TG Therapeutics

# ULTIMATE I & II Data Preview Call

April 2021

# Forward-Looking Safe Harbor Statement

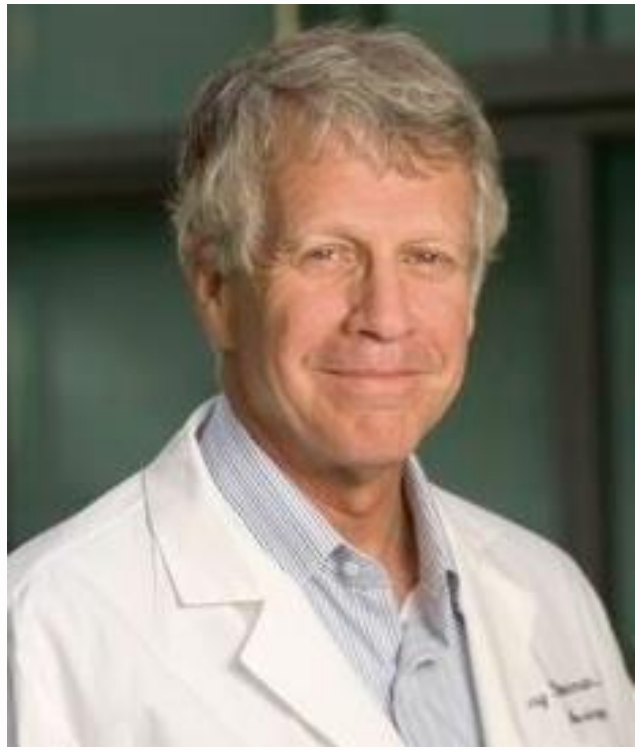
- This is presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that reflect the Company's current beliefs, expectations and assumptions. These statements include but are not limited to statements regarding the future of the Company's business, our future plans and strategies, clinical trial results, and regulatory filings and approvals. 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 forward-looking statements involve risks and uncertainties that could cause TG Therapeutics' actual results to differ materially from the anticipated results and expectations, including but not limited to: our ability to complete the BLA submission for ublituximab in relapsing multiple sclerosis (RMS) within the timeline projected; the risk that the clinical results from the ULTIMATE I & II trials will not support regulatory approval of ublituximab to treat RMS or that we will not receive regulatory approval within the timeline projected; the risk that if approved, ublituximab will not be commercially successful; our ability to expand our commercial infrastructure, and successfully launch, market and sell ublituximab in RMS if approved; the Company's reliance on third parties for manufacturing, distribution and supply, and a range of other support functions for our commercial and clinical products, including ublituximab; the uncertainties inherent in research and development; and the risk that the ongoing COVID-19 pandemic and associated government control measures have an adverse impact on our research and development plans or commercialization efforts. Further discussion about these and other risks and uncertainties can be found in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 and in our other filings with the SEC.
- Any forward-looking statements set forth in this press release speak only as of the date of this press release. We do not undertake to update any of these forward-looking statements to reflect events or circumstances that occur after the date hereof. You are cautioned not to place undue reliance on these forward-looking statements, which speak only of our views as of the date hereof.

# AGENDA

| April 16, 2021 | |
|---|---|
| 8:30 – 8:35 AM | **Welcome**<br>Jenna Bosco, TG Therapeutics |
| 8:35 – 8:40 AM | **Brief Introductions**<br>▪ Lawrence Steinman, MD, Stanford University<br>▪ Edward J. Fox, MD, PhD, Central Texas Neurology Consultants<br>▪ Enrique Alvarez, MD, PhD, University of Colorado Medicine |
| 8:40 – 8:45 AM | **Opening Remarks**<br>▪ Michael Weiss, TG Therapeutics. |
| 8:45 – 8:55 AM | **ULTIMATE I & II Phase 3 Data Preview**<br>▪ Lawrence Steinman, MD |
| 8:55 – 9:15 AM | **MS KOL Discussion**<br>▪ Steinman, Fox & Alvarez |
| 9:15 – 9:45 AM | **Q&A Session** |
| | **Closing Remarks** |

# BRIEF INTRODUCTIONS

# LAWRENCE STEINMAN, MD



**Lawrence Steinman, MD**
Zimmermann Professor of Neurology & Neurological Sciences, and Pediatrics
*Stanford University*

**Dr. Steinman** is a professor of Neurology and Neurological Sciences, Pediatrics, and Genetics. He also served as the Chair of the Stanford University Interdepartmental Program in Immunology from 2003-2011.

Dr. Steinman's research focuses on what provokes relapses and remission in multiple sclerosis (MS), the nature of the molecules that serve as a brake on the brain inflmmation, and the quest for a tolerizing vaccine for autoimmune diseases like type 1 diabetes and neuromyelitis optica. He has developed two antigen specific therapies, using DNA vaccines, for MS and type 1 diabetes. He was senior author on the seminal 1992 Nature article that reported the key role of a particular integrin in brain inflammation. This research led to the development of the drug Tysabri, which is used to treat patients with MS and Crohn's disease.

Dr. Steinman received his BA from Dartmouth College and his MD from Harvard University. He was a post-doctoral fellow in chemical immunology fellow at the Weizmann Institute of Science in Israel. Dr. Steinman returned to Stanford University Hospital as a resident in pediatric and adult neurology and then joined the faculty at Stanford in 1980.

Dr. Steinman has received numerous honors and awards, including the John M. Dystel Prize from the American Academy of Neurology and the National MS Society for his research on MS, and the Charcot Prize for Lifetime Achievement in MS research. He has twice been awarded the Senator Jacob Javits Neuroscience Investigator Award by the National Institute of Neurological Diseases and Stroke. Dr. Steinman is a member of the National Academy of Sciences and the National Academy of Medicine, formerly called the Institute of Medicine.

# EDWARD J. FOX, MD, PHD

**Edward J. Fox, MD, PhD**
Director, Multiple Sclerosis Clinic
of Central Texas
*Central Texas Neurology Consultants*

**Dr. Fox is the director of the Multiple Sclerosis Clinic of Central Texas, and is the founding partner of Central Texas Neurology Consultants in Round Rock, Texas.**

**After receiving a Bachelors Degree at Washington University in St. Louis, he completed the Medical Scientist Training Program for his M.D., Ph.D. and his Neurology residency at Baylor College of Medicine in Houston. His Ph.D. in Immunology was awarded for the thesis "Growth Requirements of Human Suppressor T Lymphocytes."**

**Since starting a private Neurology practice in the Austin area in 1992, he has been involved in numerous MS research protocols and has spoken internationally on topics related to Neuroimmunology. Dr. Fox is a Fellow of the American Academy of Neurology. He served as President of the Texas Neurological Society in 2019-2020. He has an appointment as Clinical Associate Professor of Neurology at the University of Texas Dell Medical School at Austin.**

# ENRIQUE ALVAREZ, MD, PHD

**Enrique Alvarez, MD, PhD**
Assistant Medical Director, Neurology
*University of Colorado Medicine*

**Dr. Alvarez Enrique Alvarez, MD/PhD, is a neurologist with a sub-specialization in neuroimmunology at the Rocky Mountain Multiple Sclerosis Center at the University of Colorado and Denver Health. He serves as the medical director for outpatient neurology at the University of Colorado.**

**Dr. Alvarez is particularly interested in improving outcomes in patients with MS including using biomarkers and real world data to choose the best treatment options.**

# MICHAEL S. WEISS, CEO

TG Therapeutics

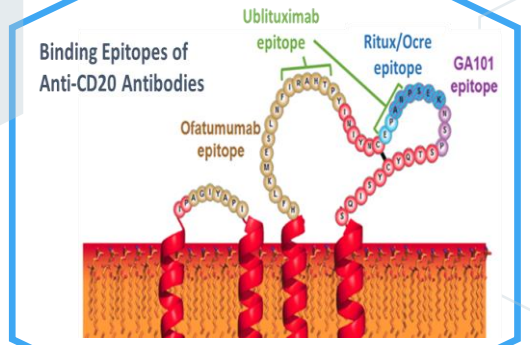
# LAWRENCE STEINMAN, MD

# Ublituximab:

*Investigational next generation anti-CD20 monoclonal antibody*


- **Targets a unique epitope on the CD20 antigen with demonstrated activity in rituximab refractory iNHL patients[1]**
- **Glycoengineered for enhanced potency**
- **1 hour infusion time, following the first infusion**
- **2,100+ patients treated with ublituximab, including 3 randomized phase 3 trials across MS and hematology**

Target
Q3 2021 BLA submission of ublituximab in MS

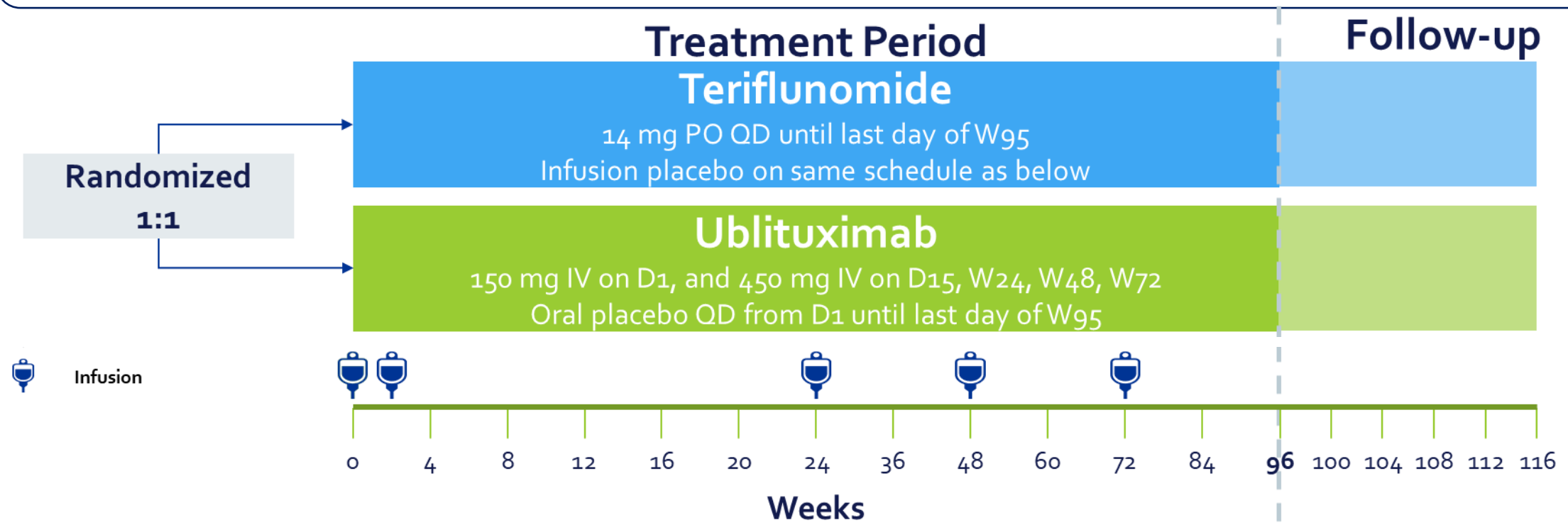



*Adapted from Klein et al, 2013*

[1]*O'Connor et al, BJH 2016*

# ULTIMATE I & II: Study Design

Identical phase 3, randomized, multi-center, double-blinded, active-controlled studies that were conducted in parallel




**Ublituximab infusions are given in one-hour, following the first infusion**



*After completing Week 96, patients entered into a 20-week safety follow-up and were eligible to enroll into an open-label extension study.

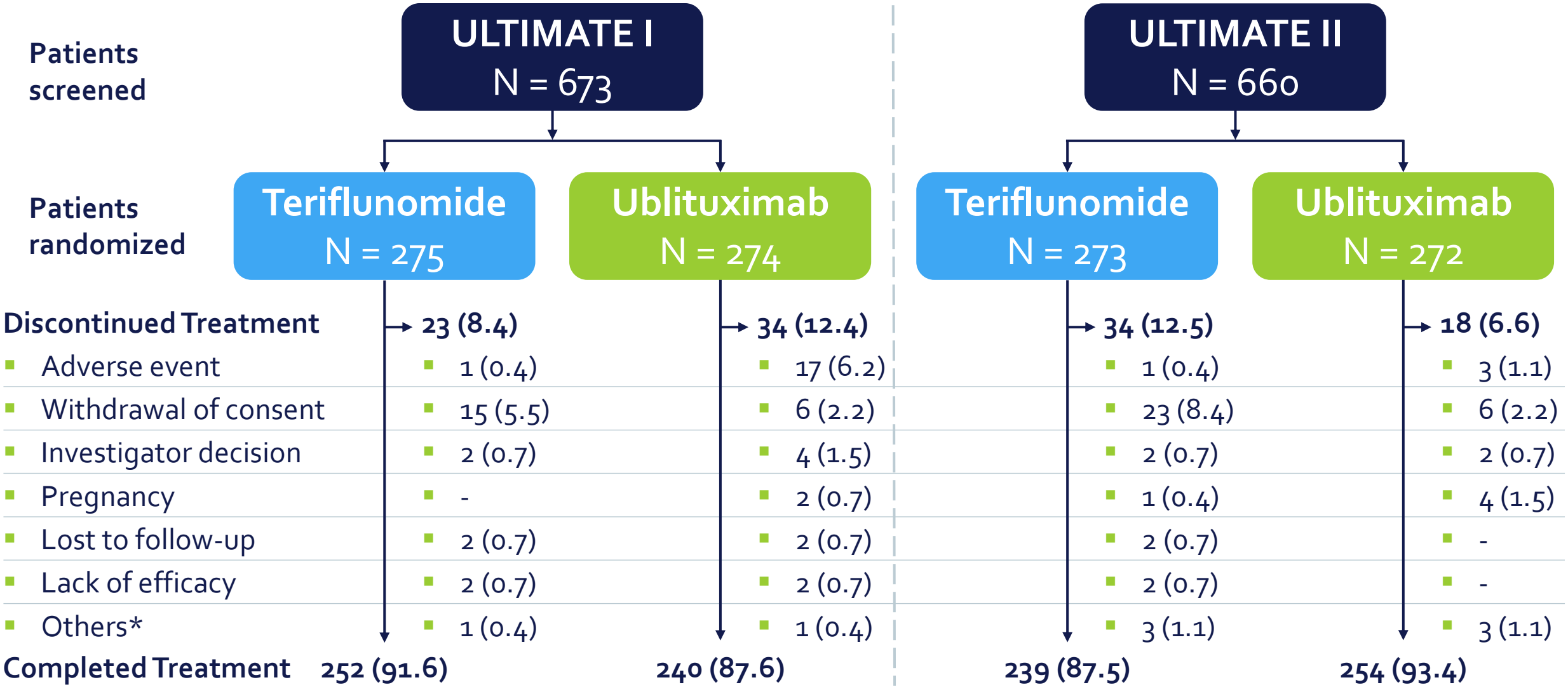
# ULTIMATE I & II: Study objective and key endpoints

**Objective**: To evaluate the efficacy and safety of ublituximab compared with teriflunomide in patients with relapsing multiple sclerosis

| | |
|---|---|
| **By individual study** | |
| **Primary endpoint** | Annualized relapse rate at 96 weeks<br>*(number of confirmed multiple sclerosis relapses in a year)* |
| **Key secondary endpoints** | ▪ Total number of Gd-enhancing T1 lesions by Week 96<br>▪ Total number of new or enlarging T2 hyperintense lesions by Week 96<br>▪ Proportion of subjects with NEDA from Week 24 to Week 96 |
| **Pre-specified pooled analysis** | |
| **Key secondary endpoints** | ▪ Time to CDP for at least 12 weeks |
| **Tertiary analyses** | ▪ Time to CDP for at least 24 weeks<br>▪ Time to CDI for at least 12 weeks<br>▪ Time to CDI for at least 24 weeks |

ARR: annualized relapse rate; CDP: confirmed disability progression; CDI: confirmed disability improvement; Gd: gadolinium; NEDA: no evidence of disease activity.

# Patient Disposition & Analysis Population




Data represented as n (%). *Others include: alternative treatment and COVID-19.

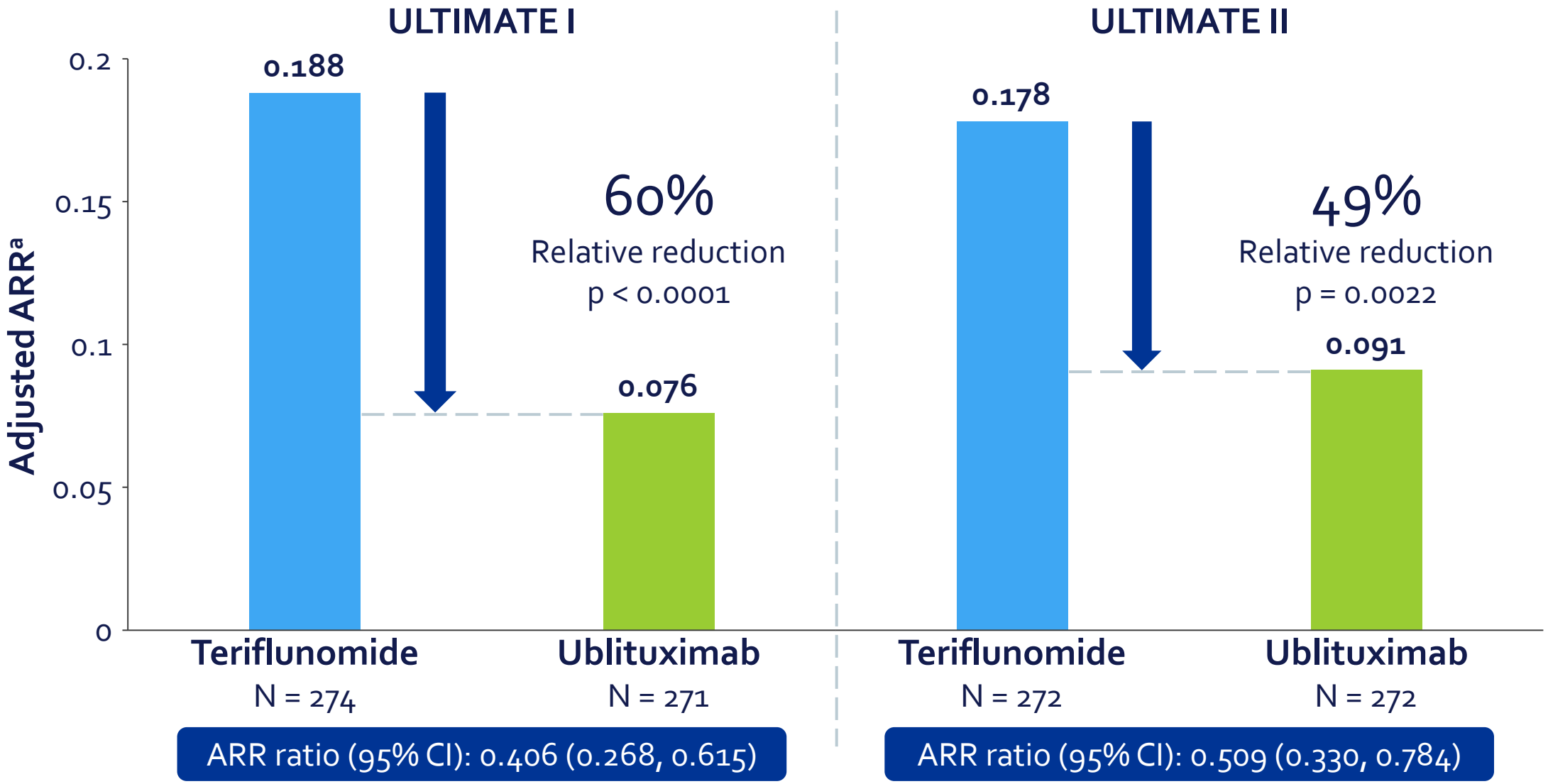
# Patient Demographics & Baseline Characteristics

*ULTIMATE I & II populations are consistent*

| Characteristic | ULTIMATE I (N = 545) | | ULTIMATE II (N = 544) | |
|---|---|---|---|---|
| *Mean ± standard deviation or n (%)* | Teriflunomide N = 274 | Ublituximab N = 271 | Teriflunomide N = 272 | Ublituximab N = 272 |
| **Age, years** | 37.0 ± 9.63 | 36.2 ± 8.24 | 36.2 ± 8.96 | 34.5 ± 8.76 |
| **Sex, Female, n (%)** | 179 (65.3) | 166 (61.3) | 176 (64.7) | 178 (65.4) |
| **Race, %** | | | | |
| Caucasian | 266 (97.1) | 264 (97.4) | 268 (98.5) | 269 (98.9) |
| African American | 6 (2.2) | 6 (2.2) | 3 (1.1) | 2 (0.7) |
| **Type of MS, n (%)** | | | | |
| Relapsing Remitting | 270 (98.5) | 264 (97.4) | 267 (98.2) | 268 (98.5) |
| Secondary Progressive | 4 (1.5) | 7 (2.6) | 5 (1.8) | 4 (1.5) |
| **Duration of MS since first symptoms, years** | 6.81 ± 5.89 | 7.52 ± 6.48 | 7.39 ± 6.26 | 7.31 ± 6.52 |
| **Previously untreated*, n (%)** | 162 (59.1) | 162 (59.8) | 155 (57.0) | 138 (50.7) |
| **Number of relapses in last 12 months** | 1.4 ± 0.67 | 1.3 ± 0.65 | 1.2 ± 0.65 | 1.3 ± 0.65 |
| **Number of relapses in last 24 months** | 2.0 ± 1.11 | 1.8 ± 0.96 | 1.8 ± 0.92 | 1.8 ± 0.94 |
| **EDSS at screening** | 2.89 ± 1.17 | 2.96 ± 1.21 | 2.96 ± 1.20 | 2.80 ± 1.31 |
| **T2 lesion volume, $cm^3$** | 14.9 ± 15.8 | 15.9 ± 16.0 | 15.7 ± 17.5 | 14.7 ± 13.5 |
| **Number of T2 lesions** | 60.4 ± 37.01 | 64.1 ± 38.59 | 64.0 ± 41.23 | 65.3 ± 41.23 |
| **Patients free of Gd+ T1 lesions, n (%)** | 156 (57.4) | 153 (56.7) | 135 (50.0) | 131 (48.2) |
| **Number of Gd+ T1 lesions at baseline** | 1.6 ± 3.67 | 2.3 ± 5.47 | 2.5 ± 5.47 | 2.6 ± 5.77 |

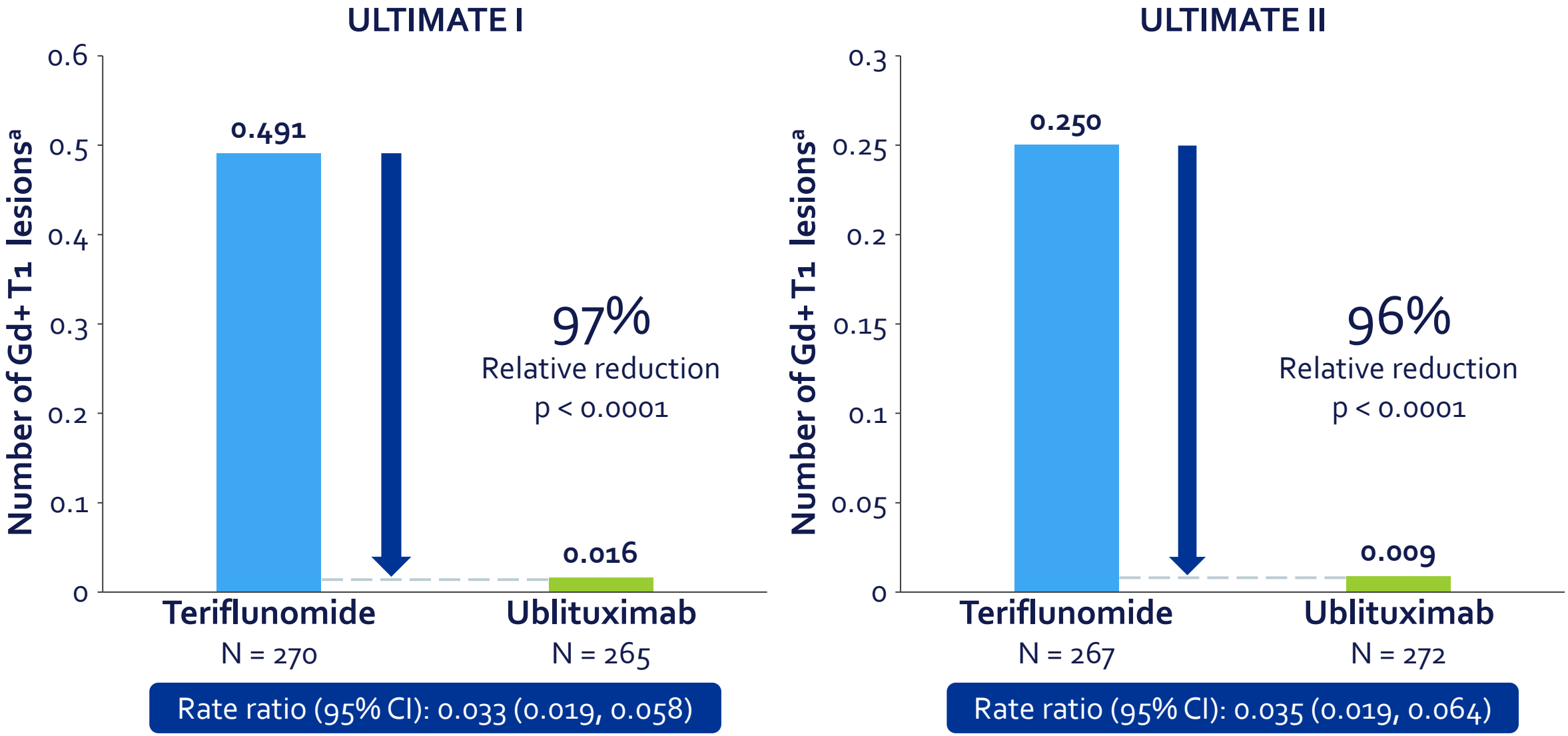
Modified Intent-to-Treat population. *Untreated with disease-modifying therapy in 5 years prior to study entry. DMT: disease-modifying therapy; EDSS: expanded disability status scale; Gd+: gadolinium-enhancing; MS: multiple sclerosis.

# Primary Endpoint: Annualized Relapse Rate (ARR)



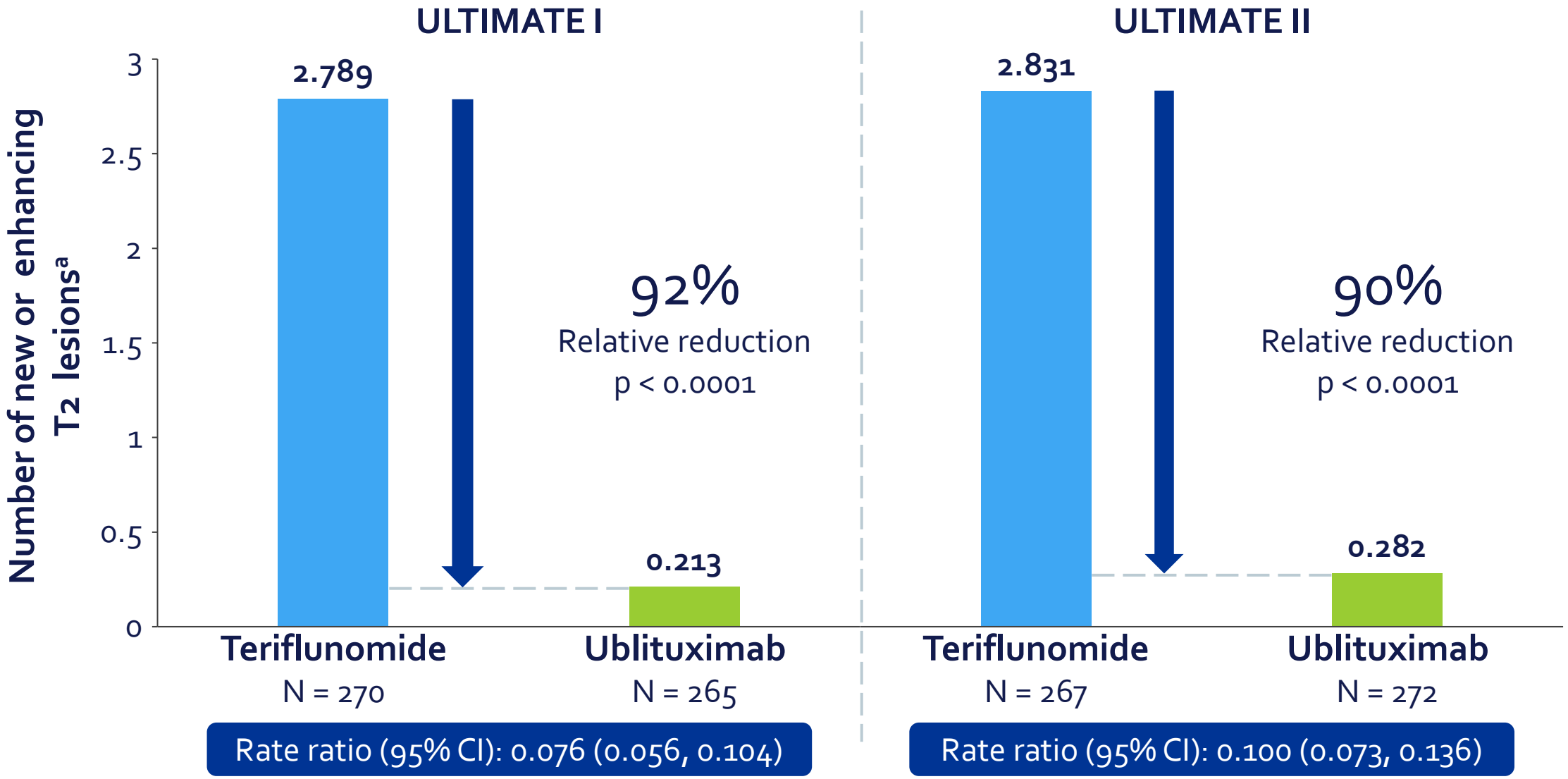

The modified Intention-to-Treat (mITT) population consists of all subjects in the ITT population who received at least one dose of study medication and had at least one baseline and post-baseline efficacy assessment. Based on negative binomial model (GEE) for the relapse count per subject with logarithmic link function, treatment, region, and baseline EDSS strata as covariates and log (years of treatment) as offset.
CI: confidence interval.

# MRI: Total Number of Gd+ T1 Lesions




The modified Intention-to-Treat MRI (mITT-MRI) population consists of all subjects in the ITT population who received at least one dose of study medication, had at least one baseline and post-baseline efficacy assessment, and had at least one baseline and post-baseline MRI efficacy assessment. Based on negative binomial model (GEE) with logarithmic link function, covariates treatment, region, baseline EDSS strata, baseline number of lesions (o/>=1) and an offset based on the log-transformed number of post-baseline MRI scans. MRI assessed by Independent Review

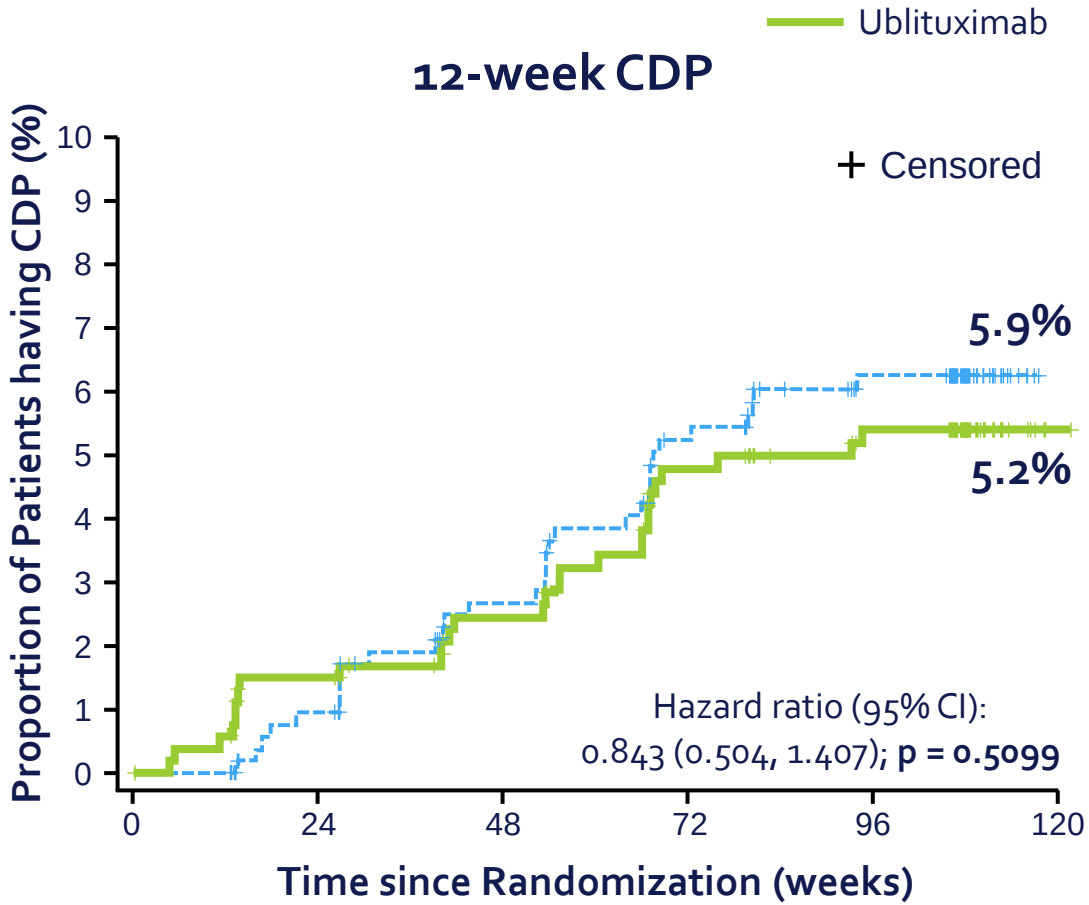
# MRI: Number of New or Enlarging T2 Lesions




The modified Intention-to-Treat MRI (mITT-MRI) population consists of all subjects in the ITT population who received at least one dose of study medication, had at least one baseline and post-baseline efficacy assessment, and had at least one baseline and post-baseline MRI efficacy assessment. Based on negative binomial model (GEE) with logarithmic link function, covariates treatment, region, baseline EDSS strata, baseline number of lesions (0/>=1) and an offset based on the log-transformed number of post-baseline MRI scans. MRI assessed by Independent Review

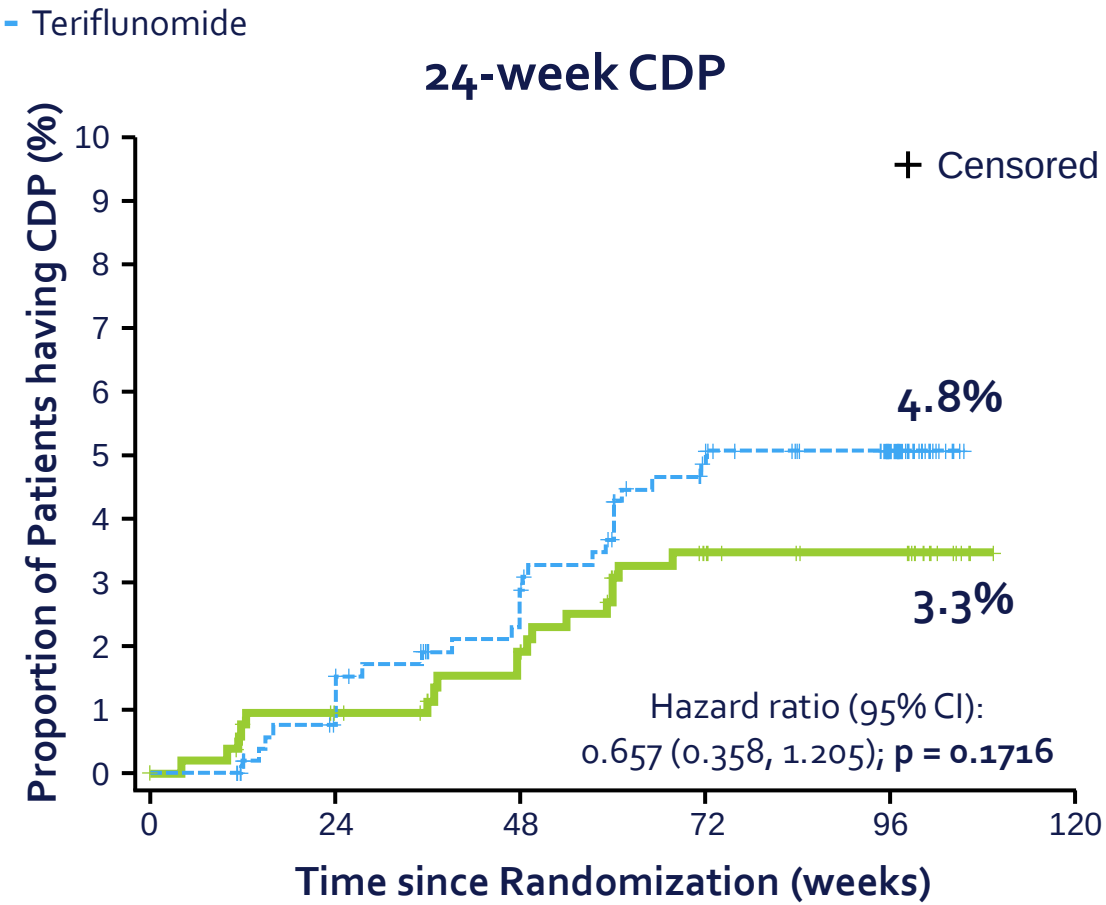
# Confirmed Disability Progression (CDP)

## Pre-specified pooled analysis




**N at risk**

| | | | | | |
|---|---|---|---|---|---|
| UTX | 543 | 522 | 506 | 481 | 345 |
| Teri | 546 | 522 | 497 | 470 | 325 |



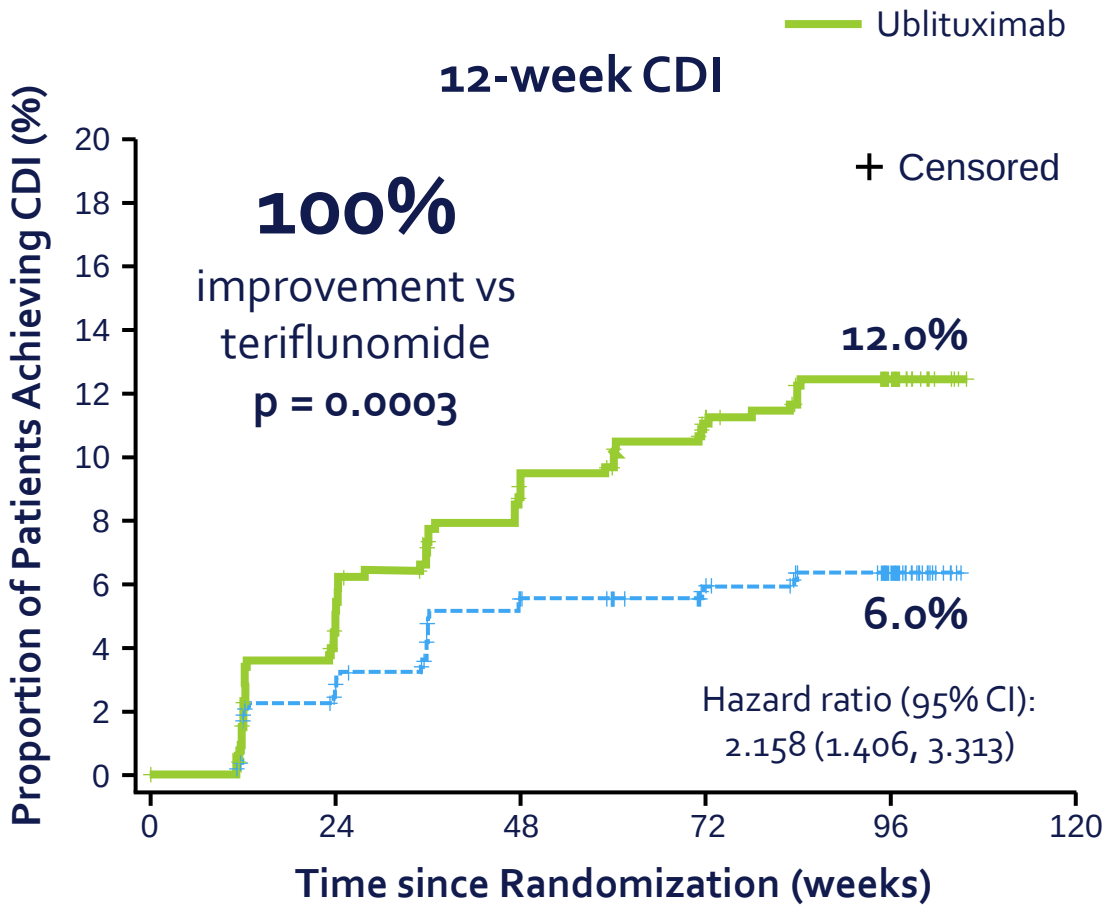

**N at risk**

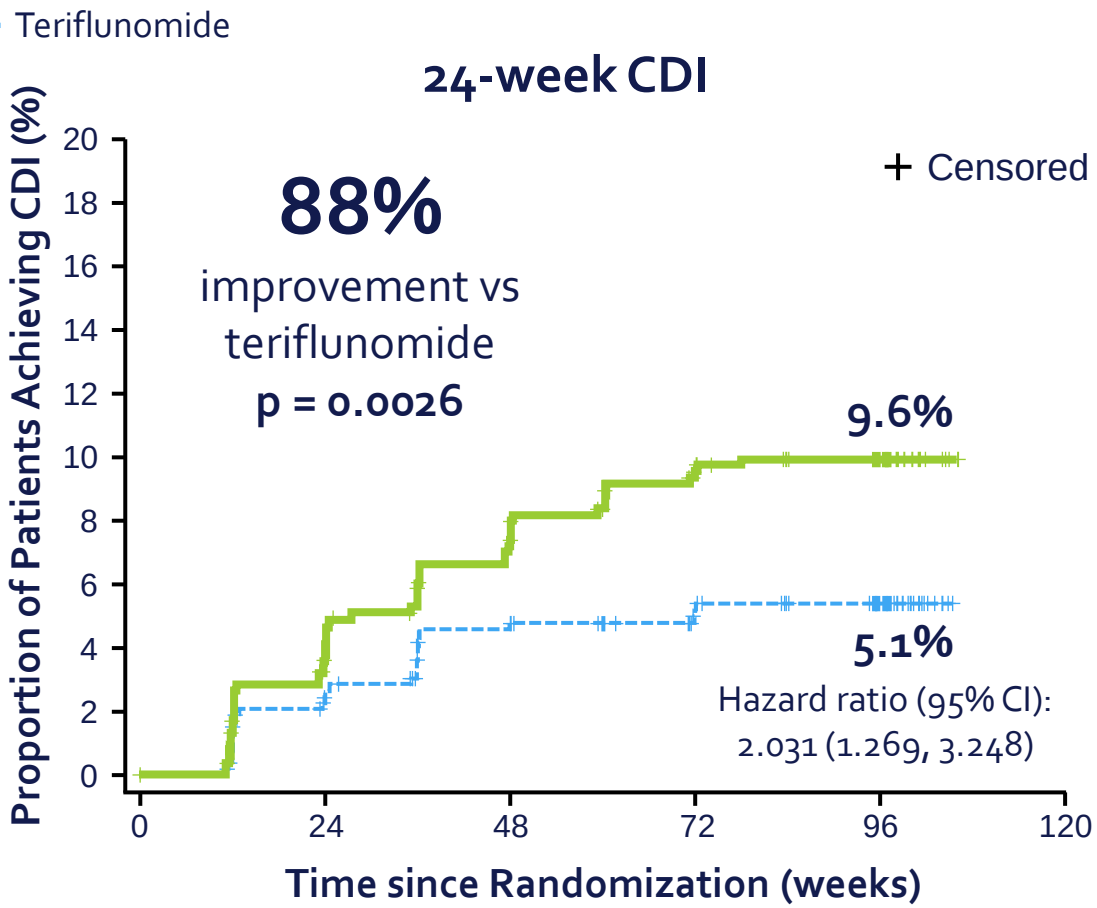
| | | | | | |
|---|---|---|---|---|---|
| UTX | 543 | 525 | 511 | 489 | 351 |
| Teri | 546 | 523 | 500 | 474 | 330 |

The modified Intention-to-Treat (mITT) population consists of all subjects in the ITT population who received at least one dose of study medication and had at least one baseline and post-baseline efficacy assessment. Hazard ratio is estimated using Cox regression model with treatment group as covariate stratified by region, baseline EDSS and study. P-value is from stratified log-rank test. UTX: ublituximab; Teri: teriflunomide

# Confirmed Disability Improvement (CDI)

## Pre-specified pooled tertiary analysis



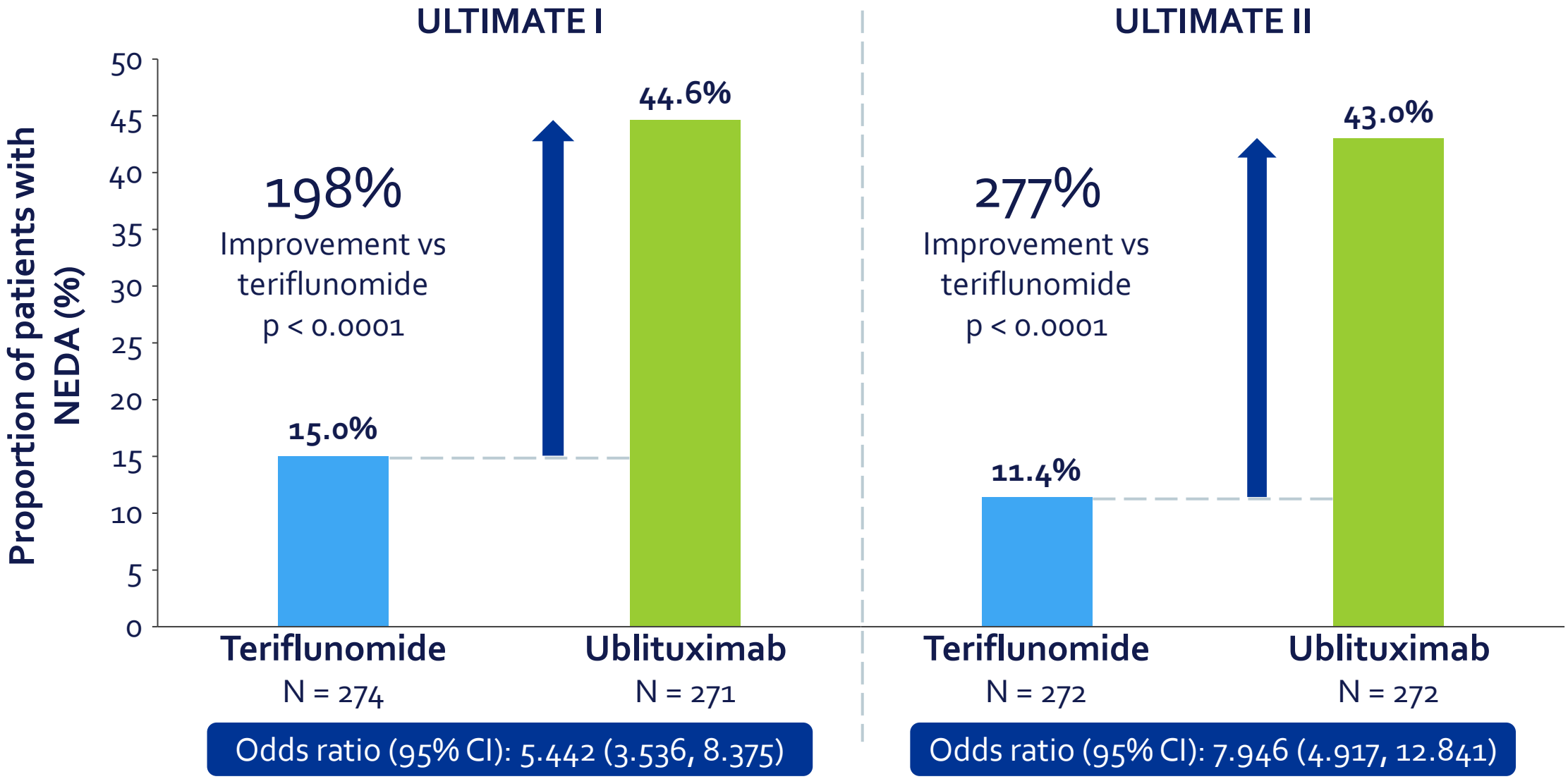




| N at risk | | | | | |
|---|---|---|---|---|---|
| UTX | 543 | 508 | 475 | 451 | 317 |
| Teri | 546 | 514 | 485 | 470 | 328 |

| N at risk | | | | | |
|---|---|---|---|---|---|
| UTX | 543 | 512 | 482 | 458 | 325 |
| Teri | 546 | 515 | 488 | 474 | 331 |

The modified Intention-to-Treat (mITT) population consists of all subjects in the ITT population who received at least one dose of study medication and had at least one baseline and post-baseline efficacy assessment. Hazard ratio is estimated using Cox regression model with treatment group as covariate stratified by region, baseline EDSS and study. P-value is from stratified log-rank test. UTX: ublituximab; Teri: teriflunomide

# No Evidence of Disease Activity (NEDA)




The modified Intention-to-Treat (mITT) population consists of all subjects in the ITT population who received at least one dose of study medication and had at least one baseline and post-baseline efficacy assessment. Logistic regression model with covariates treatment, region, baseline EDSS strata and log transformed baseline MRI counts ($T_1$ unenhancing, $T_2$, Gad enhancing).

# Adverse Events

| **Most common AEs, n (%)**<br>*≥5% in any treatment group* | **Teriflunomide**<br>N=548 | **Ublituximab**<br>N=545 |
|---|---|---|
| **Any AE** | **486 (88.7)** | **483 (88.6)** |
| IRR | 67 (12.2) | 260 (47.7) |
| Headache | 138 (25.2) | 165 (30.3) |
| Nasopharyngitis | 96 (17.5) | 97 (17.8) |
| Lymphopenia | 5 (0.9) | 51 (9.4) |
| Back pain | 53 (9.7) | 48 (8.8) |
| Respiratory tract infection viral | 31 (5.7) | 41 (7.5) |
| Respiratory tract infection | 38 (6.9) | 40 (7.3) |
| Upper respiratory tract infection | 33 (6.0) | 39 (7.2) |
| Diarrhea | 53 (9.7) | 36 (6.6) |
| Lymphocyte count decreased | 9 (1.6) | 34 (6.2) |
| Abdominal pain | 17 (3.1) | 32 (5.9) |
| Pharyngitis | 11 (2.0) | 31 (5.7) |
| Pyrexia | 23 (4.2) | 30 (5.5) |
| Insomnia | 16 (2.9) | 28 (5.1) |
| Nausea | 26 (4.7) | 28 (5.1) |
| Hypertension | 35 (6.4) | 19 (3.5) |
| Alopecia | 84 (15.3) | 18 (3.3) |

AE: adverse event. IRR: Infusion-related reaction. IRR includes AEs designated as IRR in the CRF. AEs included within IRR are not included in individual preferred terms

# Serious Adverse Events

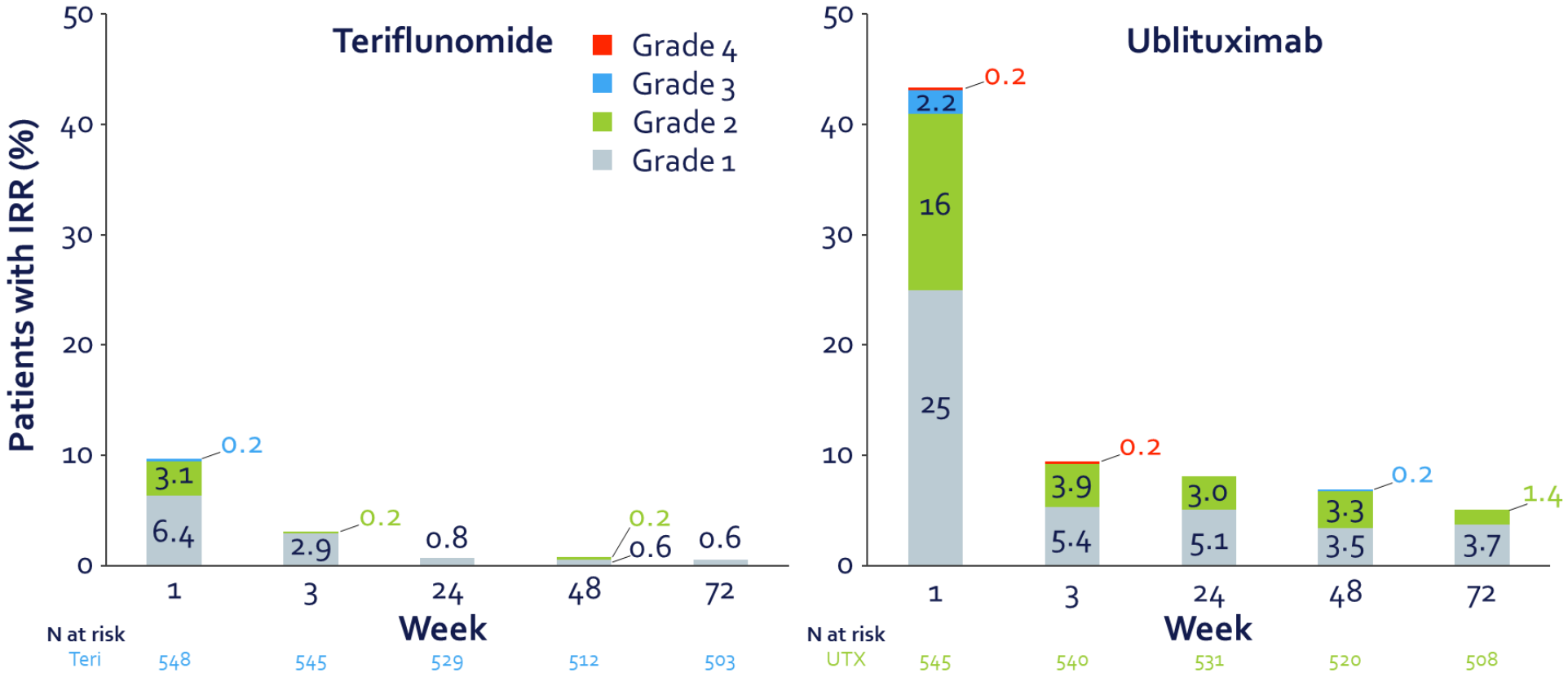
| SAEs, n (%) | Teriflunomide N = 548 | Ublituximab N = 545 |
|---|---|---|
| **Any serious AEs** | 34 (6.2) | 52 (9.5) |
| | | |
| **Most common SAEs by SOC**<br>*≥1% in any treatment group* | | |
| Infections and infestations | 14 (2.6) | 22 (4.0) |
| Nervous system disorders | 7 (1.3) | 5 (0.9) |

- Three total malignancies were reported
  - 2 ublituximab (endometrial, uterine) versus teriflunomide 1 (tongue)
- Three total deaths occurred
  - Ublituximab: pneumonia, encephalitis (post-measles), salpingitis
  - 1 death was deemed possibly related to treatment (pneumonia)
- No cases of progressive multifocal leukoencephalopathy (PML)

SAE: serious adverse event; SOC: system organ class

# Infusion Related Reactions by Dose & Severity

*Most IRRs were mild to moderate & decreased in frequency over time*




- **IRRs were most frequent on the 1st dose**
- **Discontinuations due to IRRs were rare**

IRR: infusion related reaction; Teri: teriflunomide; UTX: ublituximab.

# AAN Poster Conclusions

- In the Phase III ULTIMATE I & II studies ublituximab significantly reduced ARR and MRI parameters, compared with teriflunomide
- A very low rate of disability progression was observed with ublituximab, with >94% of patients showing no 12-week CDP, and >96% of patients showing no 24-week CDP, although neither was statistically different from teriflunomide
- Ublituximab increased the proportion of patients with 12-week confirmed disability improvement (CDI) and 24-week CDI
- A significantly higher percentage of patients treated with ublituximab compared with teriflunomide achieved NEDA
- A favorable safety and tolerability profile with no unexpected safety signals

**In ULTIMATE I & ULTIMATE II, ublituximab, a one-hour infusion, demonstrated robust efficacy and a favorable safety profile that benefited RMS patients**

# MEET THE KOLs

- **INTRODUCTIONS**
- **Lawrence Steinman, MD**
  - Zimmermann Professor of Neurology & Neurological Sciences, and Pediatrics
  - Stanford University
- **Edward J. Fox, MD, PhD**
  - Director, Multiple Sclerosis Clinic of Central Texas
  - Central Texas Neurology Consultants, PA
- **Enrique Alvarez, MD, PhD**
  - Assistant Medical Director, Neurology
  - University of Colorado Medicine

# DISCUSSION TOPICS

- How has the MS treatment landscape evolved over the past 5 years?
- In your view, what is the current role of CD20's in the treatment landscape? How might this change moving forward?
- What has been your experience with patient preference regarding sub cutaneous CD20 v IV? When selecting IV treatment, how do you factor in infusion time?

# Q&A SESSION

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# CLOSING REMARKS

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## THANK YOU!

## NASDAQ: TGTX