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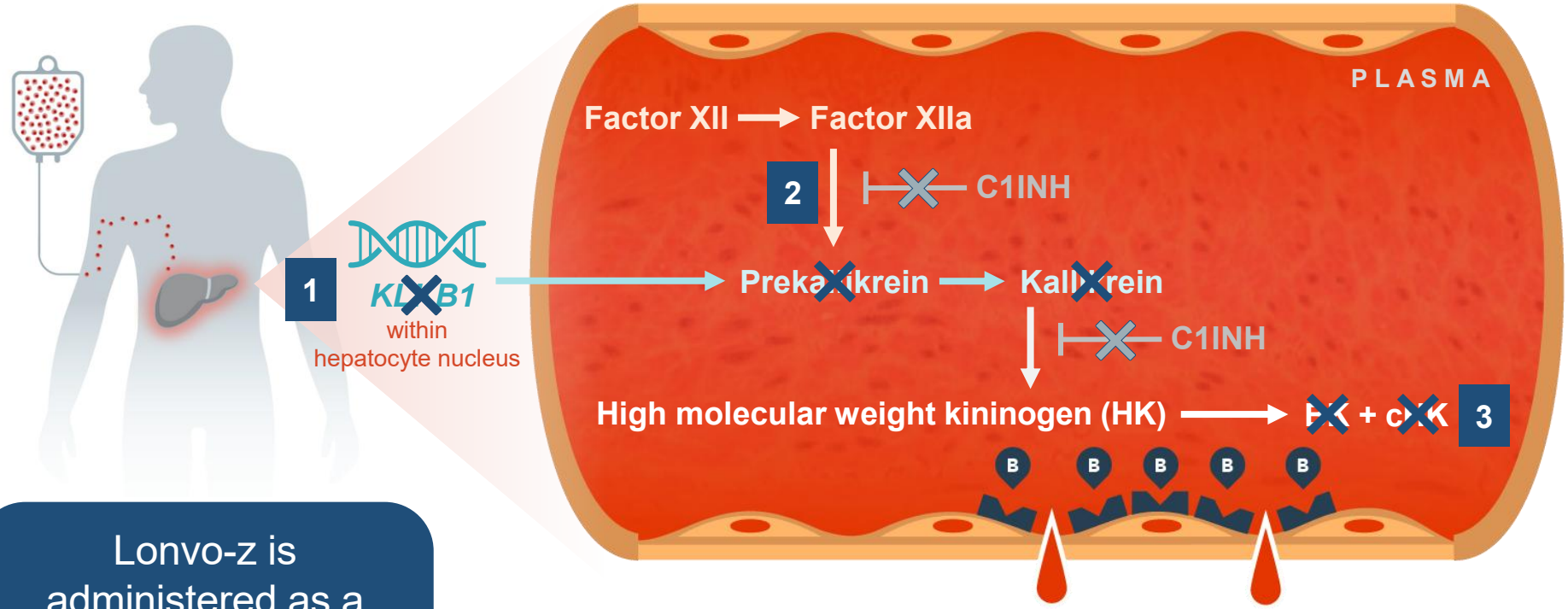
Four-Year Durability/Safety of Lonvoguran Ziclumeran (Lonvo-z) 50 mg in Patients With Hereditary Angioedema

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Lonvo-z is an investigational, *in vivo* CRISPR-based gene editing therapy intended to inactivate the *KLKB1* gene to prevent production of kallikrein and treat HAE[1-3]



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

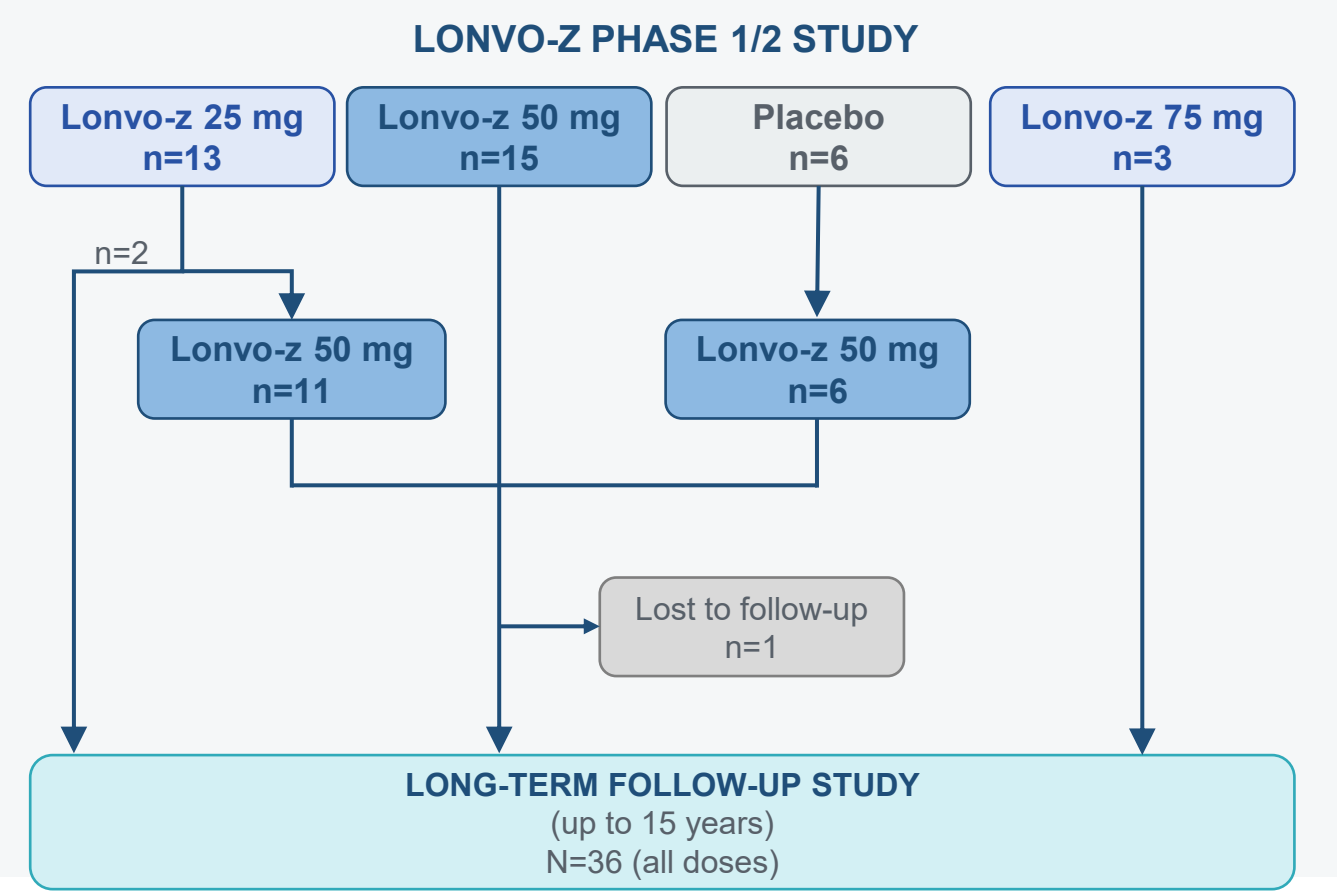
1. Lonvo-z is designed to inactivate the *KLKB1* gene to prevent production of kallikrein
2. Decreasing kallikrein resets the balance of the pathway by reducing bradykinin production
3. Reducing bradykinin reduces HAE attacks

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.

BK, bradykinin; C1INH, C1 inhibitor; cHK, cleaved high-molecular-weight kininogen; CRISPR, clustered regularly interspaced short palindromic repeats; FDA, U.S. Food and Drug Administration; HAE, hereditary angioedema; IV, intravenous.

1. Longhurst HJ, et al. *N Engl J Med*. 2024;390(5):432-441. 2. Cohn DM, et al. *N Engl J Med*. 2025;392(5):458-467. 3. Cohn DM, et al. *N Engl J Med*. 2026;395(15):1471-1482.

Lonvo-z Phase 1/2 study

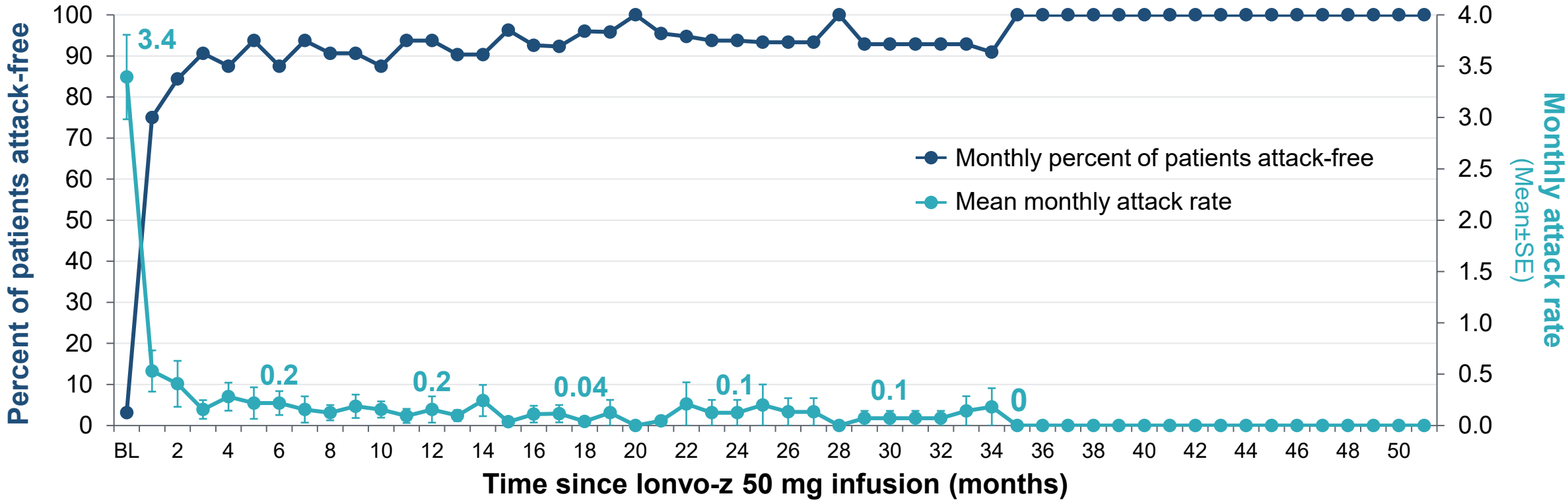


Baseline Characteristics	Lonvo-z 50 mg (n=32)
Age, median (range), years	48.5 (18-76)
Female, n (%)	16 (50)
Hereditary angioedema type, n (%)	
Type 1	26 (81)
Type 2	6 (19)
Prior long-term prophylaxis at study entry, n (%)[a]	19 (59)
Lanadelumab	4 (13)
Berotralstat	4 (13)
C1 esterase inhibitor	4 (13)
Other[b]	8 (25)
Typical attack severity (historical), n (%)	
Mild	4 (13)
Moderate	21 (66)
Severe	7 (22)
Baseline monthly attack rate, mean (SD)[c]	3.4 (2.3)

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

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LPLV: June 26, 2026 (Phase 1/2); data cutoff: July 10, 2026 (LTFU).
[a]In Phase 1, patients may have been on long-term prophylaxis at time of lonvo-z infusion. [b]Includes tranexamic acid, danazol, and stanozolol. [c]Baseline is defined as the screening period (50 mg initial dose or 25 mg to 50 mg) or for placebo to 50 mg as the time from informed consent to 50 mg infusion or start of any long-term prophylaxis, whichever occurred first. FDA, U.S. Food and Drug Administration; LPLV, last patient last visit; LTFU, long-term follow-up.

Attack rate was low with up to 4 years of follow-up, with the majority of patients treated with lonvo-z 50 mg completely attack-free at all time points



All patients treated with lonvo-z 50 mg were LTP-free at last assessment (n=32)

Median (range) time LTP-free[a]: 1.6 (0.6–3.9) years

Median percent of days attack-free and LTP-free[b]: >99% (range: 67%–100%)

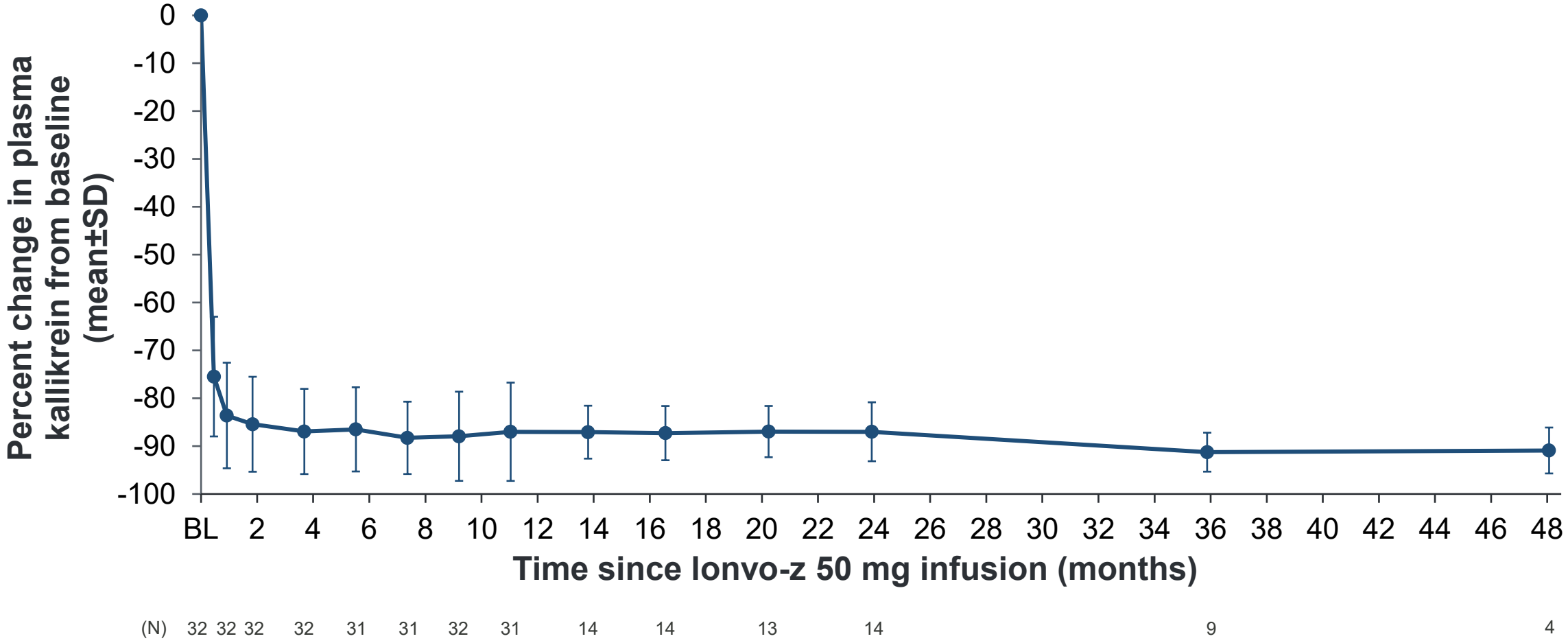
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LPLV: June 26, 2026 (Phase 1/2); data cutoff: July 10, 2026 (LTFU). 31/32 patients treated with lonvo-z 50 mg remain in long-term follow-up. N shown represents the number of patients who have reached that time point. One month=28 days. Timepoints with data from ≥3 patients are presented.

[a]Time LTP-free is defined as the last dose of LTP to the latest follow-up. [b]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.

BL, baseline; FDA, U.S. Food and Drug Administration; LPLV, last patient last visit; LTFU, long-term follow-up; LTP, long-term prophylaxis.

Kallikrein levels rapidly declined after one-time treatment with lonvo-z 50 mg and remained stable 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=30.4375 days.

BL, baseline; FDA, U.S. Food and Drug Administration; LPLV, last patient last visit; LTFU, long-term follow-up.

No long-term risks have been observed with up to 4 years of follow-up after lonvo-z infusion

	Patients treated with lonvo-z 50 mg (n=32)[a]	
	Reported within 28 days of infusion, n (%)	Reported >28 days after infusion, n (%)
Any TEAE[b] (≥10% of patients at any time)	27 (84)	31 (97)
Infusion-related reaction	17 (53)	0
Fatigue	11 (34)	0
Headache	6 (19)	2 (6)
Contusion	3 (9)	1 (3)
Abdominal discomfort	2 (6)	2 (6)
Nasopharyngitis	1 (3)	9 (28)
Upper respiratory tract infection	1 (3)	6 (19)
Arthralgia	1 (3)	6 (19)
COVID-19	1 (3)	4 (13)
Back pain	0	5 (16)
Any SAE	0	2 (6)
Perforated appendicitis	0	1 (3)[c]
Pulmonary embolism	0	1 (3)[d]

No clinically significant shifts in liver enzymes or coagulation parameters

PREGNANCY OUTCOMES

Female patient (lonvo-z 75 mg)

- Live, full-term birth delivered approximately 3 years 11 months after lonvo-z infusion
- Pregnancy occurred without complications

Male patient (lonvo-z 25 mg)

- Patient's partner was reported to be pregnant 21 months after lonvo-z infusion
- Pregnancy occurred without complications
- Live, full-term birth

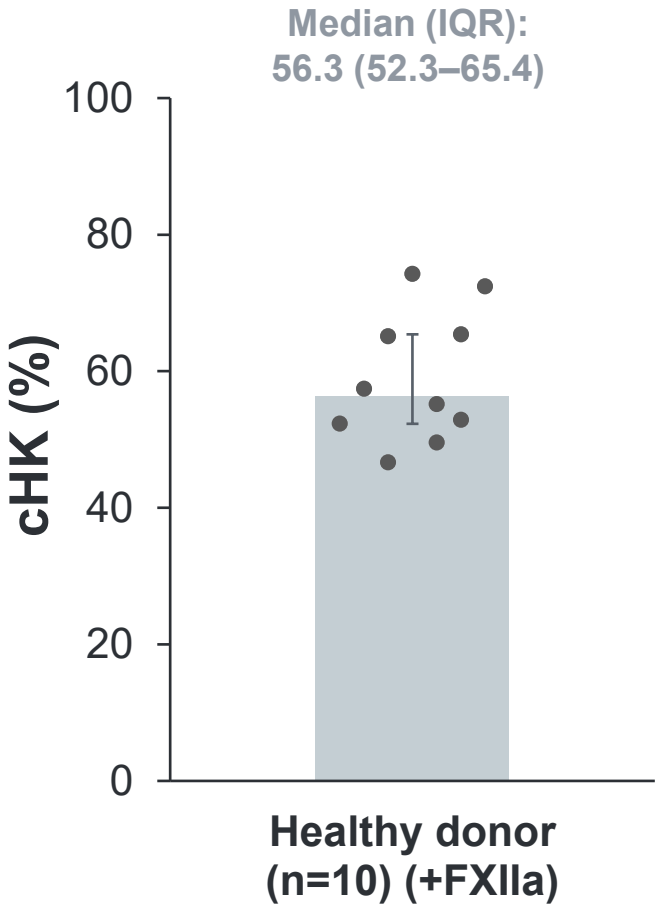
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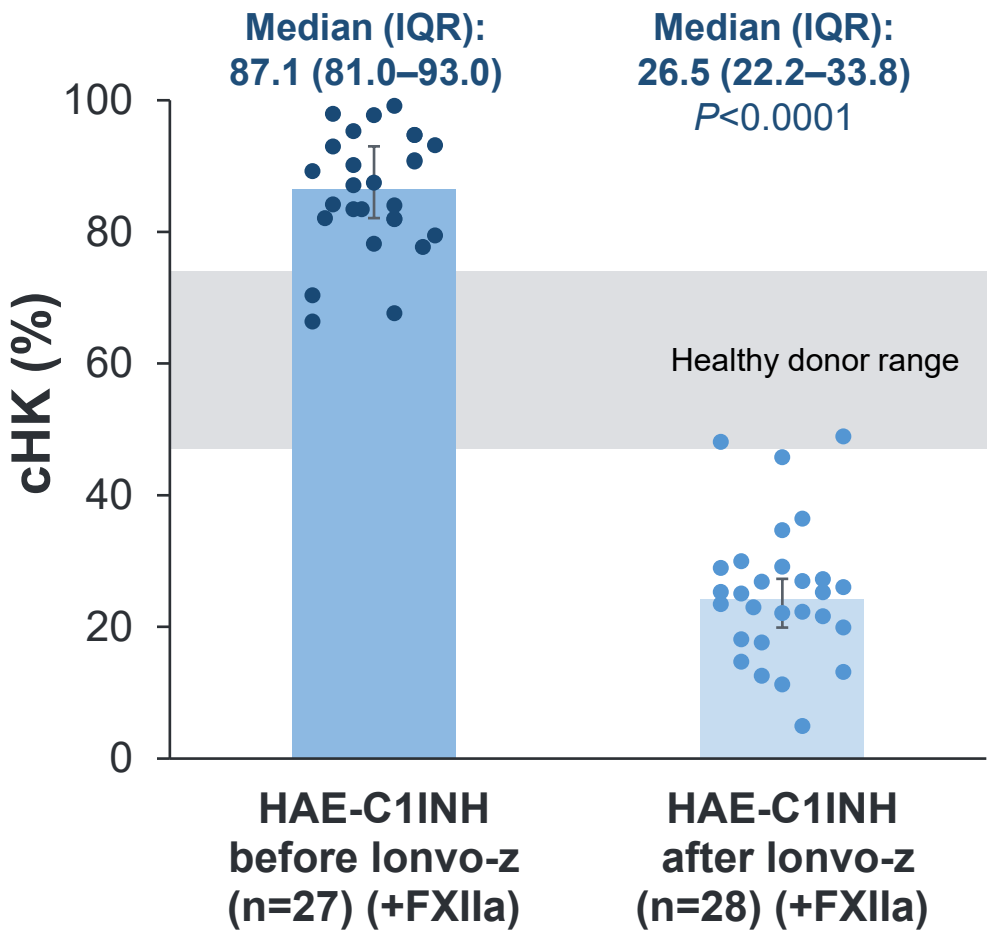
AE, adverse event; FDA, U.S. Food and Drug Administration; LPLV, last patient last visit; LTFU, long-term follow-up; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Following treatment with lonvo-z 50 mg, median cHK levels were lowered; all patients retained partial pathway activity

Healthy donors



Before and after one-time lonvo-z 50 mg



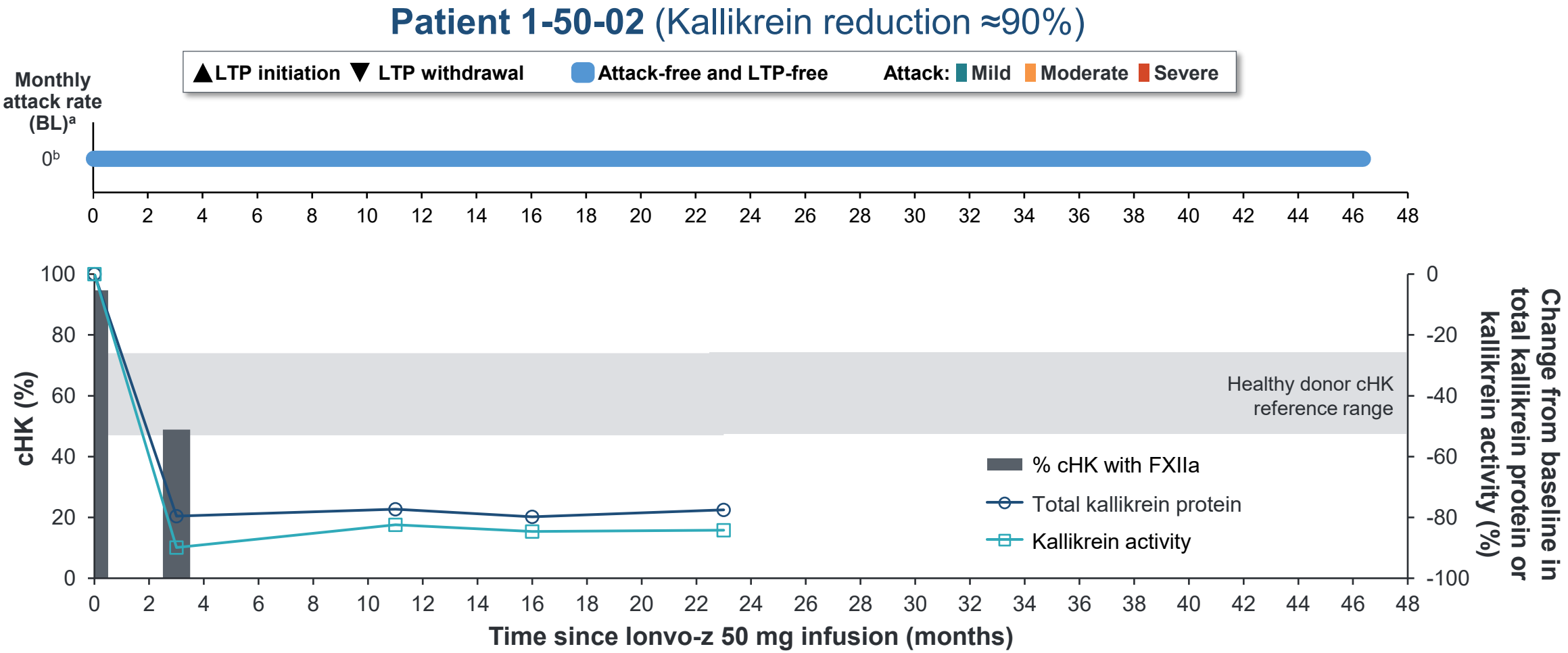
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LPLV: June 26, 2026 (Phase 1/2); data cutoff: July 10, 2026 (LTFU).

Healthy donor cHK (%) reference range: 47–74 (+FXIIa). Dots represent one individual sample. IQR represents the 25th and 75th percentile. *P* value is based on exact Wilcoxon two-sample test; nominal *P* values are presented for exploratory purposes; results should be interpreted as hypothesis generating.

C1INH, C1 inhibitor; cHK, cleaved high-molecular-weight kininogen; FDA, U.S. Food and Drug Administration; FXIIa, activated factor XII; HAE, hereditary angioedema; IQR, interquartile range; LPLV, last patient last visit; LTFU, long-term follow-up.

Patient vignette 1: cHK decreased after treatment with lonvo-z



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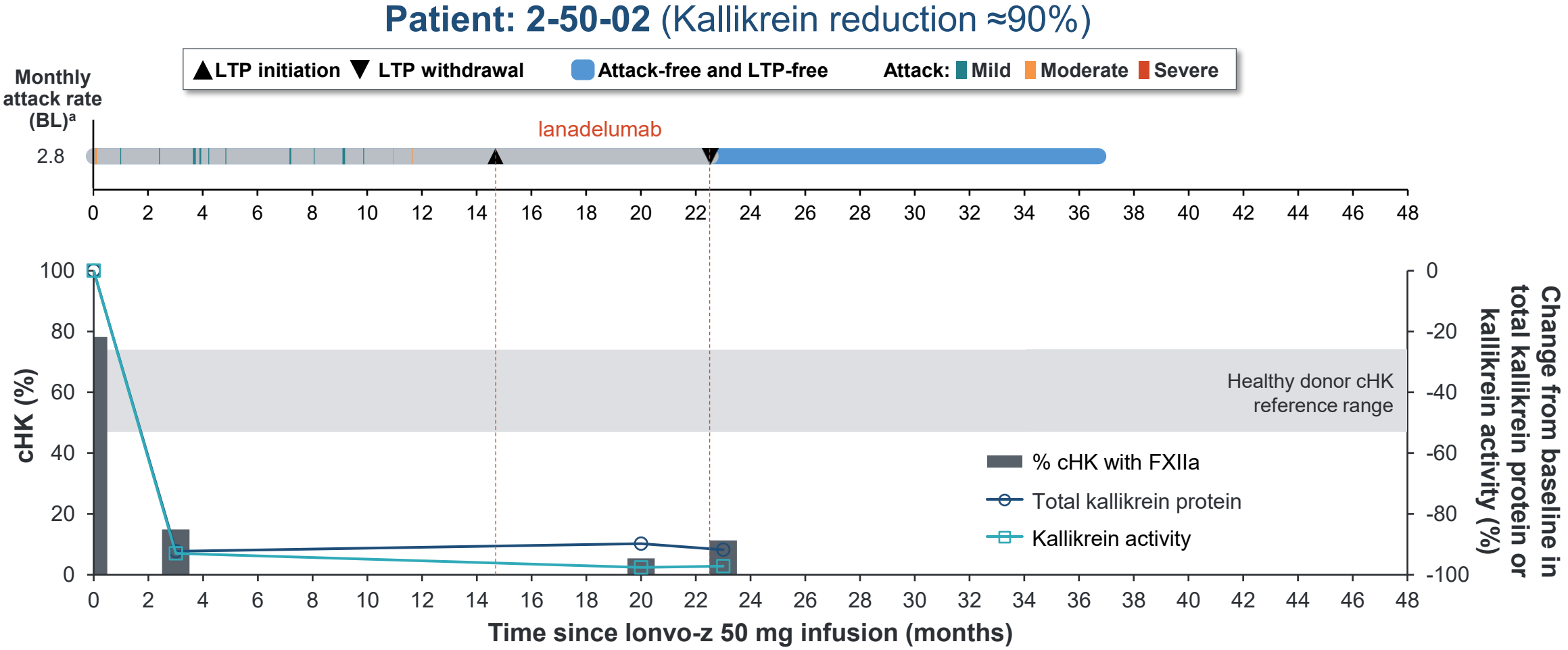
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Healthy donor cHK (%) reference range: 47–74 (+FXIIa). [a]Baseline is defined as the time from informed consent to 50 mg infusion or start of any LTP, whichever occurred first. [b]Patient had 0.9 attacks per month in the 3 months prior to screening.

BL, baseline; cHK, cleaved high-molecular weight kininogen; FDA, U.S. Food and Drug Administration; FXIIa, activated factor XII; LPLV, last patient last visit; LTFU, long-term follow-up; LTP, long-term prophylaxis.

Patient vignette 2: cHK levels decreased after treatment with lonvo-z and were similar during attack and attack-free periods

Addition of lanadelumab further reduced cHK and kallikrein activity



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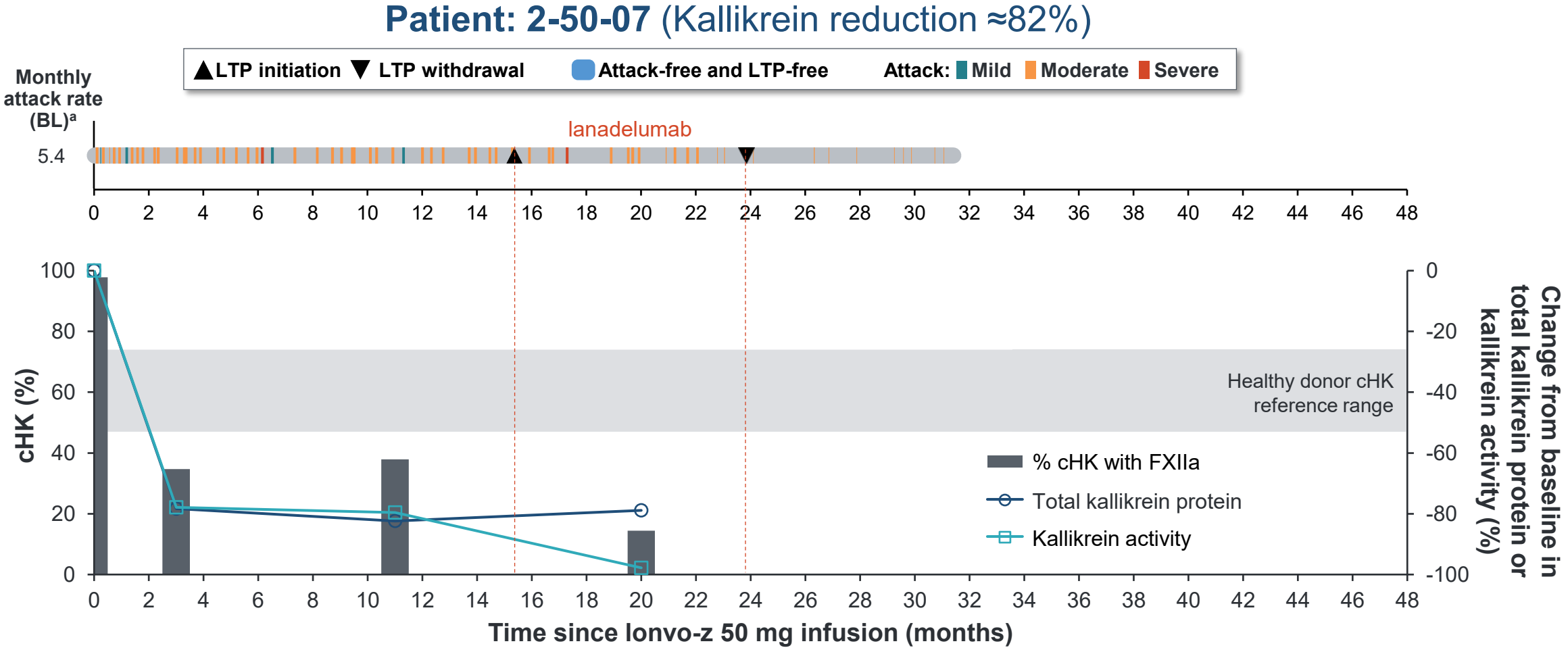
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BL, baseline; cHK, cleaved high-molecular weight kininogen; FDA, U.S. Food and Drug Administration; FXIIa, activated factor XII; LPLV, last patient last visit; LTFU, long-term follow-up; LTP, long-term prophylaxis.

Patient vignette 3: cHK levels decreased after treatment with lonvo-z and were similar during attack and attack-free periods

Addition of lanadelumab impacted the biochemical outcomes, but no meaningful effect on clinical outcomes



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Conclusions

- A one-time treatment with lonvo-z 50 mg led to robust, sustained reductions in HAE attacks without the need for LTP
  - All patients were LTP-free at last assessment
- No long-term risks have been observed with up to 4 years of follow-up after lonvo-z infusion
- These data reinforce the known mechanism of action of lonvo-z, in which inactivation of the *KLKB1* gene reduces plasma prekallikrein, which is subsequently thought to reduce overall activity of plasma kallikrein and reduce bradykinin production
- The observed attacks in patients after lonvo-z are biochemically inconsistent with an HAE attack; alternative etiologies in the one patient who continues to experience attacks should be considered
- These data support the durability of clinical and biomarker outcomes following lonvo-z treatment

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FDA, U.S. Food and Drug Administration; HAE, hereditary angioedema; LPLV, last patient last visit; LTFU, long-term follow-up LTP, long-term prophylaxis.

Acknowledgments

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