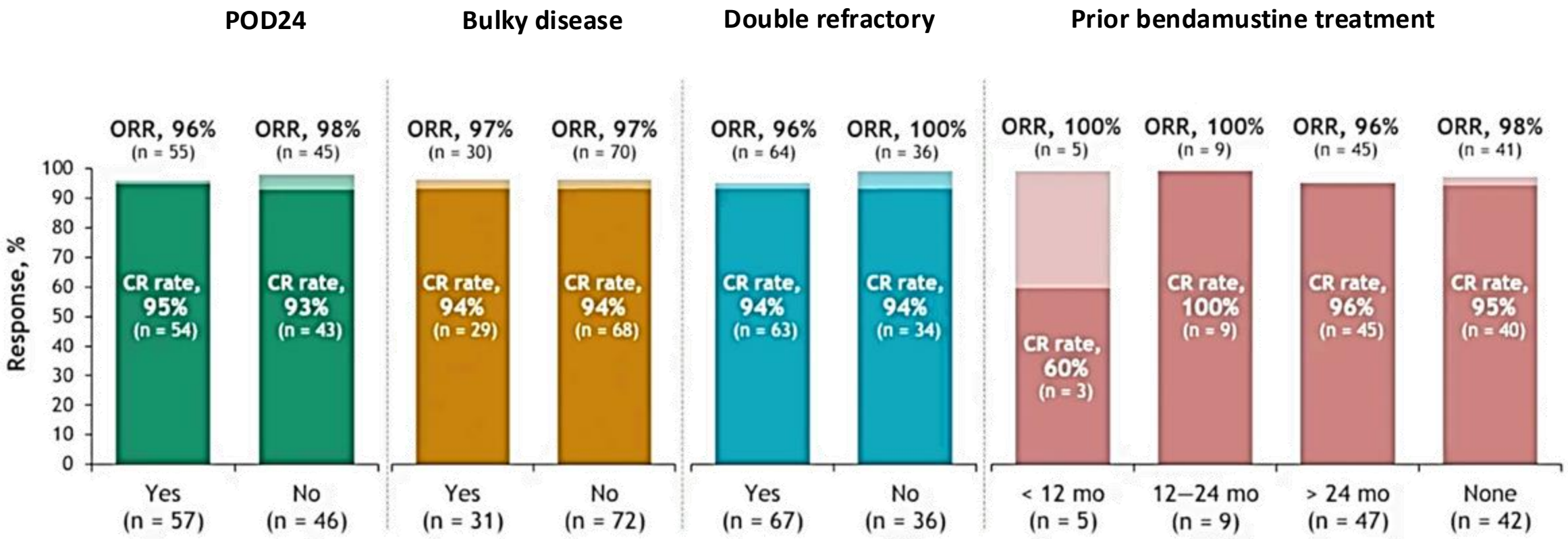
n (%)	3L + FL (n = 107)
Median (range) age, years	62 (23-80)
Met mGELF criteria at most recent relapse	57 (53)
Bulky disease	34 (32)
Median (range) prior lines of systemic therapy	3 (2-10)
Received prior HSCT	33 (31)
Received prior rituximab and lenalidomide	23 (21)
Received prior bendamustine	65 (61)
Double refractory (anti-CD20 and alkylator)	69 (64)
POD24 from initial immunochemotherapy	59 (55)
Received bridging therapy	44 (41)

mGELF: modified Groupe d'Etude des Lymphomes Folliculaires criteria; POD24: Progression of disease within 24 months from initial immunochemotherapy

KEY DATA

TRANSCEND FL: Lisocabtagene maraleucel in 3L+ FL

Primary Endpoint: Overall Response Rate across Subgroups



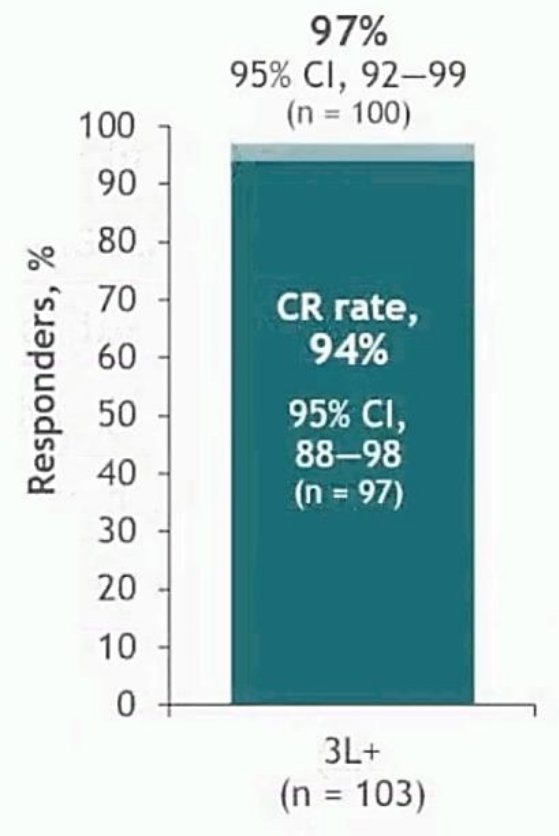
POD24: Progression of disease within 24 months from initial immunochemotherapy

KEY DATA

TRANSCEND FL: Lisocabtagene maraleucel in 3L+ FL

Secondary Endpoints

Complete Response Rate



Median DOR	**NR** (95% CI, 38.5-NR)
36-Month DOR	**70%** (95% CI, 60-78)
Media follow-up: 35.4 months (95% CI, 35.1-35.5)	
Median PFS	**NR** (95% CI, 39.4-NR)
36-Month PFS	**68%** (95% CI, 36.0-36.4)
Media follow-up: 36.3 months (95% CI, 36.0-36.4)	
Median TTNT	**NR**
36-Month TTNT	**75%** (95% CI, 70-80)
Media follow-up: 42.3 months (95% CI, 42.1-42.4)	
Median OS	**NR**
36-Month OS	**86%** (95% CI, 78-92)
Media follow-up: 42.1 months (95% CI, 41.8-42.4)	

KEY DATA

TRANSCEND FL: Lisocabtagene maraleucel in 3L+ FL

Safety Summary

n (%)	3L + FL (n = 107)
Grade ≥ 3 infection	**13 (12)**
• Treatment emergent period	7 (7)
• Post- treatment emergent period	8 (7)
Second primary malignancy	11 (10)
• Non-hematological	7 (7)
• Hematological	4 (4)
Grade ≥ 3 cytopenia at Day 90 visit	23 (21)
• Reade ≤ 2 by Day 365, n/N (%)	18/19 (95)

TRANSCEND FL

SUMMARY

- Single infusion of liso-cel demonstrated deep and durable responses (36-month DOR, 70%) with sustained survival (36-month OS, 86%)
- Liso-cel showed efficacy across subgroups with ORR of 96-100% and 3 years response rates of 60-83%, even among patients with high-risk characteristics
- Longitudinal safety analyses demonstrated favorable safety profile including low infection rates, high rates of hematologic recovery and modest supportive care needs

IMPACT

Lisocabtagene Maraleucel may considered in the third-line or late for patients with follicular lympho

FDA approved on May 15, 2024

cornerstone specialty network™

ASH 2025: RAPID REVIEWS

SEQUOIA

BGB-11417-201

KEY DATA

SEQUOIA: Zanubrutinib in treatment naïve CLL/SLL - **6 year follow up**

Study Design: Phase 3 trial

Key eligibility criteria

- Untreated CLL/SLL
- Met iwCLL criteria for treatment
- Measurable disease by CT/MRI
- Unsuitable for FCR

Arms A and B
Without del(17p)

Open label

R 1:1

Zanubrutinib
160 mg BID until PD, unacceptable toxicity or end of study
N=241

Bendamustine + rituximab
Maximum 6 cycle
N=238

Arm C
With del(17p)

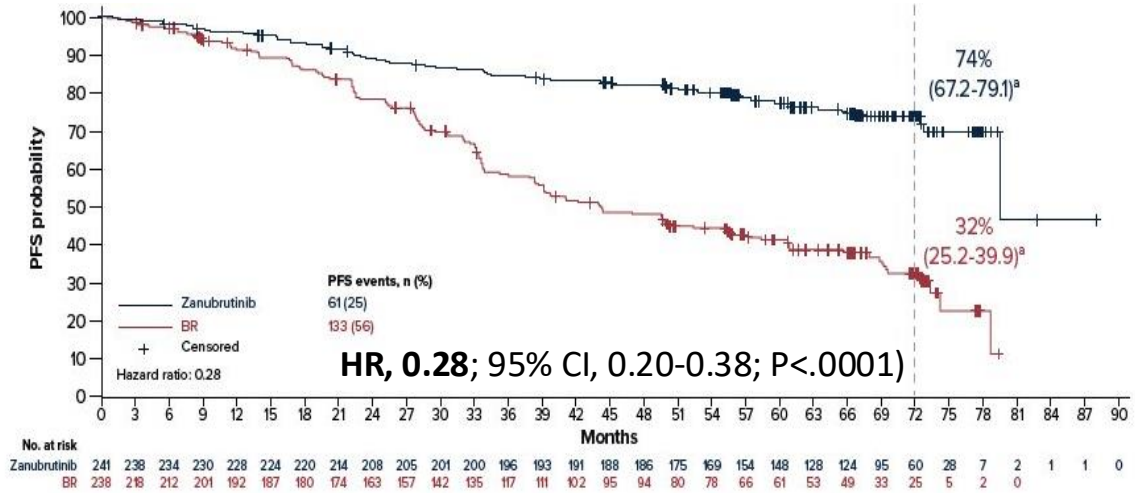
Zanubrutinib
160 mg BID until PD, unacceptable toxicity or end of study
N=111

Key endpoints: Progression-free survival (PFS), overall response rate (ORR), overall survival (OS), and safety per CTCAE

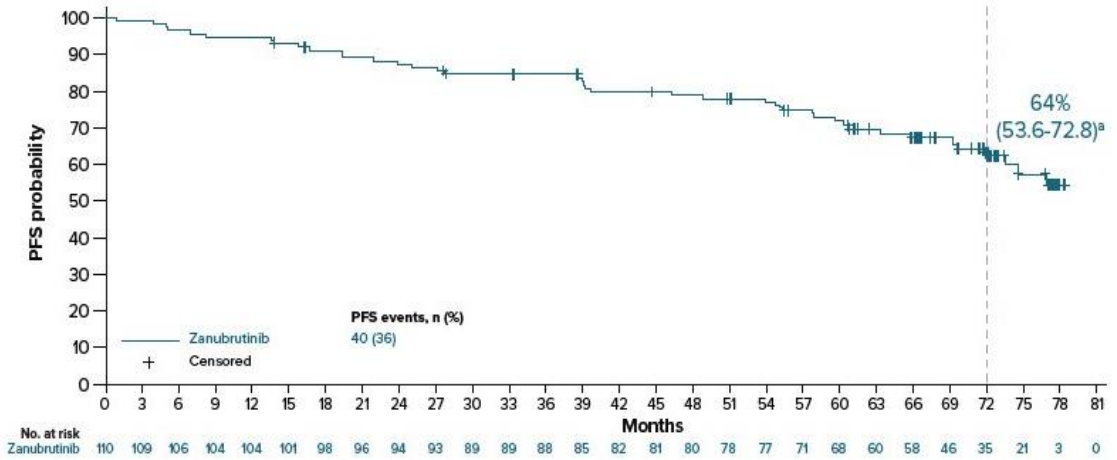
As of April 30, 2025, median follow-up in **Arms A and B was 72.8 months** (range, 0.0-90.0 months); median follow-up in **Arm C was 76.7 months** (range, 5.0-86.9 months)

Key endpoint: Progression-free survival (PFS)

Patients in Arms A and B - Without del(17p)



Patients in Arm C - With del(17p)



KEY DATA

SEQUOIA: Zanubrutinib in treatment naïve CLL/SLL - **6 year follow up**

Key Endpoints:

	Without del(17p)		With del(17p)
	Zanubrutinib n=241	BR n=238	Zanubrutinib n=110
Responders/ patients	120/125	107/123	65/66
ORR (CI 95%)	**98%** (90.9-98.7)	**89%** (79.7-92.4)	97% (91.8-100.0)
CR/CRi	24%	24%	21%

CR/CRi=complete response/complete response with incomplete hematopoietic recovery

At 72 months	Zanubrutinib n=241	BR n=238	Zanubrutinib n=110
PFS2 (CI 95%)	**84%** (78.2%-87.8%)	**76%** (69.9%-81.6%)	82% (73.6%-88.3%)

PFS2=time to second PFS event

HR 0.71; *P=0.052*

Time to next Rx (CI 95%)	**89%** (84.2%-92.6%)	**55%** (47.7%-62.2%)	83% (73.6%-88.6%)

HR 0.22; *P<0.0001*

At 72 months	Zanubrutinib n=241	BR n=238	Zanubrutinib n=110
OS	84%	80%	83%

Key Endpoint: Safety

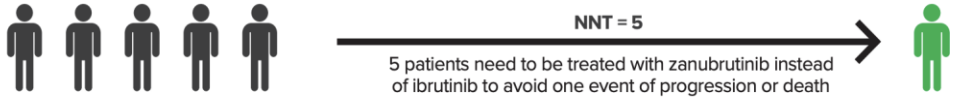
	Without del(17p)				With del(17p)	
	Zanubrutinib n=240		BR n=227		Zanubrutinib n=111	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Adverse event of special interest, n (%)	224 (93)	142 (59)	210 (93)	163 (72)	103 (93)	65 (59)
• Anemia	24 (10)	2 (1)	48 (21)	6 (3)	11 (10)	0
• Neutropenia	34 (14)	26 (11)	104 (46)	94 (41)	13 (12)	12 (11)
• Contusion	57 (24)	0	9 (4)	0	24 (22)	0
• Hypertension	49 (20)	31 (13)	29 (13)	15 (7)	21 (19)	11 (10)
• COVID-19	100 (42)	23 (10)	21 (14)	4 (2)	43 (39)	8 (7)
• Upper respiratory tract infection	51 (21)	2 (1)	34 (15)	2 (1)	32 (29)	0
• Pneumonia	38 (16)	18 (8)	27 (12)	12 (5)	18 (16)	7 (6)
• Urinary tract infection	38 (16)	4 (2)	23 (10)	6 (3)	18 (16)	3 (3)
• Basal cell carcinoma	23 (10)	2 (1)	10 (4)	1 (0)	19 (17)	0

KEY DATA

Health Economics and Outcomes Research and Real-World Evidence for Zanubrutinib

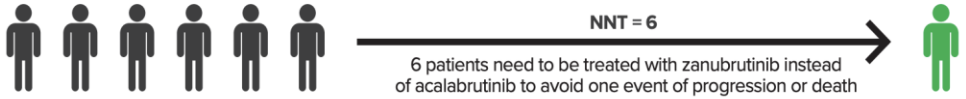
Number needed to treat (NNT): Zanubrutinib vs Ibrutinib

- The base-case results from the NNT model indicate that for the treatment of patients with high-risk R/R CLL over 24 months, every **5** patients treated with zanubrutinib instead of ibrutinib results in the avoidance of one disease progression or death



Number needed to treat (NNT): Zanubrutinib vs Acalabrutinib

- The base-case results from the NNT model indicate that for the treatment of patients with high-risk R/R CLL over 24 months, every **6** patients treated with zanubrutinib instead of acalabrutinib results in the avoidance of one disease progression or death

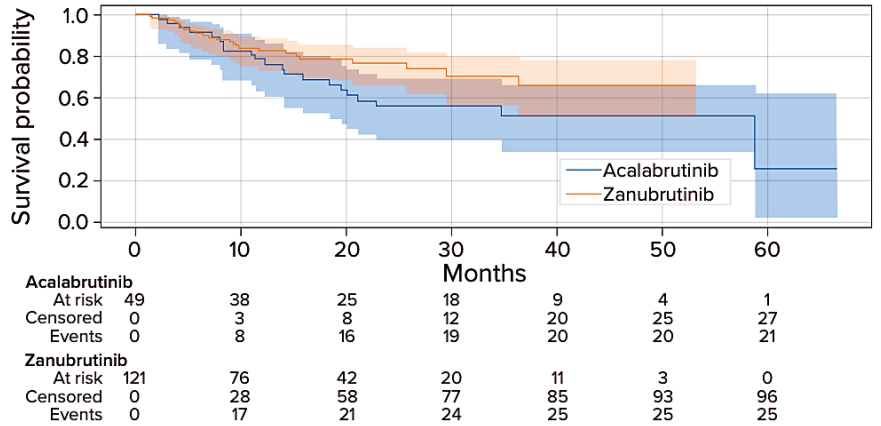


The NNT analysis suggests that among patients with high-risk R/R CLL, zanubrutinib is associated with reduced risk of progression/death compared to ibrutinib and acalabrutinib (~ 17-20 out of 100 patients will avoid disease progression events or deaths)

Kaplan-Meier Curves for Outcomes With Zanubrutinib vs Acalabrutinib

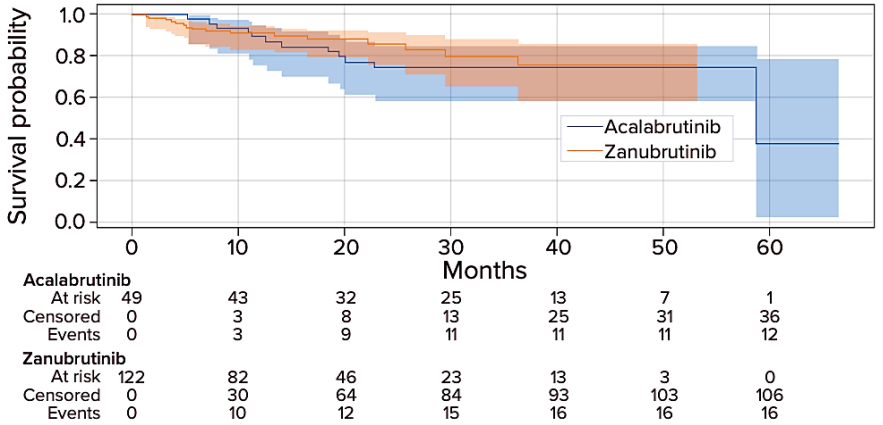
Time to Next Treatment

The median TTNT was 59 (95% CI: 20 - NR) months for acalabrutinib and **not reached** (NR) (95% CI: NR-NR) months for **zanubrutinib**



Overall Survival

The 12-month survival probabilities were 89% (95% CI: 76-95%) for acalabrutinib, and **91% (95% CI: 84-95%) for zanubrutinib**



Zanubrutinib continues to demonstrate robust efficacy and favorable safety profile for treatment naïve CLL/SLL

ASH 2025: RAPID REVIEWS

SEQUOIA

BGB-11417-201

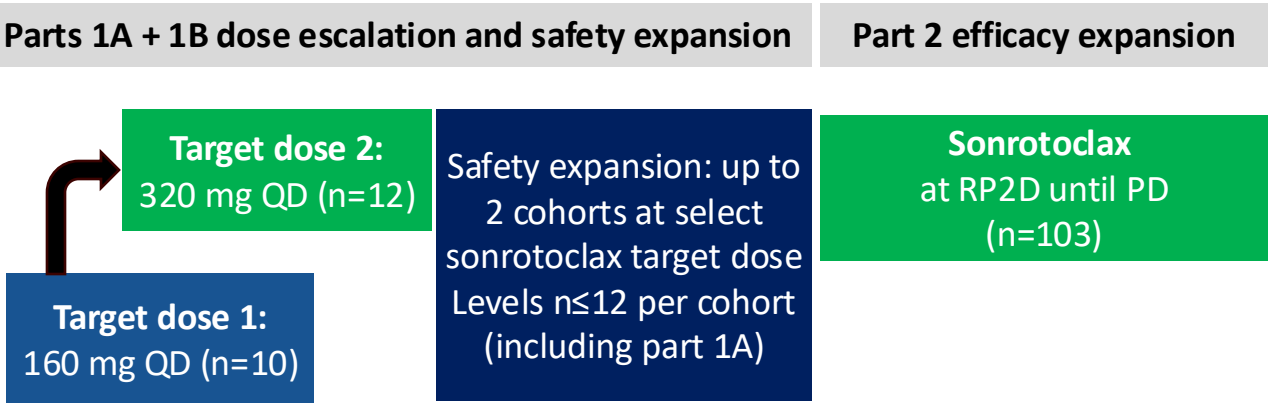
KEY DATA

BFG-11417-201: Sonrotoclax monotherapy in relapse/ refractory mantle cell lymphoma

Study Design: Phase 1/2 study

Eligibility criteria:

- Aged ≥18 years
- Histologically-confirmed MCL per WHO 2016 classification
- ≥1 line of anti-CD20-based therapy and ≥1 BTK inhibitor
- ECOG PS of 0-2
- No prior BCL2 inhibitor treatment



Part 1 Endpoints
Primary: DLTs (part 1A), TEAEs, SAEs, AAs leading to discontinuation, TLS events
Secondary: preliminary antitumor activity

Sonrotoclax target doses were achieved after a ~4 week ramp-up that did not require hospitalization or 12- or 24-hour post-dose laboratory monitoring

Part 2 Endpoints
Primary: ORR by IRC (Lugano 2014)
Secondary: ORR by INV, DOR by IRC and INV, PFS by IRC and INV, TTR by IRC and INV, HR-QOL, OS, safety

Part 2 Primary endpoints: Overall response rate (ORR) and time to response (TTR)

n (%)	Part 2: Sonrotoclax 320 mg (n=103)	
Parameters	**IRC-assessed**	**INV-assessed**
ORR	54 (52.4%)	49 (47.6%)
95% CI, %	42.4-62.4	37.6-57.6
1-sided *P* value	<.0001	N/A
CR rate	16 (15.5)	23 (22.3)
95% CI, %	9.1-24.0	14.7-31.6
TTR, median (range), months	1.9 (1.6-6.2)	1.9 (1.6-4.0)

With a median study follow-up of 14.2 months, patients who received sonrotoclax 320 mg in part 2 demonstrated:

- Median **DoR by IRC** was **15.8 months** (95% CI, 7.4 months-NE); 63% of patients who responded remained in remission after 9 months
- Median **progression-free survival (PFS) by IRC** was **6.5 months** (95% CI, 4.0-10.4 months)
- Median **overall survival (OS)** was **not reached** (95% CI, 14.8 months-NE)

Nov 26 2025: U.S. FDA Granted Priority Review to Sonrotoclax for the Treatment of Relapsed or Refractory Mantle Cell Lymphoma (approved in China Jan 6, 2026)

ASH 2025:

Lymphoma

Key Takeaways

Q&A

@SujithKalmadiMD

CLL17: Front-line fixed-duration venetoclax-obinutuzumab and venetoclax-ibrutinib achieved non-inferiority in progression-free survival vs continuous ibrutinib (3-yr PFS rate: Ven + Ibr 79.4%; Ven + Obin 81.1%; Ibr 81.0%) in patients with previously untreated chronic lymphocytic leukemia – *Not yet FDA approved*

BRUIN CLL-314: In treatment-naive and BTKi-naive CLL/SLL, first-line pirtobrutinib demonstrated noninferior ORR vs ibrutinib in the ITT (87.0% vs 78.5%) and R/R (84.0% vs 74.8%) populations compared to ibrutinib – *Not yet FDA approved*

BRUIN CLL-313: Pirtobrutinib in the first-line setting reduced risk of progressive disease or death by 80% compared to bendamustine plus rituximab for patients with treatment-naive CLL/SLL – *Not yet FDA approved*

EPCORE-FL-1: Epcoritamab plus rituximab and lenalidomide in second line or later showed a 79% reduction in the risk of progression or death (HR 0.21) and demonstrated significantly higher ORR (95% vs 79%) and CRR (83% vs 50%) compared to ^{R2} respectively for patients with relapsed/refractory follicular lymphoma – FDA approved November 2025

TRANSCEND FL: Follicular lymphoma in third-line or later, single infusion of lisocabtagene maraleucel demonstrated deep and durable responses (36-month DOR, 70%) with sustained survival (36-month OS, 86%) – *FDA approved May 2024*

SEQUOIA: In treatment naïve CLL/SLL, first-line zanubrutinib reduces the risk of progression or death 72% compared to bendamustine + rituximab – *FDA approved January 2023*

BGD-11417-201: Sonrotoxlax monotherapy showed to provide clinically beneficial outcomes of 52.4% overall response rate (ORR) and median duration of response (DoR) of 15.8 months in heavily pretreated patients with advanced mantle cell lymphoma – *Not yet FDA approved*