Nanoencapsulated Sirolimus Plus Pegadricase (NASP) Demonstrates a Reduction in Gout Flares: Results From the Phase 3 DISSOLVE Studies

Angelo Gaffo,[1,2] Herbert S.B. Baraf,[3,4] Anand Patel,[5] Tuhina Neogi,[6] Rehan Azeem,[7] Wesley DeHaan,[7] Ben Peace,[8] Hugues Santin-Janin,[9] Bhavisha Desai,[7] Naomi Schlesinger[10]

[1]University of Alabama at Birmingham, Division of Rheumatology and Clinical Immunology, Birmingham, AL, USA; [2]Birmingham VA Medical Center, Birmingham, AL, USA; [3]The Center for Rheumatology and Bone Research, Wheaton, MD, USA; [4]The George Washington University, Rheumatology, Washington, DC, USA; [5]Conquest Research, Winter Park, FL, USA; [6]Boston University Chobanian & Avedisian School of Medicine, Department of Medicine, Section of Rheumatology, Boston, MA, USA; [7]Sobi Inc., Waltham, MA, USA; [8]Sobi, Stockholm, Sweden; [9]Sobi, Basel, Switzerland; [10]University of Utah, Spencer Fox Eccles School of Medicine, Salt Lake City, UT, USA

CONCLUSIONS

Among patients from DISSOLVE I and DISSOLVE II who received 6 doses of NASP or PBO:

- At treatment initiation, there was no increase in gout flares for patients treated with nanoencapsulated sirolimus plus pegadricase (NASP) or placebo (PBO), as has been observed with urate-lowering therapy (ULT)
- Over the course of the study, the proportion of patients with gout flares decreased with NASP treatment
- Over 95% of patients who received 6 doses of high-dose (HD) NASP were flare-free at weeks 21–24
- These results highlight the potential of NASP as an effective therapy for reducing disease burden and improving a key clinical manifestation, gout flares, in patients with uncontrolled gout

References

1. Baraf HSB, et al. *Rheumatology*. 2024;63:1058–67. **2.** Chen-Xu M, et al. *Arthritis Rheumatol*. 2019;71:991–9. **3.** Fels E, Sundy JS. *Curr Opin Rheumatol*. 2008;20:198–202. **4.** Kragh N, et al. Rheumatology Nurses Society (RSN); July 17–20, 2024; Orlando, FL, USA. **5.** FitzGerald JD, et al. *Arthritis Care Res*. 2020;72:744–60. **6.** Dalbeth N, et al. *Lancet*. 2021;397:1843–55. **7.** Schlesinger N, et al. *Nat Rev Rheumatol*. 2023;19:640–9. **8.** Kishimoto TK. *Front Immunol*. 2020;11:969. **9.** Sands E, et al. *Nat Commun*. 2023;13:272. **10.** Kivitz A, et al. *Rheumatol Ther*. 2023;10:825–47. **11.** Baraf HSB, et al. Congress of Clinical Rheumatology (CCR) – East; May 9–12, 2024; Destin, FL, USA. **12.** Khanna P, et al. American College of Rheumatology (ACR); November 14–19, 2024; Washington, DC, USA. **13.** Gaffo AL, et al. *Arthritis Rheumatol*. 2018;70:462–7

Acknowledgments

The authors would like to thank the entire team involved with the DISSOLVE trials, most importantly participating patients and their families. The DISSOLVE I and II (NCT04513366 and NCT04596540) studies were jointly funded by Sobi and Selecta Biosciences, Inc. The authors wish to acknowledge the contribution of the study participants, the investigators, and their teams. The authors also acknowledge Daniela Bruni, PhD, PharmD, of Sobi for publication coordination. This poster was developed by the authors in accordance with Good Publication Practice (GPP) 2022 guidelines (https://www.ismpp.org/gpp-2022). Medical writing and editorial assistance, funded by Sobi, were provided by Hannah L. Mayberry, PhD, and Jane Moore of Peloton Advantage, LLC, an OPEN Health company (Parsippany, NJ, USA). Sobi reviewed and provided feedback on the poster. The authors had full editorial control of the poster and provided their final approval of all content.

Disclosures

AG: Consultant: Atom, Avalo Therapeutics, PK MED, Scilex, and Sobi. **HSBB:** Consultant: Arthrosi, Horizon, Olatec, Selecta Biosciences, and Sobi; Investigator: Horizon, Selecta Biosciences, and Sobi; Advisor or review panel member: Olatec. **AP:** Nothing to disclose. **TN:** Consultant: PK MED and Sobi. **RA, WD:** Stock options or bond holdings in a for-profit corporation or self-directed pension plan: Selecta Biosciences; Employee and/or shareholder: Sobi. **BP:** Contractor: Employee of Veramed contracted to Sobi. **HS-J, BD:** Employee and/or shareholder: Sobi. **NS:** Advisor or review panel member: Amgen, Arthrosi, Olatec, Protalix, Scilex, Shanton, and Sobi.

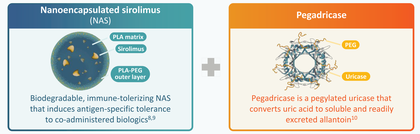
Copies of this poster obtained through QR Code are for personal use only

Presented at the Congress of Clinical Rheumatology (CCR) – East; May 1–4, 2025; Destin, FL, USA

INTRODUCTION

- Gout, caused by the deposition of monosodium urate crystals in and around joints and soft tissues, is the most common inflammatory arthritis in the US, affecting >9.2 million individuals[1,2]
- Uncontrolled gout, also known as chronic refractory gout, is characterized by a persistent elevation in serum uric acid (sUA) to ≥6 mg/dL and ongoing clinical manifestations despite the use of oral urate-lowering therapies (ULTs), resulting in joint pain, tophi, and gout flares[3,4]
  - Gout flares cause chronic pain and joint destruction, impair quality of life, and represent a critical endpoint for assessing therapeutic efficacy and guiding clinical decision-making[1,3]
- ULT is recommended to lower sUA and prevent gout flares long term[5,6]; however, an initial increase in gout flares after initiation of ULT has been observed[7]
- NASP is a novel, every 4-week, sequential infusion therapy designed to reduce sUA levels in patients with uncontrolled gout. NASP consists of targeted immunomodulating, nanoencapsulated sirolimus (NAS; formerly SEL-110) co-administered with pegadricase, a pegylated uricase (formerly SEL-037) (**Figure 1**)[1,8]

Figure 1: Nanoencapsulated sirolimus plus pegadricase



NAS, nanoencapsulated sirolimus; PEG, polyethylene glycol; PLA, polylactic acid.

- NASP is being investigated for the treatment of uncontrolled gout; efficacy and safety of NASP have been previously presented, with NASP demonstrating a statistically significant improvement (reduction) in sUA levels compared with placebo (PBO), and high-dose NASP (HD NASP) more effectively prevented the formation of anti-drug antibodies compared with low-dose NASP (LD NASP)[1,11,12]
- Here, we report gout flare outcomes in patients from the phase 3 DISSOLVE I and DISSOLVE II trials who received 6 doses of NASP or PBO (**Figure 2**)

METHODS

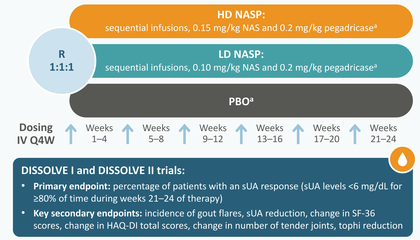
Figure 2: Design of the DISSOLVE I and DISSOLVE II trials and gout flare assessment

Pooled data[11] from:

- DISSOLVE I (NCT04513366; US)
- DISSOLVE II (NCT04596540; global)

Inclusion criteria:

- Adults with uncontrolled gout
  - ≥3 gout flares within 18 months prior to screening, **OR**
  - ≥1 tophus, **OR**
  - Current diagnosis of gouty arthritis
- Failure to normalize sUA levels and control symptoms with xanthine oxidase inhibitor
- Screening sUA level ≥7 mg/dL



Post hoc analysis:

- Patients from the pooled DISSOLVE I and DISSOLVE II ITT population[11] who received 6 doses of NASP or PBO

A validated flare assessment[13] was used:

- Gout flares were assessed by study site investigators, all of whom had experience treating and managing gout

Patients received gout flare prophylaxis and premedication for infusion reactions[b]

[a]Treatment was discontinued if the stopping rule was met: sUA <2.0 mg/dL 1 hour after infusion of the second component of the study drug during week 1 **AND** either sUA >1.0 mg/dL at the end of week 3 **OR** sUA >6.0 mg/dL at the end of any of weeks 7, 11, 15, or 19. In the overall ITT population from DISSOLVE I and DISSOLVE II, the most common reasons for treatment discontinuation among patients who received NASP were meeting the stopping rule, adverse events, and withdrawal of consent. [b]Colchicine or a nonsteroidal anti-inflammatory drug for gout flare prophylaxis and premedication with prednisone, fexofenadine, and methylprednisolone for infusion reactions.
HAQ-DI, Health Assessment Questionnaire-Disability Index; HD NASP, high-dose NASP; ITT, intent-to-treat; IV, intravenous; LD NASP, low-dose NASP; NAS, nanoencapsulated sirolimus; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; Q4W, every 4 weeks; R, randomization; SF-36, 36-Item Short Form Health Survey; sUA, serum uric acid.

RESULTS

Population

- Of 87 HD NASP, 88 LD NASP, and 90 PBO patients in the overall ITT population from the DISSOLVE I and DISSOLVE II trials, 42 HD NASP, 35 LD NASP, and 67 PBO patients received 6 doses of treatment (**Table 1**)

Table 1: Baseline characteristics in patients who received 6 doses of NASP or PBO

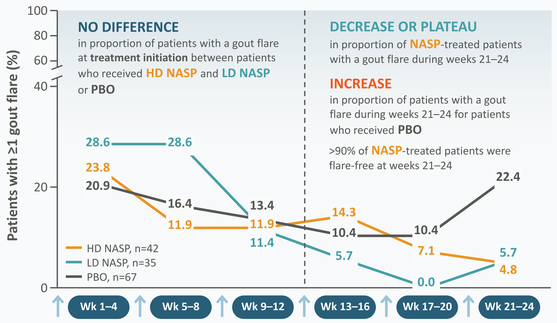
	HD NASP n=42	LD NASP n=35	PBO n=67
Patient characteristics			
Age, years, mean (SD)	57.9 (8.7)	54.7 (9.9)	56.3 (9.9)
BMI, kg/m^2, mean (SD)	33.7 (5.5)	33.1 (6.4)	33.3 (6.6)
Male, n (%)	39 (92.9)	31 (88.6)	66 (98.5)
White, n (%)	36 (85.7)	29 (82.9)	51 (76.1)
Disease characteristics			
Duration of gout diagnosis, years, mean (SD)	13.3 (10.6)	12.1 (8.5)	11.7 (8.4)
Patients with tophi, n (%)	23 (54.8)	22 (62.9)	42 (62.7)
sUA, mg/dL, mean (SD)	8.5 (1.4)	8.5 (1.3)	8.7 (1.6)
Number of tender joints, mean (SD)	5.8 (8.0)	6.1 (7.7)	7.7 (11.0)
Number of swollen joints, mean (SD)	2.9 (4.9)	3.5 (6.1)	5.2 (8.5)
Comorbidity,[a] n (%)			
Hypertension	32 (76.2)	20 (57.1)	44 (65.7)
Hyperlipidemia	17 (40.5)	8 (22.9)	23 (34.3)
Dyslipidemia	6 (14.3)	4 (11.4)	10 (14.9)
Chronic kidney disease	5 (11.9)	6 (17.1)	11 (16.4)
Obesity	5 (11.9)	6 (17.1)	9 (13.4)

[a]Comorbidities, excluding gout and related disorders, that were present in ≥10% of all patients.
BMI, body mass index; HD NASP, high-dose NASP; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; SD, standard deviation; sUA, serum uric acid.

Efficacy

- At treatment initiation (weeks 1–4), the proportion of patients who experienced a gout flare was similar between patients treated with HD NASP or LD NASP and those treated with PBO (**Figure 3**)
- During weeks 1–12 of treatment, the proportion of gout flares remained similar between patients treated with HD NASP and PBO, while a slight increase compared with HD NASP- and PBO-treated patients was seen at weeks 5–8 for patients treated with LD NASP (**Figure 3**)
- During weeks 13–24, the proportion of patients who experienced a gout flare continued to decrease in patients treated with HD NASP and LD NASP, with only 4.8% and 5.7% of patients, respectively, experiencing a gout flare during weeks 21–24 (**Figure 3**)
  - The proportion of PBO-treated patients who experienced a gout flare remained consistent with weeks 1–4 during weeks 21–24, with 22.4% of PBO-treated patients experiencing a flare
- In each arm, at weeks 21–24, 95.2% (HD NASP), 94.3% (LD NASP), and 77.6% (PBO) of patients were flare-free. Therefore, an additional 17.6% and 16.7% of patients were flare-free with HD and LD NASP, respectively, compared with PBO (**Figure 3**)

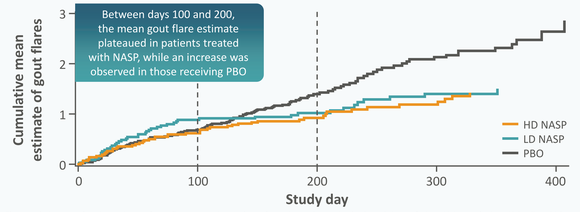
Figure 3: Percentage of patients experiencing gout flares over the study period among patients from DISSOLVE I and DISSOLVE II who received 6 doses of NASP or PBO



HD NASP, high-dose NASP; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; Wk, week(s).

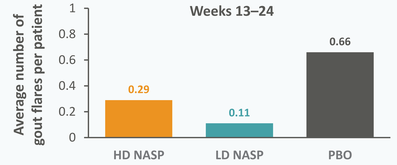
- Cumulative mean gout flare estimates between days 0 and 100 were generally similar between NASP- and PBO-treated patients (**Figure 4**)
- From day 100, gout flares plateaued in NASP-treated patients and increased with PBO (**Figure 4**)
- During weeks 13–24, HD NASP-treated patients who received 6 doses had 2.3 times fewer flares compared with PBO-treated patients who received 6 doses (HD NASP: 0.29 gout flares per patient or 1 in every 4 patients during weeks 13–24; LD NASP: 0.11 gout flares per patient or 1 in every 10 patients during weeks 13–24; PBO: 0.66 gout flares per patient or 2 in every 3 patients during weeks 13–24; **Figure 5**)

Figure 4: Cumulative mean estimate of gout flares over the study period among patients from DISSOLVE I and DISSOLVE II who received 6 doses of NASP or PBO[a]



[a]The cumulative mean function estimate of gout flares per patient is shown for patients who received at least 6 doses of HD NASP (orange), LD NASP (teal), or PBO (dark gray). The event of interest was gout flare, and multiple gout flares were considered in the cumulative mean function. Patients were censored at the end of the study.
HD NASP, high-dose NASP; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo.

Figure 5: Average number of gout flares per patient during weeks 13–24 among patients from DISSOLVE I and DISSOLVE II who received 6 doses of NASP or PBO



In weeks 13–24, gout flares were substantially reduced with NASP:

Average number of gout flares per patient was **2.3** and **5.7** times fewer with **HD NASP** and **LD NASP**, respectively, vs **PBO**

HD NASP, high-dose NASP; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo.

- Across all treatment arms, gout flares were mostly of mild to moderate intensity

Safety

- Adverse events of special interest were generally similar between the DISSOLVE I and DISSOLVE II ITT population and patients who received 6 doses of NASP or PBO (**Table 2**)[11]

Table 2: Patients with ≥1 TEAE and AESIs among patients from DISSOLVE I and DISSOLVE II who received 6 doses of NASP or PBO

	HD NASP n=42	LD NASP n=35	PBO n=67
≥1 TEAE, n (%)	31 (73.8)	23 (65.7)	45 (67.2)
AESI, n (%)			
Gout flares	18 (42.9)	17 (48.6)	29 (43.3)
Infections (including viral)	8 (19.0)	4 (11.4)	12 (17.9)
COVID-19[a]	2 (4.8)	0	5 (7.5)
Infusion-related AE within 24 h	4 (9.5)	3 (8.6)	1 (1.5)
Stomatitis[b]	3 (7.1)	3 (8.6)	0
Dyslipidemia	1 (2.4)	0	0
Hyperlipidemia	1 (2.4)	1 (2.9)	1 (1.5)
Hypertriglyceridemia	1 (2.4)	1 (2.9)	5 (7.5)
Renal impairment	1 (2.4)	0	0
Leukopenia	0	1 (2.9)	1 (1.5)

[a]There were no other infections that occurred in >3% of patients. [b]Includes stomatitis, mouth ulceration, oral ulcer, and aphthous ulcer.
AE, adverse event; AESI, adverse event of special interest; h, hour(s); HD NASP, high-dose NASP; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; TEAE, treatment-emergent adverse event.