



ECTRIMS 2019 Investor Presentation

September 13, 2019

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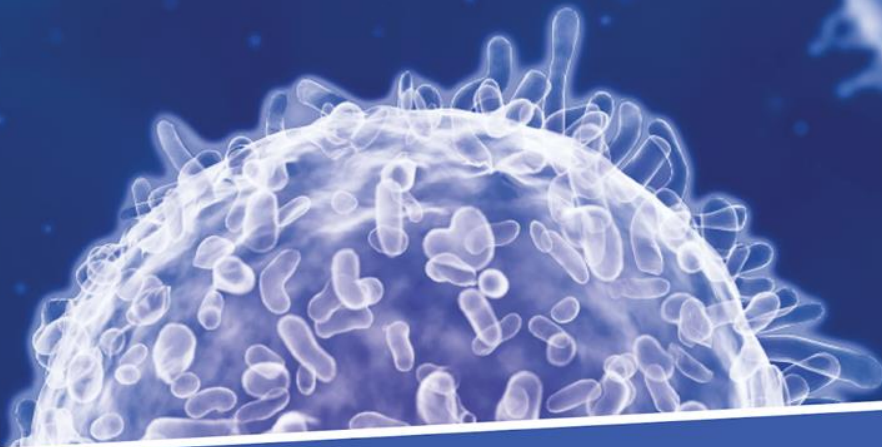


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MS Treatment Landscape Overview

Pascal Touchon

President & CEO, Atara Biotherapeutics

Evolution of the MS Treatment Landscape Toward Immunosuppression

IMMUNOSUPPRESSION

Anti-CD20 (depletes B cells)

Anti-CD52 (depletes B cells and T cells)

S1P receptor modulators (lymphocyte sequestering)

Other immunosuppression agents

IMMUNOMODULATION

Interferon beta

Glatiramer acetate

Other immunomodulatory agents

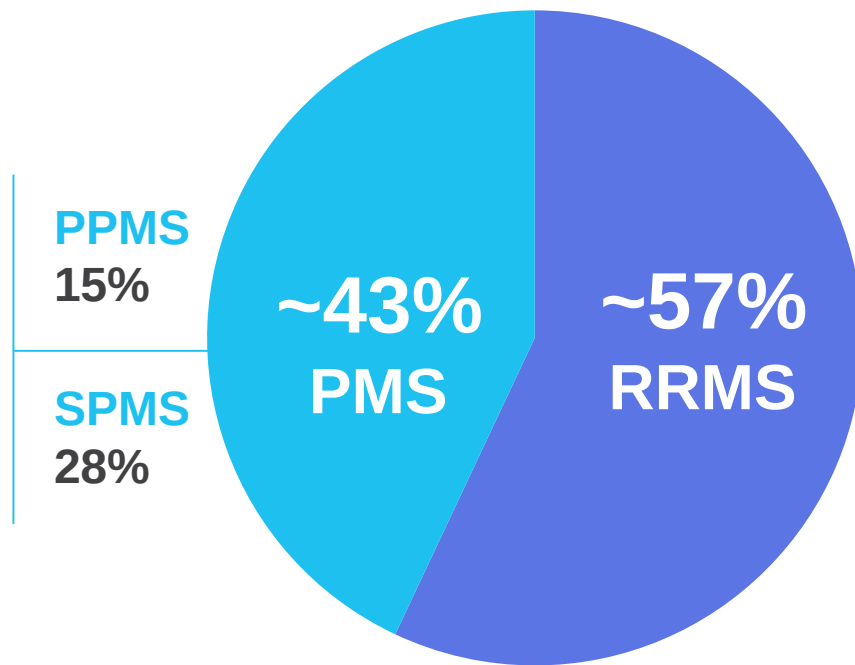
High Unmet Need Remains for Patient with Progressive MS

- ~43% of MS patients have a progressive form of the disease (PMS)
- ~80% of patients initially diagnosed with relapsing remitting MS (RRMS) are expected to transition to secondary progressive MS (SPMS)
- Limited treatment options
- Continual clinical decline is expected

New approaches with novel mechanisms of action are needed to improve outcomes in PMS

PMS: progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis; RRMS: relapsing-remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis

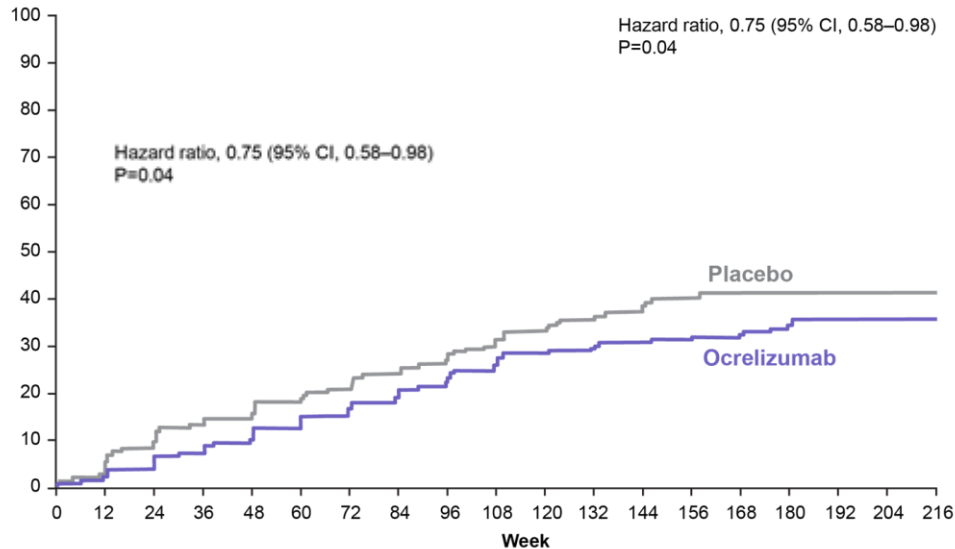
Global MS Patients *(as of 2017)*



Non-Specific B Cell Depletion Treatment in Progressive MS: Slows Disability Progression, but Does Not Improve Clinical Symptoms

Ocrelizumab Phase 3 PPMS study⁽¹⁾

Cumulative probability of 24-week disability progression (%)



Optimal Characteristics of a Progressive MS Treatment



Well-tolerated



**Reverses
disability
progression**



**Penetrates
CNS**

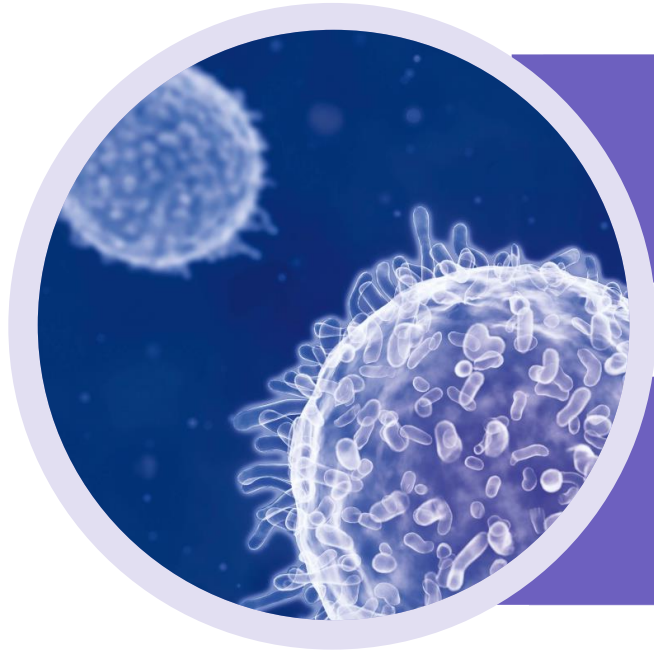


**Targets
specific
B cells and
plasma cells**



**Addresses
underlying
biology**

A Novel Approach: Adoptive T-Cell Immunotherapy Targeting EBV-Infected B Cells



ATA190 autologous

Phase 1 study completed (N=10)
Randomized Phase 2 study planned to start in H2 2019

ATA188 off-the-shelf, allogeneic

Phase 1 dose-escalation study ongoing (N=24);
Initial Ph1 efficacy results presented at ECTRIMS¹;
Phase 1b RCT vs. placebo planned²

RCT: randomized controlled trial

1. 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), September 11-13, 2019, Stockholm, Sweden

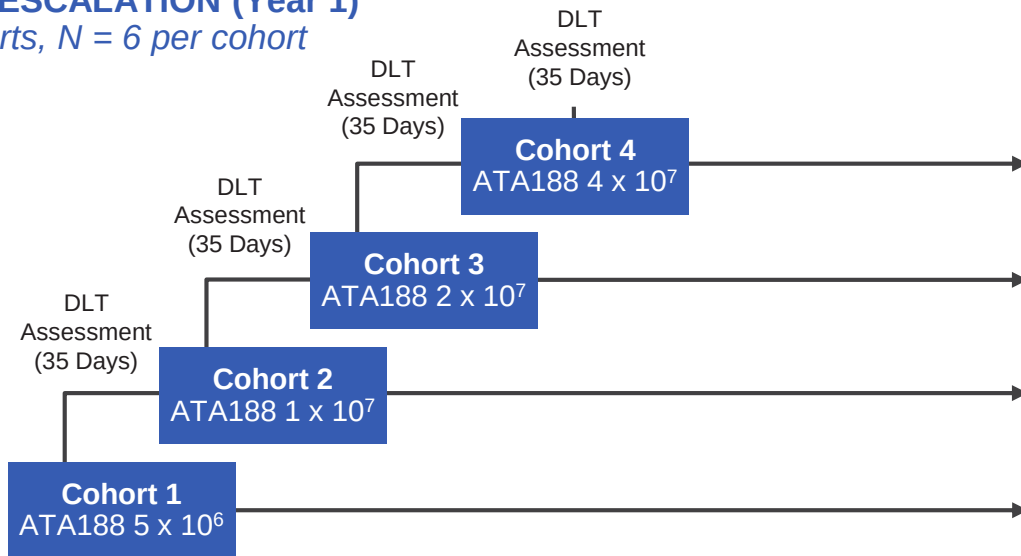
2. Randomized, double-blind, placebo-controlled Phase 1b extension period for this study using the RP2D is planned following completion of the open-label, dose-escalation period

ATA188: Early Findings of Potential Efficacy from Phase 1 Study in Patients with Progressive MS at ECTRIMS 2019

Part 1 Study Schema

DOSE-ESCALATION (Year 1)

4 Cohorts, N = 6 per cohort



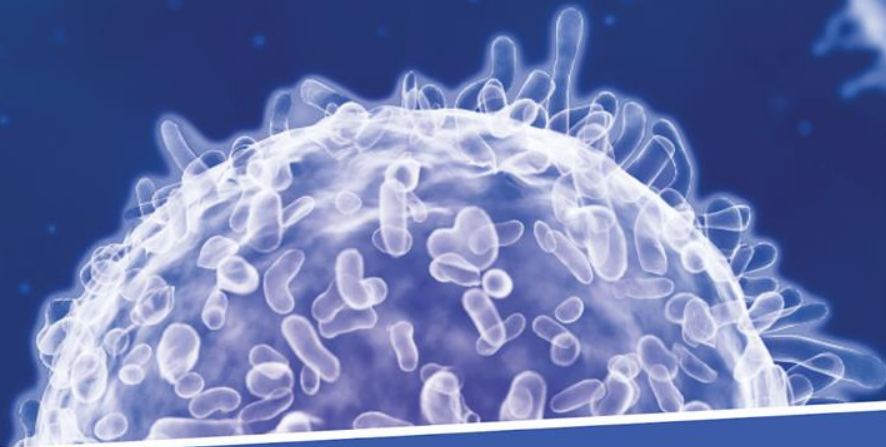
PRIMARY ENDPOINTS

Safety and identification of the recommended Phase 2 dose

CLINICAL EFFICACY CRITERIA

- EDSS
- MS Impact Scale-29
- Fatigue Severity Scale
- 12-Item MS Walking Scale
- Timed 25-foot Walk
- 9-hole Peg Test
- Visual Acuity

Enrollment in the fourth and final Phase 1 dose escalation cohort completed



The Role of Epstein-Barr Virus (EBV) in MS

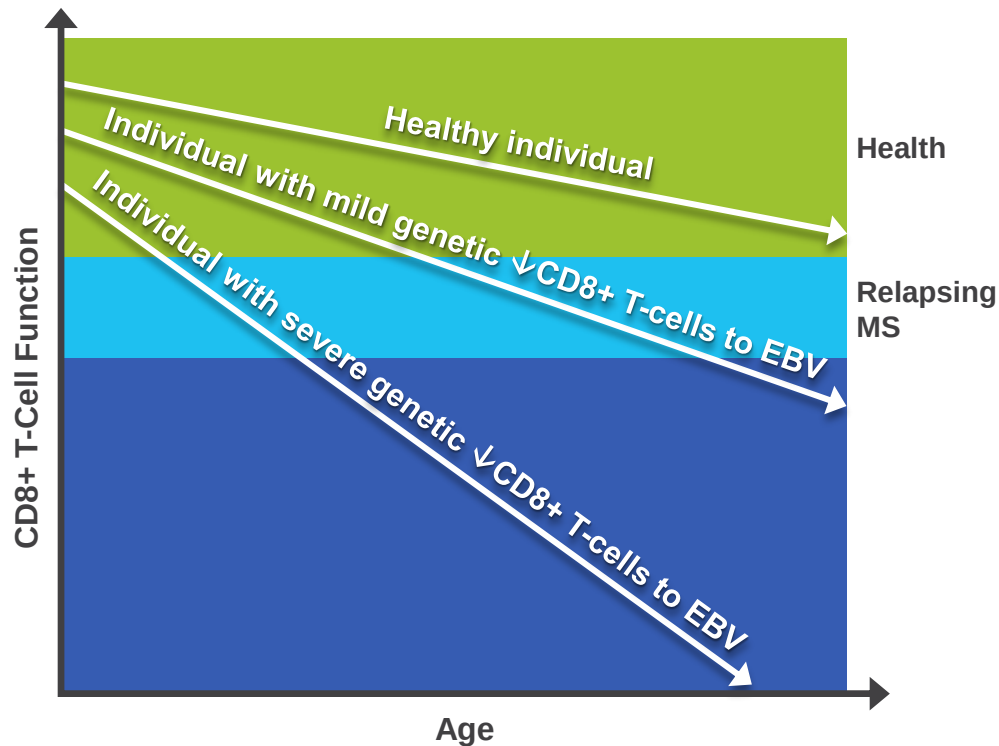
Lawrence Steinman, MD

*Professor of Neurology and Neurological Sciences,
Pediatrics and Genetics, Stanford University*

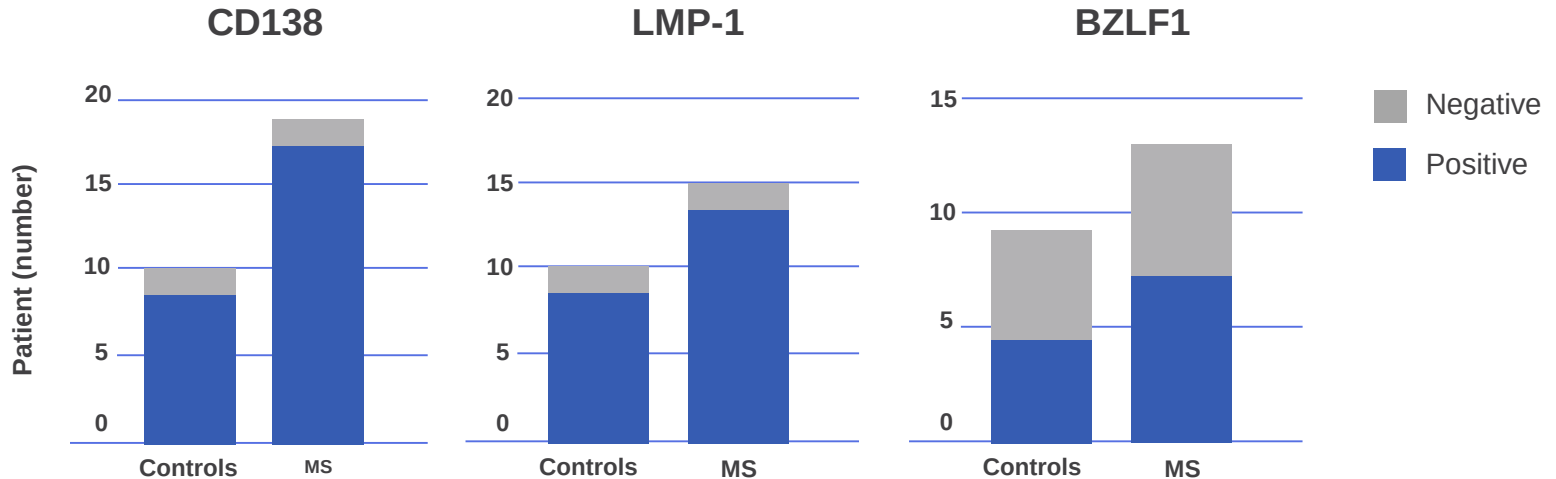
Growing Evidence that EBV Has a Major Role in the Pathogenesis of Multiple Sclerosis

Loss of EBV specific CD8+ T-cell function correlates with MS disease progression

- EBV infection increases risk of development of MS
- Genetic factors influence loss of EBV specific CD8+ T-cells and correlate with MS progression

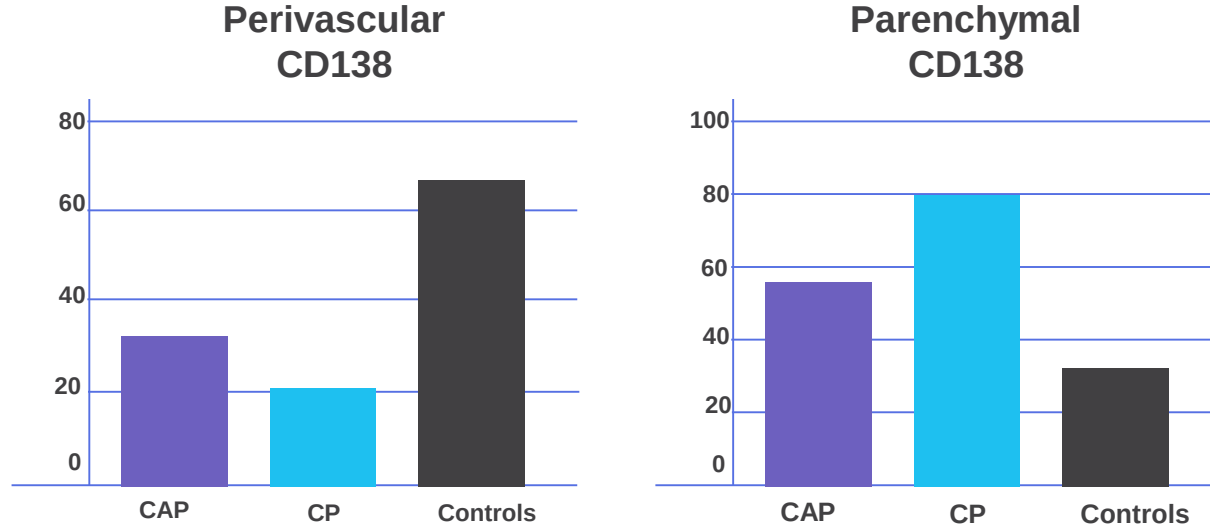


Presence of EBV Infected Cells in the Brains of MS Patients More Frequently than in Controls



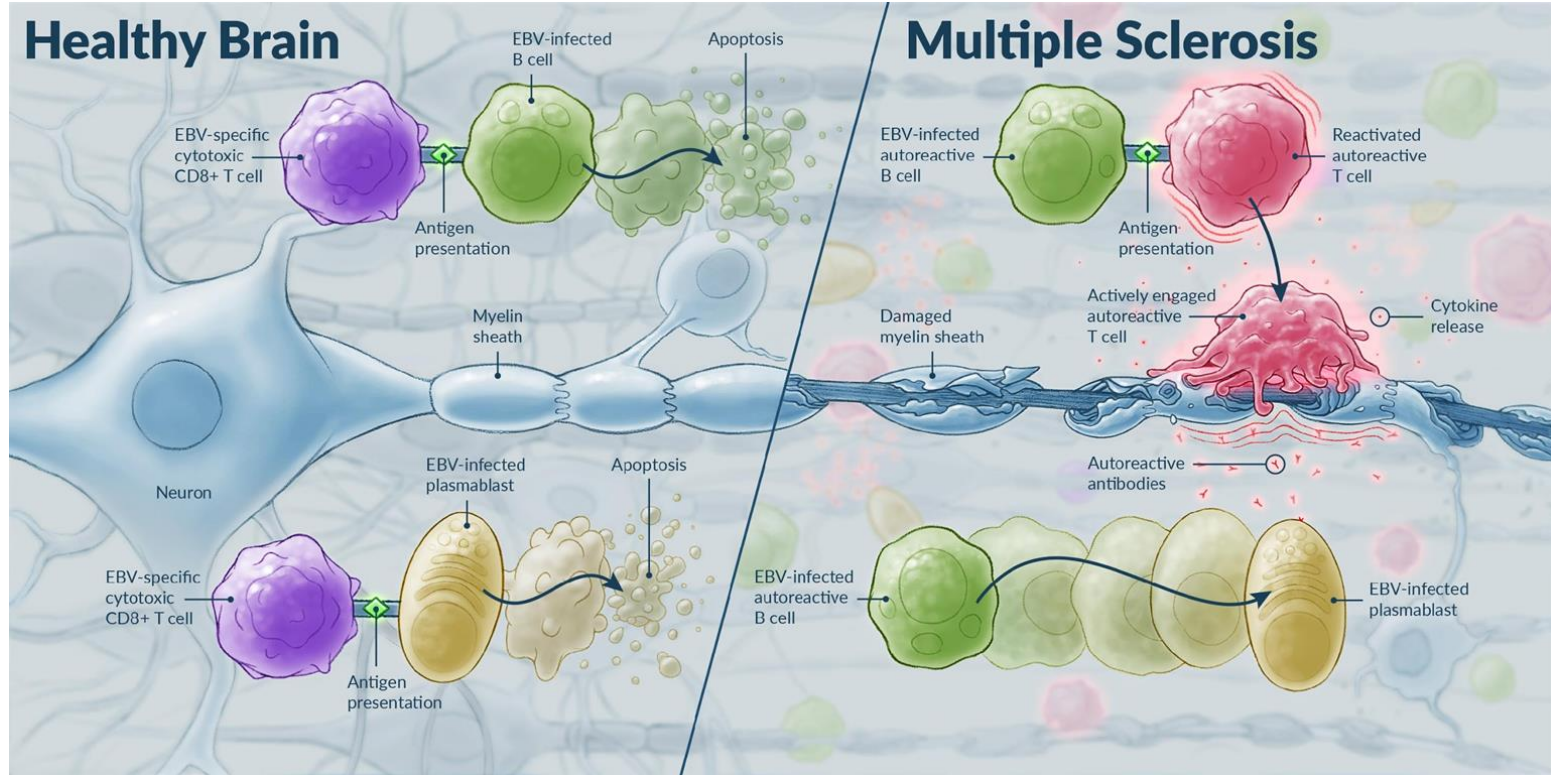
Semi-quantification of CD138 (plasma cell marker), LMP-1 (latency), and BZLF1 (early lytic) positive cells in MS and Control brain samples.

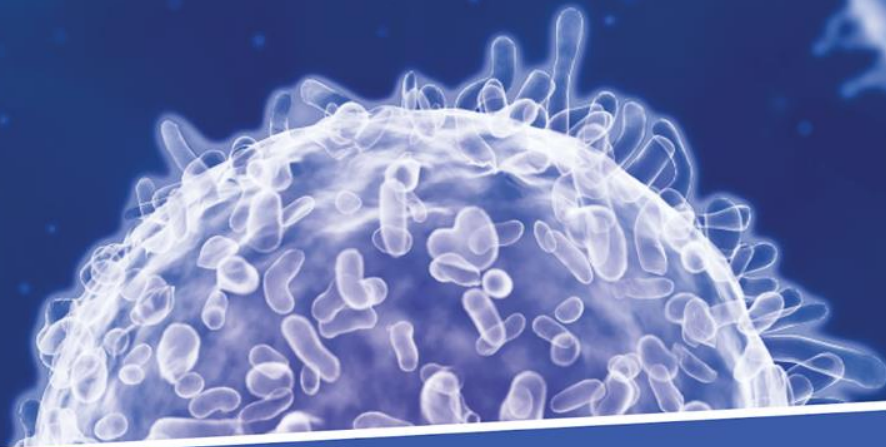
More EBV-Infected B Cells and Plasma Cells Found in Areas of Active Demyelination



33% of control samples contained parenchymal CD138+ plasma cells compared with 57% and 78% in chronic active plaques (CAPs) and chronic plaques (CPs), respectively

Auto-reactive EBV-Infected B cells and Plasma Cells Normally Controlled by EBV-Specific T Cells





ATA188 Phase 1a Results

Lawrence Steinman, MD

*Professor of Neurology and Neurological Sciences,
Pediatrics and Genetics, Stanford University*

Baseline Demographic Data

In general, baseline characteristics were similar across cohorts, with the following exceptions:

- Sex distribution
- Age
- Duration of disease from diagnosis
- Prior MS medications

	COHORT 1 (n=6)	COHORT 2 (n=6)	COHORT 3 (n=6)	COHORT 4 (n=6)	ALL PATIENTS (n=24)
Sex					
Male, n (%)	3 (50)	1 (17)	5 (83)	4 (67)	13 (54)
Female, n (%)	3 (50)	5 (83)	1 (17)	2 (33)	11 (46)
Age, median (range), years					
Age, median (range), years	58 (56–63)	56 (51–63)	49 (29–59)	54 (38–64)	56 (29–64)
Time from initial diagnosis, median (range), months					
Time from initial diagnosis, median (range), months	90 (7–357)	152 (21–237)	132 (62–345)	136 (37–249)	132 (7–357)
Prior medication for MS, n (%)					
Cladribine	0 (0)	0 (0)	2 (33)	0	2 (8)
Corticosteroids	3 (50)	1 (16.7)	3 (50)	4 (67)	11 (46)
Dimethyl Fumarate	0 (0)	1 (16.7)	3 (50)	3 (50)	7 (29)
Fingolimod	0 (0)	0 (0)	4 (67)	2 (33)	6 (25)
Glatiramer Acetate	1 (17)	0 (0)	2 (33)	2 (33)	5 (21)
Interferon	2 (33)	2 (33.3)	3 (50)	4 (67)	11 (46)
Natalizumab	1 (17)	0	2 (33)	0	3 (13)
Rituximab	0 (0)	0 (0)	1 (17)	3 (50)	4 (17)
Ocrelizumab	0 (0)	0 (0)	3 (50)	3 (50)	6 (25)
Gadolinium-enhancing lesion count, n (%)					
0	5 (83)	6 (100)	5 (83)	4 (67)	20 (83)
1	1 (17)	0	0	1 (17)	2 (8)
2	0	0	0	1 (17)	1 (4)
Missing	0	0	1 (17)	0	1 (4)
Type of progressive MS					
Secondary progressive MS	4	3	2	4	13
Primary progressive MS	2	3	4	3	12

Safety

No dose-limiting toxicities (DLTs) and no fatal AEs have been reported



As of the data cutoff date, no clinically significant laboratory abnormalities have been reported in any cohort



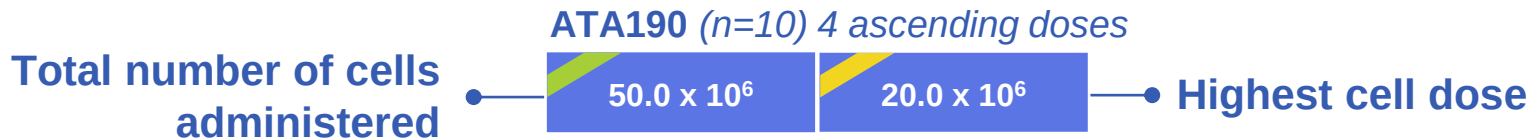
One patient in Cohort 4 dropped out due to MS relapse in the setting of ongoing URI symptoms and possible dental infection



Alignment of Off-the-Shelf, Allogeneic ATA188 Phase 1 Study Dose Cohorts with Autologous ATA190 Phase 1

ATA188 Phase 1 Study (3 infusions on days 1, 8, 15; total of two cycles)

	COHORT 1 (n=6)	COHORT 2 (n=6)	COHORT 3 (n=6)	COHORT 4 (n=6)	ALL PATIENTS (n=24)
Average cells admin/dose (10^6 cells)					
Mean (SD)	5.0 (0.0)	10.0 (0.0)	21.5 (2.4)	40.0 (0.0)	19.1 (13.8)
Total cells administered (10^6 cells)					
Mean (SD)	30.0 (0.0)	60.0 (0.0)	129.2 (14.3)	153.3 (77.6)	93.1 (63.0)



Definition of Outcome Criteria (Clinical Response)

Clinical Improvement¹

Partial Clinical Improvement²

Stable³

Clinical Decline⁴

Clinical Efficacy Criteria

assessment with clinically significant improvement



Fatigue Severity Score
-0.7



MS Impact Scale-29 (physical)
-8



T25FW⁵
-20%



9-hole peg test
-20%



MSWS-12⁶
-8



EDSS⁷
-1 (EDSS 3-5)
-0.5 (EDSS 5.5-7.0)



VA (logmar)⁸
≥ -0.1 decrease in either eye

1. Minimal clinically significant improvement or greater on 2 evaluations compared to baseline sustained over ≥ 2 consecutive timepoints compared to baseline^a

2. Minimal clinically significant improvement or greater on ≥ 2 evaluations compared to baseline at ≥ 1 post-baseline timepoint^{*}

3. Does not fulfill criteria for decline or improvement

4. Clinically significant decline in ≥ 2 scales at ≥ 1 timepoint; clinical decline takes precedence over improvement

5. Timed 25-Foot Walk

6. 12-Item Multiple Sclerosis Walking Scale

7. Expanded Disability Status Scale

8. Visual acuity

Clinical Outcomes by Cohort

(Based on Data Cut July 29, 2019)

	6 MONTHS	
RESPONSE TYPE	COHORT 1 (n=6)	COHORT 2 (n=6)
Clinical decline	4	0
Stable	0	0
Partial clinical improvement	1	4
Clinical improvement	1	2

Clinical Outcomes by Cohort

(Based on Data Cut July 29, 2019)

	6 MONTHS		12 MONTHS
RESPONSE TYPE	COHORT 1 (n=6)	COHORT 2 (n=6)	COHORT 1 (n=6)
Clinical decline	4	0	4
Stable	0	0	1
Partial clinical improvement	1	4	0
Clinical improvement	1	2	1

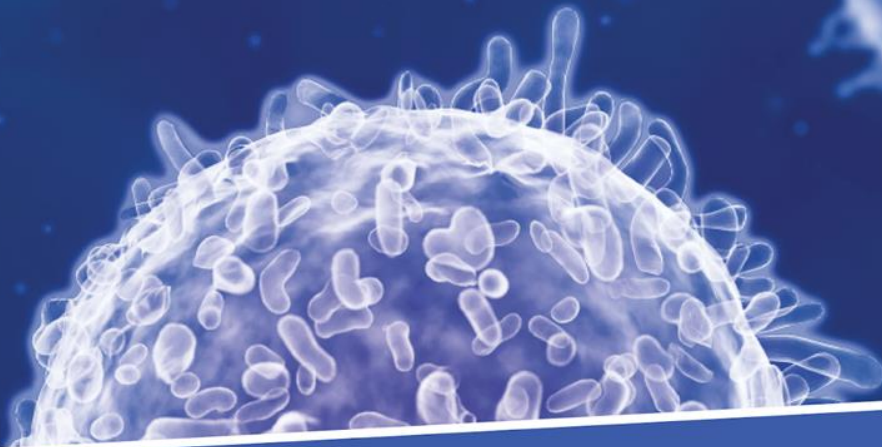
Clinically Significant Improvement/Decline by Scale

(At least One Post-Baseline Timepoint; Based on Data Cut July 29, 2019)

	COHORT 1 (n=6)		COHORT 2 (n=6)	
SCALE	IMPROVEMENT OR STABLE	DECLINE	IMPROVEMENT OR STABLE	DECLINE
Fatigue (FSS)	4	2	6	0
MSIS-20 (Physical)	5	1	6	0
MSWS-12	4	2	6	0
T25F-W ⁽¹⁾	3	3	5	1
9HPT ⁽¹⁾	5	1	6	0
EDSS ⁽¹⁾	6	0	6	0
Any disability scale ⁽¹⁾	6	4	6	1

Summary

- Safety and efficacy results highlight potential for an off-the-shelf, allogeneic T-cell immunotherapy targeting Epstein-Barr Virus (EBV)-infected B cells in patients with progressive forms of MS
- Safety results showed that across the four planned dose cohorts, ATA188 was well tolerated in patients with progressive forms of MS with no evidence of cytokine release syndrome, graft versus host disease or dose-limiting toxicities.
- Outcome classification using multiple clinically recognized MS scales is an innovative approach
- In cohort 2, an outcome classification of clinical improvement or partial clinical improvement was observed in all 6 patients at six months. No patients showed an outcome classification of stable or clinical decline.
- Results support continuing part 1 to identify the dose for both the OLE and the randomized, double-blind, placebo-controlled portion (part 2) of the study



ATA188 Development Summary

AJ Joshi, MD

Senior Vice President and Chief Medical Officer

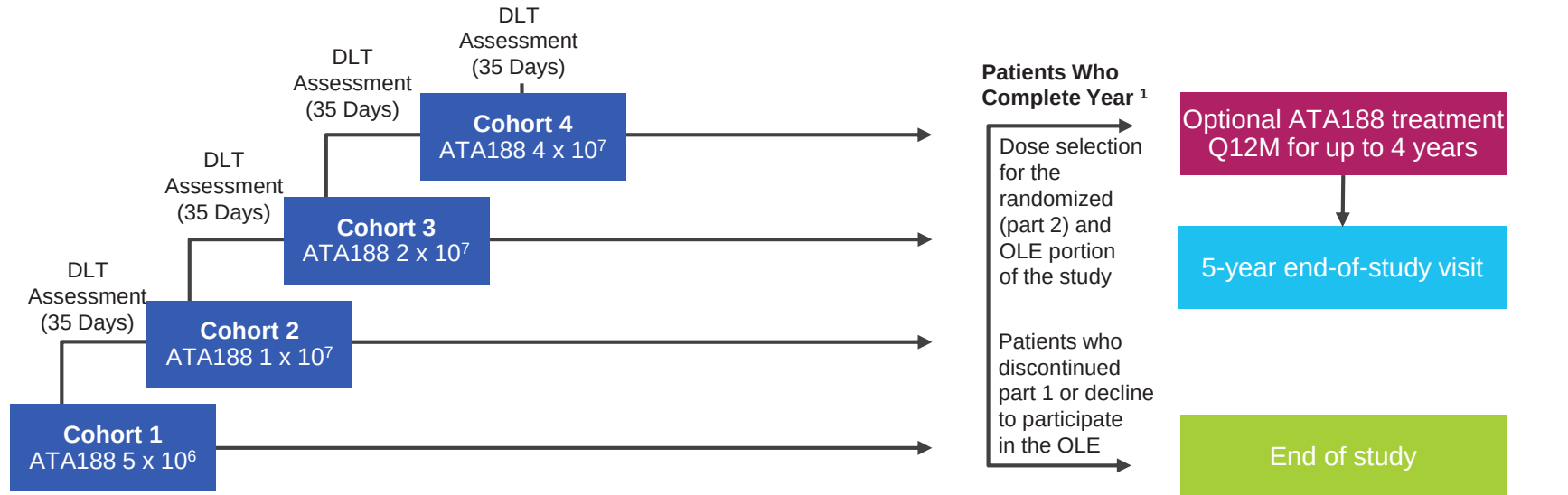
Atara Biotherapeutics

A Phase 1b Study of ATA188, an Allogeneic EBV-Targeted T-Cell Therapy for the Treatment of Progressive MS

Part 1 Study Schema

DOSE-ESCALATION (Year 1)

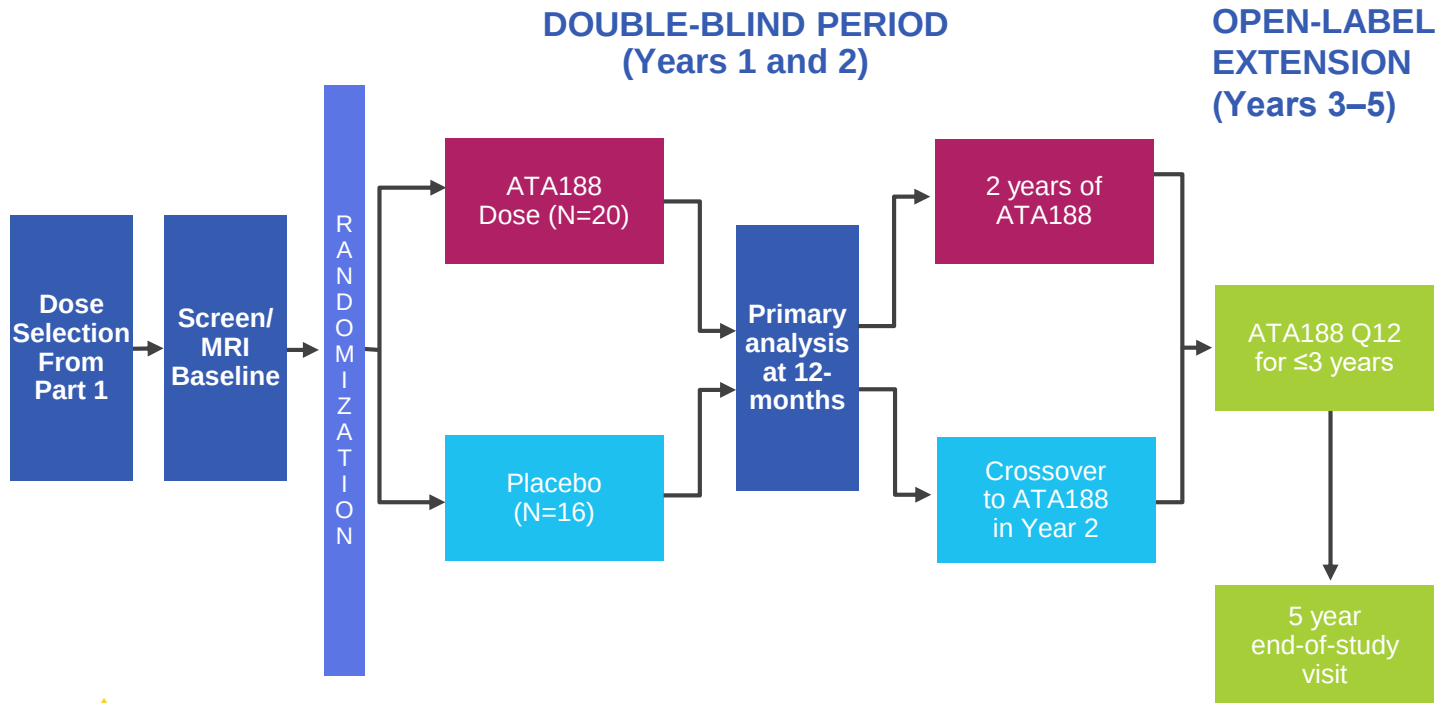
Cohorts 1–4, N = 6 per cohort



ATA188 Phase 1b Study Design

(Randomized and Open-Label Extension Periods)

Part 2 Study Schema



ENDPOINTS

- CSF, blood – IgG, oligoclonal bands, RNAseq, NFL
- MRI volumes (c-spine, whole brain), MTR, T1 & T2 lesions
- Clinical endpoints (EDSS, T25FW, 9HPT, MSFC, SDMT, Fatigue scales, activity measures, etc.)

Key ATA188 Milestones

 Multiple sclerosis		Initial safety results from off-the-shelf, allogeneic ATA188 study for patients with progressive MS to be presented at EAN	June 2019
		Initial efficacy and additional safety results from off-the-shelf, allogeneic ATA188 study for patients with progressive MS	Sept 2019
		Six and 12-month efficacy data from Phase 1a study of ATA188	2020

Identify dose to initiate a randomized,
double-blind, placebo-controlled Phase 1b

Acknowledgements



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their families, investigators, clinical site support
and all others involved in this study (NCT03283826).*

