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Cladribine tablets reduce slowly expanding lesions in gray matter-driven MRI phenotype and active lesions in all Sustain-Based MRI phenotypes of MS patients

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INTRODUCTION

Cladribine tablets (CladT) can reduce acute inflammation in relapsing-remitting (RR) multiple sclerosis (MS) patients. Acute and chronic inflammation can be measured on brain MRI. SuStaIn, an AI-driven method that stratifies patients based on their MRI characteristics, allows to identify different MS subtypes.

OBJECTIVES

To assess the 2-year accumulation rate of acute and chronic inflammation in RR-MS patients treated with cladribine tablets and stratified using SuStaIn.

METHODS

Three different datasets were used in this study:

- 376 healthy controls;
- 359 CladT-treated RRMS patients from the CLARIFY-MS (NCT03364036) trial;
- 256 CladT-treated RRMS patients with MRI acquired 10 times over a 2 years follow-up period, from the MAGNIFY-MS (NCT03369665) trial.

SuStain was trained on the healthy controls and the CLARIFY-MS cohorts. MRI features fed to SuStaIn comprise measure of white matter integrity assessed on 7 brain regions, volume of 7 grey matter regions and lesion volume. The same features were used to assign each patient of the MAGNIFY-MS to one Sustain-based MRI phenotype (Figure 1A). The cumulative number of combined unique active lesions (cum_CUA) and slowly expanding lesions (cum_SEL) were used as marker of acute and chronic inflammation, respectively. Using an in-house developed pipeline, SELs were identified as those T2 lesions showing constant and concentric expansion. For each SEL we assessed the time of occurrence defined as the first MRI time-point where the SEL intensity longitudinal profile differed from that of the surrounding WM (Figure 1B). Comparison of the slopes of cum_CUA and cum_SEL among the 3 MRI phenotypes was performed with a generalized linear mixed effect model that included subject as a random factor and an MRI-phenotype-by-time interaction term.

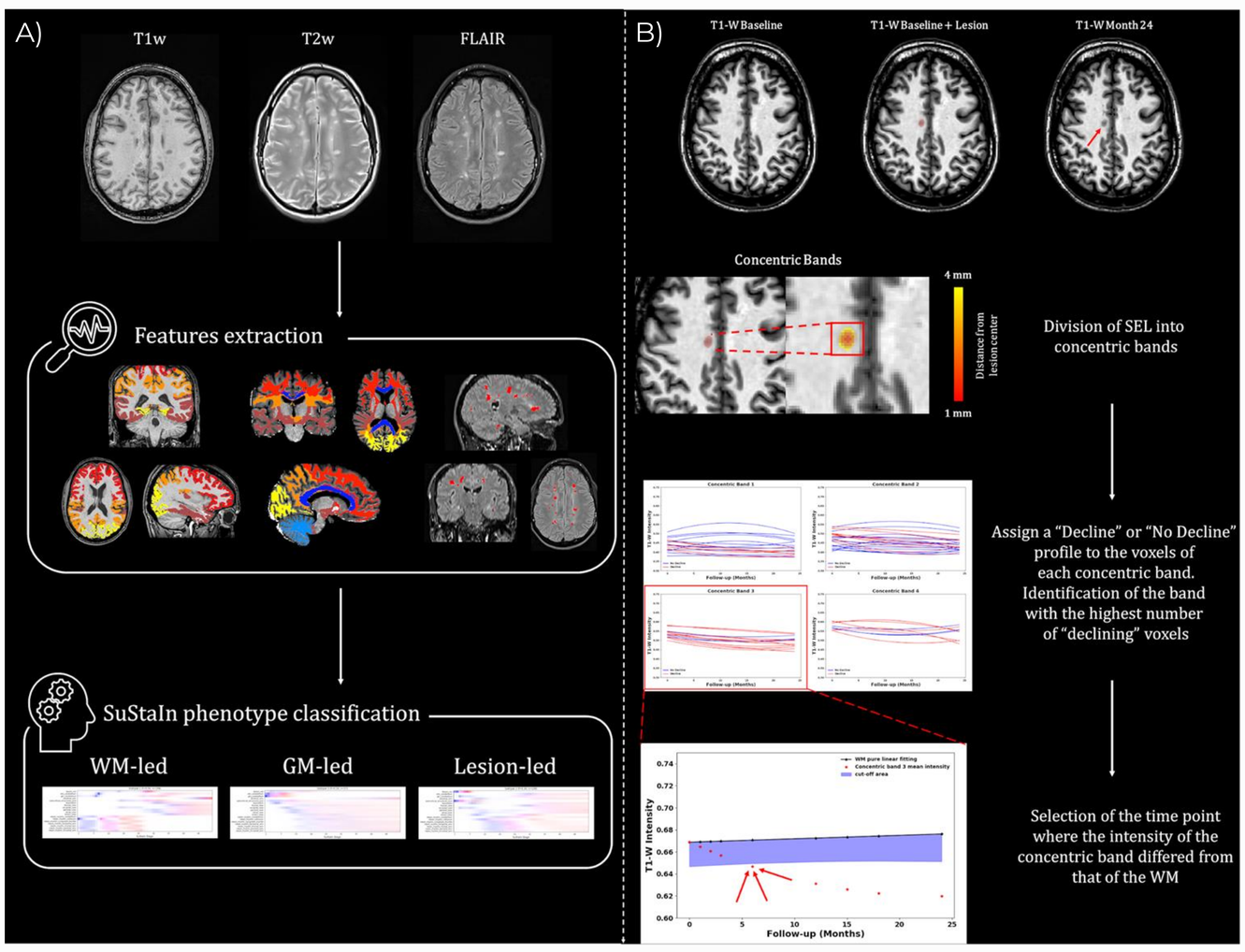

Figure 1. Depiction of SuStaIn subtype classification workflow (A). Schematic representation of the SEL occurrence time point detection process on an example lesion (B).

RESULTS

The **cum_CUA's accumulation rate** (WM-led:0.78 CUA/month, GM-led:0.7 CUA/month, Les-led:0.52 CUA/month; p>0.05) **and** that of **cum_SEL** (WM-led: 0.065 SEL/month, GM-led: 0.07 SEL/month, Les-led: 0.01 SEL/month; p>0.05) **was similar** in the three phenotypes **over 6 months**. **Over** the **next 18 months**, the cum_CUA's accumulation rate was significantly lower (WM-led:0.24 CUA/month; GM-led:0.21 CUA/month; Les-led:0.17 CUA/month; p>0.05) regardless of MR-phenotypes, while the **cum_SEL's accrual** was significantly **reduced** only in **GM-led** (0.05 SEL/month, p<0.05).

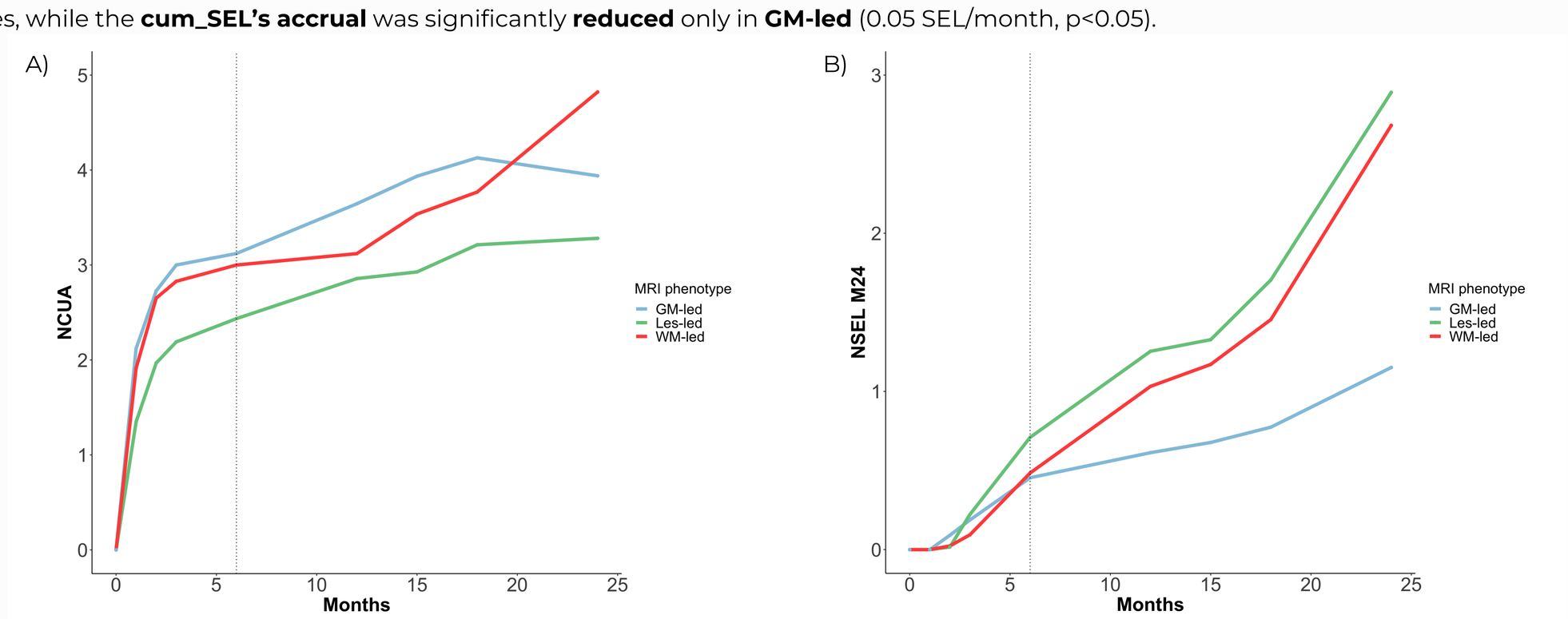

Figure 2. Number of CUA (NCUA, A) and Number of SELs (NSEL, B) over time. Different colours represent different MRI phenotypes as classified by SuStaIn. Black dotted lines indicate the first 6 months from the beginning of the MAGNIFY-MS trial

CONCLUSIONS

Cladribine tablets **slows** the **accumulation** of **acute inflammation** in all MRI phenotypes and **reduces chronic inflammation accrual** in multiple sclerosis patients with **GM-driven damage**.

DISCLOSURES

N. De Stefano: has received honoraria from Biogen-Idec, Bristol Myers Squibb, Celgene, Genzyme, Immunic, Merck, Novartis, Roche and Teva for consulting services, speaking, and travel support. He serves on advisory boards for Merck, Novartis, Biogen-Idec, Roche, and Genzyme, Immunic. He has received research grant support from the Italian MS Society and is co-founder of Siena Imaging s.r.l.
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M.Battaglini: is co-founder of Siena Imaging s.r.l.
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