Clinical Toolkit

VISIT THE AMERICAN SOCIETY OF NEURORADIOLOGY (ASNR) WEBSITE FOR

RECOMMENDED REPORTING TEMPLATES FOR ARIA

ASNR
American Society of Neuroradiology

TEMPLATE 2: MRI BRAIN ARIA

Description: Follow up imaging for patients undergoing treatment with an amyloid-lowering antibody therapy

EXAMINATION: Magnetic resonance imaging (MRI) of the brain without contrast

HISTORY: [<If information is available, include agent, doses received, date of last dose, and symptoms if present>].

TECHNIQUE: Multiplanar multi-weighted MRI of the brain and brainstem was performed without intravenous contrast using a protocol specific to assess patients with memory complaints undergoing disease modifying therapies. The protocol specifically includes T2-FLAIR to assess for potential amyloid related imaging abnormalities with edema (ARIA-E), and susceptibility sensitive sequences for detection of microhemorrhages and superficial siderosis (ARIA-H).

23. Alzheimer disease and ARIA Study Group Resources. American Society of Neuroradiology. Accessed November 14, 2023. https://www.asnr.org/education-resources/alzheimers-webinar-series/.

BASELINE MRI FOR ATT

Patients should have a recent pretreatment MRI.
The following may be contraindications to therapy:

- ❑ **Acute/subacute hemorrhage**
- ❑ **≥4 microhemorrhages**
- ❑ **≥1 area of superficial siderosis**
- ❑ **Cortical or lacunar infarct >1.5 cm**
- ❑ **Extensive diffuse white matter disease**

KEY ELEMENTS TO REPORT

- The number and location of existing **microhemorrhages**
- **Superficial siderosis**: present or absent
- Any significant imaging findings, such as infarcts

20. Cummings et al. Aducanumab: appropriate use recommendations update. *J Prev Alzheimers Dis*. 2022;9(2):221-230.

MRI MONITORING SCHEDULE

LECANEMAB[5]

Recent baseline and prior to the **5th, 7th, 14th (and 26th per AUR)** infusions

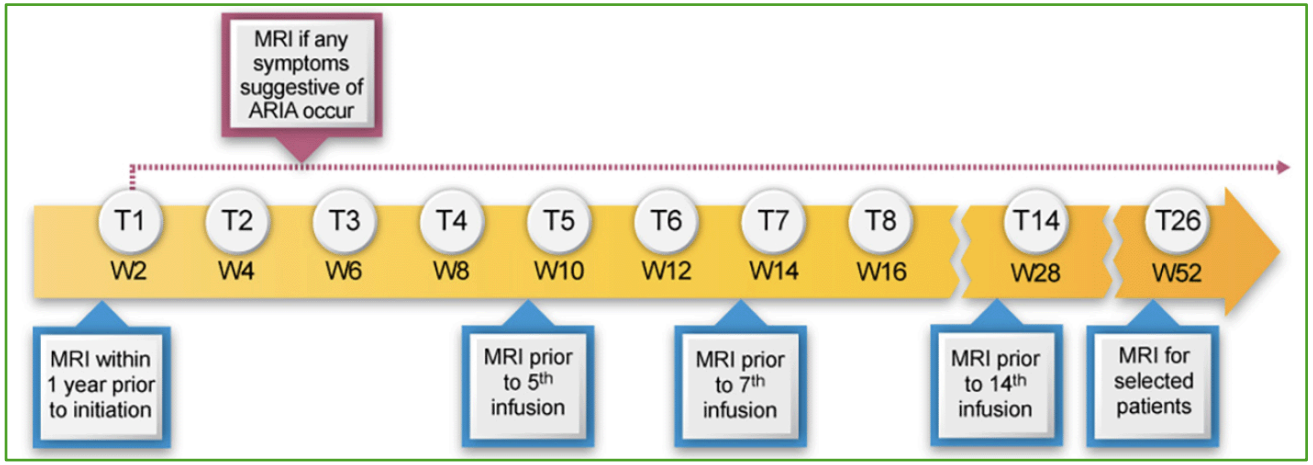
ADUCANUMAB[4]

Prior to the **5th, 7th, 9th, and 12th** infusions

Nonscheduled for ARIA symptoms + ARIA follow-up

EXAMPLE SCHEDULE: LECANEMAB

(Varies by agent)



4. ADUHELM (aducanumab-avwa). Prescribing information. Biogen Inc.; 2023. • 5. LEQEMBI (lecanemab-irmb). Prescribing information. Eisai Inc.; 2023

SUMMARY OF RECOMMENDED MRI PROTOCOLS

Optimal strategies to ensure consistency and accuracy of imaging[15,20]

SLICE THICKNESS	**5 mm**	Consistency is key
ARIA-E DETECTION	**T2-FLAIR**	Can be missed by conventional T2 due to CSF hyperintensity
ARIA-H DETECTION	**2D T2 GRE or SWI**	SWI more sensitive
ADDITIONAL IMAGING	**DWI**	To be discussed
NOTE: A general brain or stroke protocol MRI will have all the appropriate sequences		

GRE: gradient-recalled echo; **SWI:** susceptibility-weighted imaging; **T2-FLAIR**: T2-weighted-fluid-attenuated inversion recovery.

16. Barakos J et al. *J Prev Alzheimers Dis.* 2022;9(2):211-220. • 21. Cogswell PM et al. *AJNR Am J Neuroradiol.* 2022;43(9):E19-E35.

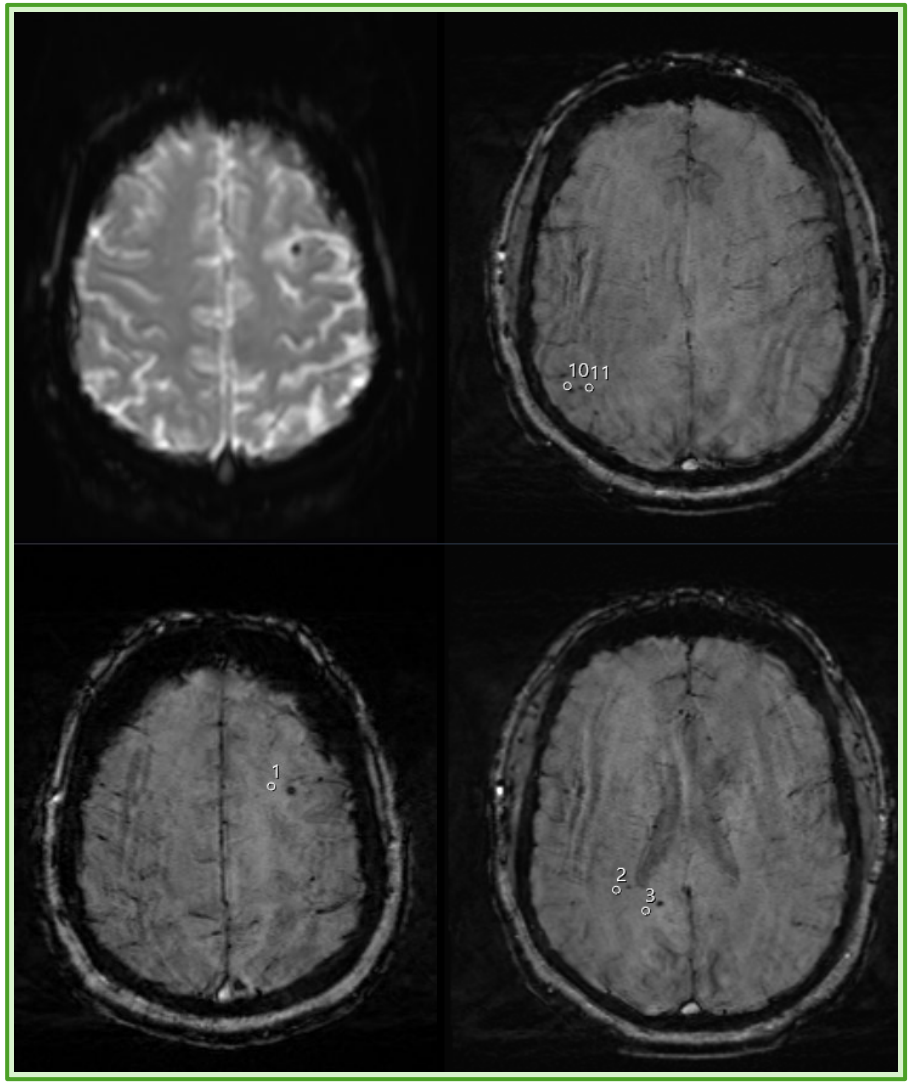
SUMMARY OF CLUES TO DIFFERENTIAL DIAGNOSES

ARIA vs. INFARCT	ARIA vs. SAH
FLAIR: ARIA will spare the cortex **DWI:** ARIA-E will not show restricted diffusion **SWI:** ARIA-H siderosis is more superficial	**SWI or GRE:** ARIA-E effusion will not have **blood products** as seen in SAH
ARIA vs. BACTERIAL MENINGITIS	**ARIA vs. PRES**
More likely to find a **mismatch in location** between edema and siderosis	PRES is more likely to be **symmetric** and will **resolve quickly** when blood pressure is controlled

Contrast may be valuable in symptomatic patients to rule out other differentials such as brain metastasis

21. Cogswell PM et al. *AJNR Am J Neuroradiol*. 2022;43(9):E19 E35

TIPS FOR TRACKING MICROBLEEDS



TECHNIQUE

Try to use the arrows, or better, use text to add numbers.

Total is important, but MORE important is **how many are NEW.**

If there is a discrepancy between different techniques, **count what you believe is real**.

COMMUNICATION

ANY ARIA:

If you see new MCH, new siderosis, new WMH or edema, please **contact the neurologist**.

MILD ARIA-E

can be called by an imaging assistant to the clinic nurse.

MODERATE or SEVERE ARIA needs a physician-to-physician conversation.

It changes management.

INITIAL REFERRAL: PRE-THERAPY

WHAT THE NEUROLOGIST IS LOOKING FOR

INCLUSION FACTORS

- ✓ Evidence of amyloid (imaging or fluid)
- ✓ MRI within 12 months of treatment initiation
- ✓ **Patient is eligible and willing to receive multiple MRIs**

Helpful to have bidirectional communication about likelihood/evidence the patient is or will be uncomfortable or uncooperative during MRIs

EXCLUSION FACTORS

- X Acute or subacute hemorrhage or infarction
- X Extensive existing cerebrovascular disease
- X Excessive ARIA-H risk
- X Intraparenchymal mass or inflammatory lesion

ARIA SEVERITY GRADING

ARIA TYPE	RADIOGRAPHIC SEVERITY		
	MILD	MODERATE	SEVERE
ARIA-E (FLAIR hyperintensities)	One (<5 cm) in sulcus or cortex/ subcortical white matter	One 5-10 cm OR more than 1 <10 cm site	>10 cm, often subcortical white matter and/or sulcal; can be >1 site
ARIA-H (new-incident microhemorrhages)	≤4	5-9	10 or more
ARIA-H (areas of superficial siderosis)	1 focal area	2 focal areas	>2 focal areas

4. ADUHELM (aducanumab-avwa). Prescribing information. Biogen Inc.; 2023. • 5. LEQEMBI (lecanemab-irmb). Prescribing information. Eisai Inc.; 2023.

ARIA SEVERITY: INFLUENCE ON CLINICAL MANAGEMENT

<table>
<tr><th rowspan="2">CLINICAL SYMPTOM SEVERITY</th><th colspan="4">RADIOGRAPHIC SEVERITY</th></tr>
<tr><th>MILD</th><th>MODERATE</th><th colspan="2">SEVERE</th></tr>
<tr><td></td><td>ARIA-E & H</td><td>ARIA-E & H</td><td>ARIA-E</td><td>ARIA-H
or macrohemorrhage</td></tr>
<tr><td>ASYMPTOMATIC</td><td rowspan="2">CONTINUE DOSING
with increased surveillance</td><td colspan="2" rowspan="2">SUSPEND DOSING
with increased surveillance

Once ARIA-E is resolved AND ARIA-H is stable, the patient may resume dosing at the same dose.</td><td rowspan="2">LIKELY PERMANENTLY DISCONTINUE DOSING
with increased surveillance</td></tr>
<tr><td>MILD TO MODERATE</td></tr>
<tr><td>SEVERE†</td><td colspan="4">Note: In the most severe symptomatic ARIA, high-dose corticosteroid therapy should be considered</td></tr>
</table>

*"**Severe" symptoms:** attributable to ARIA and involve seizure, require hospitalization, cause incapacitation, risk permanent deficits, and/or significantly impact activities of daily living*

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