

36-Week Efficacy & Safety of Atacicept 150 mg in the ORIGIN Randomized, Double-blind, Placebo-controlled Phase 2b Study in IgAN and Persistent Proteinuria

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Late Breaking Clinical Trial

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Disclosure of Interest for Richard Lafayette

- Consultant for Vera, Omeros, Calliditas, Chinook, Alexion, Otsuka, Novartis, GSK, Alnylam
- Employee of Stanford University Medical Center, which has received research funding from Vera, Omeros, ChemoCentryx, Chinook, Alexion, Otsuka, Calliditas, Roche, NIH, and University of Michigan

Forward Looking Statements

Disclaimer

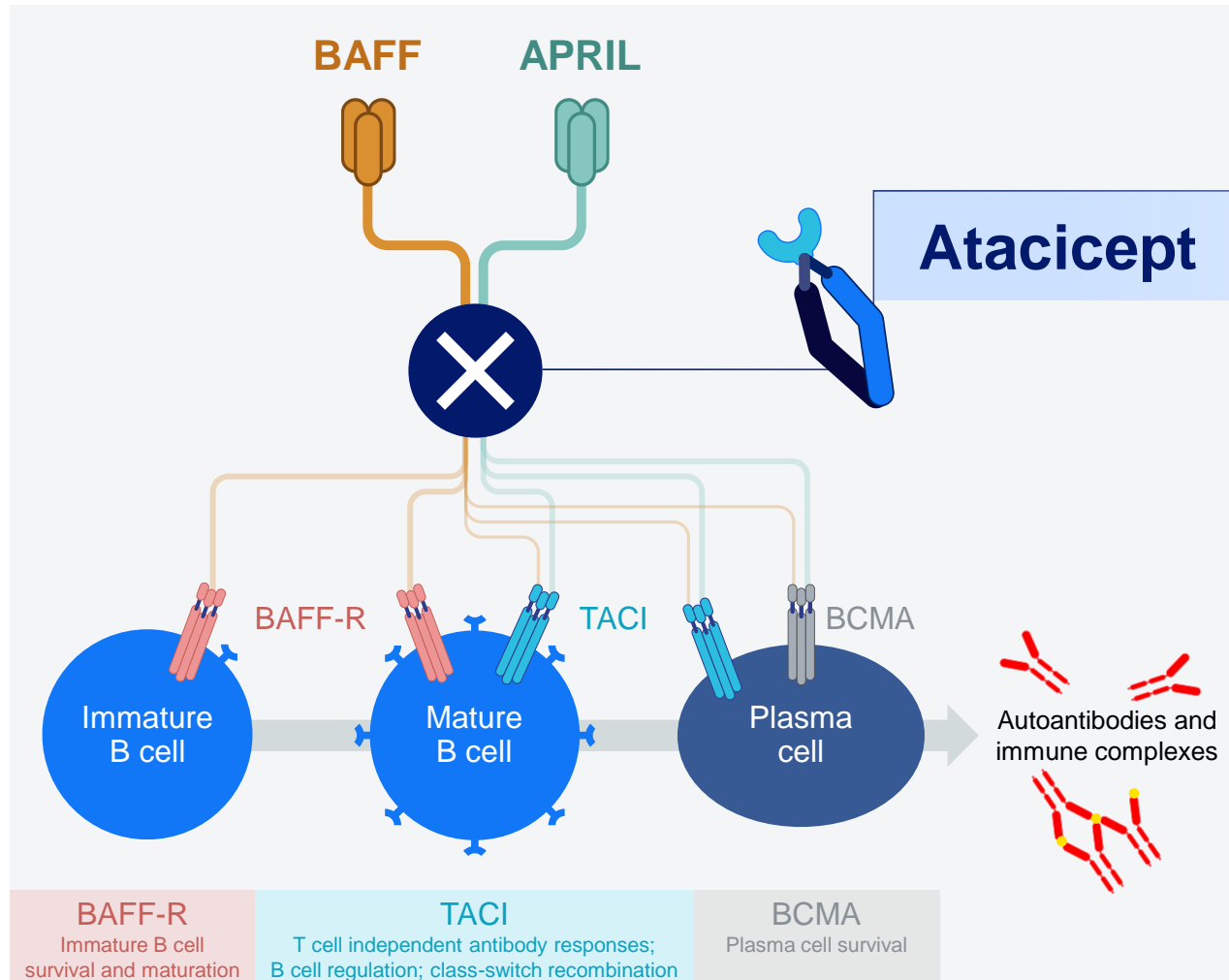
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Atacicept: Dual Inhibitor (BAFF/APRIL) of B Cells and Plasma Cells with Potential to Address Multiple Autoimmune Diseases

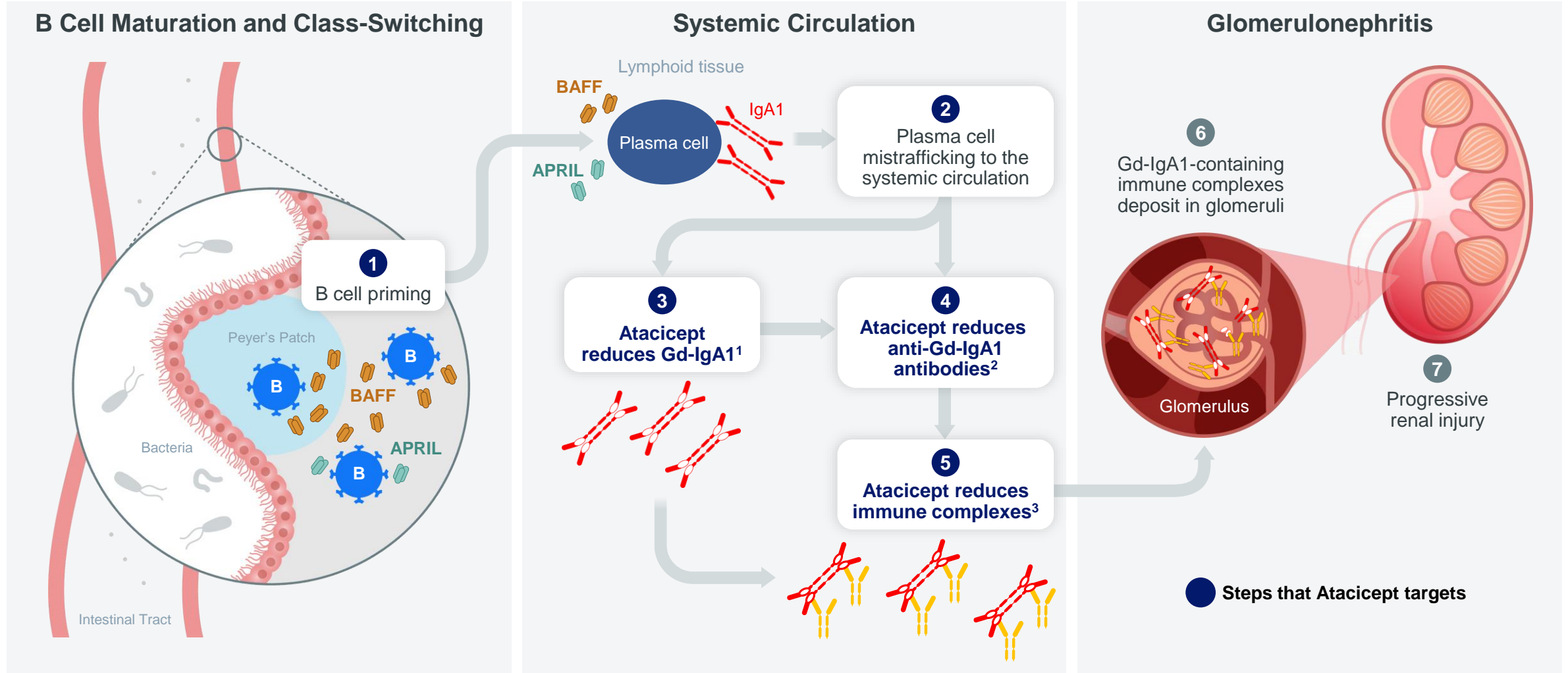


- Fully humanized TACI-Ig fusion protein, subcutaneously administered
- Low nanomolar potency vs BAFF (Kd 1.45 nM) and APRIL (Kd 0.672 nM)
- Reduces overstimulation of B cells and plasma cells¹ and autoantibody production²
- Dual inhibition more potent than either alone³, may translate to more sustained B cell modulation
- Well-characterized safety profile with exposure in >1500 patients across different indications⁴

APRIL = a proliferation-inducing ligand; BAFF = B-cell activating factor, also known as BLYS; TACI = transmembrane activator and CAML interactor.

1. Hiepe F, et al. Nat Rev Rheumatol 2011;3:170-178. 2. Gordon C, et al. Arthritis Rheumatol 2017;69:122-30. 3. Haselmayer P, et al. Eur J Immunol 2017. 4. Gordon C, et al. Rheumatol Adv Pract 2019;0:1-12. Atacicept is investigational and has not been approved by any regulatory authorities.

Atacicept Targets Upstream Hits of IgAN Pathogenesis

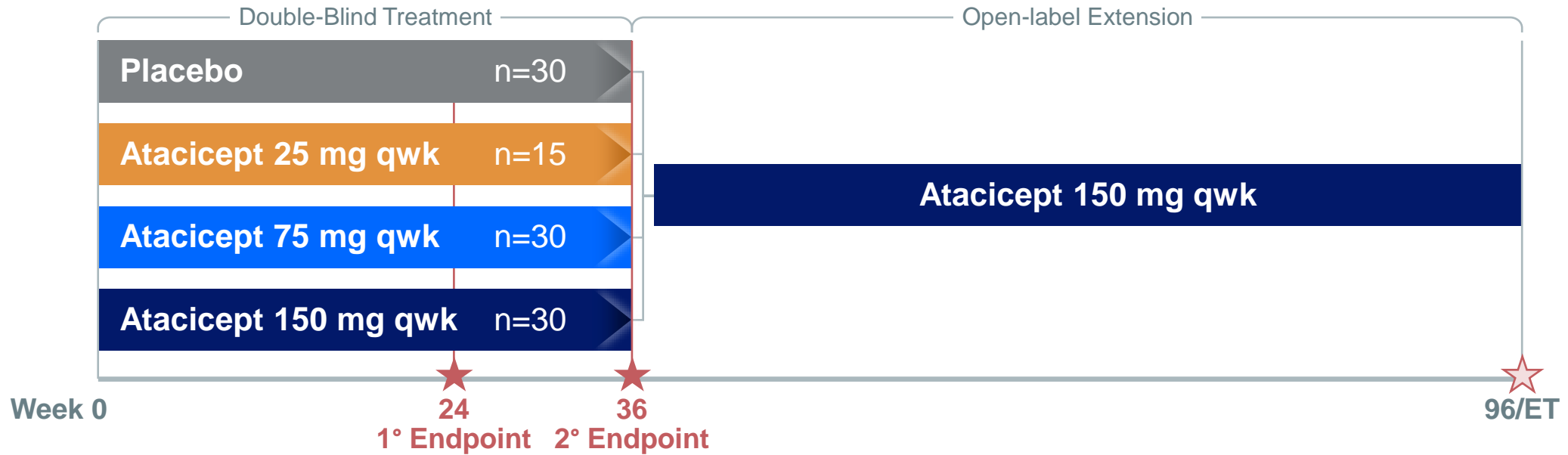


Gd-IgA1 = galactose-deficient immunoglobulin A1.

1. Vera Therapeutics Jan 30 2023 press release. 2. Barratt J, et al. Nephrol Dial Transplant 2022;3 suppl 3, abstr FC051. 3. Barratt J, et al. ASN Kidney Week 2022, abstr SA-PO655.

ORIGIN Phase 2b IgAN Trial: Study Design and Objectives

Multinational, randomized, placebo-controlled trial



Inclusion Criteria

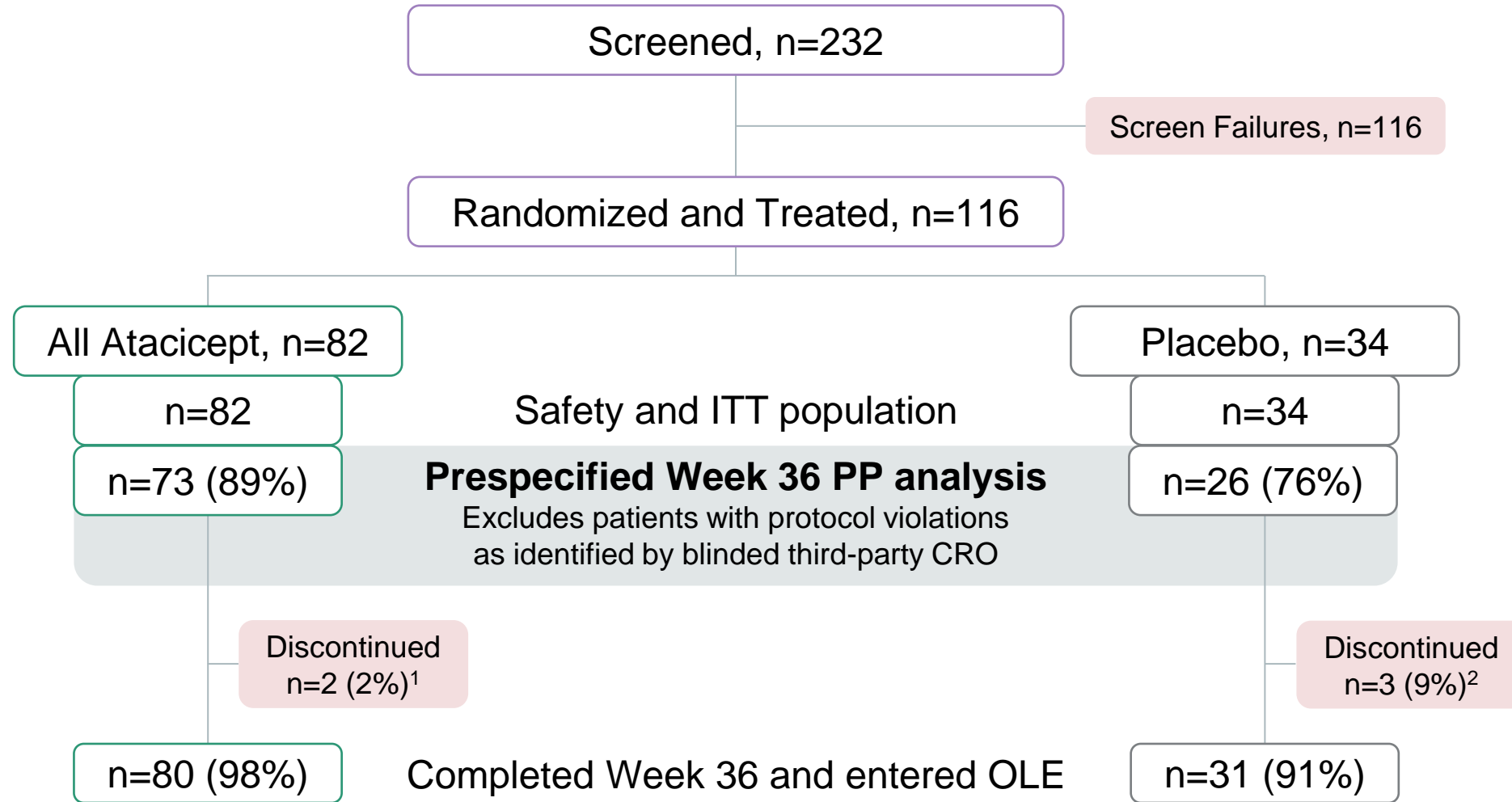
- Patients ≥ 18 years old with IgAN on renal biopsy and high risk of disease progression
- Stable and optimized RAASi for 12 weeks
- Use of SGLT2i allowed
- UPCr-24h > 0.75 g/g or UP > 0.75 g per 24h
- eGFR ≥ 30 mL/min/1.73 m²
- Blood pressure $\leq 150/90$ mmHg

Endpoints

- Primary efficacy: UPCr-24h at week 24 ★
- Key secondary: UPCr-24h at week 36 ★
- eGFR change up to week 96 ★
- Gd-IgA1 change
- Safety

eGFR = estimated glomerular filtration rate; ET = end of treatment; RAASi = renin-angiotensin-aldosterone system inhibitor; SGLT2i = sodium-glucose cotransporter-2 inhibitor; UPCr = urine protein:creatinine.

Patient Disposition



Safety data includes all post-week 36 visits available at data-cut March 09, 2023. ITT = intent to treat; PP = per protocol; OLE = open label extension.

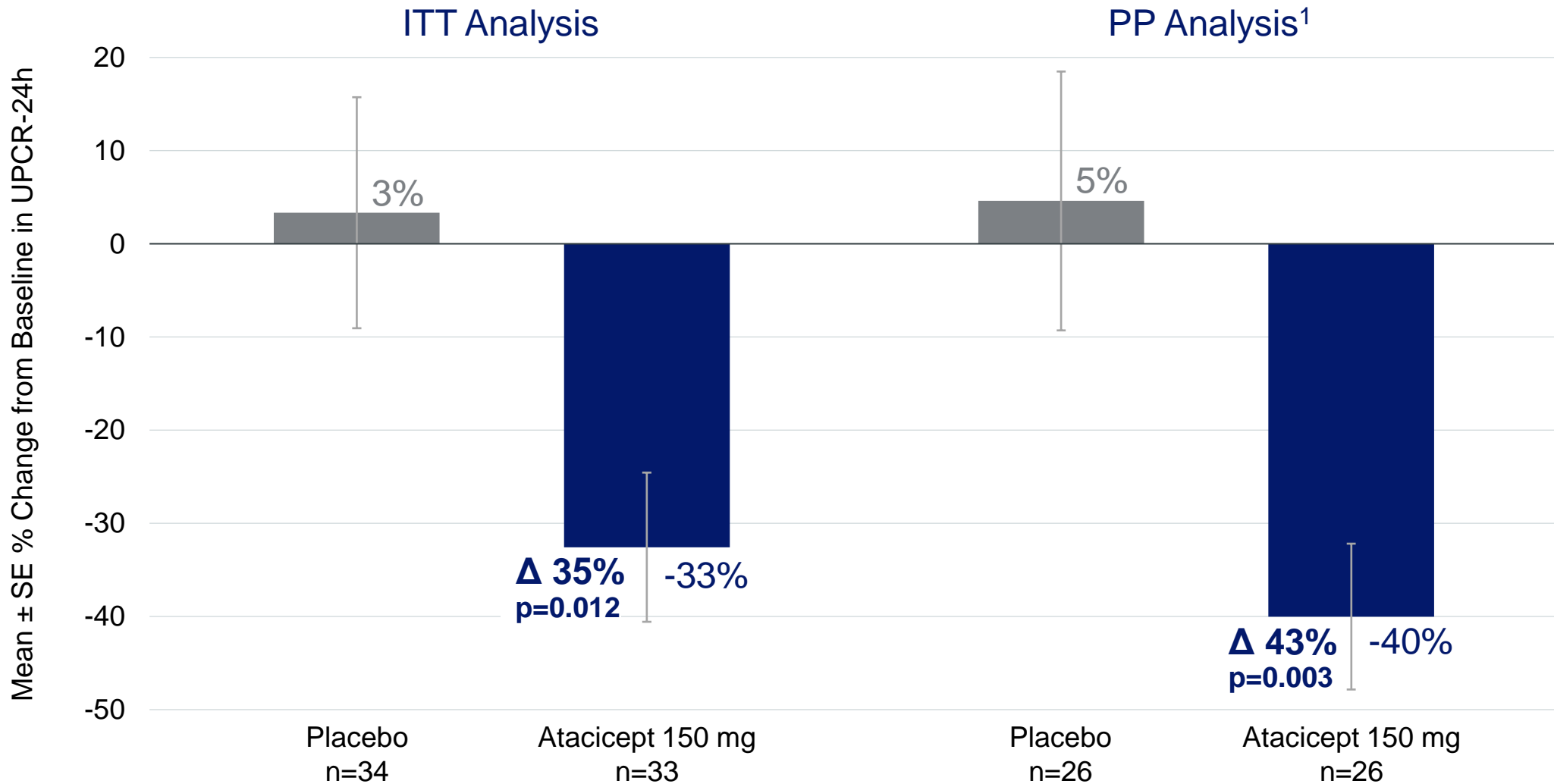
1. Discontinued to pursue elective surgery (1), discontinued due to positive hepatitis B DNA and adverse event (1).

2. Initiated prohibited medication for concomitant disease (1), discontinued due to plan to start prohibited medication for concomitant disease (1) and adverse event (1).

Demographics and Baseline Characteristics

Mean ± SD or n (%)	Overall n=116	Atacicept 25 mg n=16	Atacicept 75 mg n=33	Atacicept 150 mg n=33	Placebo n=34
Age, y	39 ± 12.6	40 ± 15.0	41 ± 12.6	38 ± 11.4	39 ± 13.0
Male sex	69 (59)	9 (56)	19 (58)	22 (67)	19 (56)
Race					
White	62 (53)	7 (44)	12 (36)	17 (52)	26 (76)
Asian	51 (44)	7 (44)	20 (61)	16 (48)	8 (24)
Other	3 (3)	2 (12)	1 (3)	0	0
eGFR, mL/min/1.73 m ²	63 ± 27.3	71 ± 28.7	64 ± 25.4	56 ± 22.7	66 ± 31.7
UPCR by 24h urine, g/g	1.6 ± 0.9	1.6 ± 0.8	1.7 ± 0.9	1.7 ± 1.0	1.6 ± 0.8
SGLT2i use	16 (14)	3 (19)	3 (9)	4 (12)	6 (18)

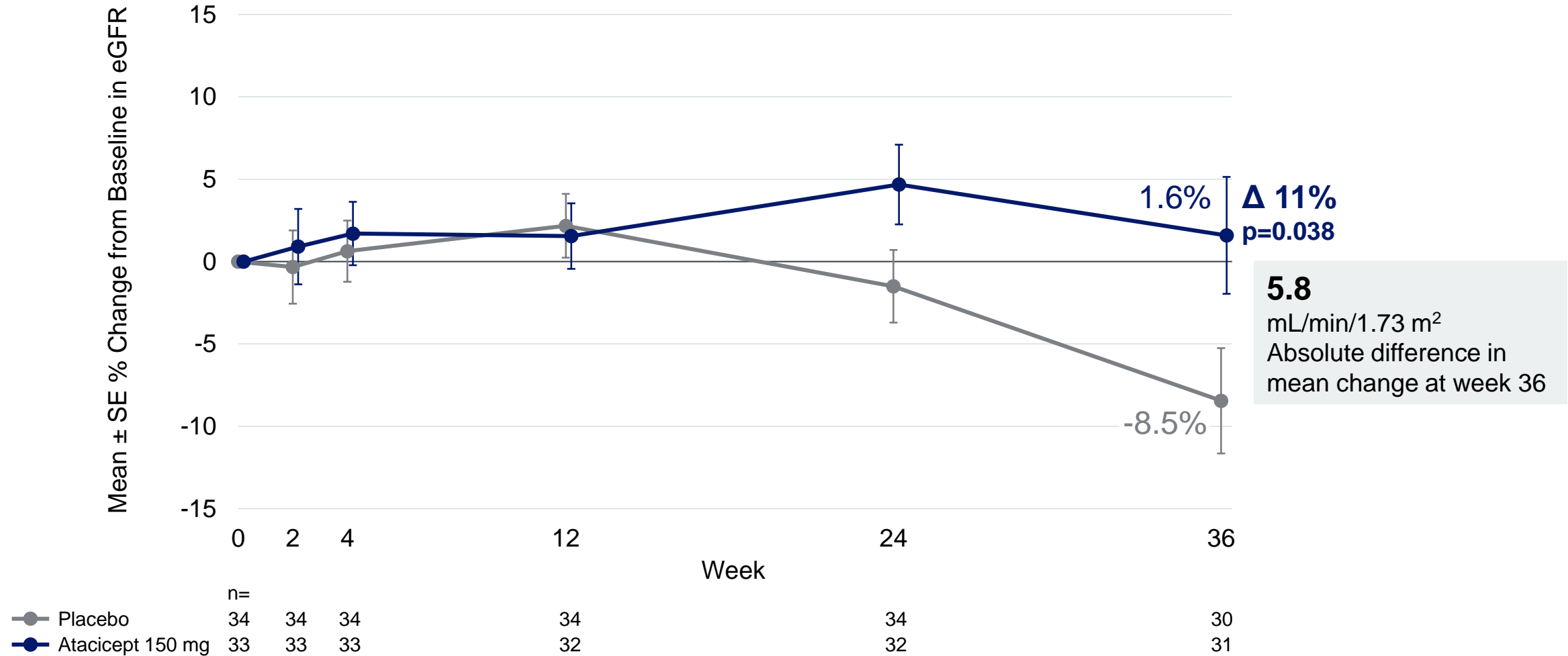
UPCR % Change with Atacicept 150 mg at Week 36



p-values, percentage changes from baseline, and treatment differences were computed using FDA-endorsed mixed-effects modeling which takes into account the effects of baseline UPCR and eGFR.

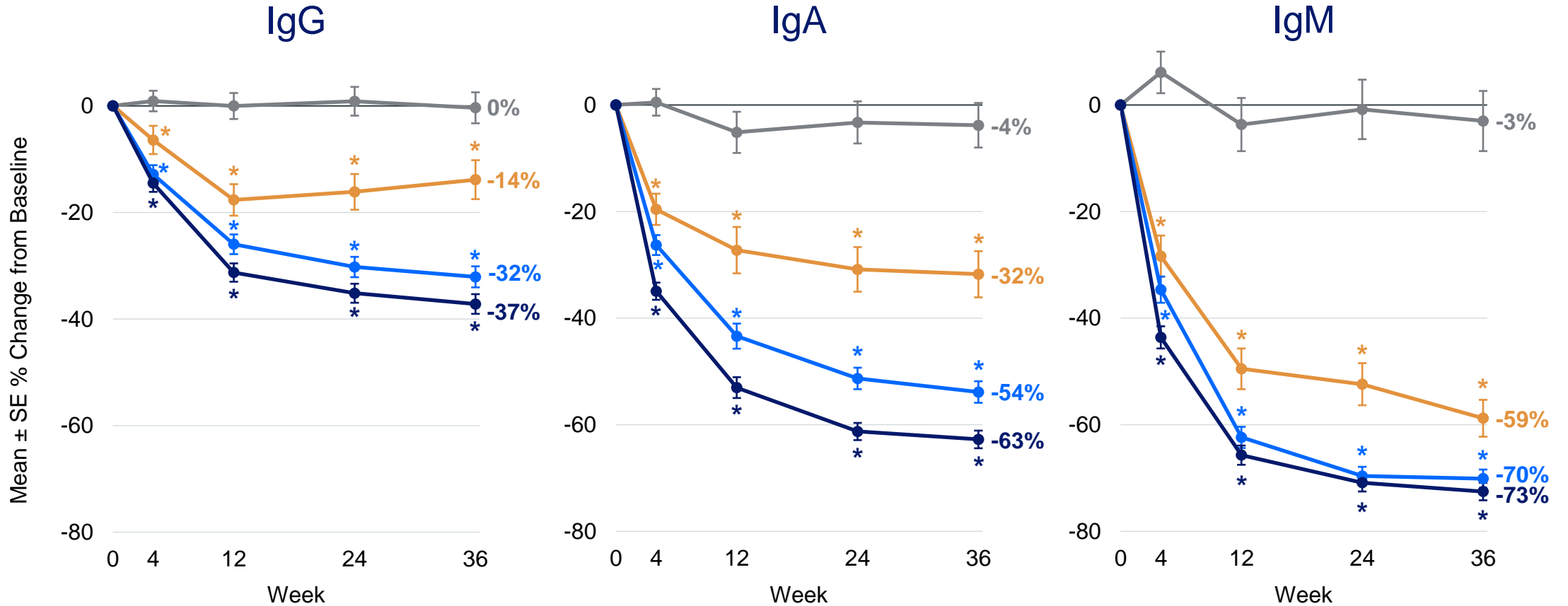
1. PP analysis excludes patients with protocol violations identified at week 36 data-cut prior to unblinding.

eGFR Change with Atacicept 150 mg Through Week 36



ITT analysis; p-values, percentage changes from baseline, and treatment differences were computed using FDA-endorsed mixed-effects modeling.

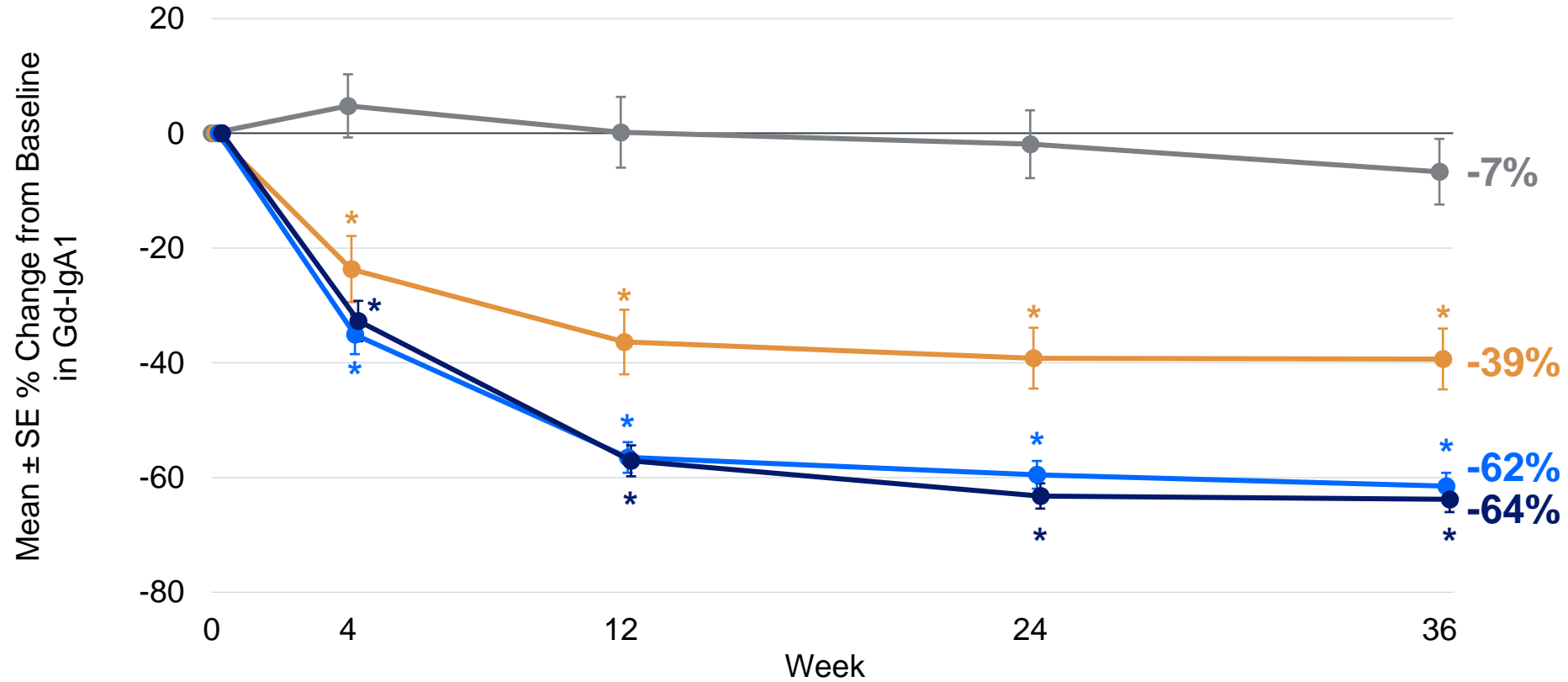
Dose-dependent Reductions Observed in Serum IgG, IgA, and IgM Through Week 36



n=	Week 0	Week 4	Week 12	Week 24	Week 36
Placebo	34	34	34	34	30
Atacicept 25 mg	16	16	16	15	15
Atacicept 75 mg	33	33	33	33	33
Atacicept 150 mg	33	33	32	32	30

ITT analysis; *p<0.05 vs placebo. p-values, percentage changes from baseline, and treatment differences were computed using FDA-endorsed mixed-effects modeling.

Gd-IgA1 % Change Through Week 36



n=	0	4	12	24	36
Placebo	33	33	33	33	29
Atacicept 25 mg	16	16	16	15	15
Atacicept 75 mg	33	33	33	33	33
Atacicept 150 mg	32	32	30	30	30

ITT analysis; *p<0.05 vs placebo. p-values, percentage changes from baseline, and treatment differences were computed using FDA-endorsed mixed-effects modeling.

Treatment-Emergent Adverse Events Through Week 36

	Atacicept 25 mg n=16	Atacicept 75 mg n=33	Atacicept 150 mg n=33	Placebo n=34
Patients, n (%)				
TEAEs	11 (69)	24 (73)	25 (76)	27 (79)
Study drug-related TEAEs ¹	6 (38)	17 (52)	19 (58)	14 (41)
Serious TEAEs	0	1 (3) ²	1 (3) ³	3 (9) ⁴
TEAEs leading to study drug discontinuation	0	0	1 (3) ⁵	1 (3) ⁶
Deaths	0	0	0	0

- No patient had study drug discontinuation or interruption due to low IgG (hypogammaglobulinemia)

1. Majority of study drug-related TEAEs were injection site reactions; one contributed to drug discontinuation.

2. Multiple fractures, resolved, unrelated to study treatment.

3. Gastroenteritis norovirus, resolved, unrelated to study treatment.

4. Anaphylactic reaction resolved (n=1); forearm fracture resolved (n=1); flank pain not resolved and ulnar nerve paralysis resolved with sequelae (n=1); all unrelated to study treatment.

5. Discontinued after 3 injections due to injection site reaction and positive hepatitis B DNA that resolved without treatment 3 weeks later, normal liver function throughout.

6. Discontinued after 31 injections due to worsening flank pain that was not resolved; unrelated to study treatment.

Infections Were Balanced Between Atacicept and Placebo Through Week 36

Patients, n (%)	Atacicept 25 mg n=16	Atacicept 75 mg n=33	Atacicept 150 mg n=33	Placebo n=34
Infections ¹	6 (38)	16 (48)	13 (39)	11 (32)
Occurring in >1 patient				
COVID-19	4 (25)	9 (27)	8 (24)	6 (18)
Upper respiratory tract infection	0	3 (9)	2 (6)	0
Nasopharyngitis	0	1 (3)	3 (9)	1 (3)
Urinary tract infection	2 (13)	1 (3)	1 (3)	0
Viral infection	0	2 (6)	0	2 (6)
Influenza	0	1 (3)	0	1 (3)
Tonsillitis	1 (6)	1 (3)	0	0

1. One severe infection (gastroenteritis norovirus, resolved and not related to study treatment); all others were mild or moderate.

Conclusions



- The Phase 2b trial met its primary endpoint of significant proteinuria reduction at week 24 in IgAN patients at high risk of disease progression
- At week 36, patients receiving atacicept 150 mg had a statistically significant 43% reduction in proteinuria compared to placebo
- Patients receiving atacicept had stable eGFR through week 36, demonstrating a statistically significant and clinically meaningful difference of 5.8 mL/min/1.73 m² compared to placebo at week 36
- Clinical safety profile was similar between atacicept and placebo
- A confirmatory Phase 3 (ORIGIN 3) trial evaluating self-administered atacicept 150 mg SC qwk (1 mL) vs placebo is currently enrolling



**Thank you to all our ORIGIN Phase 2b study volunteers
and the ORIGIN investigators and study staff**

