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XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-57

2.07 Novel therapeutic products and approaches (including gene therapy)

NXT007 PROPHYLAXIS IN PEOPLE WITH HEMOPHILIA A WITH OR WITHOUT FACTOR VIII INHIBITORS: COMBINED ANALYSIS OF TWO PHASE I/II MULTIPLE-ASCENDING-DOSE STUDIES

M.E. Mancuso[1|2], M. Shima[3], J.M. Staber[4], Y.C. Chen[5], F.J. López-Jaime[6], M.C. Shen[7], G. Ventriglia[8], M. Takeyama[9], C. Schmitt[8], Y.S. Park[10], A. Kiialainen[8], N. Mizuno[11], M. Niggli[8], T. Miyake[11], D. Matino[12], T. Saito[11], V. Jiménez-Yuste[13], R. Kobayashi[11], D. Hart[14], K. Nogami[15]

[1]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, Italy; [2]Center for Thrombosis and Hemorrhagic Diseases, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [3]Thrombosis and Hemostasis Research Center, Nara Medical University, Kashihara, Nara, Japan; [4]Stead Family Department of Pediatrics, Carver College of Medicine, University of Iowa, Iowa City, USA; [5]Hemophilia Care and Research Center, Tri-Service General Hospital, National Defense Medical University, Taipei, Taiwan; [6]Servicio de Hematología, Hospital Universitario Regional de Málaga / Instituto de Investigación Biomédica de Málaga (IBIMA), Málaga, Spain; [7]Department of Internal Medicine, Changhua Christian Hospital, Changhua, Taiwan; [8]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [9]Division of Hemophilia, National Hospital Organization, Osaka National Hospital, Osaka, Japan; [10]Department of Pediatrics, Kyung Hee University Hospital at Gangdong, Seoul, South Korea; [11]Chugai Pharmaceutical Co., Ltd, Tokyo, Japan; [12]McMaster University, Hamilton, Ontario, Canada; [13]La Paz University Hospital-IdiPAZ, Autónoma University, Madrid, Spain; [14]Roche Products Ltd, Welwyn Garden City, UK; [15]Department of Pediatrics, Nara Medical University, Kashihara, Nara, Japan

Background. NXT007, a next-generation bispecific antibody based on emicizumab that mimics activated factor (F)VIII function in people with hemophilia A (HA), was investigated in two Phase I/II, open-label, non-randomized, multicenter, multiple-ascending-dose (MAD) studies: one in Asia (NXTAGE Part B; jRCT2080224835), one Global (NCT05987449).

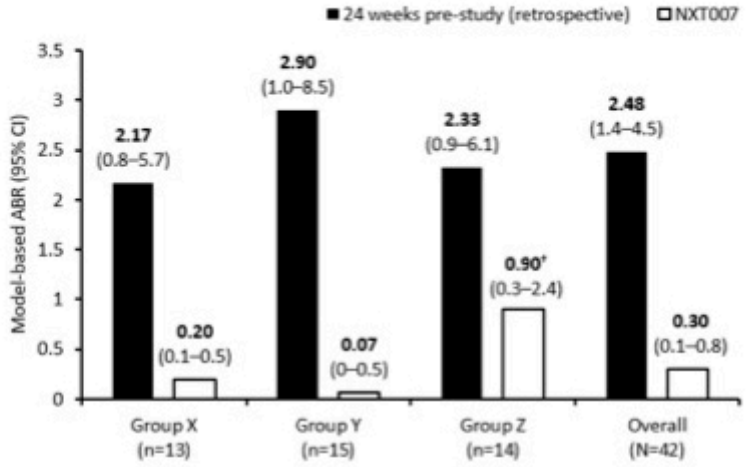
Aims. Report outcomes in three pooled NXT007 dose cohorts from two MAD studies (F. Hoffmann-La Roche Ltd/Chugai Pharmaceutical Co., Ltd) with equivalent dosing.

Methods. Eligible participants were emicizumab-naïve and aged 12–64 years (Global study: ≤59 years). Subcutaneous NXT007 maintenance doses in NXTAGE cohorts B2, B3 and B4 are identical to Global cohorts 1, 2 and 3 (0.28, 0.70, and 1.08 mg/kg, respectively, every 4 weeks; predicted to achieve non-hemophilic FVIII activity), and are pooled into Groups X, Y, and Z. Loading doses were weekly in NXTAGE Group X and Y (X: six doses; Y: four doses) and as two doses at 2-week intervals in the Global study and NXTAGE Group Z. Informed consent and ethics approval were obtained. Outcomes included safety, pharmacokinetics, pharmacodynamics, immunogenicity, and model-based annualized bleeding rates (ABRs).

Results. Overall, 42 participants received NXT007 (Group X: n=13; Group Y: n=15; Group Z: n=14). Forty (95.2%) had severe HA; one (2.4%; Global study) had FVIII inhibitors. Median (range) age was 36 (12–56) years. At cut-off (NXTAGE: 06-Nov-24; Global: 21-Apr-25), median (range) observation periods in Groups X, Y, and Z were 80.0 (61.1–113.3), 44.1 (42.1–72.4), and 21.6 (5.4–34.4) weeks, respectively. NXT007 had favorable safety outcomes across doses. D-dimer remained within normal range and prothrombin fragment 1+2 elevated slightly; neither increased dose-dependently. ABR (95% confidence interval) for treated bleeds in the maintenance period was 0.3 (0.1–0.8; Figure); 36/42 (85.7%) participants had zero treated bleeds. NXT007 plasma concentrations increased dose-dependently, with no ethnic differences. Thrombin generation peak height increased from baseline with all doses. Overall, 34/42 (81.0%) participants developed anti-drug antibodies (ADAs); one (2.4%; Group Y, NXTAGE) had ADAs impacting pharmacokinetics; none impacted safety or cross-reacted with emicizumab.

Conclusions. NXT007 had favorable safety outcomes, with low treated ABRs. One participant had ADAs impacting pharmacokinetics. These data support progression to Phase III trials.

Figure. Treated bleeding rates*



	Group X (n=13)	Group Y (n=15)	Group Z (n=14)	Overall (N=42)
Median (range) NXT007 maintenance observation duration	76.0 weeks (57.1–107.3)	40.1 weeks (38.1–68.4)	17.6 weeks (1.4–30.4)	40.1 weeks (1.4–107.3)
Participants with zero treated bleeds, n (%)	9/13 (69.2)	14/15 (93.3)	13/14 (92.9)	36/42 (85.7)

*ABRs are derived from a negative binomial regression model, and represent bleeds reported during the NXT007 maintenance dose period.

†Four treated bleeds, observed in one notable outlier in the Global study who experienced arterial bleeds secondary to direct trauma to a vessel in a replaced knee.

ABR, annualized bleeding rate; CI, confidence interval