msregister

Treatment

Cladribine therapy in multiple sclerosis: Disease activity 4+ years after initiation

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Background

- Cladribine (CLAD) is a disease-modifying therapy (DMT) for relapsing multiple sclerosis (RMS)
  - 2 annual cycles, each consisting of 2 treatment weeks 1 month apart
- After 2 cycles, treatment is typically withheld
- Limited data regarding disease activity in people with MS (pwMS) without any other DMT over several years after 2 annual CLAD cycles

Objectives

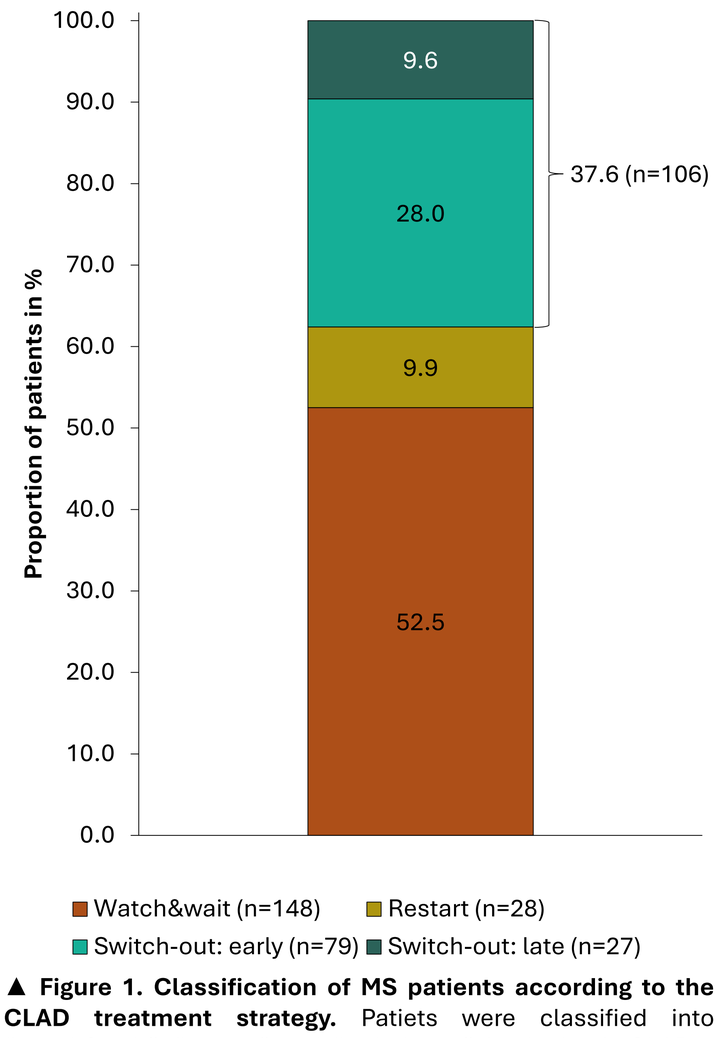
- To analyse disease activity in pwMS 4+ years after CLAD start onwards
- To compare varying CLAD treatment strategies with regard to activity of relapse and magnetic resonance imaging (MRI)

Methods

- PwMS from the German MS Register (export date: 01-08-2025) aged ≥18 years with ≥2 completed regular CLAD cycles (years 1 and 2 after CLAD start) were classified
  - "Watch&wait": 2 initial cycles, followed by persistent standby
  - "Restart": additional cycle (after the initial 2 cycles) >2 years after CLAD start
  - "Switch-out": starting another DMT after CLAD in years 1–4 (early)/after year 4 (late)
- Disease activity: annualised relapse rate (ARR) and MRI activity (gadolinium enhancing lesions and/or new T2 lesions)

Results

- 282 pwMS fulfilled inclusion criteria (Fig. 1, Table 1)



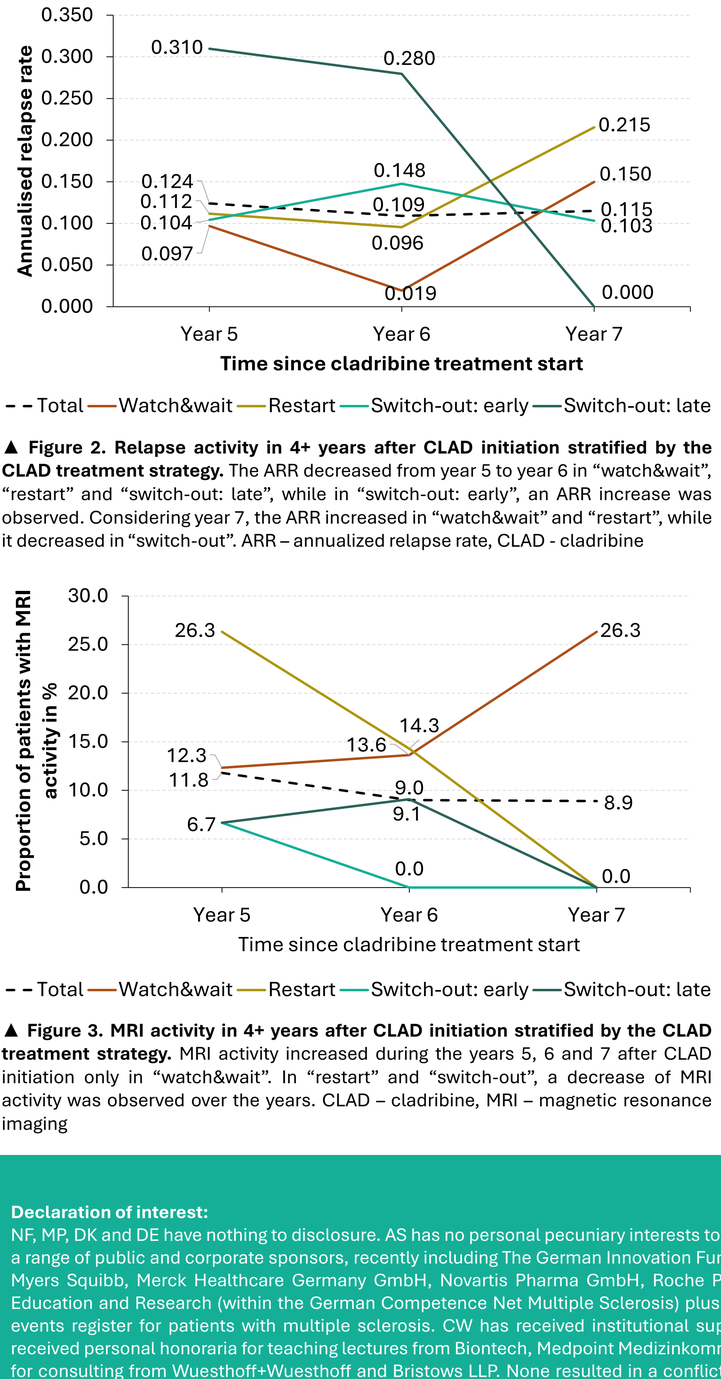
▲ **Figure 1. Classification of MS patients according to the CLAD treatment strategy.** Patiets were classified into "watch&wait", "restart" and "switch-out" (early, late). CLAD – cladribine, MS – multiple sclerosis, n – number of patients

▼ **Table 1. Clinical characterization of the study population (N=282)**

Age at CLAD start (years), *median (q1, q3)*	40.7 (33.1, 51.4)
Disease duration at CLAD start (years), *median (q1, q3)*	9.6 (3.9, 16.1)
EDSS at CLAD start, *median (q1, q3)*	3.0 (2.0, 4.0)
RRMS at CLAD start, *n (%)*	255 (90.4%)
Treatment naive before CLAD, *n (%)*	69 (24.4%)

CLAD - cladribine, MS – multiple sclerosis, n - number of patients, q1 - 25% quantile, q3 - 75% quantile, RRMS – relapsing-remitting MS

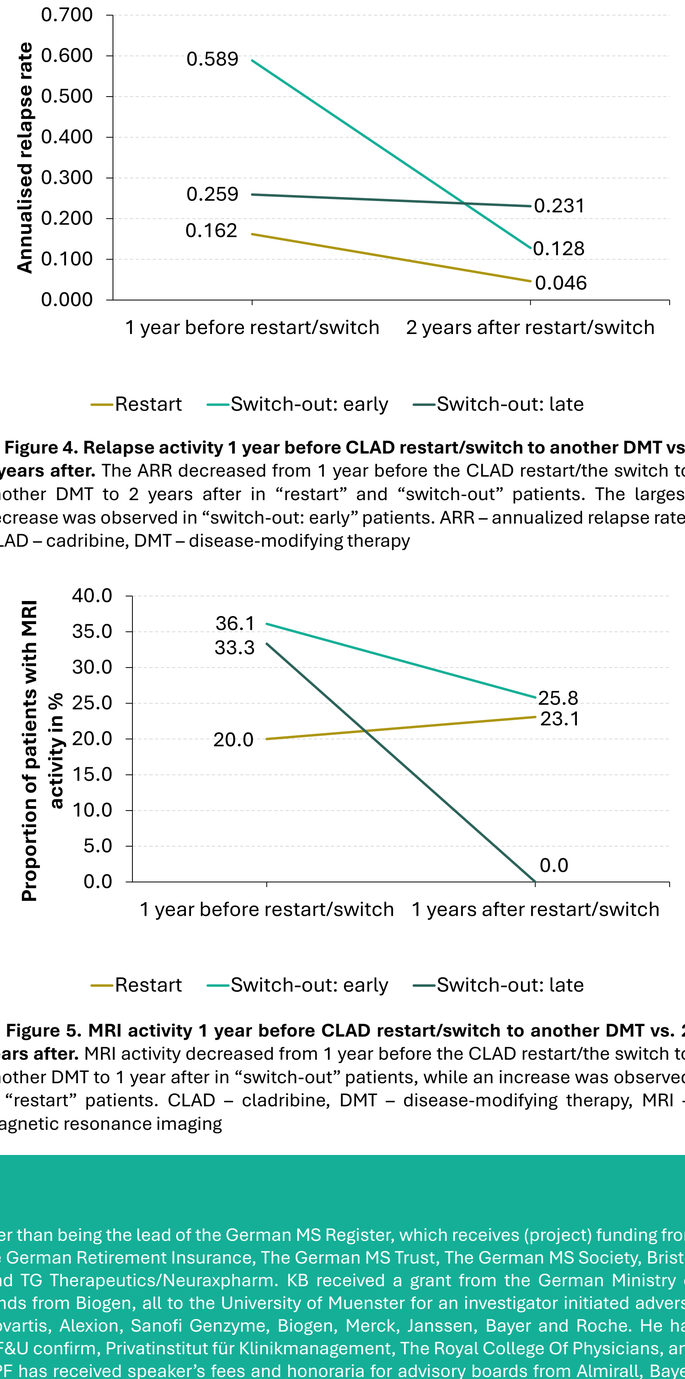
- ARR (Fig. 2):
  - Decrease during years 5 and 6 in "watch&wait" and "restart" groups, but increase in year 7
  - Decrease in year 7 among „switch-out"
- MRI activity (Fig. 3):
  - Increase from years 5 to 7 in "watch&wait"
  - Decrease over time in "restart" and "switch-out"
- Any disease activity (relapse/MRI activity) in years 5 vs. 6 vs. 7 after CLAD initiation (in total): 12.8% vs. 10.1% vs. 9.9%



▲ **Figure 2. Relapse activity in 4+ years after CLAD initiation stratified by the CLAD treatment strategy.** The ARR decreased from year 5 to year 6 in "watch&wait", "restart" and "switch-out: late", while in "switch-out: early", an ARR increase was observed. Considering year 7, the ARR increased in "watch&wait" and "restart", while it decreased in "switch-out". ARR – annualized relapse rate, CLAD - cladribine

▲ **Figure 3. MRI activity in 4+ years after CLAD initiation stratified by the CLAD treatment strategy.** MRI activity increased during the years 5, 6 and 7 after CLAD initiation only in "watch&wait". In "restart" and "switch-out", a decrease of MRI activity was observed over the years. CLAD – cladribine, MRI – magnetic resonance imaging

- Majority of „switch-out" patients switched to anti-CD20 monoclonal antibodies (early switch-out: 88.9%, late switch-out: 68.5%)
- Decrease of ARR and MRI activity after switch from CLAD to other DMTs (Fig. 4, Fig.5)
- In „restart" patients, ARR decreased after new CLAD cycle, while MRI activity increased



▲ **Figure 4. Relapse activity 1 year before CLAD restart/switch to another DMT vs. 2 years after.** The ARR decreased from 1 year before the CLAD restart/the switch to another DMT to 2 years after in "restart" and "switch-out" patients. The largest decrease was observed in "switch-out: early" patients. ARR – annualized relapse rate, CLAD – cadribine, DMT – disease-modifying therapy

▲ **Figure 5. MRI activity 1 year before CLAD restart/switch to another DMT vs. 2 years after.** MRI activity decreased from 1 year before the CLAD restart/the switch to another DMT to 1 year after in "switch-out" patients, while an increase was observed in "restart" patients. CLAD – cladribine, DMT – disease-modifying therapy, MRI – magnetic resonance imaging

Conclusions

- CLAD "watch&wait" patients may experience a resumption of disease activity (relapse and MRI activity) in year 7 after initiation, unlike "restarters" and "switch-outs"
  - Necessity of close monitoring and, if necessary, treatment adjustment after year 4 of CLAD

Declaration of interest:
NF, MP, DK and DE have nothing to disclosure. AS has no personal pecuniary interests to disclose, other than being the lead of the German MS Register, which receives (project) funding from a range of public and corporate sponsors, recently including The German Innovation Fund (G-BA), The German Retirement Insurance, The German MS Trust, The German MS Society, Bristol Myers Squibb, Merck Healthcare Germany GmbH, Novartis Pharma GmbH, Roche Pharma AG and TG Therapeutics/Neuraxpharm. KB received a grant from the German Ministry of Education and Research (within the German Competence Net Multiple Sclerosis) plus additional funds from Biogen, all to the University of Muenster for an investigator initiated adverse events register for patients with multiple sclerosis. CW has received institutional support from Novartis, Alexion, Sanofi Genzyme, Biogen, Merck, Janssen, Bayer and Roche. He has received personal honoraria for teaching lectures from Biontech, Medpoint Medizinkommunikations, F&U confirm, Privatinstitut für Klinikmanagement, The Royal College Of Physicians, and for consulting from Wuesthoff+Wuesthoff and Bristows LLP. None resulted in a conflict of interest. PF 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. FP 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. KH has received speaking fees and/or institutional grant support from Bayer, Biogen, BMS, Merck Serono, Novartis, Roche, Sanofi-Genzyme, and Teva. None resulted in a conflict of interest. UKZ 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.