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Enclosure:

- POSTER: Porsteinsson A, Chumki S, Palma A et al. Presented at Alzheimer's Association International Conference (AAIC) , July 27-31, 2025, Toronto, Canada

Efficacy of brexpiprazole on caregiver-identified bothersome agitation symptoms that influence the decision to transfer to long-term care: a 24-week *post hoc* analysis of patients with dementia due to Alzheimer's disease

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Wednesday-849

Introduction

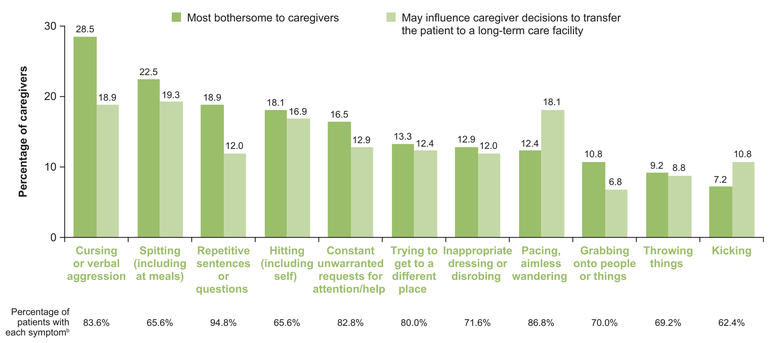
- Patients with Alzheimer's dementia can experience a wide range of bothersome agitation symptoms.[1-3]
- The presence of bothersome agitation symptoms may influence caregiver decisions to transfer their patient to a long-term care facility.[3] Agitation in dementia is associated with increased hospitalizations, and higher healthcare costs.[4]
- From the caregiver's perspective, any change in the frequency of agitation symptoms is meaningful.[2]
- Agitation symptoms may result from dysfunction in noradrenergic, serotonergic, and dopaminergic neurotransmitter systems.[5] Brexpiprazole is an atypical antipsychotic with activity in these three systems.[6]
- Brexpiprazole is approved in the US,[7] Canada,[8] and other regions for the treatment of agitation associated with dementia due to Alzheimer's disease. In Phase 3 trials, brexpiprazole showed reduction in the frequency of agitation symptoms over 12 weeks,[9,10] with continued improvement up to 24 weeks.[11]
- This *post hoc* analysis explored effects of brexpiprazole on individual agitation symptoms over 24 weeks, focusing on caregiver-identified bothersome agitation symptoms, and those that may influence the decision to transfer to long-term care.

Methods

Caregiver survey (previously reported)[3]

- In a survey, 250 caregivers indicated how often different agitation behaviors occurred, based on items of the Cohen-Mansfield Agitation Inventory (CMAI).[3]
- Caregivers were also asked "Which of the care recipient's behavior(s) are the most bothersome to you?" and "Which of the care recipient's behavior(s) are the most likely to make you consider transferring the care recipient to a long-term care facility where additional care would be available?" For each question, up to three behaviors could be selected from a list.
- The present *post hoc* analysis focuses on the effect of brexpiprazole on agitation symptoms considered "most bothersome" to caregivers, and associated with caregiver decisions to transfer the patient to a long-term care facility, as identified in the survey (Figure 1).[3]

Figure 1: Agitation symptoms most bothersome to caregivers (data previously reported)[a,3]



n=250 caregivers

[a]Figure depicts the top 10 agitation symptoms considered "most bothersome" to caregivers, and the top 10 that influence caregiver decisions to transfer patients to long-term care (11 symptoms in total due to overlap); [b]the percentage of patients in whom the behavior was observed (i.e., Cohen-Mansfield Agitation Inventory [CMAI] item score ≥2)

Sample

- Data were included for patients who received brexpiprazole 2 or 3 mg/day in a Phase 3, 12-week, fixed-dose, randomized, placebo-controlled trial (ClinicalTrials.gov: NCT03548584 [Trial 213]) and who continued to receive brexpiprazole in a 12-week, single-arm, active-treatment extension trial (NCT03594123 [Trial 182]). Specifically, participants with a CMAI assessment at baseline of Trial 213, and at any post-baseline visit of Trial 182, were analyzed.
- Data were therefore available for up to 24 weeks' treatment with brexpiprazole.
- ***For additional trial design information, please scan the QR code.***

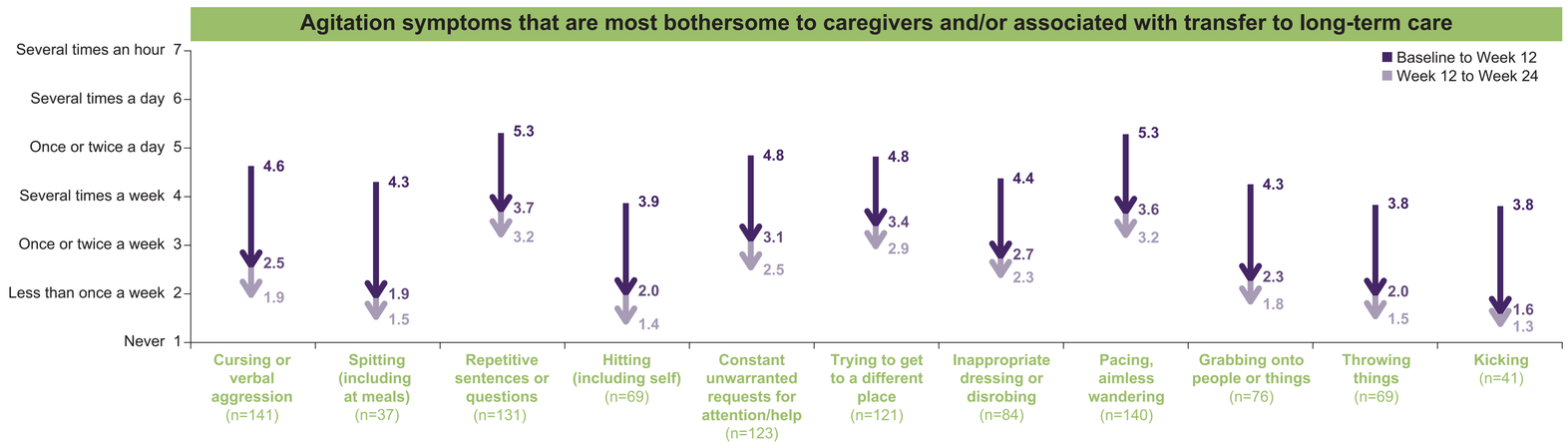
Outcomes

- Agitation symptom frequency was evaluated using the CMAI, which comprises 29 items (reflecting 29 individual agitation symptoms) each scored from 1 (never occurs) to 7 (occurs a few times an hour).[12]
- This analysis focuses on subgroups of patients who experienced a particular agitation symptom at least weekly at baseline (CMAI item score ≥3).

Results

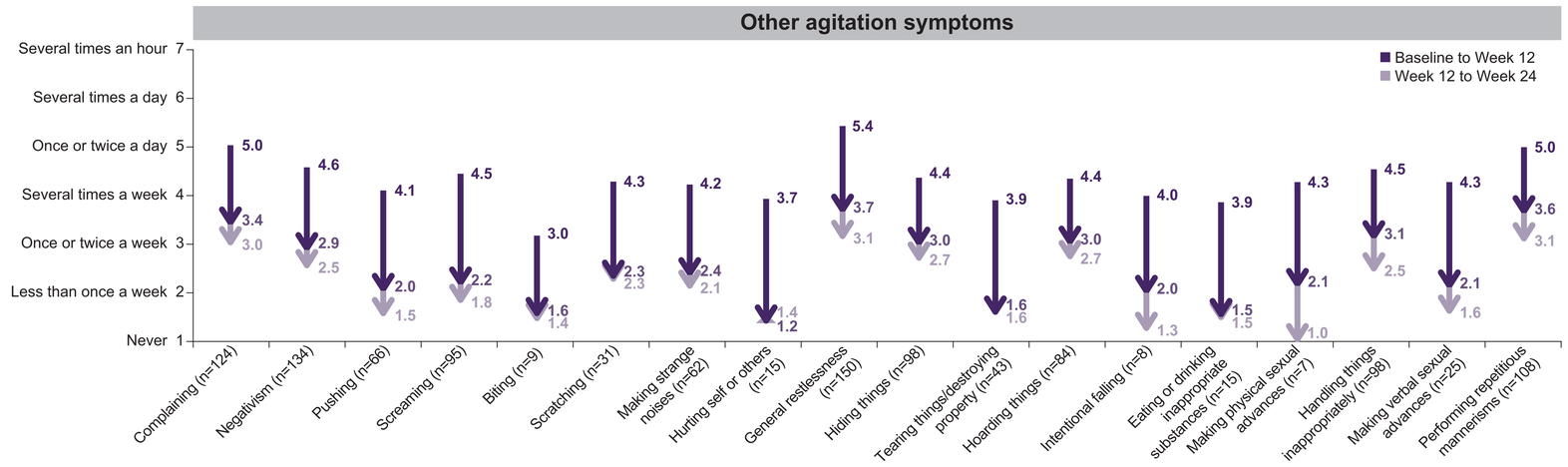
- Overall, 159 patients treated with brexpiprazole were eligible for analysis.
- Agitation symptoms considered "most bothersome" to caregivers, and/or that influence caregiver decisions to transfer patients to long-term care, reduced in frequency from baseline to Week 12, as measured by CMAI item scores. Further numerical improvements were observed from Week 12 to Week 24 (Figure 2).
- All other agitation symptoms also reduced in frequency from baseline to Week 12, and generally improved further or stabilized from Week 12 to Week 24 (Figure 3).
- Improvements were observed in non-aggressive behaviors (e.g., pacing and aimless wandering; trying to get to a different place; repetitive sentences or questions) as well as aggressive behaviors (e.g., cursing or verbal aggression) (Figure 2 & 3).

Figure 2: Change in agitation symptom frequency (CMAI item scores) over 24 weeks – symptoms most bothersome to caregivers



Agitation symptoms are arranged in descending order of "most bothersome" from the previous caregiver survey[3]
Dark arrows: the start represents baseline of Trial 213, and the point represents Week 12 of Trial 213; pale arrows: the start represents Week 12 of Trial 213, and the point represents Week 24 (i.e., Week 12 of Trial 182)
n-values indicate the number of patients in this sample who experienced each symptom at least weekly (CMAI item score ≥3) at baseline of Trial 213
CMAI=Cohen-Mansfield Agitation Inventory

Figure 3: Change in agitation symptom frequency (CMAI item scores) over 24 weeks – other agitation symptoms



Agitation symptoms are arranged in descending order of "most bothersome" from the previous caregiver survey[3]
Dark arrows: the start represents baseline of Trial 213, and the point represents Week 12 of Trial 213; pale arrows: the start represents Week 12 of Trial 213, and the point represents Week 24 (i.e., Week 12 of Trial 182)
n-values indicate the number of patients in this sample who experienced each symptom at least weekly (CMAI item score ≥3) at baseline of Trial 213
CMAI=Cohen-Mansfield Agitation Inventory

Conclusions

- Over 24 weeks, brexpiprazole 2 or 3 mg/day was associated with improvement in all studied agitation symptoms – non-aggressive (e.g., pacing and aimless wandering, or trying to get to a different place), and aggressive (e.g., cursing or verbal aggression).
- All behaviors that are most bothersome to caregivers, and that influence caregiver decisions to transfer patients to long-term care, showed continued improvements over 24 weeks.
- Overall, improvement in agitation symptoms with brexpiprazole may improve the caregiver experience, and may ultimately enable patients to remain at home for longer.

Please also visit posters **Monday-519** (brexpiprazole NNT and NNH analysis) and **Wednesday-853** (brexpiprazole efficacy and safety over 24 weeks)

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Acknowledgements

This work was supported by Otsuka Pharmaceutical Development & Commercialization Inc. (Princeton, NJ, USA) and H. Lundbeck A/S (Valby, Copenhagen, Denmark).

Medical writing support was provided by Cambridge (a division of Prime, Knutsford, UK), funded by Otsuka Pharmaceutical Development & Commercialization Inc. (Princeton, NJ, USA) and H. Lundbeck A/S (Valby, Copenhagen, Denmark).

The authors thank the patients and caregivers who were involved in these trials.

Disclosures

Anton P. Porsteinsson has received personal fees from Acadia Pharmaceuticals, Athira, BMS, Cognition Therapeutics, Eisai, IQVIA, Lundbeck, MapLight Therapeutics, Novartis, Novo Nordisk, ONO Pharmaceuticals, Otsuka, WCG, WebMD, and Xenon, and grants to institution from Athira, Biogen, Cassava, Eisai, Eli Lilly, Genentech/Roche, Vaccinex, NIA, NIMH, and DOD. He is a member of the Scientific Advisory Board of Alzheon, Athira, Cognition Therapeutics, and Oligomerix.

Sanjeda R. Chumki and Anton M. Palma are full-time employees of Otsuka Pharmaceutical Development & Commercialization Inc.

David Wang is a full-time employee of Lundbeck LLC.

Pedro Such is a full-time employee of H. Lundbeck A/S.

C. Brendan Montano has received consulting fees from AbbVie, Acadia Pharmaceuticals, Alkermes, Arbor, Eisai, Neos, Novo Nordisk, Otsuka, Sunovion, Supernus, and Takeda, and has received payment/honoraria from AbbVie, Arbor, Eisai, Otsuka, and Takeda.

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