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New Data from the Japanese Phase III Clinical Trial of Hemlibra for Acquired Hemophilia A (AGEHA Study) Presented at ISTH

- Long-term follow-up data on the use of Hemlibra in patients with acquired hemophilia A on immunosuppressive therapy and data of use in patients not eligible for immunosuppressive therapy were newly presented

TOKYO, June 26, 2023 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that the final analysis data of a Japanese phase III clinical trial (AGEHA Study) for Chugai's anti-coagulation factor IXa/X humanized bispecific monoclonal antibody/coagulation factor VIII substitute Hemlibra® [generic name: emicizumab (genetical recombination)] in acquired hemophilia A (AHA) including patients ineligible for immunosuppressive therapy was presented at the 31st International Society on Thrombosis and Haemostasis (ISTH) Annual Congress held in Montréal, Canada., on June 24 (local time).

"Acquired hemophilia A, a nationally designated intractable autoimmune disease, had limited treatment options to control bleeding for a long time. The newly presented data of Hemlibra suggest sustained bleeding control within long-term administration and reduced risk of bleeding in patients who are ineligible for immunosuppressive therapy, which is the standard of care. We will continue to build data on Hemlibra to promote its proper use so that patients, caregivers, and healthcare professionals can benefit from this drug as a treatment option that can effectively control bleeding," said Dr. Osamu Okuda, Chugai's President and CEO.

AGEHA study is a multicenter, single-arm, Japanese phase III clinical trial with two cohorts to investigate the safety, efficacy, pharmacokinetics, and pharmacodynamics of subcutaneous administration of Hemlibra in AHA. Cohort 1 enrolled 12 adults with AHA undergoing or scheduled to start immunosuppressive therapy. Cohort 2 enrolled 2 adults with AHA who were determined ineligible for immunosuppressive therapy at the time of enrollment. Participants subcutaneously received Hemlibra 6 mg/kg (body weight) on day 1, 3 mg/kg (body weight) on day 2, and 1.5 mg/kg (body weight) weekly from day 8. Dosing completion criteria for Hemlibra were specified in the study. Administration of Hemlibra was discontinued if the FVIII activity was more than 50 IU/dL and if more than 72 hours had passed since the last coagulation factor administration for the most recent bleed requiring treatment.

In this final analysis, 9 of 12 participants (75%) in cohort 1 and all two participants in cohort 2 (100%) did not experience bleeds that required treatment during the Hemlibra treatment period. Annual bleeding rates were as follows.

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AGEHA Study Annual Bleeding Rates

Efficacy evaluation period	Cohort 1*		Cohort 2**	
	Pre-treatment Period	On-treatment Period	Pre-treatment Period	On-treatment Period
Treated bleeds (times per year)	35.6 (24.91-49.42)	3.2 (0.71-9.08)	17.0 (9.88-27.18)	0.0 (NA-3.69)
Major bleeds (times per year)	66.4 (51.41-84.44)	0.0 (NA-3.69)	15.9 (9.06-25.83)	0.0 (NA-3.69)
All bleeds (times per year)	77.0 (60.80-96.27)	5.3 (1.77-12.04)	26.0 (16.98-38.09)	3.7 (0.92-9.75)

*median evaluation period: 68.0 (range: 17-168) days in the pre-treatment period, and 44.5 (range: 8-639) days in the on-treatment period

**median evaluation period: 95.5 (range: 23-168) days in the pre-treatment period, and 257 (range: 64-450) days in the on-treatment period

Adverse events related to Hemlibra were observed in three out of 12 participants (25%) in cohort 1 and in all two participants (100%) in cohort 2, with Basedow disease identified as a serious side effect in one participant. Among them, asymptomatic deep vein thrombosis was observed in one patient in the primary analysis, and there was no other thromboembolism or thrombotic microangiopathy events. No new safety signals were identified.

[Reference]

Primary Analysis of Japanese Phase III Clinical Trial of Hemlibra for Acquired Hemophilia A (AGEHA Study) Presented at ISTH (Press release issued on July 12, 2022)
https://www.chugai-pharm.co.jp/english/news/detail/20220712120001_932.html

Chugai Obtains Regulatory Approval for Hemlibra for Additional Indication of Acquired Hemophilia A (Press release issued on June 20, 2022)
https://www.chugai-pharm.co.jp/english/news/detail/20220620170002_928.html

About Hemlibra

Hemlibra is a bispecific monoclonal antibody created with Chugai's proprietary antibody engineering technologies. The drug is designed to bind factor IXa and factor X. In doing so, Hemlibra provides the cofactor function of factor VIII in people with hemophilia A, who either lack or have impaired coagulation function of factor VIII.[1,2] The product was approved by the U.S. Food and Drug Administration (FDA) in November 2017, for the first time in the world, for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors. Hemlibra has been approved in more than 110 countries for congenital hemophilia A with and without factor VIII inhibitors. In Japan, it was first approved in March 2018 for congenital hemophilia A with factor VIII inhibitors, and its indication was later expanded to include

congenital hemophilia A without factor VIII inhibitors, and acquired hemophilia A.

About acquired hemophilia A

Acquired hemophilia A is a disease in which inhibitors of blood coagulation factor VIII are acquired. The inhibitors result in a significant decrease in factor VIII activity, leading to bleeding symptoms such as spontaneous subcutaneous bleeding and intramuscular bleeding. Serious bleeding is not rare in the disease. Acquired hemophilia A is an autoimmune disease in which autoantibodies against factor VIII are produced on the basis of collagen disease, malignant tumor, and childbirth.[3,4] Acquired hemophilia A is one of the diseases included in autoimmune acquired factor deficiency, which is a nationally designated intractable disease (designated intractable disease 288). Treatment includes immunosuppressive therapy to eliminate inhibitors and treatment to improve bleeding symptoms.

Sources

1. Kitazawa, et al. Nature Medicine 2012; 18(10): 1570
2. Sampei, et al. PLoS ONE 2013; 8(2): e57479
3. Franchini M, Veneri D. Acquired coagulation inhibitor-associated bleeding disorders: an update. Hematology 2005;10:443-9.
4. Cohen AJ, Kessler CM. Acquired inhibitors. Baillieres Clin Haematol 1996;9:331-54.

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