D012

Attack-Free and Long-Term Prophylaxis-Free Status Following Treatment With Lonvoguran Ziclumeran in Hereditary Angioedema

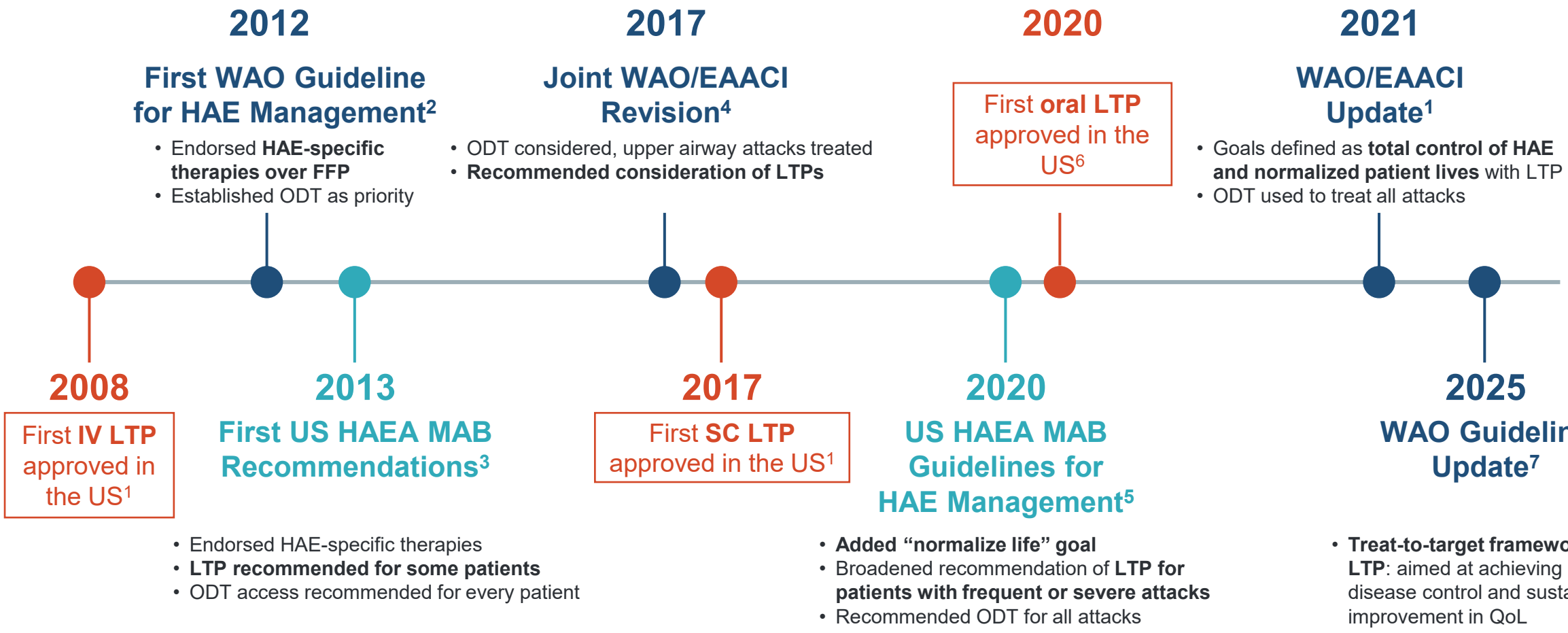
Emel Aygören-Pürsün,[1] Padmalal Gurugama,[2] Danny M. Cohn,[3] Henriette Farkas,[4] William R. Lumry,[5] Eliesha Daniels,[6] Adele Golden,[6] David Maag,[6] Catherine R. Miller,[6] Aleena Banerji[7]

[1]University Hospital Frankfurt, Goethe University Frankfurt, Frankfurt, Germany; [2]Cambridge University Hospitals, NHS Foundation Trust, Cambridge, UK; [3]Amsterdam Cardiovascular Sciences, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, the Netherlands; [4]Hungarian Angioedema Center of Reference and Excellence, Semmelweis University, Budapest, Hungary; [5]Allergy and Asthma Research Associates Research Center, Dallas, TX; [6]Intellia Therapeutics, Cambridge, MA; [7]Massachusetts General Hospital, Boston, MA, and Harvard Medical School, Boston, MA

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HAE treatment strategies and goals have evolved with the therapeutic landscape

EVOLUTION OF HAE GUIDANCE



Lonvoguran ziclumeran (lonvo-z) is an investigational product that has not been approved by the FDA or any Health Authority and for which safety and efficacy have not been established.

EAACI, European Academy of Allergy and Clinical Immunology; FDA, U.S. Food and Drug Administration; FFP, fresh frozen plasma; HAE, hereditary angioedema; HAEA, Hereditary Angioedema Association; IV, intravenous; LTP, long-term prophylaxis; MAB, Medical Advisory Board; ODT, on-demand therapy; SC, subcutaneous; QoL, quality of life; WAO, World Allergy Association.

1. Martinez-Saguer I, et al. *Clin Transl Allergy.* 2025;15(12):e70126. 2. Craig T, et al. *World Allergy Organ J.* 2012;5:182. 3. Zuraw BL, et al. *J Allergy Clin Immunol Pract.* 2013;1:458-467. 4. Maurer M, et al. *World Allergy Organ J.* 2018;11:5. 5. Busse PJ, et al. *J Allergy Clin Immunol Pract.* 2020;9(1):132-150. 6. Orladeyo (package insert). BioCryst Pharmaceuticals; 2020. 7. Vasquez DO, et al. *World Allergy Organ J.* 2026;19:101335.

Advances in HAE therapy are expanding treatment goals beyond attack prevention

Time

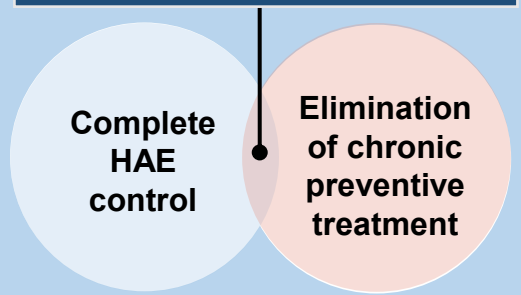
Treat	Prevent	Functional Cure	Cure
Manage symptoms or alleviate an ongoing disease	Aim to stop or slow a disease with proactive measures	Control of disease, after a finite course of treatment	Complete elimination of disease

CURRENT THERAPIES

- On-demand therapies **treat attacks** as they occur
- Long-term prophylaxis (LTP) aims to **prevent attacks**

POTENTIAL FOR FUTURE THERAPIES

- One-time treatment aims to **treat HAE**

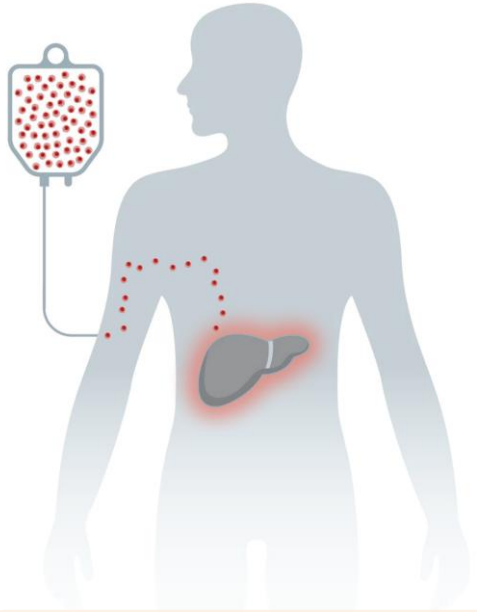


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FDA, U.S. Food and Drug Administration; HAE, hereditary angioedema.

Lonvoguran ziclumeran (lonvo-z) is being evaluated as a one-time treatment for HAE

Objective: Explore the potential for patients to become attack-free and LTP-free after lonvo-z 50 mg with up to 4 years of follow-up in the Phase 1/2 and long-term follow-up studies



Lonvo-z was administered as a **one-time IV infusion** over 2 to 4 hours in an outpatient setting

Phase 1

Lonvo-z 50 mg (n=6)
Week 1-104: Open-label

Phase 2

Lonvo-z 50 mg (n=26)
Week 1-16: Double-blind, placebo-controlled
Week 16-104: Open-label

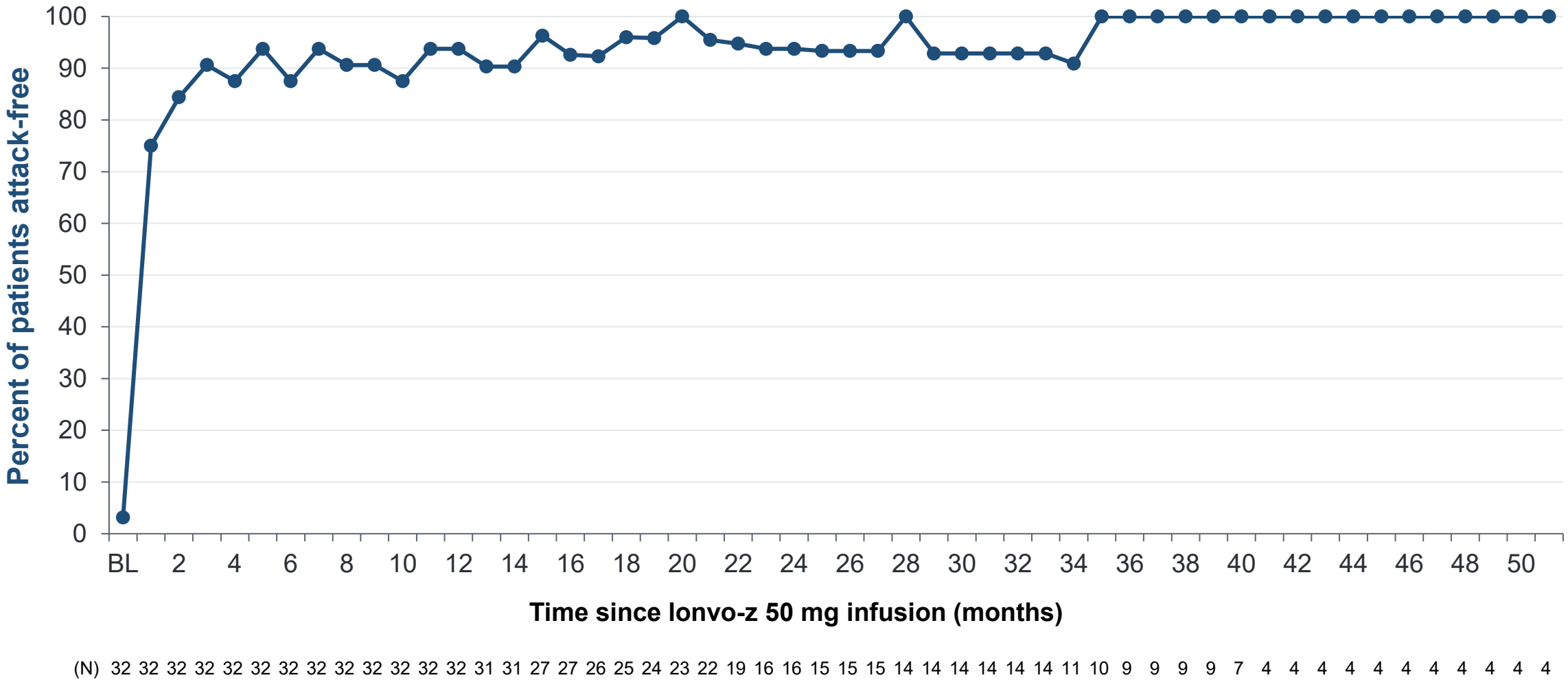
Long-term follow-up study (up to 15 years)

N=31
(1 patient lost to follow-up)

Median follow-up after receiving lonvo-z 50 mg: 20.8 months (range: 10.2–46.5 months)
in the Phase 1/2 and long-term follow-up studies

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LPLV: June 26, 2026 (Phase 1/2); data cutoff: July 10, 2026 (LTFU).
FDA, U.S. Food and Drug Administration; HAE, hereditary angioedema; IV, intravenous; LPLV, last patient last visit; LTFU, long-term follow-up; LTP, long-term prophylaxis.

The proportion of patients who were attack-free increased over time; after one year, >90% were attack-free at each month with up to 4 years of follow-up



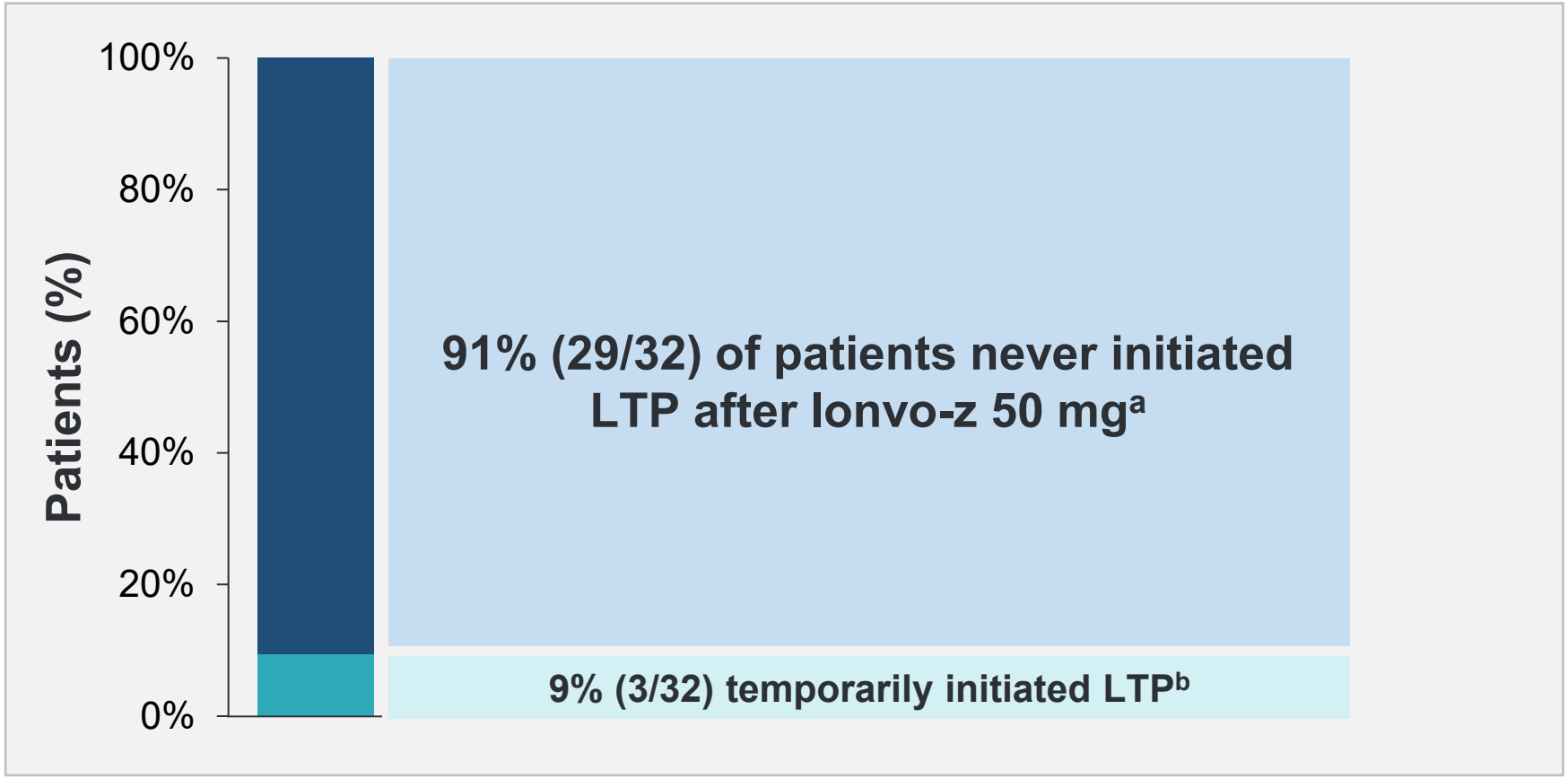
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31/32 patients treated with lonvo-z 50 mg remain in long-term follow-up. N shown represents the number of patients who have reached that time point. One month=28 days. Timepoints with data from ≥3 patients are presented.

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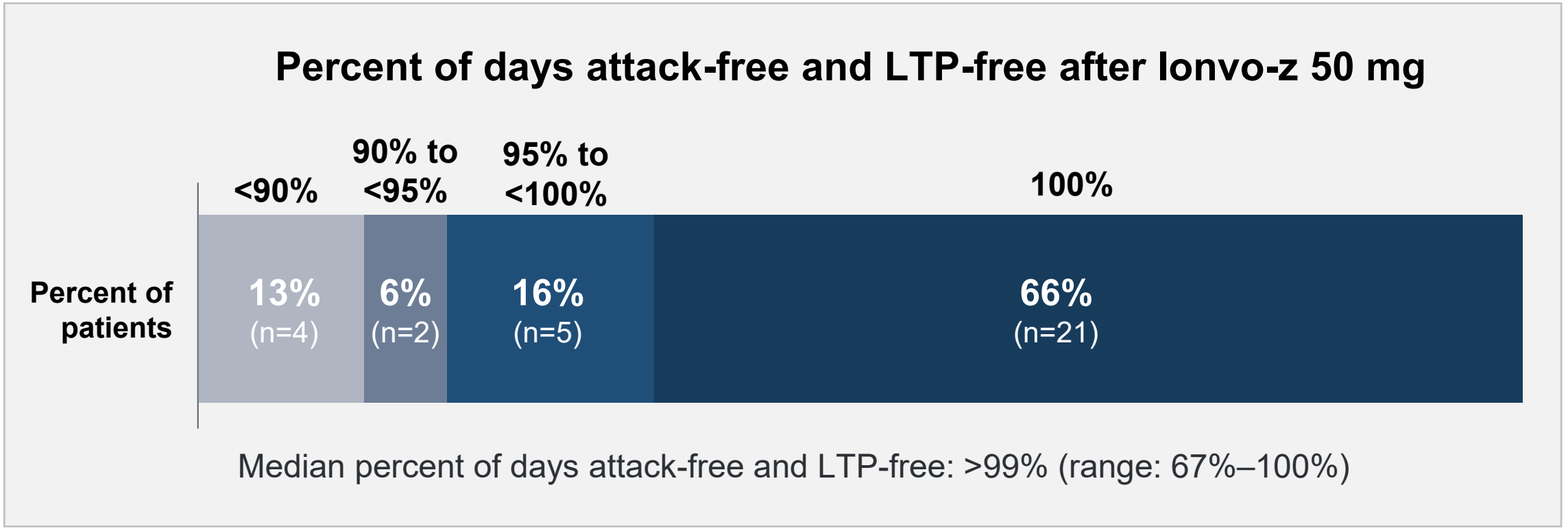
Most patients did not initiate LTP after a one-time treatment with lonvo-z 50 mg through up to 4 years of follow-up



All patients (N=32) were LTP-free at the latest follow-up
Median (range) time LTP-free[c]: 1.6 (0.6–3.9) years

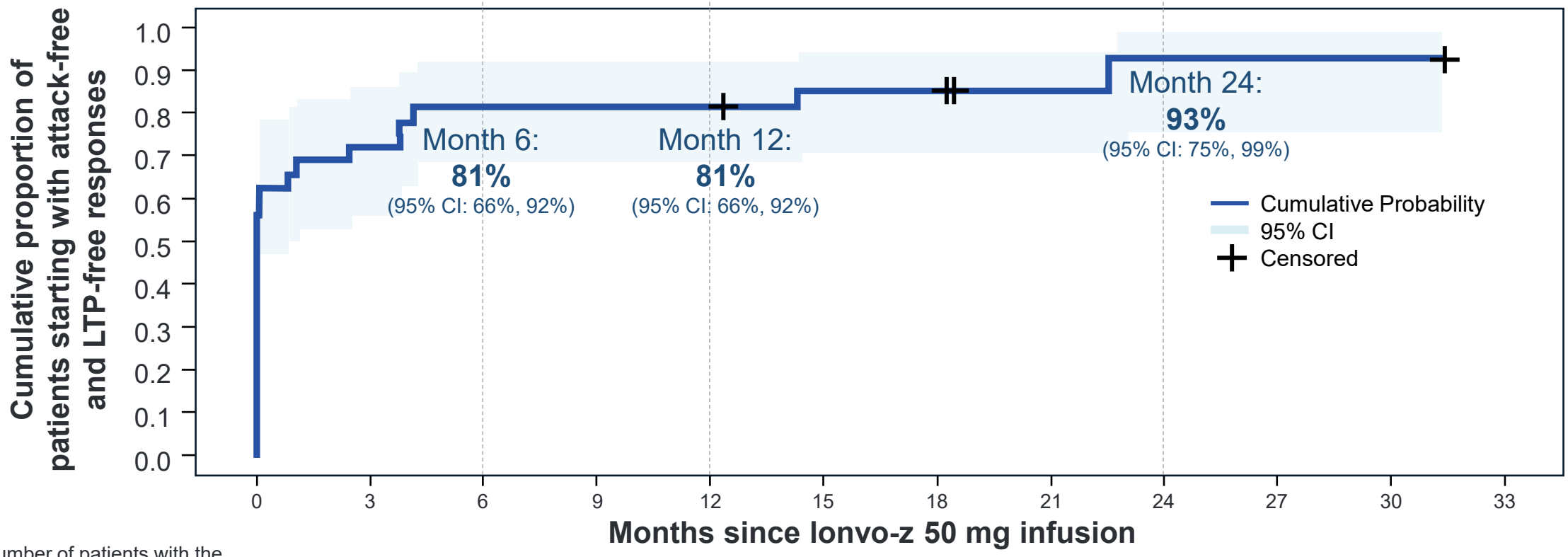
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[a]A total of 8 patients continued prior LTP through lonvo-z infusion and discontinued LTP 0-4.1 months after infusion. [b]Duration of LTP use: 3.4, 7.9, and 8.5 months. [c]Time LTP-free is defined as the last dose of LTP to the latest follow-up.
FDA, U.S. Food and Drug Administration; LPLV, last patient last visit; LTFU, long-term follow-up; LTP, long-term prophylaxis.

The majority (88%) of patients were attack-free and LTP-free for ≥90% of their follow-up time after receiving lonvo-z 50 mg



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Analysis assessed attack-free and LTP-free status for patients after lonvo-z 50 mg infusion from the start of Week 5 (ie, Day 29) to latest follow-up.
FDA, U.S. Food and Drug Administration; LPLV, last patient last visit; LTFU, long-term follow-up; LTP, long-term prophylaxis.

By Month 6, there was an 81% probability of starting an attack-free and LTP-free period lasting at least 6 months



Number of patients with the potential to become attack-free and LTP-free for ≥6 months (n)	32	9	6	6	6	4	4	2	1	1	1	0
Number of patients starting an attack-free and LTP-free interval for ≥6 months (n)	0	23	26	26	26	27	27	27	28	28	28	28

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Results are based on Kaplan-Meier estimates. Censored patients include those who have not achieved attack-free and LTP-free for ≥6 months as of the latest assessment. The median (range) estimated time to start an attack-free and LTP-free interval for ≥6 months was 1 day (1 day to 22.6 months).
FDA, U.S. Food and Drug Administration; LPLV, last patient last visit; LTFU, long-term follow-up; LTP, long-term prophylaxis.

Lonvo-z 50 mg was well tolerated with no long-term risks observed with up to 4 years of follow-up

	Lonvo-z 50 mg (N=32) n (%)[a]
Any TEAE[b] (≥10% of patients)	32 (100)
Infusion-related reaction	17 (53)
Fatigue	11 (34)
Nasopharyngitis	9 (28)
Arthralgia	7 (22)
Upper respiratory tract infection	7 (22)
Headache	6 (19)
Back pain	5 (16)
COVID-19	5 (16)
Abdominal discomfort	4 (13)
Contusion	4 (13)
Any SAE	2 (6)
Perforated appendicitis	1 (3)[c]
Pulmonary embolism	1 (3)[d]

- 78% (25/32) of patients experienced a treatment-related AE, with the most common being IRR (53%; 17/32)
- No clinically significant shifts in coagulation parameters, including aPTT
  - One pulmonary embolism with confounding risk factors including recent COVID infection
- No clinically significant shifts in liver enzymes
  - Highest reported AST/ALT elevation was Grade 2 (n=2); all changes were asymptomatic and transient
- No AEs indicative of genotoxicity or off-target editing, including malignancies
  - One squamous cell carcinoma (stage 1, curatively resected); not related to lonvo-z

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[a]AEs that occurred after each patient received lonvo-z 50 mg are reported. [b]Collected in Phase 1/2 study; TEAEs were only collected in LTFU if treatment-related, serious, or adverse events of special interest. [c]One event of Grade 3 perforated appendicitis occurred in a patient 22 months after lonvo-z 50 mg infusion and was not considered treatment-related. [d]One event of Grade 3 pulmonary embolism was reported in a patient 12 months after lonvo-z 50 mg infusion. The patient had multiple risk factors, which included recent COVID infection, ongoing history of smoking, and obesity.

AE, adverse event; ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; IRR, infusion-related reaction; LPLV, last patient last visit; LTFU, long-term follow-up; SAE, serious AE; TEAE, treatment-emergent adverse event.

Conclusions

- Most (88%) patients stayed attack-free and LTP-free for ≥90% of their follow-up time after one-time treatment with lonvo-z 50 mg
- By Month 6, the probability of starting an attack-free and LTP-free period of ≥6 months was 81%
- Lonvo-z may enable sustained attack-free and LTP-free status in most patients
  - Sustained attack-free and LTP-free status will continue to be evaluated in the LTFU study
- Lonvo-z 50 mg was well tolerated with no long-term risks observed as of last follow-up

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FDA, U.S. Food and Drug Administration; LTFU, long-term follow-up; LTP, long-term prophylaxis.

Acknowledgments

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