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POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Patient-Reported Outcomes (PROs) in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Treated with Crovalimab and Eculizumab: Results from the Phase III Randomized COMMODORE 2 and COMMODORE 1 Trials

Jens Panse, MD[1,2], *Jaroslav Cermak*[3], *Olena Kyselova, MDPhD*[4], *Akihiko Gotoh, MD PhD*[5], *Fahri Sahin*[6], *Hubert Schrezenmeier, MD*[7,8], *Alice C. Chang*[9], *Brittany Gentile, PhD*[10], *Marianne Uguen*[11], *Bing Han*[12]

[1] Department of Hematology, Oncology, Hemostaseology and Stem Cell Transplantation, Medical Faculty, RWTH Aachen University, Aachen, Germany
[2] Center of Integrated Oncology (CIO), Aachen, Bonn, Cologne, Düsseldorf (ABCD), Germany
[3] Institute of Hematology and Blood Transfusion, Prague, Czech Republic
[4] Institute of Hematology and Transfusiology, National Academy of Medical Science, Kiev, Ukraine, Kiev, Ukraine
[5] Department of Hematology, Tokyo Medical University, Tokyo, JPN
[6] Division of Hematology, Department of Internal Medicine„ Ege University, Izmir, Turkey
[7] University of Ulm, Ulm, Germany
[8] German Red Cross Blood Transfusion Service Baden-Württemberg-Hessen and University Hospital Ulm, Ulm, Germany
[9] Genentech Inc., South San Francisco, CA, SUNNYVALE, CA
[10] Genentech, Inc., South San Francisco, CA, San Francisco, CA
[11] F. Hoffman-La Roche, Basel, Switzerland
[12] Department of Hematology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, CHN

Introduction COMMODORE 2 (NCT04434092) and COMMODORE 1 (NCT04432584) are global, randomized, open-label, multicenter Phase III trials evaluating crovalimab (crova) vs eculizumab (ecu) in patients (pts) with PNH. COMMODORE 2 tested the non-inferiority of crova vs ecu in C5i-naive pts and demonstrated that crova was non-inferior to ecu for hemolysis control, transfusion avoidance, breakthrough hemolysis, and hemoglobin stabilization (Röth EHA 2023; #S181). In both studies, crova was well tolerated for both C5i-naive and C5i-experienced pts (Röth EHA 2023; #S181, Scheinberg EHA 2023; #S183). To investigate the efficacy of crova vs ecu from a pt perspective, PRO tools were used to assess fatigue, PNH-related symptoms, functioning, and global health status/quality of life (GHS/QoL) among COMMODORE 2 and COMMODORE 1 pts.
Methods In COMMODORE 2, C5i-naive pts were randomized 2:1 to receive crova or ecu during a 24-week primary treatment period. In COMMODORE 1, C5i-experienced pts receiving ecu at study start were randomized 1:1 to receive crova or ecu during a 24-week primary treatment period. Pts received crova as a weight-based tiered regimen (Liu ASH 2022; #293) that included loading doses followed by maintenance doses via subcutaneous injection every 4 weeks, or ecu via intravenous infusion every 2 weeks (900 mg per label). After completing 24 weeks of treatment, COMMODORE 1 and 2 pts randomized to crova continued crova, and those randomized to ecu switched to crova if continuing in the extension period.
Paper PRO questionnaires were completed by adult pts at baseline (BL) and at Weeks 2, 5, 9, 17, and 25 during the primary treatment period (up to Week 25) and during the crova extension period (from Week 25 onwards). Fatigue was assessed with the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scale (higher scores indicate lower fatigue severity). Additional PNH symptoms (dyspnea, dysphagia, headaches, abdominal pain, chest pain, and erectile dysfunction) were assessed using relevant questions selected from the European Organisation for Research and Treatment of Cancer (EORTC) Item Library (EORTC IL-40; higher scores indicate worse symptoms). Physical function, role function, and GHS/QoL were assessed with the EORTC Quality of Life Questionnaire Core 30 (EORTC QLQ-C30; higher scores indicate better functioning/quality of life).
Results For the primary analysis, COMMODORE 1 randomized 45 pts to crova and 44 to ecu, and enrolled 38 pts in the descriptive arm; COMMODORE 2 randomized 135 pts to crova and 69 to ecu. In COMMODORE 2, C5i-naive pts in both arms showed rapid and sustained improvement across all PRO measures during the primary treatment period. Clinically meaningful improvement (≥5 points; Cella ASH 2021; #1952) in mean FACIT-Fatigue scores from BL occurred in both arms, with numerically higher improvement with crova (crova: 7.8, 95% CI: 6.5, 9.1; ecu: 5.2, 95% CI: 3.4, 6.9; Table 1). Mean fatigue

levels of pts treated with crova improved by Week 2 and were similar to normative population values by Week 25. Analysis of the individual FACIT-Fatigue items was also conducted. Additionally, improvements were observed for both treatment arms in all EORTC IL-40 symptoms and in the functioning and GHS/QoL scales of the EORTC QLQ-C30, with numerically greater improvement with crova for most scales (Table 2). The improvements with crova treatment were maintained during the crova extension period.

In COMMODORE 1, C5i-experienced pts randomized to receive crova or ecu maintained BL levels of fatigue, PNH symptoms, functioning, and GHS/QoL scores throughout the primary treatment period (Tables 1 and 2) and with crova treatment during the extension period. There was no meaningful change in the mean values of any PRO scores after pts switched from ecu to crova at Week 25.

Conclusions C5i-naive pts inCOMMODORE 2 experienced rapid and sustained improvements from BL in fatigue, PNH symptoms, functioning, and GHS/QoL scores while on treatment with crova and ecu, with numerically greater improvement in fatigue and most GHS/QoL scales in the crova arm. C5i-experienced pts in COMMODORE 1 maintained BL levels during the first 24 weeks of treatment with crova or ecu. These trends were maintained after pts were switched from ecu to crova. These data provide supportive evidence for the treatment benefit of crovalimab for self-reported fatigue and quality of life.

Disclosures Panse: *Alexion, AstraZeneca Rare Disease:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Sanofi Ltd:* Consultancy; *Novartis:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Pfizer:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *BMS:* Consultancy; *Apellis Pharmaceuticals, Inc.:* Consultancy; *Amgen:* Consultancy; *Samsung Bioepis:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *MSD:* Consultancy; *Boehringer Ingelheim:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *F. Hoffmann-La Roche Ltd,:* Membership on an entity's Board of Directors or advisory committees, Other: Third party writing assistance by Akshaya Srinivasan, PhD, of MediTech Media Ltd and funded by F. Hoffmann-La Roche Ltd, , Speakers Bureau; *SOBI:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Blueprint Medicines:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau. **Gotoh:** *Janssen Pharmaceutical:* Honoraria; *Kyowa Kirin:* Honoraria; *Nihon Pharmaceutical:* Honoraria; *Nippon Shinyaku:* Honoraria; *Takeda Pharmaceutical:* Honoraria; *Novartis:* Honoraria; *Asahi Kasei Pharma:* Research Funding; *Daiichi Sankyo:* Honoraria, Research Funding; *Sumitomo Pharma:* Honoraria, Research Funding; *Otsuka Pharmaceutical:* Honoraria, Research Funding; *Taiho Pharmaceutical:* Honoraria, Research Funding; *Ono Pharmaceutical:* Honoraria, Research Funding; *Alexion Pharmaceuticals:* Consultancy, Honoraria; *Chugai Pharmaceuticals:* Consultancy, Honoraria, Research Funding; *PharmaEssentia Japan:* Consultancy, Honoraria; *Pfizer Japan:* Honoraria; *Sanofi:* Honoraria; *Bristol Myers Squibb:* Honoraria; *Abbvie:* Honoraria; *AstraZeneca:* Honoraria. **Sahin:** *Sobi:* Consultancy, Honoraria; *Roche:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria; *Novo Nordisk:* Consultancy, Honoraria; *Alexion:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria; *Takeda:* Consultancy, Honoraria. **Schrezenmeier:** *Roche:* Other: honoraria (to University of Ulm) ; *Apellis:* Other: honoraria (to University of Ulm) ; *Sobi:* Honoraria, Other: travel support, Research Funding; *Novartis:* Honoraria, Other: travel support, Research Funding; *Alexion, AstraZeneca Rare Disease:* Honoraria, Other: travel support, Research Funding; *Sanofi:* Other: honoraria (to University of Ulm). **Chang:** *Genentech Inc.:* Current Employment. **Gentile:** *Genentech Inc.:* Current Employment. **Uguen:** *F. Hoffmann-La Roche Ltd, Basel:* Current Employment. **Han:** *Novartis:* Honoraria, Research Funding; *Astra Zeneca:* Honoraria; *F. Hoffmann-La Roche Ltd, Basel:* Honoraria, Research Funding.

Table 1.

	COMMODORE 1[a]		COMMODORE 2[b]	
	Crova (n=38)	Ecu (n=32)	Crova (n=128)	Ecu (n=66)
FACIT-Fatigue score at Week 25, mean (95% CI)[c]	40.8 (37.6, 44.0)	38.0 (34.4, 41.6)	44.3 (43.2, 45.5)	41.4 (39.3, 43.5)
Adjusted change in FACIT-Fatigue from baseline to Week 25, mean (95% CI)[d]	1.1 (−1.5, 3.7)	−2.6 (−5.4, 0.1)	7.8 (6.5, 9.1)	5.2 (3.4, 6.9)
Difference in adjusted mean from baseline to Week 25, % (95% CI)	3.7 (0.1, 7.4)		2.6 (0.7, 4.6)	

FACIT, Functional Assessment of Chronic Illness Therapy. Clinical data cutoff: Nov 16, 2022. Only pts ≥18 years old who were recruited ≥24 weeks before clinical cutoff are included.
[a] C5 inhibitor–experienced pts. [b] C5 inhibitor–naive pts. [c] Higher scores indicate lower fatigue severity. [d] Adjusted mean change from baseline to Week 25 estimates are calculated based on a mixed-effect model of repeated measures. Clinically meaningful improvement in the FACIT-Fatigue score is an increase of ≥5 points from baseline (Cella ASH 2021;#1952).
Röth EHA 2023; #S181, Scheinberg EHA 2023; #S183.

Table 2.

	COMMODORE 1[a]		COMMODORE 2[b]	
	Crova (n=38)	Ecu (n=32)	Crova (n=128)	Ecu (n=66)
Absolute change from baseline to Week 25 in EORTC QLQ-C30 scores, mean (95% CI)[c]				
Physical functioning	0.9 (−3.9, 5.7)	0.4 (−4.7, 5.6)	12.3 (9.2, 15.4)	14.2 (9.2, 19.3)
Role functioning	1.3 (−7.1, 9.7)	−3.7 (−10.9, 3.6)	12.9 (8.1, 17.7)	11.6 (6.1, 17.2)
GHS/QoL	5.7 (−2.4, 13.8)	−1.0 (−6.9, 4.9)	13.4 (10.1, 16.7)	9.9 (4.8, 14.9)
Absolute change from baseline to Week 25 in EORTC IL-40 scores, mean (95% CI)[d]				
Dyspnea	3.2 (−3.3, 9.7)	−0.4 (−5.4, 4.7)	−13.4 (−16.9, −9.9)	−14.8 (−19.9, −9.7)
Dysphagia	0.9 (−3.1, 4.9)	−4.2 (−9.2, 0.9)	−4.4 (−7.7, −1.1)	−6.1 (−12.1, 0.0)
Headaches	−1.8 (−9.4, 5.9)	−1.0 (−11.4, 9.3)	−6.8 (−11.2, −2.4)	−4.6 (−9.1, 0.0)
Abdominal pain	−0.9 (−7.9, 6.1)	−2.1 (−8.9, 4.7)	−8.9 (−12.8, −4.9)	−7.1 (−13.7, −0.4)
Chest pain	0.0 (−2.6, 2.6)	0.0 (−5.3, 5.3)	−4.7 (−7.7, −1.7)	−8.1 (−13.3, −2.9)
Erectile dysfunction[e]	6.7 (−14.5, 27.8)	7.1 (−11.6, 25.9)	−18.0 (−24.5, −11.4)	−10.0 (−19.3, −0.7)

EORTC, European Organisation for Research and Treatment of Cancer; GHS/QoL, global health status/quality of life; IL, item library; QLQ, Quality of Life Questionnaire. Clinical data cutoff: Nov 16, 2022. All data were assessed from baseline through Week 25.
[a] C5 inhibitor–experienced pts. [b] C5 inhibitor–naive pts. [c] Higher scores indicate better functioning/quality of life. [d] Higher scores indicate worse symptoms. [e] Evaluated in male pts only. For COMMODORE 1, n=15 for crova and n=14 for ecu. For COMMODORE 2, n=65 for crova and n=30 for ecu.

Figure 1

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