INNOVATIONS IN NEUROLOGIC PRACTICE OPEN ACCESS

An Interprofessional Team for Disease-Modifying Therapy in Alzheimer Disease Implementation

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Neurology: Clinical Practice 2024;14:e200346. doi:10.1212/CPJ.0000000000200346

Abstract

Background

Lecanemab and other new amyloid-targeting immunotherapies for Alzheimer disease show notable promise but may also pose significant risk for patients.

Recent Findings

To facilitate the implementation and monitoring of lecanemab infusions at our tertiary medical center, we convened an interprofessional team. The team created a number of resources including patient handouts and medical documentation templates as well as systems and processes that are likely to be useful to other clinical care settings and centers.

Implications for Practice

It is our intent to widely share the resources and processes developed.

Background

Lecanemab and other new amyloid-targeting therapies for Alzheimer disease show notable promise for patients but also considerable risk.[1] Furthermore, the integration of lecanemab infusions into a memory disorders clinic requires systems and processes to be developed and established during routine clinical care to provide the medication in a safe and timely manner. We, therefore, assembled an interprofessional team to develop a process that would facilitate appropriate procedures, materials, and safeguards. This brief report aims to share the insights gained thus far in developing this process.

Composition and Role

An interprofessional team at VA Boston Healthcare System (VABHS) (disease-modifying therapy in Alzheimer disease, DMTAD group) consisting of attendings in the division of Cognitive Behavioral Neurology (A.E.B., K.W.T., M.K.), behavioral neurology and neuropsychiatry fellows (G.F., H.N., B.C., A.C.), geriatricians (A.N., D.A.), neuroradiologist (A.M.), infusion nurses (P.N., V.C.), geriatric clinical pharmacists (L.T., J.R.), second-year geriatric pharmacy residents (L.V., C.W.), and physician assistant (B.R.) was assembled and began meeting weekly for 1 hour. Because all team members are equally important and to facilitate open communication, we agreed to address each other using our first names (i.e., Kate and Andrew rather than Dr. Turk and Dr. Budson). The team's initial objective was to develop and streamline processes and systems for initiation of lecanemab treatment at

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Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

VABHS. Once those processes were in place, the team's purpose pivoted to assessment, review, and monitoring of patients from the VABHS memory disorders and geriatrics clinics for potential lecanemab treatment based on VA Criteria for Use. Responsibilities of the group also included placing medication orders, routinely reviewing imaging, and monitoring for any medication-related side effects and adverse reactions patients may have experienced in the preceding week.

Initial Work

Initial work of the committee included securing approval for use of lecanemab, given its high per-patient cost and thus high estimated yearly cost, from the Chief of Staff (responsible for all clinical budgeting) at VABHS, followed by drafting an infusion protocol (eAppendix 1). The infusion protocol underwent several rounds of group review and was ultimately presented to the VABHS Pharmacy and Therapeutics committee by the DMTAD pharmacists. Pharmacy team members then updated the drug files in the VA system and built order sets in the electronic VA computerized patient record system (CPRS), which were reviewed and discussed with DMTAD clinicians. A variety of note templates were created by the DMTAD committee including an infusion nursing administration template note and a templated note for the weekly DMTAD meeting for both initial eligibility and for ongoing monitoring (eAppendices 2 and 3). As a safety measure, a checkbox was added to orders of preinfusion nurses to determine that monitoring MRI before the 5th, 7th, and 14th doses was both ordered and reviewed. Infusion nursing template notes were developed (eAppendix 4). Several patient handouts were also developed by the DMTAD group to provide education regarding lecanemab and the required *APOE* genetic testing (eAppendices 5 and 6). The lecanemab medication handout was reviewed and approved by the VABHS Education and Information committee after several rounds of review and edits to achieve the appropriate fifth-grade reading level as part of VA requirements. Note that we adapt our educational approach to the appropriate level on an individual basis when patient education levels are higher.

Eligibility

Care processes of memory disorders and geriatrics clinics were developed by the DMTAD committee for determining whether patients were eligible for lecanemab. Patients in the memory disorders or geriatrics clinics who were 65 and older (per the VA Criteria for Use document, eAppendix 7) and who had (1) a clinical diagnosis of either mild cognitive impairment (MCI) due to Alzheimer disease or mild Alzheimer disease dementia as the primary etiology of their cognitive deficits, (2) no contraindication to lecanemab infusions (such as unstable medication condition, incompatible medication, or previous significant brain bleeding based on MRI within the past 3 months), and (3) a Montreal Cognitive Assessment (MoCA) score of greater than 16 or a Mini-Mental State Examination (MMSE) score of greater than 21 were offered an evaluation to determine whether they may be eligible for lecanemab (eAppendix 7, VA Criteria for Use document). Note that the age cutoff in the VA Criteria for Use document was instituted by the Pharmacy Benefits Management program in VA Central Office based on the post hoc analyses presented in the supplementary materials of the clinical trial manuscript[1] and may have been confounded by the fact that several younger patients with Alzheimer disease have 2 *APOE* ε4 alleles. It was our intention to ask the Pharmacy Benefits Management program for an exemption to treat patients younger than 65 years who were otherwise eligible for lecanemab.

If patients were interested, they were then given a handout explaining the risks and benefits of lecanemab (eAppendix 5) and were added to a secure VA tracking sheet used internally in the clinics to follow their workup and eligibility for lecanemab. The tracking sheet and monitoring data were primarily maintained and updated by the behavioral neurology/neuropsychiatry fellows.

Patients were then offered an amyloid PET scan at VABHS (if they had not already received one) or a lumbar puncture for CSF beta-amyloid (1–42) (Abeta42) total tau and phosphorylated tau (p-Tau181). If the amyloid PET scan or CSF results were consistent with AD, *APOE* genotype testing was ordered (if not ordered previously).

At the time of *APOE* ordering, a handout explaining the *APOE* gene, possible results, and potential implications for patients and family members was shared in the clinic and discussed with the patients and their family (eAppendix 6). Patients then returned to the clinic on another date and received genetic results disclosure. If *APOE* results returned as nonhomozygous for *APOE* ε4, patients were informed that they were eligible to proceed with lecanemab infusions if they so choose.

Of note, in some cases, *APOE* testing is performed before biomarker testing, but the order of testing is determined by the individual clinical scenario. When biomarker testing is needed for clinical management independent of lecanemab eligibility (e.g., prescription of the cholinesterase inhibitor or prognostic conversations with family[2]), then biomarker testing is performed first. This approach avoids exposing family members to potentially worrisome discussion of *APOE* results that are not clinically indicated if patients do not meet biomarker diagnostic criteria. By contrast, if biomarker testing is being performed solely for the determination of lecabemab eligibility, then *APOE* testing is generally performed initially because it is less costly than amyloid PET testing. An estimated 15%–20% of patients were ε4 homozygous, making them currently ineligible for lecanemab infusions.

Patients then completed the Columbia Suicide Rating Scale in the clinic to assure that they were not at risk of self-harm or suicide because it was part of the inclusion/exclusion criteria of the clinical trial.[1] Patients had their weight checked and

recorded and consented for infusions by reviewing the lecanemab patient medication handout and signing in CPRS. Finally, the eligibility progress note, filled out ahead of time by the behavioral neurology/neuropsychiatry fellow or the physician assistant with the relevant inclusion/exclusion information, was reviewed and finalized by the DMTAD team and then signed by all team members present. A nonformulary consult was entered for approval by the team clinical pharmacists, and subsequently, lecanemab orders may be entered with our order set that includes as-needed medications for infusion-related side effects.

Monitoring

The DMTAD committee decided that patients must be accompanied by a family member or other adults for infusions to take them home and assist with monitoring of any potential side effects and adverse reactions. New processes were adopted for reaching clinicians in real time if infusion reactions or side effects were to occur in the infusion suites (present on 2 campuses, Jamaica Plain and Brockton) during business hours (to the rotating behavioral neurology/neuropsychiatry fellow) or later during the evenings, nights, weekends, and holidays (to the on-call neurology resident on service). Relevant contact numbers were included in handouts given to patients. Brief resident training was conducted so that they would know what signs and symptoms to look for should they receive a call from a patient receiving lecanemab or their family.

Patients receiving infusions were reviewed weekly in the DMTAD meeting to evaluate how their infusions went the previous week and whether any complications occurred. Brain MRI scans were reviewed for signs of amyloid-related imaging abnormalities (ARIAs) at baseline and before the 5th, 7th, and 14th doses by a trained neuroradiologist and member of the DMTAD group (A.M.) before the meeting, as well as reviewed by neurologists (A.E.B., K.W.T., H.N., A.C.) and neuroradiologist during the meeting (A.M.). ARIA review of each MRI scan was performed using a standardized note template adapted from those published in the neuroradiology literature[3] to aid review (eAppendix 8). Monitoring notes were documented in the medical record during the DMTAD meeting, and a decision was made as to whether infusions can be safely continued for each patient.

Management of Infusion-Related Reactions

Our infusion protocol uses diphenhydramine as a rescue medication in the case of infusion-related reactions instead of a premedication to avoid unnecessary anticholinergic effects. However, in rare cases, a patient may have 2 episodes of infusion-related reactions and would then need premedication with antihistamines per our protocol. If a patient is tolerating infusions with diphenhydramine premedication, some studies in oncology have de-escalated to cetirizine or loratadine (H2 receptor blockers) for decreased anticholinergic effects among patients receiving oncologic immunotherapy.[4] A similar approach could be adapted with lecanemab infusions to reduce anticholinergic effects.

Patient Volume and Other Future Considerations of Group Structure

The team's current structure and membership are adequately meeting workload needs with 1 hour of dedicated meetings. However, there can be consideration for adding additional physician members from emergency medicine, stroke, and critical care and associated clinical procedures for managing patients receiving lecanemab in each setting. Future modifications of the current structure and makeup of the team may be necessary to effectively scale up to evaluate, screen, and monitor a larger number of patients. In that scenario, we anticipate potentially hiring a physician practice extender such as a nurse practitioner or physician assistant and potentially expanding the behavioral neurology/neuropsychiatry fellowship duties to include a more dedicated role on the team for multiple fellows. Finally, we have allocated more staff effort within our division (one-half day per week) to allow for a dedicated behavioral neurologist attending to lead the team and be responsible for patient eligibility and management.

Conclusions

We found that forming an interdisciplinary and interprofessional team comprising behavioral neurologists, geriatricians, pharmacists, infusion nurses, neuroradiologists, and trainees is instrumental in initiating lecanemab infusions

TAKE-HOME POINTS

- An interdisciplinary team was assembled to facilitate the initial rollout of disease modifying therapies for AD.
- The team developed patient-facing and internal documents to streamline initial medication roll out effectively.
- The team also developed policies, procedures, and weekly review processes for initial eligibility screening.
- The team has developed processes for ongoing imaging and clinical review of patients receiving infusions.
- Processes and resources developed are being disseminated for use and adaptation by others.

at a tertiary medical center. This team structure and process are also important in ongoing administration and monitoring of patients on lecanemab. We believe the approach we have outlined may be adaptable and can be used across the US medical system. Depending on each center's infrastructure, certain roles might be filled by other health care professionals such as nurses, nurse practitioners, or physician assistants instead of fellows/residents when necessary.

Study Funding

NIH support to Drs. Turk and Budson (P30-AG072978).

Disclosure

K.W. Turk reports research funding from the Alzheimer's association, US Department of Veterans Affairs, the Doris Duke Foundation and Vox Neuro incorporated. A.E. Budson reports Eli Lilly: Consultant, VoxNeuro: investigator initiated grant, Bristol Myers Squbb: investigator initiated grant, Oxford University Press: author royalties. Elsevier: author royalties. The other authors report no disclosures relevant to the manuscript. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

Publication History

Received by *Neurology: Clinical Practice* January 5, 2024. Accepted in final form April 23, 2024. Submitted and externally peer-reviewed. The handling editor was Editor Luca Bartolini, MD, FAAN, FAES.

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References

1. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388(1):9-21. doi:10.1056/NEJMoa2212948
2. Vives-Rodriguez AL, Schiloski KA, Marin A, et al. Impact of amyloid PET in the clinical care of veterans in a tertiary memory disorders clinic. *Alzheimers Dement (N Y)*. 2022;8(1):e12320. doi:10.1002/trc2.12320
3. Roytman M, Mashriqi F, Al-Tawil K, et al. Amyloid-related imaging abnormalities: an update. *AJR Am J Roentgenol*. 2023;220(4):562-574. doi:10.2214/AJR.22.28461
4. Lofy M, Jung L, Dow-Hillgartner E. Premedication strategy in cetuximab rechallenge after grade 2 hypersensitivity reactions. *J Oncol Pharm Pract*. 2024;30(2):412-416. doi:10.1177/10781552231212640

How to cite this article: Turk KW, Knobel MD, Nothern A, et al. An interprofessional team for disease-modifying therapy in Alzheimer disease implementation. *Neurol Clin Pract*. 2024;14(6):e200346. doi:10.1212/CPJ.0000000000200346.