

Jiahe Chen,^{1*2} Crystal Watson,³ Dhanalakshmi Thirumulai,^{1*} Arie Barlev,³ Eddie Jones,⁴ Sasha Bogdanovich,¹ Kiren Kresa-Reahl¹
¹Atara Biotherapeutics, Thousand Oaks, CA; ²University of Southern California, Los Angeles, CA; ³Atara Biotherapeutics, South San Francisco, CA; ⁴Adelphi Real World, Bollington, Cheshire, United Kingdom
*At the time of study

BACKGROUND

- Drug adherence is needed to maximize the effectiveness of treatments in a real-world setting, especially in chronic conditions like PMS
- Adherence to DMTs is reported to be associated with lower rates of relapse and risk of disease progression¹
 - Adherence to DMTs in patients with MS has been reported to be associated with a significantly reduced risk of relapse, hospitalization, emergency visits and significantly fewer outpatient visits, compared to patients who are non-adherent
- Factors associated with poor adherence to DMTs in patients with MS can include patient-, disease-, drug-, healthcare- and cost-related factors²
- Currently, there is a high unmet need for safe and effective DMTs in PMS, as there is only one approved product for PPMS and none approved for nonactive SPMS in the US; in addition, there is limited benefit in terms of disease modification in nonactive PPMS/SPMS

Although there are data describing adherence to DMTs in patients with MS, currently there is limited data available for patients with PMS

OBJECTIVE AND METHODS

Objective: To describe both patient- and physician-reported adherence and compliance to DMTs for patients with active/nonactive PMS

Study design

- The annual cross-sectional survey from the Adelphi Disease Specific Programme conducted independently by Adelphi Real World (Bollington, UK) in 2021 was used to collect data on adult patients with active or nonactive PMS
- Physicians (i.e. neurologists) who were qualified to practice medicine, responsible for treatment decisions for patients with MS, and made treatment decisions for ≥16 patients with MS in a typical month, were invited to participate in the cross-sectional survey
 - Participating physicians completed a physician-reported questionnaire for their next 10–15 patients with MS who consulted them
 - Information was obtained through a review of patients' medical records; there was no time limit on how far back the physician could look
- Adult patients (aged ≥18 years) with active or nonactive PMS in the US were identified and asked to participate in a patient-reported survey, which included the ADAQ, a 12-item adherence-related questionnaire about their current DMT
 - Patients with unknown status of relapses in the past year were excluded
 - Patients could not be participating in any clinical trials at the time of the survey
 - One question was not relevant to all therapies, so was excluded from this study ('how often do you plan ahead and refill your medicines before running out?')
- Patient- and physician-reported adherence data were described and characterized by route of administration (e.g. infusions, orals or injectables)

RESULTS

Patient characteristics

- Patient-reported adherence data were provided for a total of 79 patients with PMS (n=46 infusions; n=22 orals; n=11 injectables)
 - Mean age (SD) was 50.6 (9.8) years, 53.0 (10.0) years and 54.4 (11.9) years for those receiving infusions, orals and injectables, respectively
 - Mean BMI (SD) was 27.5 (5.3), 25.9 (3.7) and 25.4 (3.9) for those receiving infusions, orals and injectables, respectively

Patient-reported adherence

- For patients on infusions, at least 80% reported that they followed 8 out of 11 adherence measures and at least 70% followed the remaining 3 out of 11 adherence measures (**Figure 1**)
- For patients on orals or injectables, at least 80% reported that they followed 3 out of 11 or 4 out of 11 adherence measures, respectively (**Figure 2** and **Figure 3**)
- 64% of patients on orals forgot to take their medicine some of the time, and 48% missed taking their medicine some of the time when they were careless (**Figure 2**)
- 46% of patients on injectables forgot to take their medicine some of the time, and 64% forgot to take their medicine some of the time when feeling sick (**Figure 3**)

Figure 1. Patient-Reported Survey Responses for Patients who Received Infusions

Adherence Measure	Never (%)	Sometimes (%)	Most of the time/always (%)
Put off refilling your medicines because they cost too much money?	82.6	17.4	0
Forget to take your medicine when you are supposed to take it more than once a day?	78.3	21.7	0
Change the dose of your medicines to suit your needs (i.e. when you take more or less pills than you're supposed to)?	95.6	4.4	0
Miss taking your medicine when you are careless?	80	20	0
Miss taking your medicine when you feel sick?	76.1	23.9	0
Miss taking your medicine when you feel better?	89.1	10.8	0
Skip a dose of your medicine before you go to the doctor?	97.8	2.2	0
Run out of medicine?	84.4	15.6	0
Forget to get prescriptions filled?	80.4	19.6	0
Decide not to take your medicine?	95.7	4.4	0
Forget to take your medicine?	71.7	28.3	0

Figure 2. Patient-Reported Survey Responses for Patients who Received Orals

Adherence Measure	Never (%)	Sometimes (%)	Most of the time/always (%)	Unknown (%)
Put off refilling your medicines because they cost too much money?	68.2	31.8	0	0
Forget to take your medicine when you are supposed to take it more than once a day?	63.6	36.4	0	0
Change the dose of your medicines to suit your needs (i.e. when you take more or less pills than you're supposed to)?	81.8	13.6	4.6	0
Miss taking your medicine when you are careless?	52.4	47.6	0	0
Miss taking your medicine when you feel sick?	72.7	22.7	4.6	0
Miss taking your medicine when you feel better?	77.3	22.7	0	0
Skip a dose of your medicine before you go to the doctor?	72.7	27.3	0	0
Run out of medicine?	81	19.1	0	0
Forget to get prescriptions filled?	77.3	22.7	0	0
Decide not to take your medicine?	81.8	18.2	0	0
Forget to take your medicine?	36.4	63.6	0	0

Figure 3. Patient-Reported Survey Responses for Patients who Received Injectables

Adherence Measure	Never (%)	Sometimes (%)	Most of the time/always (%)
Put off refilling your medicines because they cost too much money?	72.7	27.3	0
Forget to take your medicine when you are supposed to take it more than once a day?	72.7	27.3	0
Change the dose of your medicines to suit your needs (i.e. when you take more or less pills than you're supposed to)?	90.9	9.1	0
Miss taking your medicine when you are careless?	72.7	27.3	0
Miss taking your medicine when you feel sick?	36.4	63.6	0
Miss taking your medicine when you feel better?	100	0	0
Skip a dose of your medicine before you go to the doctor?	100	0	0
Run out of medicine?	81.8	18.2	0
Forget to get prescriptions filled?	72.7	27.3	0
Decide not to take your medicine?	63.6	36.4	0
Forget to take your medicine?	54.5	45.5	0

Figure 4. Physician-Reported Survey Compliance (A) and Adherence (B) Results

(A) Compliance

Route of Administration	Fully compliant (%)	Fairly compliant (%)	Poorly compliant (%)
Infusions (n=207)	92.3	7.3	0.5
Orals (n=78)	92.3	6.4	1.3
Injectables (n=65)	75.4	20	4.6

(B) Adherence

Route of Administration	Completely adherent (%)	Mostly adherent (%)	Somewhat adherent/not adherent (%)
Infusions (n=212)	89.2	10.4	0.5
Orals (n=80)	73.8	25	1.3
Injectables (n=66)	57.6	34.9	7.6

Percentages may not add up to 100% due to rounding. Question asked was "How compliant/adherent do you think this patient is?"

LIMITATIONS

- Longitudinal data were not available to determine the impact of progressive MS over time
- Individuals not seen by physicians or not properly diagnosed with progressive MS were not included
- Patients with primary progressive MS were oversampled to further study this population
- Patients had to be willing and able to answer the questionnaires
- Although the ADAQ questionnaire measures adherence across many conditions and formulations, it was not developed to include infusions
- No comparisons were made as this was a descriptive study

CONCLUSIONS

- Patients with active or nonactive PMS and physicians caring for them reported the greatest adherence and compliance with infusion DMTs
 - Of the 11 relevant patient-reported adherence outcomes, at least 80% of the patients on infusions reported that they followed eight measures, while patients on orals or injectables reported that they followed only three or four measures, respectively
- Differences between patient- and physician-reported adherence and compliance were seen, especially in self-administered injectables and orals
 - Adherence and compliance may be more consistently reported between patients and physicians for infusion DMTs due to their relative infrequency of administration and also due to objective medical records documenting administration of the infusion
 - In contrast, self-administered injectables and orals may have more accurate patient-reported adherence than physician-reported adherence due to no objective medical records documenting administration other than a patient's recall during clinic visits, and a higher dose frequency that is subject to errors in recall

This study highlights that patients with PMS have the greatest adherence and compliance to infusion DMTs

ACKNOWLEDGMENTS AND DISCLOSURES

This study is sponsored and funded by Atara Biotherapeutics

Crystal Watson, Arie Barlev, Sasha Bogdanovich, and Kiren Kresa-Reahl are employees and shareholders of Atara Biotherapeutics. Eddie Jones is an employee of Adelphi Real World. Dhanalakshmi Thirumalai and Jiahe Chen were employees of Atara at the time of study

Medical writing assistance was provided by Lee Blackburn from AMICULUM Ltd, funded by Atara Biotherapeutics

REFERENCES

- Burks J, et al. *Clinicoecon Outcomes Res* 2017;9:251–260.
- Koltuniuk A & Chojdak-Lukasiewicz J. *Int J Environ Res Public Health* 2022;19:2203.

ABBREVIATIONS

ADAQ = Adelphi Adherences Questionnaire; BMI = body mass index; DMT = disease-modifying treatment; MS = multiple sclerosis; PMS = progressive multiple sclerosis; SD = standard deviation