Long-Term Phase 2 Efficacy of the MASP-2 Inhibitor Narsoplimab for Treatment of Severe IgA Nephropathy

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Disclosures

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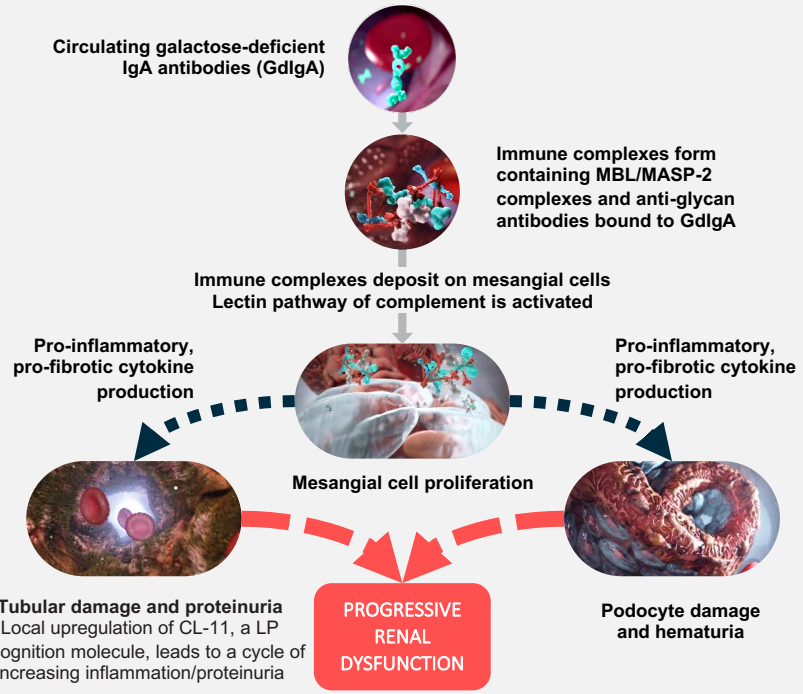
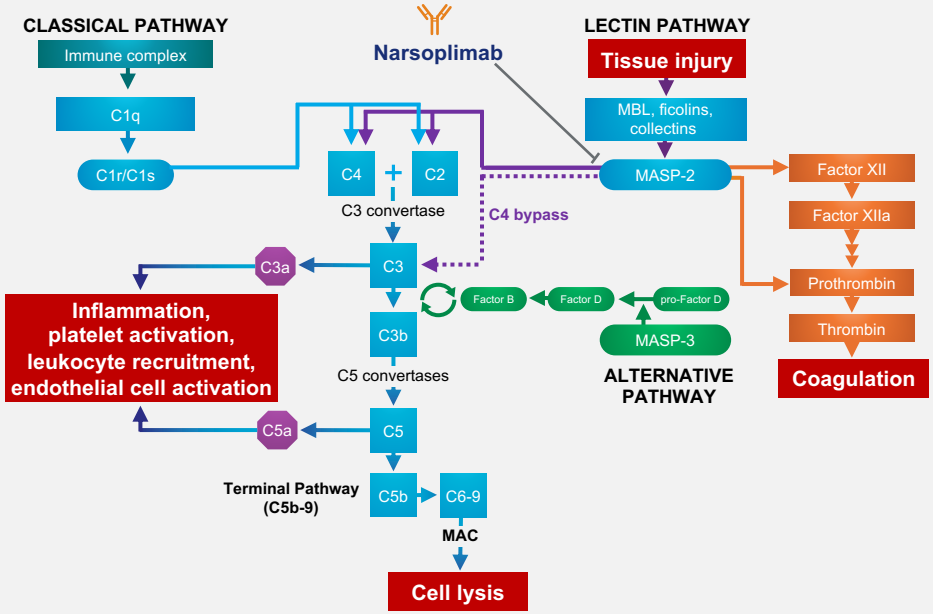
Narsoplimab is an investigational agent and has not been approved by any regulatory agency.

Narsoplimab Inhibits MASP-2, the Effector Enzyme of the Lectin Pathway, Which is Activated in IgAN

Activation of the lectin pathway contributes to tubular and podocyte damage in IgAN



Narsoplimab inhibits MASP-2, the effector enzyme of the lectin pathway



Barratt J, Lafayette R. Drugs Future. 2020;45:389–396. Merle NS, et al. Front Immunol. 2015;6:262.
CL-11, collectin-11; IgAN, IgA nephropathy; LP, lectin pathway; MAC, membrane attack complex; MASP, mannan-binding lectin-associated serine protease; MBL, mannan-binding lectin.

Staged Phase 2 Study of Narsoplimab in Adult Patients with Severe IgAN (NCT02682407)

Key inclusion criteria:

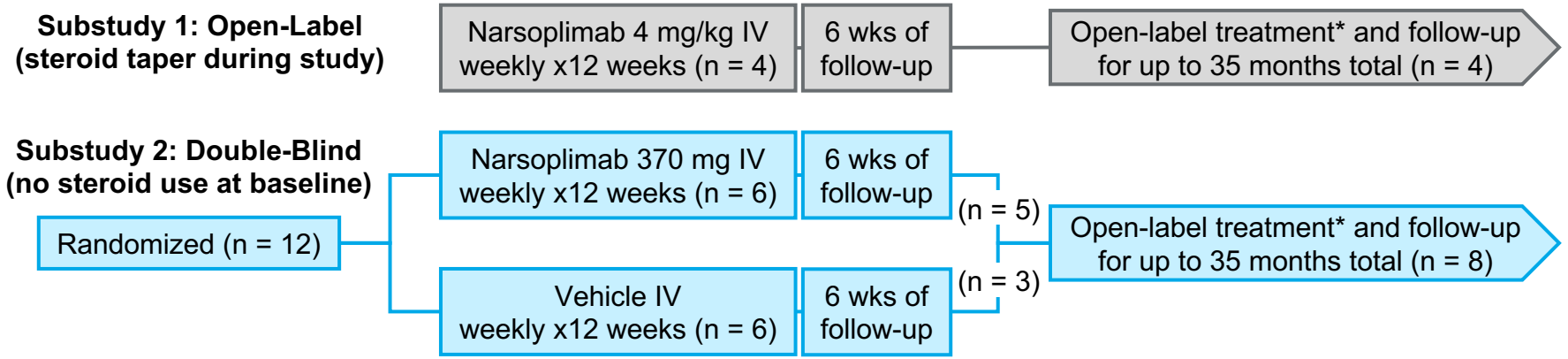
- Adults with severe IgAN
- UPE >1 g/d
- eGFR ≥30 mL/min/1.73 m^2

Primary endpoint

- Safety and tolerability of narsoplimab

Key secondary endpoints

- 24-hour UPE and eGFR, assessed by time-weighted average regression analysis



*Open-label narsoplimab 370 mg IV weekly x12 weeks could be administered if UPE was >1 g/d (or ≥50% of baseline)

eGFR, estimated glomerular filtration rate; IgAN, IgA nephropathy; IV, intravenous; UPE, urine protein excretion.

Twelve Patients Were Treated and Followed for up to 35 Months (Median, 22 Months)

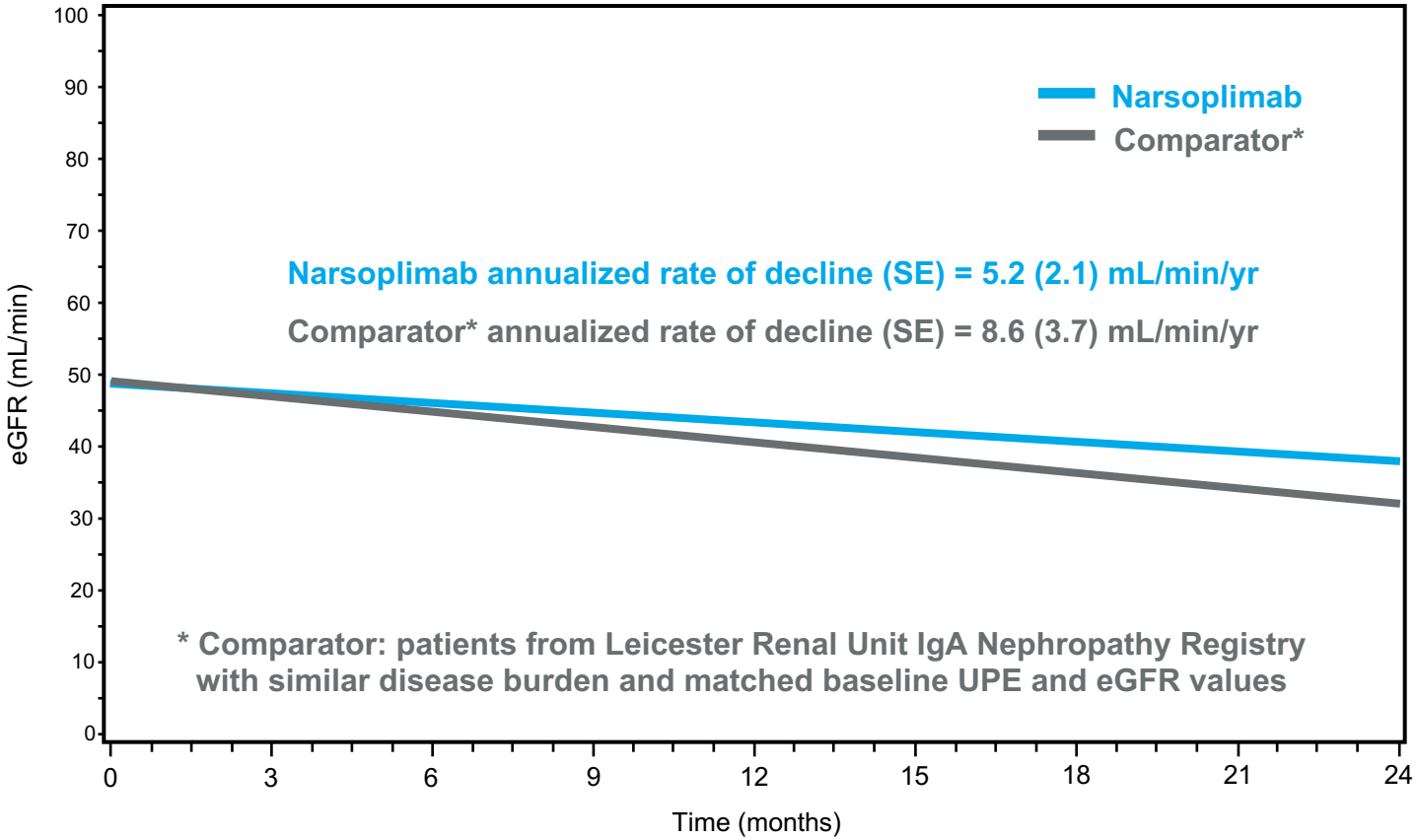
Baseline Characteristics	n (%) or median [range] (N = 12)
Age, y	35 [24 – 60]
Male	6 (50%)
White	11 (92%)
Time since IgAN diagnosis, y	6.9 [0.4 – 27.5]
eGFR, mL/min/1.73 m^2	40.7 [25.4 – 75.9]
UPE, g/d	4.2 [1.5 – 11.9]
Hypertension	10 (83%)
Systolic blood pressure, mmHg	127 [101 – 162]
Diastolic blood pressure, mmHg	84 [60 – 104]
Obesity	7 (58%)
Body mass index, kg/m^2	32.5 [24.4 – 44.3]

Narsoplimab treatment
(1 course = 12 weekly IV doses)

- Median, 1 course per year (range, 0.7–2.5)
- 7 patients (58%) received 1 course or less per year

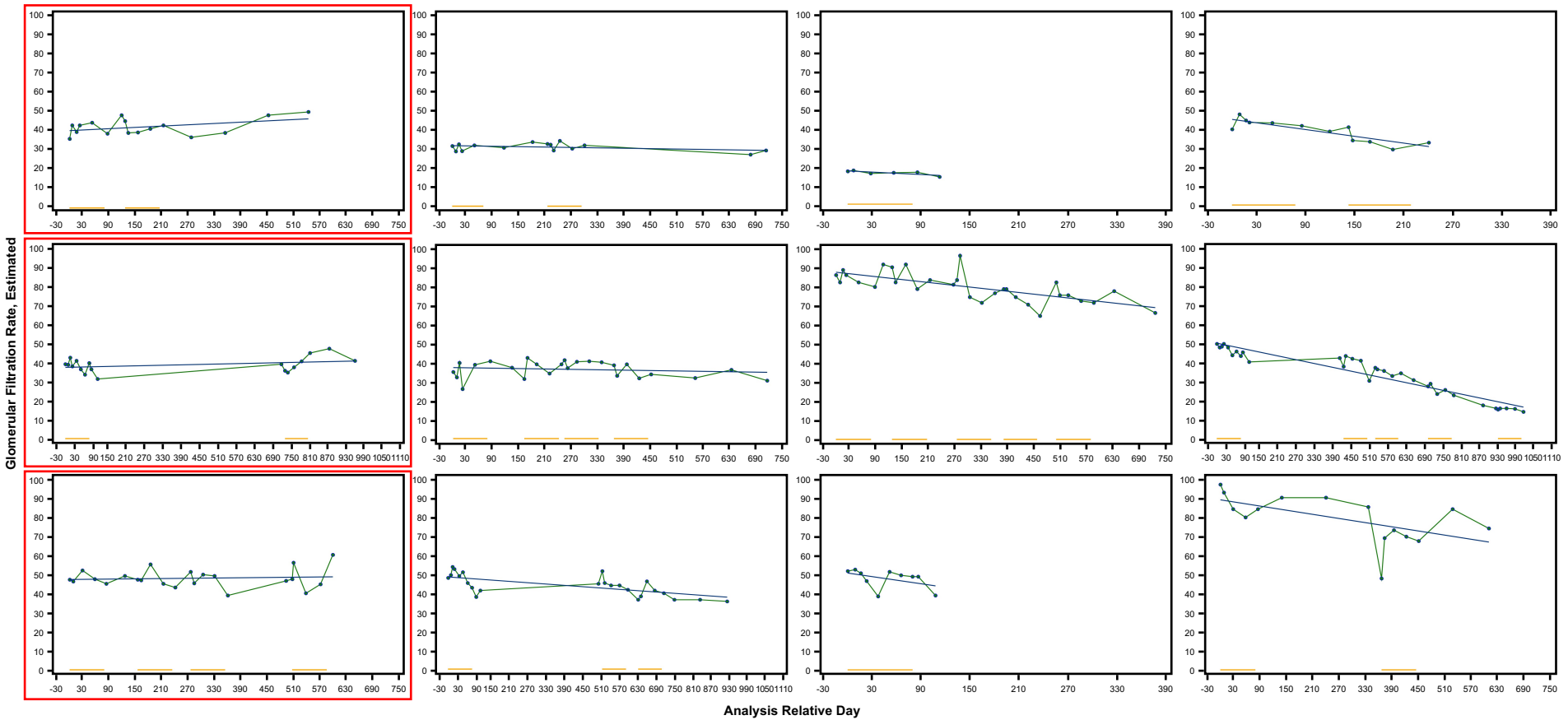
eGFR, estimated glomerular filtration rate; IgAN, IgA nephropathy; IV, intravenous; UPE, urine protein excretion.

Narsoplimab Treatment Decreased the Rate of Decline in eGFR Relative to External Comparator Group



eGFR, estimated glomerular filtration rate; SE, standard error; UPE, urine protein excretion.

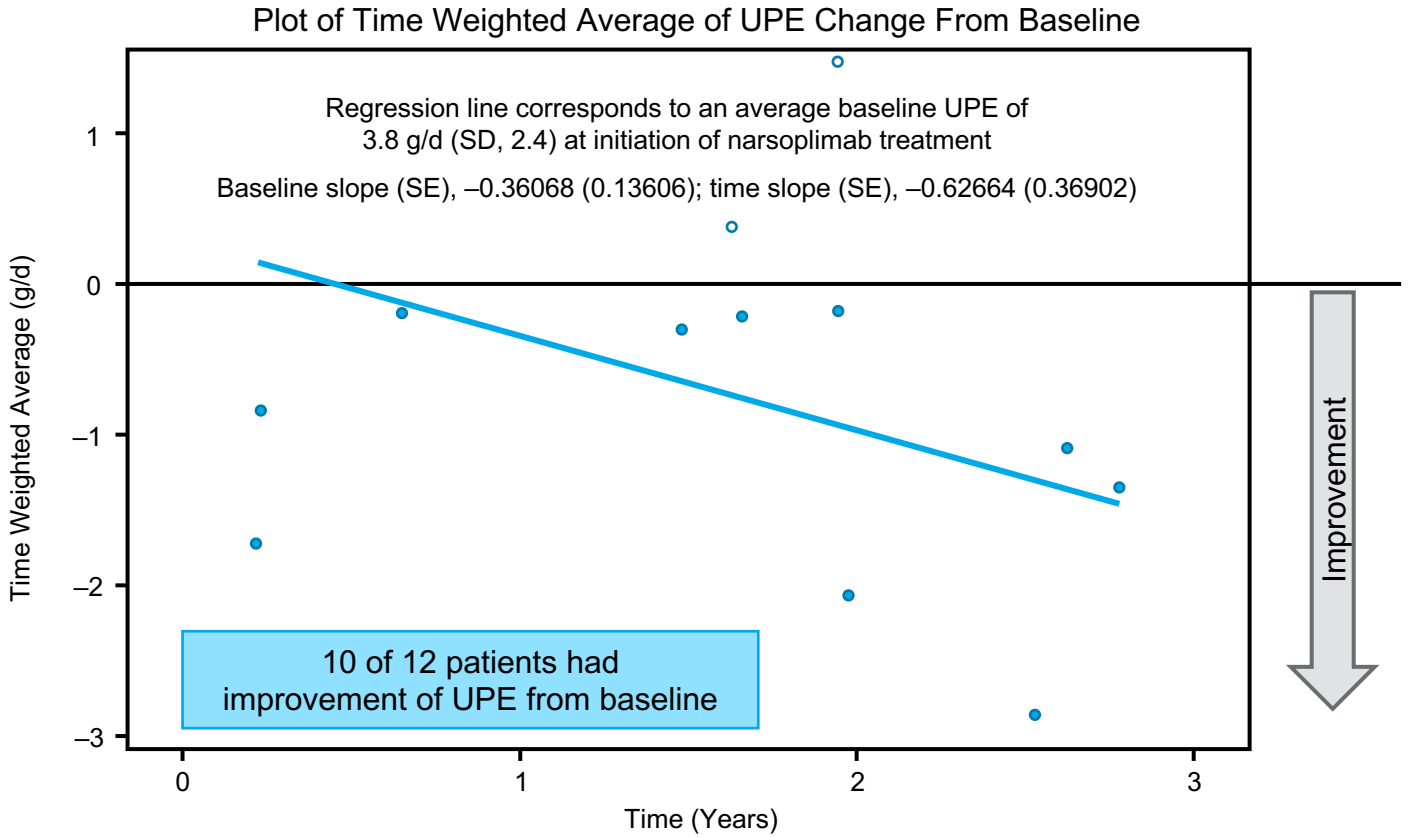
eGFR Increased in 3/12 Patients and Remained Stable for Others



eGFR, estimated glomerular filtration rate.

● eGFR Analysis Value — Regression line — 12-week courses of narsoplimab treatment

Estimated Mean UPE Decrease was 38% From Baseline Through ~3 Years



UPE, urine protein excretion.

No Subject Had a Treatment-Related Serious Adverse Event

Treatment-Emergent Adverse Event	Substudy 1 (N = 4) n (%)	Substudy 2 (N = 8) n (%)	Total (N = 12) n (%)
Fatigue	3 (75)	1 (13)	4 (33)
Upper respiratory tract infection	2 (50)	2 (25)	4 (33)
Abdominal pain	1 (25)	1 (13)	2 (17)
Acute kidney injury	0	2 (25)	2 (17)
Alopecia	2 (50)	0	2 (17)
Anxiety	1 (25)	1 (13)	2 (17)
Gout	0	2 (25)	2 (17)
Headache	2 (50)	0	2 (17)
Ligament sprain	0	2 (25)	2 (17)
Metabolic acidosis	0	2 (25)	2 (17)
Muscle spasms	1 (25)	1 (13)	2 (17)
Pharyngitis	1 (25)	1 (13)	2 (17)
Rash	1 (25)	1 (13)	2 (17)
Toothache	1 (25)	1 (13)	2 (17)
Urinary tract infection	0	2 (25)	2 (17)

Table includes adverse events that occurred in at least 2 patients.

Conclusions

- In this phase 2 study, adults with severe IgAN receiving narsoplimab treatment were followed for ~3 years
- Narsoplimab treatment improved, stabilized, or markedly slowed decline of eGFR (versus external comparator)
  - While other studies reported 1-year follow-up data in patients with IgAN, this is the first study to show sustained stabilization – or improvement – of eGFR with longer-term follow-up
- Narsoplimab treatment resulted in a mean decrease of 38% in UPE from baseline through ~3 years
- Treatment was well tolerated, with no treatment-related serious adverse events
- These results support further investigation of narsoplimab treatment in patients with IgAN
  - The ARTEMIS-IGAN phase 3 clinical trial of narsoplimab for IgAN is currently enrolling (NCT03608033)

eGFR, estimated glomerular filtration rate; IgAN, IgA nephropathy; UPE, urine protein excretion.