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Durable Efficacy of Cladribine Tablets: Cumulative Relapse Incidence over 5 years in CLARITY and CLARITY Extension

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Disclosures

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INTRODUCTION

- In the CLARITY and CLARITY Extension studies, treatment with cladribine tablets 10 mg (cumulative dose 3.5 mg/kg over 2 years [CT3.5]) significantly reduced relapse rates in patients with relapsing-remitting multiple sclerosis.^{1,2}
- Patients receiving cladribine tablets 3.5 mg/kg received their final dose of active treatment in Month 14 of CLARITY, yet had similar clinical outcomes to patients who received additional courses of cladribine tablets in the CLARITY Extension study.²
- Patients treated with cladribine tablets in CLARITY and then placebo in CLARITY Extension had a lower incidence of severe lymphopenia than patients receiving cladribine tablets in both CLARITY and CLARITY Extension.²



OBJECTIVE

To assess, *post hoc*, the temporal occurrence of relapses up to 5 years after treatment initiation with cladribine tablets.



METHODS

CLARITY

Cladribine tablets 3.5 mg/kg

Treatment arm CT3.5
N=433

Patient population

Variable bridging interval
Median: 40.3 weeks
Range: 1 day to 118 weeks

CLARITY Extension

Placebo

Treatment arm CP3.5
N=98

Cladribine tablets 3.5 mg/kg

Treatment arm CC7
N=186

Endpoint

All qualifying relapses reported in CLARITY or CLARITY Extension plus those relapses reported during the variable bridging interval

Statistical analysis

Mean Cumulative Function (MCF) estimates and 95% CI using Nelson method taking recurrent relapses into account



METHODS

CLARITY

Patient population

Variable bridging interval
Median: 40.3 weeks
Range: 1 day to 118 weeks

CLARITY Extension

Placebo

Mean cumulative function

- The Mean Cumulative Function was estimated using the Nelson-Aalen Estimate.
- The MCF is a cumulative history function that shows the cumulative number of recurrent relapses over time. It can be interpreted as the mean number of relapses cumulated over time assuming random censoring.

Endpoint

All qualified patients who were started during the variable bridging interval

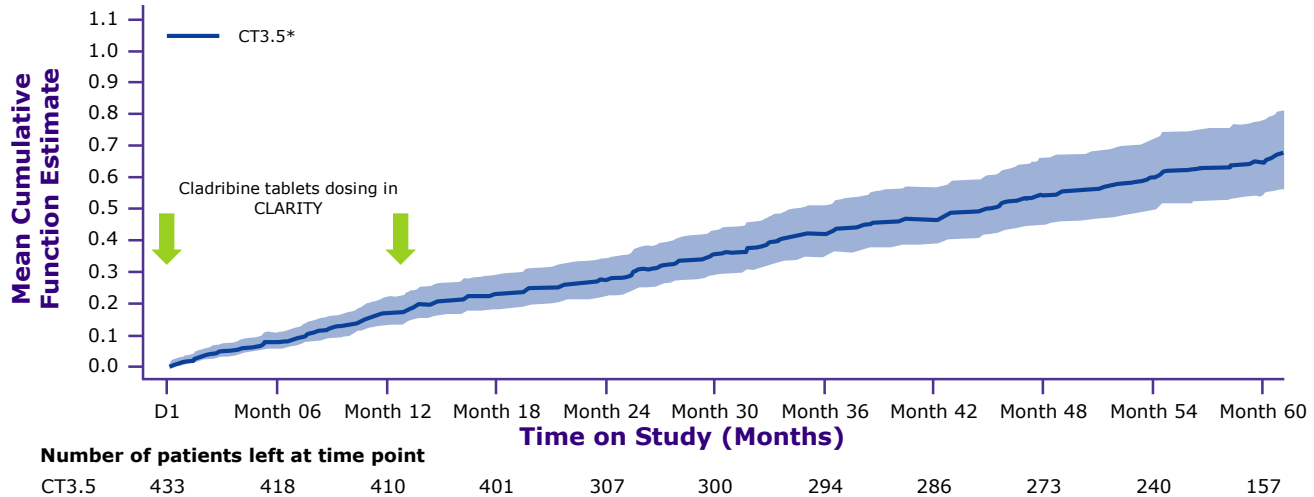
Statistical analysis

Mean Cumulative Function (MCF) estimates and 95% CI using Nelson method taking recurrent relapses into account



RESULTS

Cumulative mean number of recurrent relapses in patients randomized to cladribine tablets 3.5 mg/kg in CLARITY*



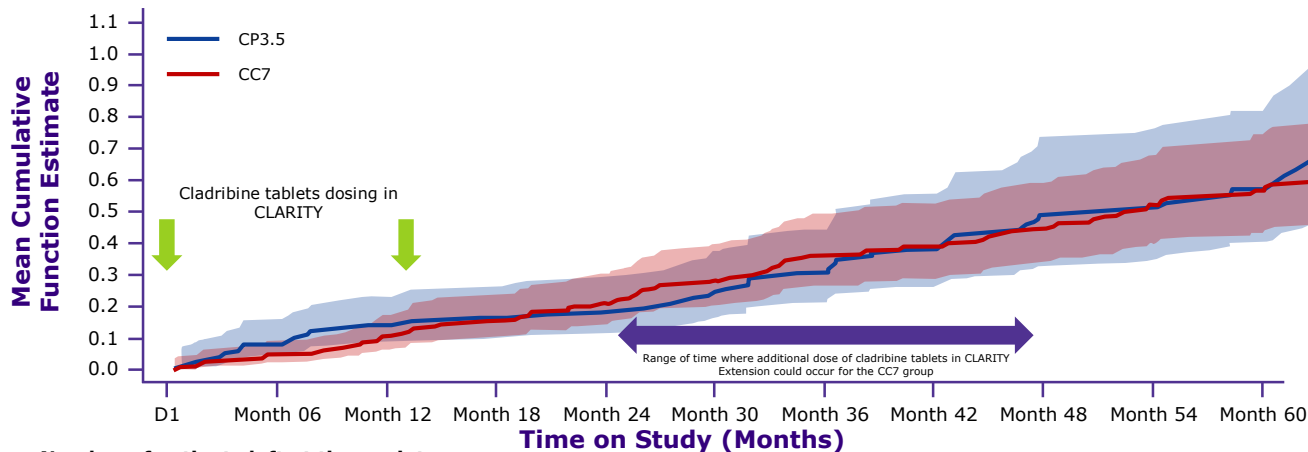
A stable and low mean daily accrual of relapses was observed following administration of cladribine tablets 3.5 mg/kg

*All patients receiving cladribine tablets 3.5 mg/kg in CLARITY and those receiving cladribine tablets 3.5 mg/kg or placebo in CLARITY Extension



RESULTS

Cumulative mean number of relapses in CP3.5 and CC7 treatment groups in CLARITY Extension



Number of patients left at time point

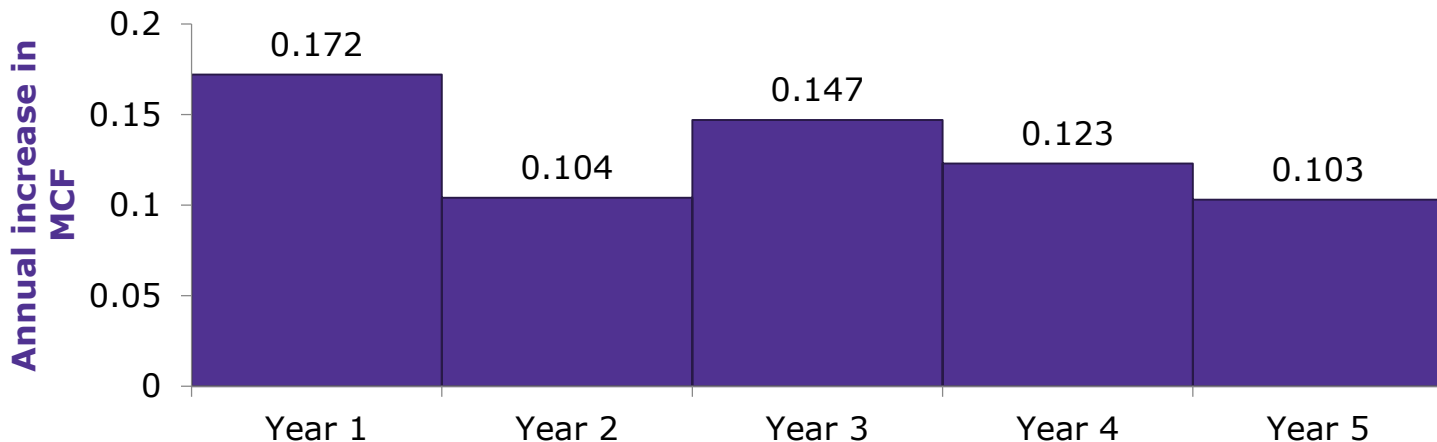
CP3.5	98	98	98	98	97	96	94	89	80	51
CC7	186	186	186	186	186	183	180	173	152	99

A similar accumulation of relapses was observed in patients treated with cladribine tablets 3.5 mg/kg in CLARITY over 2 years compared with patients who received additional courses of cladribine tablets in CLARITY Extension, justifying the pooled analysis of these two sets



RESULTS

Annual increase in Mean Cumulative Function
in patients randomized to cladribine tablets 3.5 mg/kg in CLARITY*



Number of patients at risk at end of the year

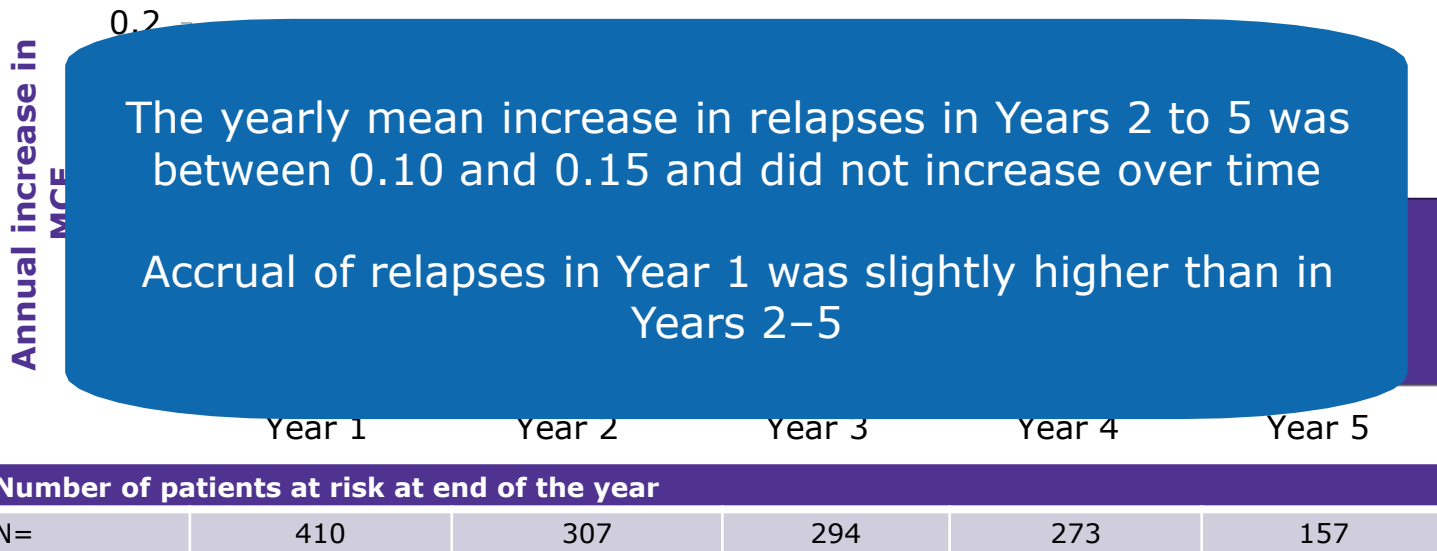
N=	410	307	294	273	157
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*All patients receiving cladribine tablets 3.5 mg/kg in CLARITY and those receiving cladribine tablets 3.5 mg/kg or placebo in CLARITY Extension
MCF, Mean Cumulative Function



RESULTS

**Annual increase in Mean Cumulative Function
in patients randomized to cladribine tablets 3.5 mg/kg in CLARITY***

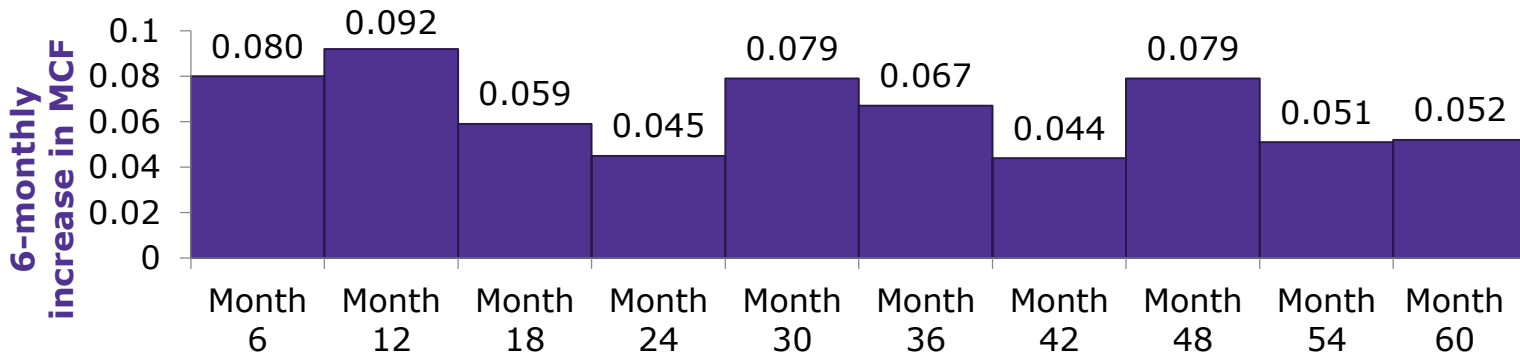


*All patients receiving cladribine tablets 3.5 mg/kg in CLARITY and those receiving cladribine tablets 3.5 mg/kg or placebo in CLARITY Extension
MCF, Mean Cumulative Function



RESULTS

6-monthly increase in mean cumulative number of relapses in patients randomized to cladribine tablets 3.5 mg/kg in CLARITY*



Number of patients at risk at end of the month

N=	418	410	401	307	300	294	286	273	240	157
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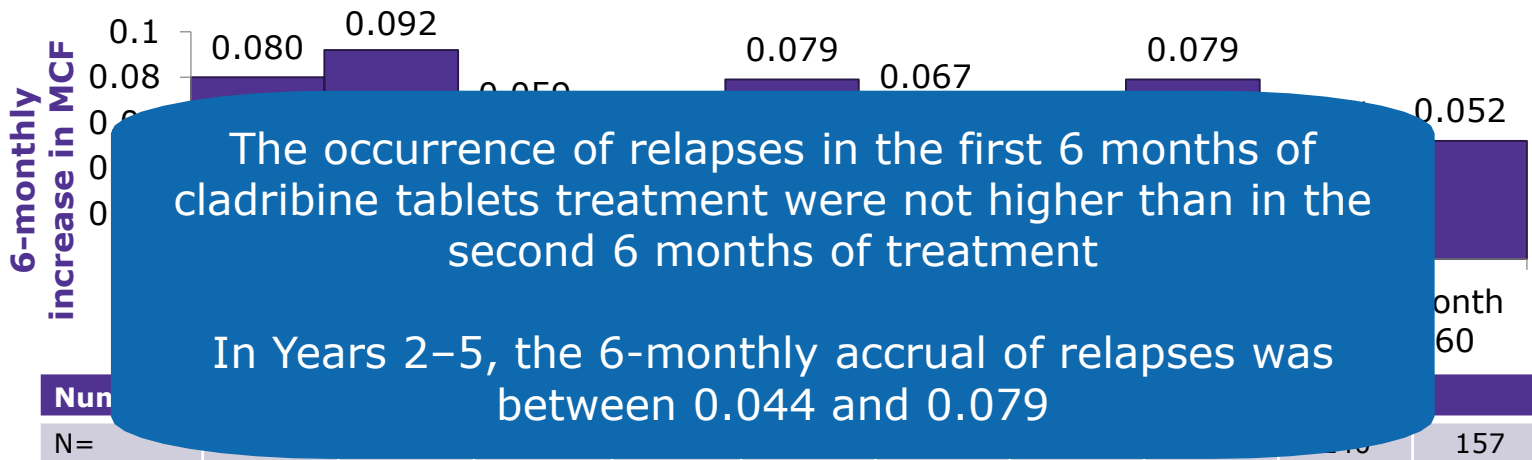
To explore the slightly higher occurrence of relapses in Year 1, the increase in mean cumulative function over 6-monthly periods was assessed

*All patients receiving cladribine tablets 3.5 mg/kg in CLARITY and those receiving cladribine tablets 3.5 mg/kg or placebo in CLARITY Extension
MCF, Mean Cumulative Function



RESULTS

6-monthly increase in mean cumulative number of relapses in patients randomized to cladribine tablets 3.5 mg/kg in CLARITY*



The occurrence of relapses in the first 6 months of cladribine tablets treatment were not higher than in the second 6 months of treatment

In Years 2–5, the 6-monthly accrual of relapses was between 0.044 and 0.079

To explore the slightly higher occurrence of relapses in Year 1, the increase in mean cumulative function over 6-monthly periods was assessed

*All patients receiving cladribine tablets 3.5 mg/kg in CLARITY and those receiving cladribine tablets 3.5 mg/kg or placebo in CLARITY Extension
MCF, Mean Cumulative Function



CONCLUSIONS



Consistent with efficacy sustained beyond dosing, patients receiving a cumulative dose of cladribine tablets 3.5 mg/kg over 2 years experienced a **stable and low yearly accrual of relapses in Years 2–5** after starting cladribine tablets.

The accrual of **relapses remained stable over time**.



The accrual of relapses was slightly higher in the first year compared to the second and subsequent years, but there was **no evidence for relapses occurring preferentially in the first 6 months** after starting cladribine tablets.