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POSTER ABSTRACTS

101.RED CELLS AND ERYTHROPOIESIS, EXCLUDING IRON

Combined Safety Data for Sutimlimab in Cold Agglutinin Disease: A Post-Hoc Analysis of the Phase 3 Cardinal and Cadenza Studies

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Background: Cold agglutinin disease (CAD) is a rare, chronic, autoimmune hemolytic anemia mediated by the classical complement pathway (CP).Sutimlimab is a first-in-class, humanized, monoclonal antibody that selectively inhibits C1s of the C1 complex, preventing CP activation and CP-mediated hemolysis. CARDINAL (NCT03347396) was an open-label, single-arm, Phase 3 study of sutimlimab in patients with CAD and recent history of transfusion; CADENZA (NCT03347422) was a randomized, double-blind, placebo-controlled, Phase 3 study of sutimlimab in patients with CAD and no recent history of transfusion. Both studies had a 26-week treatment period (Part A) followed by a long-term extension (Part B), reporting data up to 2 years after the last patient finished Part A of CARDINAL and up to 1 year after the last patient finished Part A of CADENZA. With long-term treatment in both studies, sutimlimab demonstrated sustained efficacy with improvements in hemolysis and anemia, sustained clinically meaningful improvements in quality of life, and it had a favorable safety profile.
Aims: To report combined safety data from Part A and B of the Phase 3 CARDINAL and CADENZA studies in sutimlimab-treated patients with CAD.
Methods: In CARDINAL Part A, patients received sutimlimab on Days 0 & 7, then biweekly until the end of Part B. In CADENZA Part A, patients received sutimlimab or placebo on Days 0 & 7, then biweekly; in Part B, patients continued to receive biweekly sutimlimab or switched from placebo to receive sutimlimab on Days 0 & 7, then biweekly. Data fromall enrolled patients who received at least 1 dose of sutimlimab in CARDINAL (N=24) and CADENZA (N=42), including a post-treatment follow-up 9 weeks after the last dose, were combined into the Safety Analysis Set. Endpoints for this analysis included the incidence of treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), and adverse events of special interest (AESIs). AESIs were selected based on a list of important identified risks and important potential risks for sutimlimab.
Results: The Safety Analysis Set included 66 patients. At baseline, the median age was 69.5 years (range 46-88) and the majority (72.7%) were female, with a median duration since CAD diagnosis of 5.7 years (range 0-33). The median patient follow-up was 129.1 weeks (range 5-175). Sixty-four (97.0%) patients experienced ≥1 TEAE (*Table 1*). Eighty-six TEAEs assessed as related to sutimlimab by the investigator occurred in 30 (45.5%) patients. Fifty-three TESAEs were reported in 22 (33.3%) patients. Three (4.6%) patients each experienced one TESAE assessed as related or possibly related to sutimlimab by the investigator (related vitreous hemorrhage, related viral infection, and possibly related severe cerebral venous thrombosis). Seven patients discontinued sutimlimab treatment and/or the studies due to ≥1 TEAE, 4 in CARDINAL and 3 in CADENZA. Four patients died during the studies: 1 in CADENZA with a TESAE of lung squamous cell carcinoma and sutimlimab was withdrawn due to this TESAE prior to the patient's death; 3 in CARDINAL, 1 patient died after premature discontinuation of sutimlimab due to AEs (fatal infection of *Klebsiella pneumoniae*, acrocyanosis), 1 patient died due to a newly diagnosed hepatic cancer in the first month of the study, and 1 patient died due to exacerbation of CAD during the 9-week washout

period approximately 1.5 months after the last dose of sutimlimab. No deaths were assessed as related to sutimlimab by the investigator.

Treatment-emergent AESIs (selected based on a list of important identified risks and important potential risks for sutimlimab) are presented in *Table 1*. Fourteen TEAEs of serious infection were reported in 9 patients (13.6%; one assessed as related to sutimlimab by the investigator), 31 TEAEs of hypertension were reported in 17 patients (25.8%), 28 TEAEs of acrocyanosis and/or Raynaud's phenomenon were reported in 13 patients (19.7%), and 4 TEAEs of thromboembolic events were reported in 4 patients (6.1%). No TEAEs of serious hypersensitivity reaction and/or anaphylaxis, meningococcal infection or development of systemic lupus erythematosus were reported.

Conclusion: The combined safety analysis of the Phase 3 CARDINAL and CADENZA studies (Part A and B) demonstrated that sutimlimab was generally well tolerated, with the type and frequency of TEAE consistent with an older and medically complex population.

Disclosures Broome: *Apellis:* Honoraria; *Sanofi:* Honoraria; *Alexion:* Honoraria; *Argenx:* Honoraria. **Barcellini:** *Alexion, AstraZeneca Rare Disease:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Novartis:* Consultancy, Honoraria, Speakers Bureau. **Ueda:** *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Janssen:* Consultancy; *Chugai:* Consultancy, Honoraria, Research Funding; *Asahi Kase:* Consultancy; *Alexion:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Sanofi:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *SOBI:* Consultancy, Honoraria. **Khan:** *Sanofi:* Current Employment. **Patel:** *Sanofi:* Current Employment. **Wardęcki:** *Sanofi:* Current Employment, Current equity holder in publicly-traded company, Divested equity in a private or publicly-traded company in the past 24 months, Patents & Royalties. **Kralova:** *Sanofi:* Current Employment. **Srivastava:** *Sanofi:* Current Employment, Current holder of *stock options* in a privately-held company. **Roeth:** *Roche:* Consultancy, Honoraria, Research Funding; *Alexion, AstraZeneca Rare Disease:* Consultancy, Honoraria; *Biocryst:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *Apellis Apellis Pharmaceuticals:* Consultancy, Honoraria; *Sanofi:* Consultancy, Honoraria; *Bioverativ:* Consultancy, Honoraria.

Table 1. Incidence of TEAEs, TESAEs, and AESIs by study and overall in the Safety Analysis Set.

	CARDINAL (N=24)	CADENZA (N=42)	OVERALL (N=66)
TEAEs			
Number of TEAEs, n	385	425	810
Patients with ≥1 TEAEs, n (%)[a]	24 (100)	40 (95.2)	64 (97.0)
Related TEAEs			
Number of related TEAEs, n	16	70	86
Patients with ≥1 related TEAEs, n (%)[a]	11 (45.9)	19 (45.2)	30 (45.5)
TESAEs			
Number of TESAEs, n	40	13	53
Patients with ≥1 TESAEs, n (%)[a]	14 (58.3)	8 (19.1)	22 (33.3)
Related TESAEs			
Number of related TESAEs, n	2	1	3
Patients with ≥1 related TESAEs, n (%)[a]	2 (8.3)	1 (2.4)	3 (4.6)
AESIs			
Serious infections[b]			
Number of TEAEs, n	12	2	14
Patients with ≥1 TEAEs, n (%)[a]	7 (29.2)	2 (4.8)	9 (13.6)
Hypertension[c]			
Number of TEAEs, n	10	21	31
Patients with ≥1 TEAEs, n (%)[a]	5 (20.8)	12 (28.6)	17 (25.8)
Acrocyanosis and/or Raynaud's phenomenon[d]			
Number of TEAEs, n	10	18	28
Patients with ≥1 TEAEs, n (%)[a]	5 (20.8)	8 (19.1)	13 (19.7)
Thromboembolic events[e]			
Number of TEAEs, n	2	2	4
Patients with ≥1 TEAEs, n (%)[a]	2 (8.3)	2 (4.8)	4 (6.1)
Serious hypersensitivity reactions and/or anaphylaxis[f]			
Number of TESAEs, n	0	0	0
Meningococcal infections[f]			
Number of TEAEs, n	0	0	0
Development of systemic lupus erythematosus[f]			
Number of TEAEs, n	0	0	0

Events are coded using MedDRA version 21.0. [a]Percentages are based on the number of subjects in each study cohort (or total) of the Safety Analysis Set; [b]Serious Infections were identified based on a search for all preferred terms with System Organ Class matching 'Infections and Infestations' and marked as serious; [c]Identified based on a search for the following AE preferred terms ('Hypertension', 'Blood pressure increased', 'Essential hypertension', 'Hypertensive crisis', 'White coat hypertension'); [d]Acrocyanosis and/or Raynaud's phenomenon were identified based on a search for the following AE preferred terms ('Cyanosis', 'Raynaud's phenomenon'); [e]Thromboembolic events were identified based on a search for the following AE preferred terms ('Ischemic stroke', 'Device related thrombosis', 'Peripheral artery thrombosis', 'Transient ischemic attack', 'Deep vein thrombosis'); [f]There were no preferred terms identified for serious hypersensitivity reactions and/or anaphylaxis, meningococcal infections or development of systemic lupus erythematosus.
AE, adverse event; AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

Figure 1

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