Rationale and Design of Classic-MS Study Evaluating Long-Term Efficacy for Patients with Multiple Sclerosis Treated with Cladribine Tablets

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CONCLUSION

CLASSIC-MS is an exploratory study that may provide valuable information on the long-term efficacy of patients with multiple sclerosis (MS) treated with cladribine tablets.

The results from this study may benefit patients with MS and clinicians by helping to inform future treatment approaches and treatment decision-making.

INTRODUCTION

- Cladribine tablets 10 mg (cumulative dose 3.5mg/kg over 2 years demonstrated efficacy versus placebo over 2 years in CLARITY,[1] CLARITY Extension,[2] and ORACLE-MS,[3] showing sustained efficacy in MS patients without further active treatment in CLARITY Extension.
- Long-term safety in this population has been previously assessed in the PREMIERE registry.[4]
- **CLASSIC-MS** is an exploratory, low-interventional, multicenter, ambispective, Phase IV study of patients with MS, or those with a first clinical demyelinating event enrolled into the Phase III trials and who received ≥1 course of cladribine tablets or placebo.

OBJECTIVES

CLASSIC-MS will explore long-term efficacy and real-world treatment patterns in CLARITY, CLARITY Extension and ORACLE-MS trial patients.

METHODS

- Following pre-baseline screening and assessment for eligibility, long-term retrospective data will be obtained from medical records at Study Visit 1; prospective data will be collected at Study Visits 1 and 2.
- Patients will be enrolled during 17 months between Q3 2019–Q4 2020.
- The last Patient Last Visit is expected in Q1 2021.

Figure 1. CLASSIC-MS Study Visit and Data Collection

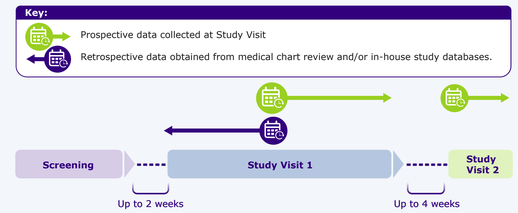

Table 1. CLASSIC-MS Study Objectives

Objective	
Primary	Evaluation of long-term mobility
Secondary	Differences in clinical and MRI characteristics between long-term responders* and non-responders
	Real-world treatment patterns
	Durability of clinical outcomes, quality of life, and cognitive outcomes after treatment with IMP
	Durability of outcome on brain imaging after treatment with IMP
Tertiary	Association between high-disease activity and long-term response
	Differences in genetics between long-term responders* and study participants requiring alternate therapies following treatment with IMP

*Study participants who did not demonstrate any evidence of disease reactivation based on Investigator assessment of clinical and imaging outcomes until Year 4 or later following their last dose of IMP and who did not receive disease-modifying treatment until Year 4 or later following their last dose of IMP.

IMP, investigational medicinal product (cladribine tablets or placebo); **MRI**, magnetic resonance imaging.

Table 2. CLASSIC-MS Schedule of Data Collection

Assessments & Procedures	Screening	Study Visit 1*	Study Visit 2†
Informed consent	X		
Inclusion and exclusion criteria	X		
Sociodemographic and clinical characteristics	X		
Prospective Data Collection			
Physical examination		X	
EDSS telephone assessment		X	
EDSS, EQ-5D-3L, BVMT-R, SDMT		X	
Optional blood sample for pharmacogenetic testing		X	
Adverse events and concomitant medications		X	X
End of study form		X	X
Retrospective data collection (based on chart review)			
Medical and disease history	X		
EDSS from end of parent study to Study Visit 1		X	
Details of subsequent DMDs, including physician questions on treatment decisions		X	
Date of first use of an ambulatory device or wheelchair		X	
Date of first time bedridden		X	
Relapse history from end of parent study to Study Visit 1		X	
SPMS conversion		X	
CDMS conversion		X	
PPMS diagnosis		X	
Adverse drug reactions related to cladribine tablets		X	
MRI sub-study			
Urine pregnancy test			X
MRI assessment			X

*Within 2 weeks of Screening. †Within 4 weeks of Study Visit 1. **BVMT-R**, Brief Visuospatial Memory Test Revised; **CDMS**, clinically definite MS; **DMD**, disease-modifying drug; **EDSS**, Expanded Disability Status Scale; **EQ-5D-3L**, EuroQoL-5 Dimensions; **MRI**, magnetic resonance imaging; **PPMS**, primary progressive MS; **SDMT**, Symbol Digit Modalities Test; **SPMS**, secondary progressive MS.

RESULTS

Figure 2. Enrollment of Sites into CLASSIC-MS

In 2018, a feasibility survey was sent to 225 centers

110 centers provided positive responses and were included, representing **48%** of sites originally enrolled in the Phase III studies

115 centers were not included:
81 were not willing to participate
13 were dropped*
16 were non-responders
5 were rejected

*Following agreement to participate these sites finally declined citing reasons such as budgeting or resourcing issues.

The CLASSIC-MS Study: NCT03961204

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