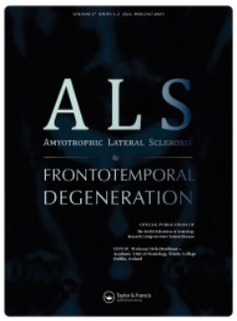

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RESEARCH ARTICLE

Dextromethorphan/quinidine (DMQ) for reducing bulbar symptoms in amyotrophic lateral sclerosis – assessment of treatment experience in a multicenter study

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Abstract

Background: In amyotrophic lateral sclerosis (ALS), dextromethorphan/quinidine (DMQ) has been reported to reduce bulbar symptoms, including dysarthria and dysphagia. However, data on patients' perceptions of DMQ treatment are limited. *Methods*: Data on DMQ treatment were collected from 1065 ALS patients treated at 13 ALS centers between 10–2015 and 06–2025. Patient-reported outcome measures (PROM) of 179 participants were remotely assessed via the "ALS App". PROM included the self-explanatory version of the ALS Functional Rating Scale (ALSFRS-R-SE), the Net Promoter Score (NPS); and Treatment Satisfaction Questionnaire for Medication (TSQM-9). *Results*: Mean disease

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duration was 29.3 months (SD 38.1). ALS progression before treatment was 0.82 points/month (ALSFRS-R). Mean DMQ treatment duration was 8.4 months (SD 10.8), including 35.2% ($n = 374$) of shorter (<3 months), 35.3% ($n = 375$) of longer (3–9 months), and 29.5% ($n = 313$) of very long DMQ treatment (>9 months). Patients' recommendation ($n = 178$) was positive (NPS: +23) with higher scores after very long DMQ treatment (NPS +37) compared to longer (NPS +15) and shorter treatment (NPS +7.5), respectively. TSQM-9 scores ($n = 163$) demonstrated high satisfaction for effectiveness 60.0 (SD 25.9), convenience 73.8 (SD 18.2), and global satisfaction 63.4 (SD 29.8). *Interpretation*: The positive perception in PROM underscores the value of DMQ as an individualized treatment option for bulbar symptoms in ALS. However, shortage of clinical data, online assessment, and selection biases are among the limitations of this study that need to be addressed in further investigations.

Keywords: *Amyotrophic lateral sclerosis, dextromethorphan/quinidine (DMQ), bulbar symptoms, dysarthria, dysphagia, patient-reported outcomes*

Background

Amyotrophic lateral sclerosis (ALS) is a severe and progressive neurodegenerative disorder of the upper and lower motor neurons (1,2). In ALS, about 30% of the patients exhibit bulbar symptoms at onset, including dysarthria, dysphagia, and sialorrhea. Moreover, most patients develop bulbar impairments as the disease progresses (3–5). The treatment of bulbar dysfunction is a major challenge in ALS care. Anticholinergic drugs (e.g. ipratropium bromide) are commonly used to reduce sialorrhea in ALS patients (6). However, effective drug therapy options for managing dysarthria and dysphagia in ALS are currently limited. Dextromethorphan/quinidine (DMQ) has been proposed as a symptom-reducing treatment for dysarthria and dysphagia (7–9). The pharmaceutical compound DMQ is a combination medication of dextromethorphan (DM), an uncompetitive N-methyl-D-aspartate (NMDA) glutamate receptor antagonist, a sigma-1 receptor agonist, and a serotonin and norepinephrine reuptake inhibitor (10), and quinidine (Q), a cytochrome P450 2D6 inhibitor that is co-administered to increase DM bioavailability (11). Nuedexta (20 mg DM/10 mg Q) was approved by the Food and Drug Administration (FDA) in 2011 for the treatment of pseudobulbar affect (PBA) associated with ALS or other neurologic disorders (10,12). Beyond its effects on PBA, studies have found that DMQ moderately improves bulbar deficits, including dysarthria, dysphagia, and hypersalivation (13). In 2017, Smith et al. reported that DMQ treatment significantly improved the bulbar subscore (questions 1–3) of the ALS Functional Rating Scale (ALSFRS-R) (7). This study further supports the beneficial effects of DMQ on bulbar motor function and speech. Subsequent findings in 2018 also indicated quantifiable improvements in speech (9). A recent 2023 study further confirmed the positive effects of DMQ on bulbar function, demonstrating a significant increase in the bulbar subscore of the ALSFRS-R, and confirming positive outcomes in speech and swallowing (8).

DMQ is not commercially available as a finished drug in Germany, but it is compounded by specialty pharmacies into a drug formulation. It has been increasingly used in Germany, particularly for its effects on bulbar function in ALS patients (6). Yet, a lack of patient-reported data on perspectives and treatment satisfaction remains. This study therefore aims to: 1) investigate the clinical characteristics of patients receiving DMQ for bulbar symptom control, 2) determine the duration of DMQ medication in clinical practice, 3) explore patients' recommendation of the drug using the Net Promoter Score (NPS), and 4) assess the subjective perception of the drug in terms of the Treatment Satisfaction Questionnaire of Medication (TSQM-9).

Methods

Study design

This study is a secondary use of existing data from a multicenter study, in which clinical, data, the standard of care and PROM data are collected (ClinicalTrials.gov ID NCT05852418). The investigation was reported following the STROBE criteria (14).

Participants

Subjects who participated in the cohort study met the following criteria: 1) diagnosis of ALS (ICD-10 G12.2) according to the Gold Coast criteria (15); 2) presence of dysarthria; 3) treatment with DMQ; 4) participation in an ALS case-management program for medication (6); 5) consent to remote digital assessment using the research platform "APST" or via the "ALS-App" (16–18).

Setting

Secondary use of existing data on DMQ treatment. The study analyzed existing data from APST's "ALS Pharmacy Program", which provides symptom-specific medications via specialized pharmacies, including DMQ formulations (6,16). Data on DMQ usage were collected through the program's platform. Although established in January 2013, the analysis focused on patients on DMQ treatments from October 2015 to June 2025.

Data selection of DMQ treatment for bulbar symptoms. Analysis focused on DMQ's impact on bulbar symptoms such as dysarthria, dysphagia, and sialorrhea. Treatment decisions were made independently of this data analysis, and data related to PBA were excluded from the study.

Assessment of treatment satisfaction. Data on treatment satisfaction were collected via an online survey provided through the "ALS App" (mobile application) or the "APST platform" (desktop) (17).

Data capture

Demographic data, clinical characteristics, medication data, and ALSFRS-R scores were collected on the APST platform (www.ambulanzpartner.de) (16). Survey data from the "ALS App" were collected through this platform.

Variables

Demographic data and clinical characteristics. The following demographic data and clinical characteristics were collected for all participants: age, sex, diagnosis, and disease duration.

ALS functional rating scale - revised (ALSFRS-R) and self-explanatory (ALSFRS-R-SE). The ALSFRS-R is a validated 48-point scale assessing ALS functional impairment, with higher scores indicating better function (19,20). The self-explanatory version (ALSFRS-R-SE), which provides item descriptions and response options, was used remotely via the "ALS App" alongside the DMQ satisfaction survey (18,21). The first ALSFRS-R scores were collected within 6 months prior to DMQ treatment, while the last ALSFRS-R scores were collected at least 1 month post-treatment.

ALS progression rate (ALSPR). ALSPR was measured from the time of onset and by the monthly slope of ALSFRS-R scale points as previously described (18). It was calculated using the following formula: (48 -ALSFRS-R divided by disease duration (months)). A classification of ALSPR of slower (<0.5 ALSFRS-R/month), intermediate (≥ 0.5 and ≤ 1.0 ALSFRS-R/month), and faster ALS progression (> 1.0 ALSFRS-R/month) was applied (22).

Treatment with DMQ

DMQ dosage and administration form. Data on dosage and administration form of DMQ were analyzed (Supplementary file 3).

Duration of DMQ treatment. The duration of DMQ treatment was determined by analyzing the start and end dates of therapy. Three groups were defined based on the length of DMQ therapy: shorter (<3 months), longer (3–9 months), and very long (>9 months).

Net promoter score (NPS)

NPS was used to examine patients' attitudes toward their treatment with DMQ, based on the single question: "How likely is it that you would recommend DMQ to a fellow ALS patient?" Responses ranged from 0 (very unlikely) to 10 (very likely), categorizing patients as "promoters" (scores 9–10), "passives" (scores 7–8), or "detractors" (scores 0–6). NPS is calculated by subtracting the percentage of detractors from the percentage of promoters, yielding a score from +100 to −100 (Supplementary file 1). A positive NPS (>0) indicates a supporting recommendation. An NPS of +50 is considered excellent (23,24).

Treatment satisfaction Questionnaire for medication (TSQM-9)

DMQ treatment satisfaction was assessed using the TSQM-9, a validated nine-item questionnaire covering three dimensions: effectiveness (questions 1–3), convenience (questions 4–6), and global satisfaction (questions 7–9) (25–27). The questions are answered on five- or seven-point scales and converted into scores ranging from 0 to 100, with higher scores indicating greater satisfaction. Score calculation details are provided in Supplementary file 1.

Protocol approvals and registrations

The study protocol was approved by the Ethics Committee of the Charité – Universitätsmedizin Berlin, Germany (EA1/219/15). All participants provided written informed consent.

Data analysis

Descriptive statistics were used for the statistical analysis (frequency in percent, mean, median, standard deviation). Significant differences were determined using the Mann-Whitney U test, with p values reported at a 95% confidence interval. The data were analyzed using SPSS version 29.0.

Results

Sample characteristics

Among the 4562 ALS patients enrolled in the ALS Pharmacy Program between 01/2013 and 06/2025, 1065 patients (23.3%) received DMQ treatment. During the 13-month DMQ satisfaction survey period, 552 patients on active DMQ therapy were invited to participate. Of these, 179 ALS patients (32.4%) completed the online survey assessing their DMQ treatment experience (Figure 1).

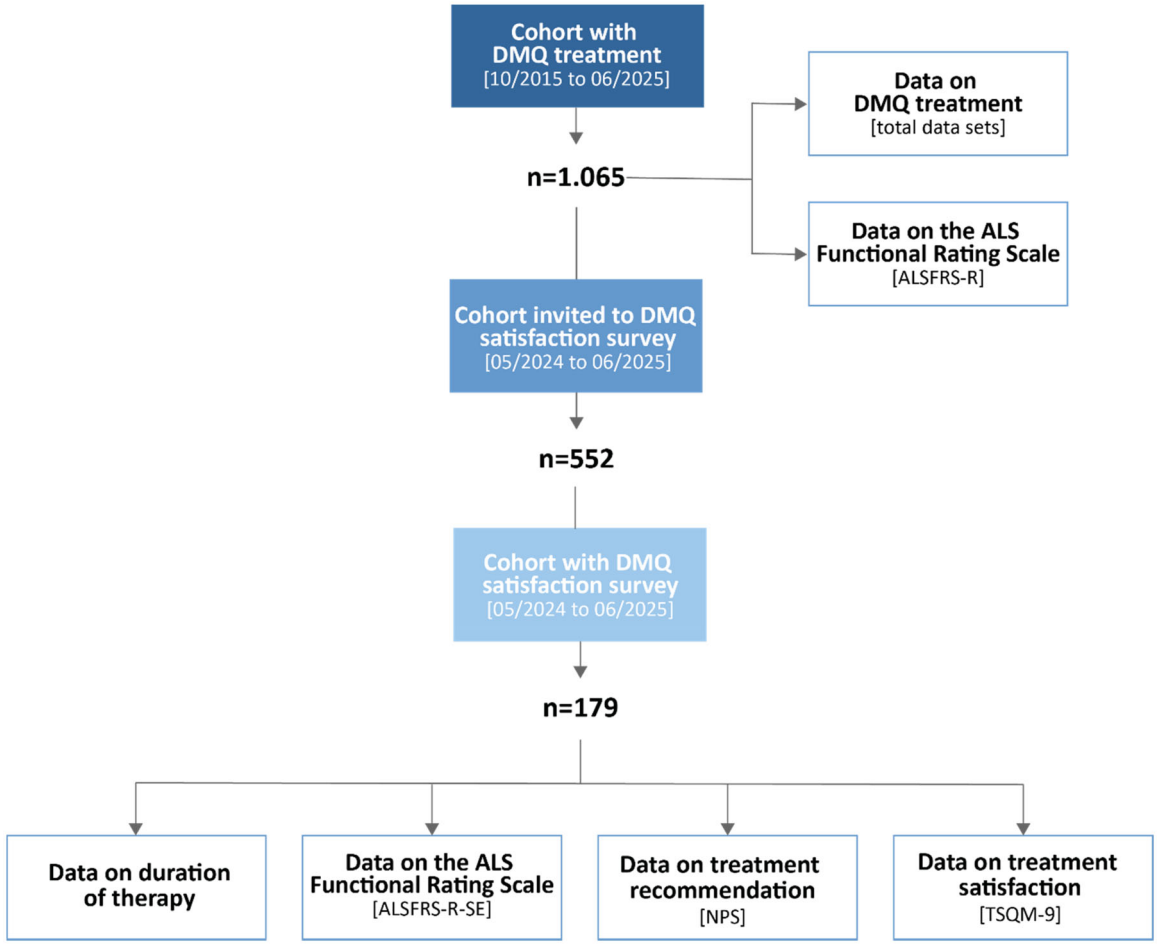


Figure 1. Sample characteristics. Among the 4562 ALS patients enrolled in the ALS Pharmacy Program, 1065 patients (23.3%) received DMQ treatment. Over the 13-month DMQ satisfaction survey period, 552 patients were currently on DMQ treatment and invited to participate. From this cohort, a subset of 179 ALS patients completed the online satisfaction survey. Survey data were collected via the ALS-App. The survey was conducted between May 2024 and June 2025 and included patients actively undergoing DMQ therapy at the time of invitation. Data sets for duration of therapy, recommendation of treatment (Net Promoter Score, NPS), and treatment satisfaction (Treatment Satisfaction Questionnaire for Medication, TSQM-9) were obtained. n = number of patients and analyzable datasets, respectively.

Demographic data and clinical characteristics

In the DMQ-treated group ($n = 1065$), 52.3% were female, and ages at treatment start ranged from 31 to 90 years. Bulbar function was moderately impaired at baseline (mean sub-score 8.3 out of 12 points), but by the end of the observation period, the mean sub-score had declined to 5.4 points. Detailed demographics and clinical data are provided in Table 1.

Treatment with DMQ

Frequency and duration of DMQ treatment. Among current ALS drug management program participants ($n = 917$), 28.1% ($n = 258$) received DMQ as of June 2025 (Supplementary file 2), with a mean treatment duration of 8.4 months (Table 1). Treatment duration subgroups included 35.2% ($n = 374$; <3 months), 35.3% ($n = 375$; 3–9 months), and 29.5% ($n = 313$; >9 months).

Dosage and formulation of DMQ treatment. In all 1065 patients, DMQ was used as a compounded drug in a DM/Q composition of 20mg/10mg, mostly in suspension formulation (87%, Supplementary file 3).

Net promoter score (NPS). The overall NPS for DMQ treatment was +23, with 50% of patients (promoters) likely to recommend DMQ, 27% (detractors) unlikely to recommend it, and 23% (passives) indifferent. NPS was highest among patients with slower ALS progression (+32), followed by those with intermediate progression (+13), and faster progression (+4) (Figure 2). Patients with very long DMQ treatment (>9 months) had a significantly higher NPS (+37, $p = 0.036$) than those with longer (3–9 months; +15) or shorter (<3 months; +7.5) durations (Figure 3).

Treatment satisfaction questionnaire for medication (TSQM-9)

Detailed results for individual TSQM-9 questions. Patient satisfaction with DMQ, as assessed by TSQM-9 (Figure 4), was high across domains.

Table 1. Demographical and clinical characteristics.

Characteristics	Description	Cohort with DMQ treatment ($n = 1.065$)	Cohort with DMQ survey ($n = 179$)
Age (years)	at onset, mean (SD, R)	61.7 (11.3, 25.3–89.5)	60.1 (11.7; 24.9–89.4)
	at start of DMQ treatment, mean (SD, R)	64.1 (10.8; 31.0–90.4)	63.2 (11.0; 31.5–90.1)
Sex	male, % (*n*)	47.7 (508)	55.3 (99)
	female, % (*n*)	52.3 (557)	44.7 (80)
Disease duration (months)	at start of DMQ treatment, mean (SD, R)	29.3 (38.1; 1.6–350.5)	34.4 (39.1; 3.8–251.2)
ALSFRS-R, total	first assessment, mean (SD, R)[1]	37.1 (6.8, 2–48)	38.3 (7.0, 16–48)
	last assessment, mean (SD, R)[2]	26.2 (10.3, 0–48)	28.8 (10.2, 5–48)
ALSFRS-R, bulbar sub-score (item 1–3)	first assessment, mean (SD, R)[1]	8.3 (2.1, 1–12)	8.4 (1.7, 2–12)
	last assessment, mean (SD, R)[2]	5.4 (3.2, 0–12)	6.0 (3.0, 0–12)
ALSFRS-R, Dysarthria (item 1)	first assessment, mean (SD, R)[1]	2.5 (0.8, 0–4)	2.5 (0.8, 1–4)
	last assessment, mean (SD, R)[2]	1.4 (1.1, 0–4)	1.6 (1.1, 0–4)
ALSFRS-R, Salivation (item 2)	first assessment, mean (SD, R)[1]	3.0 (1.0, 0–4)	3.0 (0.9, 0–4)
	last assessment, mean (SD, R)[2]	2.1 (1.3, 0–4)	2.2 (1.3, 0–4)
ALSFRS-R, Dysphagia (item 3)	first assessment, mean (SD, R)[1]	2.9 (0.8, 0–4)	2.9 (0.6, 1–4)
	last assessment, mean (SD, R)[2]	1.9 (1.2, 0–4)	2.2 (1.2, 0–4)
ALSPR, total	mean (SD, R)	0.82 (0.86, 0.01–9.08)	069 (0.93; 0.01–5.84)
ALSPR, classification	slower progression ALS, % (*n*)	44.3 (381)	58.1 (97)
	intermediate progression ALS, % (*n*)	29.3 (252)	26.9 (45)
	faster progression ALS, % (*n*)	26.5 (228)	15.0 (25)
DMQ treatment duration	months, mean (SD, R)	8.4 (10.8, <0.1–100.9)	11.2 (13.9; 0.8–100.9)

A classification of patient's progression was applied as follows: slower progression (<0.5 ALSFRS-R/ month), intermediate progression (≥0.5 and ≤1.0 ALSFRS-R/ month), and faster progression (>1.0 ALSFRS-R/ month) (22).
ALSPR: ALS progression rate; SD: standard deviation; R: range; *n*: number of patients.
[1]The first ALSFRS-R score was collected within 6 months prior to DMQ treatment.
[2]The last ALSFRS-R score was collected at least 1 month after DMQ treatment.

In the effectiveness domain, 82% were satisfied with DMQ's ability to treat bulbar symptoms (Question 1), 78% were satisfied with symptom relief (Question 2), and 77% with the time to take effect (Question 3). In the convenience domain, 89% found DMQ easy to use in its current form and plan (Questions 4 & 5), and 93% found administration easy (Question 6). For the global satisfaction domain, 78.5% believed DMQ was beneficial (Question 7), 78% felt that the benefits outweighed the drawbacks (Question 8), and 80% were satisfied overall. However, around 20% expressed some degree of dissatisfaction or uncertainty (Question 9).

Total scores for TSQM-9. Table 2 shows the total TSQM-9 scores, with the highest satisfaction in the convenience domain (73.8), followed by global satisfaction (63.4), and effectiveness (60.0). Patients with slower ALSPR had significantly higher satisfaction across different TSQM-9 items compared to those with faster ALSPR (Figure 5). Figure 6 illustrates that mean subscores for effectiveness were also significantly higher in the slower ALSPR group.

Discussion

Two pivotal studies on DMQ's effectiveness in alleviating bulbar symptoms have led to its use as a symptomatic treatment for ALS. Earlier findings demonstrated improvements in clinical scores and functional measures of speech and swallowing during DMQ therapy (7,8). However, the present study shifts the focus to the patient experience with DMQ specifically for reducing bulbar symptoms, employing two research strategies: analyzing existing real-world data on patients' characteristics and DMQ treatment duration, and assessing PROMs to gauge patients' subjective perception of their treatment.

Sample selection

The study utilized prescription data from the digital case-management platform (6), which includes approximately 30% of ALS patients in Germany (around 2000 individuals with ALS) (28). While the advantages of the platform-based registry provide a substantial dataset for analysis, particularly regarding DMQ treatment patterns, the limitations need to be addressed. The satisfaction survey component, targeting DMQ users, had a relatively small sample size of 179 participants out of 552 invited, resulting in a response rate of 32.4% over a 13-month survey period. Non-response reasons were not systematically explored, which may introduce potential bias. Additionally, using the platform approach and the study sites

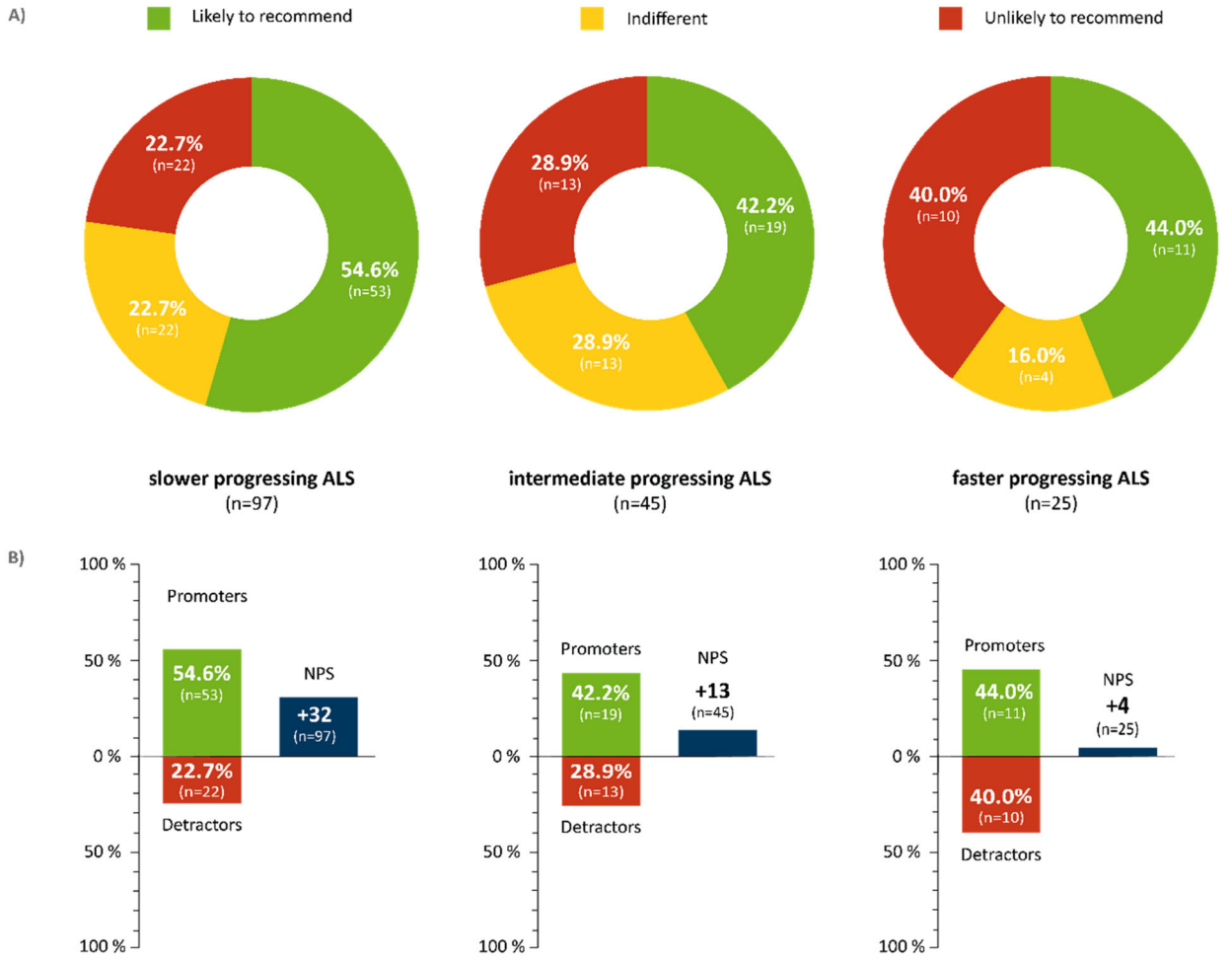


Figure 2. Patients' recommendation of DMQ in relation to the ALS progression rate. The likelihood of recommendation of DMQ in the overall cohort and in subgroups of different ALS progression rates (a) was assessed using the Net Promoter Score (NPS): unlikely recommendation (0 to 6 points); indifferent recommendation (7 to 8 points); likely recommendation (9 to 10 points). Patients were considered "promoters" (10 or 9 score points), "passives" (8 or 7 points), or "detractors" (6 to 0 points). The total NPS (b) was calculated by subtracting the percentage of "detractors" from "promoters". Progression rate of ALSFRS-R was distinguished between slower ALS progression (<0.5 ALSFRS-R/month), intermediate ALS progression (≥0.5 and ≤1.0 ALSFRS-R/month), and faster ALS progression (>1.0 ALSFRS-R/month) (22). *n* = number of patients.

being tertiary ALS centers may have introduced observational bias, potentially overrepresenting patients who receive complex treatments. Consequently, the pharmacological management of less complex ALS phenotypes might have occurred independently of the platform and outside the analyzed data set.

Frequency and duration of DMQ treatment

In the current ALS pharmacy program participant group, 28% of patients were treated with DMQ, reflecting an increase from previous reports (7,8). Despite this growth, DMQ may still be underutilized, given that 30% of ALS patients present with bulbar-onset symptoms and up to 70% develop bulbar symptoms over time (1,29,30). Further research is necessary to ascertain the maximum addressable patient group of bulbar symptoms that would potentially benefit from DMQ. The mean duration of DMQ treatment exceeded 8 months, with nearly one-third of patients with having very long DMQ treatment for more than 9 months. This observation period exceeds the previously reported 28-d course of DMQ pharmacologic intervention by far (7,8). Treatment durations are categorized into short, longer, and very long, based on prescription intervals of every 3 months. While shorter durations offer limited insight into adherence, longer treatments may indicate perceived benefits from both patient and neurologist perspectives. Also, the high proportion of long-term users suggests that many patients experience prolonged symptom relief. Given the retrospective nature of the data analysis, a distinction of between ongoing and stopped treatment has not been made. Therefore, it is conceivable that the proportion of longer and very long treatments is underestimated. Additionally, pharmacokinetic data for DMQ were not available due to the secondary use of existing real-world data. Notwithstanding of these limitations, the findings indicate both the feasibility of chronic treatment and sufficient adherence to DMQ medication.

Figure 3. Patients' recommendation of DMQ in relation to treatment duration. The likelihood of recommendation of DMQ in the overall cohort and in subgroups of different ALS progression rates (a) was assessed using the Net Promoter Score (NPS): unlikely recommendation (0 to 6 points); indifferent recommendation (7 to 8 points); likely recommendation (9 to 10 points). Patients were considered "promoters" (10 or 9 score points), "passives" (8 or 7 points), or "detractors" (6 to 0 points). The total NPS (b) was calculated by subtracting the percentage of "detractors" from "promoters". n = number of patients.

Clinical characteristics

This study provided real-world data on the clinical characteristics of ALS patients being treated with DMQ in Germany. The findings indicate a representative ALS cohort in terms of age at onset and disease progression (31). Notably, women constituted a higher proportion of DMQ-treated patients, consistent with previous findings that female patients more frequently experience bulbar-onset symptoms (29). Bulbar function was moderately impaired before treatment (ALSFRS-R subscale 8.3; SD 2.1) and decreased until the end of the observed treatment period (5.4; SD 3.2). There was no improvement in the bulbar subscore, as suggested in previously reported 28-d DMQ treatment trials, which that reported a mean difference of less than one point in this subscale (7,8).

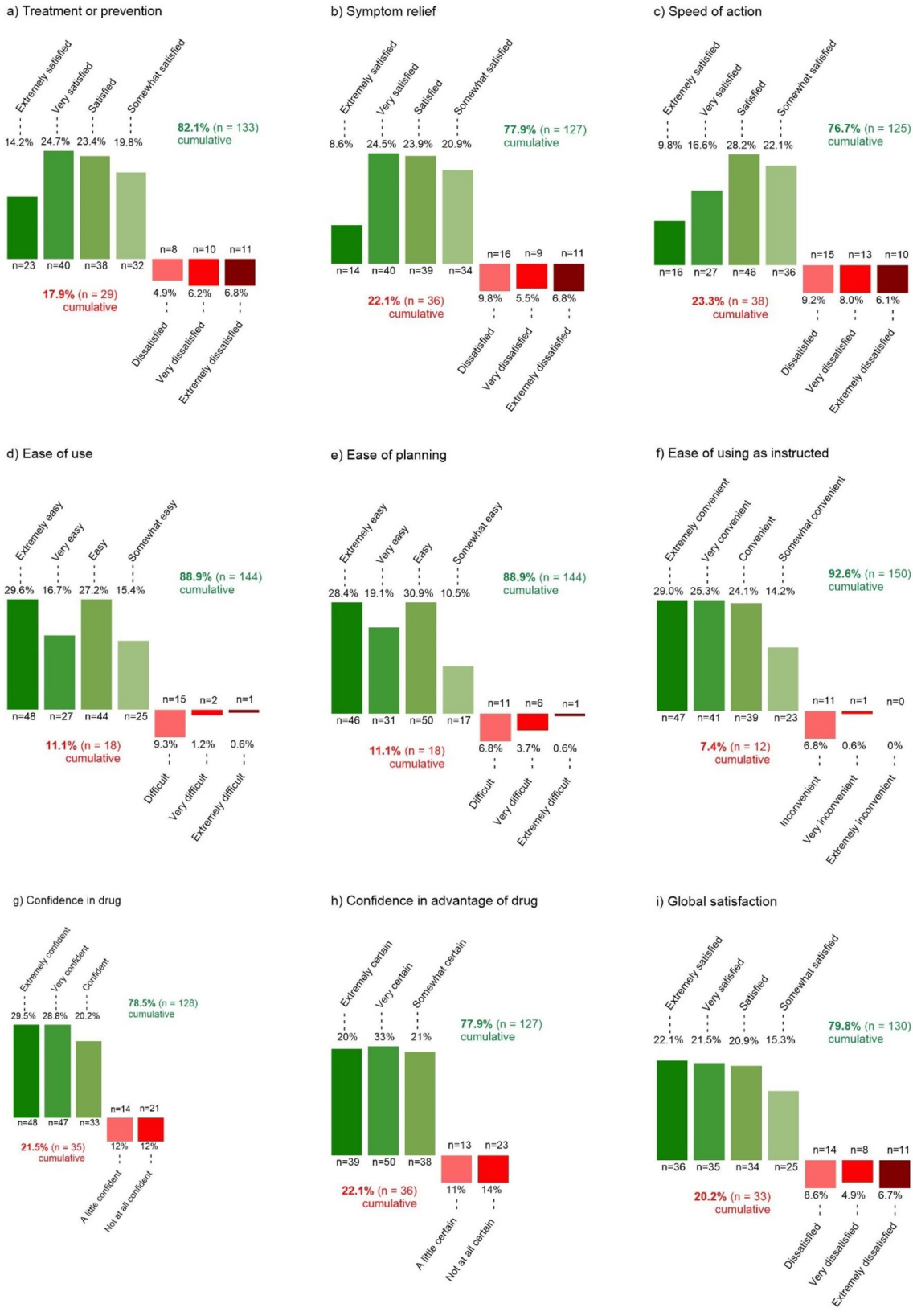
However, given ALS's progressive nature and the prolonged observation duration, it is expected that bulbar dysfunction would naturally decline. Consequently, any potential benefits of DMQ on speech and swallowing are likely overshadowed by disease progression.

In addition, a limitation of this study is the absence of a specific quantitative measure to differentiate upper versus lower motor neuron involvement. The available clinical data did not allow for a reliable stratification of participants based on the relative burden of upper and lower motor neuron signs. Future studies should incorporate a classification of patients into motor phenotypes (32), to enable a more systematic evaluation of potential differential treatment effects across phenotypic subgroups.

Amidst their worsening disease progression, the study employed PROMs, such as the NPS and TSQM-9, to gauge patients' perceptions regarding the net benefit of DMQ.

Recommendation of DMQ by patients assessed by the NPS

The study employed the NPS to gauge patients' attitudes toward DMQ treatment for bulbar symptoms. The NPS score was +23, indicating a positive sentiment, as it is above zero, which is generally considered favorable (23,24). Moreover,



patients with longer DMQ treatment durations showed higher recommendation rates: very long duration had an NPS of +37, compared to +15 for long and +7.5 for shorter durations, suggesting good patient acceptance. Remarkably, NPS was highly related to disease progression. Patients with slower ALS progression had high recommendation rates (+32), while those with intermediate or faster progression showed lower scores (+13 and +4). Despite this, most patients still recommended DMQ treatment. The reduced promoter proportion among faster-progressing patients may be due

Figure 4. The patient's treatment satisfaction with DMQ, as assessed by the Treatment Satisfaction Questionnaire for Medication (TSQM-9). The score was evaluated separately in nine questions, which are as follows. Question 1 (a) – ability of DMQ to prevent or treat bulbar symptoms: "How satisfied or dissatisfied are you with the ability of DMQ to prevent or treat your bulbar symptoms?"; Question 2 (b) – the way DMQ relieves bulbar symptoms: "How satisfied or dissatisfied are you with the way DMQ relieves your symptoms?"; Question 3 (c) – amount of time it takes DMQ to start working: "How satisfied or dissatisfied are you with the amount of time it takes the medication to start working?"; Question 4 (d) – usability of DMQ: "How easy or difficult is it to use the medication in its current form?"; Question 5 (e) – planning when to use DMQ: "How easy or difficult is it to plan when you will use the medication each time?"; Question 6 (f) – administration of DMQ as instructed: "How convenient or inconvenient is it to take the medication as instructed?"; Question 7 (g) – taking DMQ is a good thing: "Overall, how confident are you that taking this medication is a good thing for you?"; Question 8 (h) – the good things about DMQ outweigh the bad things: "How satisfied are you that the good things about this medication outweigh the bad things?"; Question 9 (i) – overall satisfaction DMQ: "Taking all things into account, how satisfied or dissatisfied are you with this medication"; Bulbar deficits include dysarthria, dysphagia, and hypersalivation. n = number of patients.

Table 2. Total score of treatment satisfaction questionnaire for medication (TSQM-9).

Question no.	Variables of TSQM-9	Value mean (SD, R)
	Effectiveness	60.0 (25.9, 0–100)
TSQM-9, Q1	Treatment or prevention	63.0 (28.0, 0–100)
TSQM-9, Q2	Symptom relief	59.6 (27.0, 0–100)
TSQM-9, Q3	Speed of action	57.9 (26.8, 0–100)
	Convenience	73.8 (18.2, 27.8–100)
TSQM-9, Q4	Ease of use	72.6 (23.4, 0–100)
TSQM-9, Q5	Ease of planning	73.1 (23.6, 0–100)
TSQM-9, Q6	Ease of using as instructed	75.6 (21.1, 16.7–100)
	Global satisfaction	63.4 (29.8, 0–100)
TSQM-9, Q7	Confidence in drug	63.3 (33.5, 0–100)
TSQM-9, Q8	Confidence in advantage of drug	60.6 (33.0, 0–100)
TSQM-9, Q9	Global satisfaction	65.2 (29.5, 0–100)

to a lack of drug response or symptoms outweighing benefits.

A limitation of the study is that no formal measure of PBA was included as the PROMs focused on speech and swallowing. It cannot be excluded that, in patients with PBA, changes in this symptom contributed to perceived treatment benefit, given a reported overlap between symptoms of depression and crying in PBA (33). Similarly, any potential effect of DMQ on depressive symptoms, as suggested in a previous trial (34), was not assessed and cannot be evaluated in this study. It also remains to be determined whether potential effects of DMQ on depressive or bulbar symptoms could influence overall survival in ALS patients, which warrants further investigation.

Because of the study design, PROMs could only be obtained retrospectively; prospective collection alongside established clinical outcome measures (such as ALSFRFS-R domains), as used in pivotal trials (35), may be required to better evaluate DMQ to treat bulbar function. Digital remote assessment using the ALS App is an existing tool that can be used for real-time PROM collection. Thus, frequent remote assessment using the self-administered ALS Functional Rating Scale (ALSFRS-R-SE) could serve as a treatment monitoring tool if collected before, immediately after, and periodically during treatment (17,18,21). Another limitation pertains to the methodology of NPS, which is an established tool for evaluating products and services. Its application in the medical realm is still in its nascent stages and necessitates caution (36–41). Nonetheless, the study highlights varied patient perceptions of DMQ benefits, reflecting differing rates of bulbar symptom progression in ALS.

Treatment satisfaction measured by the TSQM-9

The TSQM-9 has been validated as a reliable measure for assessing treatment satisfaction in various clinical settings, enabling the evaluation of treatment satisfaction across domains such as effectiveness, convenience, and global satisfaction (27). The overall outcomes reported through TSQM-9 demonstrate a high level of satisfaction with DMQ treatment among most ALS patients studied, with 80% of patients expressing positive results for global satisfaction (question 9). Interestingly, this substantial proportion of patients reporting high satisfaction with DMQ somehow contrasts with the smaller percentage willing to recommend the treatment to others (50%, positive NPS results). This discrepancy suggests that TSQM-9 (satisfaction) and NPS (recommendation) capture distinct aspects of the patient experience. While there is no direct comparison between TSQM-9 and NPS, it is plausible that patients approach the recommendation of a therapy (NPS) with greater caution and stricter criteria than when assessing their personal satisfaction (TSQM-9). While both tools aim to capture patient

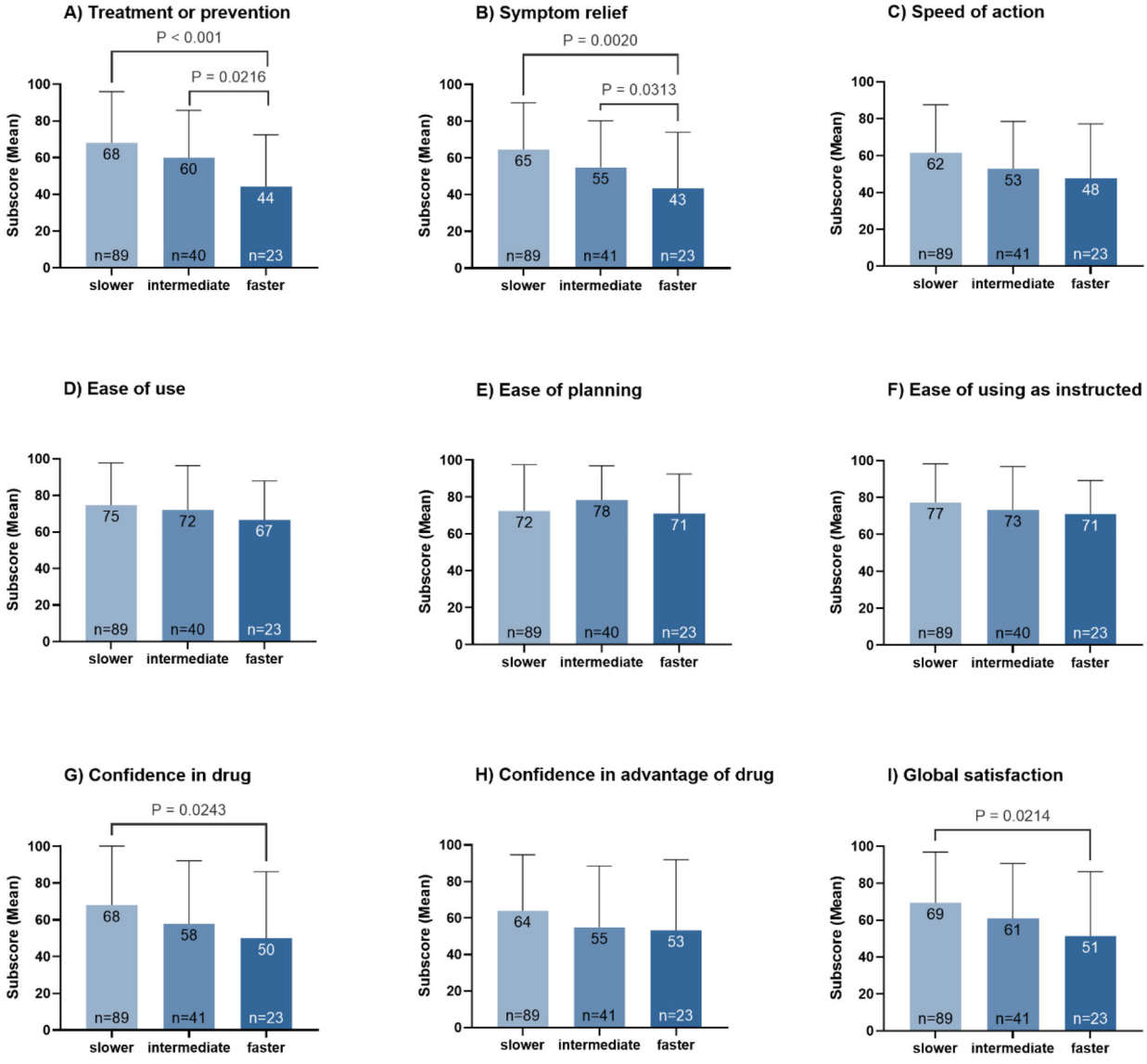


Figure 5. The patient's treatment satisfaction with DMQ in relation to ALSPR. The score was evaluated separately in nine questions, which are as follows. Question 1 (a) – ability of DMQ to treat bulbar symptoms; Question 2 (b) – the way DMQ relieves bulbar symptoms; Question 3 (c) – amount of time it takes DMQ to start working; Question 4 (d) – usability of DMQ; Question 5 (e) – planning when to use DMQ; Question 6 (f) – administration of DMQ as instructed; Question 7 (g) – taking DMQ is a good thing; Question 8 (h) – the good things about DMQ outweigh the bad things; Question 9 (i) – overall satisfaction DMQ. Bulbar symptoms include dysarthria, dysphagia, and hypersalivation. ALS progression rate (ALSPR) is defined as follows: slower (<0.5 ALSFRS-R/month), intermediate (≥0.5 and ≤1.0 ALSFRS-R/month), and faster ALS progression (>1.0 ALSFRS-R/month) (22). *n*=number of patients.

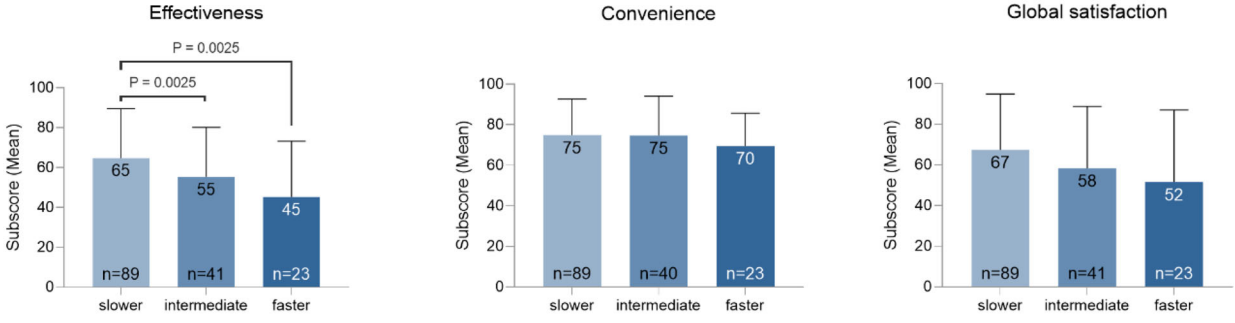


Figure 6. The patient's perceived effectiveness, convenience, and global satisfaction with DMQ in relation to ALSPR. The score was evaluated in the three main TSQM-9 domains: effectiveness, convenience, and global satisfaction. ALS progression rate (ALSPR) is defined as follows: slower (<0.5 ALSFRS-R/month), intermediate (≥0.5 and ≤1.0 ALSFRS-R/month), and faster ALS progression (>1.0 ALSFRS-R/month) (22). *n*=number of patients.

perspectives, they assess distinct dimensions – the TSQM-9 focuses on specific treatment satisfaction parameters, whereas the NPS gauges overall willingness to recommend (27,42). A notable limitation, however, is the lack of comparative TSQM-9 data for other symptomatic drugs to treat bulbar dysfunction, such as other cholinergic drugs (e.g. pyridostigmine). This underscores a broader issue in clinical ALS research, where systematic studies on PROM for symptomatic and palliative medications remain scarce. In light of this gap, the TSQM-9 data presented here should be regarded as exploratory.

Conclusion

DMQ is increasingly recognized as a valuable treatment option for reducing bulbar symptoms in ALS. The average treatment duration of more than 8 months indicates a remarkable adherence to this symptomatic medication. Notably, patients with slower or intermediate disease progression reported higher treatment satisfaction with DMQ, whereas faster disease progression outweighed the benefits of the drug. This highly variable perception of DMQ in relation to ALS progression should be taken into account when counseling patients on the treatment expectations of DMQ. In further studies, the effect of DMQ on the progression of dysphagia and the prolongation of the need for PEG is of interest. Thus, the full potential of DMQ remains to be explored, and a prospective trial will be essential to validate these real-world findings for regulatory purposes.

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Authors' contributions

SS designed and conceptualized the study, analyzed and interpreted the data, visualized the data, and drafted the manuscript for intellectual content. TM and AM had a major role in data acquisition, data interpretation, writing, review and editing, visualization, validation, methodology, and revising the manuscript for intellectual content. BW had a major role in data collection and preparation of data. SKS had a major role in reviewing and editing the manuscript. TG, PW, DK, RF, SB, AR, US, RS, UW, SP, RL, BB, PL, JG, BMG, WP, WS, JD, AP, JS, JN, BH, and CM had a major role in data acquisition and revised the manuscript for intellectual content.

Ethics approval and consent to participate

The study protocol was approved by the Medical Ethics Committee of the Charité – Universitätsmedizin Berlin, Germany, under the number EA1/219/15. A signed patient information and informed consent form was obtained from all participating patients.

Declaration of interest

TM has received grants, personal fees, non-financial support and research support from AL-S Pharma, Amylyx, Cytokinetics, Ferrer, Mitsubishi Tanabe, Sanofi, Orphazyme, and has served on the advisory boards of Amylyx, Biogen, and ITF Pharma outside of the submitted work. TM and CM are founders of the internet platform Ambulanzpartner and hold shares of Ambulanzpartner Soziotechnologie APST GmbH. TG has received personal fees from ITF Pharma and served on the advisory boards of Amylyx, and ITF Pharma outside of the submitted work. SP has received speaker fees, non-financial support and research support from Biogen, Roche, ALS Pharma, Amylyx, Cytokinetics, Ferrer, ITF Pharma, and Sanofi and served on advisory boards of Amylyx, Biogen, Roche, Zambon, and ITF Pharma outside of the submitted work. BB received compensation for travel expenses from ITF Pharma GmbH outside of the submitted work. AM has received personal fees, non-financial support, and research support from ITF Pharma and Zambon outside the submitted work. The other authors declare no conflicts of interest.

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Data availability statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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