Long-term Efficacy of Cladribine Tablets in Patients with Relapsing-Remitting or Secondary Progressive Multiple Sclerosis: Analysis of Real-World Data From the Italian Multiple Sclerosis Registry (CLARINET-MS)

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CONCLUSION

CLARINET-MS suggests that approximately 2/3 of patients with either RRMS or SPMS were free of relapse in the 3 years after their last dose of cladribine tablets. More than 50% were free of disability progression.

Patients who were switched from treatment with cladribine tablets in the longer term were treated with a variety of immunomodulatory and immunosuppressive therapies.

INTRODUCTION

- The collection of real-world data (RWD) from large patient registries allow for the investigation of long-term safety and efficacy of treatment in chronic diseases like multiple sclerosis (MS).
- Analysis of RWD alongside clinical data would therefore complement clinical trial data and may provide evidence for the sustained effectiveness of cladribine tablets.
- The Italian MS Registry merges data of approximately 55,000 Italian MS patients from regional registries and local databases, consisting of 134 Italian MS centers in total.
- **CLARINET-MS** was a non-interventional, exploratory investigation of Italian MS patients using data available from the Italian MS Registry, who received at least one course of cladribine tablets in CLARITY,[1] CLARITY Extension,[2] ONWARD,[3] or ORACLE-MS.[4]

Italian MS Registry

OBJECTIVE

To assess the long-term effectiveness of cladribine tablets in patients with:

RRMS
Relapsing-Remitting MS

SPMS
Secondary-Progressive MS

using data available from the Italian MS Registry.

METHODS

Study Population:

- Previously enrolled into CLARITY, CLARITY Extension, ONWARD, or ORACLE-MS randomized clinical trials (RCTs) with at least one full course of treatment with cladribine tablets 3.5 mg/kg (approved dose) or 5.25 mg/kg (investigational dose only, not approved) in both year 1 and year 2.
- Patient participation in the RCTs also must have ended.
- Patients were required to have given written informed consent to be included in the patient registry.

Data Analysis:

- The data are descriptive, with no formal comparison with other treatments. Only aggregated, anonymized data were obtained from the database.
- The analysis of all objectives was based on a time-to-event analysis based on the Kaplan-Meier (KM) method. Median duration and associated 95% confidence intervals (CI) were estimated from the model.

Patient Flow Chart

Access Here

RESULTS

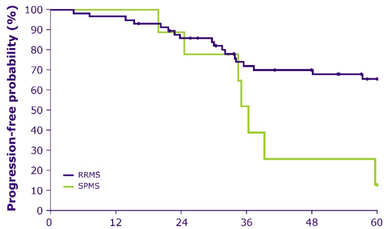
Table 1. Patient Demographics

Characteristic	Patients (N=70)
Age, years, mean ± SD	39.2 ± 10.2
Female, n (%)	40 (57.1)
MS phenotype, n (%)	
RRMS	60 (85.7)
SPMS	10 (14.3)
EDSS = 0, n/pts* (%)	13/70 (18.8)
EDSS = 1–5, n/pts* (%)	51/70 (73.9)
EDSS ≥ 5.5, n/pts* (%)	5/70 (7.2)

Phenotype of patients included in this analysis as determined at baseline of the initial randomized clinical trial.
EDSS, Expanded Disability Status Scale; **MS**, multiple sclerosis; pts*, patients with ≥ 1 EDSS score available; **RRMS**, relapsing-remitting MS; **SD**, standard deviation; **SPMS**, secondary-progressive MS.

Treatment received by patients after the last course of cladribine tablets

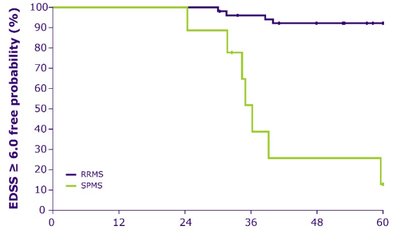
Figure 1. Time-to-disability progression, by MS phenotype



RRMS	Number at risk	57	55	47	36	33	27
	Survival Estimates (95% CI)		96.5 (91.8-100.0%)		72.0 (60.9-85.2%)		65.6 (53.7-80.0%)
SPMS	Number at risk	9	9	8	4	2	1
	Survival Estimates (95% CI)		100.0 (100.0-100.0%)		51.9 (26.7-100.0%)		13.0 (2.1-80.2%)

- The KM estimates for the probability of being free of disability progression at 12 months after the last dose were **96.5%** for RRMS patients and **100.0%** for SPMS patients.
- KM estimates for the probability of being free of disability progression: RRMS 36 months, **72.0%**, 60 months, **51.9%**; SPMS 36 months **65.6%**, 60 months, **13.0%**.

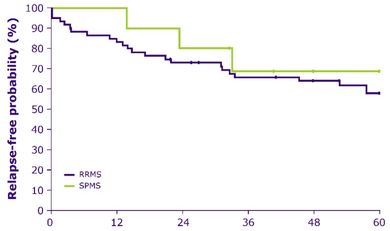
Figure 2. Time-to-EDSS ≥ 6.0, by MS phenotype



RRMS	Number at risk	56	56	54	48	44	40
	Survival Estimates (95% CI)		100.0 (100.0-100.0%)		96.1 (91.0-100.0%)		92.1 (85.0-99.8%)
SPMS	Number at risk	9	9	9	4	2	1
	Survival Estimates (95% CI)		100.0 (100.0-100.0%)		51.9 (26.7-100.0%)		13.0 (2.1-80.2%)

- The KM estimates for the probability of EDSS score ≥ 6.0 at 12 months after the last dose were **100.0%** for RRMS and **100.0%** for SPMS patients.
- KM estimates for the probability of EDSS score ≥ 6.0: RRMS 36 months, **96.1%**, 60 months, **51.9%**; SPMS 36 months, **92.1%**, 60 months, **13.0%**.

Figure 3. Time-to-first confirmed relapse, by MS phenotype



RRMS	Number at risk	60	49	42	36	33	29
	Survival Estimates (95% CI)		83.2 (74.2-93.3%)		65.7 (54.5-79.1%)		57.8 (46.2-72.4%)
SPMS	Number at risk	10	10	8	6	4	4
	Survival Estimates (95% CI)		100.0 (100.0-100.0%)		68.6 (44.5-100.0%)		68.6 (44.5-100.0%)

- By MS phenotype, the KM estimates for the probability of being relapse-free at 12 months after the last dose were **83.2%** for RRMS patients and **100.0%** for SPMS patients.
- KM estimates for the probability of being relapse-free: RRMS 36 months, **65.7%**, 60 months, **68.6%**; SPMS 36 months, **57.8%**, 60 months, **68.6%**.

1. Giovannoni G, et al. *N Engl J Med*. 2010;362:416–426. 2. Giovannoni G, et al. *Mult Scler*. 2018;24:1594–1604. 3. Montalban X, et al. *Neurol Neuroimmunol Neuroinflamm*. 2018;5:e477. 4. Leist TP, et al. *Lancet Neurol*. 2014;13:257–267.

Cladribine tablets 10 mg (3.5 mg/kg cumulative dose over 2 years) are indicated for the treatment of patients with MS in the United States (relapsing forms of MS, including relapsing-remitting disease and active secondary progressive disease, in adults). The CLARITY study: NCT00213135; The CLARITY Extension study: NCT00641537; The ONWARD study: NCT00436826; The ORACLE-MS study: NCT00725985
The authors would like to thank Dominic Jack of Global Medical Affairs, Merck KGaA, for assisting with the interpretation of the study data. The authors would also like to thank patients and their families, the Italian MS Registry, Mosconi and Lepore of STO, investigators, co-investigators and the study teams at each of the 17 participating Italian MS centers and at Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by Joseph Ward of inScience Communications, Springer Healthcare Ltd, UK, and was funded by Merck KGaA, Darmstadt, Germany.
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Presented at the American Academy of Neurology (AAN) 2020 Virtual Congress | 25 April – 1 May

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