

ASSOCIATE EDITORS

HENRY C. BARRY, MD, MS
Professor Emeritus, Department of Family
Medicine, and Senior Associate
Dean Emeritus, College of Human Medicine,
Michigan State University, East Lansing

KATE ROWLAND, MD, MS, FAAFP
Rush University, Chicago

RICHARD P. USATINE, MD
University of Texas Health,
San Antonio (Photo Rounds)

ASSISTANT EDITORS

DOUG CAMPOS-OUTCALT, MD, MPA
University of Arizona

RICK GUTHMANN, MD, MPH
Advocate Health Care Illinois Masonic Medical
Center Program, Chicago

GARY KELSBERG, MD, FAAFP
University of Washington, Renton

COREY LYON, DO
University of Colorado, Denver

E. CHRIS VINCENT, MD
University of Washington, Seattle

SAMINA YUNUS, MD, MPH
Cleveland Clinic, Chagrin Falls, OH

EDITORIAL BOARD

FREDERICK CHEN, MD, MPH
University of Washington, Seattle

MARK S. JOHNSON, MD, MPH
Howard University College of Medicine
Washington, DC

JEFFREY T. KIRCHNER, DO, FAAFP, AAHIVS
Penn Medicine/Lancaster General Hospital, PA

TRACY MAHVAN, PHARM D
University of Wyoming, Laramie

MICHAEL MENDOZA, MD, MPH, MS, FAAFP
University of Rochester, NY

FRED MISER, MD, MA
The Ohio State University, Columbus

KATE ROWLAND, MD, MS, FAAFP
Rush University, Chicago

LINDA SPEER, MD
University of Toledo, OH

DIRECT INQUIRIES TO:

Frontline Medical Communications
283 - 299 Market St.
(2 Gateway Building), 4th Floor
Newark, NJ 07102
Telephone: (973) 206-3434
Fax: (973) 206-9378

Have a comment or
feedback?

Email: jfp.eic@mdedge.com

**GUEST
EDITORIAL**

Henry C. Barry, MD, MS
Professor Emeritus, Department of Family
Medicine, and Senior Associate Dean Emeritus,
College of Human Medicine,
Michigan State University, East Lansing

*The author reported no potential conflict of interest relevant
to this editorial. Dr. Barry is an associate editor for
The Journal of Family Practice.*

jfp.eic@mdedge.com

doi: 10.12788/jfp.0562



Meaningful improvement for patients like Tante Ilse

Last year, after a long delay due to COVID, my father's ashes were finally laid to rest at Arlington National Cemetery. Among the loved ones who came was my favorite aunt, Tante Ilse, who was suffering from dementia. While she wasn't "following" everything that was going on, she did perk up when she heard my father's name and would comment on how she liked him and how wonderful he had been to her.

After the ceremony, our family of about 30 gathered at a restaurant where we shared stories and old pictures. Tante Ilse seemed to relish the photos and the time with family. She was doing so well that when we went back to my mom's home after

the reception, my cousins decided to bring Tante Ilse there, too. She had a great time, as evidenced by her famous total-body laugh. In the months before her death, we all commented about that day and how happy she seemed.

My aunt's decline comes to mind as I reflect on media reports of 2 Alzheimer drugs—aducanumab and lecanemab—that have been billed by some as "gamechangers." These new drugs are monoclonal antibodies directed at

amyloid, one of several agents thought to cause Alzheimer disease. The details of aducanumab's approval by the US Food and Drug Administration (FDA) generated a great deal of criticism—with good reason.

Two manufacturer-sponsored studies of aducanumab were halted due to futility of finding a benefit.¹ The FDA's scientific advisory panel recommended *against* approval due to a lack of evidence that it did anything more than remove amyloid plaque from the brain. And yet aducanumab received accelerated approval from the FDA. (This author collaborated on an additional analysis using data presented to the FDA, after its approval, which also reported no clinically meaningful effects.²) The other agent, lecanemab, also reduces markers of amyloid and was shown to be only moderately better than placebo in decreasing the rate of decline on various measures of cognition.³ Quite notably, both aducanumab and lecanemab, which are administered parenterally, cost more than \$25,000 per year^{4,5} and cause amyloid-related imaging abnormalities (brain edema or hemorrhage).

Expensive agents without meaningful benefit. So far, neither of these agents has shown a reduction in things that are truly important to our patients and their families/caregivers: a reduction in caregiver burden and a reduction in the need for placement in long-term care facilities.

This is in contrast to cholinesterase inhibitors, which also slow the rate of cognitive decline.⁶ Among the differences that exist between these agents: Cholinester-

CONTINUED ON PAGE 92

- the US. Published December 6, 2022. Accessed February 2, 2023. www.cdc.gov/vaccines/covid-19/downloads/summary-interim-clinical-considerations.pdf
- CDC. COVID-19 vaccine: interim COVID-19 immunization schedule for persons 6 months of age and older. Published December 8, 2022. Accessed February 2, 2023. www.cdc.gov/vaccines/covid-19/downloads/COVID-19-immunization-schedule-ages-6months-older.pdf
 - Krow-Lucal E, Marin M, Shepersky L, et al. Measles, mumps, rubella vaccine (PRIORIX): recommendations of the Advisory Committee on Immunization Practices—United States, 2022. *MMWR Morb Mortal Wkly Rep.* 2022;71:1465-1470. doi: 10.15585/mmwr.mm7146a1
 - CDC. ACIP evidence to recommendations framework for use of PRIORIX for prevention of measles, mumps, and rubella. Updated October 27, 2022. Accessed February 2, 2023. www.cdc.gov/vaccines/acip/recs/grade/mmr-PRIORIX-etr.html
 - Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-valent pneumococcal conjugate vaccine and 20-valent pneumococcal conjugate vaccine among US adults: updated recommendations of the Advisory Committee on Immunization Practices—United States, 2022. *MMWR Morb Mortal Wkly Rep.* 2022;71:109-117. doi: 10.15585/mmwr.mm7104a1
 - Campos-Outcalt D. Vaccine update: the latest recommendations from ACIP. *J Fam Pract.* 2022;71:80-84. doi: 10.12788/jfp.0362
 - Kobayashi M. Proposed updates to clinical guidance on pneumococcal vaccine use among adults. Presented to the ACIP on October 19, 2022. Accessed February 2, 2023. www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/04-Pneumococcal-Kobayashi-508.pdf
 - Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-valent pneumococcal conjugate vaccine among US children: updated recommendations of the Advisory Committee on Immunization Practices—United States, 2022. *MMWR Morb Mortal Wkly Rep.* 2022;71:1174-1181. doi: 10.15585/mmwr.mm7137a3
 - CDC. Immunization schedules. Updated February 17, 2022. Accessed February 6, 2022. www.cdc.gov/vaccines/schedules/hcp/index.html
 - Campos-Outcalt D. Vaccine update for the 2022-2023 influenza season. *J Fam Pract.* 2022;71:362-365. doi: 10.12788/jfp.0487
 - Hills S. Tick-borne encephalitis. Presented to the ACIP on February 23, 2022. Accessed February 2, 2023. www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-02-23-24/02-TBE-Hills-508.pdf
 - CDC. Tick-borne encephalitis. Updated March 11, 2022. Accessed February 2, 2023. www.cdc.gov/tick-borne-encephalitis/
 - Ticovac. Package insert. Pfizer; 2022. Accessed February 6, 2023. www.fda.gov/media/151502/download
 - Collins JP, Ryan ET, Wong KK, et al. Cholera vaccine: recommendations of the Advisory Committee on Immunization Practices, 2022. *MMWR Recomm Rep.* 2022;71:1-8. doi: 10.15585/mmwr.r7102a1
 - Global Task Force on Cholera Control. Cholera outbreak response field manual. Published October 2019. Accessed February 16, 2023. www.gtfcc.org/wp-content/uploads/2020/05/gtfcc-cholera-outbreak-response-field-manual.pdf
 - WHO. Health topics: cholera. Accessed February 16, 2023. www.who.int/health-topics/cholera#tab=tab_1

GUEST EDITORIAL

CONTINUED FROM PAGE 54

ase inhibitors are taken orally and are available as generics, which cost less than a thousand dollars per year.⁷ Limited data also suggest that they are associated with a lower risk for nursing home placement.^{8,9} (A February 2023 search of clinicaltrials.gov did not reveal any completed or planned head-to-head comparisons of monoclonal antibodies and anticholinergic agents.)

Our patients, their families, and caregivers hold out hope for something that will improve the patient's cognition and extend the meaningful time they have with their

loved ones. So far, the best we have to offer falls far short of these goals. I certainly would have hoped for something better than merely clearing amyloid for my aunt.

It's time that the FDA adopt more rigorous standards requiring new drugs to, among other things, demonstrate meaningful clinical benefits, provide real cost savings, and be safer than currently available therapies. Other nations seem to be able to do this.^{10,11} It is bad enough to provide "hope in a bottle"; it is worse when what is offered is false hope. **JFP**

References

- Budd Haerberlein S, Aisen PS, Barkhof F, et al. Two randomized phase 3 studies of aducanumab in early Alzheimer's disease. *J Prev Alzheimers Dis.* 2022;9:197-210. doi: 10.14283/jpad.2022.30
- Ebell MH, Barry HC. Why physicians should not prescribe aducanumab for Alzheimer disease. *Am Fam Physician.* 2022;105:353-354.
- van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med.* 2023;388:9-21. doi: 10.1056/NEJMoa2212948
- Reardon S. FDA approves Alzheimer's drug lecanemab amid safety concerns. *Nature.* 2023; 613:227-228. doi: 10.1038/d41586-023-00030-3
- Biogen announces reduced price for Aduhelm to improve access for patients with early Alzheimer's disease. December 20, 2021. Accessed February 20, 2023. <https://investors.biogen.com/news-releases/news-release-details/biogen-announces-reduced-price-aduhelm-improve-access-patients>
- Takramah WK, Asem L. The efficacy of pharmacological interventions to improve cognitive and behavior symptoms in people with dementia: A systematic review and meta-analysis. *Health Sci Rep.* 2022;5:e913. doi: 10.1002/hsr2.913
- GoodRx. Donepezil generic Aricept. Accessed February 20, 2023. www.goodrx.com/donepezil
- Howard R, McShane R, Lindesay J, et al. Nursing home placement in the donepezil and memantine in moderate to severe Alzheimer's disease (DOMINO-AD) trial: secondary and post-hoc analyses. *Lancet Neurol.* 2015;14:1171-1181. doi: 10.1016/S1474-4422(15)00258-6
- Geldmacher DS, Provenzano G, McRae T, et al. Donepezil is associated with delayed nursing home placement in patients with Alzheimer's disease. *J Am Geriatr Soc.* 2003;51:937-944. doi: 10.1046/j.1365-2389.2003.51306.x
- Pham C, Le K, Draves M, et al. Assessment of FDA-approved drugs not recommended for use or reimbursement in other countries, 2017-2020. *JAMA Intern Med.* Published online February 13, 2023. doi: 10.1001/jamainternmed.2022.6787
- Johnston JL, Ross JS, Ramachandran R. US Food and Drug Administration approval of drugs not meeting pivotal trial primary end points, 2018-2021. *JAMA Intern Med.* Published online February 13, 2023. doi: 10.1001/jamainternmed.2022.6444