

Sentiment analysis of social media responses to the approval of lecanemab for the treatment of Alzheimer's disease in Japan

Journal of Alzheimer's

Disease Reports

Volume 9: 1–7

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DOI: 10.1177/25424823241307639

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Abstract

Lecanemab, an anti-amyloid therapy for early Alzheimer's disease, received approval by the FDA and Japan in 2023. Public response on social media was scrutinized, aiming to obtain insights into communication and treatment development. For 478 posts from X and Facebook, their sentiments on efficacy, safety, societal significance, and overall lecanemab impression were assessed by GPT-4 and the authors. Results indicated impressions were 43.7% negative, 26.6% neutral, and 29.7% positive. Social significance concerns dominated negative views. Specific attitude patterns were observed in the overall impression to lecanemab's approval. These insights highlight the need for targeted communication and research on anti-amyloid therapies.

Keywords

Alzheimer's disease, large language model, lecanemab, sentiment analysis, social media

Received: 14 May 2024; accepted: 26 November 2024

Introduction

Lecanemab (LeqembiTM), an anti-amyloid therapy for mild cognitive impairment and the mild dementia stage of Alzheimer's disease (AD),¹ received full FDA approval and Medicare coverage in July 2023.² In Japan, this therapeutic subsequently received the endorsement of the Minister and Ministry of Health, Labor, and Welfare (MHLW) in September 2023, marking significant news in Japan.

Japan's health system, which is largely tax and insurance-funded, is challenged by the aging population and rising healthcare costs.^{3,4} Moreover, the high acquisition cost of lecanemab (e.g., \$26,500/year in the U.S. and approximately \$20,000/year in Japan)⁵ and high AD prevalence among older individuals⁶ fuel debate on its societal value considering national budget impacts and its low degree of efficacy demonstrated in earlier trials.¹

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Accurate drug information is critical to ensure appropriate use and further development. Misconceptions, whether positive or negative, can lead to misuse, potentially harming patient welfare.⁷ Thus, understanding the public's perception on lecanemab's approval could help to guide future communications in the development and dissemination of disease-modifying therapy drugs, not limited to lecanemab. For example, it could inform what types of explanations may be especially needed in clinical practice of lecanemab treatment and in ensuring accountability to the public regarding approved drugs and future research and development expenditures.

Social media sentiment analysis can provide insights into public perception,^{8,9} including in the identification of opinions being disseminated on social media. Social media is characterized by its ability to enable rapid communication and shape public opinions.¹⁰ In this study, we aimed to analyze social media responses to the approval of lecanemab in Japan, particularly focusing on X (formerly Twitter) and Facebook.

Methods

About the study

This retrospective study analyzed public posts written in Japanese on X (formerly Twitter) (<https://twitter.com/>) and Facebook (<https://www.facebook.com/>), two major text-based social networking services (SNS) with a 20–30% usage rate among individuals in their 50s and 60s in Japan in 2021.¹¹ No informed consent was required, as this study used publicly available data.

Data acquisition

We focused on two key events in 2023: the MHLW's expert panel's agreement to approve lecanemab on August 21 (the first event), and the Minister's official approval on September 25 (the second event). Posts submitted within one week of these events containing the Japanese words corresponding to "lecanemab" or "Leqembi" were collected. The one-week time window was determined because of the rapid decline in the number of daily posts within a few days following each event date (Supplemental Figure 1A and B). The web-searches to identify response regarding the first and second events were performed on August 30 and October 4, 2023, respectively. News media posts were excluded.

Posts by medical doctors were identified as the posters' attribution based on the user profile page, and we examined their characteristics. Although SNS profile may not always be reliable, we nevertheless referred to this information, pursuant to the Article 18 of the Medical Practitioners Act, which prohibits the use of the title of medical practitioner by any person without a medical license.

Data formatting

Hashtags, URLs, and quoted news article titles were removed from the collected posts. Posts lacking substantive text after removal were discarded.

Text analysis

GPT-4 (<https://chat.openai.com>) was applied for text evaluation in early October 2023. GPT-4 is known to accurately handle text-based tasks, including text rating,¹² and is reportedly capable of passing medical licensing examinations^{13,14} and bar exams.¹⁵ The version used was trained up to September 2021.

Based on the entered Japanese-written prompt as instructions, for each individual post, GPT-4 rated the submitters' attitudes on the four aspects of lecanemab: (#1) drug efficacy, (#2) drug side effects, (#3) social significance, and (#4) overall impression. We defined the societal significance of the drug primarily in terms of its impact on the national health insurance budget. The prompt included five sections: (I) prerequisite of AD pathology and anti-amyloid therapy background, (II) GPT-4's role as a clinician or researcher, (III) task instructions, (IV) response language/format, and (V) text presentation for evaluation. For aspects #1–3, rating results were classified as negative / neutral / positive / not referred, and for aspect #4, rating results were classified as negative / neutral / positive. Table 1 includes an English translation of the entered prompt. Outputs were refreshed after each response to avoid bias from previous results.

Ratings by GPT-4 were validated against the authors' evaluations using kappa coefficients¹⁶ to examine inter-rater reliability, by the R package *{psych}*. Kappa values are interpreted as follows: ≤ 0.2 slight reliability, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, and > 0.8 almost perfect reliability, respectively.^{16,17}

Analysis

GPT-4 ratings were summarized and examined via Fisher's exact test or Chi-squared test. Kappa coefficients assessed the degree of correspondence between attitudes towards drug aspects (#1–3) and overall impression (#4).

We also conducted a logistic regression analysis to evaluate the contribution of poster attribution and the type of platform to the negative impression in each aspect, using the following model:

$$\ln(\text{Odds of negative impression in aspect } \#k) = \beta_1 + \beta_2 \text{Platform} + \beta_3 Dr,$$

where *Dr* refers to whether the posting is made by medical doctor, and *Platform* denotes the place and timing of the post (i.e., posts on X in August, X in September, and Facebook).

Table 1. English translations of search prompts.

(I) Prerequisites	Alzheimer's disease (AD), which accounts for 60–70% of dementia cases, develops as the result of the accumulation of amyloid beta, an abnormal protein, in the brain, which is an upstream initiator of dysfunction and cell death of brain neurons, which occurs through multiple processes including tau protein accumulation and synaptic damage. This leads to the onset of cognitive symptoms and brain atrophy. Antibody drugs (anti-A β monoclonal antibody) that aim to eliminate amyloid- β include aducanumab and lecanemab. Of these, lecanemab (Leqembi TM), which is being developed by the pharmaceutical companies Eisai and Biogen, met its primary endpoint of slowing the progression of cognitive decline in a Phase III clinical trial (Clarity-AD trial) in patients in the mild cognitive impairment stage of AD to mild AD dementia in 2023. The characteristic side effects of anti-A β antibody drugs, such as mild edema of the brain and microhemorrhages, termed amyloid-related imaging abnormality (ARIA), are observed in approximately 10–20% of patients. Although ARIA symptoms are infrequent and generally mild, there have been rare reports of serious side effects. In the U.S., the acquisition cost of lecanemab is estimated to be about 4 million Japanese Yen per year, and is anticipated to be similarly high in Japan. Given the high prevalence of AD among the older population, there is a concern that the medical costs of insuring this drug will be enormous, placing an undue burden on national finances. In the U.S., lecanemab was officially approved as a treatment for AD by the FDA in July 2023, and is to be covered by Medicare. In Japan, a panel of experts of the Ministry of Health, Labor and Welfare (MHLW) approved the domestic production and marketing of lecanemab on August 21, 2023, and subsequently, lecanemab (product name Leqembi) was officially approved by the Minister of the MHLW on September 25 of the same year.
(II) Role	You are a Japanese-speaking physician or academic researcher and have certain knowledge of the above (I) Prerequisites.
(III) Task	Below are the numbered tweets/posts responding to the MHLW's approval of lecanemab (Leqembi) on August 21 and September 25, 2023. For each, indicate your estimation about the submitters' attitude (negative/neutral/positive) towards lecanemab's: (1) efficacy, (2) side effects, (3) social impact, and (4) overall impression. For the aspects (1), (2), and (3), if an assessment is not applicable, reply N/A.
(IV) Constraints	The format of your response should be one line for each tweet, stating (1) through (4) in that order. The example of format is as follows: No. 3, (1) - efficacy, positive, (2) - side effect, negative, (3) - significance, N/A, (4) - overall, neutral.
(V) Input	(5–10 posts as input, 1 post per line).

Results

In total, 478 eligible posts (446 X posts and 32 Facebook posts) were included in the analysis, among which 226 X posts and 30 Facebook posts were submitted in the first period (August 21–27, 2023), and 188 X posts and 2 Facebook posts were submitted in the second period (September 25–October 1, 2023). Approximately 90% of the submitters posted only 2 or fewer eligible posts. Approximately 16% among all posts were considered to be posted by medical doctors.

Evaluation by GPT-4 revealed that the overall impression (aspect #4) in these posts was negative in 43.7%, neutral in 26.6%, and positive in 29.7% of the posts (Figure 1(A)). Among aspects (#1) - (#3), social significance was most frequently negatively referred to (in 18.4% of posts on efficacy, 11.7% on adverse effects, and 33.1% on social significance, respectively). Adverse events were not referred to in most of the posts (83.5%). These ratings by GPT-4 showed substantial to almost perfect alignment with the authors' evaluations (kappa coefficient [κ] = 0.719 (95% confidence interval (CI): 0.533 ~ 0.905) for efficacy, κ = 1.000 (95% CI: 1.000 ~ 1.000) for adverse effects, κ = 0.602 (95% CI: 0.404 ~ 0.801) for social significance, and κ = 0.706 (95% CI: 0.533 ~ 0.878)) for overall impression in 40 randomly selected samples.

When stratified by the period and type of SNS (Figure 1(B)-(D)), negative attitudes on overall impression were most frequently observed in X of the second period (47.4%) (Figure 1(C)), followed by X of the first period (42.2%) (Figure 1(B)), and Facebook of both periods (21.9%) (Figure 1(D)); the proportion of attitudes on the overall impression (#4) by these subgroups barely differed by the submitted SNS (X versus Facebook, p = 0.048 in Fisher's exact test). When considering both the posting platform and the posters' attribution to the overall impression (#4) (Supplemental Figure 1C), posts on Facebook (in August and September) were less likely to be negative compared to the posts on X in August. However, posts on X in September showed no significant difference in their likelihood of expressing a negative overall impression.

Next, we visualized the distribution of attitudes on aspects #1~#3 based on the results of overall impression (Figure 2), to examine attitude patterns. Attitudes on efficacy and social significance largely aligned with the direction of overall impressions: a negative attitude on efficacy (Figure 2(A)) was observed largely in conjunction with the overall impression of the same attitude (κ = 0.441), whereas a negative attitude on social significance was observed largely simultaneously with a negative overall impression (κ = 0.698). Positive attitudes on efficacy or social significance were observed largely simultaneously with the positive

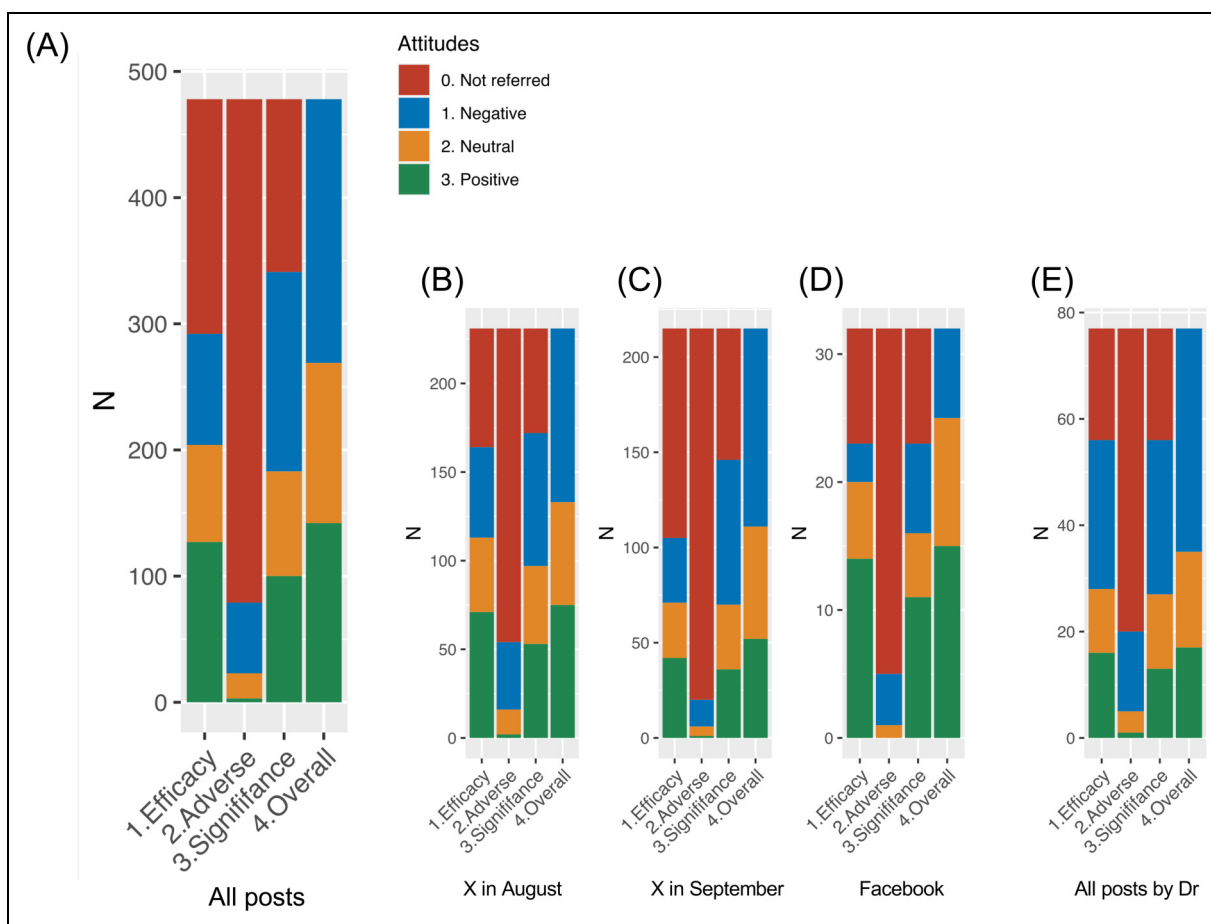


Figure 1. Evaluation of aspects #1–4 by GPT-4.

Evaluation by GPT-4 revealed that overall impression (aspect #4) in these posts was negative in 43.7%, neutral in 26.6%, and positive in 29.7% of the posts (A). Among aspects (#1) - (#3), social significance was most frequently negatively referred to (in 18.4% of posts on efficacy, 11.7% on adverse effects, and 33.1% on social significance). Adverse events were not referred to in most of the posts (83.5%). When stratified by the period and type of SNS (B-D), negative attitudes on overall impression were most frequently observed in X of the second period (47.4%) (C), followed by X of the first period (42.2%) (B), and Facebook of both periods (21.9%) (D).

overall impression ($\kappa=0.695$ and 0.671 , respectively) (Figure 2(C)). However, attitudes on adverse effect did not align with the direction of overall impressions, whichever negative or positive ($\kappa<0.2$) (Figure 2(A)-(C)). Neutral attitudes on either aspect were also not simultaneously observed with the neutral overall impression ($\kappa<0.4$) (Figure 2(B)).

Finally, posts submitted by medical doctors (Figure 1(E)) were more likely to show negative overall impression to lecanemab's approval (odds ratio = 1.679, 95%CI: 1.020~2.821). Additionally, when simultaneously considering the posting platform and the posters' attribution, posts by medical doctors were more likely to show negative impression in terms of efficacy (#1) and overall impression (#4) (Supplemental Figure 1D).

Discussion

In this study, we conducted a sentiment analysis on posts submitted to text-based SNS sites (X and Facebook), in

order to characterize the prevailing opinions regarding the approval of lecanemab in social networking spaces in Japan. As a result, we identified that the majority (approximately 44%) of posts referring to lecanemab's approval exhibited a negative attitude towards it, with some specific patterns of attitudes identified in the four aspects of the content, each with varied points of focus. This study highlights the diverse social media perspectives on lecanemab's approval, guiding future information provision and research direction for anti-amyloid therapies: it could inform what types of explanations may be especially needed in clinical practice of lecanemab treatment and in ensuring accountability to the public regarding approved drugs and future research and development expenditures.

This study comprised a survey on social media responses, which is one of its characteristics. Unlike traditional opinion surveys—whichever they are web-based, paper-based, or in-person—a review survey on social media posts might have some advantages that it enables

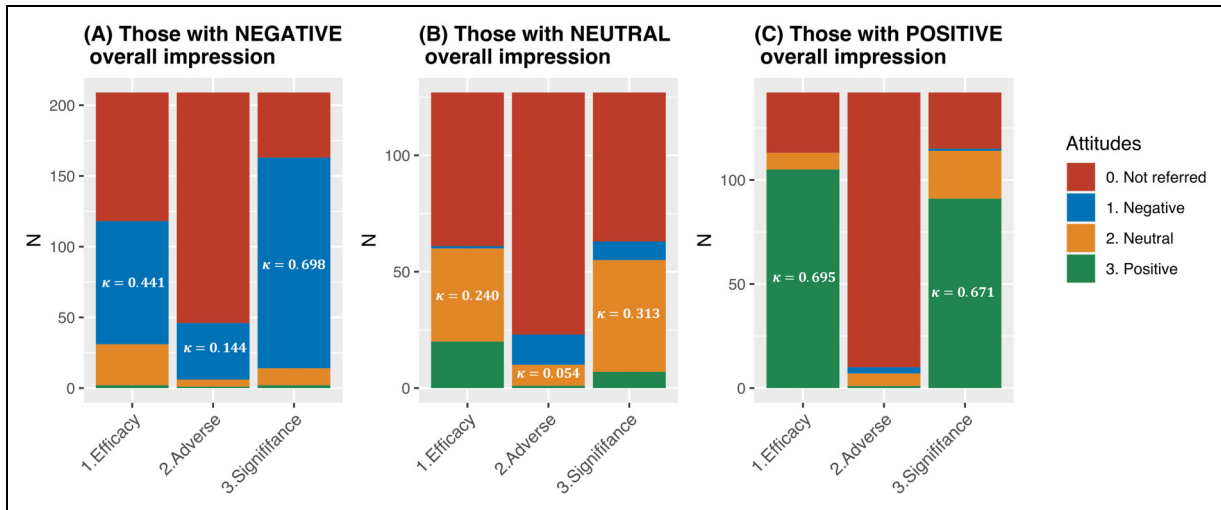


Figure 2. Evaluation aspects #1–3 by GPT-4, depending on the result for aspect #4.

We firstly examined patterns in attitude. Attitudes on efficacy and social significance largely aligned with the direction of overall impressions: negative attitude on efficacy (A) was generally observed simultaneously with overall impression of the same attitude ($\kappa = 0.441$), and a negative attitude on social significance was observed largely simultaneously with the negative overall impression ($\kappa = 0.698$). Positive attitudes on efficacy or social significance were observed largely in conjunction with the positive overall impression ($\kappa = 0.695$ and 0.671 , respectively) (C). However, attitudes on adverse effect did not align with the direction of overall impressions, either negative or positive ($\kappa < 0.2$) (A–C). Neutral attitudes on either aspect were also not simultaneously observed with the neutral overall impression ($\kappa < 0.4$) (B).

researchers to possess insights into public perception without delay, helping them shape hypothesis to examine by conventional but more robust methods of opinion survey. Meanwhile, it should be noted that current study design may have introduced some inherent disadvantages. For example, the number of SNS users in the total population is not necessarily sufficient to represent the entire population, especially older individuals, as only approximately 20–30% of people aged 50–60 in Japan were on SNS in 2021,¹¹ and the number of posters is further limited. It is also reported that more than half of frequent Japanese X users are in their 20s and 30s, and approximately half of frequent Japanese X users being single or living with their parents.¹⁸ Individuals with such profiles are less likely to have direct concern about AD for themselves or their parents. Meanwhile, it is reported that Facebook users are mostly in their 40s or older,¹⁸ which may partly explain why Facebook users were less negative about the approval of lecanemab, as they would have more direct concerns about developing AD or dementia for themselves or their relatives. Additionally, it is known that some SNS users tend to exaggerate their posts.^{19,20} Results on the current attitudes (positive/neutral/negative) towards the approval of lecanemab thus cannot be equated with the true public perception, which should be estimated based on conventional opinion polls. In other words, the proportion of different attitudes as identified in this study cannot be interpreted as representative of proportions reflected by the perception of the entire public. Nevertheless, social media survey is

still considered useful, as long as it is applied to obtain a sample of opinion patterns, although it may not be exhaustive. In the future, questionnaire surveys applied to a diverse population²¹ may be useful in validating the current results.

In the examined posts, we identified several specific patterns of attitudes from which we could infer some public perceptions. As such, these results help us to ascertain what kind of information is sought and should be provided, as well as what kind of evidence needs to be built. For example, social significance was most frequently negatively referred to in combination with the negative overall impression, which suggests this aspect may have been the prevailing reason for the submitters to have a negative overall impression compared to efficacy, or that it may have had a higher profile than efficacy for most people. This might be due to the growing number of individuals with dementia in Japan (e.g., an estimated 13% of the elderly population in 2025²²), the increasing burden on the national health insurance budget, and the anticipated rise in health insurance premiums for residents of Japan. This implies the practical societal significance or meaning for all patients must be demonstrated over the medical efficacy for individual patients.

Additionally, efficacy and social significance were positively referred to at a similar level as the positive overall impression (Figure 2(C)), suggesting they are both similarly important as the reason for the submitters to have a positive overall impression. Most posters did not present an attitude, even neutral, on adverse effects. This means people with

favorable attitudes to lecanemab may be less topical or less interested regarding its adverse effects. Otherwise, this may simply have occurred because of the posters' limited knowledge about the adverse effect of lecanemab, or because of the lower priority of the aspect of the adverse effect, as X places a character limit of 140 Japanese characters on posts, unless users have the paid version of X. Whatever the reason, prior to treatment, such patients will need to be clearly informed of the major safety concerns of anti-amyloid therapies such as lecanemab, including amyloid related imaging abnormalities, which can be serious in some very rare cases.²

Another feature of this study is that we used GPT4 to rate posts. This method is advantageous as it can help save authors' labor, maintain constant rating criteria, and prevent subtle fluctuations in rating criteria along with the processing of many texts. Although there is room for improvement, the rating performance was indeed acceptable, showing a good correspondence of the selected samples with the authors' rating results ($\kappa > 0.6$). Such strength of using large language models (LLM) for coding SNS posts will be better demonstrated in studies with large-scale data.

Medical doctors have made significantly much more of negative posts about the efficacy of lecanemab (#1) and its approval overall (#4), while no notable difference was observed between doctors and non-doctors in terms of other aspects (#2, #3). Conversely, non-doctors have posted fewer negative comments on lecanemab's efficacy and overall impression. These observations align line with our recent online survey in late 2023, where non-clinicians had stronger expectations regarding the efficacy of lecanemab compared to medical specialists in the field of dementia treatment.²³ It remains uncertain whether these trends of doctors' perceptions, as represented in the posts, will influence the prescription behavior of lecanemab for eligible AD patients, or the reverse. Similarly, it is unclear whether non-doctors' perceptions will affect dementia patients' willingness to receive lecanemab treatment, and vice versa.

Our study has some other limitations in addition to those already mentioned. For example, we could not examine all of the relevant posts on SNS, especially from X, as we only examined posts which included the Japanese words for lecanemab or its tradename. As such, successive posts following the eligible posts were not analyzed. In addition, in relation to this, the fact that a particular content is not mentioned in a post does not mean that it has not been taken into account by the submitter. Based on the limitation of words or characters in each post, the content may be simply less prioritized for reference. This made the interpretation of the obtained results less straightforward. Furthermore, only a few earlier studies have used LLM such as GPT-4 to code each text,²⁴ meaning that the methodology has not been properly evaluated. Potential biases specific to the LLM used (in this case, GPT-4) should also be

considered. Comparing results with other available LLMs, such as Gemini or Claude3, may help address these limitations of the current study. Finally, the small number of posts on Facebook prevented us from robustly examining the difference between posts on Facebook and posts on X.

In conclusion, the present study suggests several specific patterns of social media responses to lecanemab's approval, with a varied point of focus. These findings can guide future information provision and research direction for anti-amyloid therapies.

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Statements and declarations

Author contributions

Kenichiro Sato (Conceptualization; Data curation; Formal analysis; Writing – original draft); Yoshiaki Niimi (Conceptualization; Writing – review & editing); Ryoko Ihara (Writing – review & editing); Atsushi Iwata (Writing – review & editing); Kiyotaka Nemoto (Writing – review & editing); Tetsuaki Arai (Writing – review & editing); Shinji Higashi (Writing – review & editing); Ataru Igarashi (Writing – review & editing); Kensaku Kasuga (Writing – review & editing); Takeshi Iwatsubo (Supervision).

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by AMED Grant Numbers JP23dk0207048 (T.I) and JP23dk0207054 (Y.N), and MHLW Special Research Program Grant Number JPMH23CA2008 (T.A). The sponsors had no role in the design and conduct of the study; collection, analysis, and interpretation of data; preparation of the manuscript; or review or approval of the manuscript.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data availability

The data supporting the findings of this study are openly available from X and Facebook contents.

Supplemental material

Supplemental material for this article is available online.

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