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Reduced Grey Matter Atrophy in Patients with Relapsing Multiple Sclerosis Treated with Cladribine Tablets

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Disclosures

This study was sponsored by Merck KGaA, Darmstadt, Germany.

- **MB, LL, and GG** have no conflicts to declare.
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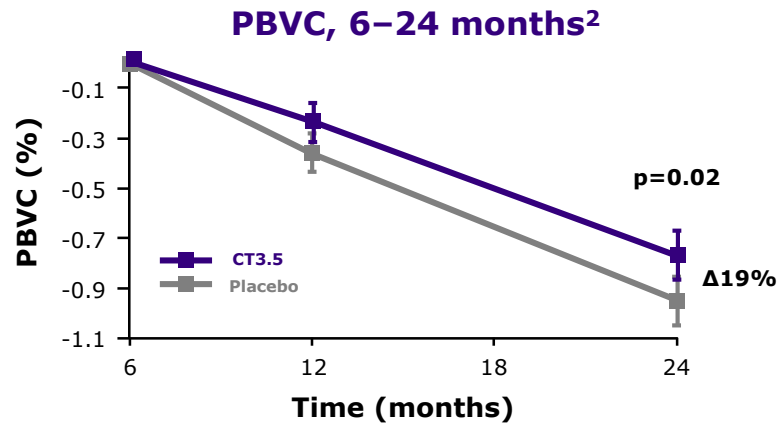
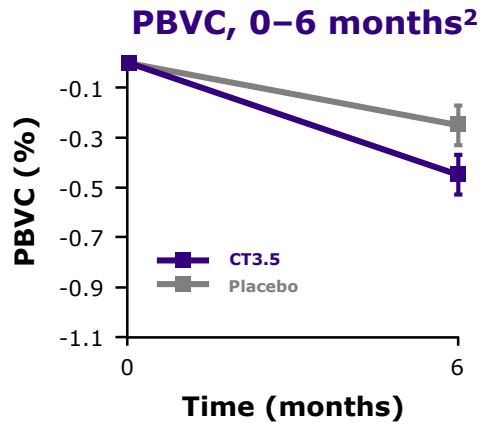
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The CLARITY study: NCT00213135



INTRODUCTION

- Grey matter atrophy is associated with disability progression and cognitive decline in patients with MS.¹
- In the **CLARITY study**, treatment with cladribine tablets decreased brain atrophy compared with placebo which was associated with a lower risk of disability progression.²

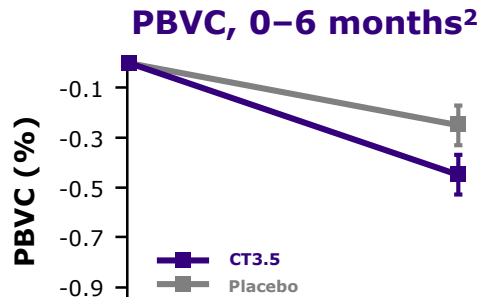


1. De Stefano N, et al. *CNS Drugs*. 2014;28:147–156. 2. De Stefano N, et al. *Mult Scler*. 2018;24:222–226.
CT3.5, cladribine tablets 3.5 mg/kg (cumulative dose over 2 years); MS, multiple sclerosis; PBVC, percentage brain volume change

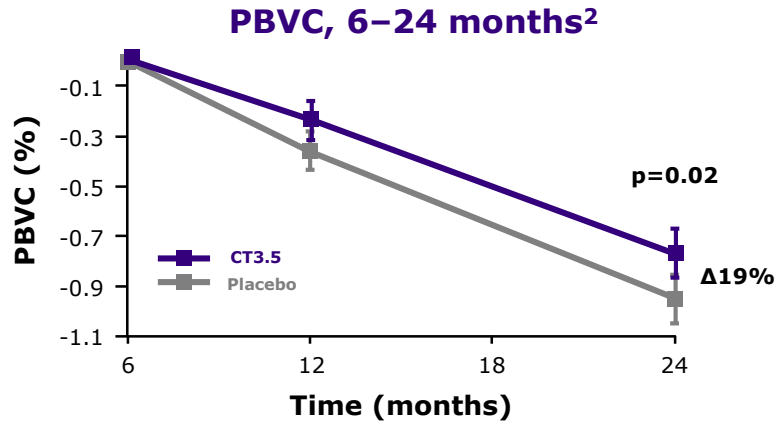


INTRODUCTION

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Pseudoatrophy¹
Anti-inflammatory effect early in the course of cladribine treatment



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OBJECTIVES

***Post hoc* evaluation of grey matter and white matter volume changes in patients with relapsing MS randomized to cladribine tablets or placebo in the CLARITY study.**



METHODS

CLARITY: GM/WM atrophy study

Patients randomized to cladribine tablets 3.5 mg/kg or placebo for 2 years in CLARITY with images from pre-gadolinium T1-weighted magnetic resonance imaging scans evaluated using SIENA-XL software¹

Pseudoatrophy analysis

GM/WM changes
0–6 months

CT3.5 (n=267) Placebo (n=265)

Atrophy analysis

GM/WM changes
6–24 months

CT3.5 (n=184) Placebo (n=186)

- Images from 0–6 months were analyzed independently of images from 6–24 months to account for possible pseudoatrophy.
- Annualized mean % changes in GM/WM volume over time were compared using a variance model.

Scan here for more on
CLARITY primary paper



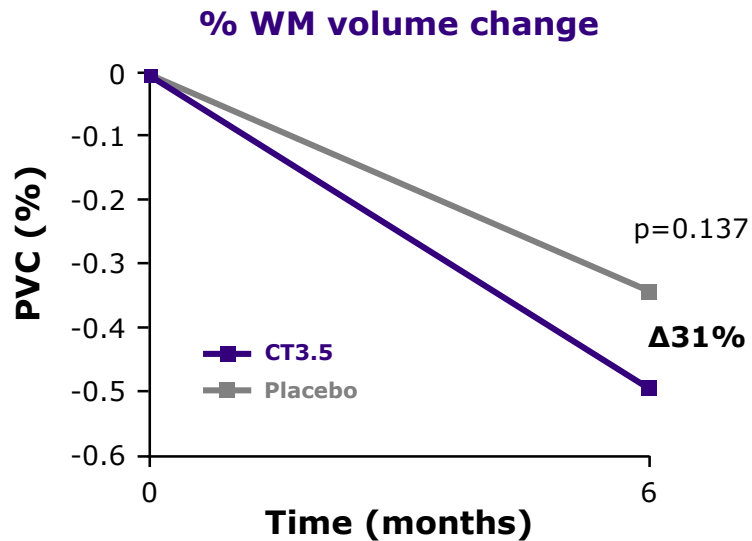
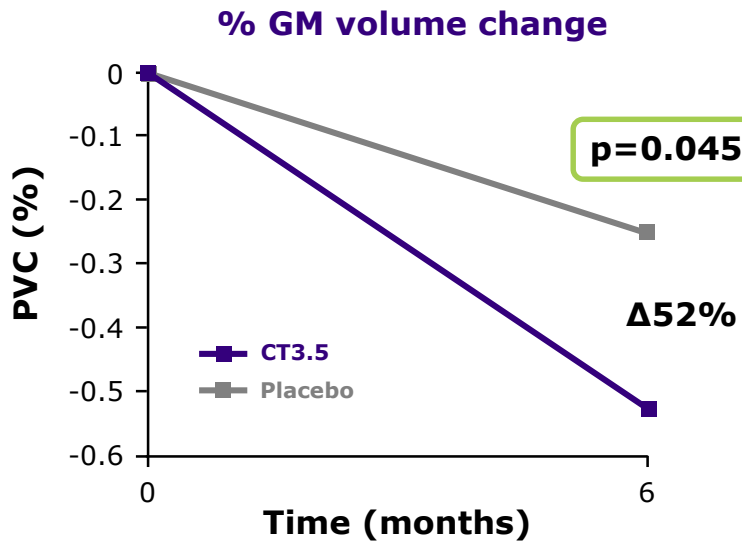
1. Battaglini M, et al. *Hum Brain Mapp.* 2018;39:1063–1077.

CT3.5, cladribine tablets 3.5 mg/kg (cumulative dose over 2 years); GM, grey matter; WM, white matter



RESULTS

Pseudoatrophy analysis, 0–6 months

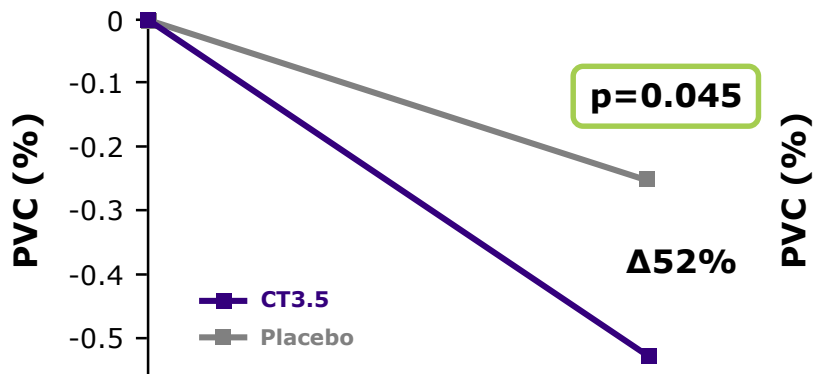




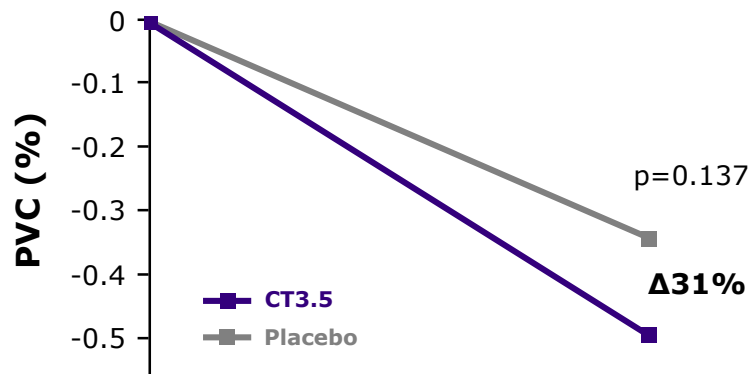
RESULTS

Pseudoatrophy analysis, 0–6 months

% GM volume change



% WM volume change



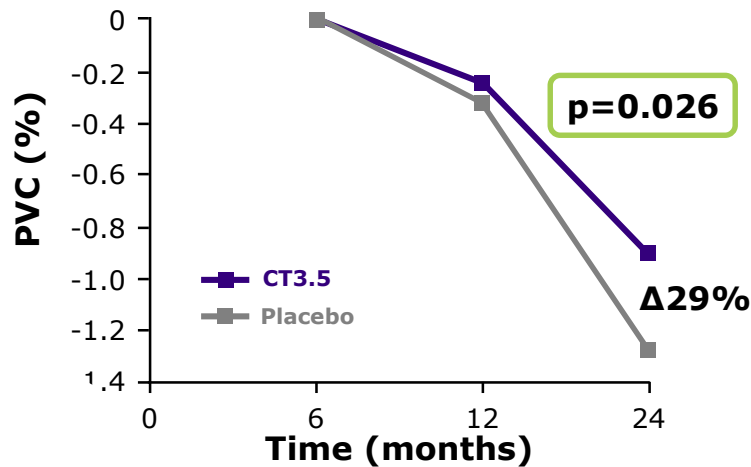
Pseudoatrophy is present both in GM and WM during the first 6 months of therapy
- Significant difference in volume change between CT3.5 and placebo for GM only



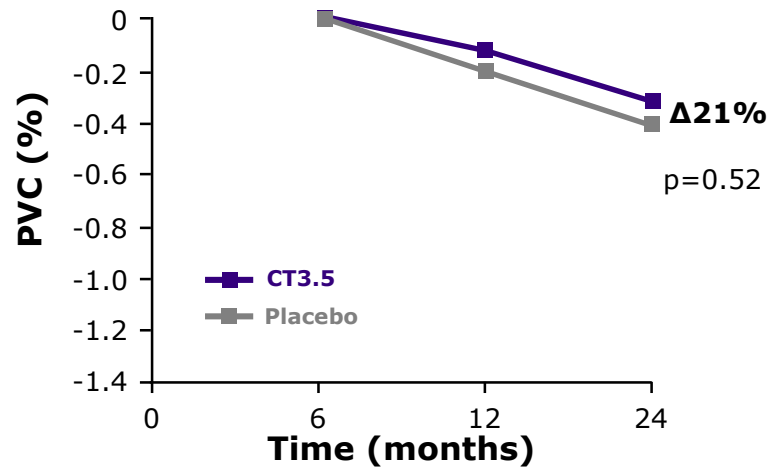
RESULTS

Atrophy analysis, 6–24 months

% GM volume change



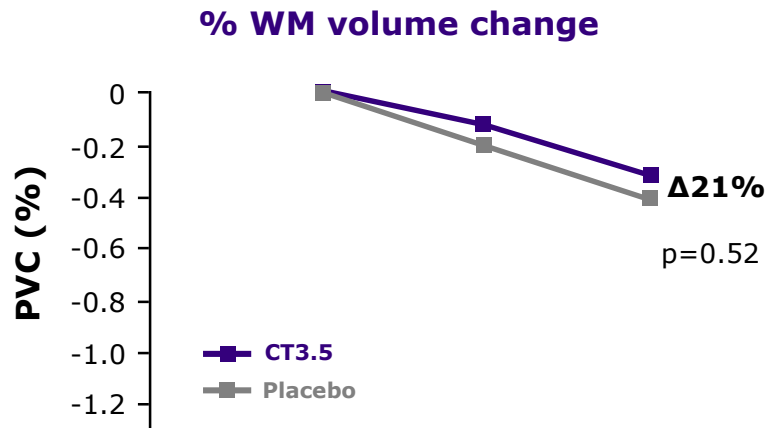
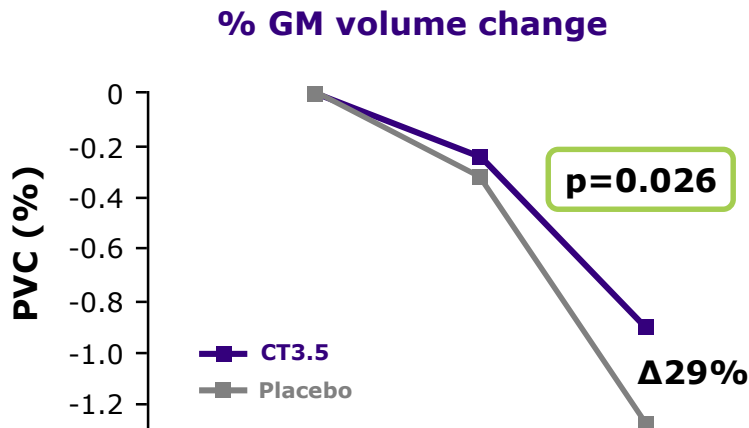
% WM volume change





RESULTS

Atrophy analysis, 6–24 months



Brain volume loss from 6–24 months was reduced in patients treated with CT3.5 - Significant difference in volume change between CT3.5 and placebo for GM only



CONCLUSIONS



A reduction in grey matter volume loss was noted from 6–24 months in cladribine-treated patients versus placebo, after a period of pseudoatrophy (0–6 months).



Findings suggest that cladribine tablets 3.5 mg/kg significantly reduces brain atrophy predominantly in the grey matter, an effect that may contribute to a lower risk of disability progression.