# ARIA ESSENTIALS

## Interdisciplinary Perspectives

## Elevating Care with Evidence-Based Imaging and Collaboration

This activity is supported by an educational grant from Lilly.

# FACULTY

**Alireza Atri, MD, PhD**

Chief Medical Officer,
Banner Research
Director, Banner Sun Health
Research Institute
Sun City, AZ, USA

**Anton P. Porsteinsson, MD**

William B. and Sheila Konar
Professor of Psychiatry, Neurology,
Neuroscience, and Medicine
Director, Alzheimer's Disease Care,
Research and Education Program
(AD-CARE)
University of Rochester School of
Medicine and Dentistry
Rochester, NY, USA

**Petrice M. Cogswell MD, PhD**

Chair, Neuroradiology Research
Mayo Clinic
Rochester, MN, USA

**Maria Vittoria Spampinato, MD**

Assistant Professor, Radiology
Medical University of South Carolina
Charleston, SC, USA

# Activity Overview

## Target Audience

This activity is designed for neuroradiologists and radiologists as well as other members of the interdisciplinary team who are involved in the care of patients with Alzheimer's disease globally.

## Educational Objectives

After completing this activity, learners will be better able to:

- **Identify** pathophysiologic features that put patients taking anti-amyloid monoclonal antibodies at increased risk for amyloid-related imaging abnormalities (ARIA)
- **Apply** standardized magnetic resonance imaging (MRI) protocols and grading scales to optimally monitor for, detect, and assess the severity of ARIA in patients receiving anti-amyloid monoclonal antibodies
- **Integrate** best practices for interdisciplinary communication to enhance coordination among radiologists, neurologists, and geriatricians in the management of ARIA

## Agenda

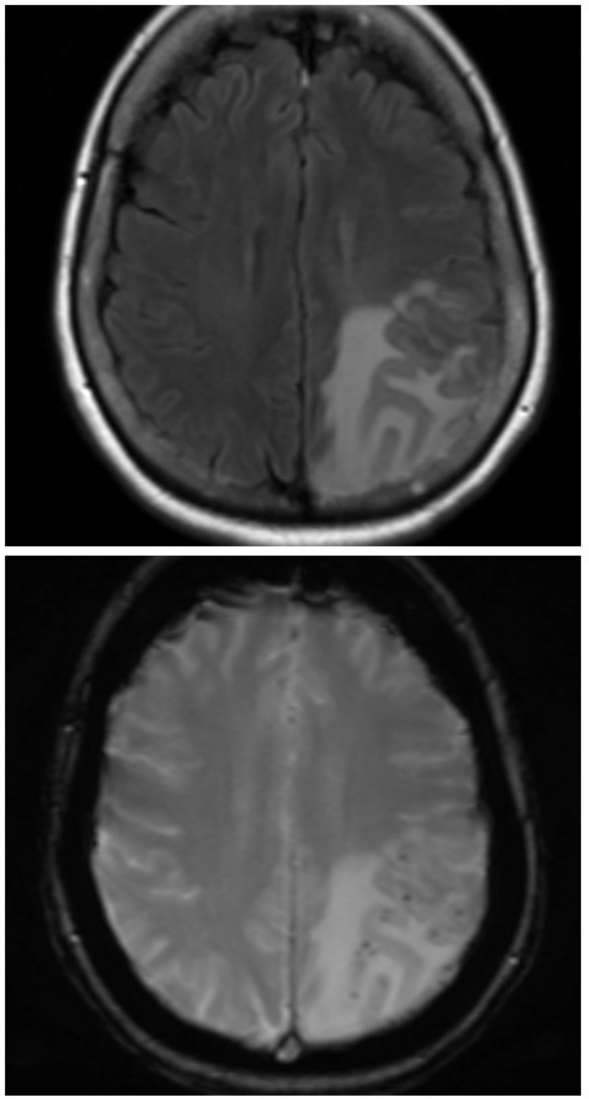
- Pathophysiology and risk factors of ARIA
- Standardized MRI protocols and grading scales for ARIA detection
- Interdisciplinary communication for effective ARIA management

Part 1:

# Pathophysiology of and Risk Factors for ARIA

# Amyloid-Related Imaging Abnormalities (ARIA)

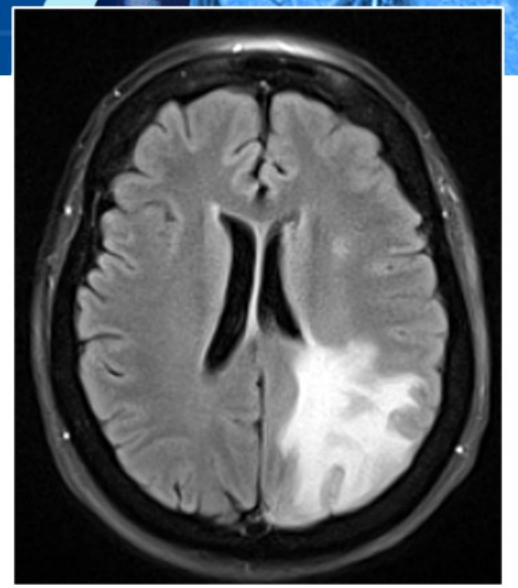
- Edema (ARIA-E) and hemorrhage (ARIA-H) that occur in the setting of immunotherapies targeting beta-amyloid
- Common mechanism
  - Leak of exudate from vessel into extracellular or subarachnoid space
- Etiology
  - Vessel wall infiltration by amyloid, loss of vascular integrity when amyloid is removed from the vessels as well as the parenchyma

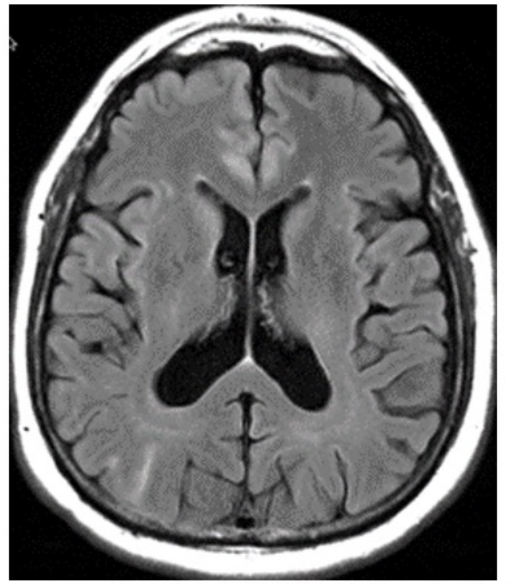


ARIA-E, amyloid-related imaging abnormalities-edema; ARIA-H, amyloid-related imaging abnormalities-hemorrhage.
Haller S et al. *Radiology*. 2024;310(2):e233381.

# ARIA-E on Imaging

- E = edema, effusion/exudate
- Imaging sequence: T2 FLAIR
- Imaging appearance
  - Parenchymal: vasogenic edema
    - T2 hyperintense signal in white matter ± gray matter
    - May have associated gyral swelling
  - Leptomeninges: sulcal effusion or exudate
- No restricted diffusion
- Occipital > parietal > frontal > cerebellum, brainstem
- Transient



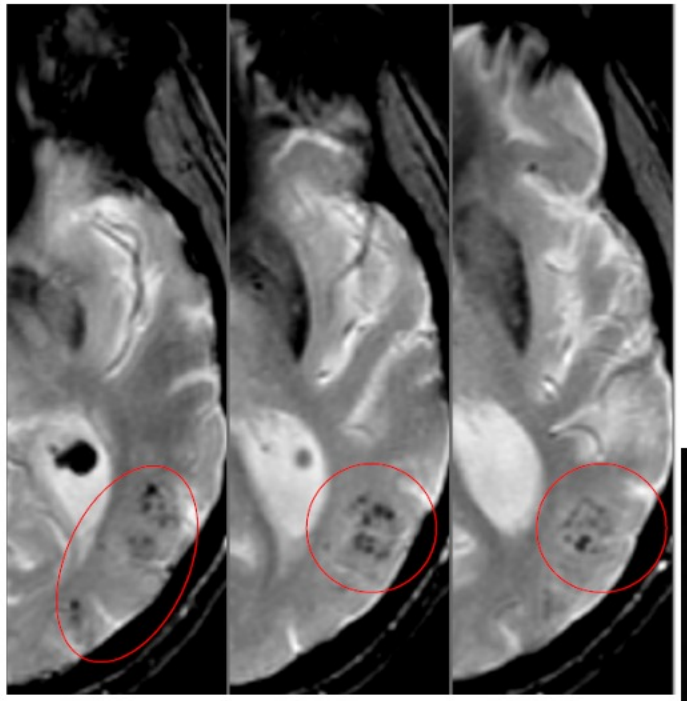


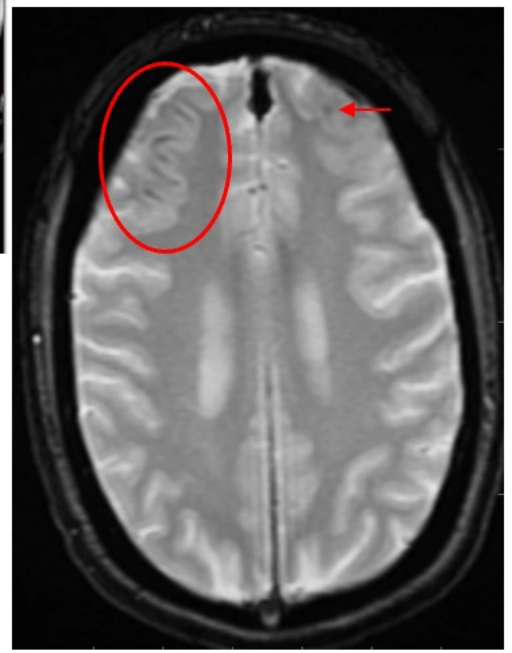
ARIA-E, amyloid-related imaging abnormalities-edema; FLAIR, fluid-attenuated-inversion recovery.

Cogswell PM et al. *AJNR Am J Neuroradiol*. 2022;43(9):E19-E35. Published 2025 Jan 8.

# ARIA-H on Imaging

- Imaging sequence: GRE ± SWI
- Imaging appearance
  - Parenchyma: microhemorrhage
    - Focal, hypointensity that does not track with a vessel
    - In the brain parenchyma
  - Leptomeninges: superficial siderosis
    - Curvilinear hypointensity
    - Along the brain surface





ARIA-H, amyloid-related imaging abnormalities-hemorrhage; GRE, gradient echo; SWI, susceptibility-weighted imaging.
Cogswell PM et al. *AJNR Am J Neuroradiol*. 2022;43(9):E19-E35.

# ARIA-E and ARIA-H

- ARIA-E occurs in 15% to 40% of patients with AD receiving amyloid-targeting therapies
- Most cases of ARIA-E are mild and reversible
  - Only a minority of cases (< 7%) are severe
- ARIA-H does not resolve with drug discontinuation and persists after identification on MRI
- ARIA typically occurs early during treatment
  - Resuming amyloid-targeting therapies at a lower dose is associated with ~15% development of ARIA-E relapse

AD, Alzheimer disease; ARIA-E, amyloid-related imaging abnormalities-edema; ARIA-H, amyloid-related imaging abnormalities-hemorrhage; MRI, magnetic resonance imaging.
Haller S et al. *Radiology*. 2024;310(2):e233381. Doran SJ et al. *Front Neurosci*. 2024;18:1326784.

# ARIA Symptoms

## Common

- Headache
- Confusion
- Visual changes
- Dizziness
- Nausea
- Gait difficulty

## Severe

- Seizures
- Status epilepticus
- Focal neurologic deficits
- Malignant HTN
- Intracerebral hemorrhages > 1 cm (some fatal)

ARIA, amyloid-related imaging abnormalities; HTN, hypertension.
Vukmir RB. *Ann Clin Transl Neurol*. 2024;11(7):1669-1680.

# ARIA Risk and Cerebrovascular Conditions

- Risk factors for ARIA-E and ARIA-H
  - Positive APOE4 carrier status
  - Prior multiple cerebral microhemorrhages
- Risk factors for ARIA-H
  - Age
  - Antithrombotic use
  - History of prior strokes

Apoε4, apolipoprotein E ε4; ARIA-E, amyloid-related imaging abnormalities-edema; ARIA-H, amyloid-related imaging abnormalities-hemorrhage.
Doran SJ et al. *Front Neurosci.* 2024;18:1326784.

# Differentiating ARIA

- Other processes have imaging appearances similar to ARIA
  - CAA-RI: spontaneous sulcal effusions/edema and microhemorrhages/siderosis
  - PRES: edema and hemorrhages, including microbleeds, subarachnoid hemorrhage, and intraparenchymal hematoma
- Differences between ARIA and other processes
  - Use/non-use of monoclonal antibodies that remove amyloid plaque
  - Clinical presentation and components of imaging findings may differ

ARIA, amyloid-related imaging abnormalities; CAA-RI, cerebral amyloid angiopathy-related inflammation; PRES, posterior reversible encephalopathy syndrome.

Haller S et al. *Radiology*. 2024;310(2):e233381. Cogswell PM et al. *AJNR Am J Neuroradiol*. 2022;43(9):E19-E35. Published 2025 Jan 8.

Part 2:

# MRI Protocols and Grading Scales for ARIA Detection

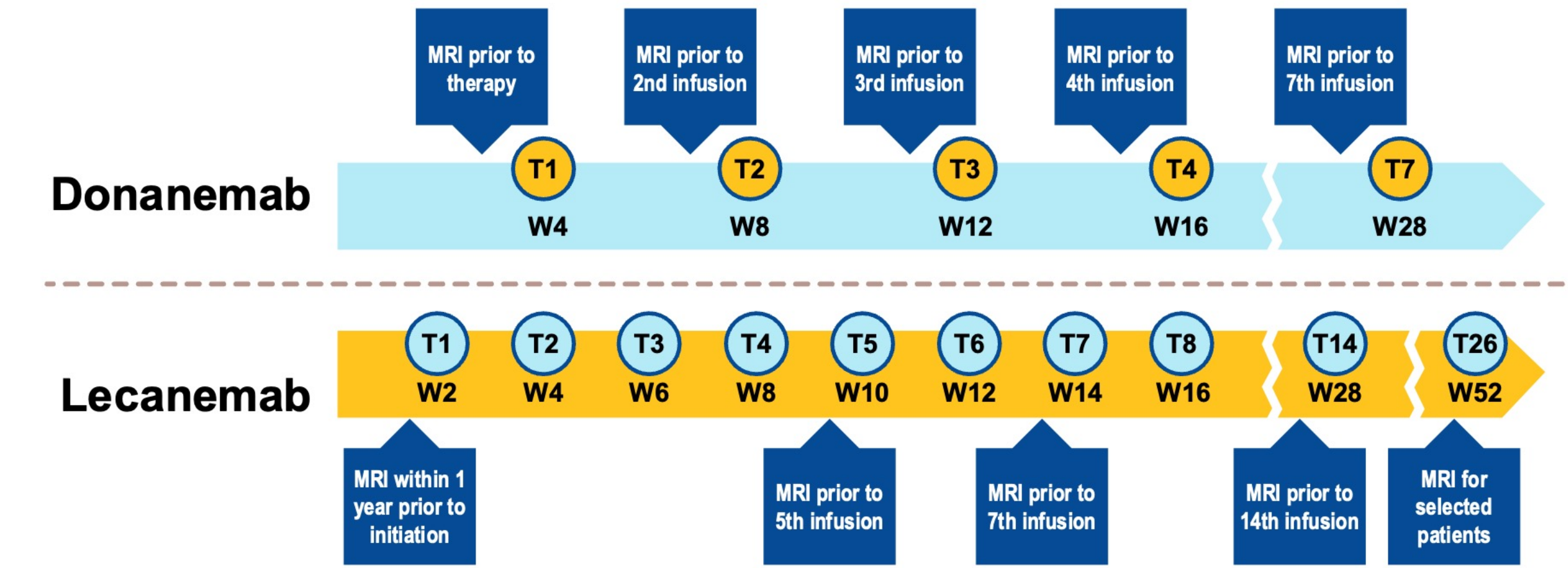
# Appropriate Use Recommendations

- Consider disease, clinical, and biomarker characteristics when selecting candidates for treatment
- Importance of APOE4 genotyping for predicting risk of amyloid-related imaging abnormalities
- Need for pretreatment MRI to exclude patients with white matter disease or evidence of cerebral amyloid angiopathy
- Advisement against treatment for patients taking anticoagulants
- Contraindication of thrombolytics for patients on active anti-amyloid immunotherapy therapy

MRI, magnetic resonance imaging.

17th annual Clinical Trials on Alzheimer's Disease (CTAD) conference. Donanemab: appropriate use recommendations. *Pract Neurol*. https://practicalneurology.com/news/donanemab-appropriate-use-recommendations-presented-at-ctad-2024sease (CTAD) Conference. Donanemab: Appropriate Use Recommendations. Practical Neurology. https://practicalneurology.com/news/donanemab-appropriate-use-recommendations-presented-at-ctad-2024.

# Baseline and Follow-Up MRI Scans




***Perform MRI if any symptoms suggestive of ARIA occur***

ARIA, amyloid-related imaging abnormalities; MRI, magnetic resonance imaging.

Donanemab. Prescribing information. Eli Lilly and Company; 2024. Lecanemab. Prescribing information. Eisai Inc.; 2025. Cummings J et al. *J Prev Alzheimers Dis*. 2023;10(3):362-377.

# Standard Reporting for ARIA and Emerging AD Therapeutics

| TECHNIQUE: Blood-Sensitive sequence: [<SWI>][<GRE/T2*>] Field strength: [<3 T>][<1.5 T>] | |
|---|---|
| **Category** | **Details** |
| **Findings** | |
| Total microhemorrhages | Total number<br>Describe locations in general, deep vs lobar |
| Superficial siderosis | None / < 1 focal area / < 2 focal areas / > 2 focal areas<br>Describe locations |
| Extent of white matter hyperintensities | Mild, moderate, severe |
| Infarcts | Describe cortical and subcortical infarcts if present |
| Other findings | General description of other acute or chronic findings |
| **Impression** | |
| Total microhemorrhages | 0-4 / 5-9 / ≥ 10 |
| Superficial siderosis | Not detected vs present |
| Other findings | General description of other findings |

AD, Alzheimer disease; ARIA, amyloid-related imaging abnormalities; GRE, gradient echo; SWI, susceptibility-weighted imaging.

**Report templates available at: https://www.alznetproviders.org/Clinical-Care-Resources/Imaging-Resources**

# Assessment of ARIA + Therapy Monitoring

| ARIA Type | Radiographic Severity | | |
|---|---|---|---|
| | Mild | Moderate | Severe |
| ARIA-E | FLAIR hyperintensity confined to sulcus and/or cortex/subcortical white matter in 1 location < 5 cm | FLAIR hyperintensity 5-10 cm, or more than 1 site of involvement, each measuring < 10 cm | FLAIR hyperintensity measuring > 10 cm, often with significant subcortical white matter and/or sulcal involvement; ≥ 1 separate sites of involvement |
| ARIA-H microhemorrhage | ≤ 4 new incident microhemorrhages | 5-9 new incident microhemorrhages | ≥ 10 new incident microhemorrhages |
| ARIA-H superficial siderosis | 1 focal area of superficial siderosis | 2 focal areas of superficial siderosis | > 2 focal areas of superficial siderosis |

Adapted from Aducanumab label. Adapted from Lecanemab. Prescribing information. Eisai Inc.; 2025.
ARIA-E, amyloid-related imaging abnormalities-edema; ARIA-H, amyloid-related imaging abnormalities-hemorrhage; FDA, U.S. Food and Drug Administration; FLAIR, fluid-attenuated-inversion recovery.

# Patient Management Based on ARIA Severity and Symptoms

| Clinical Symptom Severity | ARIA-E Severity | | | ARIA-H Severity | | |
|---|---|---|---|---|---|---|
| | Mild | Moderate | Severe | Mild | Moderate | Severe |
| Asymptomatic | C | S | D | C | S | D |
| Mild | S | S | D | S | S | D |
| Moderate | S | S | D | S | S | D |
| Severe | D | D | D | D | D | D |

C = continue dosing

S = suspend dosing until resolution of ARIA-E and stabilization of ARIA-H, resumption of dosing based on patient-specific risk-benefit assessment

D = discontinue dosing due to serious symptoms

Adapted from Aducanumab label. Adapted from Lecanemab. Prescribing information. Eisai Inc.; 2025.
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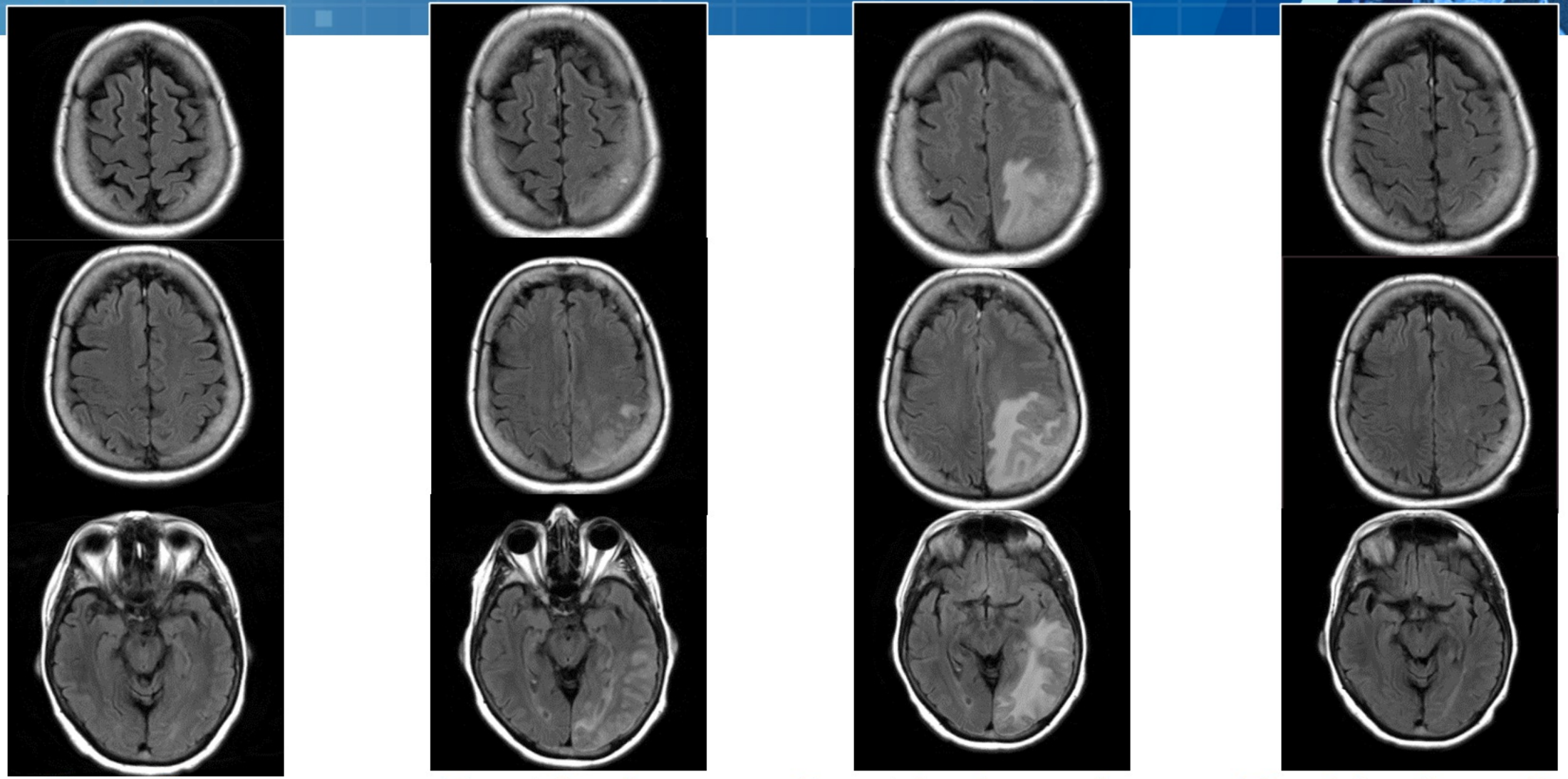
Cogswell PM et al. *AJNR Am J Neuroradiol*. 2022;43(9):E19-E35. Published 2025 Jan 8.

# Severe ARIA-E
# > 10 cm



Baseline | Postdosing | Postdosing +1 mo | Postdosing +2 mo

ARIA-E, amyloid-related imaging abnormalities-edema.

# Severe ARIA-H
# > 10 mH


ARIA-E, amyloid-related imaging abnormalities-hemorrhage.

Part 3:

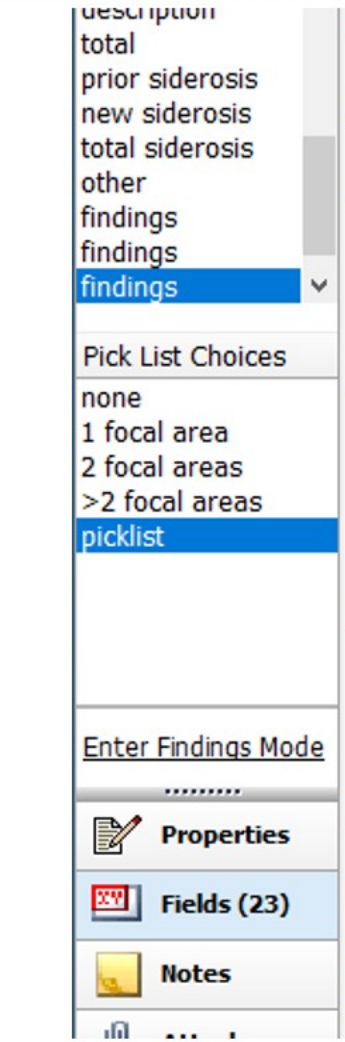
# Interdisciplinary Communication for Effective ARIA Management

# Interdisciplinary Discussions

- Establish clear communication channels
- Align imaging review with clinical context
- Foster timely decision-making on treatment adjustments
- Streamline interdisciplinary collaboration
- Standardize follow-up and documentation

Cogswell PM et al. *AJNR Am J Neuroradiol*. 2022;43(9):E19-E35. Published 2025 Jan 8.

# Standardized Terminology and Structured Reporting Templates for ARIA




**FINDINGS**:

ASSESSMENT FOR ARIA:

ARIA-E
- Prior FLAIR hyperintensities concerning for ARIA-E: [describe location(s) and size][describe change]
- New/incident FLAIR hyperintensities concerning for ARIA-E: [describe location(s) and size]
- Total current regions of FLAIR hyperintensities concerning for ARIA-E: [picklist]

ARIA-H, Microhemorrhages
- Microhemorrhages at pre-treatment baseline: [number of microhemorrhages at pre-treatment baseline][describe locations]
- Prior treatment emergent microhemorrhages: [number of microhemorrhages present on prior monitoring exam][describe locations]
- New microhemorrhages: [number of new microhemorrhages since prior exam][describe locations]
- Total treatment emergent microhemorrhages = prior treatment emergent + new microhemorrhages: [picklist]

ARIA-H, superficial siderosis
- Prior treatment emergent siderosis: [number of prior focal areas of superficial siderosis]
- New siderosis: [number of new focal area of superficial siderosis]
- Total treatment emergent focal areas of superficial siderosis: [picklist]

ADDITIONAL FINDINGS: [...]

**IMPRESSION**:
1. Findings of [picklist] ARIA-E.
Findings of [picklist] ARIA-H related microhemorrhages.
Findings of [picklist] ARIA-H related siderosis.

**Report templates available at: https://www.alznetproviders.org/Clinical-Care-Resources/Imaging-Resources**

ARIA-E, amyloid-related imaging abnormalities-edema; ARIA-H, amyloid-related imaging abnormalities-hemorrhage; FLAIR, fluid-attenuated-inversion recovery.

# THANK YOU!

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This activity is supported by an educational grant from Eli Lily and Company.