Understanding the treatment landscape in mild cognitive impairment/Alzheimer's disease dementia and physicians' opinions on future developments in disease-modifying therapies: a real-world survey.

Pascual Sanchez-Juan[1], Simona Vasileva-Metodiev[2], Brenda Botello Estrada[2], Sarah Cotton[3], Diego Novick[2]

[1]Research Foundation for Neurological Diseases Fundación CIEN, Madrid, Spain, [2]Eli Lilly and Company, Bracknell, United Kingdom, [3]Adelphi Real World, Bollington, United Kingdom

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OBJECTIVE

- To examine the treatment landscape in mild cognitive impairment (MCI) and Alzheimer's disease (AD) by physician-determined disease severity level.
- To assess the factors that specialist physicians most value about new DMTs.

CONCLUSION

- Our results indicate that physicians used currently approved symptomatic medications principally to slow progression of MCI/AD, and secondly, to preserve short-term memory (except in patients with severe dementia due to AD).
- As DMTs become available for clinical use, education about the therapeutic effect of symptomatic medications versus DMTs may help to inform PCP on treatment expectations.
- Finally, specialist physicians want new DMTs to improve quality of life and slow disease progression in MCI/AD.

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STUDY DESIGN

- Data were drawn from the Adelphi Real World AD Disease Specific Programme™ (DSP), a cross-sectional survey with elements of retrospective data collection of primary care physicians (PCP) and specialists (neurologists, geriatric psychiatrists, geriatricians, psychiatrists, neuropsychiatrists and neurosurgeons), in Germany, France, Italy, Spain, the United Kingdom, Japan and the United States.
- The survey was conducted between December 2022 and March 2024, before approval of donanemab (Food and Drug Administration [FDA] and Japan)[2,3] and lecanemab (Medicines and Healthcare products Regulatory Agency)[4].
- The DSP methodology has been previously published, validated[5-7], and found to be consistent over time[8].
- Analyses were descriptive and sample size varied among variables, as there was no imputation of missing data.
- Physicians reported information on the treatment patterns and reasons for prescribing specific treatments for their next 9 consecutively consulting patients aged ≥50 years with a diagnosis of MCI (due to suspected or uncertain AD etiology) or AD. This data have been segmented by physician-determined disease severity (MCI or mild, moderate or severe dementia due to AD).
- Physicians also completed a survey capturing their attitudes and experience in the management of patients with dementia, including attributes they would most value in new DMTs.

References:

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BACKGROUND

- AD is a progressive and deteriorating illness, represented by a continuum that stretches from the asymptomatic stage through the MCI stage and culminates in dementia.[1]
- Until recently, treatments for AD were mainly represented by acetylcholinesterase inhibitors (AChEIs) and N-methyl-D-aspartate receptor antagonist (NMDA) memantine, which are symptomatic cognitive enhancing agents[1]. They may transiently improve cognitive function or temporarily postpone cognitive decline, but they do not slow the rate of progression of disease.
- Important discoveries have been made in relation to AD pathology, biomarker-driven diagnosis, along with approval of DMTs, which target amyloid pathology with the aim to remove the amyloid plaques and slow disease progression[1].
- Consequently, it is important to understand the current treatment management and perspectives of physicians on the rapidly changing treatment landscape.

KEY RESULT

Table 1: Patients' treatment characteristics.

Treatment characteristic	MCI [N= 2017]	Mild dementia due to AD [N= 935]	Moderate dementia due to AD [N= 1684]	Severe dementia due to AD [N= 785]
Current treatment, n (%)				
On treatment	1072 (53.1)	680 (72.7)	1272 (75.5)	518 (66.0)
AChEIs	821 (40.7)	594 (63.5)	966 (57.4)	329 (41.9)
NMDA Antagonist	304 (15.1)	148 (15.8)	547 (32.5)	293 (37.3)
No treatment	945 (46.9)	255 (27.3)	412 (24.5)	267 (34.0)
Number of treatments, med (IQR)	[N= 1072] 2 (1.0- 2.0)	[N= 680] 1 (1.0-2.0)	[N= 1272] 2 (1.0-3.0)	[N= 518] 2 (2.0-3.0)
Duration of current treatment (weeks), mean (SD)	[N= 841] 74.4 (95.1)	[N= 561] 54.5 (57.2)	[N= 991] 85.1 (89.1)	[N= 353] 129.1 (121.6)

Results

- Overall, 779 physicians reported data on 5,551 patients. Of these, 765 physicians completed an attitudinal survey.
- Of those with a physician-defined severity level, 2,017 patients had MCI, 935 mild dementia due to AD, 1,684 moderate dementia due to AD, and 785 severe dementia due to AD (their treatment characteristics are listed in table 1).
- Overall, patients had a mean (standard deviation [SD]) age of 76.5 (8.4) years, with 51.5% of the patients being female. For patients receiving treatment, the median (interquartile range) number of treatments per patient was 2.0 (1.0 - 3.0) with mean (SD) duration of 81.2 (93.0) weeks.
- Overall, 50.0% of patients were receiving AChEIs.
- Of patients with MCI, 49.9% were receiving donepezil, 6.3% galantamine, 6.2% rivastigmine oral, 15.0% rivastigmine patch, and 27.7% received memantine.
- Of patients with mild dementia due to AD, 57.1% were receiving donepezil; 5.9% galantamine; 10.1% rivastigmine oral; 14.6% rivastigmine patch, and 21.8% received memantine.
- Slowing disease progression on cognitive and functional outcomes is the key reason physicians choose their patients' current therapy (83.3% of patients), regardless of disease severity, although these treatments are not indicated for it[1]. However, results varied by disease severity for the other most common reasons for current therapy choice (Figure 2).
- Only specialists (N=428) were asked to indicate the features of new DMTs they expect and would like most, due to their expertise on AD (Figure 1).

Figure 1. Key attributes specialists would expect and most like for new disease-modifying therapies.

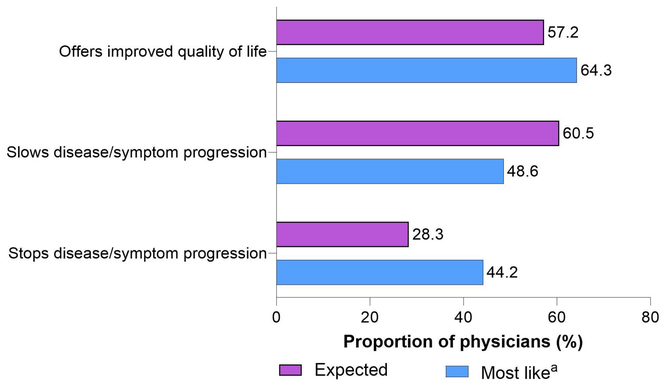
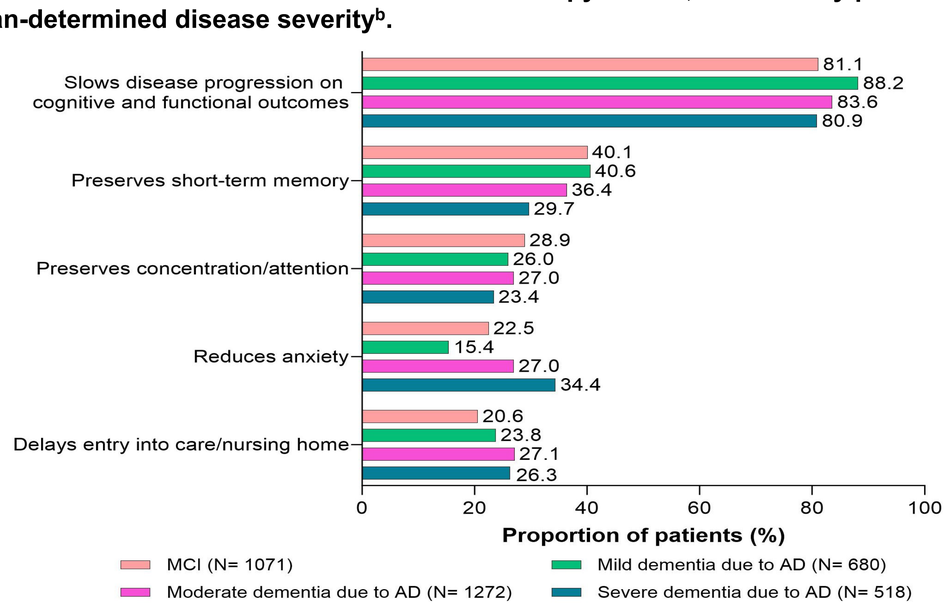


Figure 2. Five most common reasons for current therapy choice, stratified by patient's physician-determined disease severity[b].



Limitations

- The DSP is based on a pseudo-random sampling of physicians or patients. While minimal inclusion criteria governed the selection of the participating physicians, participation is influenced by willingness to complete the survey. Patients were actively consulting, which may limit the generalizability of the results to all patients with AD.

Abbreviations: AChEIs, acetylcholinesterase inhibitors; AD, Alzheimer's disease; DMTs, disease-modifying therapies; DSP, Disease Specific Programme™; IQR, interquartile range; MCI, mild cognitive impairment; med, median n, number; NMDA, N-methyl-D-aspartate; PCP, primary care physicians; SD, standard deviation.
[a] Multiple-choice question, maximum 5 choices. [b] Multiple choice question, no maximum choices.

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