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Nanoencapsulated Sirolimus Plus Pegadricase Reduced Disease Burden in Patients With Uncontrolled Gout: Results From the Phase 3 DISSOLVE Trials

Post Hoc Analysis in Patients Who Received 6 Doses of Treatment

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Disclosures

Puja P. Khanna has the following relevant financial relationships to disclose:

- Grant/research: Arthrosi, Olatec, Selecta Biosciences
- Consultant: Sobi

Please see the published abstract for a full list of author disclosures.

Uncontrolled gout

Uncontrolled gout (UG) is characterized by **persistent elevation of serum uric acid (sUA)** of ≥6 mg/dL and **ongoing clinical manifestations** despite the use of oral urate-lowering therapy[1]

UG has a **substantial impact on health-related quality of life (HRQOL)**, which has been emphasized through its inclusion in previously established gout remission criteria[2-5]

To achieve **disease control**, it is imperative to reduce sUA to <6 mg/dL, which in turn **mitigates disease burden** by reducing tophi and incidence of flares, resulting in a reduction in the number of tender and swollen joints and initiating a path toward **clinical remission**[6,7]

HRQOL, health-related quality of life; sUA, serum uric acid; UG, uncontrolled gout.

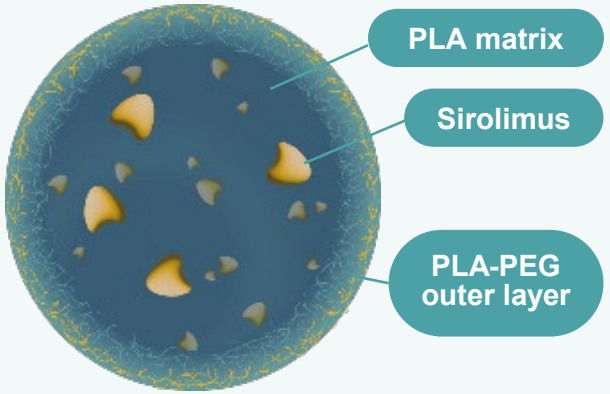
1. Fels E, Sundy JS. *Curr Opin Rheumatol*. 2008;20:198–202. **2.** Botson J, et al. *Rheumatol Adv Pract*. 2024;8:rkae145. **3.** Watson L, et al. *Rheumatology*. 2023;62:2748–56. **4.** Strand V, et al. *J Rheumatol*. 2012;39:1450–7. **5.** de Lautour H, et al. *Arthritis Care Res*. 2016;68:667–72. **6.** Abdellatif A, et al. *Front Immunol*. 2025;16:1516146. **7.** Tabi-Amponsah AD, et al. *Ann Rheum Dis*. 2025; online ahead of print.

NASP

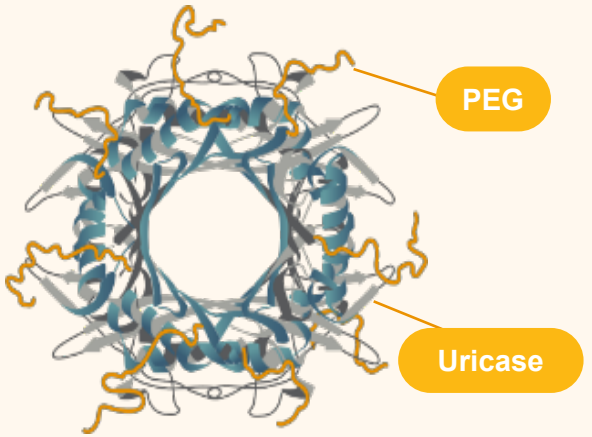
Nanoencapsulated sirolimus plus pegadricase (NASP; formerly SEL-212) is a **novel**, **every 4-week**, **sequential infusion therapy** designed to **reduce sUA levels** in patients with UG,[1] **consisting of co-administered:**

Nanoencapsulated sirolimus (NAS)
formerly SEL-110

Biodegradable, immune-tolerizing agent that induces antigen-specific tolerance to co-administered biologics[2,3]



Pegadricase
formerly SEL-037



Pegylated uricase that converts uric acid to soluble and readily excreted allantoin[4]

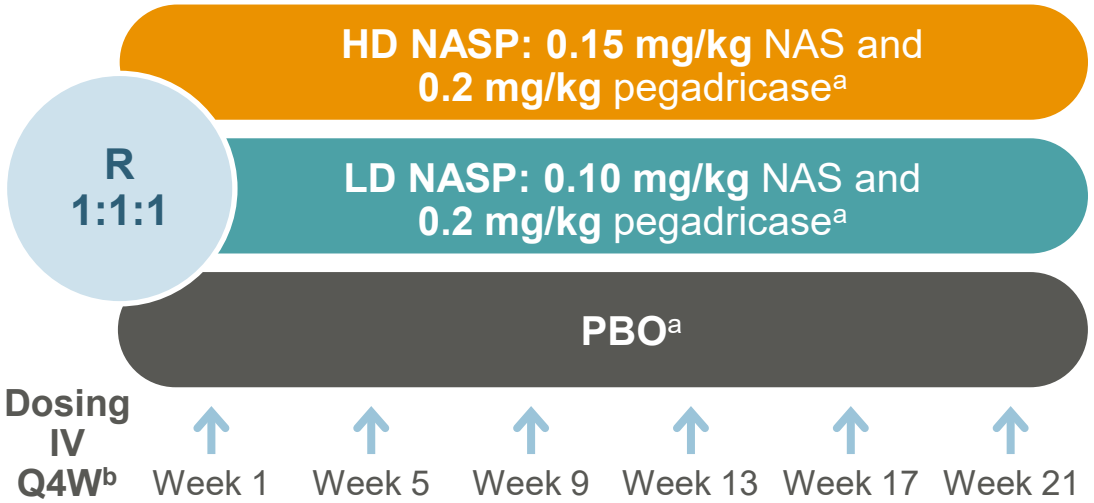
- ✓ NASP has demonstrated **significant reductions in sUA levels** compared with placebo (PBO) in patients with UG[5]
- ✓ NASP has led to improvements in **key clinical manifestations** of UG, including a decrease in gout flares and significant tophus resolution[6,7]

NAS, nanoencapsulated sirolimus; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; PEG, polyethylene glycol; PLA, polylactic acid; sUA, serum uric acid; UG, uncontrolled gout.

1. Baraf HSB, et al. *Rheumatology*. 2024;63:1058–67. **2.** Kishimoto TK. *Front Immunol*. 2020;11:969. **3.** Sands E, et al. *Nat Commun*. 2022;13:272. **4.** Kivitz A, et al. *Rheumatol Ther*. 2023;10:825–47. **5.** Khanna P, et al. American College of Rheumatology (ACR); November 14–19, 2024; Washington, DC, USA. Poster 2005. **6.** Gaffo A, et al. Congress of Clinical Rheumatology (CCR) – East; May 1–4, 2025; Destin, FL, USA. **7.** Baraf HSB, et al. Congress of Clinical Rheumatology (CCR) – East; May 1–4, 2025; Destin, FL, USA.

Design of the DISSOLVE I and DISSOLVE II randomized controlled trials

DISSOLVE I (NCT04513366; US) and DISSOLVE II (NCT04596540; global) are 2 parallel, randomized, double-blind, PBO-controlled, phase 3 trials (RCTs)[1-4]



DISSOLVE I and II inclusion criteria:

- Adults with UG
  - ≥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 XOIs (or contraindication to XOIs)
- Screening sUA level ≥7 mg/dL

[a]Administered as sequential infusions; for patients who received NASP, pegadricase infusion began within 30 minutes of completion of NAS infusion. [b]Arrows indicate time of study drug administration.
HD NASP, high-dose NASP; IV, intravenous; LD NASP, low-dose NASP; NAS, nanoencapsulated sirolimus; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; Q4W, every 4 weeks; R, randomization; RCT, randomized controlled trial; sUA, serum uric acid; UG, uncontrolled gout; US, United States; XOI, xanthine oxidase inhibitor.

1. Gaffo A, et al. Congress of Clinical Rheumatology (CCR) – East; May 1–4, 2025; Destin, FL, USA. **2.** Baraf HSB, et al. Congress of Clinical Rheumatology (CCR) – East; May 1–4, 2025; Destin, FL, USA. **3.** Khanna P, et al. American College of Rheumatology (ACR); November 14–19, 2024; Washington, DC, USA. Poster 2005. **4.** Baraf HSB, et al. European Congress of Rheumatology (EULAR); June 12–15, 2024; Vienna, Austria. Poster POS0260.

Study design and key endpoints

Primary endpoint:

- Percentage of patients with an sUA response (sUA levels <6 mg/dL for ≥80% of time during weeks 21–24 of therapy)

Select secondary endpoints:

- sUA reduction
  - Mean and median sUA were assessed at baseline and prescheduled time points throughout treatment
- Change in number of tender and swollen joints
  - Assessed at baseline and week 24
- Change in SF-36 physical component summary and HAQ-DI scores
  - Assessed at baseline and week 24
- Safety/tolerability

Post hoc analysis:

This analysis reports outcomes in patients from the pooled DISSOLVE I and II intent-to-treat (ITT) population who received 6 doses of NASP or PBO[a]:

- sUA levels
- Tender and swollen joint exam findings
- HRQOL: SF-36 physical component summary
- VAS pain scores

[a]While presenting data on patients who received the full dosing schedule (6 doses) introduces selection bias, it is useful to examine the performance of the full dosing schedule.
HAQ-DI, Health Assessment Questionnaire-Disability Index; HRQOL, health-related quality of life; ITT, intent-to-treat; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; SF-36, 36-Item Short Form Health Survey; sUA, serum uric acid; VAS, visual analogue scale.

Baseline characteristics

Patients who received 6 doses of NASP or PBO

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Similar to the ITT population,[1,a] the subset of patients who received 6 doses of NASP or PBO had a high baseline burden of disease, reflected by a large proportion of patients with tophi, high mean sUA, and high mean number of tender and swollen joints

Patient characteristics	HD NASP n=42	LD NASP n=35	PBO n=67
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)
Race, n (%)			
White	36 (85.7)	29 (82.9)	51 (76.1)
Black or African American	6 (14.3)	6 (17.1)	9 (13.4)
Asian	0	0	3 (4.5)
Comorbidity,[b] 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)
Obesity	5 (11.9)	6 (17.1)	9 (13.4)

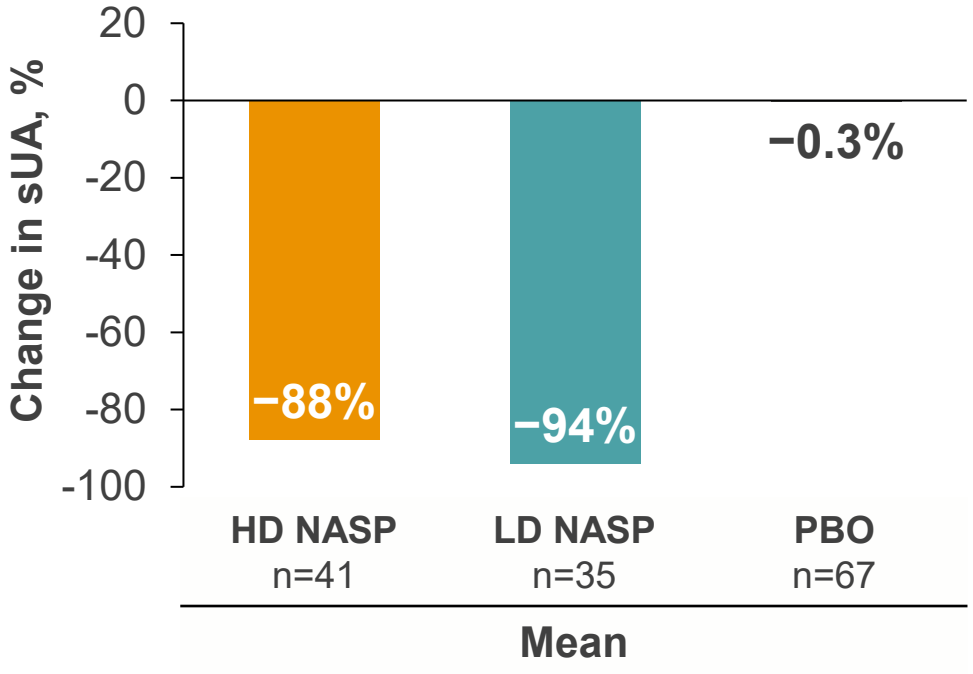
Disease characteristics	HD NASP n=42	LD NASP n=35	PBO n=67
Time since gout diagnosis, years, mean (SD)	13.3 (10.6)	12.1 (8.5)	11.7 (8.4)
Patients with tophi, n (%)	23 (54.8)	22 (62.9)	42 (62.7)
sUA, mg/dL, mean (SD)	8.5 (1.4)	8.5 (1.3)	8.7 (1.6)
Number of tender joints, mean (SD)	5.8 (8.0)	6.1 (7.7)	7.7 (11.0)
Number of swollen joints, mean (SD)	2.9 (4.9)	3.5 (6.1)	5.2 (8.5)

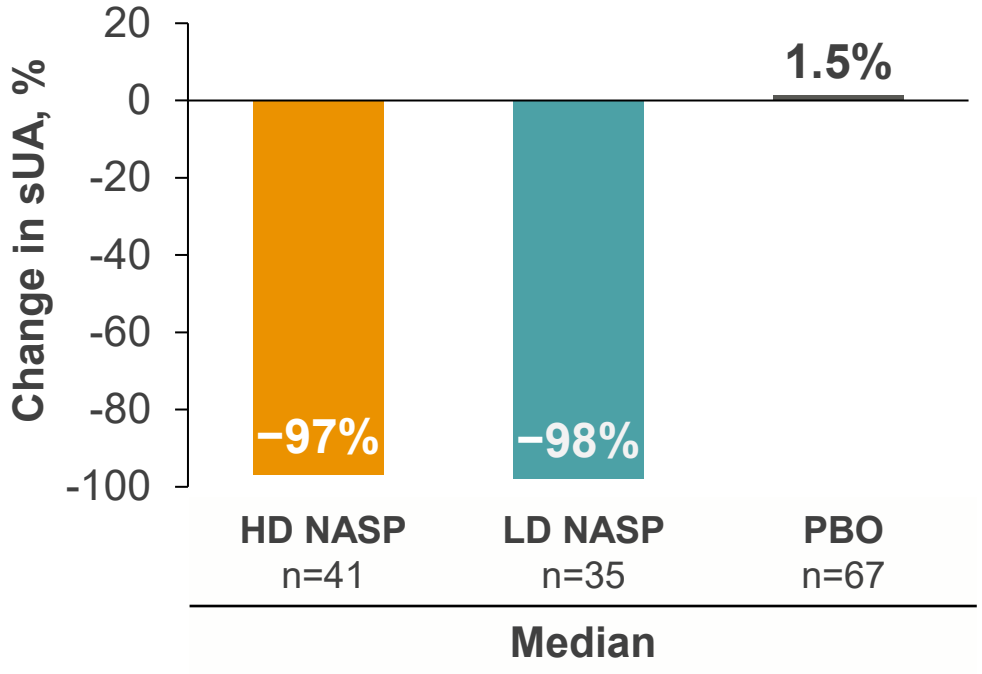
[a]Among patients in the DISSOLVE I and II ITT population, 48% (42/87) of patients treated with HD NASP, 40% (35/88) of patients treated with LD NASP, and 74% (67/90) of patients treated with PBO received 6 doses of treatment; overall, 54% (144/265) of patients received 6 doses of treatment. [b]Comorbidities, excluding gout and related disorders, that were present in ≥10% of all patients.
BMI, body mass index; HD NASP, high-dose NASP; ITT, intent-to-treat; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; SD, standard deviation; sUA, serum uric acid.

1. Baraf HSB, et al. European Congress of Rheumatology (EULAR); June 12–15, 2024; Vienna, Austria. Poster POS0260.

Change in sUA from baseline to the last treatment period

Patients who received 6 doses of NASP or PBO





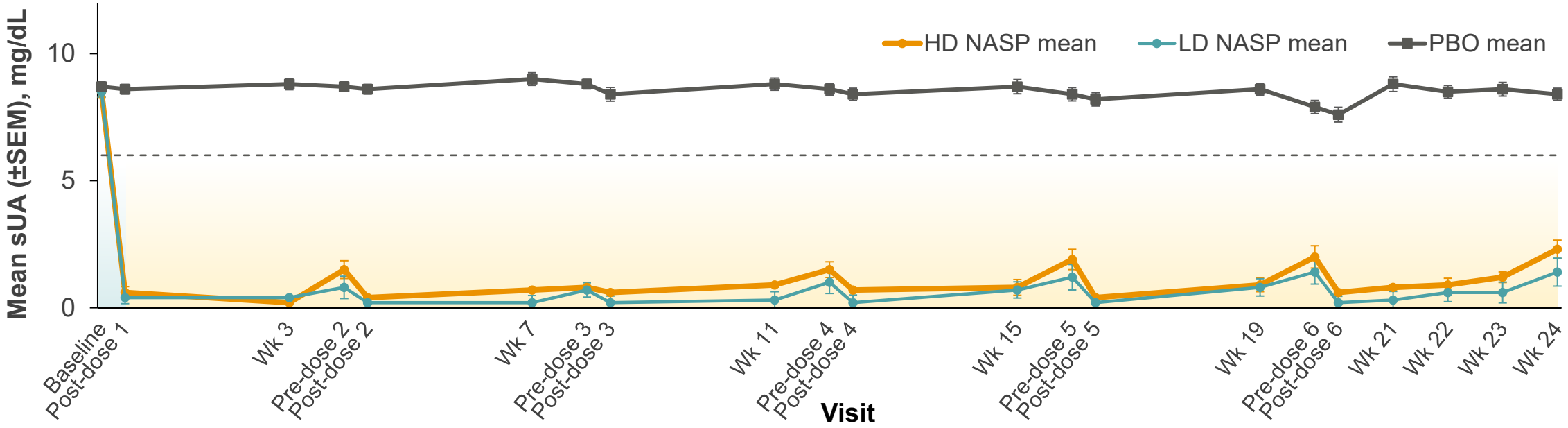
From baseline to the last treatment period (weeks 21–24), mean and median sUA decreased substantially in NASP-treated patients

In PBO-treated patients, sUA levels remained similar to baseline levels throughout the trial

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

sUA over time

Patients who received 6 doses of NASP or PBO



Patients, n	BL	Dose 1		Dose 2			Dose 3			Dose 4			Dose 5			Dose 6					
		Post	Wk 3	Pre	Post	Wk 7	Pre	Post	Wk 11	Pre	Post	Wk 15	Pre	Post	Wk 19	Pre	Post	Wk 21	Wk 22	Wk 23	Wk 24
HD NASP	42	41	41	41	41	42	42	42	42	41	41	42	41	40	42	39	38	35	35	40	37
LD NASP	35	33	35	35	34	35	35	35	35	34	34	35	33	33	34	33	33	31	31	34	35
PBO	67	66	66	67	67	67	67	67	67	67	67	67	64	64	67	61	61	64	62	64	67

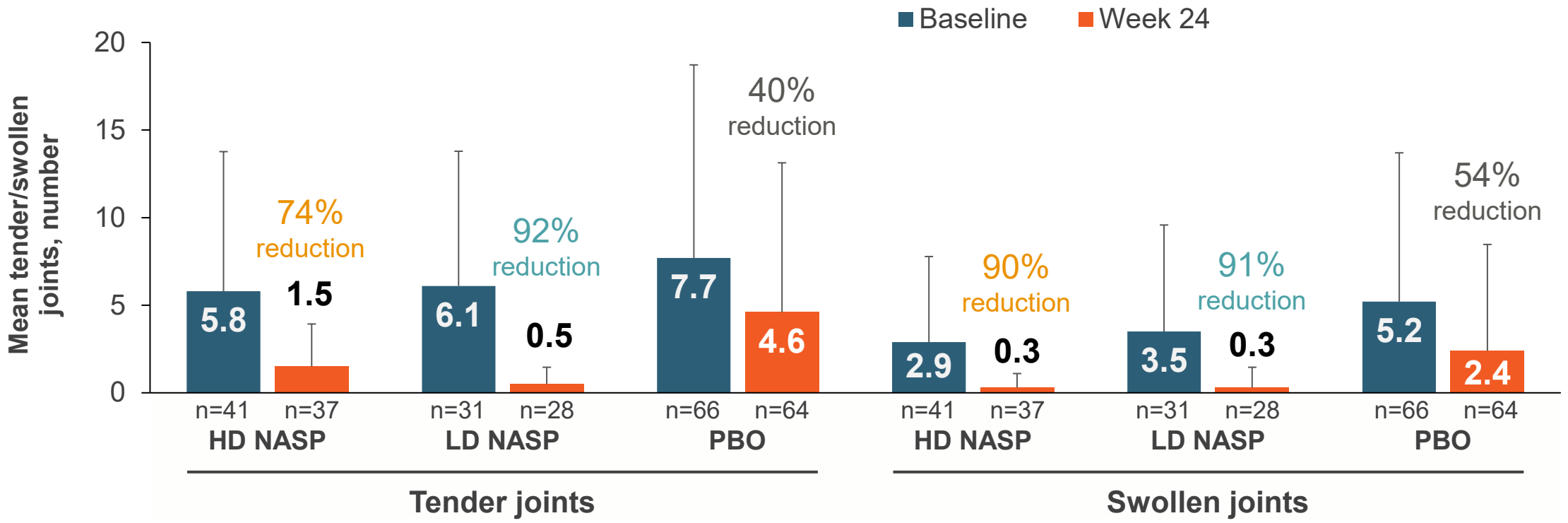
sUA reduction was seen immediately after the first dose of NASP and within 1 hour of each subsequent dose

Mean sUA was generally sustained at ≤2 mg/dL throughout the trial

Error bars show standard error of the mean. Dotted line shows sUA of 6 mg/dL; the primary endpoint of the DISSOLVE I and II trials was the percentage of patients with an sUA response (sUA levels <6 mg/dL for ≥80% of time during weeks 21–24 of therapy). BL, baseline; HD NASP, high-dose NASP; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; pre, pre-dose; post, post-dose; SEM, standard error of the mean; sUA, serum uric acid; Wk, week.

Tender and swollen joints at baseline and week 24

Patients who received 6 doses of NASP or PBO

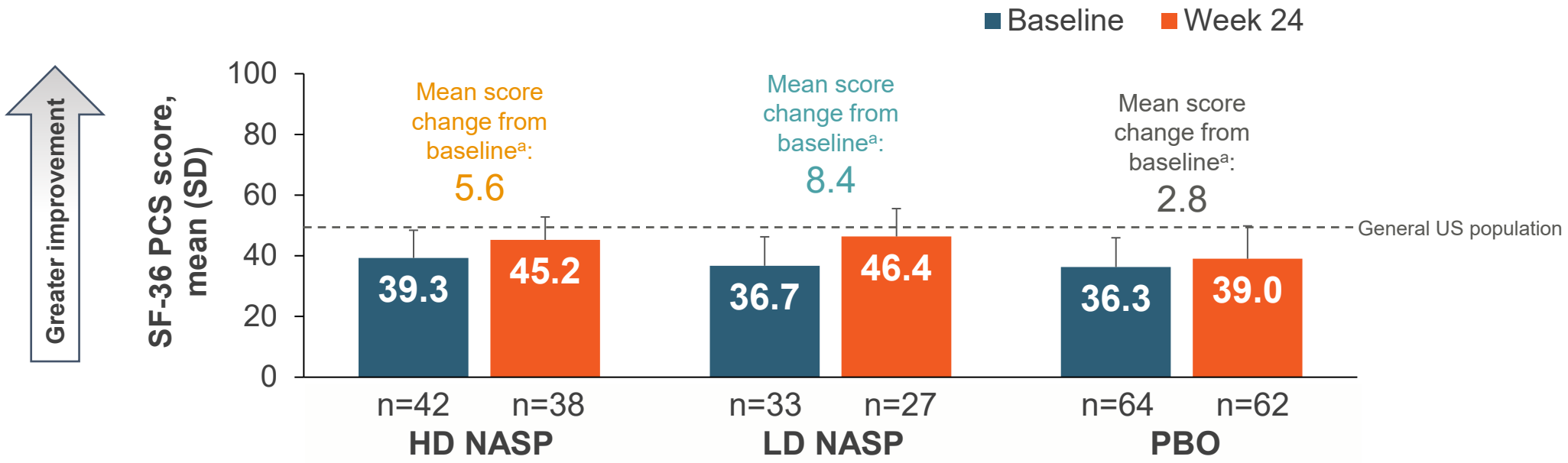


NASP treatment substantially reduced the number of tender and swollen joints over 24 weeks of treatment; ~2-fold greater reductions were observed with HD NASP and LD NASP versus PBO

Error bars show standard deviation.
HD NASP, high-dose NASP; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo.

HRQOL: SF-36 PCS scores at baseline and week 24

Patients who received 6 doses of NASP or PBO



NASP-treated patients reported improvements in mean SF-36 PCS scores from baseline to week 24 that exceeded the MCID of 2.5[1] and were ≥2-fold higher than changes in PBO-treated patients

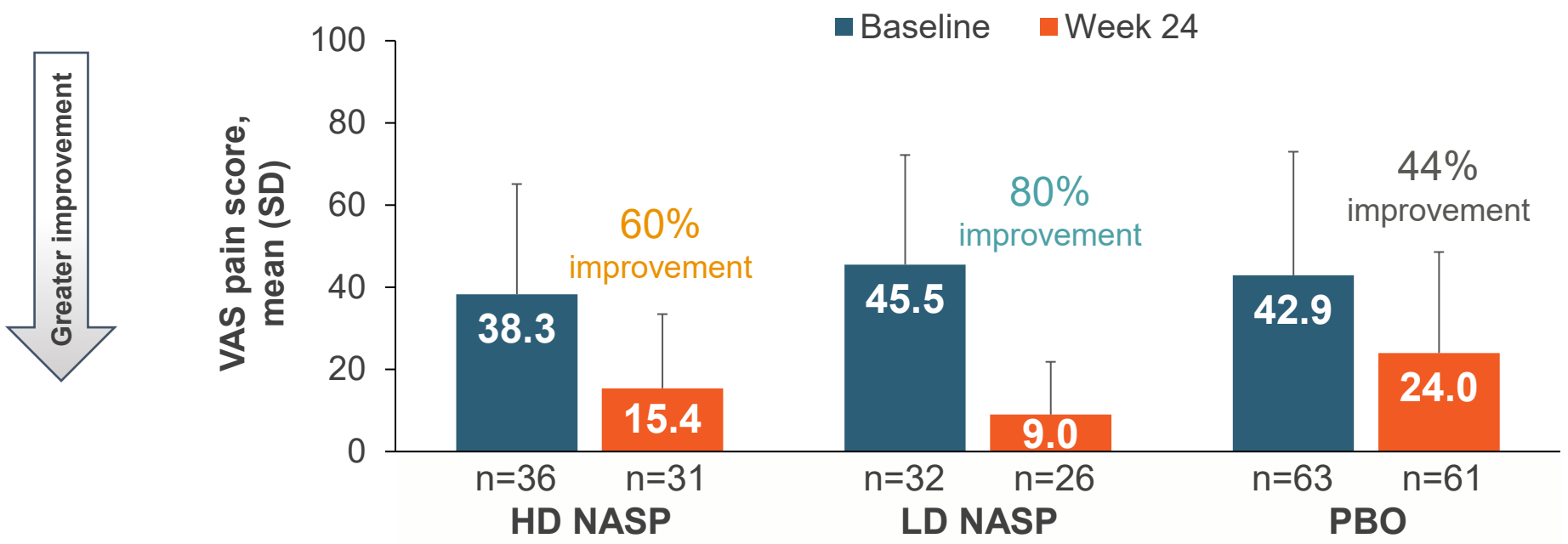
At week 24, scores in NASP-treated patients were comparable to the general US population (49.2)[2]

Error bars show standard deviation. Higher SF-36 scores indicate greater improvement in HRQOL.
[a]Mean change from baseline in patients with a 24-week assessment.
HD NASP, high-dose NASP; HRQOL, health-related quality of life; LD NASP, low-dose NASP; MCID, minimal clinically important difference; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; PCS, physical component summary; SD, standard deviation; SF-36, 36-Item Short Form Health Survey; US, United States.

1. Sundy JS, et al. *JAMA*. 2011;306:711–20. **2.** Maglinte GA, et al. *J Clin Epidemiol*. 2012;65:497–502.

VAS pain scores at baseline and 24 weeks

Patients who received 6 doses of NASP or PBO



Mean improvements in VAS pain scores from baseline to week 24 were 1.4-fold higher with HD NASP and 1.8-fold higher with LD NASP versus PBO

Error bars show standard deviation. Lower VAS scores indicate less pain. The MCID for the VAS of pain severity is 18.[1]

HD NASP, high-dose NASP; LD NASP, low-dose NASP; MCID, minimal clinically important difference; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; SD, standard deviation; VAS, visual analogue scale.

1. Todd KH, Funk JP. *Acad Emerg Med*. 1996;3:142–6.

Adverse events of special interest

Patients 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 hours	4 (9.5)	3 (8.6)	1 (1.5)
Infusion-related AE within 1 hour	0	0	0
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)

Adverse events of special interest in patients who received 6 doses of NASP or PBO were generally similar to those observed in the overall ITT population (previously presented)[1]

[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; HD NASP, high-dose NASP; ITT, intent-to-treat; LD NASP, low-dose NASP; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; TEAE, treatment-emergent adverse event.

1. Baraf HSB, et al. European Congress of Rheumatology (EULAR); June 12–15, 2024; Vienna, Austria. Poster POS0260.

Conclusions

- In patients with UG who received 6 doses of treatment, NASP demonstrated:
  - Rapid and sustained sUA control
  - A substantial reduction in the number of tender and swollen joints
  - An improvement in physical functioning and pain measures reported by patients
- No new safety signals were detected

These results show NASP had a noteworthy impact on resolving gout symptoms and improving patient-reported outcomes over 6 treatments

NASP, nanoencapsulated sirolimus plus pegadricase; sUA, serum uric acid; UG, uncontrolled gout.

Acknowledgments

The authors would like to thank the **entire team** involved with the DISSOLVE trials, most importantly **participating patients** and **their families**.

The authors also acknowledge:

- Adrianne Spencer, PhD, Hannah L. Mayberry, PhD, and Pamela Barendt, PhD, of Peloton Advantage, LLC, an OPEN Health company (Parsippany, NJ, USA), for medical writing and editorial assistance
- Daniela Bruni, PhD, PharmD, of Sobi (Basel, Switzerland) for publication coordination

The DISSOLVE I and II (NCT04513366 and NCT04596540) trials were jointly funded by Sobi and Selecta Biosciences, Inc. Medical writing and editorial assistance were funded by Sobi.

This presentation was developed by the authors in accordance with Good Publication Practice (GPP) 2022 guidelines (https://www.ismpp.org/gpp-2022). Sobi reviewed and provided feedback on the presentation. The authors had full editorial control of the presentation and provided their final approval of all content.