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Lilly ConnectAD™

Welcome to ConnectAD™, a clinical case series created by the Eli Lilly and Company Neuroscience medical education team. This series is intended to connect healthcare professionals to resources that help them detect, diagnose, and manage Alzheimer's disease.

Disclaimer

The content for this case was created by Eli Lilly and Company and is inspired by scenarios clinicians may encounter while caring for patients with Alzheimer's disease.

Inclusion of a specific approach to treatment and monitoring in this clinical case does not imply endorsement or recommendation by Lilly.

Learning Objective

Through completing this course, you will have a deeper understanding of:

Potential options to approach treatment initiation and monitoring in Alzheimer's disease

Lilly ConnectAD™

Connect *with Beverly*

Treat · Monitor

Diagnosis: Mild Dementia Due to AD

Click here to access Beverly's detection and diagnosis case to learn more about her path to diagnosis

Patient overview:

Beverly is a 79-year-old Black female with:

- Type 2 diabetes
- Hypertension
- Urinary incontinence
- High cholesterol

Initial clinical assessment

- Alert and responsive
- Self-reported that she was able to complete all activities of daily living
- Beverly's daughter noted that her mom needed help with many activities of daily living, including managing finances and taking medication
- Cognitive impairment (MoCA below threshold)

Additional testing

Beverly's clinical history and cognitive assessment warranted further testing.

The additional tests selected included:

- Blood work
- Brain MRI
- Amyloid PET

Amyloid PET results

Positive with moderate-to-frequent Aβ deposition

Aβ=Amyloid Beta; AD=Alzheimer's Disease; MoCA=Montreal Cognitive Assessment; MRI=Magnetic Resonance Imaging; PET=Positron Emission Tomography.

Treatment Options

Non-pharmacologic or behavioral interventions:

- Non-pharmacologic interventions that may improve or maintain cognition/function, help to support independence in usual activities of daily living, or address behavioral symptoms[1]
- Eg, cognitive therapy, physical exercise, nutrition

Symptomatic therapy:

- Pharmacotherapy that may improve cognitive and behavioral symptoms, but does not alter the course of the disease[2]

Disease-modifying therapy:

- Pharmacotherapy that modifies the clinical course of disease but does not stop or reverse the disease[3]
- Eg, amyloid-targeting therapy (ATT)

Note: The treatment plan is under the discretion of the HCP and patient via shared decision making and a combination of treatments may be chosen

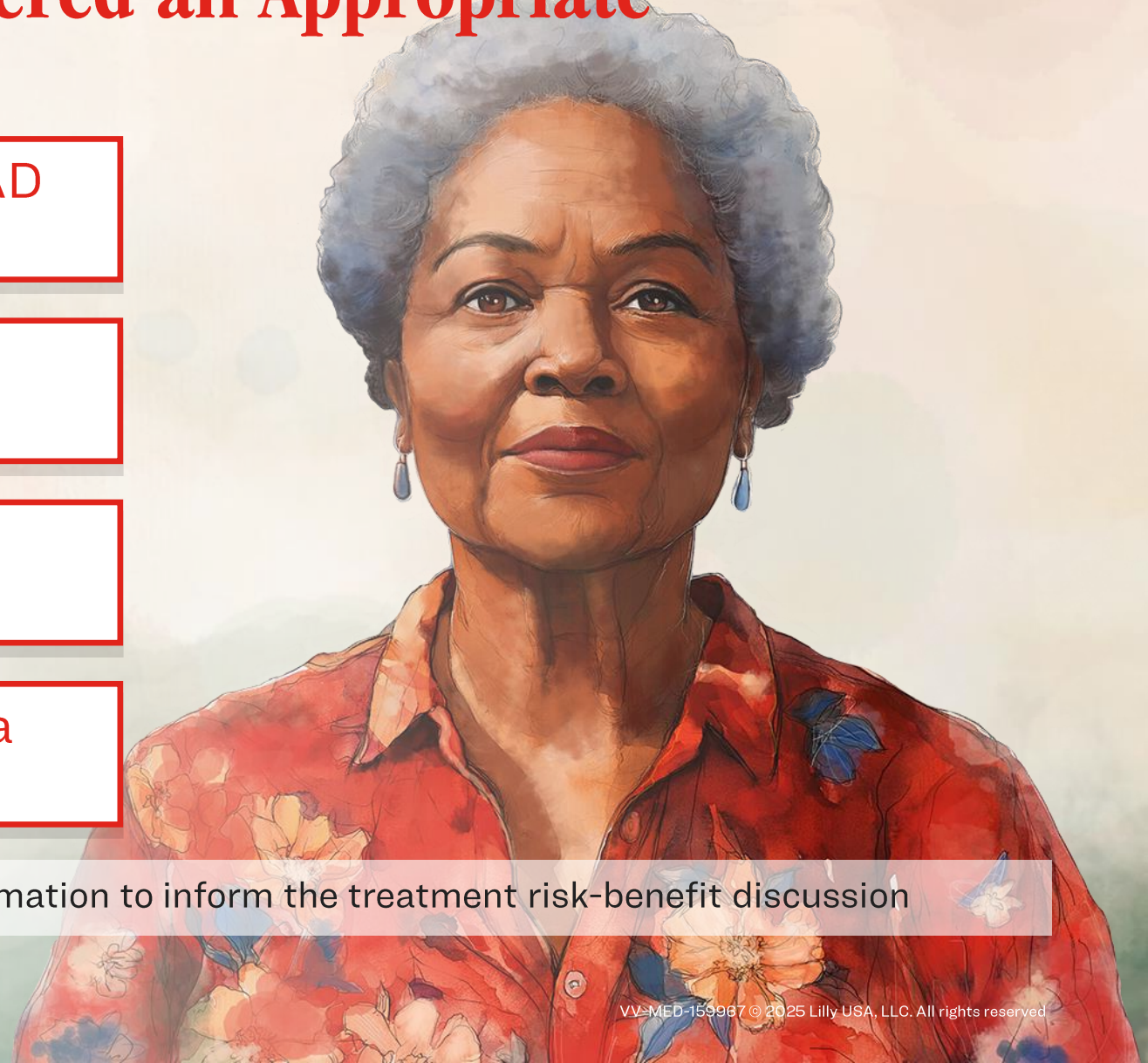
HCP=Healthcare Provider.

1. Li X, et al. *Neurol Ther*. 2023;12(1):39-72. 2. Cummings J. *Mol Neurodegener*. 2021;16(1):2. 3. Huang LK, et al. *J Biomed Sci*. 2023;30(1):83.

JUSTIFICATION FOR STARTING BEVERLY ON ATT

Why Could Beverly Be Considered an Appropriate Candidate for an ATT?

1. Diagnosis of mild dementia due to AD with confirmed Aβ pathology
2. No other known cause for cognitive decline
3. No contraindications to treatment
4. Brain MRI has no evidence of edema or cerebral amyloid angiopathy



Note: *APOE* ε4 genotyping would provide additional information to inform the treatment risk-benefit discussion

Aβ=Amyloid Beta; AD=Alzheimer's Disease; *APOE*=Apolipoprotein E; ATT=Amyloid-targeting Therapy; MRI=Magnetic Resonance Imaging.

Ramanan VK, et al. *Neurology*. 2023;101(19):842-852.

ATT Class Boxed Warning: *APOE* ε4 & ARIA

Among patients treated with the ATT class of medications, those who are *APOE* ε4 homozygotes have a higher incidence of amyloid-related imaging abnormalities (ARIA) – including symptomatic and serious ARIA – than those who are heterozygotes or noncarriers.[1-2]

Testing for *APOE* ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA.[1-2]

APOE=Apolipoprotein E; ATT=Amyloid-targeting Therapy.

1. Kisunla (donanemab-azbt). Prescribing Information. Lilly USA, LLC. 2. Leqembi (lecanemab-irmb) injection, for intravenous use [package insert]. Nutley, NJ: Eisai Inc.

ATT Class Boxed Warning: Risk of ARIA

ATTs are monoclonal antibodies directed against aggregated forms of Aβ and can cause amyloid-related imaging abnormalities (ARIA), as ARIA with edema or effusion (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). ARIA is usually asymptomatic, although serious and life-threatening events can rarely occur. Serious intracerebral hemorrhages >1 cm have occurred in patients treated with this class of medications. ARIA-E can cause focal neurologic deficits that can mimic ischemic stroke.[1-2]

Consider the benefit for the treatment of Alzheimer's disease and risk of ARIA when deciding to treat with an ATT.[1-2]

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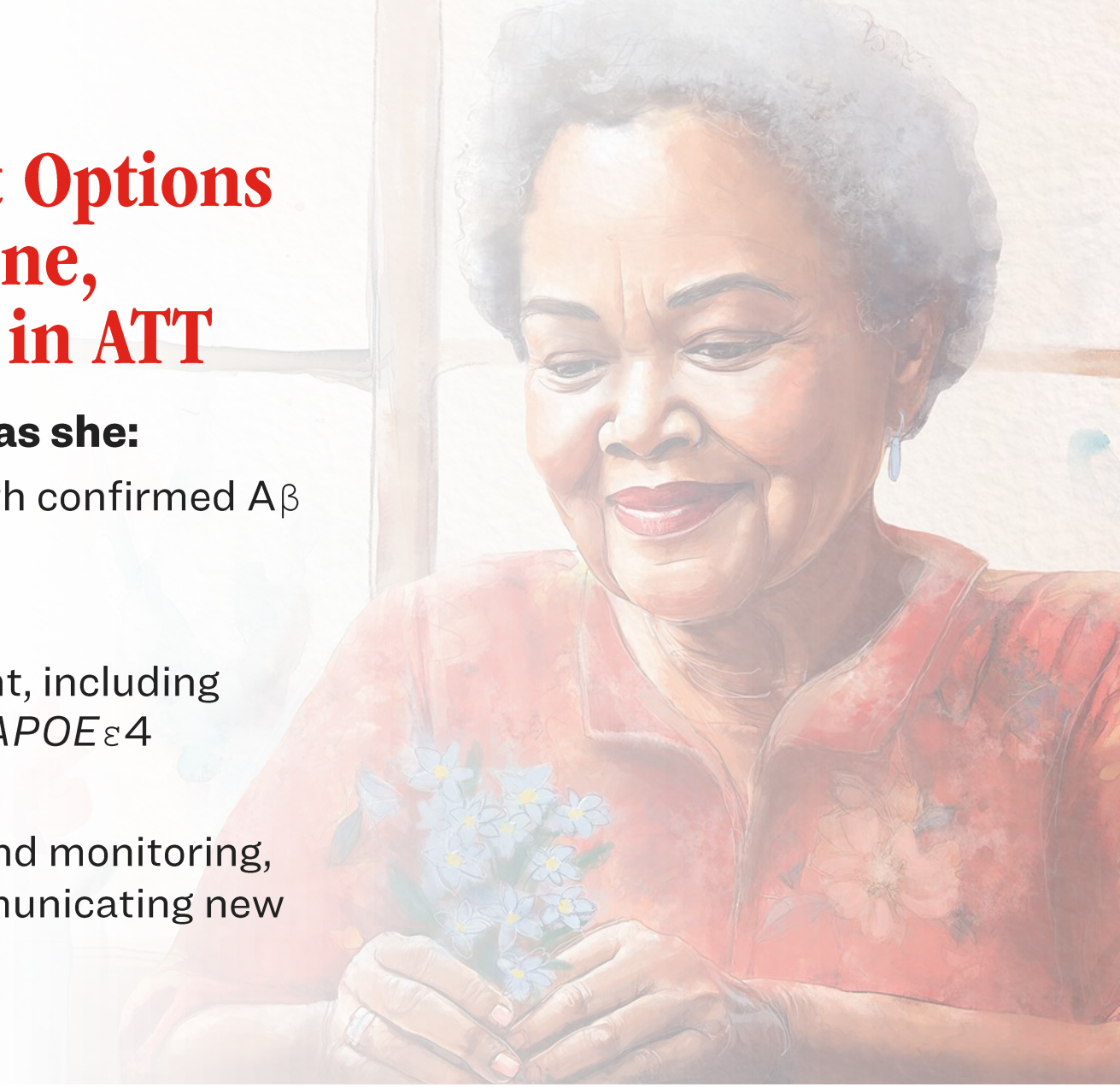
After Discussion of Treatment Options with Beverly and Her Loved One, Beverly Expresses an Interest in ATT



Beverly is an appropriate candidate for ATT as she:

- Has a diagnosis of mild dementia due to AD with confirmed Aβ pathology
- Has no contraindications
- Understands the risks and benefits of treatment, including the rationale, process, and resulting impact of *APOE*ε4 genotype testing
- Understands the requirements for treatment and monitoring, including infusion and MRI schedule, and communicating new symptoms to the clinician
- Has additional support from loved ones

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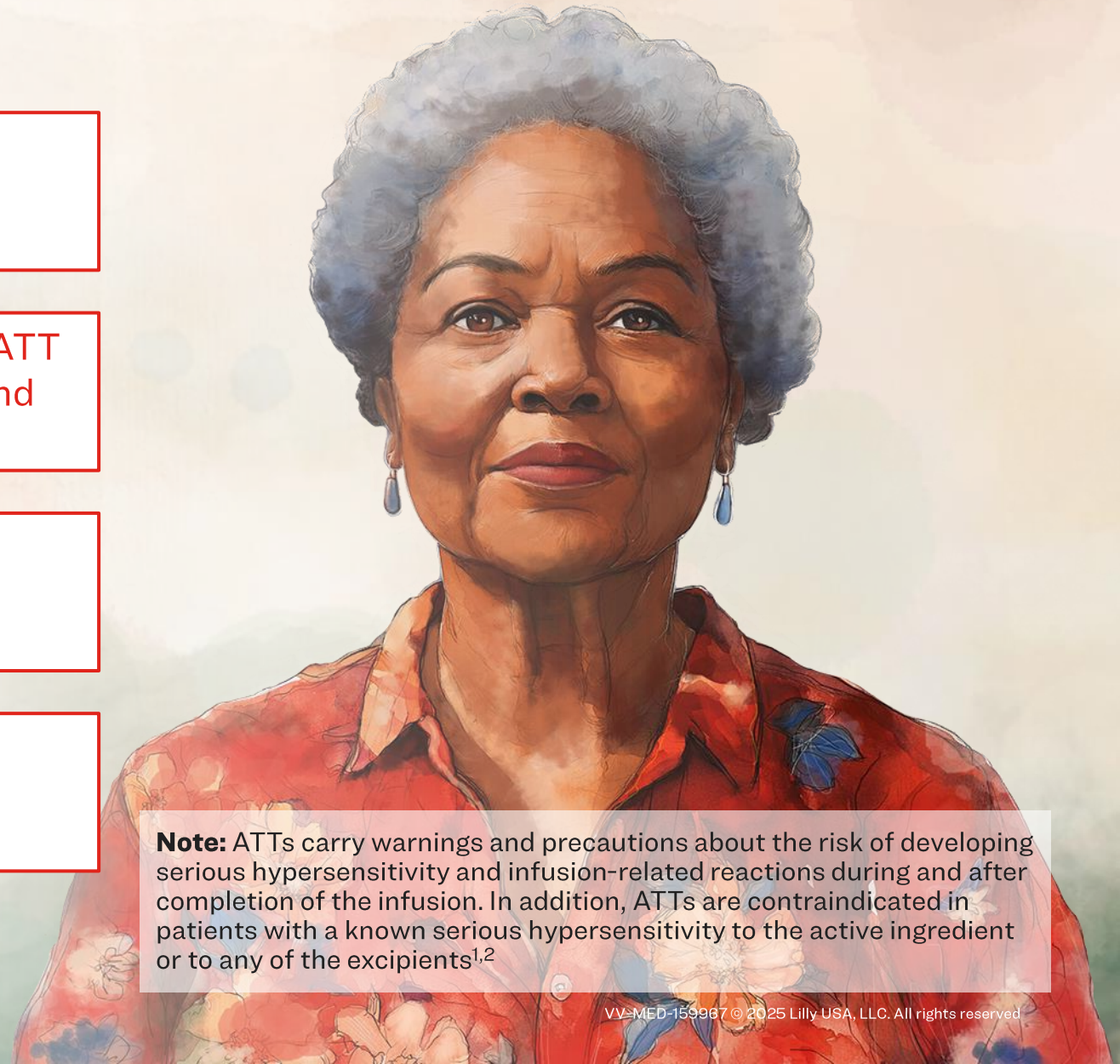
Initiation of an ATT

- Beverly begins ATT infusions
- During monitoring, after completion of her first ATT infusion, she developed symptoms of flushing and generalized pruritus
- Symptoms resolved in 30 minutes without additional treatment and did not recur in subsequent treatment infusions
- Premedication was not required



Note: ATTs carry warnings and precautions about the risk of developing serious hypersensitivity and infusion-related reactions during and after completion of the infusion. In addition, ATTs are contraindicated in patients with a known serious hypersensitivity to the active ingredient or to any of the excipients[1,2]

ATT=Amyloid-targeting Therapy.

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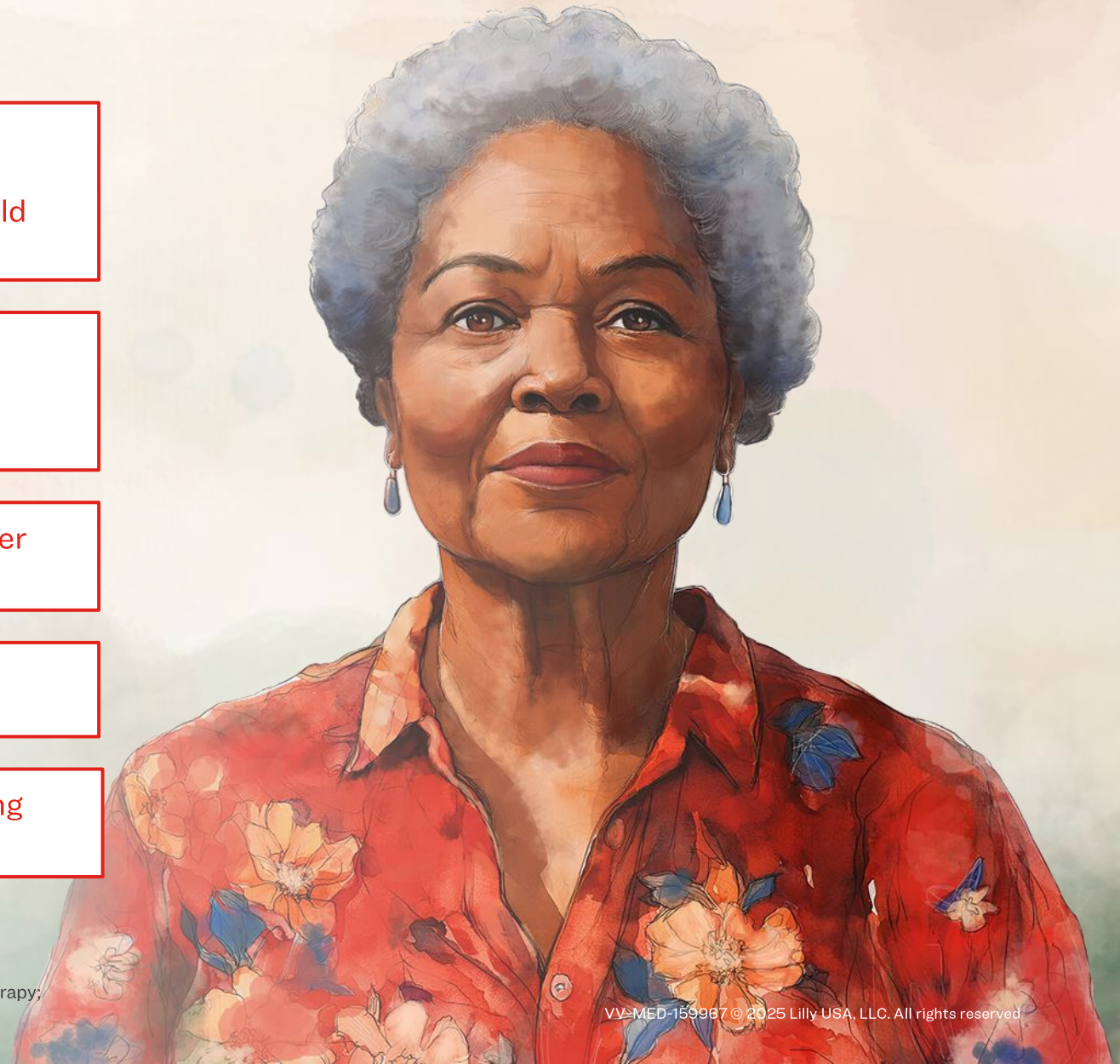
2. Leqembi (lecanemab-irmb) injection, for intravenous use [package insert]. Nutley, NJ: Eisai Inc.

Monitoring of an ATT

- After a few months of treatment, ARIA-E was found or demonstrated on a scheduled monitoring MRI in the right parieto-occipital region, categorized as radiographically mild (<5 cm, single area involved)
- The prescribing neurologist reviewed the MRI results with Beverly and her loved one. During this conversation, it was determined there were no associated symptoms
- Follow-up MRIs demonstrated resolution of the ARIA-E over 8 weeks
- Treatment was continued per the dosing schedule
- No new ARIA was detected on monitoring MRI scans during treatment over the following year



ARIA=Amyloid-related Imaging Abnormalities; ARIA-E=ARIA-Edema or Effusion; ATT=Amyloid-targeting Therapy; MRI=Magnetic Resonance Imaging.

Monitoring of an ATT

- ATTs require periodic monitoring for ARIA with MRI at baseline and throughout treatment. If a patient experiences symptoms suggestive of ARIA, clinical evaluation should be performed, including an MRI if indicated.
- Dose adjustments for ARIA depend on type, radiographic severity, and clinical symptoms.[1,2]

ARIA=Amyloid Related Imaging Abnormalities; ATT=Amyloid-targeting Therapy; MRI=Magnetic Resonance Imaging.

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2. Leqembi (lecanemab-irmb) injection, for intravenous use [package insert]. Nutley, NJ: Eisai Inc.

Key Learnings in Beverly's Case

Treatment with ATTs requires monitoring for infusion-related reactions and adherence to scheduled MRIs to monitor for ARIA.

- Clinicians administering the infusion should be trained to recognize the signs and symptoms of hypersensitivity reactions and how to manage them when they occur[1]
- Infusion-related reactions should be documented and communicated to the prescribing clinician[1]
- Adherence to scheduled brain MRI scans prior to infusions are necessary to identify ARIA and to modify dosing if needed[2]
- Multi-disciplinary collaboration between the prescribing clinician, radiologist, infusion center, and the primary care provider is necessary for optimal treatment monitoring[2]
- Patients and their loved ones should be educated about symptoms associated with ARIA and should communicate new symptoms to the prescribing clinician and infusion clinicians[2,3]

ARIA=Amyloid-related Imaging Abnormalities; ATT=Amyloid-targeting Therapy; MRI=Magnetic Resonance Imaging.

1. Sims JR, et al. *JAMA*. 2023;330(6):512-527. 2. Agarwal A, et al. *Radiographics*. 2023;43(9):e230009. 3. Ramanan VK, et al. *Neurology*. 2023;101(19):842-852.

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Thank you for Connecting *with Beverly*

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