

# A-beta Oligomer Lowering Treatment With PRI-002 Does Not Cause Aria In Ongoing Phase 2 Trial

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Poster Number: Monday-1173

## Abstract

- Background:** Amyloid related imaging abnormalities (ARIA) are common side effects of monoclonal anti-amyloid antibodies and limit the benefit risk ratio substantially. Here we investigate the safety and efficacy of the anti-oligomeric small molecule PRI-002 in early AD. PRI-002 is an orally available, all-D-peptide developed to disassemble neurotoxic and synaptotoxic A $\beta$  oligomers into harmless A $\beta$  monomers.
- Methods:** PRImus-AD (NCT06182085) is an ongoing randomized, double-blind, placebo-controlled phase 2 study of PRI-002 in early symptomatic AD. Primary efficacy outcome is CDR-SB and will be evaluated after 12 months. MRI monitoring to detect ARIA events is performed.
- Results:** 304 patients 70.4 $\pm$ 6.5 years on age, with a MMSE of 25.2 $\pm$ 2.2, 155 with MCI (51.0%) and 149 (49.0%) with mild dementia were randomized. CDR-SB at baseline was 3.3 $\pm$ 1.4 and RBANS-DMI 54.8 $\pm$ 12.7. 208 patients have at least one APOE4 allele (68.4%). After 90 patients, irrespective of the treatment arm, had passed the first 24 weeks of treatment, the incidence of ARIA was evaluated. Within these 90 patients ARIA-E occurred in 2 (2.2%) and ARIA-H were detected in 6 (6.7%) subjects. An unblinded DSMB reviewed the ARIA incidence in all three study arms and recommended to stop ARIA monitoring until the end of study.
- Conclusions:** In an ongoing phase 2 trial with oral PRI-002 that was designed to disassemble synaptotoxic A $\beta$  aggregates into harmless A $\beta$  monomers, the study drug is well tolerated and the safety profile favorable. Efficacy data are expected in Q4 2026.

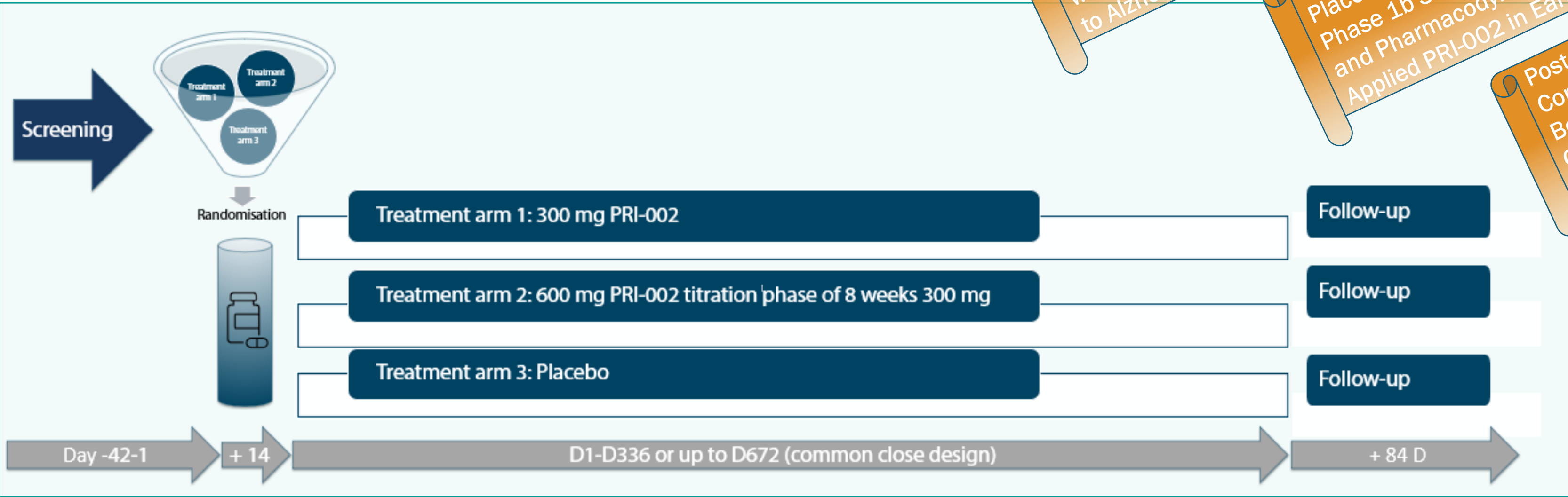
## PRImus-AD Key Points

- Phase 2b study
- Acronym: PRImus-AD
- EU Clinical Trial Number: 2022-503148-41
- Sponsor: PRInnovation, Germany
- Funded by SPRIND, Germany



- Targeting MCI and mild dementia due to AD**
- 38 active study sites in 6 countries:** The Netherlands, Germany, Poland, Czech Republic, Spain and Italy
- Oral treatment**
- 3 treatment arms:** placebo, 300 mg PRI-002, 600 mg PRI-002
- Common close design:** 48 to 96 weeks treatment duration
- Primary efficacy endpoint:** CDR-SB
- 540 patients screened, 304 enrolled in 11 months**
- FPFV February 2024**
- LPLV June 2026**
- Results expected in October 2026**

## Common Close Study Design



Poster Number Wednesday-0048: Design of a Phase 2 Study (PRImus-AD) Treating Patients with MCI or Mild Dementia Due to Alzheimer's Disease

Poster Number Tuesday-0023: A Placebo-Controlled, Double-Blind, Phase 1b Study to Evaluate Safety and Pharmacodynamics of Orally Applied PRI-002 in Early AD

Poster: The A-Beta Targeting Compound PRI-002 Reduces A-Beta Oligomers and Prevents Cognitive Decline in Various AD Animal Models

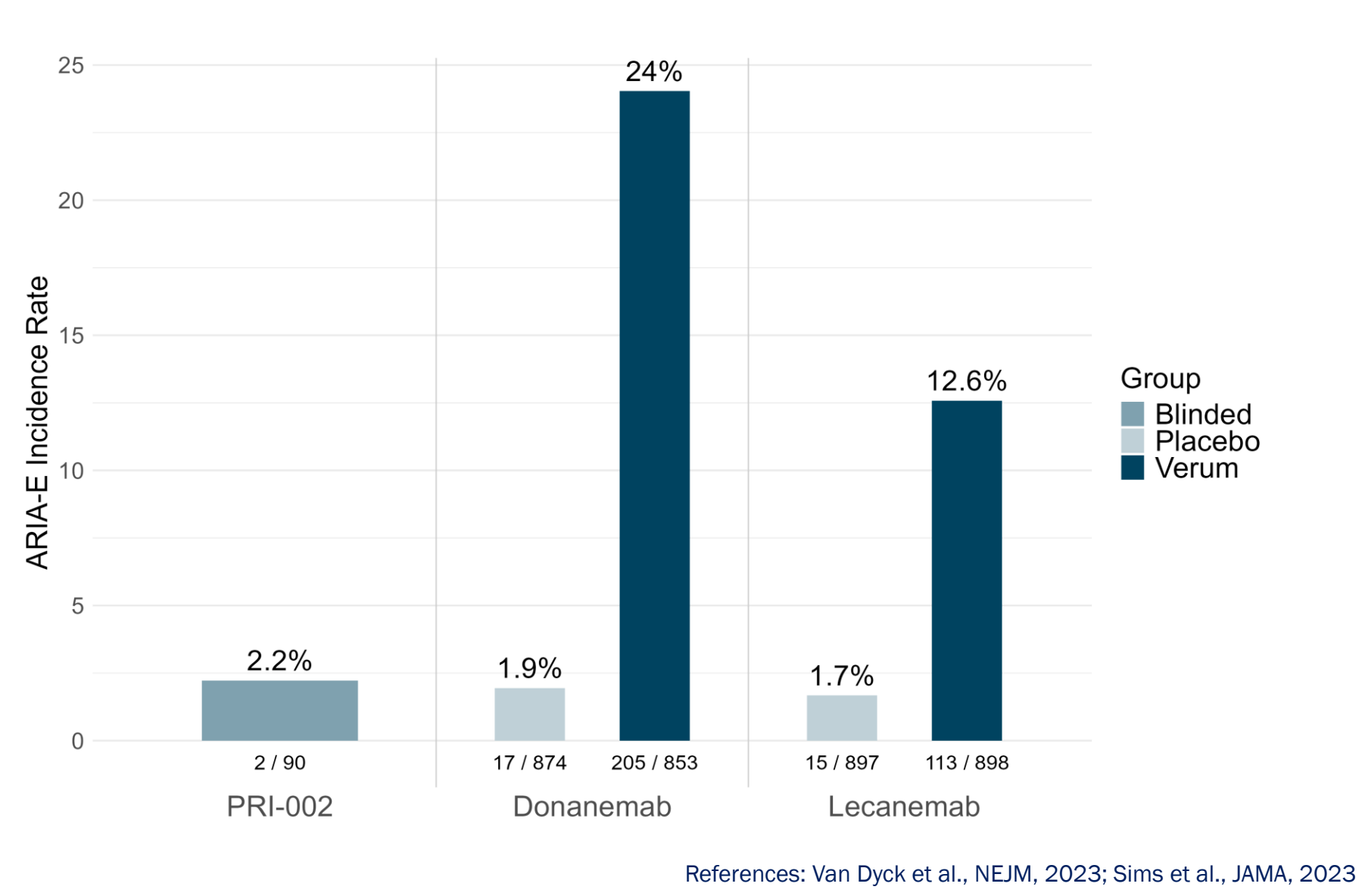
## Baseline Demographics I

|                      |               |              |
|----------------------|---------------|--------------|
| Disease status       | MCI           | 154 (50.8 %) |
|                      | mild dementia | 149 (49.2 %) |
| sex                  | female        | 158 (52.1 %) |
|                      | male          | 145 (47.9 %) |
| ApoE e4              | no            | 96 (31.7 %)  |
|                      | yes           | 207 (68.3 %) |
| Positive PET         | no            | 225 (74.3 %) |
|                      | yes           | 78 (25.7 %)  |
| Age at screening (y) | n             | 304          |
|                      | mean (SD)     | 70.4 (6.5)   |
|                      | min, max      | 55, 80       |

## Baseline Demographics II

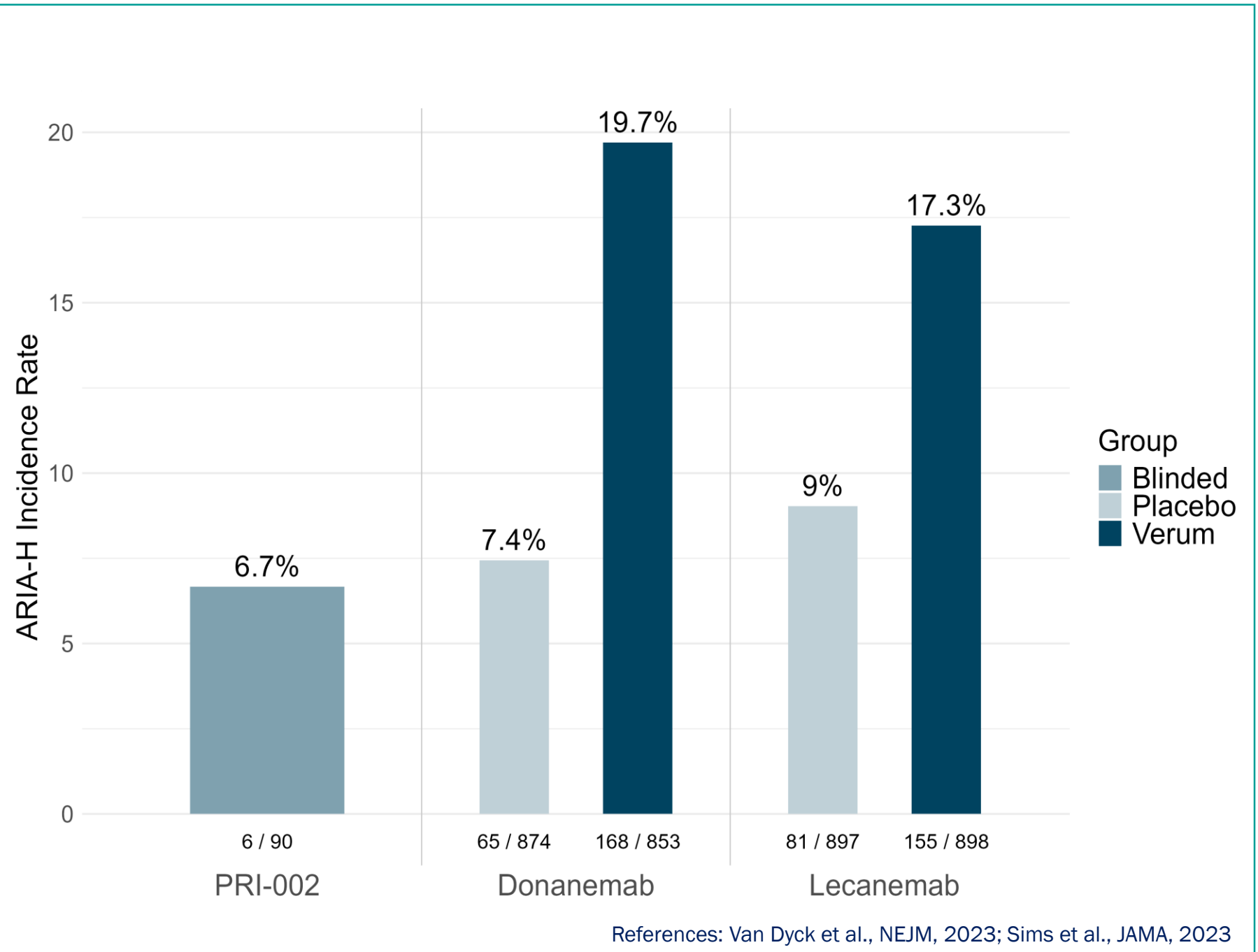
|        |                   |              |
|--------|-------------------|--------------|
| MMSE   | <22               | 40 (13.2 %)  |
|        | 22-26 (inclusive) | 182 (60.1 %) |
|        | >26               | 81 (26.7 %)  |
| MMSE   | Mean (SD)         | 24.5 (2.9)   |
|        | Median            | 24.0         |
|        | Min, max          | 16, 30       |
| CDR-G  | Mean (SD)         | 0.61 (0.22)  |
|        | Median            | 0.5          |
|        | Min, max          | 0.0, 2.0     |
| CDR-SB | Mean (SD)         | 3.38 (1.51)  |
|        | Median            | 3.00         |
|        | Min, max          | 0.5, 10.0    |

## ARIA-E Monitoring



References: Van Dyck et al., NEJM, 2023; Sims et al., JAMA, 2023

## ARIA-H Monitoring



References: Van Dyck et al., NEJM, 2023; Sims et al., JAMA, 2023

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Special thanks go to the patients and their families for their willingness to participate. We would like to extend our heartfelt thanks to all participating study centers.

### Selected Publications:

- Kutzsche J, Jürgens D, Willuweit A, Adermann K, Fuchs C, Simons S, Windisch M, Hümpel M, Rossberg W, Wolzt M and Willbold D. Safety and pharmacokinetics of the orally available antiprionic compound PRI-002: A single and multiple ascending dose phase I study. *Alzheimers Dement* (N Y), 2020. 6(1): p. e12001.
- Kutzsche J, Cosma N, Kauselmann G, Fenski F, Bieniek C, Bujnicki T, Pils M, Bannach O, Willbold D, Peters O. Oral PRI-002 treatment in patients with MCI or mild AD: a randomized, double-blind phase 1b trial. *Nat Commun*. 2025 May 6;16(1):4180. doi: 10.1038/s41467-025-59295-z.