Cladribine personalised dosing to treat multiple sclerosis: observations in 208 patients

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Disclosures

KAP, SDT, AS, OY, AA, LB and DA have nothing to disclose.
JM has received advisory board fees from Biogen, Novartis and Merck and meeting support from Biogen, Novartis, Merck, Roche and Sanofi Genzyme.
DB has received compensation for consultancy and speaking for Canbex Therapeutics, Japan Tobacco, Merck Serono, Roche, Sanofi-Genzyme.
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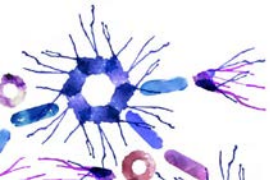
Development of Cladribine Personalised Dosing

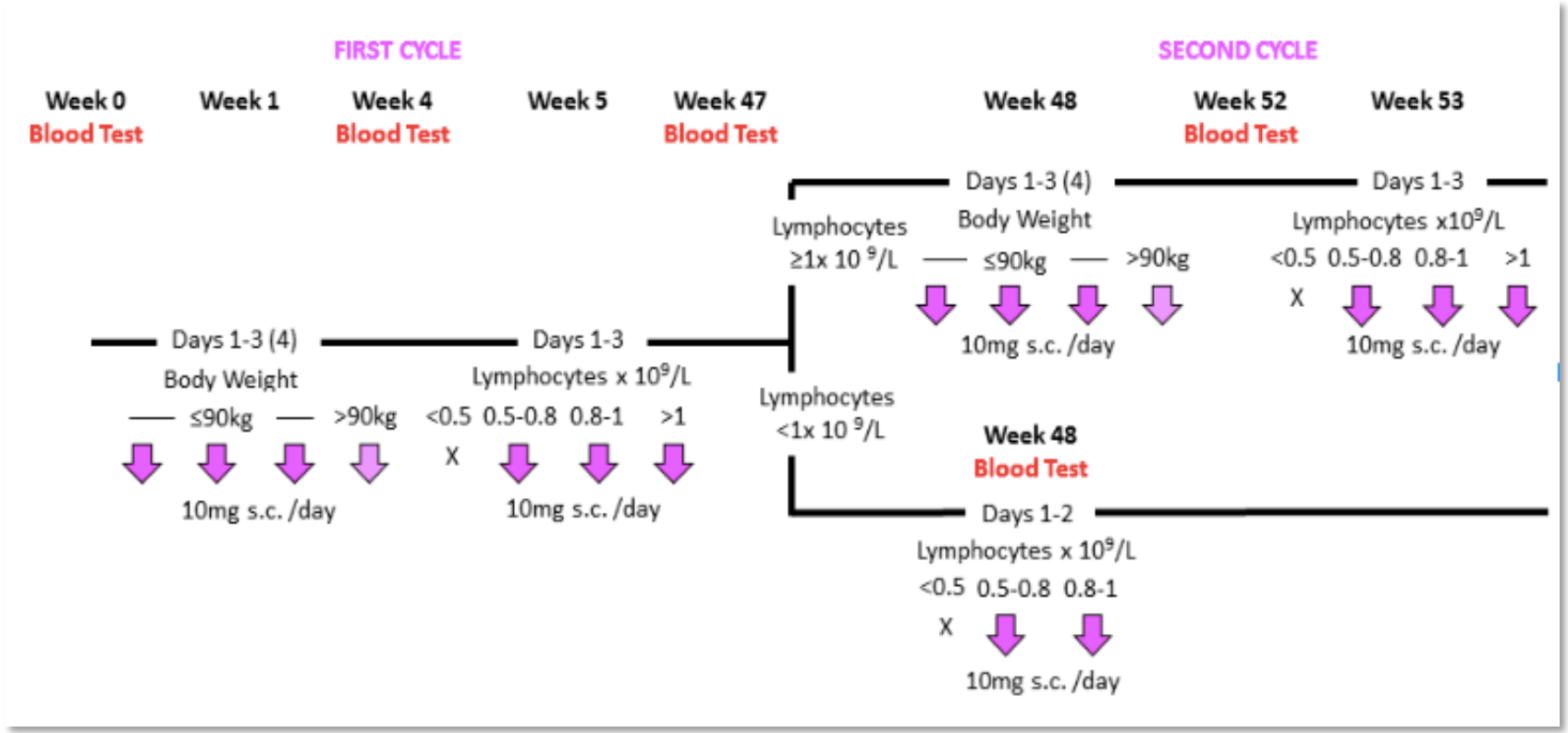
CLADRIBINE

- Selective lymphocyte depleting immunotherapy
- Original use: Hairy Cell Leukaemia
- Oral form licensed for relapsing/ active MS
- BartsMS Off-label programme (2014)
- **Favourable profile**:
  - Efficacy[1-5]
  - CNS penetrant[6-7]
  - Safety[8-9]
  - Convenience[10-11]



[1]Giovannoni, et al. NEJM 2010; [2]Leist, et al. Lancet Neurol 2014; [3]Sipe, et al. Lancet 1994; [4]Beutler, et al. Proc Nat Acad Sci USA 1996; [5]Rice, et al. Neurology 2000; [6]Santana, et al. Blood 1994; [7]Kearns Cancer Res 1994; [8]Pakpoor, et al. Neurol Neuroimmunol Neuroinflamm 2015; [9]Baker, et al. JAMA Neurol 2017; [10]Mao, et al. JNNP 2017; [11]Mao, et al. MSARD 2019.

Dosing schedule



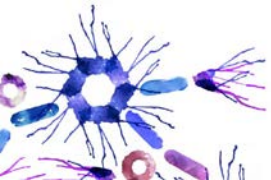
Methods

- **Service evaluation** — Barts Health Clinical Effectiveness Unit #11483
- **Treatment eligibility** — **Disease activity** demonstrated by Gd^+ and/or new/enlarging T_2 lesion(s) on MRI[1], and/or elevated CSF neurofilament light chain[2]

  Safety checklist passed[3]
- **Follow-up** — Safety and para-/clinical efficacy at 2 years compared to baseline

Results

Demographics	Total n = 208
Female/male	131/77
Relapsing Progressive	100 108
Age (years)	44 (17-72)
Disease duration (years)	11 (1-48)
Median EDSS	5.5 (0-8.5)
Eligible for NHS England DMTs?	Yes 113 No 95



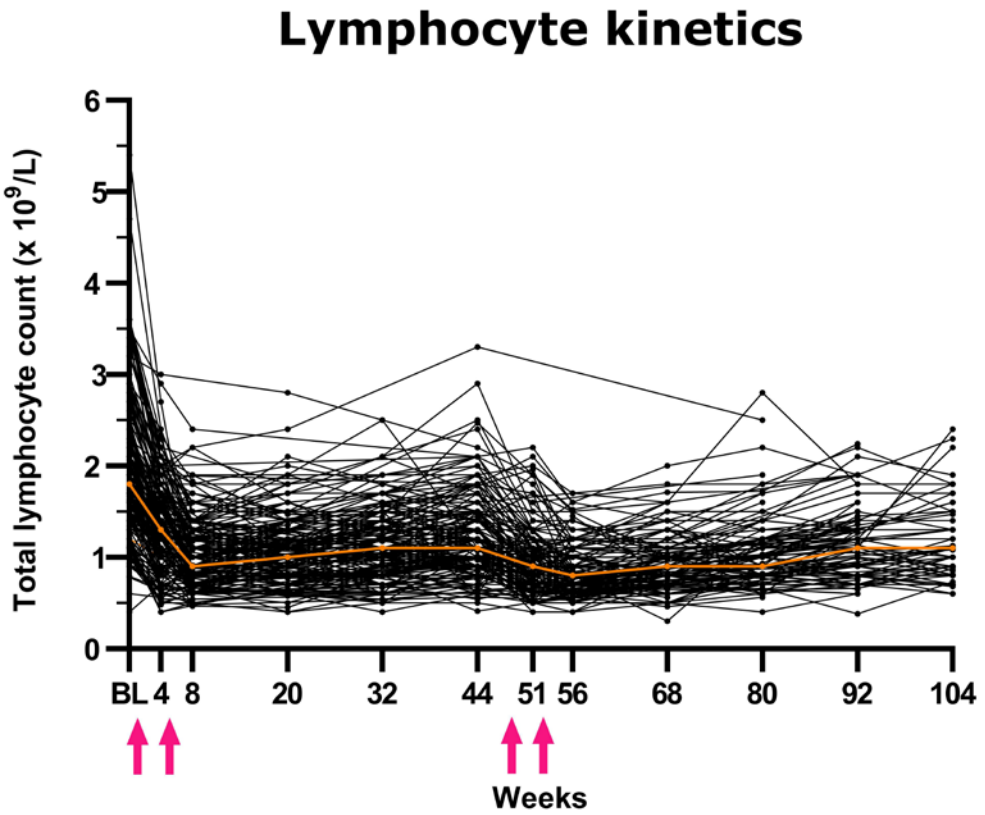
[1] Mao Z, et al. Mult Scler Relat Disord 2019;27:247-53. [2]Yildiz O, et al. Mult Scler Relat Disord 2018;24:20-7. [3]https://www.slideshare.net/KlausSchmierer/bartsms-infosafetyconsentpackjuly-2018

Follow-up

Safety & tolerability generally very good, with some exceptions[1]

94% pwMS free from severe lymphopenia

WHO grade lymphopenia	N patients (%)
0	34 (16.3)
1 (≥ 0.8 – 1.0 x 10^9/L)	49 (23.6)
2 (≥ 0.5 – 0.8 x 10^9/L)	113 (54.3)
3 (0.2 - 0.5 x 10^9/L)	11 (5.3)
4 (<0.2 x 10^9/L)	1 (0.5)



[1] Mateo-Casas M, et al. Mult Scler Relat Disord 2020;43:102140

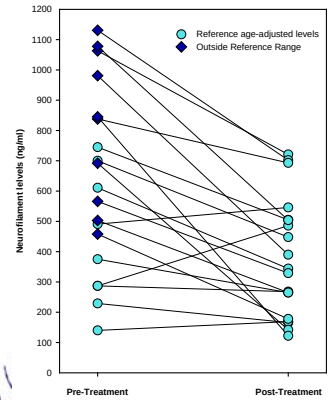
Follow-up

Efficacy

23 pwMS had elevated baseline CSF NfL with normal levels at follow-up in 22 pwMS.

Median CSF-NfL levels were 652 pg/mL (IQR 458-1063) and 344 pg/mL (IQR 186-505) at baseline and follow-up, respectively.

CSF neurofilament light chain



Efficacy

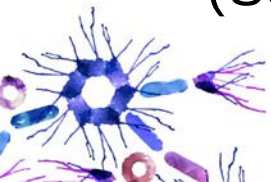
196/208 received a second treatment cycle.

Outcome	Baseline	2-year follow-up
EDSS (n=116)	**Median 5.0**	**Median 5.5**
Stable or improved/ Deteriorated		956 (82%)/ 21 (18%)
MRI (n= 147)		
Gd⁺ and/or new T_2 lesions No new lesions	71 (48%) 76 (52%)	26 (18%) 121 (82%)
Relapses (n= 130)		
Patients (%)	36 (28%)	8 (6%)

NEDA 66% (95% CI 49%, 80%) in n= 38 pwRMS
NEPAD 62% (95% CI 32%, 86%) in n= 13 pwPMS

Conclusions

- Our uncontrolled real-world data suggest CPD may be a safe, well-tolerated, and effective alternative for pwMS with active MS.
- Efficacy in pwRMS was similar to controlled trial data.
- NEPAD rates in the proportion of pwPMS with full datasets was promising.
- Long-term follow-up of this cohort continues.
- Underpins multi-centre, placebo-controlled trial of cladribine tablets starting recruitment from January 2021 (See poster 0196).



CHARIOT MS