Reduction in Tophi Observed in Patients With Chronic Refractory Gout Treated With NASP: Results From Phase 3 DISSOLVE Studies

Herbert S.B. Baraf,[1,2] Puja Khanna,[3] Frédéric Lioté,[4] Rehan Azeem,[5] Wesley DeHaan,[5] Ben Peace,[6] Hugues Santin-Janin,[7] Bhavisha Desai,[5] Alan Kivitz[8]

[1]The Center for Rheumatology and Bone Research, Wheaton, MD, USA; [2]The George Washington University, Rheumatology, Washington, DC, USA; [3]University of Michigan, Division of Rheumatology, Ann Arbor, MI, USA; [4]Université Paris Cité, Inserm UMR 1132, GH Paris Saint-Joseph, Rheumatology Department, Institut Arthur Vernes, Paris, France; [5]Sobi Inc., Waltham, MA, USA; [6]Sobi, Stockholm, Sweden; [7]Sobi, Basel, Switzerland; [8]Altoona Center for Clinical Research, Duncansville, PA, USA

CONCLUSIONS

Lowered serum uric acid (sUA) area-under-the-curve levels were associated with significant tophus resolution and/or reduction in tophus size, with higher response rates observed in patients who received 6 doses of nanoencapsulated sirolimus plus pegadricase (NASP) compared with patients who received placebo (PBO)

NASP-treated patients in the ITT population and patients who received 6 doses of NASP demonstrated higher rates of complete resolution of tophus compared with patients who received PBO

The high rate of partial target tophus response to PBO was statistically significantly inferior to that of NASP-treated patients but indicative of the limitations of photographic monitoring of tophus size in clinical trials; complete response criteria provide a more reliable measure of clinical response

These results highlight the effectiveness of NASP in lowering sUA levels and promoting tophus resolution, thus alleviating a clinical manifestation of uncontrolled gout

References

1. Dalbeth N, *et al. Lancet.* 2021;397:1843–55. **2.** Schlesinger N, Lipsky PE. *Semin Arthritis Rheum.* 2020;50:531–8. **3.** Fels E, Sundy JS. *Curr Opin Rheumatol.* 2008;20:198–202. **4.** Dalbeth N, et al. *Nat Rev Dis Primers.* 2019;5:69. **5.** Schlesinger N, et al. *Nat Rev Rheumatol.* 2023;19:640–9. **6.** Laurent V, et al. *RMD Open.* 2023;9:e003725. **7.** Baraf HSB, et al. *Rheumatology.* 2024;63:1058–67. **8.** Baraf HSB, et al. British Society for Rheumatology (BSR); April 24–26, 2024; Liverpool, UK. Poster P084. **9.** Krishnaiah TK. *Front Immunol.* 2020;11:969. **10.** Baraf HSB, et al. Congress of Clinical Rheumatology (CCR) – East; May 9–12, 2024; Destin, FL, USA. **11.** Baraf HSB, et al. European Congress of Rheumatology (EULAR); June 12–15, 2024; Vienna, Austria. Poster POS0260.

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 Long Dao, 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

HSBB: Consultant: Arthrosi, Horizon, Olatec, Selecta Biosciences, and Sobi; Investigator: Horizon, Selecta Biosciences, and Sobi; Advisor or review panel member: Olatec. **PK:** Grant/research: Arthrosi, Horizon, Olatec, and Selecta Biosciences; Consultant: Horizon and Sobi. **FL:** Consultant: Horizon, Selecta Biosciences, and Sobi; Data monitoring committee: Olatec; Advisor: Horizon and Sobi; Speaker: Sobi; Unrestricted educational grants for European Crystal Network (ECN) workshops: Amgen Rare Disease, Arthrosi, Bristol Myers Squibb, Crystalys, Fresenius Kabi, Horizon, Olatec, 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. **AK:** Consultant or speaker/honoraria: AbbVie; Stock options or bond holdings: Amgen; Consultant: Covis, Ecofit, Grünenthal, Innovaderm, Promethera, SynAct, and XBiotech; Advisor/review panel member or consultant: Fresenius Kabi, Horizon, Janssen, Takeda, and UCB; Scientific expert: Genzyme; Consultant or stocks/bonds: Gilead; Consultant, speaker/honoraria, or stocks/bonds: GSK; Speaker/honoraria: Lilly and Sanofi/Regeneron; Advisor/review panel member or stocks/bonds: Novartis; Speaker/honoraria or stocks/bonds: Pfizer; Educational: Prime.

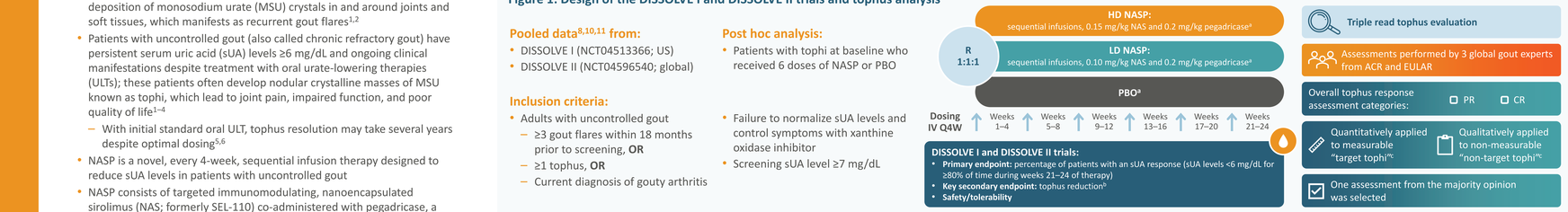
Presented at the Congress of Clinical Rheumatology (CCR) – East; May 1–4, 2025; Destin, FL, USA

INTRODUCTION

- Gout, caused by uncontrolled, sustained hyperuricemia, results in the deposition of monosodium urate (MSU) crystals in and around joints and soft tissues, which manifests as recurrent gout flares[1,2]
- Patients with uncontrolled gout (also called chronic refractory gout) have persistent serum uric acid (sUA) levels ≥6 mg/dL and ongoing clinical manifestations despite treatment with oral urate-lowering therapies (ULTs); these patients often develop nodular crystalline masses of MSU known as tophi, which lead to joint pain, impaired function, and poor quality of life[1–4]
  - With initial standard oral ULT, tophus resolution may take several years despite optimal dosing[5,6]
- 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)[7–9]
- Here, we report the pooled tophus outcomes from the DISSOLVE I and DISSOLVE II trials (**Figure 1**)

METHODS

Figure 1: Design of the DISSOLVE I and DISSOLVE II trials and tophus analysis



[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. Patients received colchicine or a nonsteroidal anti-inflammatory drug for gout flare prophylaxis and premedication with prednisone, fexofenadine, and methylprednisolone for infusion reactions. [b]Secondary endpoint was below the broken hierarchy; therefore, it could not be formally tested for significance. *P* values are provided for descriptive purposes. [c]Tophi were considered measurable if they were ≥5 mm in the longest dimension at baseline and had borders distinguishable to the independent reader.
ACR, American College of Rheumatology; CR, complete response; EULAR, European Alliance of Associations for Rheumatology; 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; PR, partial response; Q4W, every 4 weeks; R, randomization; sUA, serum uric acid.

- **Partial response (PR)** was defined as **≥50% and <100% reduction** in the area of a tophus without enlargement of any existing tophus and no new tophus
- **Complete response (CR)** was defined as **100% reduction** in the area or complete disappearance of a tophus without enlargement of any existing tophus and no new tophus

RESULTS

Population

- Of the overall ITT population from the DISSOLVE I and DISSOLVE II trials, 23, 22, and 42 patients in the HD NASP, LD NASP, and PBO groups, respectively, had tophi at baseline and received 6 doses of treatment (**Table 1**)
  - At least 1 tophus was observed at baseline in 63.0% of patients in the overall ITT population and in 60.4% of patients who received 6 doses of NASP or PBO
  - Patients who had tophi at baseline and received 6 doses of treatment had similar disease characteristics to those in the ITT population (baseline characteristics not shown)[10]

Table 1: Baseline characteristics in patients with tophi at baseline who received 6 doses of NASP or PBO

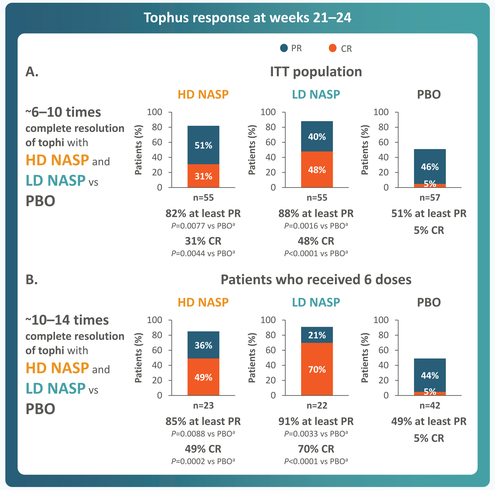
	HD NASP n=23	LD NASP n=22	PBO n=42
Patient characteristics			
Age, years, mean (SD)	56.0 (9.4)	54.4 (9.4)	57.5 (8.5)
BMI, kg/m^2, mean (SD)	34.5 (6.1)	32.3 (5.6)	32.4 (6.7)
Male, n (%)	23 (100)	20 (90.9)	41 (97.6)
White, n (%)	20 (87.0)	18 (81.8)	33 (78.6)
Disease characteristics			
Duration of gout diagnosis, years, mean (SD)	15.8 (9.6)	12.3 (8.7)	13.1 (9.1)
Patients with tophi, n (%)	23 (100)	22 (100)	42 (100)
Number of tophi, mean (SD)	5.5 (5.2)	5.6 (5.0)	6.0 (5.6)
sUA, mg/dL, mean (SD)	8.9 (1.4)	8.6 (1.5)	9.1 (1.6)
Number of tender joints, mean (SD)	8.6 (8.6)	7.4 (8.3)	8.6 (12.4)
Number of swollen joints, mean (SD)	4.0 (5.9)	4.7 (7.1)	5.8 (9.8)

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

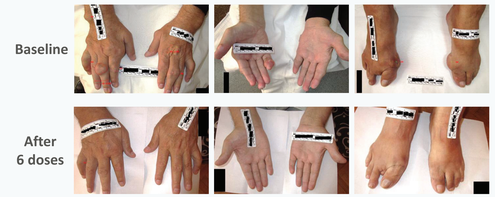
- In the ITT population, patients treated with NASP had a significantly greater response in total tophus area reduction (weeks 21–24 vs baseline) compared with those who received PBO (**Figure 2A**)
  - HD NASP- and LD NASP-treated patients had approximately 6–10-fold higher CR rates compared with PBO-treated patients
  - >80% of NASP-treated patients had at least PR
- In patients who received 6 doses, those treated with NASP had a significantly greater response in tophus area reduction (weeks 21–24 vs baseline) compared with those who received PBO (**Figure 2B;** example patient images in **Figure 3**)
  - HD NASP- and LD NASP-treated patients had approximately 10–14-fold higher CR rates compared with PBO-treated patients
  - ≥85% of NASP-treated patients had at least PR

Figure 2: Tophus response at weeks 21–24 in the ITT population (A) and patients who received 6 doses (B)



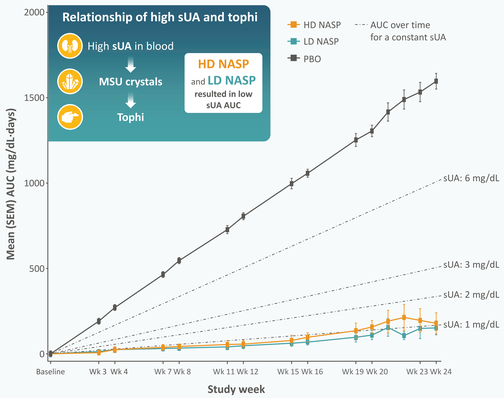
[a]Secondary endpoint was below the broken hierarchy; therefore, it could not be formally tested for significance. *P* values are provided for descriptive purposes.
Responses were evaluated using the blinded triple read model. The percentage of responders was estimated using a logistic regression model that includes treatment and study as categorical factors. An N−1 correction chi-square test comparing each treatment to PBO was used to generate *P* values. The logistic method considering treatment group was used to impute missing values for response.
CR, complete response; HD NASP, high-dose NASP; ITT, intent-to-treat; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; PR, partial response.

Figure 3: Example of tophus response in a patient with uncontrolled gout who received 6 doses of HD NASP and had tophi at baseline and CR after treatment, at the end of the double-blind phase



CR, complete response; HD NASP, high-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase.

Figure 4: Mean cumulative sUA AUC[a] through week 24 in patients who received 6 doses of NASP or PBO with tophi at baseline



[a]Cumulative sUA is a measure of the duration and intensity of sUA exposure over time, defined in this study as AUC at each time point (average of the current and previous sUA values multiplied by the time between the current and previous sUA values). The cumulative sUA AUC at each study week in the figure was the total AUC from D1 up to that week. sUA assessments were performed at the end of each week. Dashed lines show what the cumulative AUC would be at each point in time for a patient who had a constant sUA level.
AUC, area under the curve; D, day; HD NASP, high-dose NASP; LD NASP, low-dose NASP; MSU, monosodium urate; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; SEM, standard error of mean; sUA, serum uric acid; Wk, week.

- Mean sUA remained low throughout the course of treatment in patients who received NASP, which led to a low sUA area under the curve (AUC), whereas patients receiving PBO had consistently higher sUA levels that were reflected in a higher sUA AUC (**Figure 4**)

Safety

- Treatment-emergent adverse events were generally similar between the DISSOLVE I and DISSOLVE II ITT population and patients with tophi at baseline who received 6 doses of NASP or PBO[11]
- Adverse events of special interest in patients who received 6 doses of HD NASP, LD NASP, or PBO with tophi at baseline (**Table 2**) were similar to those in the ITT population (previously presented)[11]

Table 2: Patients with ≥1 TEAE and AESIs

	HD NASP n=23	LD NASP n=22	PBO n=42
≥1 TEAE, n (%)	15 (65.2)	15 (68.2)	27 (64.3)
AESI, n (%)			
Gout flares	9 (39.1)	11 (50.0)	17 (40.5)
Infections (including viral)	4 (17.4)	3 (13.6)	7 (16.7)
COVID-19[a]	0	0	2 (4.8)
Nasopharyngitis[a]	1 (4.3)	0	1 (2.4)
Infusion-related AE within 24 h	3 (13.0)	0	0
Stomatitis[b]	2 (8.7)	2 (9.1)	0
Hyperlipidemia	1 (4.3)	1 (4.5)	0
Hypertriglyceridemia	1 (4.3)	1 (4.5)	3 (7.1)
Renal impairment	1 (4.3)	0	0
Leukopenia	0	1 (4.5)	1 (2.4)

[a]Infections in >1 patient are shown. [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.