

#### Cladribine personalised dosing to treat multiple sclerosis:

#### observations in 208 patients

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#### MSVirtual2020

## 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.

**GG** has received either research support or received personal compensation for participating on advisory boards, trial steering/data and safety monitoring committees from AbbVie, Atara Bio, Bayer-Schering Healthcare, Biogen, Canbex, Eisai, Elan, Fiveprime, Genzyme, Genzyme-Sanofi, Genentech, GSK, GW Pharma, Ironwood, Merck, Merck-Serono, Merz, Novartis, Roche, Sanofi-Aventis, Synthon BV, Teva, UCB Pharma and Vertex Pharmaceuticals.

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**BT** has received travel bursaries, grants and advisory board fees from Biogen, Roche, Sanofi-Aventis, Novartis and Merck.

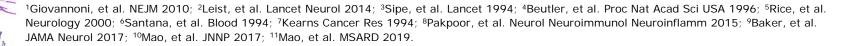
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# **Development of Cladribine Personalised Dosing**

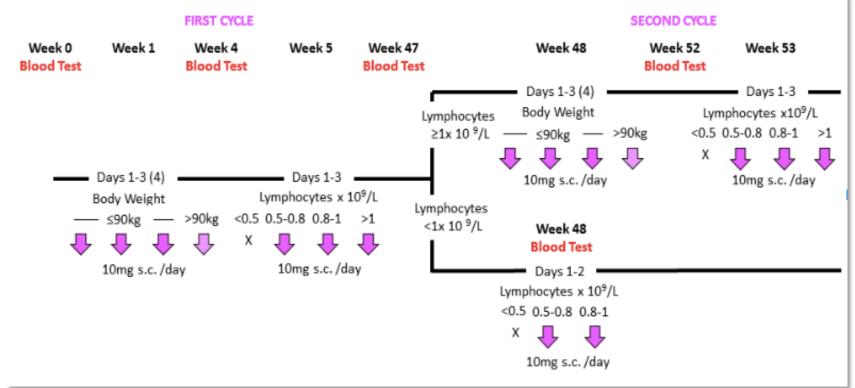
#### CLADRIBINE

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

	Both cladribine and alemtuzumab may				
	affect MS via B-cell depletion				
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## **Dosing schedule**





## Methods

- Service evaluation
- Treatment eligibility

Barts Health Clinical Effectiveness Unit #11483

**Disease activity** demonstrated by Gd<sup>+</sup> and/or new/enlarging T<sub>2</sub> lesion(s) on MRI<sup>1</sup>, and/or elevated CSF neurofilament light chain<sup>2</sup>

#### Safety checklist passed<sup>3</sup>

Safety and para-/clinical efficacy at 2 years compared to baseline

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

## Results

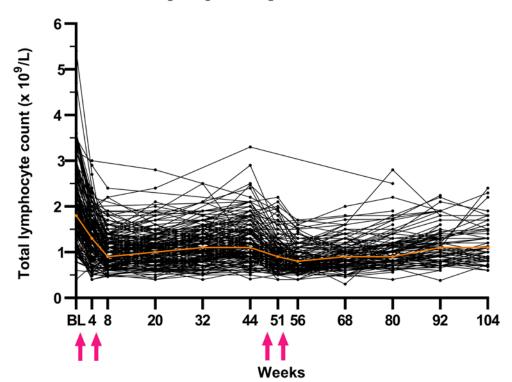


### Follow-up

Safety & tolerability generally very good, with some exceptions<sup>1</sup>

# 94% pwMS free from severe lymphopenia

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



Lymphocyte kinetics

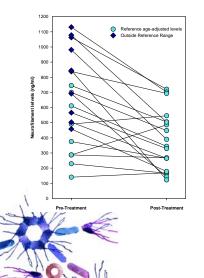
## Follow-up

#### 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 <sup>+</sup> and/or new T <sub>2</sub> 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).

