Low discontinuation rate and side-effect burden after switching to cladribine tablets: Canadian experience from the adveva™ patient support program

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DISCLOSURES

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Introduction

- The efficacy and safety of cladribine tablets have been characterised in a comprehensive clinical trial program[1-5]
- Cladribine tablets were approved in Canada in November 2017
- Experience from using cladribine tablets in the real world setting can help complement data obtained in randomised clinical trial[6]
- All patients prescribed cladribine tablets in Canada are enrolled with their consent in the adveva™ patient support program (PSP), which provides drug education, assistance with reimbursement and patient support services
- Analysis of data routinely collected through the adveva™ program can assist with characterizing the use of cladribine tablets in everyday clinical practice in Canada

Objectives

To examine clinical characteristics of patients initiating cladribine tablets in Canada, assess the discontinuation rates, and describe reported adverse events (AEs)

PATIENT

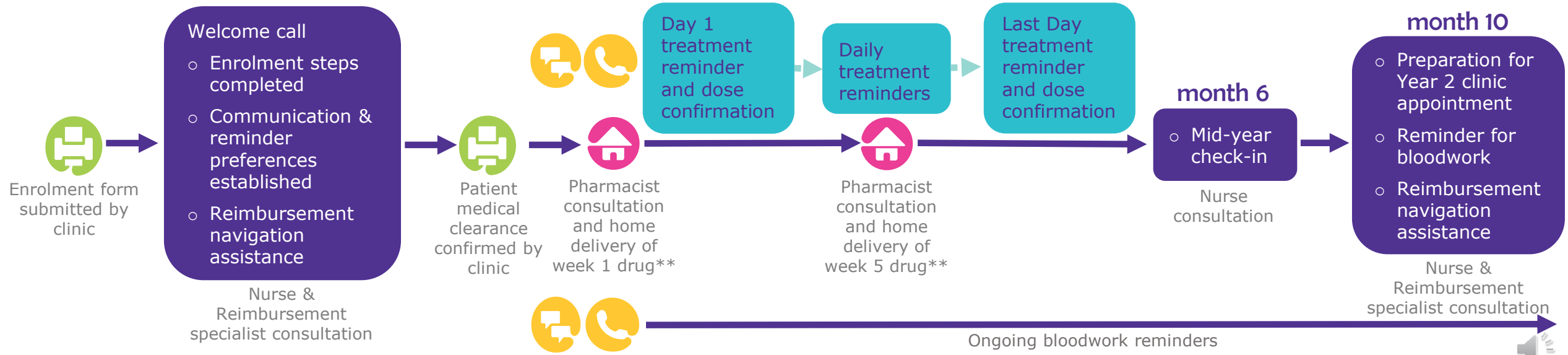
Abbreviations: PSP, patient support program; **AE**, adverse events;

References: 1. Giovannoni G et al. *N Engl J Med* 2010;362:416–26; **2.** Giovannoni G et al. Mult Scler. 2018 Oct;24(12):1594-1604; **3.** Montalban X et al. Neurol Neuroimmunol Neuroinflamm. 2018 Jul 11;5(5):e477 **4.** Leist TP et al. *Lancet Neurol* 2014;13:257–67 **5.** PREMIERE registry (NCT01013350) Available at: https://clinicaltrials.gov/ct2/show/NCT01013350?term=NCT01013350&rank=1 [Accessed 14 Aug 2020]; **6.** Katkade VB et al. *J Multidiscip Healthc* 2018 Jul 2;11:295-304.

Methods

- Anonymized data routinely collected by adveva™ team from the time of first patient enrollment in December 2017 to January 2020 were analyzed
- Patients were included if they consented to enroll in the adveva™ PSP
- All patients were contacted at enrollment and periodically thereafter by a nurse, a reimbursement specialist (to facilitate drug coverage process for patient) and a pharmacist **(Figure 1)**. Patient medical clearance (pre-treatment evaluation completion) was confirmed by clinic. Patient follow-up ceased when treatment was completed or discontinued
- All AEs were reported to EMD Inc., Canada (a business of Merck KGaA, Darmstadt, Germany), in accordance with local reporting guidelines

Figure 1: Adveva™ PSP Year 1*



*Program repeats for Year 2 (until month 18); **The recommended cumulative dose of MAVENCLAD is 3.5 mg/kg body weight over 2 years. Each treatment course consists of 2 treatment weeks, one at the beginning of the first month (week 1) and one at the beginning of the second month (week 5) of the respective year.

Results

Baseline Demographics

- N=1864 patients were enrolled in the adveva™ program between December 2017 and January 2020 **(Table 1)**
  - N=1373 were female (73.7%)
  - Mean age was 41.5 years
  - All patients were previously treated with another disease-modifying drug (DMD)
- Most patients (n=1191; 63.9%) had received only one prior DMD before their enrollment

Table 1. Baseline demographics of patients enrolled in the adveva™ PSP

Patients enrolled in adveva™	
Patients enrolled, n	1864
Female, n (%)	1373 (73.7%)
Mean age at enrollment, years (SD)	41.5 (10.34)
Mean body weight (kg)	81.2
Prior DMD, n (%)	1864 (100%)
Number of prior DMDs, n (%) 1 2 3 >3	 1191 (63.9%) 405 (21.7%) 180 (9.7%) 88 (4.7%)

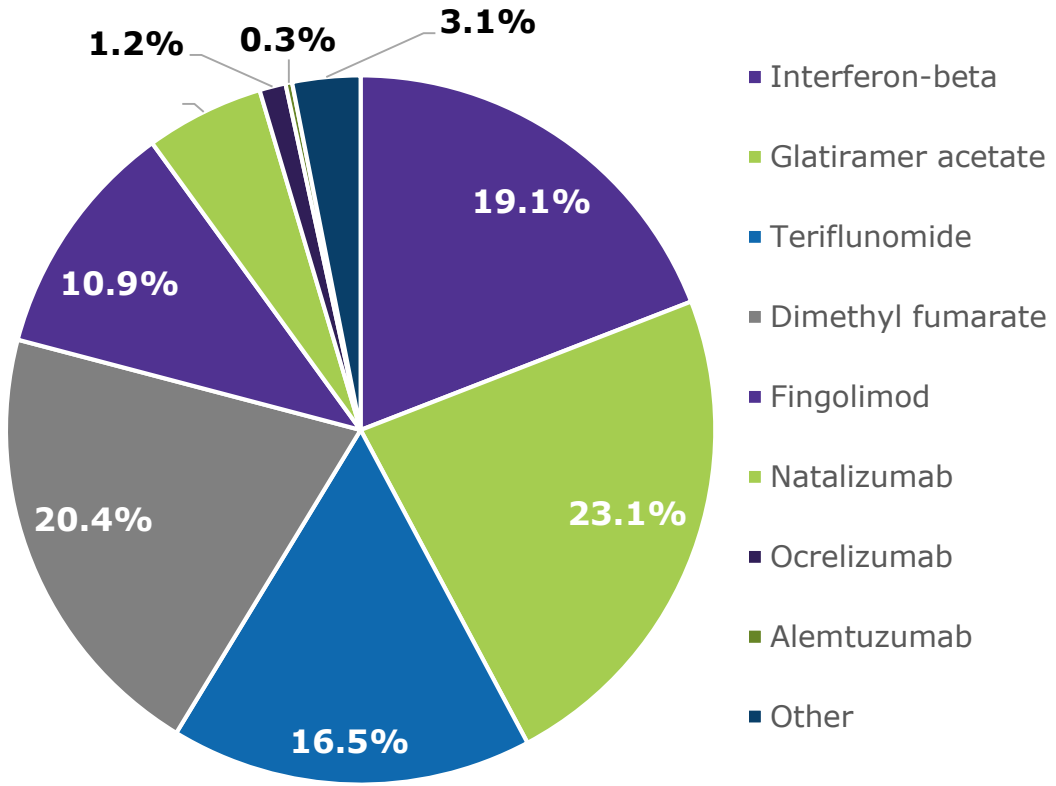
Abbreviations: DMD, disease modifying drug

Results – cont'd

Prior DMDs before switching to cladribine tablets

- The most recent prior DMDs prior to enrollment (n=1864) were glatiramer acetate formulations (23.1%), dimethyl fumarate (20.4%), interferon-beta formulations (19.1%), teriflunomide (16.5%), and fingolimod (10.9%), **(Figure 2)**
- Although most patient did not cite a reason for switching, of the n=74 patients that did, the most common reasons cited were adverse effects (62.3%) and physician/patient-reported lack of efficacy (24.3%)

Figure 2: Most recent prior DMDs

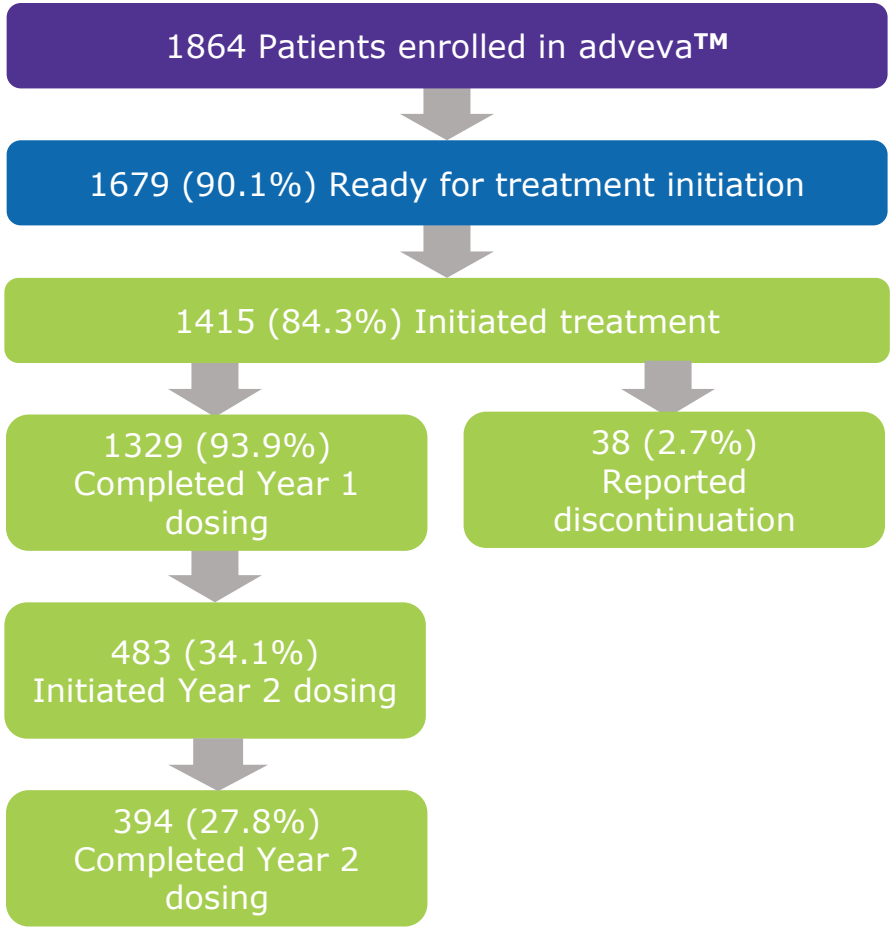


Results – cont'd

Cladribine tablets – treatment experience

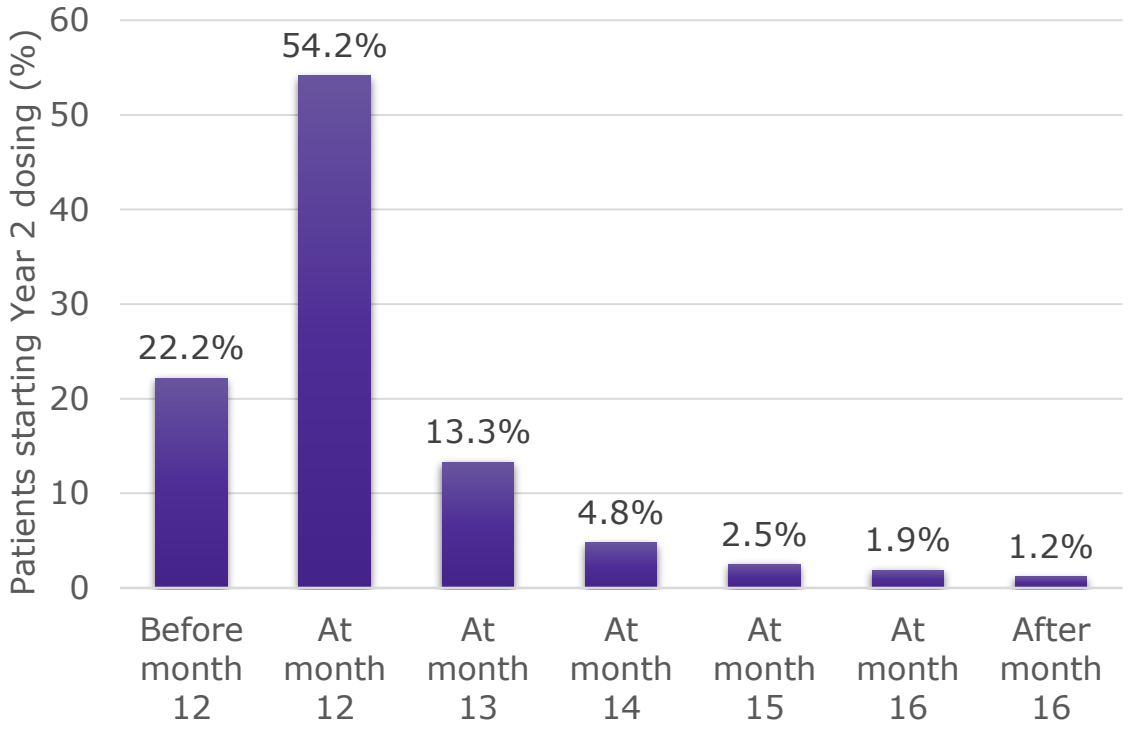
- Of 1864 patients enrolled in adveva™, 1679 (90.1%) had completed the pre-treatment evaluation (medical clearance) by the data cut-off and were confirmed ready by clinic for treatment initiation **(Figure 3)**
- In the treatment-ready group, 1415 of 1679 patients (84.3%) had started Year 1 of treatment by data cut-off
- Among those 1415 initiated patients:
  - N=1329 (93.9%) completed Year 1 dosing
  - N=483 (34.1%) initiated Year 2 dosing
  - N=394 (27.8%) completed the full two-year treatment course and
  - N=38 (2.7%) reported discontinuation

Figure 3: Treatment experience with cladribine tablets



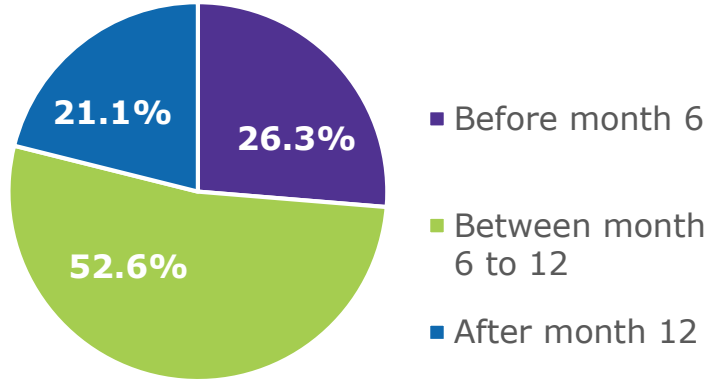
Results – cont'd

Figure 4: Patients starting Year 2 dosing at different time points



- Among the patients that started Year 2 (n=483), the mean time to Year 2 dosing initiation was 12.75 (SD 1.27) months. The majority of patients (89.7%) started Year 2 dosing by month 13 **(Figure 4)**

Figure 5: Discontinuations occurring at different time points



- N=38 (2.7%) of patients reported treatment discontinuation
- Discontinuations occurring within first 6 months of treatment initiation (26.3%), between month 6 to 12 (52.6%) and after month 12 (21.1%) **(Figure 5)**
- The reasons reported for treatment discontinuation (n=38) were adverse events other than flu-like symptoms and lymphopenia (21.1%), worsening disease (18.4%), patient decision (10.5%), family planning/pregnancy (10.5%), laboratory result/low lymphocyte count (7.9%), flu-like symptoms (2.6%) and unknown (28.9%)

Results – cont'd

Adverse Events

- A total of 843 of 1415 patients (59.6%) reported at least one AE. Among the total AEs reported (n=3525), the most frequent were fatigue (8.0%), headache (5.4%), nausea (4.7%), MS relapse (2.7%) and decrease in lymphocyte count (2.5%) **(Table 2)**

Table 2: Reported AEs (preferred term) (>1.5% of reported terms)

Adverse events reported, n	3525
Fatigue, n (%)	282 (8.0%)
Headache, n (%)	191 (5.4%)
Nausea, n (%)	164 (4.7%)
MS relapse, n (%)	94 (2.7%)
Lymphocyte count decrease, n (%)	87 (2.5%)
Nasopharyngitis, n (%)	86 (2.4%)
Alopecia, n (%)	59 (1.7%)
Dizziness, n (%)	59 (1.7%)
Hypoesthesia, n (%)	59 (1.7%)

Conclusions

- The majority of patients registered in the Canadian adveva™ program started treatment with cladribine tablets and >90% had completed the Year 1 treatment course at the time of data cut-off
- Cladribine tablets had a low discontinuation rate and most patients successfully self-administered the drug
- The majority of patients initiated Year 2 dosing within one month of scheduled start, suggesting a low proportion of patients with persistent lymphopenia at the end of Year 1
- Treatment was well tolerated, with few patients discontinuing treatment
- Reported adverse events were not severe