Phase 2 Multicenter Study Results of Ublituximab, a Novel Glycoengineered AntiCD20 Monoclonal Antibody (mAb), in Patients with Relapsing Multiple Sclerosis (RMS)

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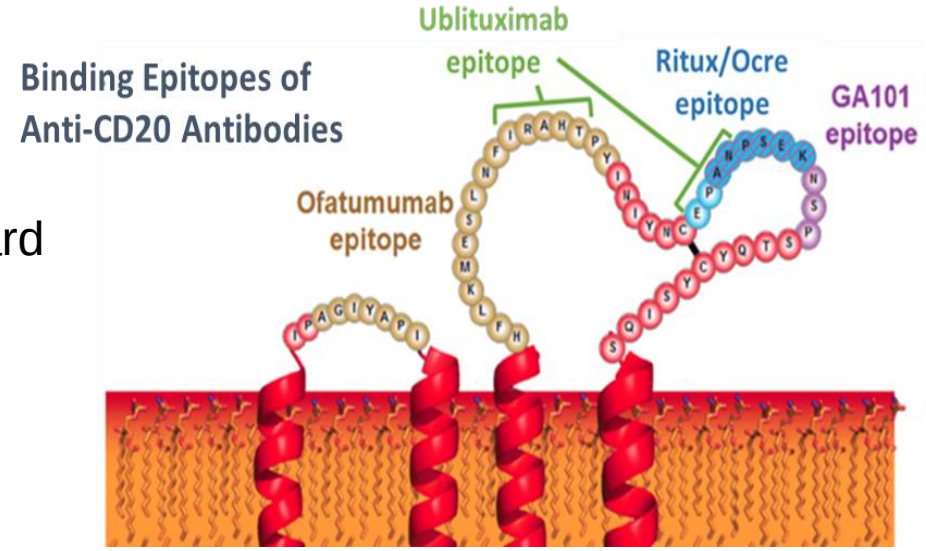
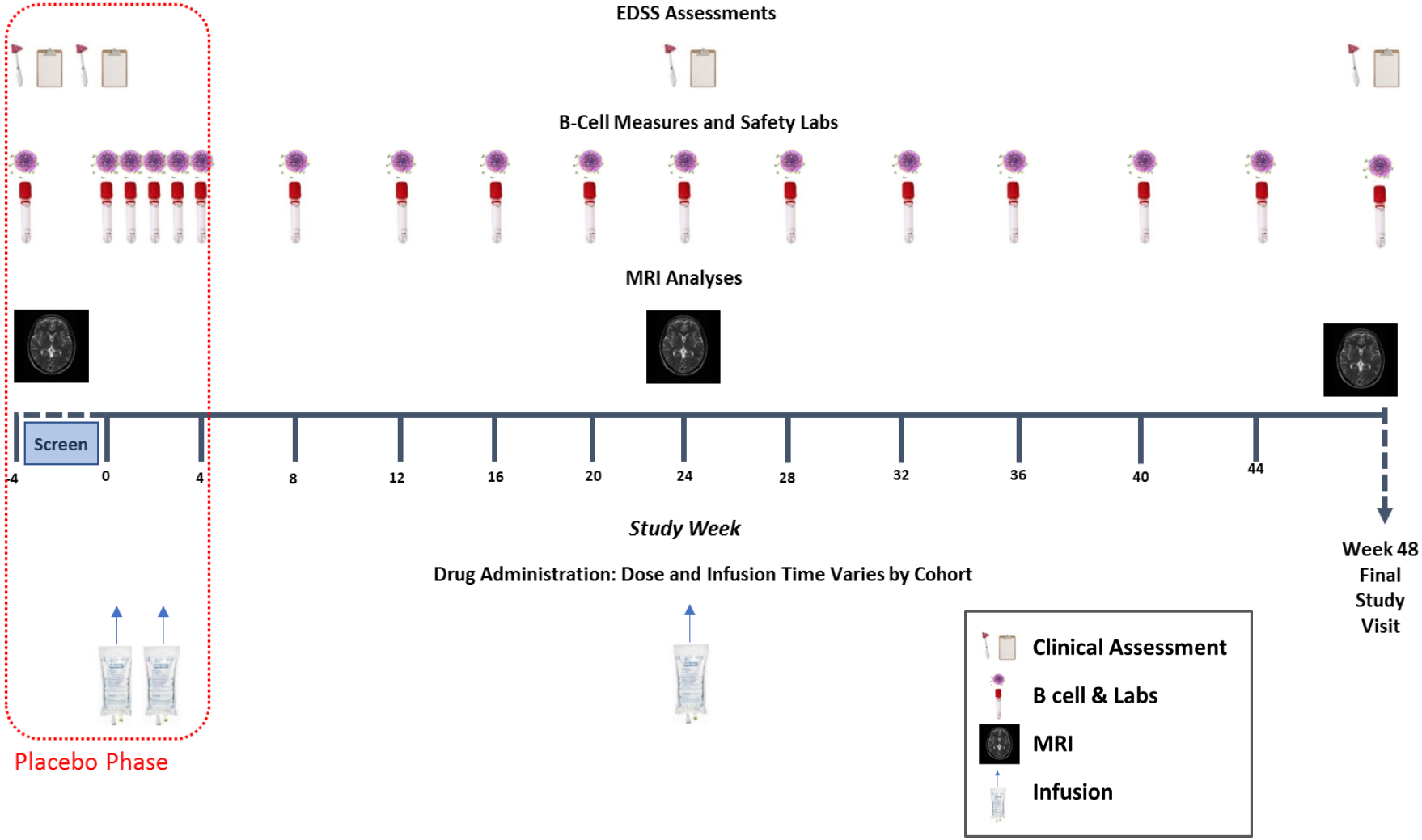
Ublituximab (TG-1101)

- Novel Glycoengineered Anti-CD20 mAb
- Unique protein sequence
- Type 1 Chimeric IgG1 mAb
- Potential advantages over current standard of care:
  - Glycoengineered for significantly enhanced ADCC
  - Activity in “low” CD20 expressing cell lines, a characteristic of rituximab resistance
  - Binds to a novel epitope on CD20



Source: Adapted from Ruuls et al 2008

Ublituximab Phase II: Design



Ublituximab Phase II: Design

	Randomization	Treatment Period		
Cohort	Treatment	Day 1/ Infusion Time	Day 15/ Infusion Time	Week 24/ Infusion Time
1	Placebo (n=2)	Placebo / 4h	Placebo / 3h	-
	UTX (n=6)	150 mg / 4h	450 mg / 3h	450 mg / 1.5h
2	Placebo (n=2)	Placebo / 4h	Placebo / 1.5h	-
	UTX (n=6)	150 mg / 4h	450 mg / 1.5h	450 mg / 1h
3	Placebo (n=2)	Placebo / 4h	Placebo / 1h	-
	UTX (n=6)	150 mg / 4h	450 mg / 1h	600 mg / 1h
4	Placebo (n=2)	Placebo / 3h	Placebo / 1h	-
	UTX (n=6)	150 mg / 3h	600 mg / 1h	600 mg/ 1h
5	Placebo (n=2)	Placebo / 2h	Placebo / 1h	-
	UTX (n=6)	150 mg / 2h	600 mg / 1h	600 mg/ 1h
6	Placebo (n=2)	Placebo / 1h	Placebo/ 1h	-
	UTX (n=6)	150 mg / 1h	600 mg / 1h	600 mg/ 1h

TG1101-RMS201
PHASE II PRELIMINARY RESULTS:

- 24 Week Data, All Cohorts
- 48 Week Data, Cohorts 1 and 2

Ublituximab Phase II Results: Baseline Characteristics

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
4	Placebo (n=2)	31±1	67%	6.8±7.7
	UTX (n=6)	39±12	50%	0.20±0.10
5	Placebo (n=2)	36±12	100%	15.4±9.6
	UTX (n=6)	46±1	100%	6.3±5.6
6	Placebo (n=2)	28±1	50%	5.7±2.5
	UTX (n=6)	40±8	33%	8.5±8.4
Total	N=48	40±10	65%	8.0±8.1

[1] **Mean ± Standard Deviation**

[2] **Distribution of time from diagnosis: 22 subjects (46%) were less than 5 years, 10 (21%) were 5-10 years, and 16 (33%) were greater than 10 years**

Ublituximab Phase II Results: Patient Disposition

- 48 subjects were randomized to treatment in Cohort 1 through Cohort 6

- 46/48 subjects completed 6 months of ublituximab treatment; 12 subjects (2 per cohort) received placebo infusions, before crossing over to the ublituximab arm
  - One subject in Cohort 2 withdrew from the study due to pregnancy, after having received 2 ublituximab infusions, but continued to be followed with safety lab monitoring and immunological analyses
  - One subject in Cohort 6 missed the week 24 infusion

Ublituximab Phase II Results: Safety & Tolerability

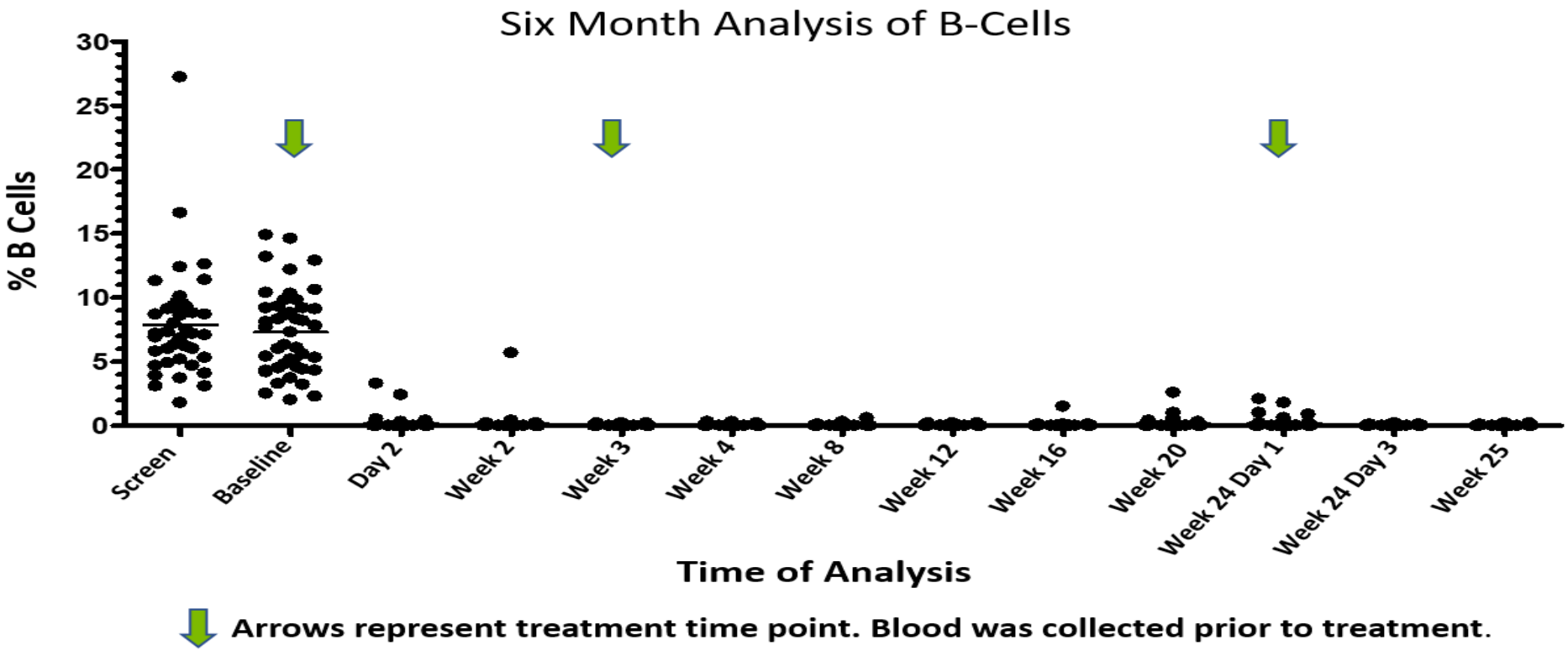
All AEs >10% Regardless of Causality

Event, n (%)	(N=48)	
Any adverse event[1]	41 (85%)	
Most frequently reported adverse events[2]	All Grades	Grade 3/4
Infusion-related reaction	20 (42%)	- (-)
Fatigue	12 (25%)	3 (6%)
Headache	11 (23%)	- (-)
Numbness	7 (15%)	- (-)
Common Cold	7 (15%)	- (-)
Dizziness	7 (15%)	- (-)
Nausea/Vomiting	7 (15%)	- (-)
Upper Respiratory Infection	7 (15%)	1 (2%)

[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.

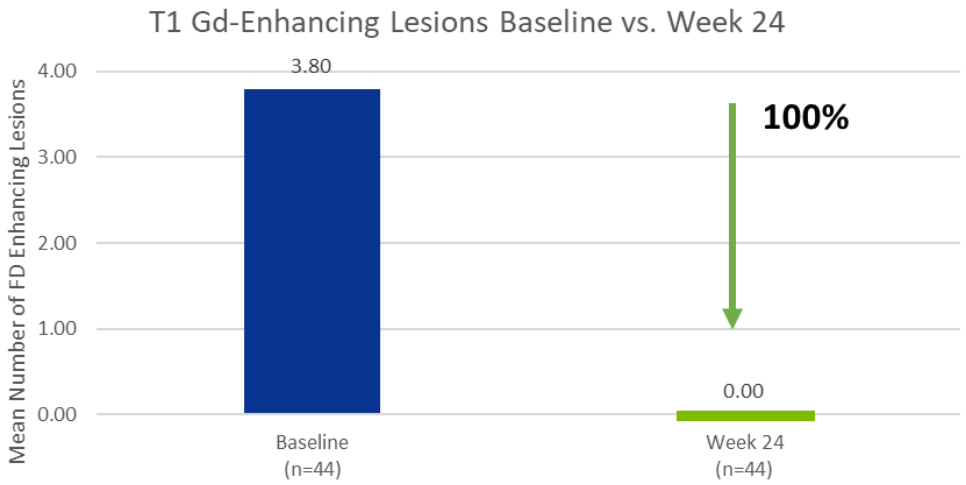
- **Median duration of follow up ~11 months**
- **Ublituximab was well tolerated and no drug related discontinuations from study have occurred to date.**
- No Grade 3/4 Adverse Events (AEs) were deemed possibly related to ublituximab.
- A total of 41 infusion related reactions (IRRs) were reported in 20 subjects. All were Grade 1 or Grade 2.
- No events of death reported on study.
- The Data Safety Monitoring Board (DSMB) has reviewed safety labs & adverse events for all subjects, and has not found any lab abnormalities or safety signals that would warrant a change in protocol.

Ublituximab Phase II Results: B-Cell Depletion



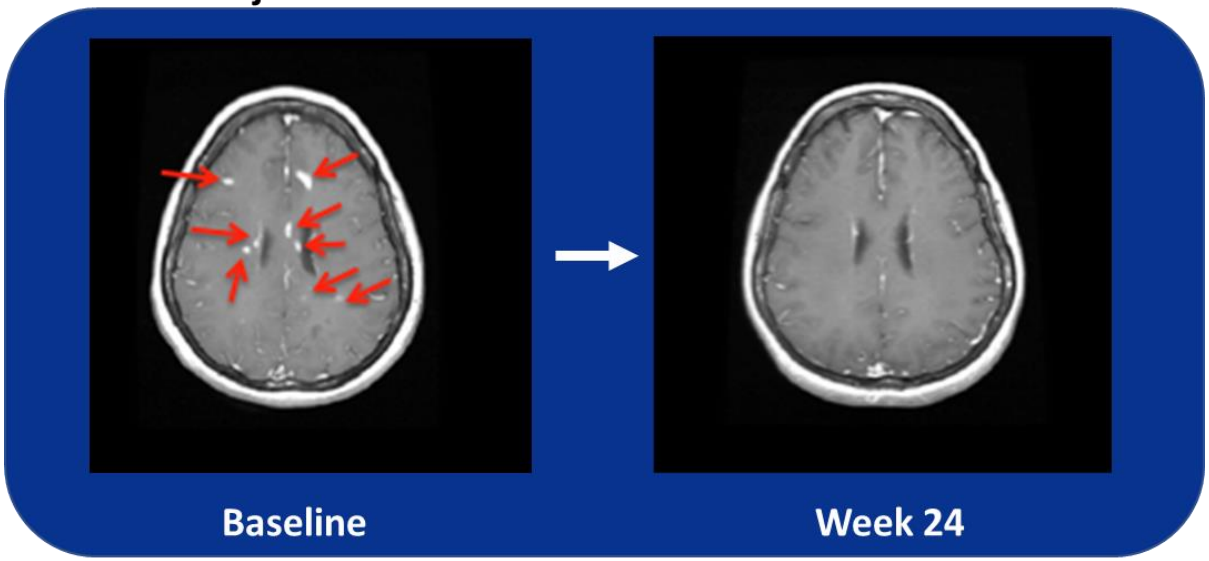
- At week 4, median 99% B cell depletion was observed and maintained at Week 24 (n=44)

Ublituximab Phase II 24 Week Results: MRI-Gd Enhancing Lesions

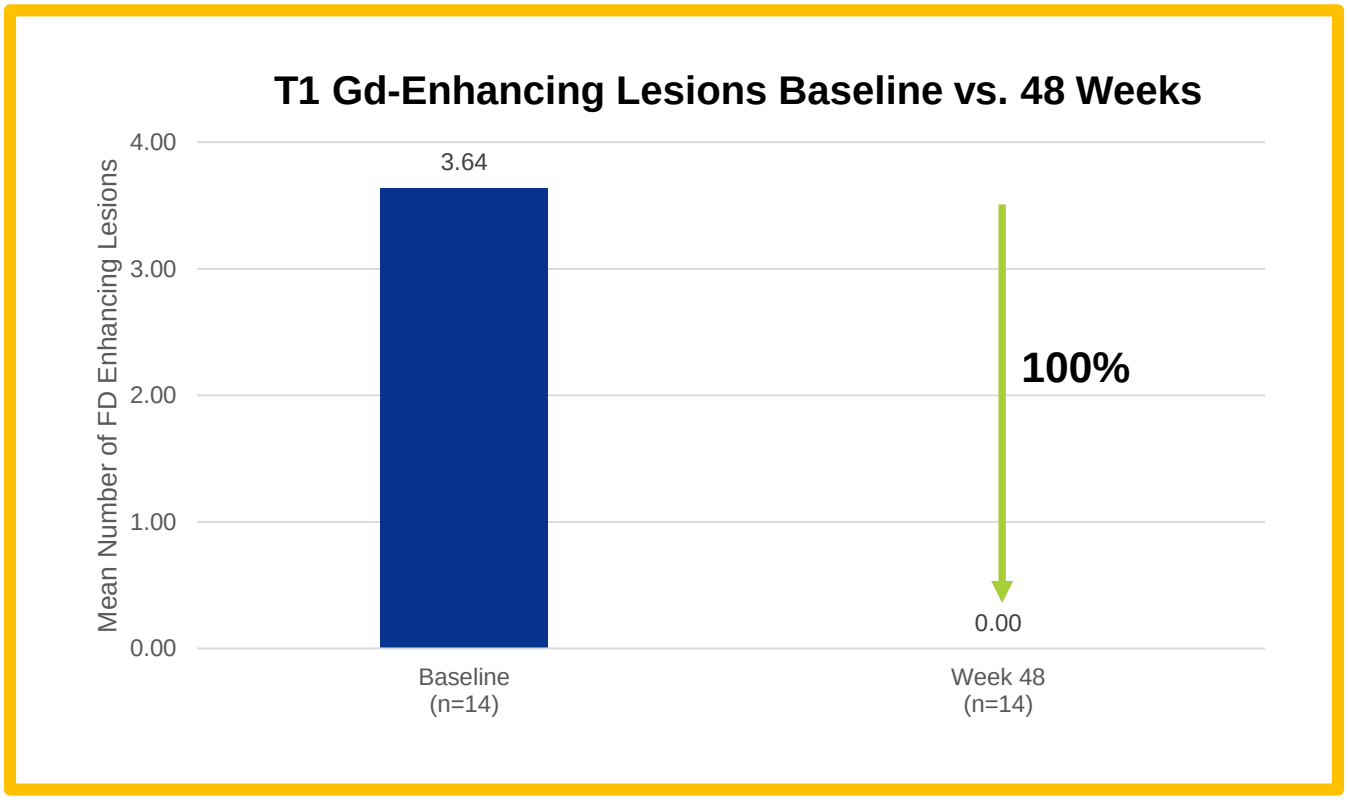


- *No T1 Gd-enhancing lesions detected in any subjects at Week 24 (n=44; p=0.003)*
- Mean number of T1 Gd lesions at baseline was 3.80

Subject T1 Gd MRI at Baseline and Week 24

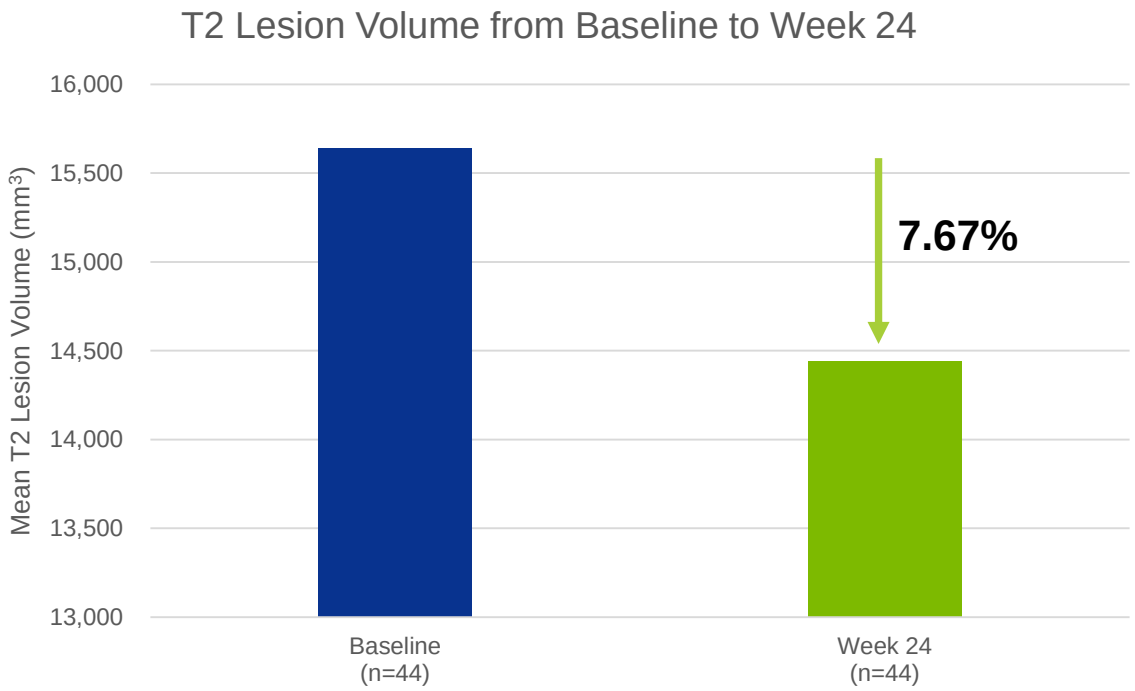


Ublituximab Phase II 48 Week MRI Results: Gd-Enhancing Lesions: Cohorts 1-2



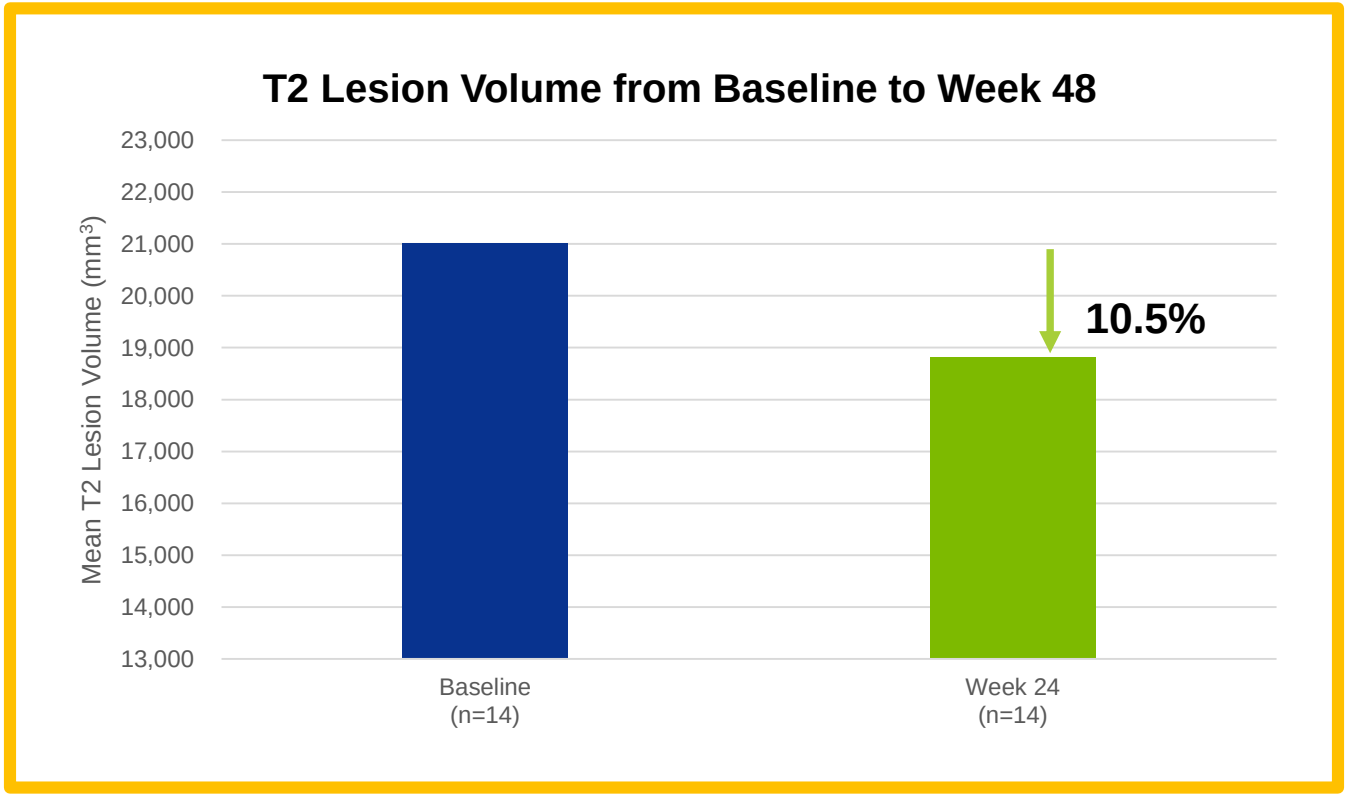
- *No T1 Gd-enhancing lesions detected in any subjects in Cohorts 1-2 at Week 48 (n=14)*
- Mean number of T1 Gd lesions at baseline for Cohorts 1-2 was 3.64 (n=14)

Ublituximab Phase II 24 Week Results: MRI-T2 Lesion Volume



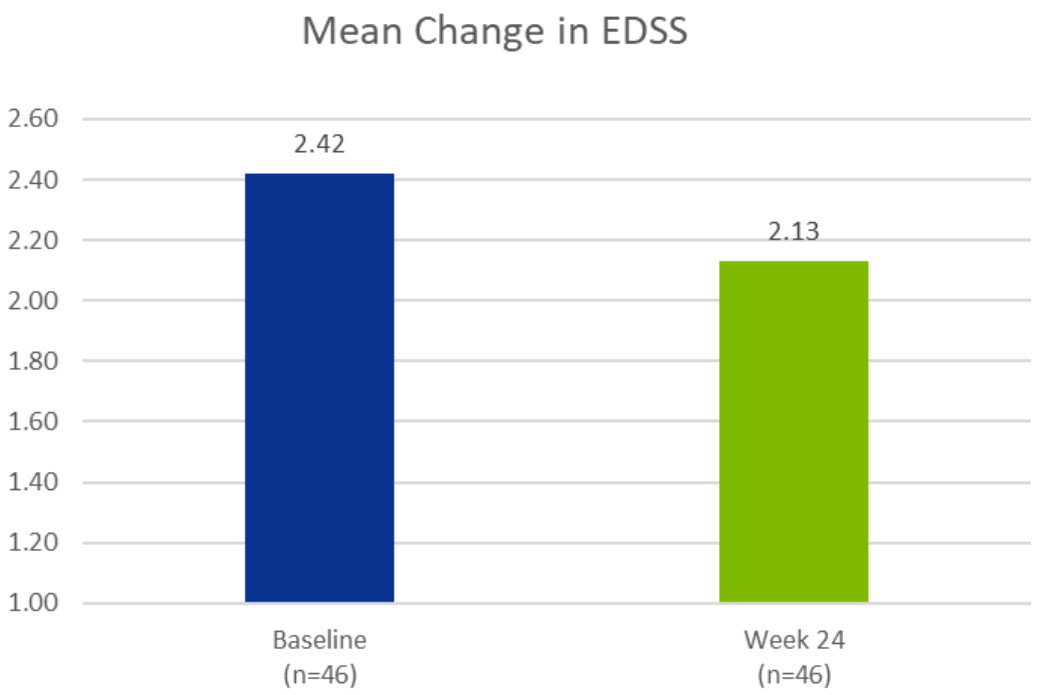
- There was a decrease of 7.67% (p=0.004) in T2 lesion volume at Week 24 compared to baseline
- The mean number of New/Enlarging T2 lesions from baseline to Week 24 was 0.2 ± 0.45

Ublituximab Phase II 48 Week Results: MRI-T2 Lesion Volume, Cohorts 1-2



- There was a decrease of 10.5% in T2 lesion volume at Week 48 compared to baseline for Cohorts 1-2 (n=14)

Ublituximab Phase II 24 Week Results: EDSS

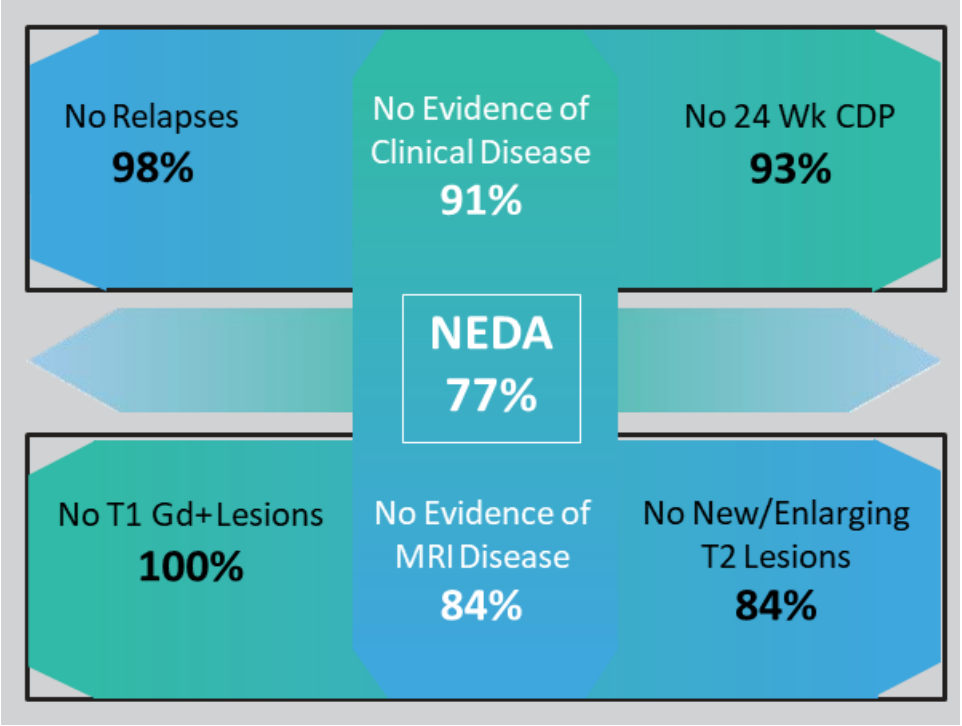


- 83% of subjects showed improved or stable EDSS
- Mean EDSS at baseline was 2.41 ±1.41; Median=2.5
- At Week 24, the mean EDSS was 2.12. The mean change from baseline was an improvement of 0.29 ±0.93 points.

** 2 of the total 48 patients did not complete the week 24 EDSS evaluation*

Ublituximab Phase 2 RMS Update: NEDA at Week 24

- At Week 24, 43* of 48 subjects had received all assessments to be evaluated for NEDA:
  - 98% of subjects were relapse free
  - 93% of subjects did not experience 24 week confirmed disability progression
  - 100% of subjects did not have any Gd-enhancing lesions
  - 84% of subjects did not have any new/enlarging T2 lesions
  - 76% of subjects achieved clinical and MRI outcomes consistent with NEDA



** 3 of the total 48 patients did not have week 24 MRI, 1 patient did not have week 24 MRI or week 24 EDSS evaluation and 1 additional patient did not have a week 24 EDSS evaluation therefore only 43 patients had received all assessments to be evaluated for NEDA*

CDP is defined as an increase of ≥ 1.0 point from the baseline EDSS score that is not attributable to another etiology (e.g. fever, concurrent illness, or concomitant medication) when the baseline score is 5.5 or less, and ≥ 0.5 when the baseline score is above 5.5.

Ublituximab Phase II Results: Cumulative ARR

- Annualized Relapse Rate of 0.07
  - ARR calculated cumulatively, based on 48 subjects with a mean of approximately 11 months of follow-up

Conclusions

- B-cells are efficiently depleted in most patients within 24 hours of receiving the first dose of ublituximab, with >99% depletion in all patients by Week 4, and significant reductions from baseline maintained at Week 24

- Ublituximab was well tolerated and the most frequent AEs were infusion related reactions (IRRs); all Grade 1 or 2

- A rapid infusion time, as low as one hour, of 450mg was well tolerated, produced high levels of B cell depletion and is now being studied in the Phase 3 ULTIMATE trials

Conclusions

- **Cumulative Annualized Relapse Rate (ARR) of 0.07**
- No T1 Gd-enhancing lesions were detected in any subjects at Week 24 (n=44) or at Week 48 (n=14)
- 7.67% Reduction in T2 lesion volume at Week 24 from baseline, suggestive of a decrease in burden of disease (n=44)
  - 10.5% reduction in T2 lesion volume at Week 48 from baseline (n=14)
- Final Week 48 results from this Phase 2 are expected to be presented at an upcoming major medical meeting and support the currently ongoing ULTIMATE Phase 3 trials in relapsing forms of Multiple Sclerosis (RMS)

Thank You to Our Study Sites

- Hope Neurology, Knoxville, TN: Sibyl Wray, MD
  - Coordinator: Brenda Whitehead, CCRP
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