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Background

Cladribine (CLAD) was approved by the European Medicines Agency (EMA) for the therapy of people with multiple sclerosis (PwMS) in 2017. Previous analyses showed that treatment switches from CLAD to ocrelizumab (OCR; EMA approval 2018) occur frequently.

Objective

To assess the outcome after the switch (CLAD to OCR). PwMS who remained on CLAD were used as comparator.

Methods

In this retrospective cohort study from the German MS Registry, all PwMS who switched from CLAD to OCR between 2017 and 2023 were analysed regarding annualized relapse rate (ARR), MRI activity (gd+/new T2 lesions) and EDSS scores and compared with PwMS who remained on CLAD (non-switchers). Non-switchers were evaluated at comparable follow-up times compared to switchers.

Results

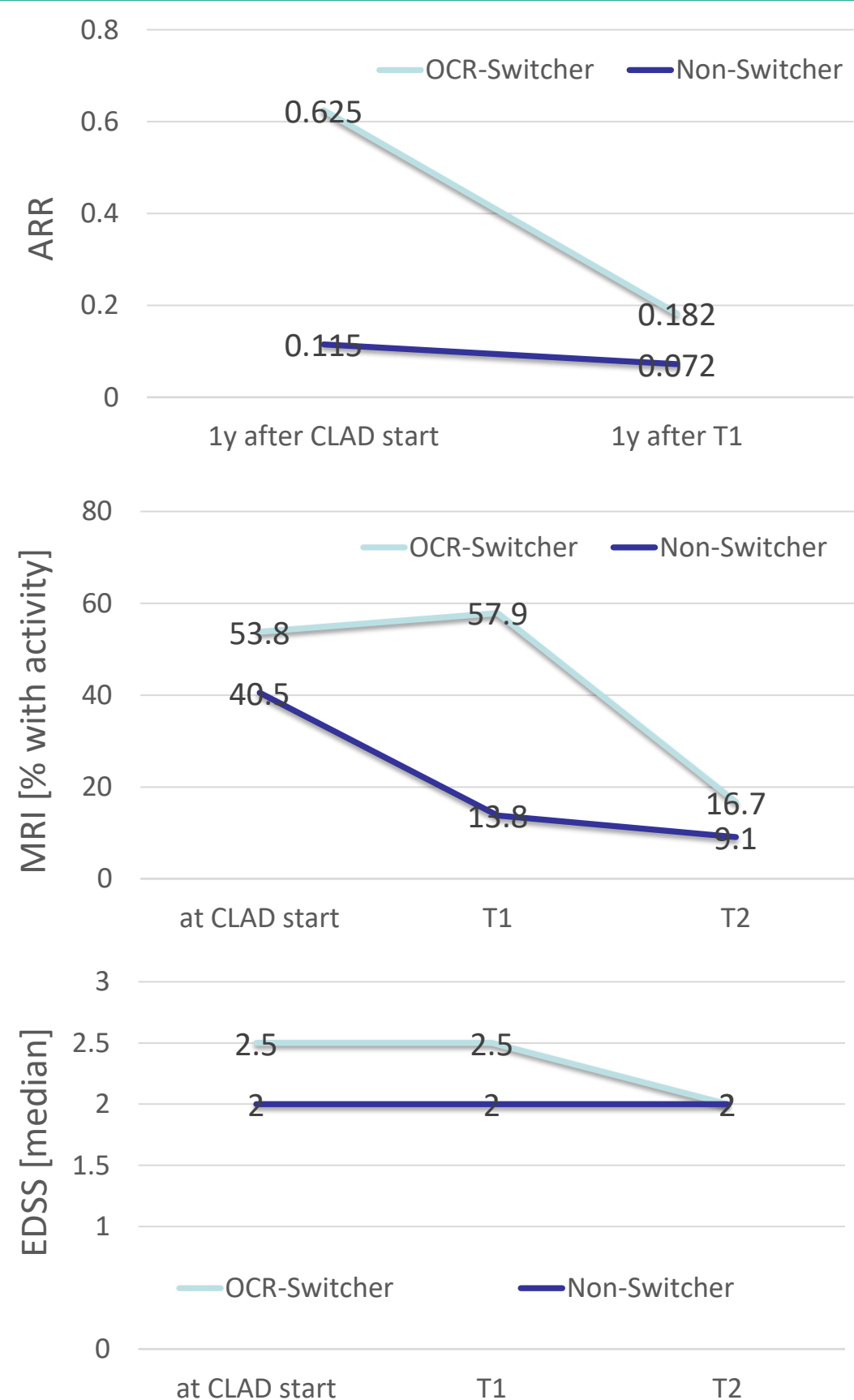


Figure 2. Comparison of OCR-switcher and non-switcher.

T1: at OCR start (switcher) or 1.9y after CLAD start (non-switcher)

T2: 1y after T1, i.e. 1y after OCR start (switcher) or 2.9y after CLAD start (non-switcher).

Declaration of interest: David Ellenberger, Firas Fneish and Melanie Peters had no personal financial interests to disclose other than being employees of the German MS Registry. Niklas Frahm is an employee of the MSFP. Moreover, he is an employee of Rostock's University Medical Center and received travel funds for research meetings from Novartis. None resulted in a conflict of interest. Alexander Stahmann has no personal financial interests to disclose, other than being the leader of the German MS Registry, which receives (project) funding from a range of public and corporate sponsors, recently including G-BA, The German Retirement Insurance, The German MS Trust, German MS Society, Biogen, Bristol Myers Squibb, Merck, Novartis and Roche. None resulted in a conflict of interest. Peter Flachenecker has received speaker's fees and honoraria for advisory boards from Almirall, Bayer, Biogen Idec, BMS-Celgene, Coloplast, Genzyme, GW Pharma, Hexal, Janssen-Cilag, Novartis, Merck, Roche, Sanofi, Stadapharm and Teva. None resulted in a conflict of interest. Tim Friede has received personal fees for consultancies (including data monitoring committees) in the past three years from Bayer, BiosenseWebster, Boehringer Ingelheim, Cardialysis, CSL Behring, DaiichiSankyo, Enanta, Feldmann Patent Attorneys, Fresenius Kabi, Galapagos, IQVIA, Janssen, Medicomics, Novartis, Penumbra, Roche, SGS, Vifor. None resulted in a conflict of interest. Friedemann Paul has received speaking fees, travel support, honoraria from advisory boards and/or financial support for research activities from Bayer, Novartis, Biogen, Bristol Myers Squibb, Teva, Sanofi-Aventis/Genzyme, Merck Serono, Alexion, Chugai, MedImmune, Shire, German Research Council, Werth Stiftung of the City of Cologne, German Ministry of Education and Research, EU FP7 Framework Program, Arthur Arnstein Foundation Berlin, Guthy Jackson Charitable Foundation and National Multiple Sclerosis of the USA. He serves as academic editor for PLoS ONE and associate editor for Neurology, Neuroimmunology and Neuroinflammation. None resulted in a conflict of interest. Clemens Warnke has received institutional support from Novartis, Alexion, Sanofi Genzyme, Biogen, Merck and Roche. None resulted in a conflict of interest. Uwe K. Zettl has received speaking fees, travel support and/or financial support for research activities from Alexion, Almirall, Bayer, Biogen, Bristol Myers Squibb, Janssen, Merck Serono, Novartis, Octapharma, Roche, Sanofi Genzyme, Teva as well as EU, BMBF, BMWI and DFG. None resulted in a conflict of interest.

In total, the German MS Register observed 586 CLAD patients, with a median observation time on CLAD of 1.7 years. In this cohort, 90 started (/switched to) another DMD during follow-up, while 496 had not yet switched at last follow-up. Within the PwMS who switched, a relative majority of 40 PwMS switched to OCR. Switch to OCR occurred after a median period of 1.9 years (Q1, Q3: 1.1, 2.9 years) post CLAD start, with 22 PwMS having switched ≤ 2 years, 15 PwMS 2-4 years and 3 PwMS >4 years after treatment start with CLAD.

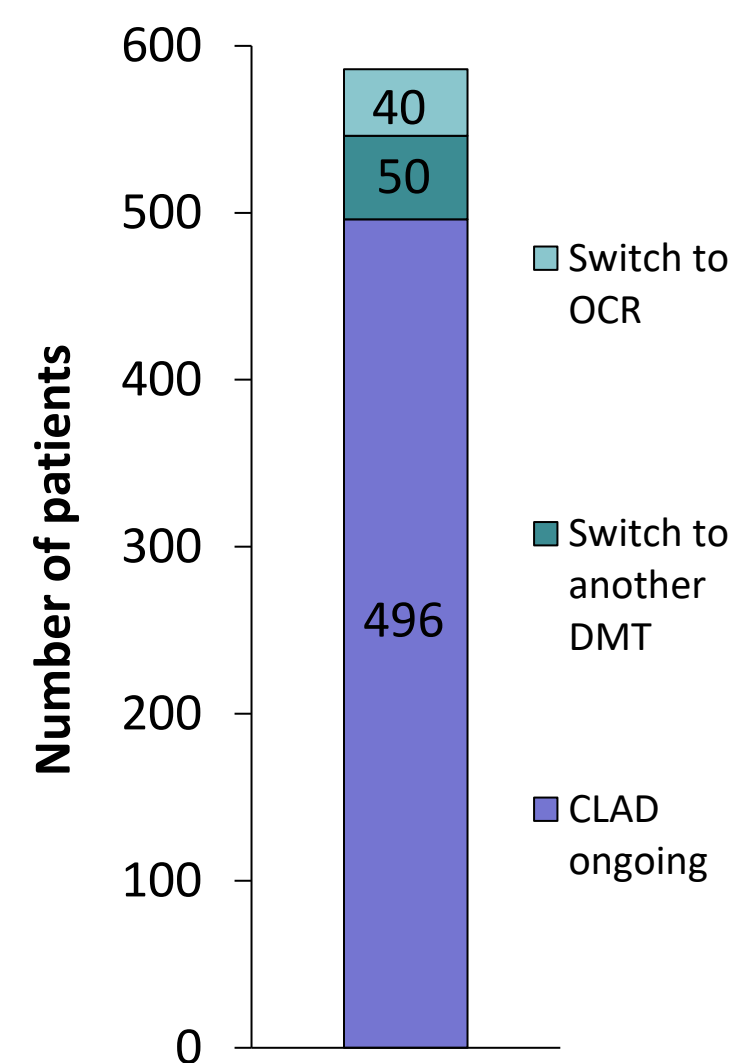


Figure 1. Overview of treatment discontinuation in PwMS treated with cladribine in GMSR (N=586).

Table 1. Demographics of CLAD to OCR switcher and non-switcher. CLAD – cladribine

	OCR-Switcher (N=40)	Non-Switcher (N=496)
sex [female, %]	29 (72.5%)	366 (73.8%)
age at CLAD start (y) median/mean(SD)	36.2 / 36.7 (± 12.5)	39.9 / 41.7 (± 11.8)
age at last visit (y)	39.2 / 40.6 (± 12.8)	42.0 / 43.8 (± 12.0)
disease duration at last visit (years)	13.5 / 14.3 (± 8.8)	11.0 / 12.7 (± 8.7)

Conclusions

- Only 15% (90/586) of CLAD patients switched medication, of which most switched to OCR. The low rate, as well as low disease activity in non-switchers, may be an indicator for treatment efficacy.
- Recent research showed ongoing disease activity in response to OCR after switches from other DMDs.¹ Patients who previously showed signs of disease activity under CLAD could be effectively stabilized with a switch to OCR, indicated by lower relapse and MRI activity after starting OCR.
- Patients unresponsive to CLAD-treatment are responding well to therapy escalation to OCR for controlling disease activity, thus choosing CLAD as a therapy doesn't limit follow-up treatment options.
- Additional data on CLAD therapy (beyond year 4) can be found in Poster **P747**.

References

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