024 Briquilimab, An Anti-CD117 Antibody, Prevents Passive Systemic Anaphylaxis In Mice Expressing Chimeric Human And Mouse CD117 Through Mast Cell Depletion

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RATIONALE: Mast cells (MC) are the primary cells responsible for triggering life-threatening anaphylactic reactions. Stem cell factor (SCF) signaling through CD117 receptor plays an essential role in MC development, survival, and function. Briquilimab is a humanized aglycosylated monoclonal antibody against CD117 that inhibits SCF signaling and can deplete human mast cells.

METHODS: The effect of briquilimab on passive systemic anaphylaxis (PSA) was evaluated in transgenic mice expressing chimeric CD117 consisting of extracellular human and intracellular mouse regions (hmCD117) instead of wild-type mouse CD117. PSA was performed by sensitization with anti-DNP IgE prior to challenge with DNP-HSA. A single 25mg/kg dose of briquilimab was given to treated animals 2 weeks before challenge (n=3). Control animals received only DNP-HSA (n=6). Core body temperature (CBT) was recorded for 60 minutes after challenge, and statistical analysis of CBT changes was performed by 1-way ANOVA. Fixed tissue sections were stained with toluidine blue for MC quantification.

RESULTS: Briquilimab-treated animals were protected from anaphylactic reactions after PSA challenge, with average CBT of 36.8±1.0°C similar to 37.8±0.8°C in control animals (P=0.440). In contrast, untreated animals exhibited severe anaphylaxis, with average CBT of 33.1±2.3°C after PSA challenge (n=3; P<0.001). MC numbers were decreased in normally MC-abundant tissues including stomach, ear, and tongue ten days after briquilimab treatment compared to control hmCD117 mice without briquilimab treatment, suggesting a single dose of briquilimab effectively blocks PSA response in hmCD117 mice through MC depletion.

CONCLUSIONS: This study provides early proof of concept that briquilimab may be a promising treatment option for MC-mediated disorders including anaphylaxis.

025 Real-world Treatment Outcomes of Lanadelumab in the Prevention of Hereditary Angioedema Attacks: an Interim Analysis of a Polish, Prospective, Multicenter, Observational Study (CHOPIN)

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RATIONALE: CHOPIN is a noninterventional, multicenter study assessing the effectiveness and safety of lanadelumab in Polish patients with hereditary angioedema (HAE) in the National Drug Program (NCT05147181).

METHODS: HAE type-1 or type-2 prophylactic treatment–naïve patients (≥12 years) were enrolled. Primary outcomes: change from baseline in total number and characteristics of HAE attacks. Secondary outcomes: change from baseline to the end of therapy (EOT; 6 months after lanadelumab initiation) in Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH) and Angioedema Quality of Life (AE-QoL). Exploratory outcome: Angioedema Control Test (AECT) total score.

RESULTS: Data for 16 HAE patients (median age 37.0 years, 87.5% female) receiving lanadelumab (March 2022–May 2023) were collected. Median time from diagnosis to lanadelumab initiation was 14.4 years. Among all patients, 172 HAE attacks occurred before and 5 occurred after lanadelumab initiation (severe, 126 versus 2; moderate, 37 versus 1; mild, 9 versus 2). Total incidence of HAE attacks/4 weeks was 2.63 and 0.05 before and at EOT, respectively. Mean baseline and EOT WPAI:GH scores for absenteeism, presenteeism, overall work impairment and activity impairment were: 7.4% (n=11) versus 0.0% (n=12); 50.0% (n=11) versus 0.0% (n=12); 53.3% (n=11) versus 0.0% (n=12); and 51.9% (n=16) versus 3.3% (n=15), respectively. Mean total AE-QoL and AECT scores at baseline and EOT were 59.9 (n=16) versus 7.9 (n=15) and 4.4 (n=15) versus 15.3 (n=15), respectively. Four nonserious lanadelumab-related adverse events were reported.

CONCLUSIONS: Lanadelumab reduced the frequency and severity of HAE attacks, improved patient-reported outcomes, and was well-tolerated in Poland.

026 Understanding The Reasons Not To Treat All HAE Attacks And Patient Satisfaction For On-Demand Treatment (ODT). Results From The HAE Wave II Disease Specific Program™ (DSP™) 2023

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RATIONALE: The notion that HAE patients do not treat all attacks is familiar to experts but the reasons have not been thoroughly documented in literature.

METHODS: Data were drawn from an interim analysis of the ongoing Adelphi HAE Wave II DSP™, a real-world cross-sectional survey of physicians and their patients in France, Germany, Italy, Spain, the United Kingdom and the United States. Physicians used patients' medical chart data alongside clinical judgement to report demographics, reasons to use/not use ODT to treat attacks and characteristics of non-treated attacks.

RESULTS: 65 physicians reported data for 258 HAE patients (53% female; mean [range] age 33 [7-77] years). Mean (SD) time since diagnosis was 9 (9) years. Of these patients, 77% were receiving ODT, for a mean (SD) 4.2 (3.8) years. Most patients (80%) treated their most recent attack with icatibant (53%), pdC1-INH (33%), rC1-INH (12%), or steroids (3%). For patients not treating their most recent attack, reasons (≥10%) included attack was mild/not severe (60%) and patient was not prescribed any ODT (17%). Of the non-treated attacks, 28% were reported by physicians to be moderate/severe, most experienced external swelling of the hands, arms, feet, legs, fingers or toes (59%), followed by abdominal pain (24%), and 13% resulted in the patient attending the ER.

CONCLUSIONS: Physicians reported their patients reserve ODT for more severe attacks, despite the US HAEA Medical Advisory Board/WAO/EAACI recommendation that all attacks are considered for ODT. Prescription and use of ODT for all attacks may reduce attack severity and use of healthcare services.