TG

TG Therapeutics

2017 Post ECTRIMS – ACTRIMS
Data Review Call
November 2017

TG Therapeutics

Michael S. Weiss, CEO

Forward Looking Safe Harbor Statement

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are often, but not always, made through the use of words or phrases such as "anticipates", "expects", "plans", "believes", "intends", and similar words or phrases. Such statements involve risks and uncertainties that could cause TG Therapeutics' actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in clinical trials, drug development, and commercialization. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement and TG Therapeutics undertakes no obligation to update these statements, except as required by law.

TG Therapeutics, Inc.

- Biopharmaceutical company focused on B-cell cancers (CLL and NHL) & autoimmune-related diseases (**MS**, RA, Lupus)
- **Headquarters:** New York, NY
- **NASDAQ:** TGTX

- Developing portfolio of B-cell targeted agents
- **TG-1101 – (ublituximab) Novel Glycoengineered, Anti-CD20 monoclonal antibody**
  - Enhanced ADCC profile for increased potency, similar to Gazyva® (GA101)
  - Robust activity demonstrated in CLL and NHL in Phase 1/2 studies
  - **GENUINE Phase 3 Registration Trial in CLL positive results announced!**
  - **ULTIMATE I & II Phase 3 Trials in Multiple Sclerosis under SPA**

- **TGR-1202 – (umbralisib) – Novel PI3Kδ inhibitor**
  - Highly active and well tolerated as monotherapy and in combination treatment
  - Demonstrated best-in-class attributes
  - **UNITY- CLL Phase 3 trial under FDA-Special Protocol Assessment (SPA)**
    - **Completion of full enrollment has been met, targeting top-line ORR data in 2Q18**

TG-1101(ublituximab) Phase 2 Multiple Sclerosis ECTRIMS-ACTRIMS Data

Edward Fox, MD, PhD

Study Design & Primary Endpoint

- TG1101 RMS201 (clinicaltrials.gov NCT02738775) is a randomized, placebo controlled, multi-center study to test the safety and efficacy of TG-1101 (ublituximab), at doses markedly less than used in ongoing Phase 3 oncology studies, and at a range of infusion times, with a goal of rapid infusions

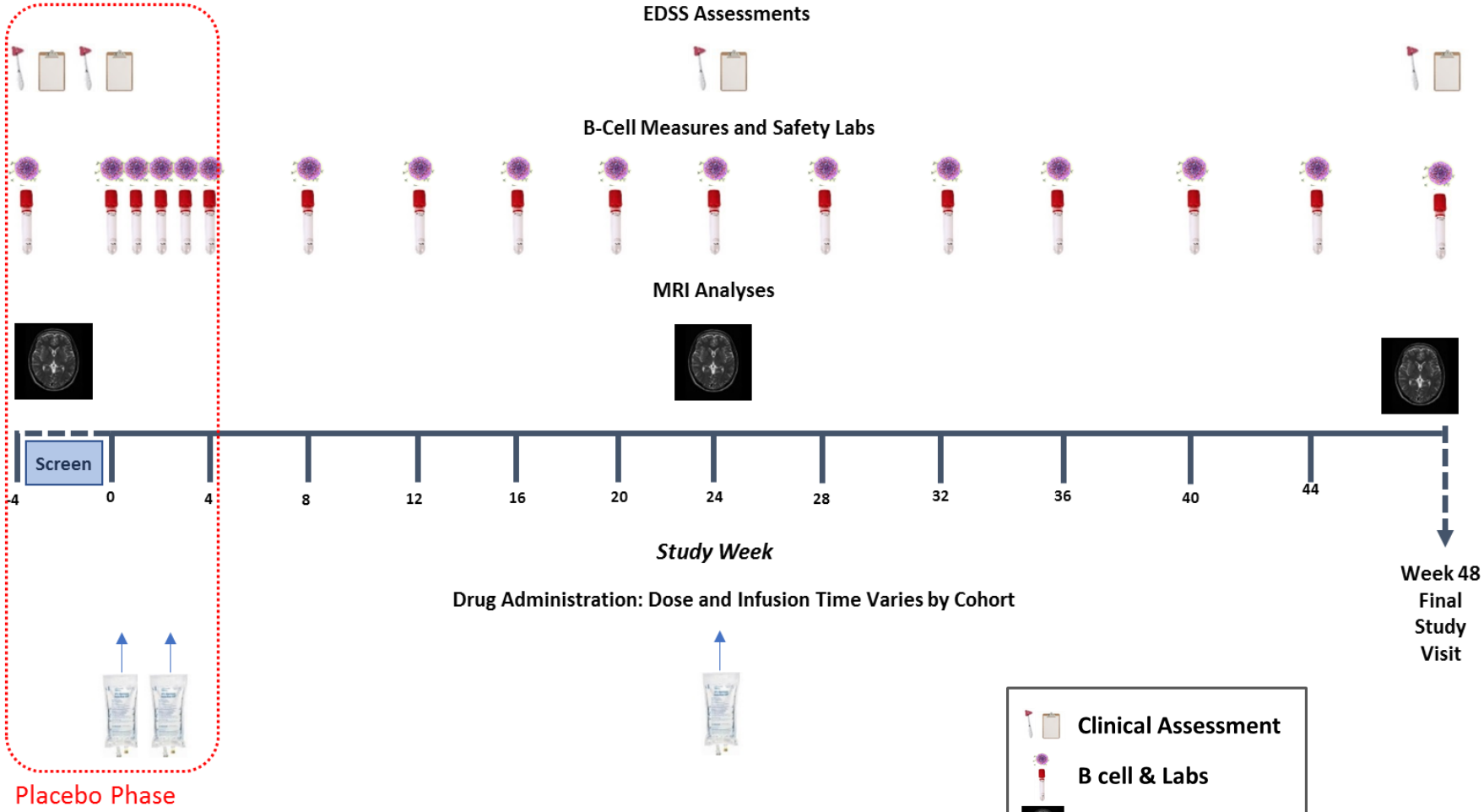
- Primary endpoint is the Responders Rate, defined as percent of subjects with ≥95% reduction in peripheral CD19+ B-cells within 2 weeks after the second infusion (day 15)

- The TG1101 RMS201 study in ongoing and will incorporate additional clinical and MRI measures (see Study Design)

Secondary Efficacy Endpoints

- Number of new Gd-enhancing lesions at 24 and 48 weeks
- Number of new or enlarging T2 lesions at 24 and 48 weeks
- Annualized relapse rate (ARR)
- Relapse rate reduction (RRR)
- Percent of relapse free patients
- Reduction in B cells (CD19+), memory (CD19+CD27+) and naïve (CD19+CD27-) B cells at baseline, day 1 (pre dose), 2, 8, 15 (pre-dose), 30 and every 4 weeks thereafter until the next infusion at week 24 (day 180; pre-dose) and day 182, and 188, and weeks 28, 36, 40, 44 and 48.
- Sustained B cell reduction during the first and third infusions
- Additional immune profiling (CD4+, CD8+, IL10 and NK cells) at baseline, day 1 (pre dose), 2, 8, 15 (pre-dose), 30 and every 4 weeks thereafter until the next infusion at week 24 (day 180; pre-dose) and day 182, and 188, and weeks 28, 36, 40, 44 and 48.
- PK (ADME) profile of ublituximab at day 1 and 15 and week 24

Phase 2 Study Design



Ublituximab Phase 2 RMS: Design

Randomization		Treatment Period		
Cohort	**Subjects and treatment**	**Day 1/ infusion time**	**Day 15/ infusion time**	**Week 24/ infusion time**
1	Placebo (n=2)[b]	Placebo / 4h	Placebo / 3h	-
	UTX (n=6)	150 mg / 4h	450 mg / 3h	450 mg / 1.5h
2	Placebo (n=2)[b]	Placebo / 4h	Placebo / 1.5h	-
	UTX (n=6)	150 mg / 4h	450 mg / 1.5h	450 mg / 1h
3	Placebo (n=2)[b]	Placebo / 4h	Placebo / 1h	-
	UTX (n=6)	150 mg / 4h	450 mg / 1h	600 mg / 1h
4	Placebo (n=2)[b]	Placebo / 3h	Placebo / 1h	-
	UTX (n=6)	150 mg / 3h	600 mg / 1h	600 mg / 1h
5	Placebo (n=2)[b]	Placebo / 2h	Placebo / 1h	-
	UTX (n=6)	150 mg / 2h	600 mg / 1h	600 mg / 1h
6	Placebo (n=2)[b]	Placebo / 1h	Placebo / 1h	-
	UTX (n=6)	150 mg / 1h	600 mg / 1h	600 mg / 1h
Cohort expansion[a]	*Up to 100*	*To be explored at selected doses pending on the results of the above doses*		

UTX = ublituximab = TG-1101

Patient Demographics

Baseline Demographics				
Cohort	**Subjects and Treatment**	**Age (Years)[1]**	**Gender (% Female)**	**Disease Duration (Years)[1,2]**
1	Placebo (n=2)	39±14	50%	15.5±20.4
	UTX (n=6)	43±12	67%	7.1±7.3
2	Placebo (n=2)	44±1	0%	0.9±1.2
	UTX (n=6)	33±10	100%	5.3±6.4
3	Placebo (n=2)	38±7	50%	11.5±7.5
	UTX (n=6)	40±11	67%	13.4±10.0
Total	**n=24**	**40±11**	**67%**	**8.8 ± 9.0**

[1] Mean ± Standard Deviation

[2] Distribution of times from diagnosis: 11 subjects (45.8%) were less than 5 years, 7 (29.2%) were 5-10 years, and 6 (25%) were greater than 10 years.

UTX = ublituximab = TG-1101

Safety and Tolerability at Week 24

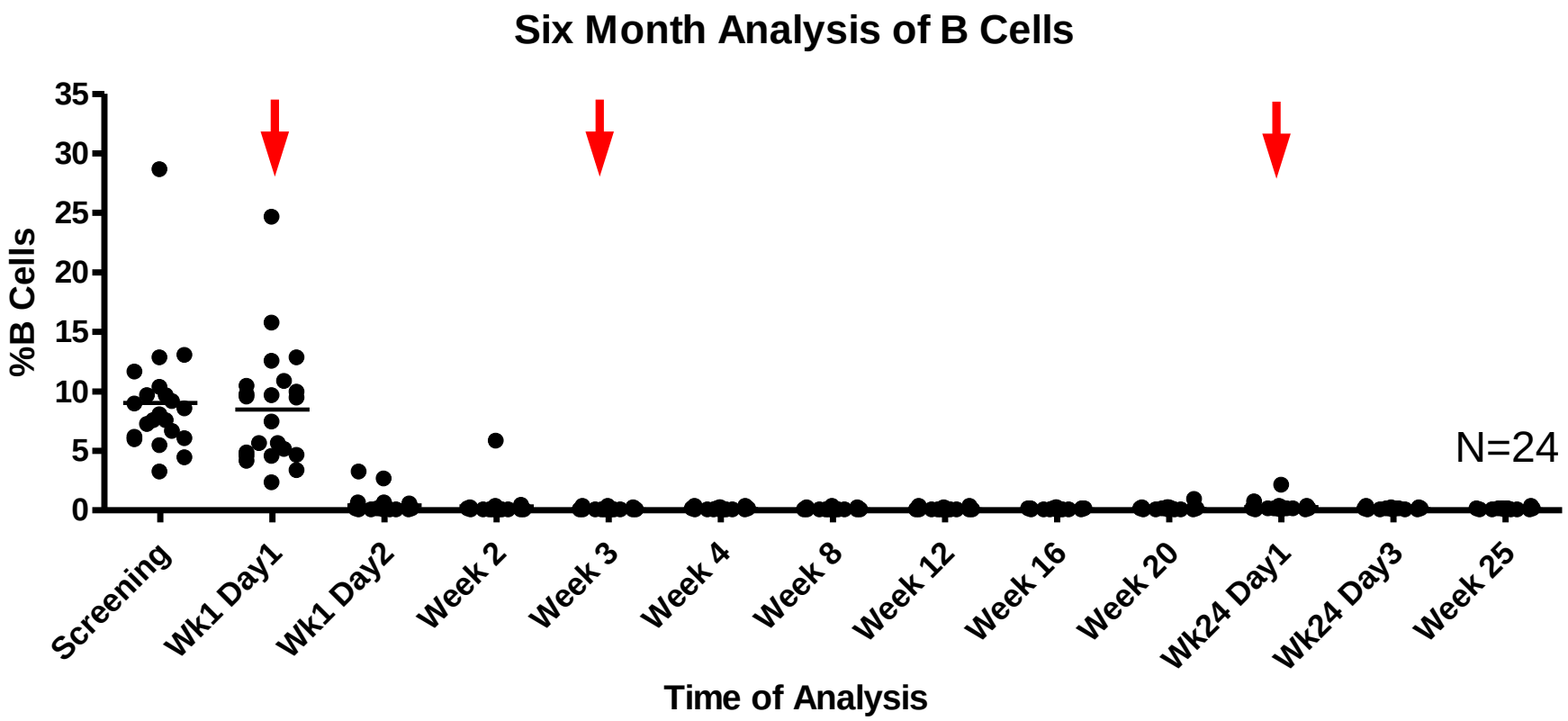
Event, n (%)		(N=24)	
Any adverse event[1]		18 (75%)	
Most frequently reported adverse events[2]		All Grades	Grade 3/4
	Infusion-related reaction	7 (29%)	- (-)
	Nausea/Vomiting	5 (21%)	- (-)
	Numbness	5 (21%)	- (-)
	Urinary tract infection	5 (21%)	- (-)
	Fatigue	4 (17%)	2 (8%)
	Headache	4 (17%)	- (-)
	Upper respiratory infection	4 (17%)	1 (4%)
	Yeast infection	3 (12%)	1 (4%)
Infusion-related reactions			
	Patients with at least one infusion-related reaction	7 (29%)	
	Total number of reactions	15	
	Grade	(N=24)	
	1	2 (8%)	
	2	5 (21%)	
	3	- (-)	
	4	- (-)	
	5	- (-)	

[1] Reflects total number of patients that experienced one or more adverse event.
[2] These events were reported by at least 10% of patients and are listed by decreasing incidence.

- **Ublituximab was well tolerated and no drug related discontinuation from study has occurred to date.**
- **A total of 15 infusion related adverse events (AEs) were reported in 7 subjects, all Grade 1 or 2.**
- No infusion related AEs were deemed related to ublituximab in Cohort 3, which had the fastest infusion times, and highest combined dose.
- There were a total of 11 Adverse Events ≥ Grade 3, only one of which was deemed possibly related to ublituximab, an MS relapse occurring 12 days after the subject's first infusion of 150mg of ublituximab. This subject was initially randomized to the placebo arm.
- There were no events of death reported on study.
- The Data Safety Monitoring Board (DSMB) has reviewed safety labs and adverse events for all subjects to date, and has not found any lab abnormalities or safety signals that would warrant a change in protocol.

Fox E et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P793

B Cell Depletion at Week 24

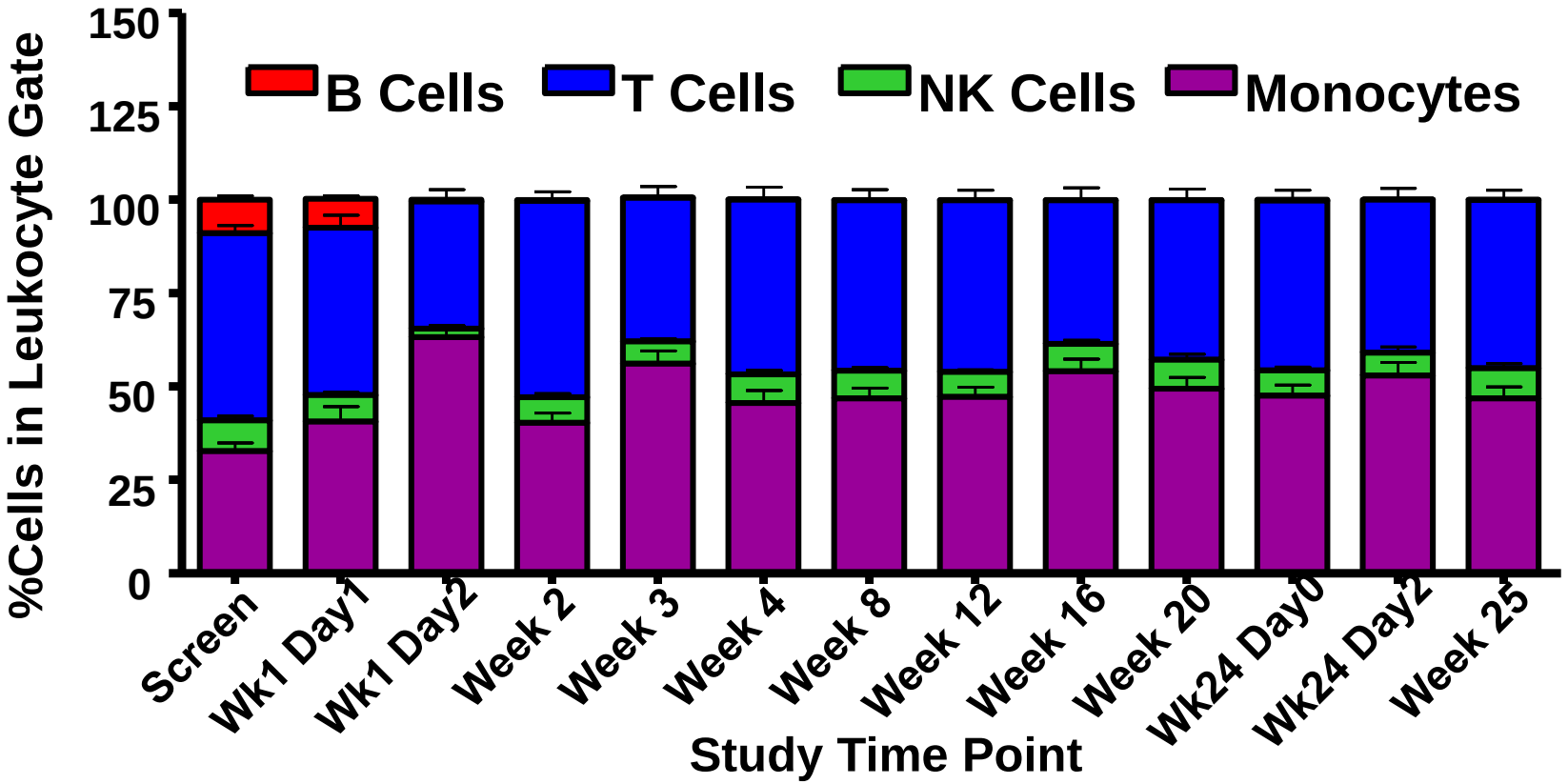


Arrows represent treatment timepoints. Blood analysis was done pre-treatment.

99% B Cell depletion at Week 4 and sustained until Week 24

Fox E et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P793
Lovett-Racke A et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P1158

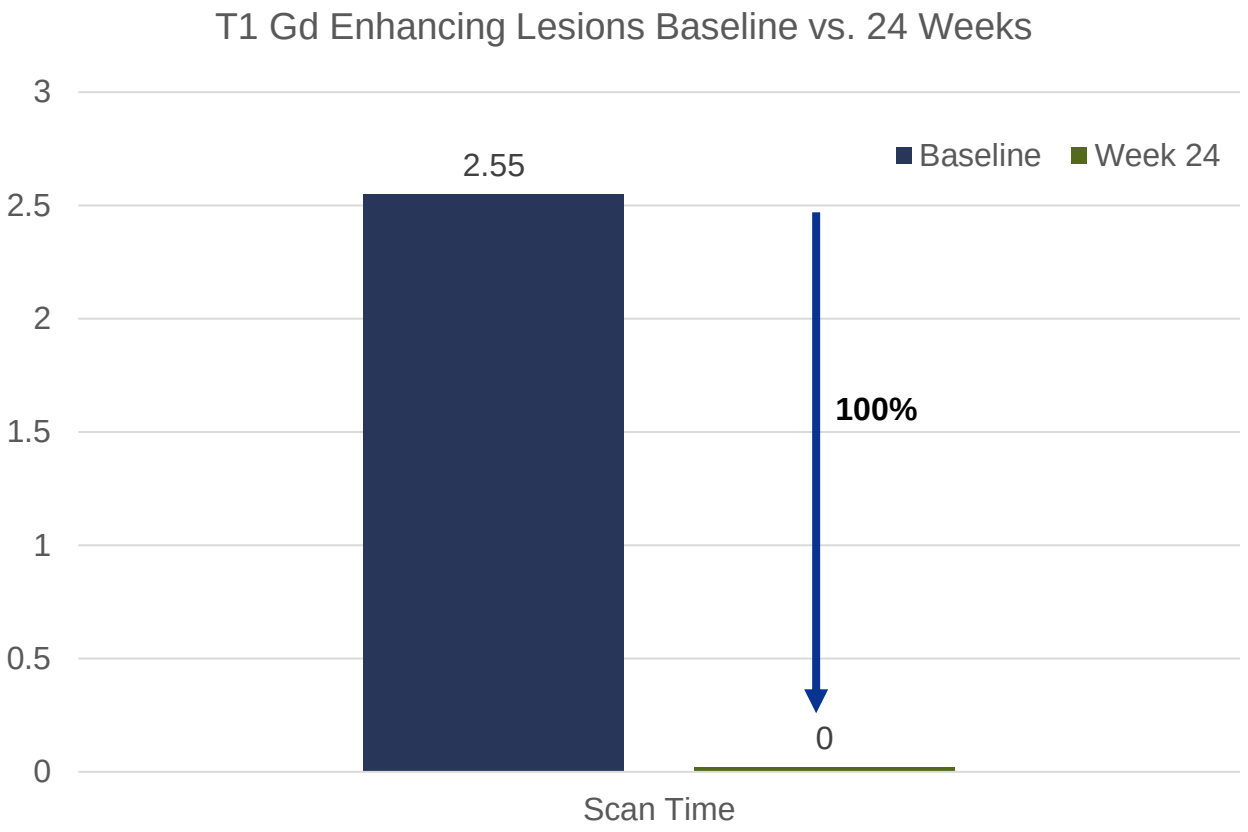
Ratio of B/T/NK/Monocytes Over 6 Months



Immune homeostasis is restored and maintained in the T cell, NK cell and monocyte populations.

Lovett-Racke A et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P1158

MRI: Total Reduction of Gd-Enhancing Lesions

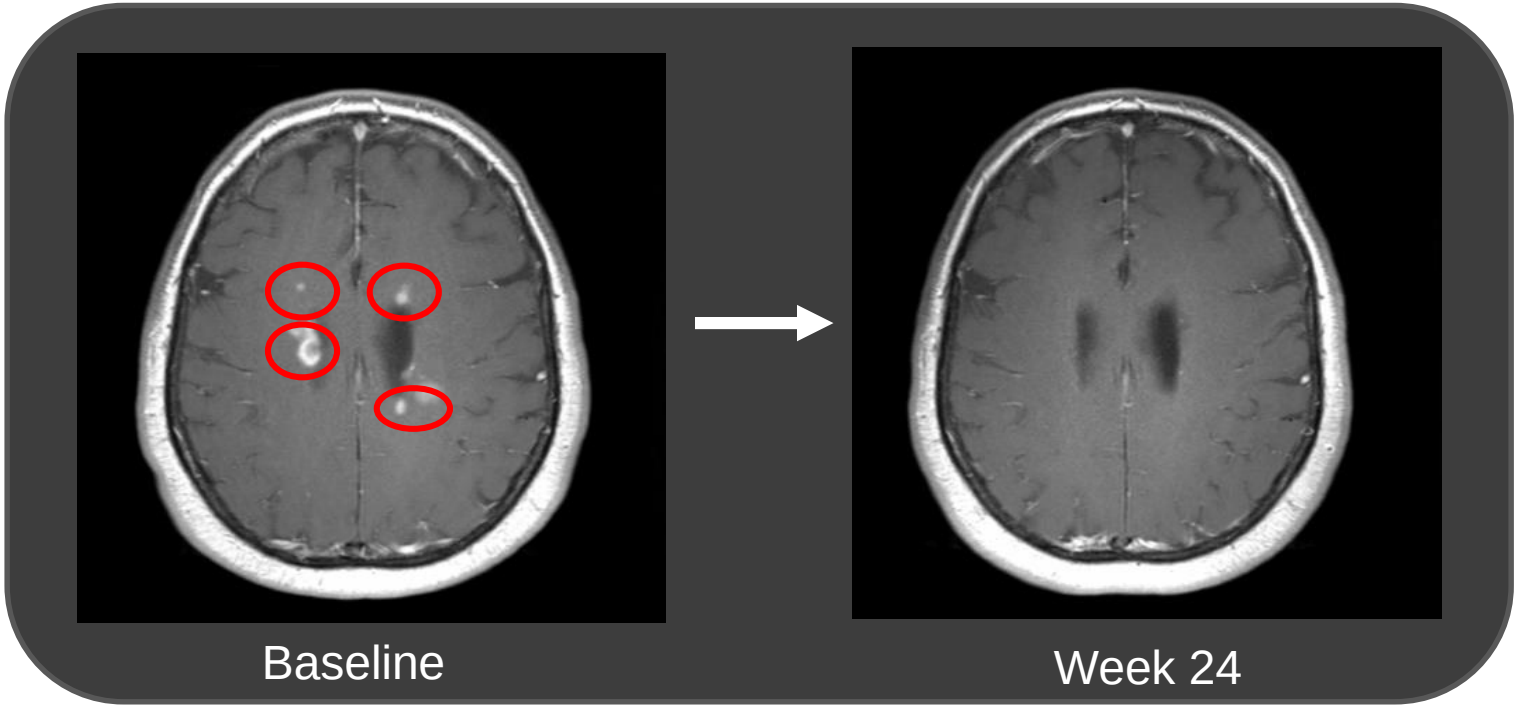


No T1 Gd enhancing lesions were detected in any subjects at Week 24

Fox E et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P793
Inglese M et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P798

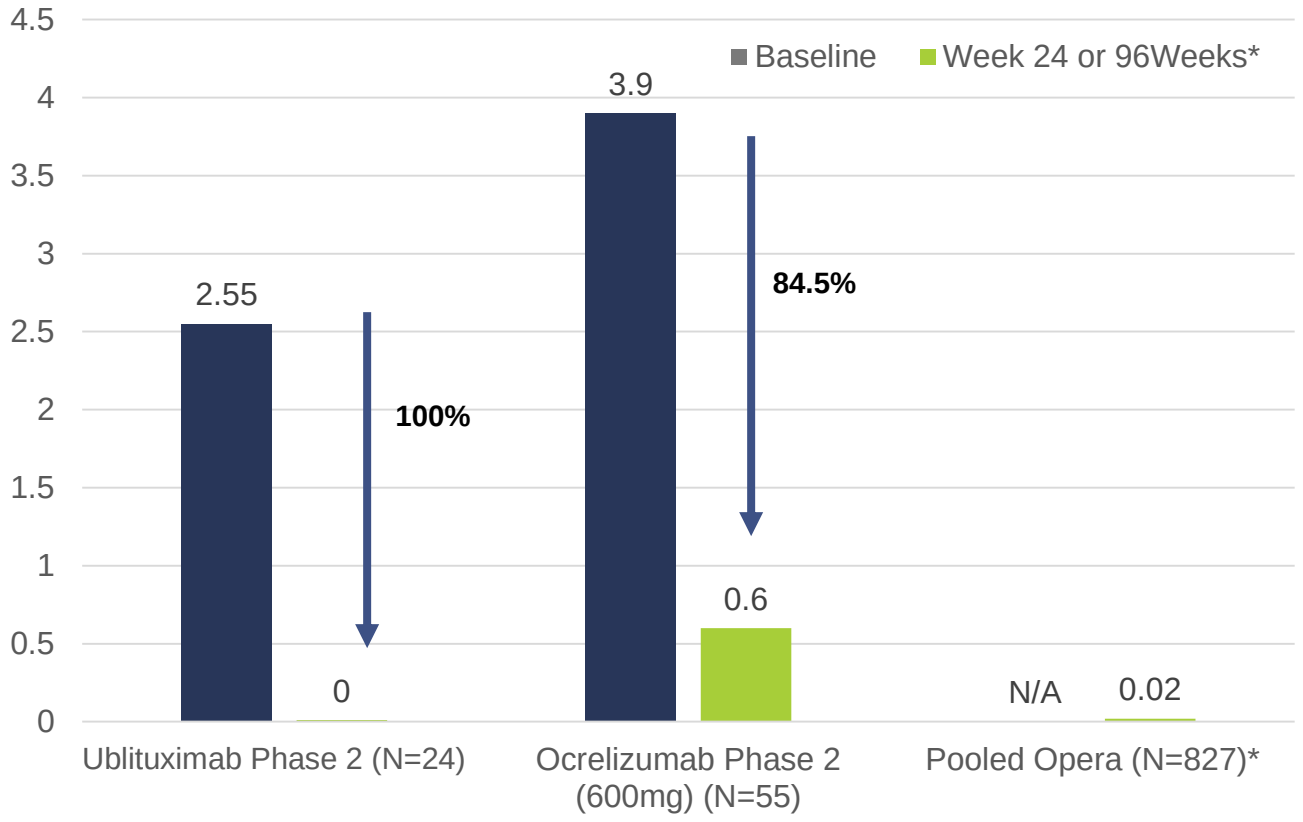
T1-Gd MRI at Baseline and Week 24: Study Subject

Subject T1-Gd MRI at Baseline and Week 24



Inglese M et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P798

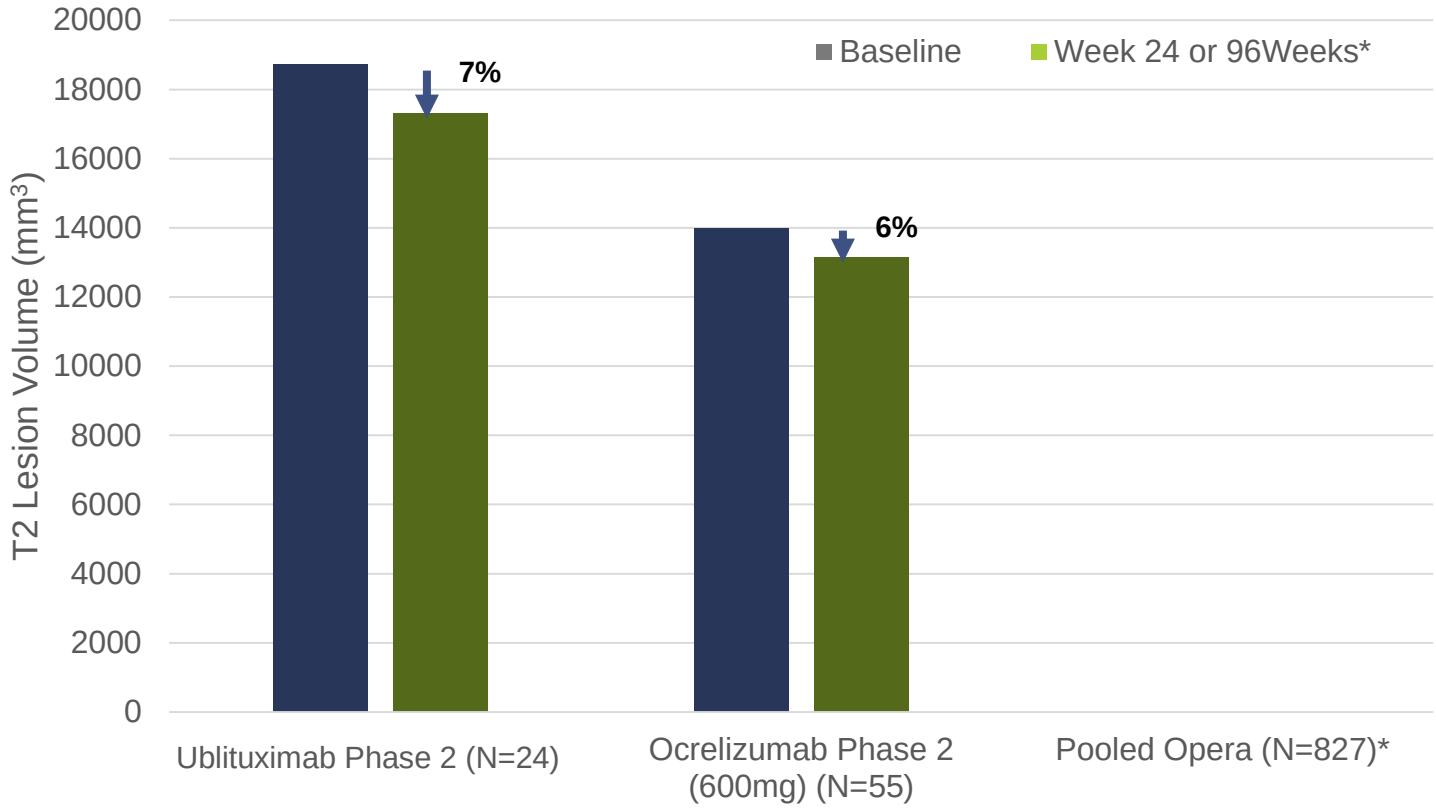
MRI: Total Reduction of Gd-Enhancing Lesions



Note: Pooled Opera I& II: Gd enhancing lesions decreased by 94% when compared to Rebif

Fox E et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P793
Inglese M et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P798
Kappos L et al. Lancet. 2011; 378:1779-1787
Hauser SL et al. NEJM. 2017; 376:221-234

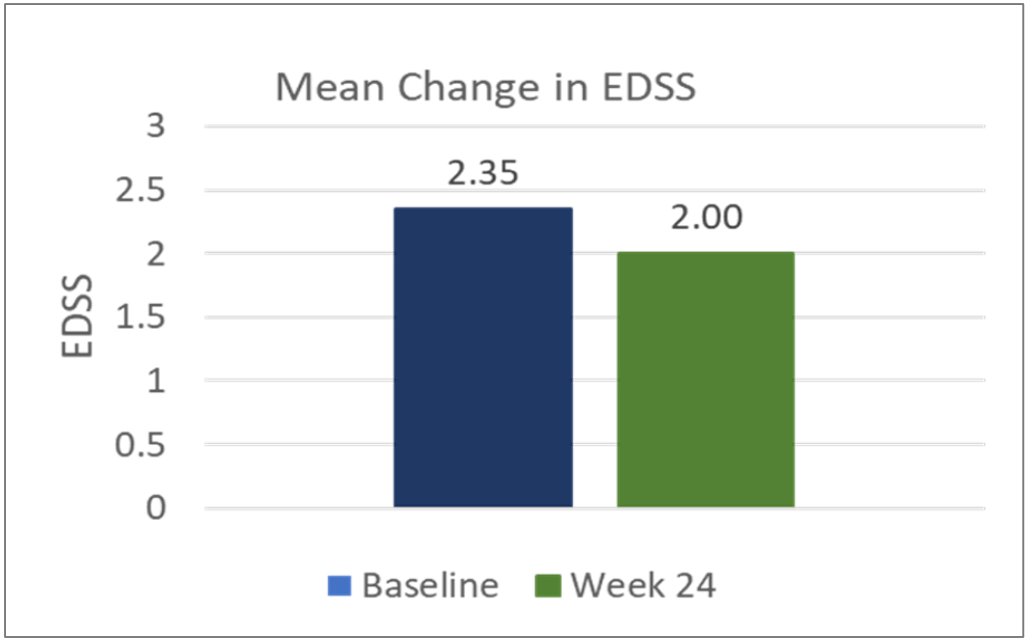
MRI: Reduction in T2 Lesion Volume at Week 24



- **There was a decrease of 7.5% (p=0.02) in T2 lesion volume at Week 24 compared to baseline (N=20)**
- **The mean number of New/Enlarging T2 lesions from baseline to Week 24 was 0.3 ± 0.4 (N=20)**

Inglese M et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P798
Kappos L et al. Lancet. 2011; 378:1779-1787
Hauser SL et al. NEJM. 2017; 376:221-234

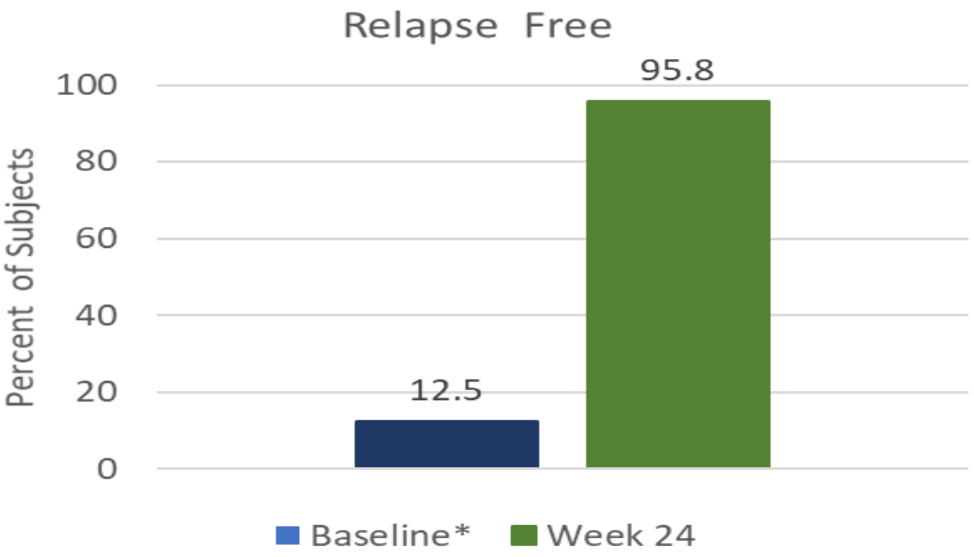
MS Relapse Data at Week 24



- **23/24 (95.8%) of subjects were confirmed relapse free at 24 weeks.**
  - One confirmed relapse was reported. The subject was initially randomized to the placebo arm. The relapse occurred 12 days after the subject's first infusion of 150mg of TG-1101. The subject remains on study and has received the second and third infusions of TG-1101. To date, the subject has remained relapse free.
- 21/24 (87.5%) subjects had experienced one relapse in the past year or two relapses in the past two years.
  - Among patients who had relapses in the year prior to screening, the mean number of relapses per subject was 1.42
  - The mean time between last reported relapse and enrollment was 5.77 months

Fox E et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P793

Relapse at Week 24



- 23/24 (95.8%) of subjects were confirmed relapse free at Week 24
- 1 Subject relapsed 12 days after first infusion
- At Week 24, ARR for Ublituximab was 0.09

Disability Endpoint	TG-1101 Phase 2 (N=24) (24 Weeks)	Ocrelizumab Phase 2 (N=55) (24 Weeks)	Opera I&II (96 Weeks)
ARR	0.09	0.13	0.156
% Relapse Free	95.8%	87%	80%

Fox E et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P793
Kappos L et al. Lancet. 2011; 378:1779-1787
Hauser SL et al. NEJM. 2017; 376:221-234

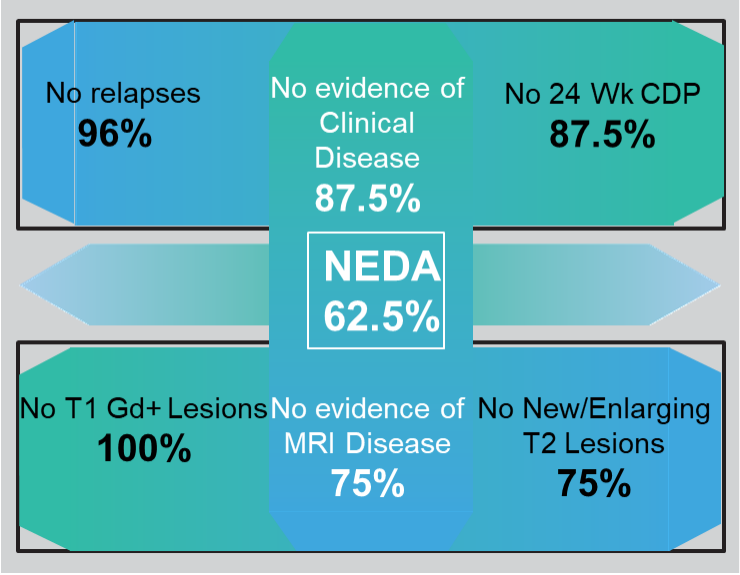
Disability as Measured By EDSS

Disability Endpoint	TG-1101 Phase 2 (N=24) (24 Weeks)	Ocrelizumab Phase 2 (N=55) (24 Weeks)	Opera I&II (N=827) (96 Weeks)
Patients with no confirmed disability progression	87%	N/A	90.6% (Opera I) 86.8% (Opera II)
Confirmed Disability Improvement	29.2%	N/A	20.7%
Mean change EDSS from baseline	-0.35	N/A	N/A

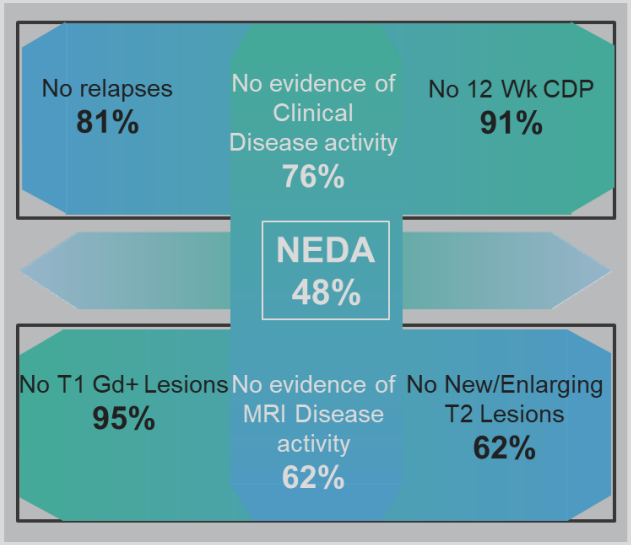
Fox E et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P793
Kappos L et al. Lancet. 2011; 378:1779-1787
Hauser SL et al. NEJM. 2017; 376:221-234

NEDA: Ublituximab Phase 2 & OPERA I & II

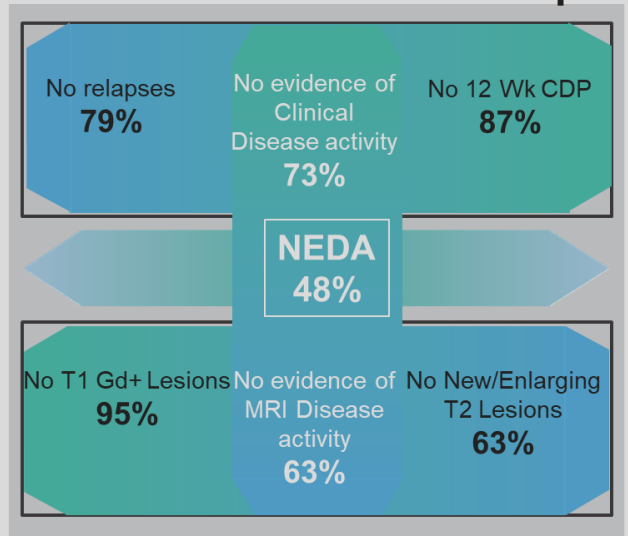
Ublituximab at Week 24



Ocrelizumab at Week 96 – Opera I



Ocrelizumab at Week 96 – Opera II



Fox E et al., Presented at ECTRIMS Annual Meeting Paris October 25-28 2017 P793
Traboulsee A et al. Presented at the 2016 American Academy of Neurology Meeting, Vancouver, Canada. April 15 - 22. Neurology. 2016;

ECTRIMS-ACTRIMS 2017

Poster Highlights:

- 99% median B-cell depletion was observed at week 4 and maintained at week 24 (6 months) (n=24)

- 96% of subjects (23/24) were relapse free at week 24
  - One confirmed relapse was reported in a patient initially randomized to the placebo arm. The relapse occurred 12 days after the patients first infusion of 150mg of TG-1101. The patient remains on study and has received the second and third infusions of TG-1101 and to date has remained relapse free.
- Mean EDSS improvement from baseline of 0.35 with 79% of subjects showing improved or stable EDSS

- TG-1101 was well tolerated across all patients including those receiving rapid infusions, as low as a one hour for the 450mg Phase 3 dose, and produced similar levels of B-cell depletion with no identified change in IRR or overall safety profile.

E. Fox, ECTRIMS-ACTRIMS, 2017

ECTRIMS - ACTRIMS 2017

Poster Highlights:

- TG-1101 completely eliminated all (100%) of T1 Gd-enhancing lesions at week 24 (n=20) (p=0.005)
- 7% Reduction in the T2 lesion volume at Week 24 from baseline (p=0.02), suggestive of a decrease in burden of disease
- 6.5% Reduction in T1 hypointense lesion volume at Week 24 from baseline (p=0.03)

ECTRIMS - ACTRIMS 2017

Poster Highlights:

- B-cell are efficiently depleted in most patients within 24 hours of receiving the first dose of TG-1101, with 99% depletion observed at week 4 and maintained at week 24 (6 months) (n=24)

- The fluctuation in NK cells, T cells and monocytes that occurred in response to B-cell depletion is corrected within 4 weeks post initial TG-1101 treatment

- Due to the sustained B-cell depletion, there is no significant affect of TG-1101 treatment at Week 24 on the NK cells, T cells or monocytes, illustrating the immune homeostasis in the non-B cell

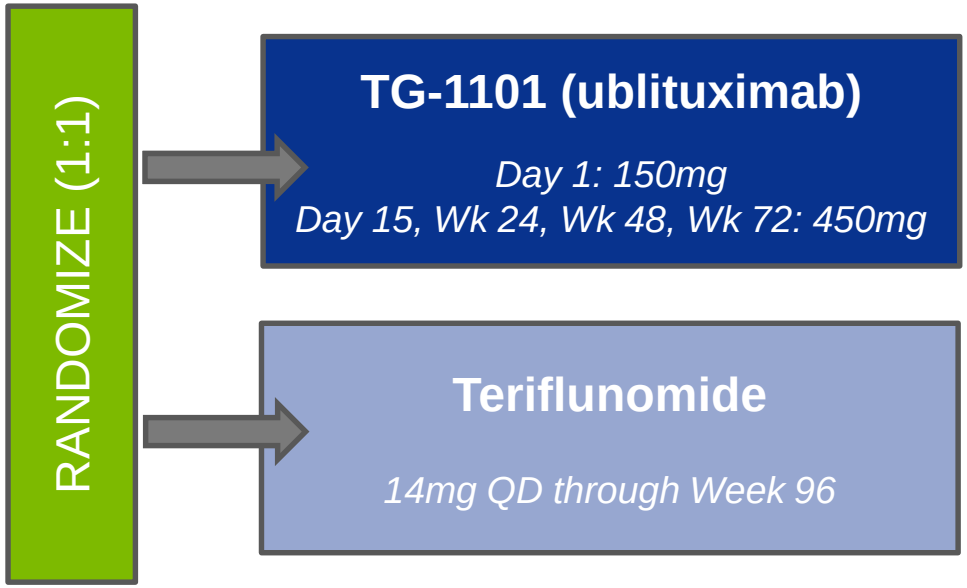
TG-1101(ublituximab)
Phase 3
ULTIMATE I & II Trials

Edward Fox, MD, PhD

ULTIMATE I and II Study Design

- ULTIMATE I and II are two independently conducted Phase 3 registration trials for ublituximab in relapsing MS
- Identical in design and balanced with respect to location of study sites
- Randomized, Double-Blind, Double-Dummy, Active Comparator
  - Patients randomized 1:1 to ublituximab plus oral placebo or teriflunomide plus IV placebo
  - 116 Week Duration: 96 week treatment period plus 20 week follow-up

ULTIMATE I & II MS Phase 3 Trials

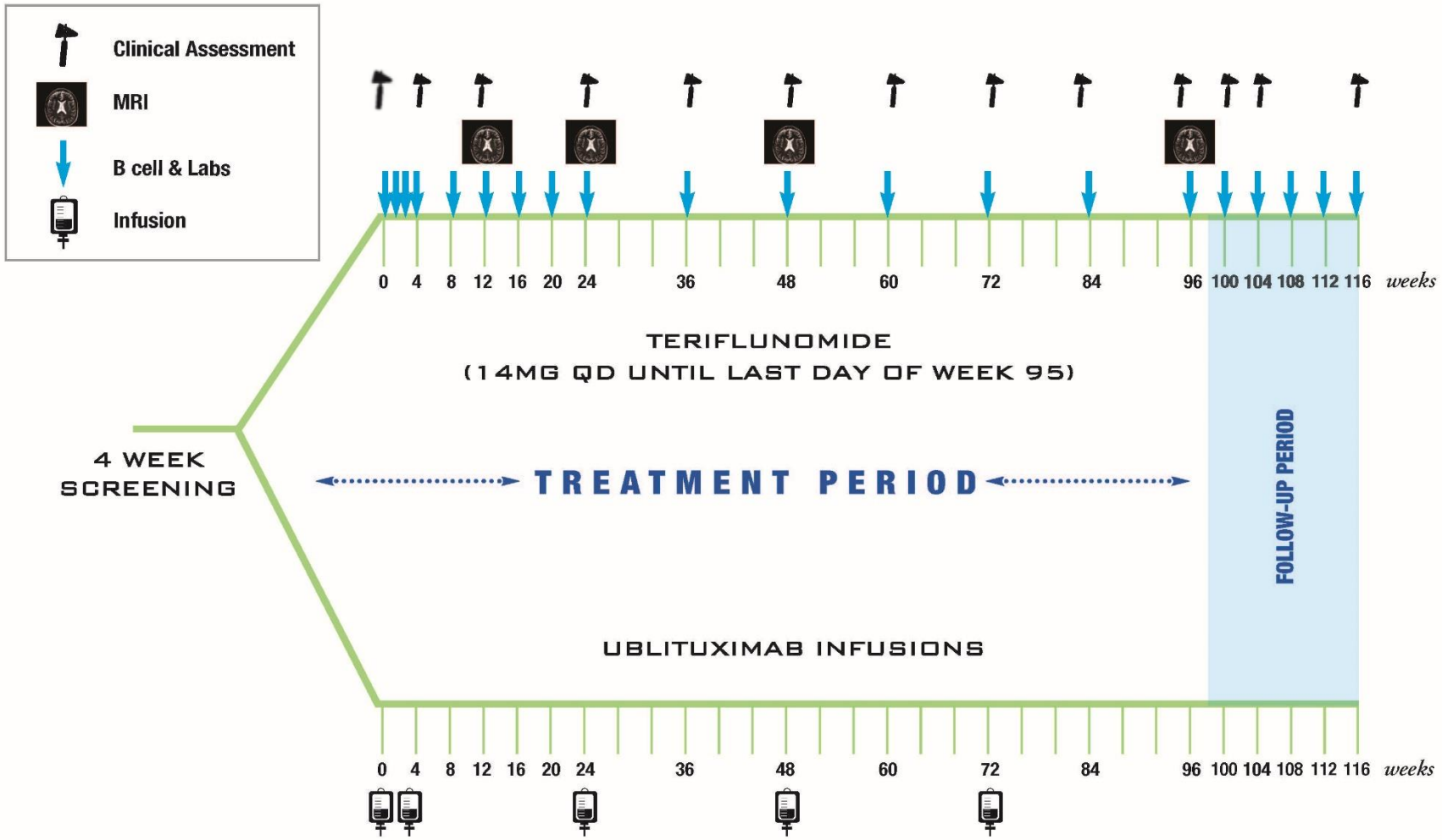


- Two independent Phase III, randomized, multi-center, double-blinded, double-dummy, active-controlled studies

- **Design, Endpoints, and Statistics agreed to via Special Protocol Assessment (SPA)**
- Enrolling ~440 patients per study (880 patients total) with relapsing forms of Multiple Sclerosis (RMS)
- Primary Endpoint: Annualized Relapse Rate (ARR) following 96 weeks of treatment
- Study Chair: Dr. Lawrence Steinman, Stanford University
- ***Currently open for enrollment in the US, Ex-US sites to follow***

ULTIMATE I & ULTIMATE II Phase 3 Trials

Evaluating Ublituximab in Relapsing Forms of Multiple Sclerosis



Primary Endpoint

- Annualized Relapse Rate (ARR) defined as the number of confirmed relapsed per-subject year
  - The estimate of ARR for a treatment group will be the total number of relapses for subjects in the respective treatment group divided by the sum of duration on study for subjects in that specific treatment group
  - Subjects will be treated up to 96 weeks

QUESTIONS?