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Oral Presentation #901

CARDINAL: A Phase 1 Study of TERN-701, a Novel, Investigational Allosteric BCR::ABL1 Inhibitor for Patients with Previously Treated CML

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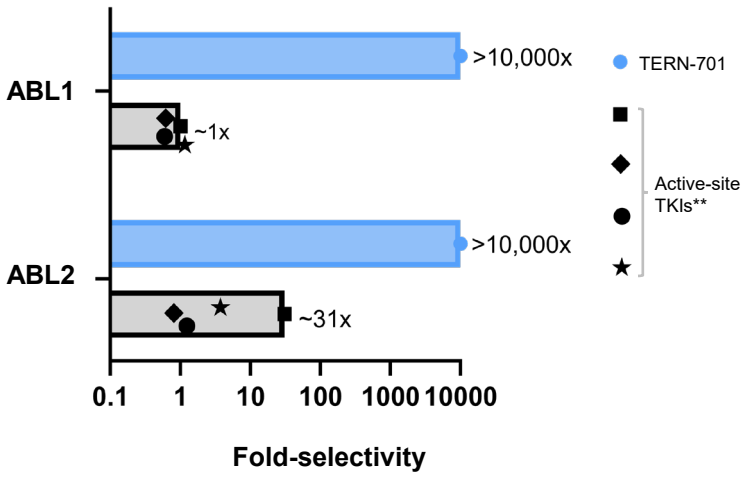
This study is sponsored by Terns Pharmaceuticals. For more information, please refer to https://clinicaltrials.gov/study/NCT06163430/

Oral presentation at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL, and online.

TERN-701: Background

Highly selective binding to BCR::ABL1 myristate pocket

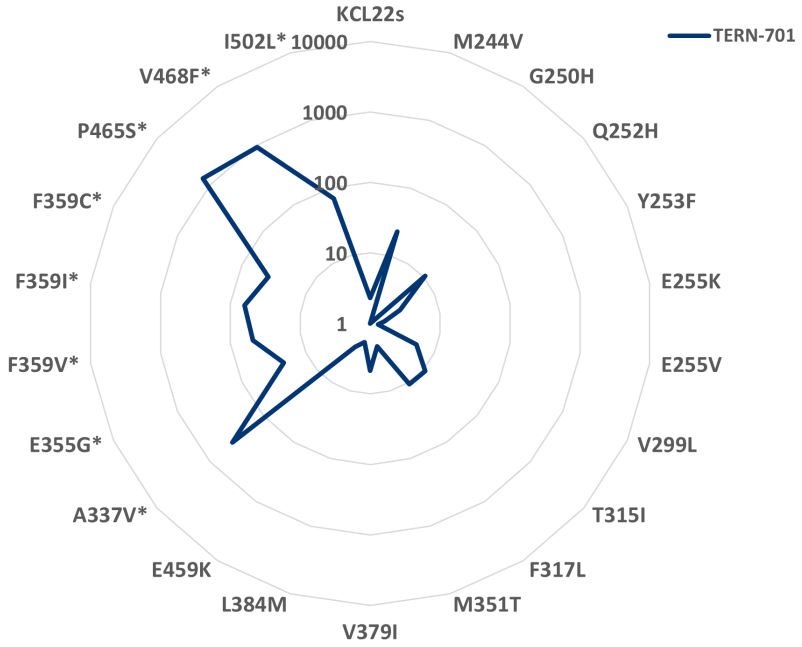
Selectivity* of TERN-701 vs Active-Site TKIs



*BCR::ABL1 potency derived from KCL22-s cytotoxicity assay (n=3).
**Active-site TKIs include imatinib, dasatinib, ponatinib & ELVN-001. ELVN-001 selectivity data derived from Enliven Company Overview, April 2024.

Highly Potent against native and mutated BCR::ABL1 *in vitro*

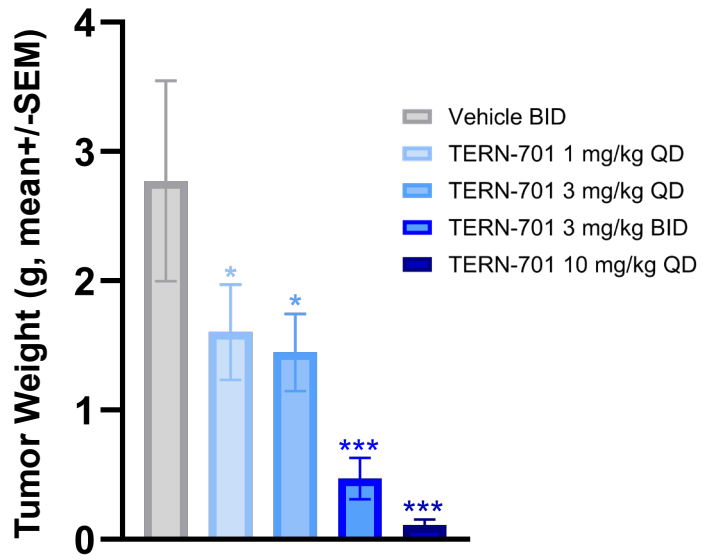
Cell-Based Potency (IC_{50}, nM)



*Denotes myristoyl mutations or mutations indicated in resistance to allosteric inhibition of BCR::ABL1. IC_{50}=concentration of inhibitor required to bring about 50% inhibition/measurable effect.

Dose-dependent ***in vivo*** **anti-tumor activity**

K562 Xenograft (Day 14)



*p<0.05, ***p<0.001.

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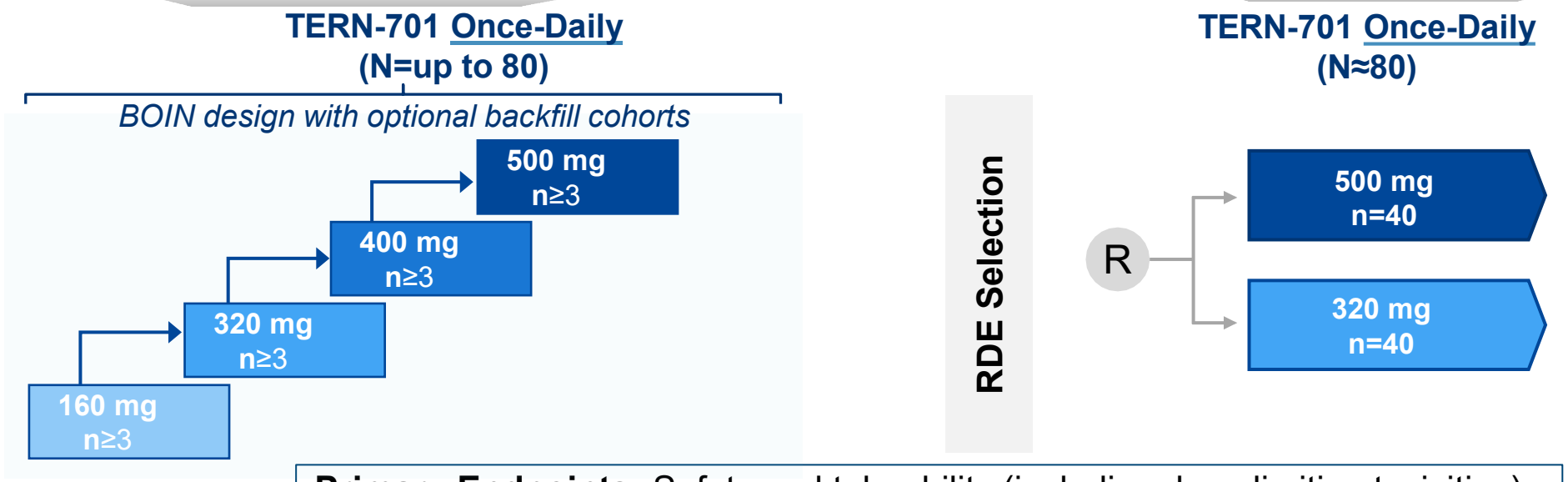
TERN-701 Phase 1 CARDINAL Trial in CP-CML

Part 1 Dose Escalation

- Received ≥2 TKIs OR had treatment failure/suboptimal response to frontline 2G TKI
- Prior asciminib/ponatinib failure/intolerance allowed; myristate pocket resistance mutations excluded
- T315I and non-T315I mutations allowed

Part 2 Dose Expansion

- Treatment failure OR suboptimal response to ≥1 prior TKI
- Prior asciminib/ponatinib treatment failure/intolerance allowed; myristate pocket resistance mutations excluded
- Only non-T315I mutations allowed



Data cutoff:
September 13, 2025

Primary Endpoints: Safety and tolerability (including dose-limiting toxicities)

Secondary Endpoints: Efficacy (molecular responses) and pharmacokinetics

CP-CML=chronic-phase chronic myeloid leukemia; TKI=tyrosine kinase inhibitor. Jabbour E., et al. Oral presentation at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL. Presentation #901.

TERN-701 Phase 1: Baseline Characteristics

	All Patients (N=63)	
Age, median (range), years	57 (29–86)	
Baseline *BCR::ABL1*^{IS}, n (%)		
>10%	28 (44%)	
>1% to 10%	8 (13%)	
>0.1% to 1%	16 (25%)	
≤0.1%	11 (18%)	
Discontinuation to last TKI, n (%)		
Lack of efficacy (per ELN 2020 criteria)	40 (64%)	
Lack of tolerability	18 (29%)	
Other	5 (8%)	
Median number of prior unique TKIs (range)	3 (1–6)	
≥3 prior, n (%)	38 (60%)	
Prior asciminib	24 (38%)	
Prior ponatinib	14 (22%)	
BCR::ABL1 mutations, n (%)	T315I	6 (10%)
	F317L	2 (3%)
	E255K	1 (2%)

IS=International Scale for *BCR::ABL1* transcript measurement; TKI=tyrosine kinase inhibitor; ELN=European LeukemiaNet.

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TERN-701 Phase 1: Patient Disposition

	All patients (N=63)
Median duration of treatment, months (range)	6.1 (0.2–19)
Treatment ongoing	55 (87%)
Discontinued from treatment	8 (13%)
Treatment failure	4
Adverse events	1
Physician decision	1
Other (withdrew consent/lost to follow up)	2

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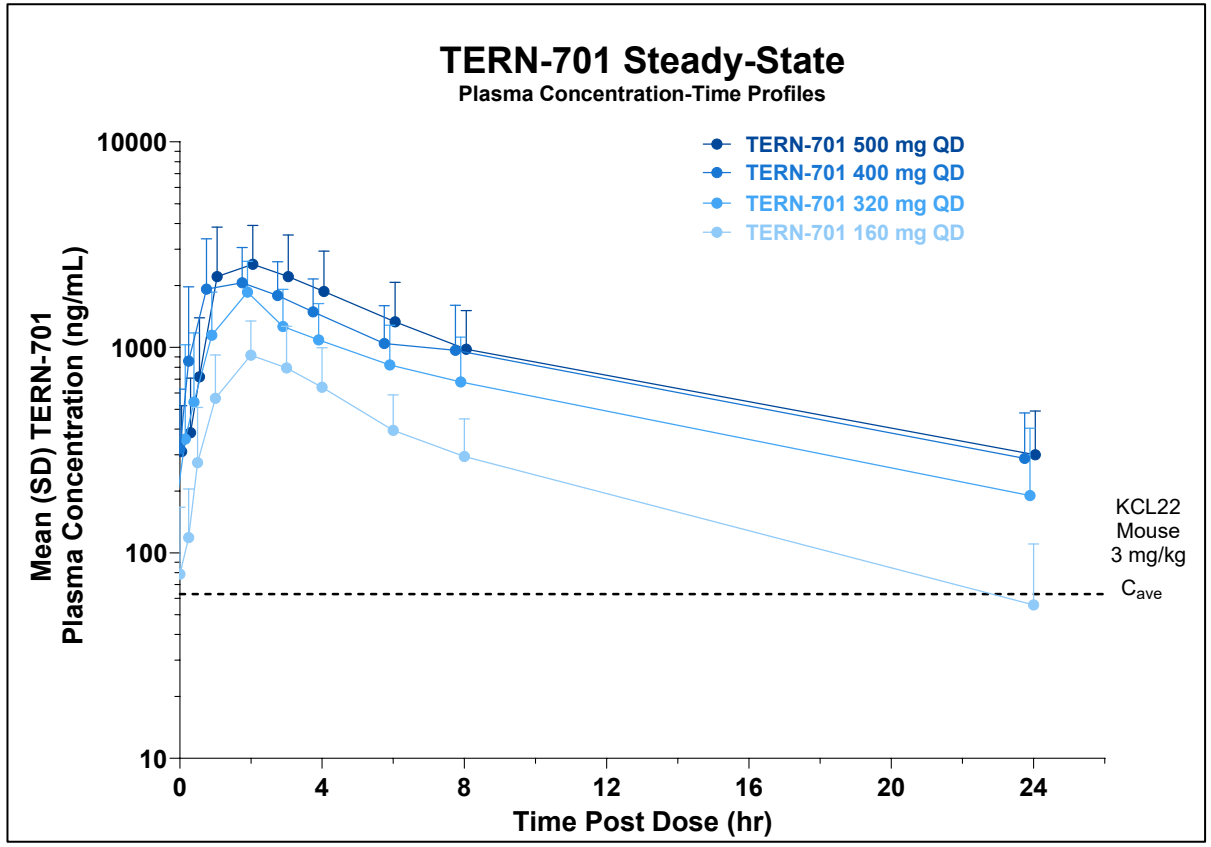
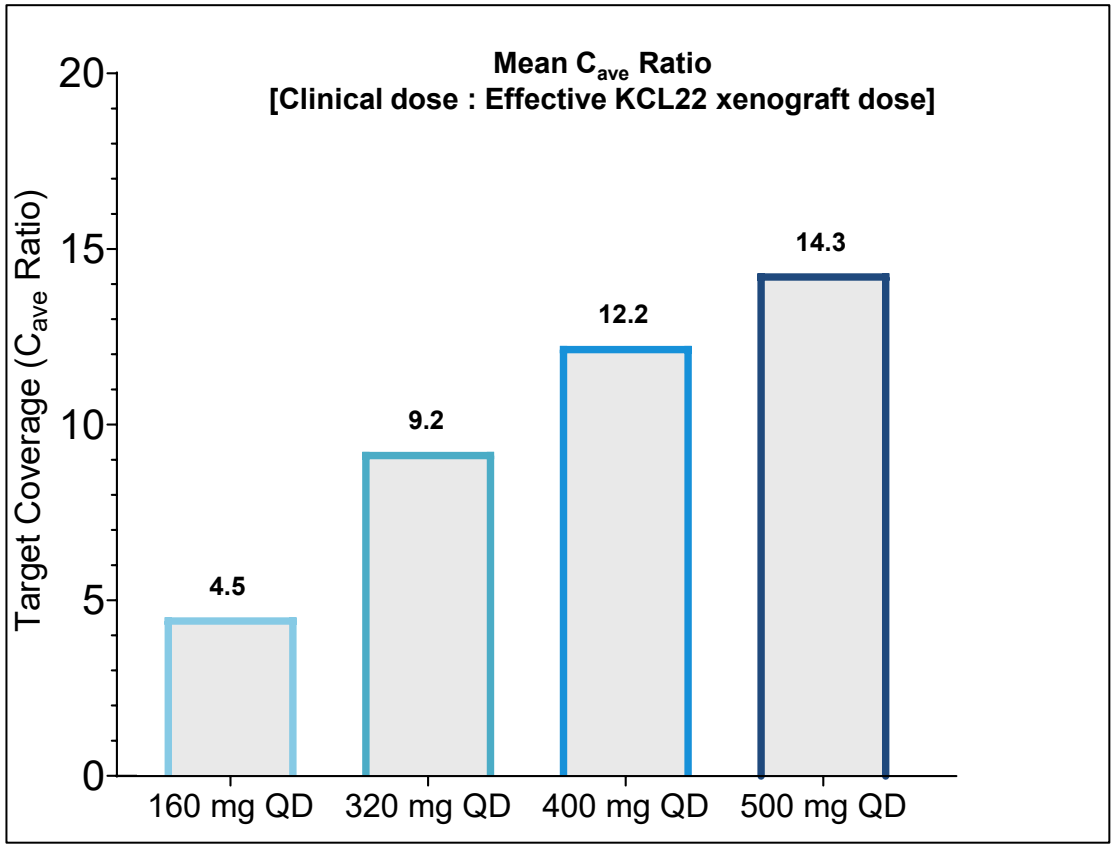
TERN-701 Phase 1: Pharmacokinetic Profile





- Linear PK with approximately **dose-proportional increase in exposure** from 160–500 mg exceeding efficacious exposures in KCL-22 mouse model by up to 14-fold
- No **clinically significant difference** in exposure (AUC) when dosed fasted or with a high-fat meal

QD=once daily; C_{ave}=average concentration; SD=standard deviation; PK=pharmacokinetics; AUC=area under curve.

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TERN-701 Phase 1: Overall Safety Summary

Patient Incidence, n (%)	All patients (N=63)
Treatment-Emergent Adverse Events (TEAEs)	
Overall, Any Grade	51 (81%)
Overall, Grade 3 or Higher	20 (32%)
Dose Limiting Toxicities	0 (0%)
Leading to Treatment Discontinuation	1 (2%)

- No DLTs in dose escalation and MTD was not reached

DLTs=dose-limiting toxicities; MTD=maximum tolerated dose. Jabbour E., et al. Oral presentation at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL. Presentation #901.

TERN-701 Phase 1: AEs Regardless of Causality in ≥10% of Patients

Preferred Term, n (%)	160 mg QD n=10		320 mg QD n=21		400 mg QD n=13		500 mg QD n=19		All patients (N=63)	
	All Grade	≥Grade 3	All Grade	≥Grade 3	All Grade	≥Grade 3	All Grade	≥Grade 3	All Grade	≥Grade 3
Hematologic										
Thrombocytopenia	2 (20%)	0	5 (24%)	3 (14%)	2 (15%)	2 (15%)	1 (5%)	0	10 (16%)	5 (8%)
Neutropenia	1 (10%)	0	4 (19%)	2 (10%)	2 (15%)	2 (15%)	1 (5%)	1 (5%)	8 (13%)	5 (8%)
Anemia	1 (10%)	0	2 (10%)	1 (5%)	1 (8%)	0	2 (11%)	0	6 (10%)	1 (2%)
Non-Hematologic										
Diarrhoea	1 (10%)	0	5 (24%)	0	3 (23%)	0	4 (21%)	0	13 (21%)	0
Headache	3 (30%)	0	6 (29%)	0	2 (15%)	0	1 (5%)	0	12 (19%)	0
Nausea	4 (40%)	0	4 (19%)	0	2 (15%)	0	2 (11%)	0	12 (19%)	0
Fatigue	1 (10%)	0	4 (19%)	0	2 (15%)	1 (8%)	2 (11%)	0	9 (14%)	1 (2%)
Abdominal pain	3 (30%)	1 (10%)	2 (10%)	0	1 (8%)	0	2 (11%)	0	8 (13%)	1 (2%)
Myalgia	0	0	4 (19%)	0	3 (23%)	0	1 (5%)	0	8 (13%)	0
Back pain	1 (10%)	0	2 (10%)	0	1 (8%)	0	3 (16%)	0	7 (11%)	0
Rashes	2 (20%)	0	1 (5%)	1 (5%)	2 (15%)	0	2 (11%)	0	7 (11%)	1 (2%)
ALT increased	1 (10%)	0	2 (10%)	0	0	0	3 (16%)	0	6 (10%)	0
Dizziness	1 (10%)	0	4 (19%)	0	1 (8%)	0	0	0	6 (10%)	0

- No clinically significant changes in blood pressure were reported
- No clinical pancreatitis or symptomatic lipase elevations of any grade

AEs=adverse events; QD=once daily. Jabbour E., et al. Oral presentation at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL. Presentation #901.

TERN-701 Phase 1: Grade ≥3 AEs Regardless of Causality (>1 patient)

Preferred Term, n (%)	160 mg QD n=10	320 mg QD n=21	400 mg QD n=13	500 mg QD n=19	All patients (N=63)
Thrombocytopenia	0	3 (14%)	2 (15%)	0	5 (8%)
Neutropenia	0	2 (10%)	2 (15%)	1 (5%)	5 (8%)
Leukopenia	0	1 (5%)	1 (8%)	0	2 (3%)

- Low rate of ≥G3 TEAEs (all <10%)
- One patient with G3 peripheral ischemia (foot) unrelated to treatment
  - Patient had a 5-year history of peripheral vascular disease with chronic ponatinib treatment
  - AE occurred ~2 months after ponatinib discontinuation

AEs=adverse events; QD=once daily; G3=Grade 3; TEAEs=treatment-emergent adverse events. Jabbour E., et al. Oral presentation at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL. Presentation #901.

TERN-701 Phase 1: Efficacy Evaluable Criteria

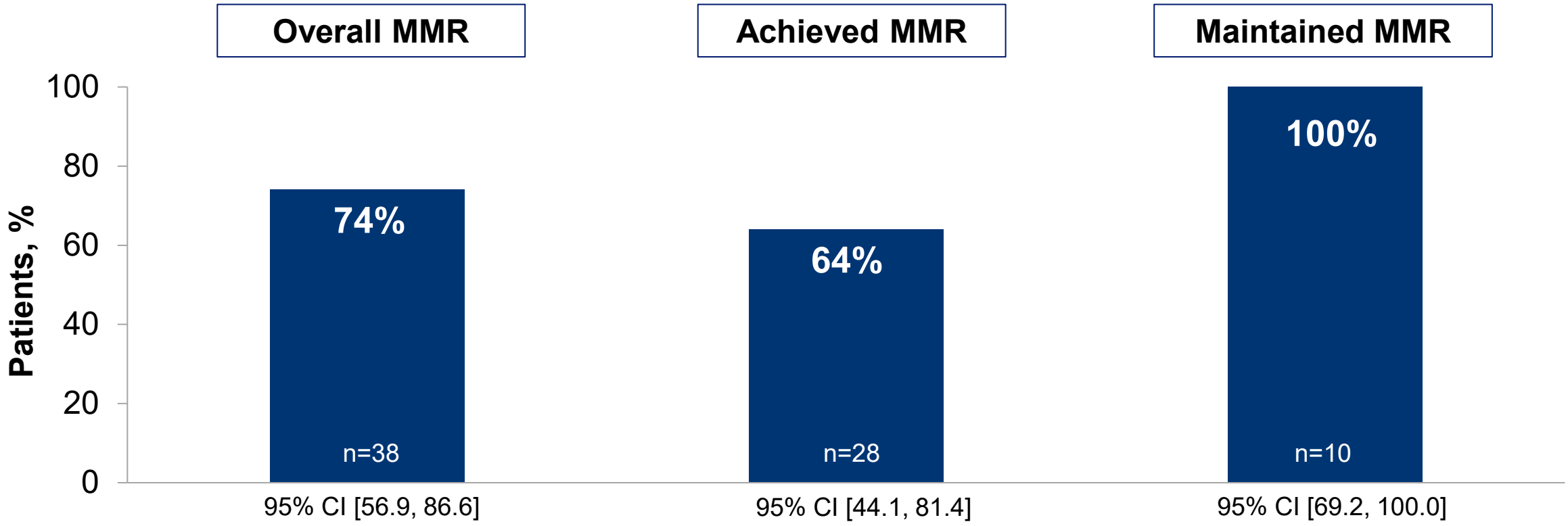
- Efficacy evaluable cohort includes patients **without T315I or atypical transcripts**
- As of September 13, 2025, **38 patients were evaluable for MMR by 24 weeks** assessed centrally

Efficacy Evaluable Criteria

- Received TERN-701 for at least 24 weeks, OR
- **Achieved** MMR or better prior to 24 weeks (if no MMR at baseline), OR
- **Maintained** MMR or better for ≥24 weeks (if in MMR at baseline), OR
- Discontinued treatment for any reason prior to 24 weeks

MMR=major molecular response. Jabbour E., et al. Oral presentation at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL. Presentation #901.

TERN-701 Phase 1: MMR Achievement Rates by Week 24 (N=38)



MMR=major molecular response; CI=confidence interval.

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TERN-701 Phase 1: Categorical MR Shift from Baseline by 24 Weeks

Post-treatment *BCR::ABL1*^{IS}	Baseline *BCR::ABL1*^{IS} level						
N=38	**MR5** ≤0.001% (n=0)	**MR4.5** >0.001 to 0.0032% (n=1)	**MR4** >0.0032 to 0.01% (n=3)	**MR3 (MMR)** >0.01 to 0.1% (n=6)	**MR2** >0.1 to 1% (n=11)	**MR1** >1 to 10% (n=6)	>10% (n=11)
MR5 ≤0.001%		1	2	1	1	1	1
MR4.5 >0.001 to 0.0032%			1		3		
MR4 >0.0032 to 0.01%				1	1	1	
MR3 (MMR) >0.01 to 0.1%				4	6		4
MR2 >0.1 to 1%						3	
MR1 >1 to 10%						1	1
>10%							5

Compared with baseline, *BCR::ABL1*^{IS} level category by week 24: Stable | Lack of Efficacy | Improvement in MR category

IS=International Scale for *BCR::ABL1* transcript measurement;; MR=molecular response; MMR=major molecular response.

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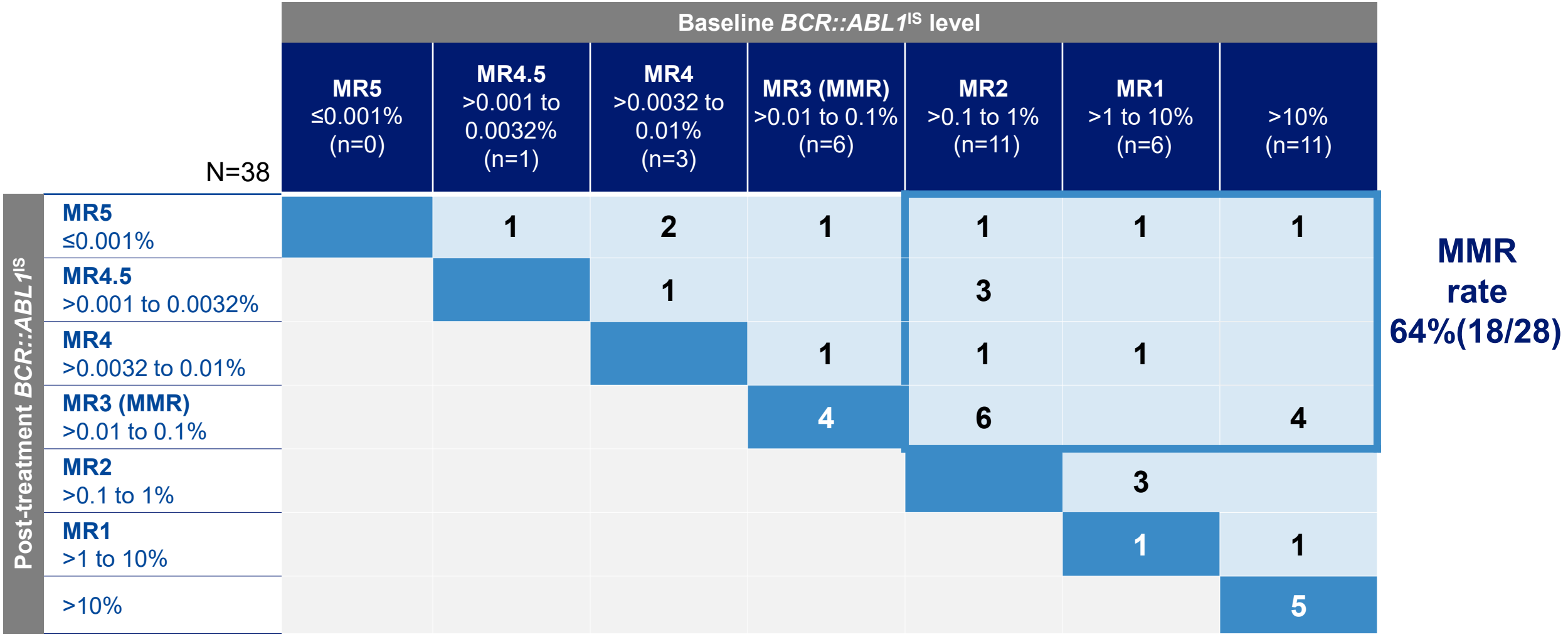
TERN-701 Phase 1: 64% MMR Achievement by 24 Weeks



Compared with baseline, *BCR::ABL1*^{IS} level category by week 24: Stable | Lack of Efficacy | Improvement in MR category

IS=International Scale for *BCR::ABL1* transcript measurement; MR=molecular response; MMR=major molecular response.

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TERN-701 Phase 1: MMR Achievement Rate in Patients with High Baseline Transcript Levels

Post-treatment *BCR::ABL1*^{IS}	Baseline *BCR::ABL1*^{IS} level						
N=38	**MR5** ≤0.001% (n=0)	**MR4.5** >0.001 to 0.0032% (n=1)	**MR4** >0.0032 to 0.01% (n=3)	**MR3 (MMR)** >0.01 to 0.1% (n=6)	**MR2** >0.1 to 1% (n=11)	**MR1** >1 to 10% (n=6)	>10% (n=11)
MR5 ≤0.001%		1	2	1	1	1	1
MR4.5 >0.001 to 0.0032%			1		3		
MR4 >0.0032 to 0.01%				1	1	1	
MR3 (MMR) >0.01 to 0.1%				4	6		4
MR2 >0.1 to 1%						3	
MR1 >1 to 10%						1	1
>10%							5

MMR rate in pts with baseline transcripts >10%
45% (5/11)

Compared with baseline, *BCR::ABL1*^{IS} level category by week 24: Stable | Lack of Efficacy | Improvement in MR category

IS=International Scale for *BCR::ABL1* transcript measurement; MR=molecular response; MMR=major molecular response; Pts=patients.

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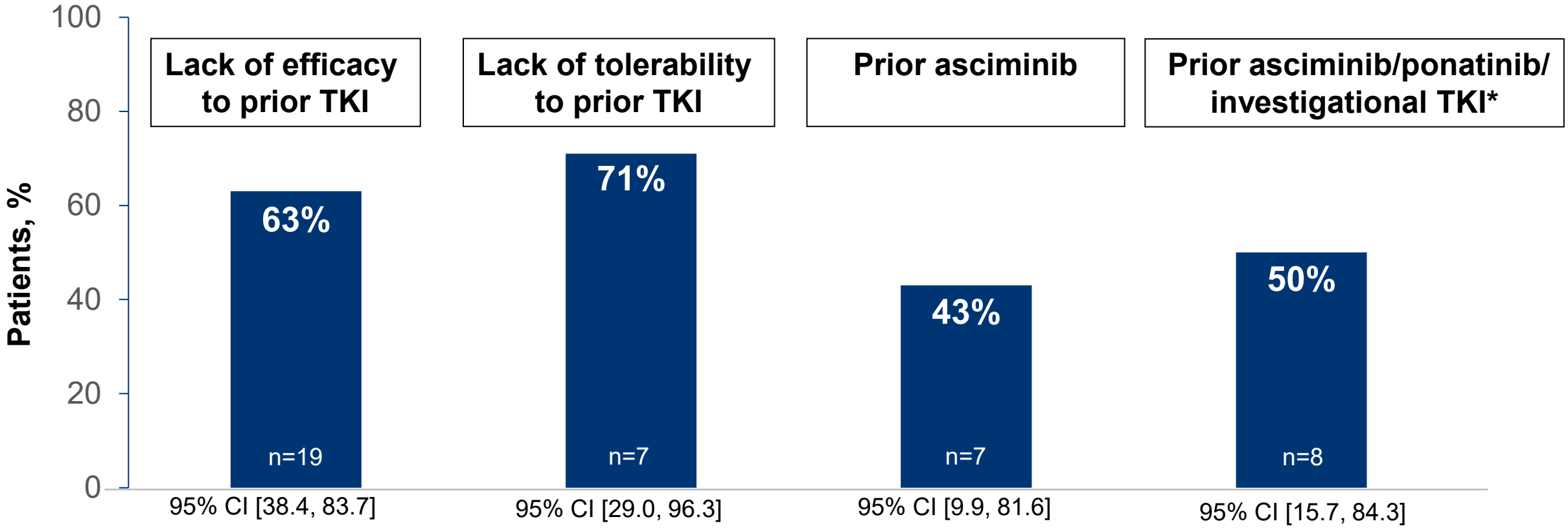
TERN-701 Phase 1: MMR Achievement by 24 Weeks Across Key Patient Subgroups



*Investigational TKI: ELVN-001; MMR=major molecular response; TKI=tyrosine kinase inhibitor.

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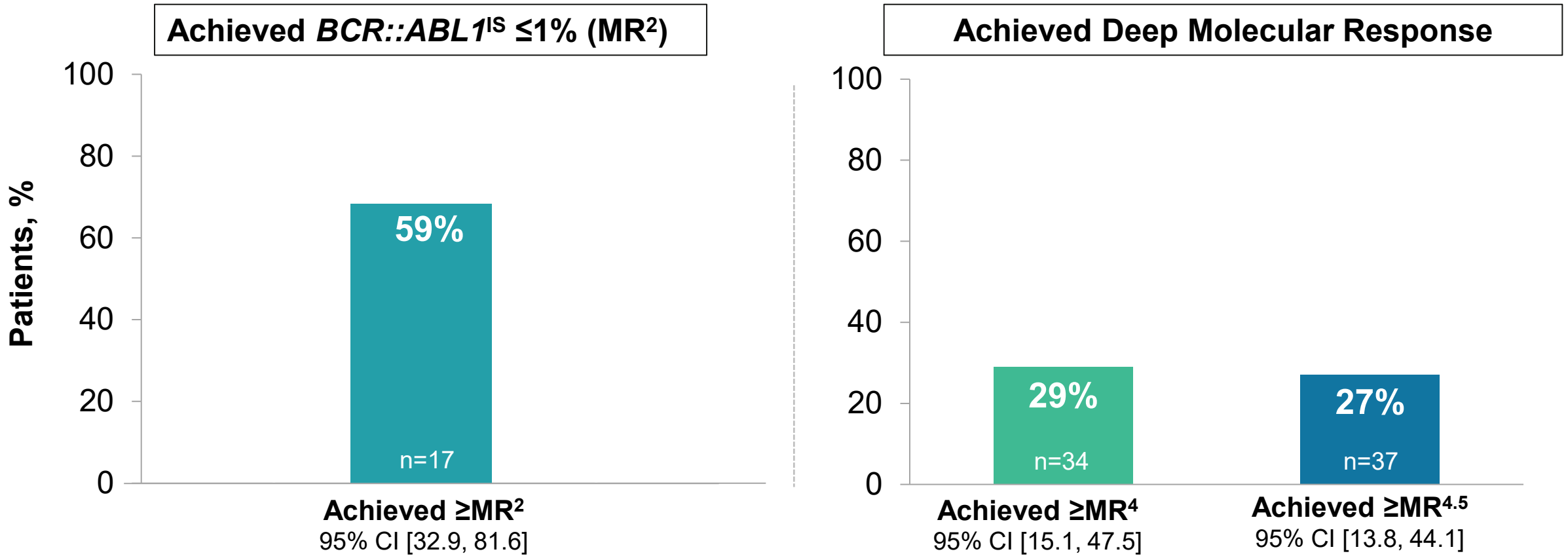
TERN-701 Phase 1: MR^2 and DMR Achievement by 24 Weeks



MR=molecular response; DMR=deep molecular response; IS=International Scale for *BCR::ABL1* transcript measurement; CI=confidence interval.
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TERN-701 Phase 1: BL Demographics at RP2D Dose Range (≥320 mg QD)

	All Patients (N=53)	
Age, median (range), years	57 (30–82)	
Baseline *BCR::ABL1*^{IS}, n (%)		
>10%	25 (47%)	
>1% to 10%	5 (9%)	
>0.1% to 1%	16 (30%)	
≤0.1%	7 (13%)	
Discontinuation to last TKI, n (%)		
Lack of efficacy (per ELN 2020)	36 (68%)	
Lack of tolerability	12 (23%)	
Other	5 (9%)	
Median number of prior unique TKIs (range)	3 (1–6)	
≥3 prior, n (%)	32 (60%)	
Prior ponatinib	11 (21%)	
Prior asciminib	20 (38%)	
BCR::ABL1 mutations, n (%)	T315I	5 (9%)
	F317L	2 (4%)
	E255K	1 (2%)

BL=baseline; RP2D=Recommended Phase 2 dose; IS=International Scale for *BCR::ABL1* transcript measurement; QD=once daily; TKI=tyrosine kinase inhibitor; ELN=European LeukemiaNet

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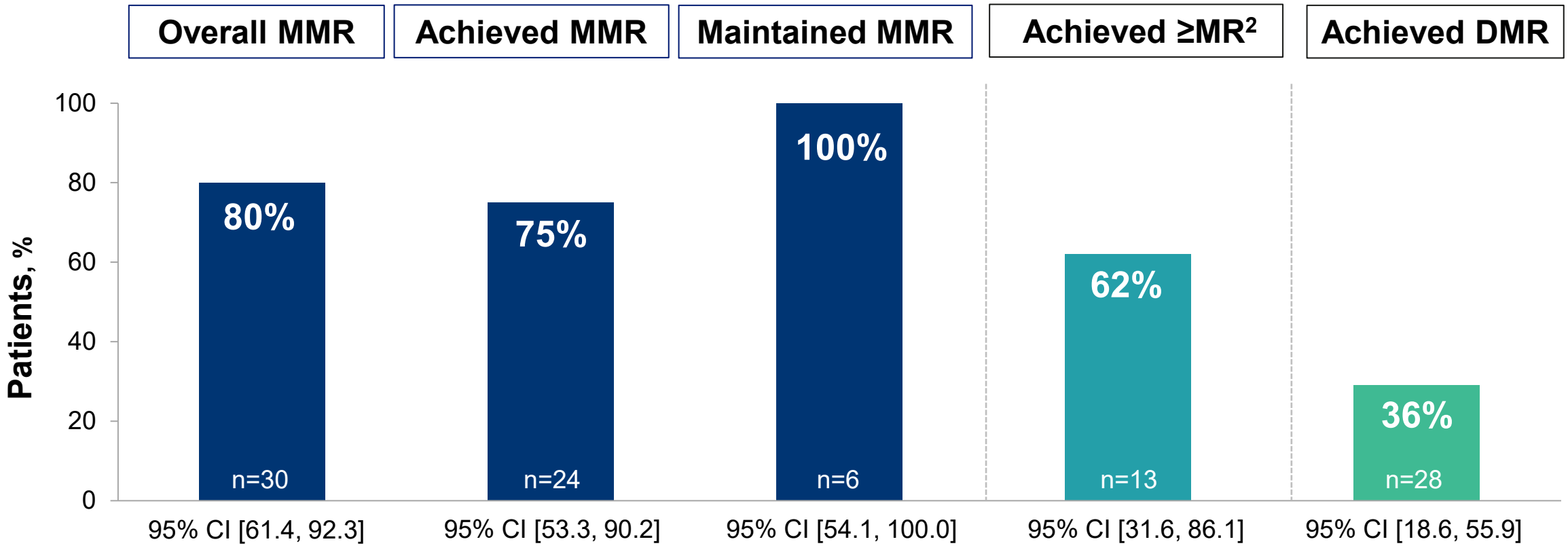
TERN-701 Phase 1: Response Rates at RP2D Dose Range (≥320 mg QD) by 24 Weeks



MMR=major molecular response; RP2D=recommended Phase 2 dose; QD=once daily; CI=confidence interval.

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TERN-701 Phase 1: Conclusions

- Favorable safety and tolerability in **heavily pre-treated (3L+)** CML-CP patients
  - **No DLTs/MTD** identified
  - Majority of **TEAEs low grade**; **G3** AEs <10%
- Encouraging efficacy in refractory non-T315Im CML including prior asciminib and ponatinib treatment failures
  - **64% MMR achievement** with **29% DMR achievement** by 24 weeks **at all doses**
  - **75% MMR achievement** with **36% DMR achievement** by 24 weeks **at RP2D dose range** (≥320 mg QD)
- Doses of 320 mg and 500 mg QD selected as recommended doses for further evaluation in the randomized dose expansion (currently enrolling)

3L=third line; CP-CML=chronic-phase chronic myeloid leukemia; DLTs=dose-limiting toxicities; MTD=maximum tolerated dose; TEAEs-treatment emergent adverse events; G3=Grade 3; AEs-adverse events; MMR=major molecular response; DMR=deep molecular response; R2PD=recommended Phase 2 dose; QD=once daily.

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Acknowledgment

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