

PLASMA PROTEOMIC SIGNATURES OF LECANEMAB RESPONSE AND ARIA RISK IN CHINESE PATIENTS WITH ALZHEIMER'S DISEASE: A PROSPECTIVE REAL-WORLD COHORT STUDY

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Background

Response to lecanemab varies, and markers of amyloid-related imaging abnormalities (ARIA) are incomplete. We examined whether plasma proteins were associated with efficacy, ARIA, and treatment-period biology in Chinese patients with Alzheimer's disease (AD).

Methods

In 96 treated patients, proteomics was profiled at baseline (n = 52) and paired baseline/Week 28 visits (n = 48). Response was benchmarked to a weighted natural-history reference. Analyses used Firth regression, Elastic Net, stability selection, limma, and linear mixed-effects models.

Results

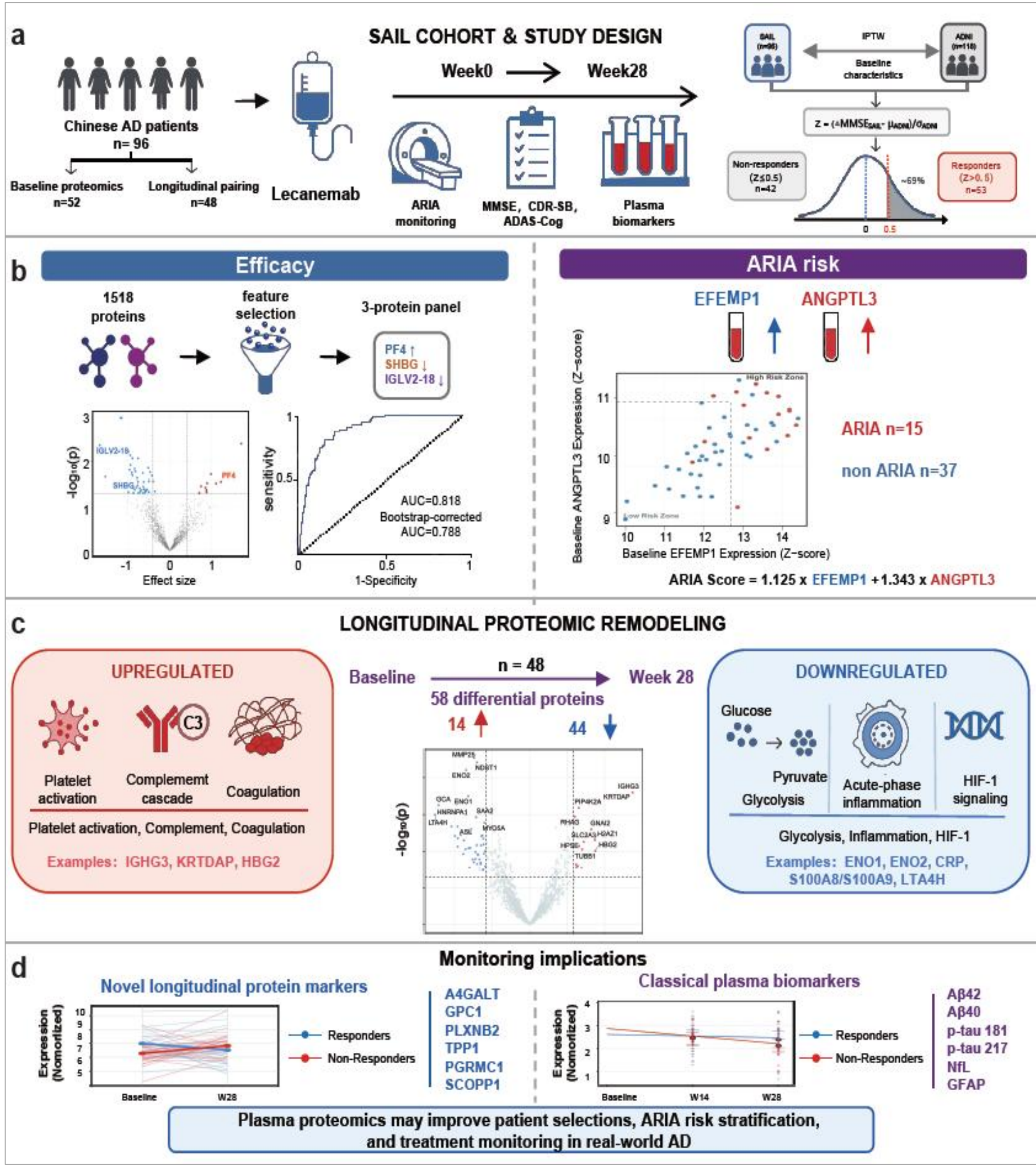
A baseline PF4, SHBG, and IGLV2-18 panel discriminated responders from non-responders (AUC=0.818). EFEMP1–ANGPTL3 marked an exploratory ARIA risk signal correlated with plasma Aβ42 change (r = −0.41; p = 0.017). Longitudinal protein changes suggested candidate monitoring signals, whereas standard biomarkers showed no response-group-specific trajectories.

Table 1. Baseline characteristics of subjects

Variables	Total (n = 96)	Non responder (n = 43)	Responder (n = 53)	p
Age, Mean ± SD	71.1 ± 9.3	73.5 ± 8.4	69.1 ± 9.6	0.019
Sex, n (%)				0.809
Male	59 (61.5)	27 (62.8)	32 (60.4)	
Female	37 (38.5)	16 (37.2)	21 (39.6)	
Education, n (%)				0.804
<6 years	22 (21.9)	8 (18.6)	14 (24.5)	
6-12 years	37 (38.5)	17 (39.5)	20 (37.7)	
>12years	37 (38.5)	18 (41.9)	19 (35.8)	
APOE, n (%)				0.383
E2/E3	8 (8.3)	4 (9.3)	4 (7.5)	
E2/E4	3 (3.1)	3 (7)	0 (0)	
E3/E3	36 (37.5)	16 (37.2)	20 (37.7)	
E3/E4	37 (38.5)	16 (37.2)	21 (39.6)	
E4/E4	12 (12.5)	4 (9.3)	8 (15.1)	

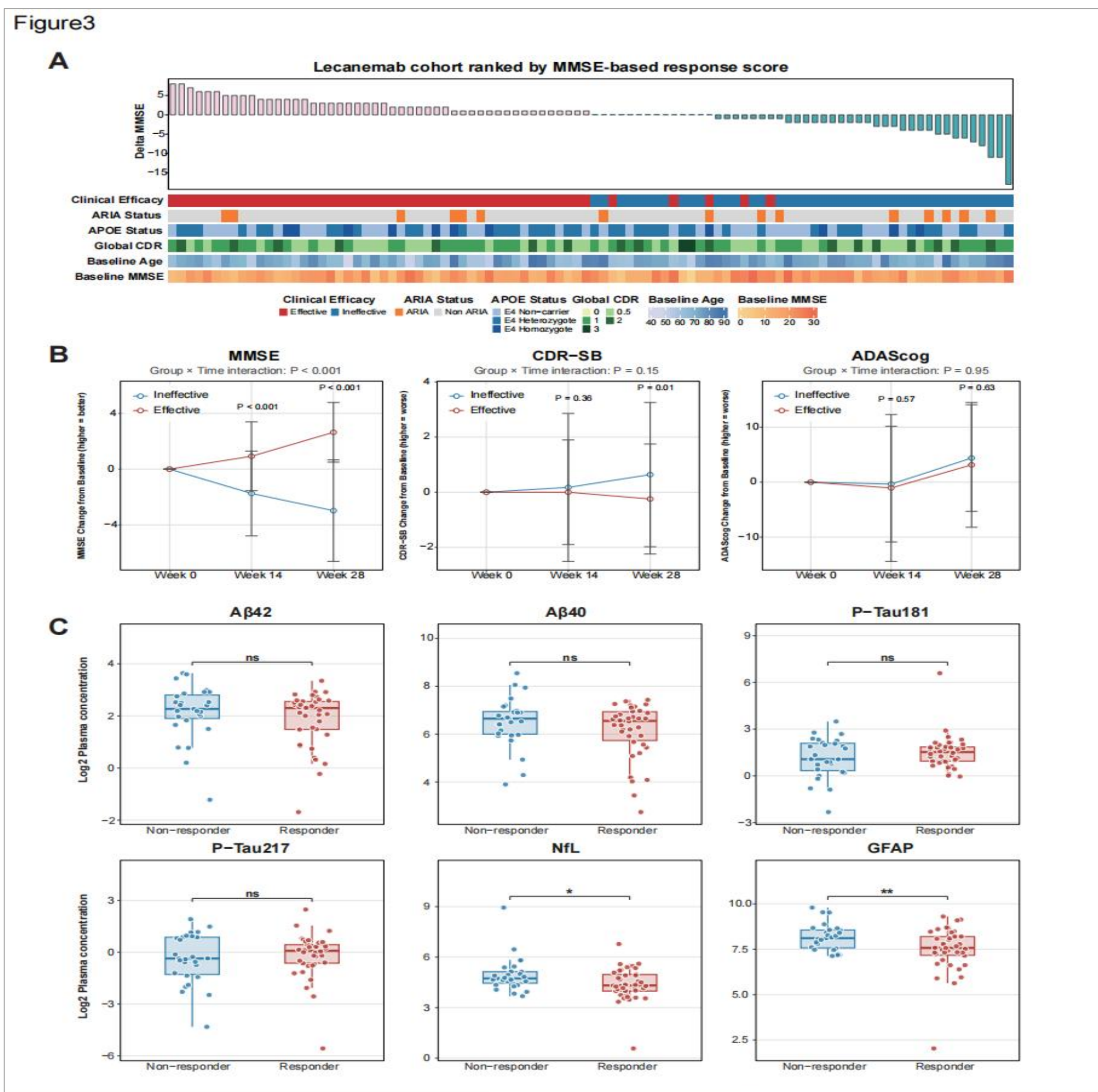
The final analysis cohort included 96 participants. Age was 71.1 ± 9.3 years (mean ± SD), 37 participants (38.5%) were male, and 59 (61.5%) were female. APOE ε4 carriers accounted for 52 participants (54.2%).

Figure 1 Graphical abstract



The SAIL cohort followed Chinese patients with AD treated with lecanemab from baseline to Week 28. Response was benchmarked against an IPTW-weighted ADNI natural-history reference. Paired proteomics showed treatment-period remodeling enriched for platelet/coagulation, myeloid/megakaryocyte, bone marrow, glycolytic, and inflammatory pathways. Aβ, amyloid beta; AD, Alzheimer's disease; ADNI, Alzheimer's Disease Neuroimaging Initiative; ARIA, amyloid-related imaging abnormalities; IPTW, inverse probability of treatment weighting; SAIL, South China Alzheimer's Disease Investigation with Lecanemab A Real-World Study.

Figure 2 Clinical response stratification, cognitive trajectories, and baseline blood biomarkers during lecanemab treatment



(A)MMSE change from baseline to Week 28, ordered by individual change and annotated by response group, ARIA status, APOE ε4 status, CDR, age, and baseline MMSE. Responders were defined using an IPTW-weighted ADNI reference. (B) MMSE, CDR-SB, and ADAS-Cog13 trajectories by response group. (C) Baseline plasma biomarkers by response group after log2 transformation. *p < 0.05; **p < 0.01. Aβ, amyloid beta; ADAS-Cog13, Alzheimer's Disease Assessment Scale-Cognitive Subscale 13; ARIA, amyloid-related imaging abnormalities; CDR-SB, Clinical Dementia Rating Sum of Boxes; MMSE, Mini-Mental State Examination.

Conclusions

Plasma proteomics identified discovery-stage signals for lecanemab response, ARIA susceptibility, and treatment monitoring.