

Implementing Personalized Endpoints to Assess Treatment Outcomes: A Case of Goal Attainment Scaling (GAS) in Alzheimer’s Disease



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Background

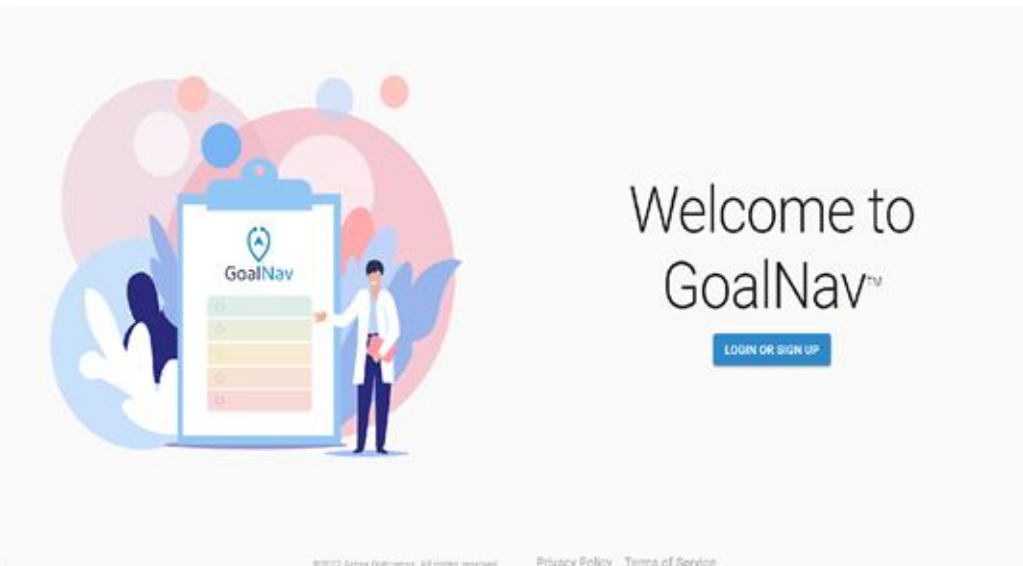
Alzheimer’s disease (AD) exhibits substantial clinical heterogeneity. When testing new therapies with novel MOAs one cannot know in advance which clinically meaningful disease dimension will be most impacted. Traditional measures can miss important changes in daily functioning and may furthermore not align with each patient’s priorities. GAS offers a structured, patient-centered approach to quantifying such individualized change, especially when collected using standardized implementation methods and facilitated by goal inventories. We report the feasibility of inventory-guided GAS to evaluate treatment response in a Phase 2 AD trial with a novel MOA.¹

Methods

GAS was utilized as a secondary endpoint in a global, six-month, randomized, double-blind, placebo-controlled Phase 2 trial of pegipanermin (XPro1595) in 206 patients with early AD and biomarkers of inflammation (Clinical Trial Registry NCT05318976). GAS standardization strategies included:

- trial-specific **goal inventory** encompassing cognition, behavior, daily function, executive function, and physical manifestations.
- structured **patient orientation** & centralized **clinician training** and certification.
- GAS-focused electronic clinical outcome assessment platform (**GoalNav®**).

Methods



Goal Title	Rating
Much more than expected	+2
Somewhat more than expected	+1
The expected level of outcome	0
Somewhat less than expected	-1
Much less than expected	-2

Clinician & Care Partner Rating

+2	+2
+1	+1
0	0
-1	-1
-2	-2

Set & Scale Goals

Rank

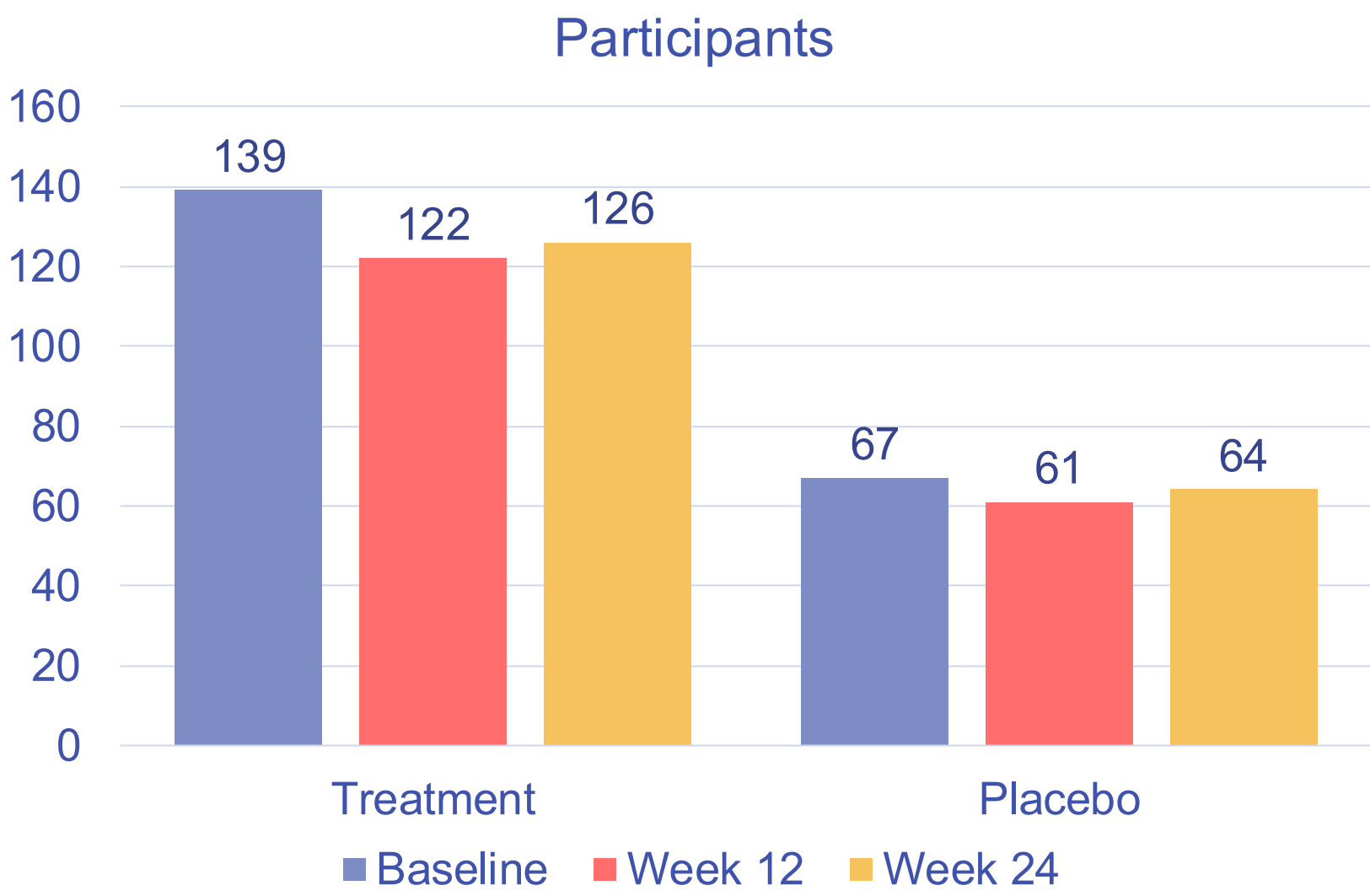
Rate Attainment

The primary endpoint was six-month change in cognition measured by the Early Mild Alzheimer’s Cognitive Composite (EMACC). GAS assessed meaningful within-patient change aligned with individualized treatment goals.

Results

Participants (n = 206) successfully set 431 individualized goals (median =3), demonstrating the practicality of inventory-guided GAS in a global, multicenter trial. The attrition rate remained low at 12.0% (n=25).

Participants



Group	Baseline	Week 12	Week 24
Treatment	139	122	126
Placebo	67	61	64

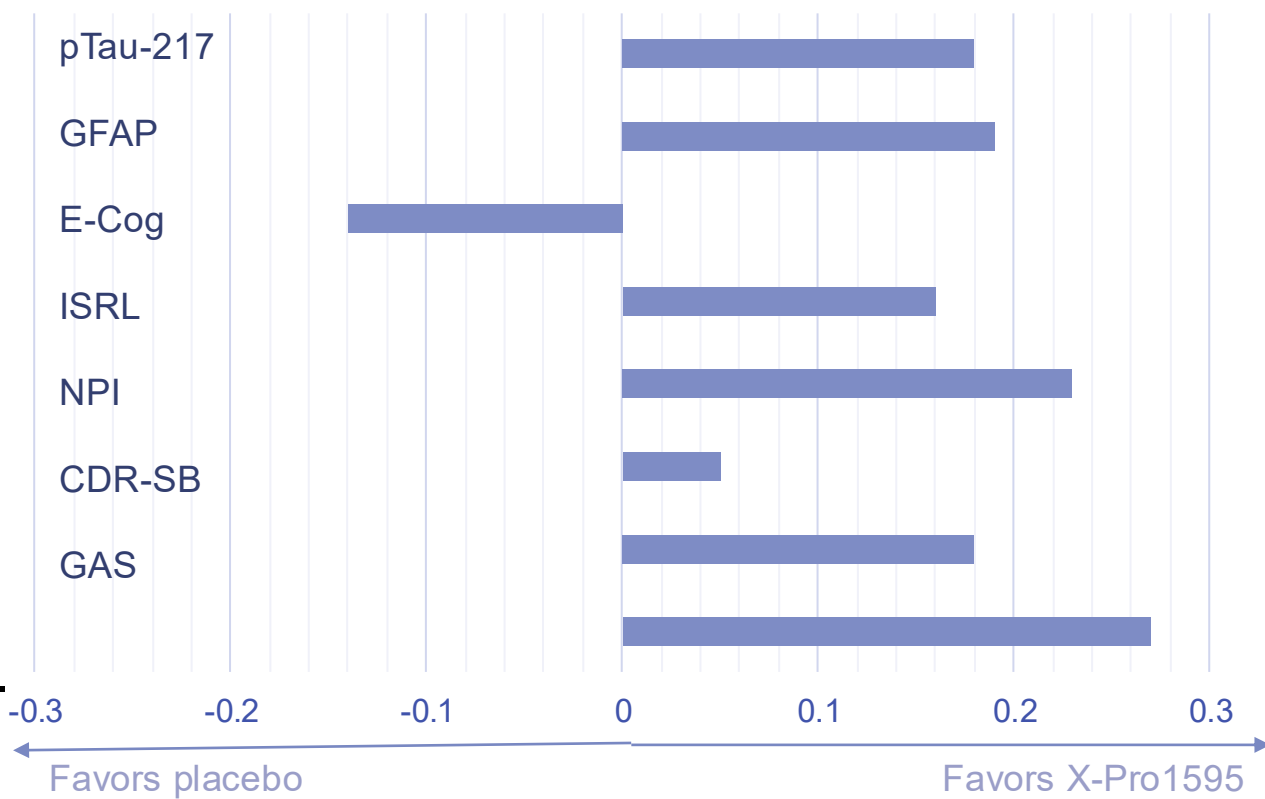
■ Baseline ■ Week 12 ■ Week 24

With 98.55% of participants meeting the protocol requirement of setting 3 or more goals, the implementation of GAS demonstrated high procedural fidelity among 79 GAS interviewer roles across 9 countries.

The primary efficacy endpoint, EMACC, did not demonstrate difference between drug and placebo in the The mITT population (n = 200, (p = 0.67).

Results

Cohen's d



Endpoint	Cohen's d
pTau-217	0.18
GFAP	0.18
E-Cog	-0.12
ISRL	0.15
NPI	0.22
CDR-SB	0.05
GAS	0.27

In a biologically defined subgroup of amyloid-positive participants with high inflammatory burden (ADi; n = 100), there was a consistent trend favoring treatment, observed across multiple endpoints:

EMACC (LSM difference = 0.086 (90% CI: -0.015 to +0.186; p = 0.16, d = 0.27) GAS (LSM difference = 2.00, 90% CI: -3.00 to 7.00, p = 0.42, d = 0.18). Convergent patterns across endpoints suggest a potential treatment-related signal. GAS results were consistent with the broader trend that includes cognition and behavior.

Discussion and Conclusion

GAS captured individualized, patient-relevant changes that aligned with established clinical measures. The observed numerical improvements with XPro1595, particularly in the ADi subgroup, indicate that GAS may be responsive to clinically meaningful change in targeted populations. Overall, these findings reinforce the value of GAS as a complementary endpoint that can enhance the interpretation of treatment effects by incorporating patient-defined goals, particularly in heterogeneous neurodegenerative disease populations. Further studies are warranted to confirm its sensitivity.

References

1 Jaeger, J., Staats, K. A., Barnum, S., Pope, P., Kingery, L., Buitendyk, M., ... & Barnum, C. J. (2026). XPro1595 in early Alzheimer’s disease with inflammation: results from the phase 2 MINDFUL trial. npj Dementia, 2(1), 37. Manufacturer Pegipanermin (XPro1595), INmune Bio, Inc., San Diego, CA, USA



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