

ENABLE: UPDATED EFFICACY AND SAFETY RESULTS OF ELVN-001, A NOVEL SELECTIVE ATP-COMPETITIVE INHIBITOR OF BCR::ABL1, IN PATIENTS WITH PREVIOUSLY TREATED CP-CML

Dragana Milojkovic¹, Dennis Kim², Fabian Lang³, Koji Sasaki⁴, Dw Kim⁵, Michael Mauro⁶, Maria Raquel De Paz Arias⁷, Susanne Saussele⁸, Franck Emmanuel Nicolini⁹, Nicole Blijlevens¹⁰, Michael Heinrich¹¹, Naranie Shanmuganathan¹², Philipp Le Coutre¹³, Sarah Altmeyer¹⁴, Elvira Mora¹⁵, Valerie Coiteux¹⁶, Gabriel Etienne¹⁷, Yingsi Yang¹⁸, Qi Wang¹⁸, Brianna Hoffner¹⁸, M. Damiette Smit¹⁸, Andreas Hochhaus¹⁹

¹ Hammersmith Hospital, Imperial College NHS Trust, London, United Kingdom, ² Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, Canada, ³ Goethe University Hospital, Frankfurt, Germany, ⁴ The University of Texas MD Anderson Cancer Center, Houston, USA, ⁵ Uijeongbu Eulji Medical Center, Uijeongbu-si, South Korea, ⁶ Memorial Sloan Kettering Cancer Center, New York, USA, ⁷ Hospital Universitario La Paz, Madrid, Spain, ⁸ Medizinische Fakultät Mannheim der Universität, Heidelberg, Germany, ⁹ Centre Léon Bérard & INSERM U1052 CRCL, Lyon, France, ¹⁰ Department of Hematology, Radboud University Medical Centre, Nijmegen, The Netherlands, ¹¹ Knight Cancer Institute, Portland, USA, ¹² Royal Adelaide Hospital, Adelaide, Australia, ¹³ Charité-Universitätsmedizin Berlin, Berlin, Germany, ¹⁴ Universitätsklinikum des Saarlandes, Homburg, Germany, ¹⁵ Hospital Universitario y Politécnico La Fe, Valencia, Spain, ¹⁶ Service des Maladies du Sang Hôpital Huriez - CHRU de Lille, Lille, France, ¹⁷ Institut Bergonie - Centre Régional de Lutte Contre Le Cancer de Bordeaux et Sud Ouest, Bordeaux, France, ¹⁸ Enliven Therapeutics, Burlingame, USA, ¹⁹ Universitätsklinikum Jena, Jena, Germany

Dr. Dragana Milojkovic

Research Grant	Novartis, Ascentage, ELVN, TERN, Pfizer, Takeda
Consultant	ELVN
Speakers Bureau	Novartis, Takeda, ELVN
Honoraria	Novartis, Ascentage, ELVN, TERN, Takeda
Employee	
Shareholder	

ELVN-001: A Highly Selective ATP-Competitive Inhibitor of BCR::ABL1



ELVN-001 was designed to address key unmet challenges in CML

Potency without Off-Target Toxicity¹

- ELVN-001 delivers **potent** inhibition of BCR::ABL1 with **high ABL1 selectivity**: >100-fold selectivity against >99% of 370 kinases; no inhibition of KIT, VEGFR2, PDGFR, or SRC

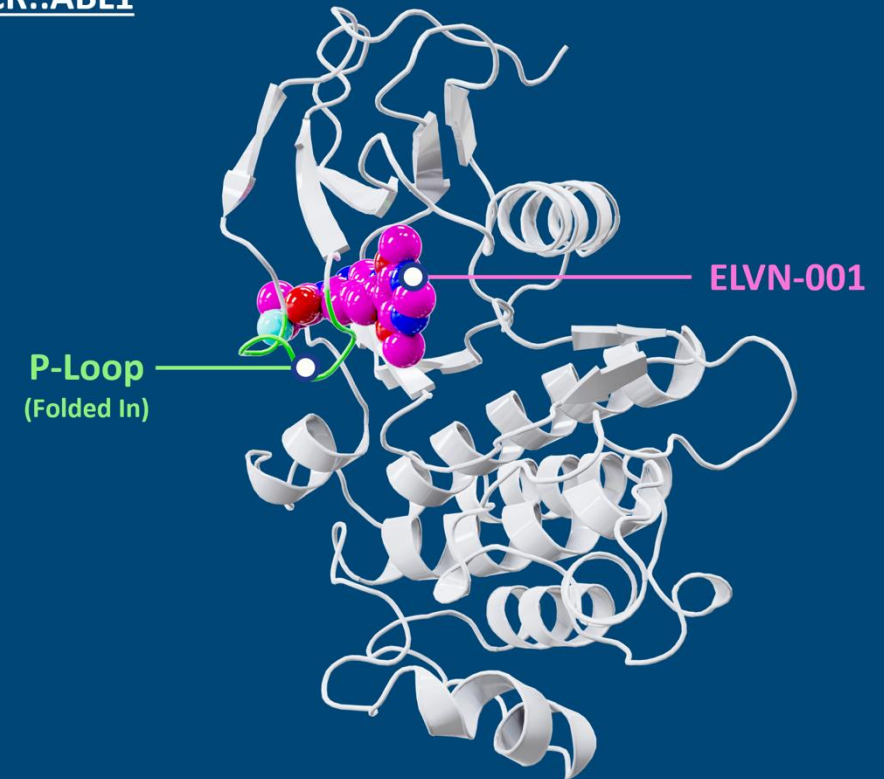
Resistance^{2,3}

- ELVN-001 showed activity against T315I and the emerging class of mutations associated with resistance to allosteric inhibition
- Not a P-gp or BCRP substrate or inhibitor

Administration Limitations^{4,5}

- Once daily administration of ELVN-001 with or without food
- Potential for concomitant administration with CYP3A4 substrates or inhibitors and proton pump inhibitors

BCR::ABL1



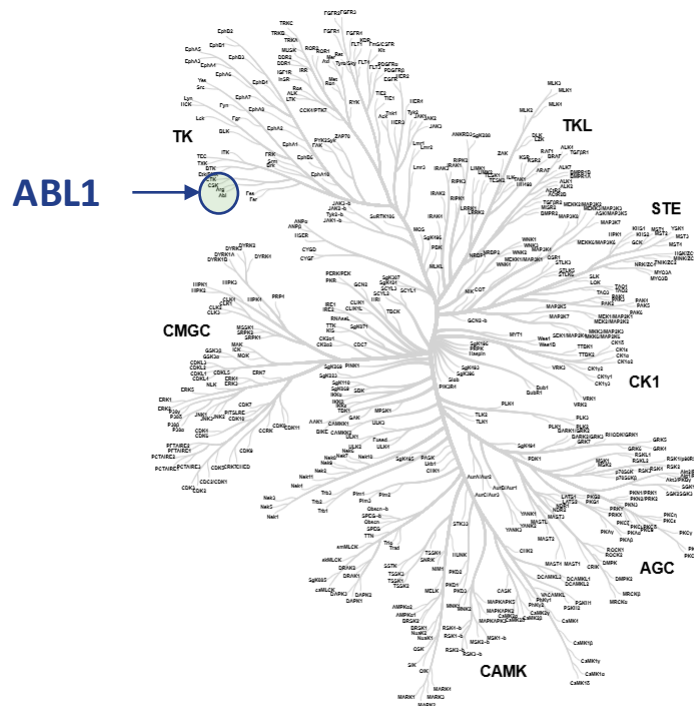
ELVN-001 has a unique P-loop folded-in binding mode

ATP, adenosine triphosphate; BCR::ABL1, breakpoint cluster region-Abelson leukemia virus 1; BCRP, breast cancer resistant protein; P-gp, P-glycoprotein

¹Lee H, et al. Int J Hematol. 2021; ²Hegedus, et al. Clin Transl Sci. 2022; ³Braun T, et al. Cancer Cell. 2020; ⁴Osorio S, et al. Ann Hematol. 2018; ⁵Cheng F, et al. Crit Rev Oncol Hematol. 2024

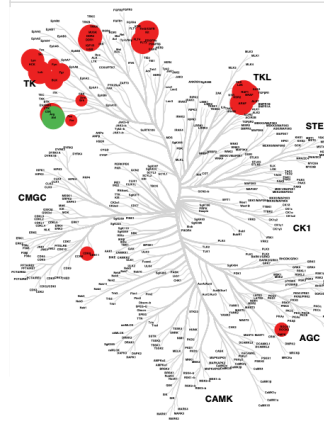
ELVN-001: Differentiated by its Selective ABL1 Inhibition

ELVN-001



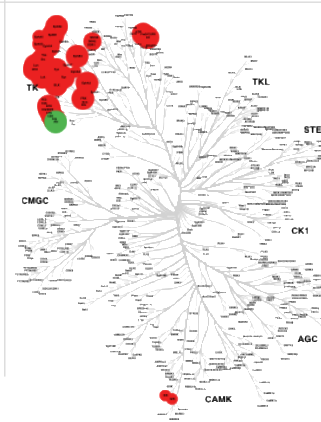
Imatinib

Also inhibits:
KIT, CSFR-1, PDGFR



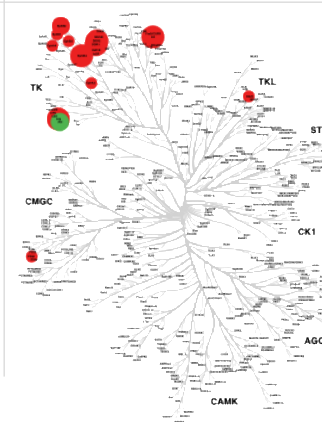
Dasatinib

Also inhibits:
SRC family, KIT,
PDGFR



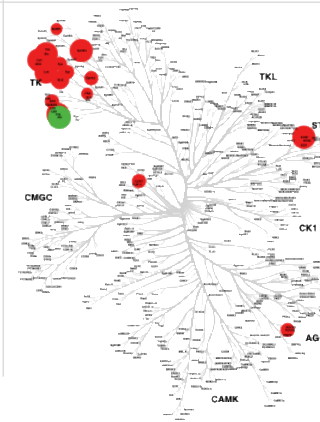
Nilotinib

Also inhibits:
KIT, PDGFR, CSFR-1,
DDR-1, hERG channel



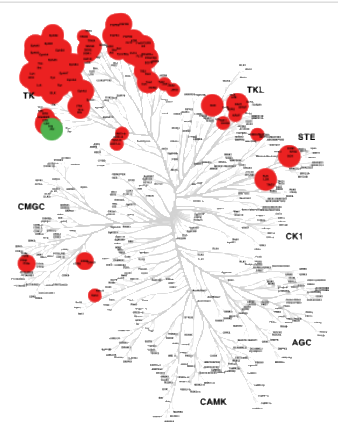
Bosutinib

Also inhibits:
SRC family



Ponatinib

Also inhibits:
KDR, FGFR, KIT, RET,
FLT3, PDGFR



ELVN-001 provides greater selectivity than available ATP inhibitors^a, with potential for better tolerability

^aEach of these active site TKIs was profiled at 30x its respective ABL1 IC₅₀ value against a panel of 377 protein kinases in biochemical assays with 100 mM ATP concentration in the screen (Reaction Biology) (Metz KS et al. Cell Systems. 2018).

ELVN-001: Phase 1 Trial Design and Status

Key Eligibility Criteria:

- Chronic phase CML
- Failed, intolerant to, or not a candidate for available therapies known to be active for treatment of their CML
- Typical or atypical transcripts

Primary Endpoints

- Incidence of DLTs, AEs, clinically significant laboratory and ECG abnormalities

Key Secondary Endpoints

- Molecular response by central qPCR
- PK parameters

Phase 1a Dose Escalation

10 mg–120 mg QD
60 mg–120 mg BID
N = up to ~80

✓ Complete

Phase 1b Dose Expansion (non-T315I)

60 mg QD
N = 20

80 mg QD
N = 20

120 mg QD
N = 21

✓ Complete

**Optimal Biological Dose (OBD)
identified as 80 mg QD**
Based on safety/tolerability, anti-CML
activity, and PK/PD modeling

80 mg QD
N = 40

● Enrolling

Phase 1 is ongoing (NCT05304377). AE, adverse event; DLT, dose-limiting toxicity; ECG, electrocardiogram; BID, twice daily; OBD, optimal biological dose; CML, chronic myeloid leukemia; PD, pharmacodynamics; PK, pharmacokinetics; QD, once daily; qPCR, quantitative polymerase chain reaction.

Patient Demographics and Baseline Characteristics

Parameter	All Patients (N = 161 ^a)	80 mg QD (Phase 1b) (N = 49)
Median age in years (range)	59 (19–82)	57 (19–82)
Typical BCR::ABL1 transcript (e13a2/e14a2), n (%)	150 (93%)	47 (96%)
Baseline BCR::ABL1 transcript ^b ≤0.1%	26 (17%)	8 (17%)
>0.1% – 1%	37 (25%)	11 (23%)
>1% – 10%	28 (19%)	10 (21%)
>10%	50 (33%)	10 (21%)
Baseline BCR::ABL1 mutation (Sanger), n (%)	39 (24%)	5 (10%)
T315I mutation	12 (7%)	n/a
Mutations associated with resistance to allosteric inhibition	13 (8%)	2 (4%)
Other mutations	9 (6%)	3 (6%)

^a Includes 3 re-enrolled patients (158 individual patients)

Parameter	All Patients (N = 161 ^a)	80 mg QD (Phase 1b) (N = 49)
Median lines of prior TKI therapy, n (range)	4 (1–10)	3 (1–9)
Median number of prior unique TKIs, n (range)	3 (1–7)	3 (1–6)
1–2 prior, n (%)	46 (29%)	19 (39%)
3 prior, n (%)	39 (24%)	11 (22%)
4 prior, n (%)	37 (23%)	11 (22%)
≥ 5 prior, n (%)	37 (23%)	7 (14%)
Prior asciminib or ponatinib at any time, n (%)		
Asciminib ^b	100 (62%)	27 (55%)
Ponatinib	60 (37%)	13 (27%)
Reason for discontinuation of last TKI, n (%) ^c		
Lack of efficacy	99 (61%)	25 (51%)
Lack of tolerability	51 (32%)	20 (41%)

^b Most received asciminib in late line and the majority discontinued asciminib due to lack of efficacy

^c Unknown/other in 9 patients (all patients) and 3 patients (80 mg QD)

Majority of patients received ≥ 3 prior TKIs (70%) and prior ponatinib and/or asciminib (72%)

Patient Disposition: Majority of Patients Remain on Study

Disposition	All Patients (N = 161)	80 mg QD (Phase 1b) (N = 49)
Median duration of exposure, weeks (range)	35 (0.1–156)	16.1 (0.3–86.7)
Ongoing, n (%)	123 (76%)	40 (82%)
Discontinued, total n (%)	38 (24%)	9 (18%)
Lack of efficacy	21 (13%)	1 (2.0%)
Adverse event	10 (6.2%)	3 (6.1%)
Death	1 (0.6%)	1 (2.0%)
Other ^a	6 (3.7%)	4 (8.2%)

^a Protocol violation, investigator decision, and consent withdrawal

Overall, 146 person-years of exposure and 118 patients treated at doses $\geq$ 80 mg QD

At 80 mg QD in phase 1b:

- 82% of patients remain on study
- Current median duration of exposure of 16 weeks (cohort actively enrolling)
- Low rate of discontinuation due to adverse events

- No patients progressed to blast phase
- Death was due to post-operative complication (not related to ELVN-001)

ELVN-001 had Favorable Safety and Tolerability

- **Wide therapeutic window**
 - 80 mg BID determined to be MTD:
 - 2 patients with DLT at 120 mg BID (one Grade 3 hallucination in patient with history of hallucinations and one Grade 3 myalgia)
 - Low incidence of AOE^{*}:
 - 7 patients (4.4%) with any grade; 3 (1.9%) with Grade 3, all with CV disease/risk factors incl. prior nilotinib and/or ponatinib
- **Safety of 80 mg QD similar to overall safety; determination of optimal biological dose based on PK/PD modeling**

Most Common TEAEs (by Preferred Term), n (%)	All Patients (N = 158 Safety Analysis Set)		80 mg QD (N = 62 Safety Analysis Set)	
	Any	≥ Grade 3	Any	≥ Grade 3
Any TEAE	142 (90%)	53 (34%)	51 (82%)	15 (24%)
Hematologic TEAEs ≥ 5%				
Thrombocytopenia ^a	23 (15%)	10 (6.3%)	10 (16%)	4 (6.5%)
Neutropenia ^a	11 (7.0%)	10 (6.3%)	1 (1.6%)	0
Non-hematologic TEAEs ≥ 10%				
Lipase increased	35 (22%)	9 (5.7%) ^b	13 (21%)	3 (4.8%) ^b
Fatigue	28 (18%)	2 (1.3%) ^b	7 (11%)	1 (1.6%) ^b
Headache	24 (15%)	1 (0.6%) ^b	11 (18%)	1 (1.6%) ^b
Arthralgia	22 (14%)	2 (1.3%) ^b	10 (16%)	1 (1.6%) ^b
Myalgia	22 (14%)	1 (0.6%) ^b	7 (11%)	0
Nausea	19 (12%)	0	8 (13%)	0
Diarrhea	18 (11%)	0	6 (9.7%)	0
Amylase increased	16 (10%)	0	5 (8.1%)	0

^a Grouped terms: platelet count decreased/thrombocytopenia and neutrophil count decreased/neutropenia

^b Grade 3 only

Data cutoff: 10 March 2026.

TEAE, treatment-emergent adverse event. *AOEs (arterial occlusive events) identified by MedDRA. TEAE of hypertension, any grade, reported in 5.7% of patients, 1.9% Grade 3.

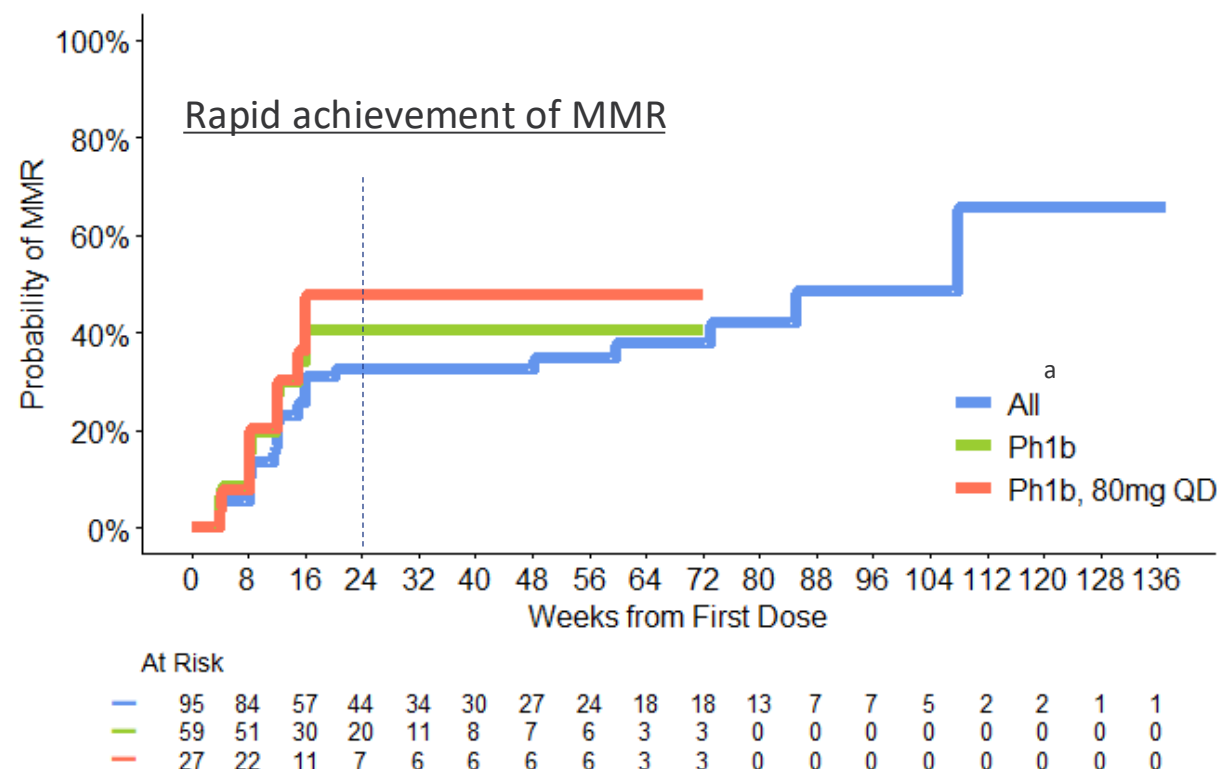
ESH-icMLf 2026: October 2-4, 2026; Gothenburg, Sweden

Encouraging Anti-CML Activity in Phase 1b

Key Efficacy Milestones by Week 24 for Phase 1b

	Total QD (Phase 1b) (N = 90)	80 mg QD (Phase 1b) (N = 49)
Median exposure (weeks)	28.0 (0.3-86.7)	16.1 (0.3-86.7)
MMR ($BCR::ABL1 \leq 0.1\%$)		
Overall MMR	37/69 (54%)	17/28 (61%)
MMR achieved	21/53 (40%)	10/21 (48%)
MMR maintained	16/16 (100%)	7/7 (100%)
MR2 ($BCR::ABL1 \leq 1\%$)		
MR2 achieved	19/33 (58%)	9/13 (69%)
DMR ($BCR::ABL1 \leq 0.01\%$)		
DMR achieved	14/64 (22%)	8/27 (30%)

Cumulative Incidence of MMR in Patients Not in MMR at Baseline



Data cutoff: 10 March 2026.

DMR, deep molecular response; MMR, major molecular response; NOTE: Patients were included if they had baseline typical $BCR::ABL1$ transcript, and postbaseline assessment of $BCR::ABL1$ transcript at 24 weeks or achieved $MMR/\leq 1\%$ within 24 weeks or discontinued treatment before 24 weeks without achieving $MMR/\leq 1\%$. For patients with $MMR/\leq 1\%$ at baseline, only postbaseline assessments beyond 70 days were included in the analysis.

All Patients in Phase 1b had Improved or Stable MR Category

Change in *BCR::ABL1* Transcript in Patients Evaluable for MMR by Week 24 (N = 69)

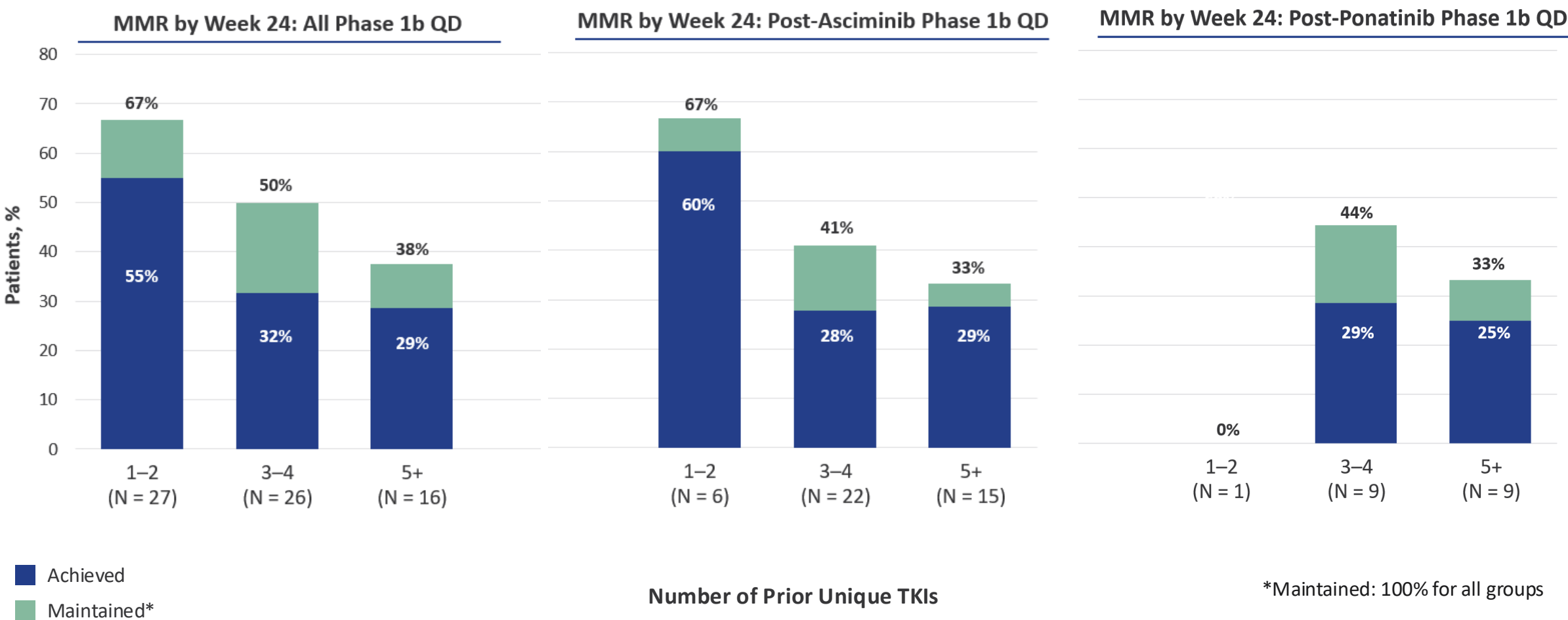
		<i>BCR::ABL1</i> transcript (%) at baseline					
		≥MR4.5 ≤0.0032 (N = 4)	MR4 > 0.0032 to 0.01 (N = 1)	MR3 > 0.01 to 0.1 (N = 11)	> 0.1 to 1 (N = 21)	> 1 to 10 (N = 15)	> 10 (N = 17)
<i>BCR::ABL1</i> transcript (%) by Week 24	≥MR4.5 ≤0.0032	4	1	4	5	2	
	MR4 > 0.0032 to 0.01			1	1	1	
	MR3 > 0.01 to 0.1			6	6	4	2
	> 0.1 to 1				9	4	5
	> 1 to 10					4	3
	> 10						7

In subgroup with baseline transcript >10%:
59% (10/17) had improved MR category

Data cutoff: 10 March 2026.

NOTE: Evaluable patients had baseline typical *BCR::ABL1* transcript without T315I mutation and post-baseline assessment of *BCR::ABL1* transcript at 24 weeks or achieved MMR within 24 weeks or discontinued treatment before 24 weeks without achieving MMR. For patients with MMR at baseline, only post-baseline assessments beyond 70 days were included in the analysis.

Encouraging MMR Rates Across Lines of Therapy and After Asciminib and Ponatinib Failure

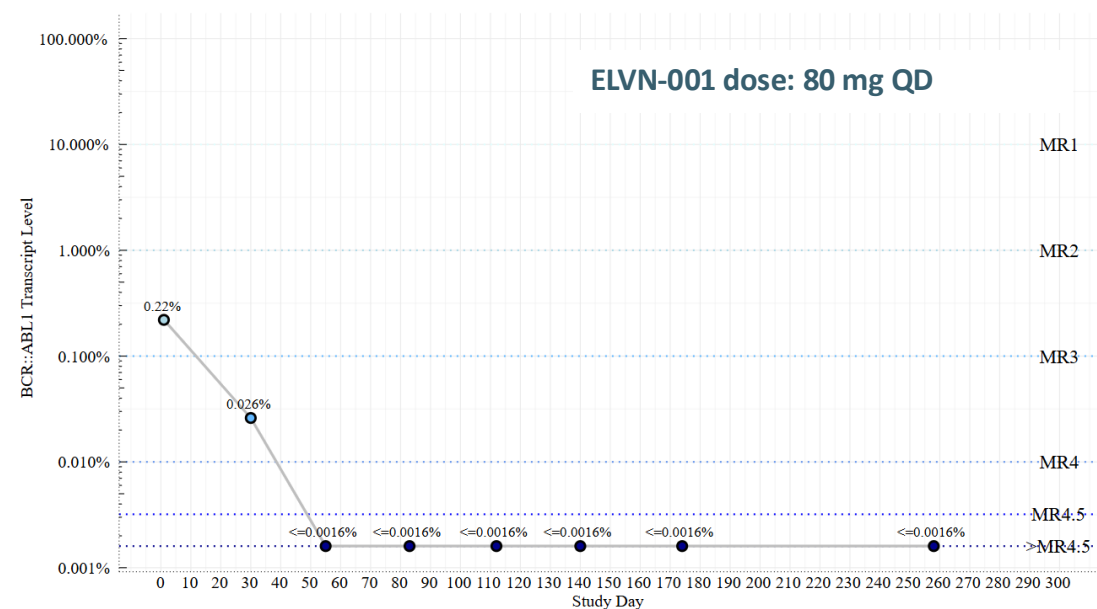


Data cutoff: 10 March 2026.
NOTE: Analysis by number of prior TKIs done with prior *unique* TKIs. Evaluable patients had baseline typical BCR::ABL1 transcript without T315I mutation and post-baseline assessment of BCR::ABL1 transcript at 24 weeks or achieved MMR within 24 weeks or discontinued treatment before 24 weeks without achieving MMR. For patients with MMR at baseline, only post-baseline assessments beyond 70 days were included in the analysis.

Case Studies: A344D and V299L mutation

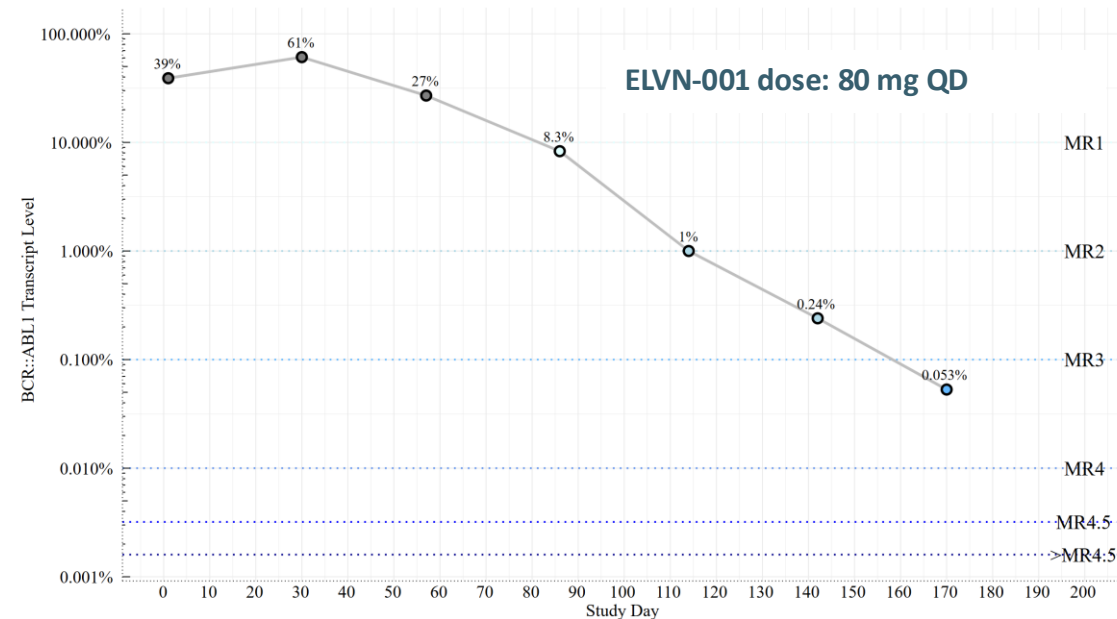
57 y/o F with CML since 2021 and A344D^a

Prior TKI	Reason for Discontinuation	Best molecular response	Time on TKI (approx.)
Imatinib	Lack of efficacy	>1-≤10%	9 months
Bosutinib	Lack of efficacy	>1-≤10%	8 months
Asciminib	Lack of efficacy	MR5	2.8 years



75 y/o F with CML since 2017 and V299L^b

Prior TKI	Reason for Discontinuation	Best molecular response	Time on TKI (approx.)
Imatinib	Lack of efficacy	unknown	9 months
Dasatinib	Pleural effusion	MR2	5 years
Asciminib ^c	Lack of efficacy	MR2	2.5 years



Data as of 24 Sept 2026 (from ongoing study, not part of aggregate data snapshot)

^aNGS 99.73%, ^bNGS 99.72%. ^c ~1 yr of peginterferon-alpha 2a combination

ESH-iCMLf 2026: October 2-4, 2026; Gothenburg, Sweden

Conclusions

ELVN-001 showed favorable safety and tolerability with longer follow-up

- Low rate of discontinuations due to TEAEs
- The safety profile is consistent with ELVN-001's selectivity for ABL1
- No evidence of increased cardiovascular toxicity to date

The Optimal Biological Dose was determined to be 80 mg QD based on safety, efficacy, PK/PD

Encouraging anti-CML activity continued to be observed

- At the OBD of 80 mg QD in Phase 1b: 61% overall MMR with 48% achieving MMR by Week 24
- MR stable or improved in all patients enrolled in Phase 1b
- Encouraging MMR rates even in heavily pretreated patients and after asciminib and ponatinib failure

Phase 3 ENABLE-2 pivotal trial is expected to initiate in the second half of 2026

ELVN-001, an ATP-competitive BCR::ABL1 TKI with high selectivity for ABL1, demonstrated favorable safety and efficacy profile at biologically active doses

Thank you

**to all investigators and site staff, and to the patients and their
families for their participation in the study**

This study was funded by Enliven Therapeutics, Inc.