



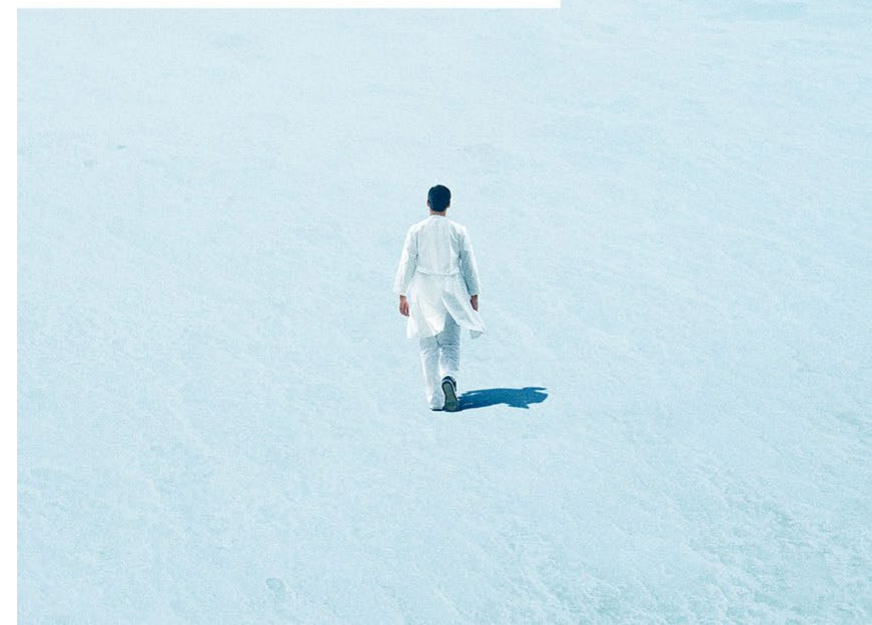
NXT007: Study Session on ISTH Presentation

24 June 2025

CHUGAI PHARMACEUTICAL CO., LTD.



INNOVATION BEYOND IMAGINATION



Important Reminders

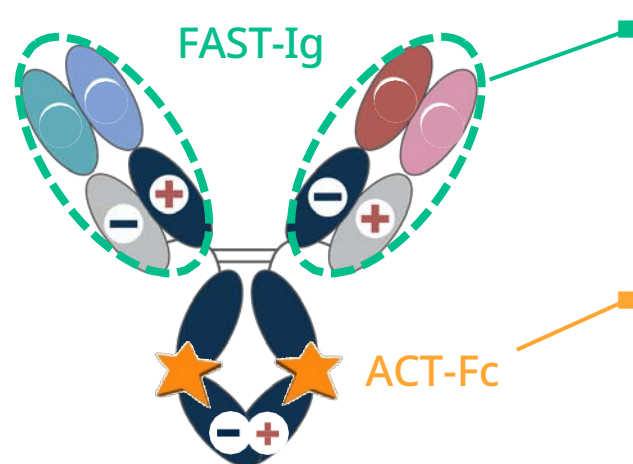
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Please note that Japanese is the preferred language in expression and content, since the official language of this presentation is Japanese.

NXT007: Providing New Value to People with Hemophilia A

- Chugai's proprietary antibody engineering technologies are applied. The ongoing Phase 2 trial results will be presented at a medical conference in 2025
- Three Phase 3 trials, including head to head vs. Hemlibra[®], are planned to start in 2026



Anti-coagulation factor IXa/X bispecific antibody applying FAST-Ig[™]: Higher efficacy is expected by optimizing the variable region of Hemlibra[®]

Expecting high convenience by improving antibody pharmacokinetics through the application of ACT-Fc[®]

Engineered based on Hemlibra[®], to enhance binding affinities, extend half-life, and allow for low volume, infrequent subcutaneous injections

- ~30-fold more potent than Hemlibra[®] and in vitro assay indicates that thrombin generation is within the range of people without Hemophilia A*
- High convenience in dosing (~10-week half-life** and subcutaneous injection)

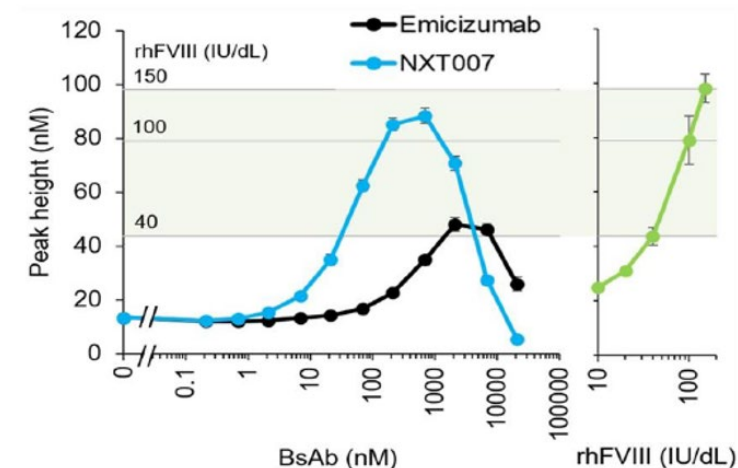
*A bispecific antibody NXT007 exerts a hemostatic activity in hemophilia A monkeys enough to keep a non-hemophiliac state (<https://doi.org/10.1016/j.jtha.2023.09.034>)

**Data of healthy adult part in the NXT001JG study presented at 2023 ISTH

¹ Yuri Teranishi-Ikawa et. al *Journal of Thrombosis and Haemostasis* 2023 ^a tissue factor triggered

P1	P2	P3
P1/2		Data in 2025
vs. FVIII		P3 start exp.2026
vs. Hemlibra [®]		P3 start exp.2026
Pediatric patients		P3 start exp.2026

in vitro Thrombin Generation Assay ^{1,a}



(OC 20.3)

NXT007 Prophylaxis in Emicizumab-Naive Persons with Hemophilia A without Inhibitor: Phase I/II Study (NXTAGE)

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Overview of NXTAGE Part B

Multiple ascending dose part in emicizumab-naïve PwHA to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics and efficacy of NXT007

Key Inclusion Criteria:

- Severe Hemophilia A
- Without FVIII inhibitors
- Ages ≥ 12 to < 65 years



Patients received NXT007 via subcutaneous (SC) administration every 4 weeks (Q4W) in ascending dose cohorts after loading doses

(N=6-8/cohort*¹)

B-4: 4 weeks loading dose → Maintenance dose: **1.08 mg/kg Q4W SC**

B-3: 4 weeks loading dose → Maintenance dose: **0.7 mg/kg Q4W SC**

B-2: 6 weeks loading dose → Maintenance dose: **0.28 mg/kg Q4W SC***²

B-1: 4 weeks loading dose → Maintenance dose: **0.072 mg/kg Q4W SC**

*¹ For B-1, 10 patients were enrolled.

*² Dosing regimen was switched from 0.14 mg/kg Q2W to reflect study protocol amendment.

Timing of the primary analysis:

- At least 6 patients completed 16 weeks of NXT007 treatment in all Part B cohorts
- First patient in: 1-Feb-2022
- Data cutoff date: 6-Nov-2024

Concept of Dose Setting

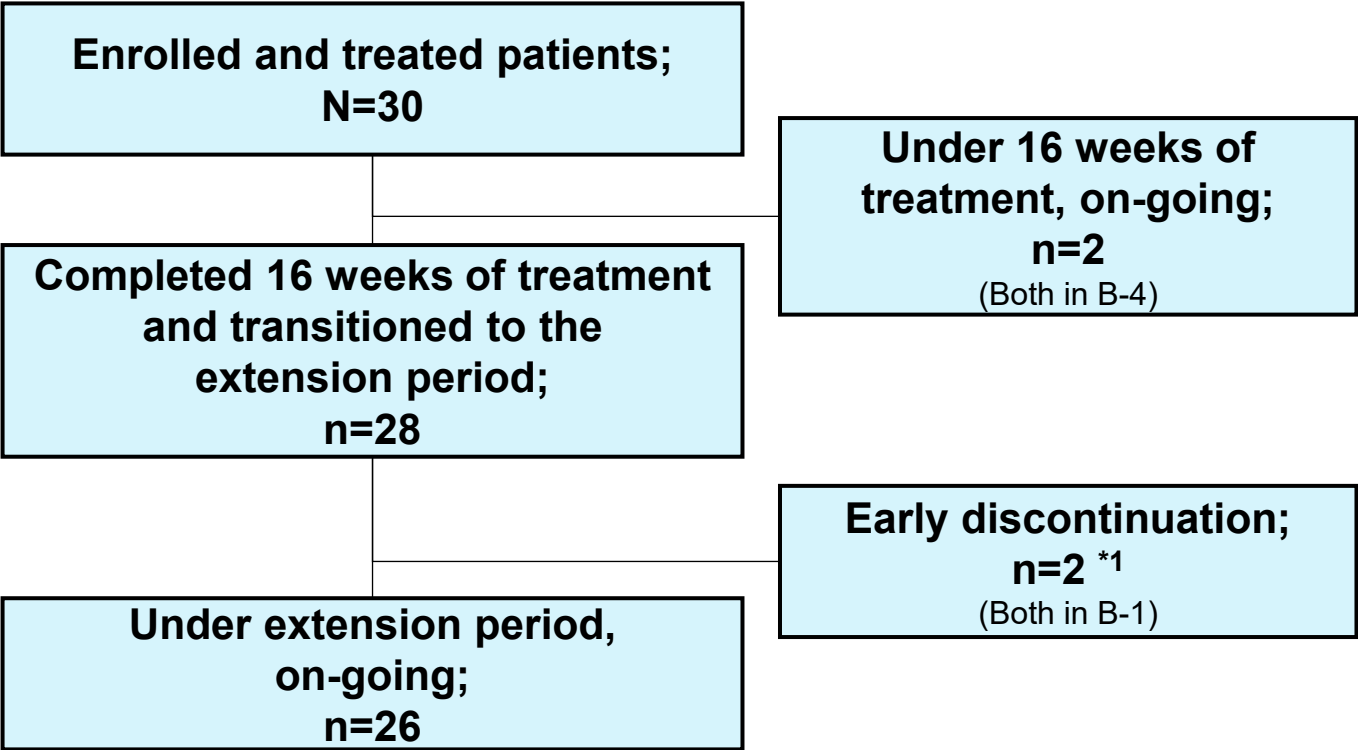
- NXT007 doses were adapted by population PK simulations using the PK data from healthy volunteers who participated in NXTAGE to achieve the target FVIII-equivalent activity predicted based on FIX-NXT007-FX ternary complex concentrations.
- FVIII-equivalent activity was predicted to reach non-hemophilic level in B-2 onwards.

Cohort	Maintenance dose	Predicted trough levels at steady state	
		Plasma NXT007 concentration	FVIII-equivalent activity* ¹
B-4	1.08 mg/kg Q4W	24.8 µg/mL	93.1 IU/dL
B-3	0.7 mg/kg Q4W	16.1 µg/mL	73.8 IU/dL
B-2	0.28 mg/kg Q4W	7.27 µg/mL	40.1 IU/dL
B-1	0.072 mg/kg Q4W	2.29 µg/mL	13.8 IU/dL

*¹ The FVIII-equivalent activity prediction was performed based on Yoneyama et.al., Blood (2022) 140 (Supplement 1): 11295–11296

Patient Disposition and Duration of Exposure

Patient Disposition



*1 One patient discontinued NXT007-treatments due to unrelated adverse event, lower limb fracture. Another patient discontinued NXT007-treatments due to development of anti-drug antibody (ADA) impacting PK. Both discontinued the study due to consent withdrawal thereafter.

Duration of NXT007 Exposure by Cohort

Cohort	Duration of Exposure; week (median, min-max)
B-1 (N=10)	114.1 (29-140)
B-2 (N=6)	96.4 (88-112)
B-3 (N=6)	58.1 (52-72)
B-4 (N=8)	22.2 (4-28)
Total (N=30)	68.4 (4-140)

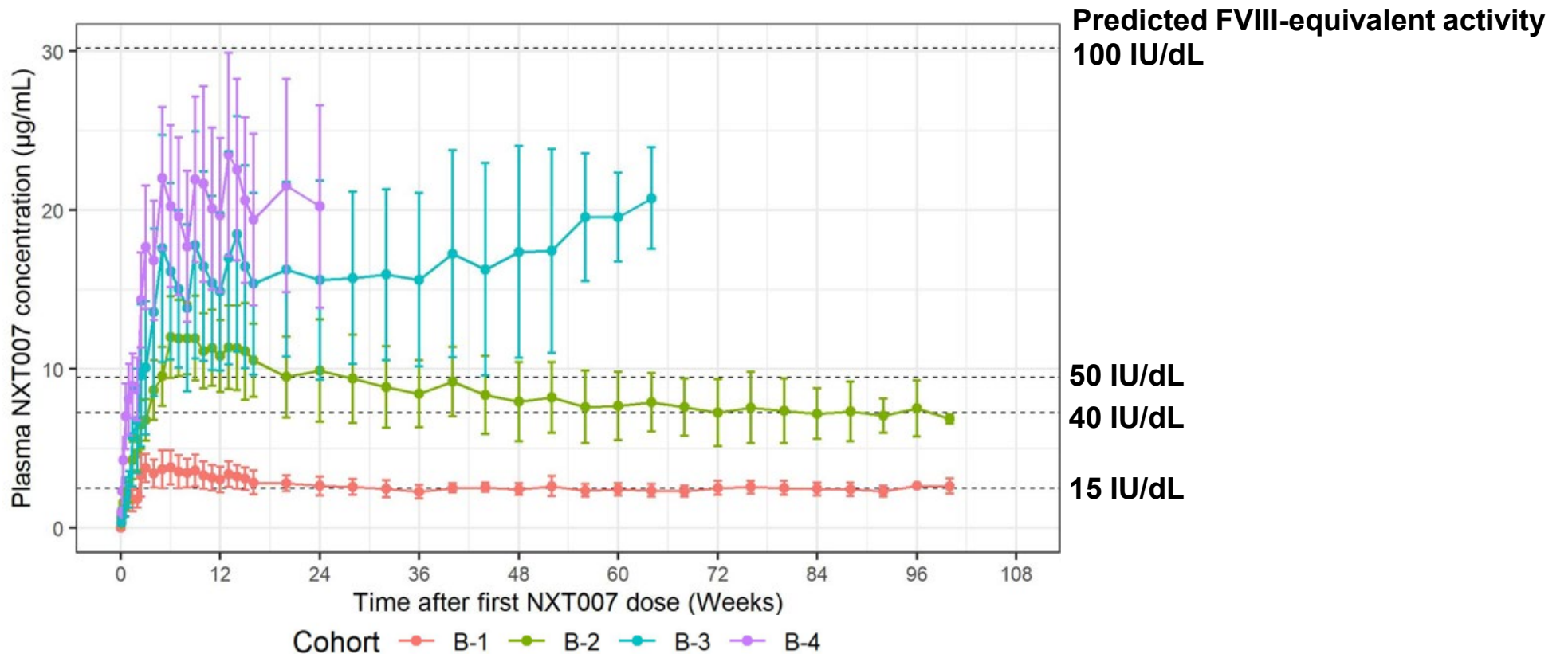
Patient Demographics

Most of the patients (96.7%) received FVIII prophylaxis before enrollment.

	B-1 (N=10)	B-2 (N=6)	B-3 (N=6)	B-4 (N=8)	Total (N=30)
Age, years, median (range)	39.5 (20 - 57)	22 (12 – 54)	37 (18 - 52)	51.0 (25 - 56)	39.5 (12-57)
Weight, kg, median (range)	68.75 (53.8 – 93.9)	78.30 (40.6 – 89.6)	60.70 (52.6 – 82.0)	70.55 (56.2 – 81.5)	69.65 (40.6-93.9)
Patients with Target joint, n (%)	3 (30.0%)	1 (16.7%)	1 (16.7%)	1 (12.5%)	6 (20.0%)
Prior treatment regimen					
Prophylaxis, n (%)	9 (90%)	6 (100%)	6 (100%)	8 (100%)	29 (96.7%)
Episodic, n (%)	1 (10%)	0	0	0	1 (3.3 %)

PK and Predicted FVIII-equivalent Activity

- Dose-dependent increase of NXT007 plasma concentration was observed.
- In B-3 and B-4, plasma concentrations beyond non-hemophilic levels of FVIII-equivalent activity were maintained, consistent with the dose setting concept.

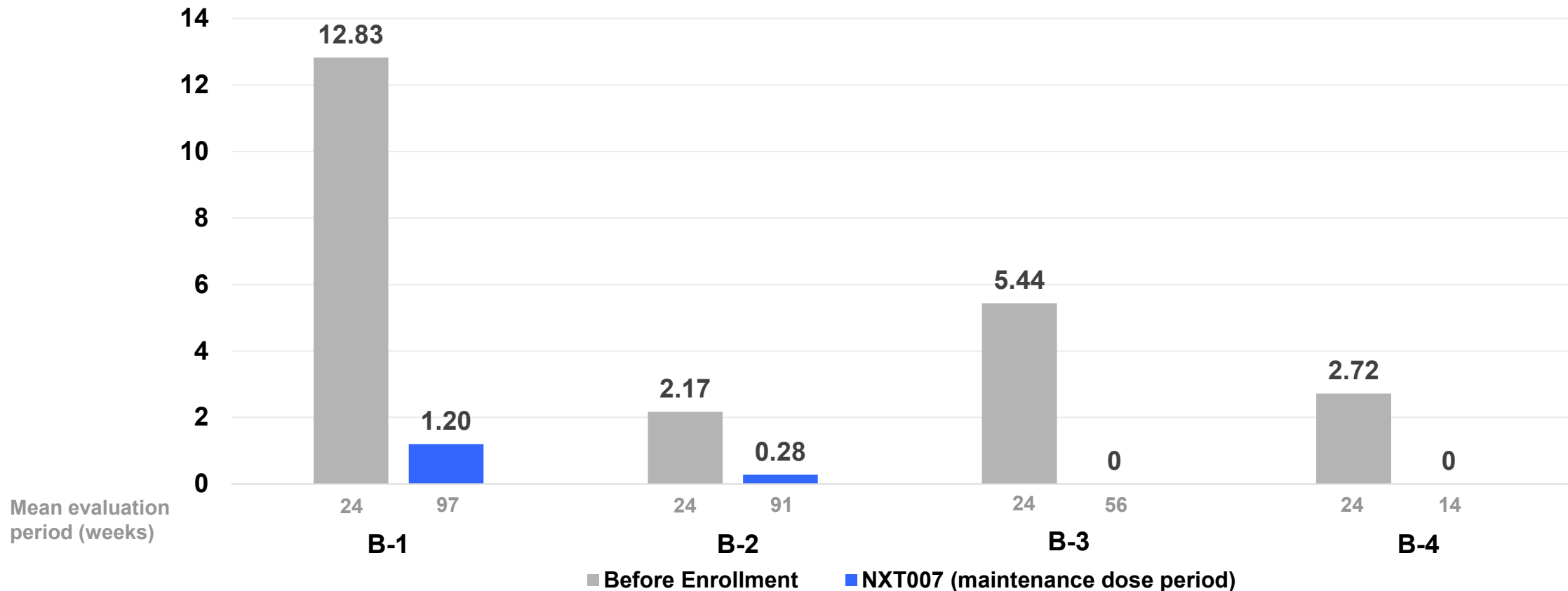


Excluding 4 PK outliers, and 2 patients with PK decrease presumably due to anti-drug antibody. The PK data after up-titration in 3 B-1 patients were also excluded. Data not shown if the number of measured values is less than two.

Efficacy: Annualized Bleed Rate (ABR)

ABR decreased during NXT007 prophylaxis compared to baseline*¹.

Mean ABR for treated bleeds*²



*¹ 96.7% of patients received prophylactic therapy with FVIII agents.

*² Bleeding information before study was collected from 24 weeks before the study in a retrospective manner. Calculated ABR is displayed.

Safety and Tolerability

NXT007 was well tolerated:

- No dose-dependent increases in AEs were observed.
- All serious AEs were NOT related to NXT007.
- **No thromboembolic events were observed.**
- Injection site reactions were reported in 4 patients (13.3%), all of which were mild.

	B-1 (N=10)	B-2 (N=6)	B-3 (N=6)	B-4 (N=8)	Total (N=30)
Total No. of patients with at least one AE	7 (70.0%)	5 (83.3%)	3 (50.0%)	6 (75.0%)	21 (70.0%)
Total No. of AEs	17	51	10	11	89
Total No. of patients with at least one:					
Serious AE ^{*1}	3	0	0	0	3
Led to treatment discontinuation ^{*1}	1	0	0	0	1
NXT007-related ^{*1}	0	0	0	0	0
Thromboembolic event	0	0	0	0	0
NXT007-related AE ^{*2}	2	1	0	3	6
Injection site reactions	2	0	0	2	4

^{*1} Serious AEs include lower limb fracture, ankle fracture, and carbon monoxide poisoning, among which the lower limb fracture led to study drug discontinuation.

^{*2} Injection site erythema (1 event in B-1, 1 event in B-4), injection site reaction (2 events in B-1), rash (1 event in B-2), hepatic function abnormal (1 event in B-4), and injection site rash (1 event in B-4).

Immunogenicity: Anti-Drug Antibody (ADA)

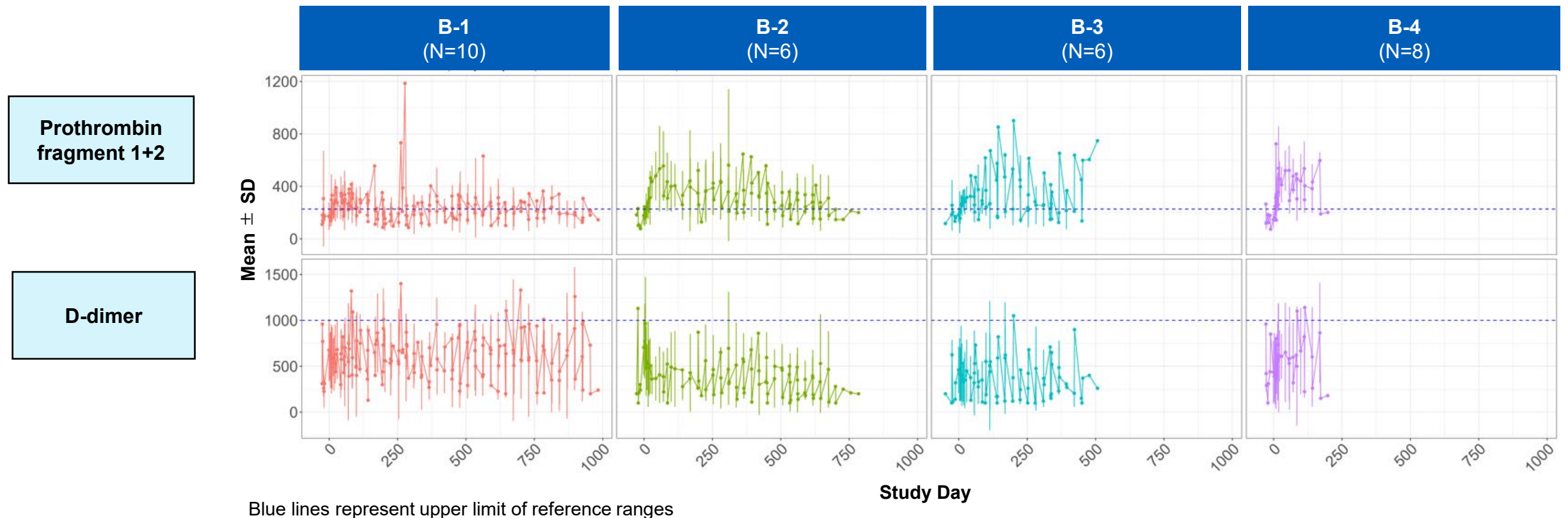
- ADA was observed in 22 out of 30 patients; the number of ADA positive patients at the final observation before the data cutoff was 9.
- ADA impacting PK was observed in 2 patients.
 - One patient in B-1 completely lost NXT007 plasma concentration due to ADA, and discontinued treatment.
 - The other patient in B-3 experienced a decrease in plasma concentration to B-1 levels, and was continuing NXT007 treatment without bleeding events.
- No ADA cross-reacting with emicizumab was observed.

	B-1 (N=10)	B-2 (N=6)	B-3 (N=6)	B-4 (N=8)	Total (N=30)
ADA post-baseline incidence *1	7	6	4	5	22
ADA impacting PK	1	0	1	0	2
ADA cross-reacting with emicizumab	0	0	0	0	0

*1 No patients were ADA positive at baseline.

Coagulation Markers

- Prothrombin fragment 1+2 levels showed an increasing trend above the reference range, suggesting increased coagulation potential.
- No increasing trend was observed in D-dimer, suggesting no significant systemic hypercoagulability.



Conclusions

NXTAGE Part B examined NXT007, the emicizumab-based next generation bispecific antibody, in PwHA with Q4W SC dosing for the first time.

NXT007 prophylaxis led to a decrease in ABR compared to baseline.

No treated bleeds were observed during maintenance dose period in B-3 and B-4 with predicted FVIII-equivalent activity beyond the non-hemophilic level.

No safety concerns were observed up to the highest dose cohort (B-4).



The results suggest that NXT007 has a potential to provide a hemostatic normalization in PwHA with acceptable safety profile, supporting advancement to next phase clinical studies. The efficacy and safety of NXT007, including hypercoagulability and ADA, should be further investigated.

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A member of the Roche group