Download the *Blood* publication

Enjaymo®
sutimlimab-jome
Injection for intravenous use
1100 mg/22 mL

SUTIMLIMAB IN PATIENTS WITH COLD AGGLUTININ DISEASE:

Results of the randomized placebo-controlled phase 3 CADENZA trial

Alexander Röth, Sigbjørn Berentsen, Wilma Barcellini, Shirley D'Sa, Bernd Jilma, Marc Michel, Ilene C. Weitz, Masaki Yamaguchi, Jun-ichi Nishimura, Josephine M.I. Vos, Michael Storek, Nancy Wong, Parija Patel, Xiaoyu Jiang, Deepthi S. Vagge, Marek Wardęcki, Frank Shafer, Michelle Lee, Catherine M. Broome

September 2022

Background[1,2]

Cold Agglutinin Disease (CAD) is a rare autoimmune hemolytic anemia characterized by chronic hemolysis mediated entirely by activation of the classical complement pathway. ENJAYMO is a humanized monoclonal antibody designed to target C1s, which is responsible for activating the complement pathway. By selectively inhibiting the classical complement pathway as the C1s level, ENJAYMO does not inhibit the lectin and alternative pathways.

CADENZA is the first placebo-controlled trial in CAD and strengthens the results with ENJAYMO from the previous single-arm, open-label CARDINAL study of ENJAYMO in CAD.

ENJAYMO, the first and only approved treatment for CAD[1,3]

ENJAYMO® (sutimlimab-jome) is indicated for the treatment of hemolysis in adults with Cold Agglutinin Disease (CAD)

CAD=Cold Agglutinin Disease.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ENJAYMO is contraindicated in patients with known hypersensitivity to sutimlimab-jome or any of the inactive ingredients.

WARNINGS AND PRECAUTIONS

Serious Infections Including Those Caused by Encapsulated Bacteria

- ENJAYMO, a proximal classical complement C1s inhibitor, increases susceptibility to serious infections, including infections caused by encapsulated bacteria e.g. *Neisseria meningitidis* (any serogroup, including non-groupable strains), *Streptococcus pneumoniae*, and *Haemophilus influenzae* type B.
- Life-threatening and fatal infections with encapsulated bacteria have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.
- Serious infections (bacterial and viral) were reported in 15% (10/66) of patients receiving ENJAYMO in the two phase 3 trials. These infections included urinary tract infection with sepsis, respiratory tract infection, pneumonia, otomastoiditis, and skin infections. One patient (1.5%) died due to *Klebsiella pneumoniae*.
- Complete or update vaccination against encapsulated bacteria at least 2 weeks prior to administration of the first dose of ENJAYMO, according to the most current ACIP recommendations for patients receiving a complement inhibitor.
- If urgent ENJAYMO therapy is indicated in a patient who is not up to date on their vaccine(s), administer as soon as possible.

Please see Important Safety Information throughout and full Prescribing Information.

CADENZA study design[1,3,4]

CADENZA, a phase 3, global, multicenter, randomized, double-blind, placebo-controlled trial, confirmed the efficacy and safety of ENJAYMO in 42 patients with CAD and no history of transfusion.* Following the completion of the 6-month treatment period, patients from both arms continued to receive ENJAYMO in a long-term safety and durability of response extension phase for a minimum of 1 year. Efficacy was based on the proportion of patients who met the trial's composite endpoint.

ENJAYMO demonstrated a significant benefit vs placebo across key efficacy measures[1,3]

73%
(16/22)

ACHIEVED ALL 3 COMPOSITE ENDPOINT MEASURES†

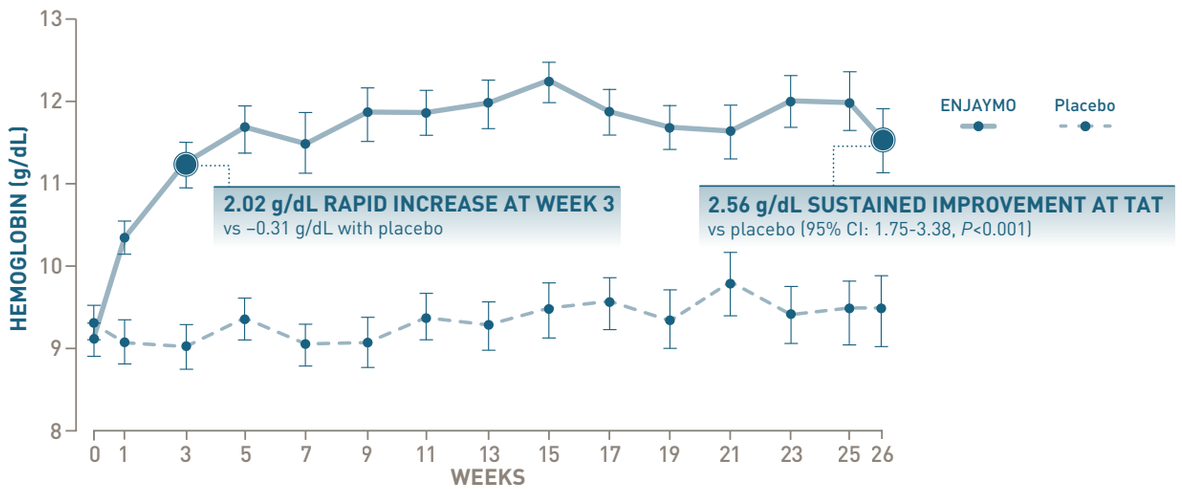
- **ACHIEVED SIGNIFICANT Hb INCREASE** of ≥1.5 g/dL at TAT from baseline (9.15 g/dL)
- **MAINTAINED TRANSFUSION INDEPENDENCE** from baseline through Weeks 5 to 26
- **RECEIVED NO ADDITIONAL TREATMENT** from Weeks 5 to 26‡

vs 15% (3/20) with placebo (Responder rate difference: 58.8%, 95% CI: 34.6%-83.0%, *P*=0.0004)

Treatment assessment time point (TAT) was defined as the mean value from Weeks 23, 25, and 26.

ENJAYMO significantly improved anemia at TAT, with a rapid and sustained increase in hemoglobin levels[1,3]

Mean Hb levels through Week 26 with ENJAYMO vs placebo (N=42)§



ENJAYMO (n)	22	22	21	22	19	20	17	19	17	18	19	19	18	19	19
Placebo (n)	20	19	19	19	19	19	19	19	19	19	19	19	20	19	19

Data at TAT (mean values from Weeks 23, 25, and 26) were tested for significance. Between baseline and Week 26, data at each time point were the observed mean. Interpret these data with discretion given small sample.

*Patients with confirmed CAD and no history of transfusion within 6 months or >1 in 12 months prior to enrollment (N=42). Patients with CAS secondary to infection, rheumatologic disease, SLE, or overt hematologic malignancy were excluded, whereas patients with a history of or concomitant low-grade lymphoproliferative disease (bone marrow involvement <10%) were not excluded.

†Two patients discontinued prior to Week 23 and their status was considered unknown for the purposes of this analysis.

‡Prohibited therapies included rituximab alone or in combination with cytotoxic agents.

§Mean baseline values: Hb was 9.15 g/dL for ENJAYMO and 9.33 g/dL for placebo. LS mean improvement at TAT was 2.66 g/dL for ENJAYMO and 0.09 g/dL for placebo.

CAS=cold agglutinin syndrome; Hb=hemoglobin; LS=least squares; SLE=systemic lupus erythematosus; TAT=treatment assessment time point.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

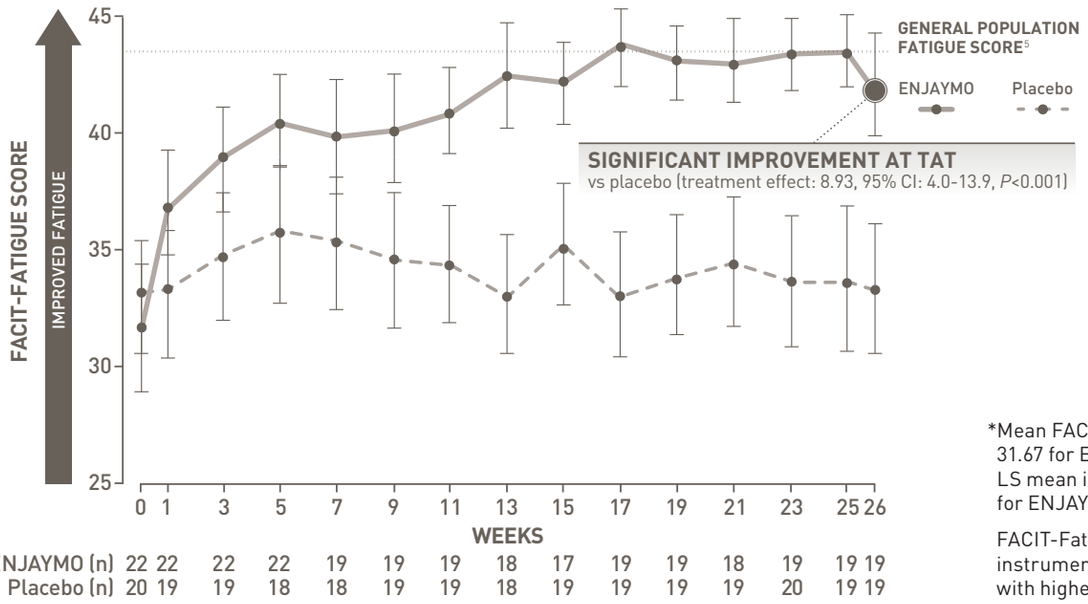
Serious Infections Including Those Caused by Encapsulated Bacteria (continued)

- Vaccination does not eliminate the risk of serious encapsulated bacterial infections. Closely monitor patients for early signs and symptoms of serious infection and evaluate patients immediately if an infection is suspected.

Please see Important Safety Information throughout and full Prescribing Information.

Patients experienced significant improvement in the symptoms and impact of fatigue at TAT[1,3]

Mean FACIT-Fatigue scores through Week 26 with ENJAYMO vs placebo (N=42)*



ENJAYMO (n)	22	22	22	22	19	19	19	18	17	19	19	18	19	19	19
Placebo (n)	20	19	19	18	18	19	19	18	19	19	19	19	20	19	19

*Mean FACIT-Fatigue score at baseline was 31.67 for ENJAYMO and 32.99 for placebo. LS mean improvement at TAT was 10.83 points for ENJAYMO and 1.91 points for placebo.

FACIT-Fatigue is a patient-reported outcome instrument with scores ranging from 0 to 52, with higher scores indicating less fatigue.

Data at TAT (mean values from Weeks 23, 25, and 26) were tested for significance. Between baseline and Week 26, data at each time point were the observed mean. Interpret these data with discretion given small sample.

A well-tolerated safety profile studied over 2.5 years[1,3]

ENJAYMO safety was evaluated in CADENZA, a 6-month placebo-controlled study (Part A [n=42]), followed by a 1 year open-label, single-arm study (Part B [n=39]) and CARDINAL (an open-label, single-arm study [n=24])

Adverse reactions (≥10%) in patients receiving ENJAYMO with a difference >5% vs placebo (CADENZA Part A)

Adverse reaction	ENJAYMO (n=22)	Placebo (n=20)
Headache	5 (23%)	2 (10%)
Hypertension	5 (23%)	0
Rhinitis	4 (18%)	0
Acrocyanosis	4 (18%)	0
Raynaud's phenomenon	4 (18%)	0

- Serious adverse reactions were Raynaud's phenomenon (n=1) and febrile infection (n=1)
- Adverse reactions leading to discontinuation were Raynaud's phenomenon (n=1), acrocyanosis (n=1), and infusion-related reactions (n=1)

FACIT=Functional Assessment of Chronic Illness Therapy; TAT=treatment assessment time point.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Serious Infections Including Those Caused by Encapsulated Bacteria (continued)

- If ENJAYMO treatment is administered to patients with active systemic infections, monitor closely for signs and symptoms of worsening infection. Some infections may become rapidly life-threatening or fatal if not recognized and treated promptly. Inform patients of these signs and symptoms and steps to be taken to seek immediate medical care.
  - Consider interruption of ENJAYMO treatment in patients who are undergoing treatment for serious infection.
  - Consider patients' immune status when initiating treatment with ENJAYMO.

Infusion-Related Reactions

- Administration of ENJAYMO may result in infusion-related reactions. In the two phase 3 trials, 29% (19/66) of patients treated with ENJAYMO experienced infusion-related reactions. One patient permanently discontinued ENJAYMO due to an infusion-related reaction.
- Monitor patients for infusion-related reactions and interrupt if a reaction occurs.

Please see Important Safety Information throughout and full Prescribing Information.

Download the *Blood* publication

Enjaymo®
sutimlimab-jome
Injection for intravenous use
1100 mg/22 mL

Conclusions[1,3]

Most patients experienced improvement in anemia and fatigue

73% (16/22) **OF PATIENTS ACHIEVED THE COMPOSITE ENDPOINT, INCLUDING*:**

- **A significant Hb increase**
- **Transfusion avoidance**
- **No use of additional CAD medication†**

SIGNIFICANT AND SUSTAINED RESULTS:

- **2.02 g/dL rapid increase in mean Hb levels at Week 3 with sustained 2.56 g/dL improvement at TAT vs placebo** (95% CI: 1.75-3.38; *P*<0.001)
- **Significant and sustained improvements in fatigue through TAT** (95% CI: 4.0-13.9; *P*<0.001)‡

CADENZA reinforces ENJAYMO as an effective and well-tolerated treatment for hemolysis in patients with Cold Agglutinin Disease[1]

These data show that targeting the classical complement pathway at C1s represents an effective therapeutic approach for CAD management with significant treatment responses as early as Week 3

*Efficacy was based on the proportion of patients who met the following criteria: an increase from baseline in Hb level ≥1.5 g/dL, did not require blood transfusion from Weeks 5 through 26, and did not use protocol-prohibited treatment for CAD from Weeks 5 through 26.
†Prohibited therapies included rituximab alone or in combination with cytotoxic agents.
‡According to the FACIT-Fatigue Scale.

TAT=treatment assessment time point.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Infusion-Related Reactions (continued)

- Discontinue ENJAYMO infusion and institute appropriate supportive measures if signs of hypersensitivity reactions, such as cardiovascular instability or respiratory compromise, occur.

Risk of Autoimmune Disease

- Based on its mechanism of action, ENJAYMO may potentially increase the risk for developing autoimmune diseases such as systemic lupus erythematosus (SLE). Development of SLE has been associated with inherited classical complement deficiency.
- In clinical trials, 4.5% (3/66) of patients developed a relapse or worsening of previously diagnosed autoimmune disease.
- Monitor ENJAYMO patients for signs and symptoms and manage medically.

Recurrent Hemolysis After ENJAYMO Discontinuation

- If treatment with ENJAYMO is interrupted, closely monitor patients for signs and symptoms of recurrent hemolysis, eg, elevated levels of total bilirubin or lactate dehydrogenase (LDH) accompanied by a decrease in hemoglobin, or reappearance of symptoms such as fatigue, dyspnea, palpitations, or hemoglobinuria. Consider restarting ENJAYMO if signs and symptoms of hemolysis occur after discontinuation.

ADVERSE REACTIONS

- The most common adverse reactions in the CADENZA trial (Part A) (incidence ≥18%) are rhinitis, headache, hypertension, acrocyanosis, and Raynaud's phenomenon. The most common adverse reactions in the CARDINAL trial (incidence ≥25%) are urinary tract infection, respiratory tract infection, bacterial infection, dizziness, fatigue, peripheral edema, arthralgia, cough, hypertension, and nausea.

Please see Important Safety Information throughout and full Prescribing Information.

References: 1. Röth A, Berentsen S, Barcellini W, et al. Sutimlimab in patients with cold agglutinin disease: results of the randomized placebo-controlled phase 3 CADENZA trial. *Blood*. 2022;140(9):980-991. doi:10.1182/blood.2021014955 **2.** Röth A, Barcellini W, D'Sa S, et al. Sutimlimab in Cold Agglutinin Disease. *N Engl J Med*. 2021;384(14):1323-1334. doi:10.1056/NEJMoa2027760 **3.** ENJAYMO. Prescribing information. Genzyme Corporation. **4.** Data on file. Sanofi. **5.** Cella D, Lai J-S, Chang C-H, Peterman A, Slavin M. Fatigue in cancer patients compared with fatigue in the general United States population. *Cancer*. 2002;94(2):528-538. doi:10.1002/cncr.10245

sanofi

MAT-US-2209731-v2.0-02/2024