Emerging Therapies

Multiple Sclerosis Research Update

CAN DO MULTIPLE SCLEROSIS

WEBINAR WEDNESDAYS

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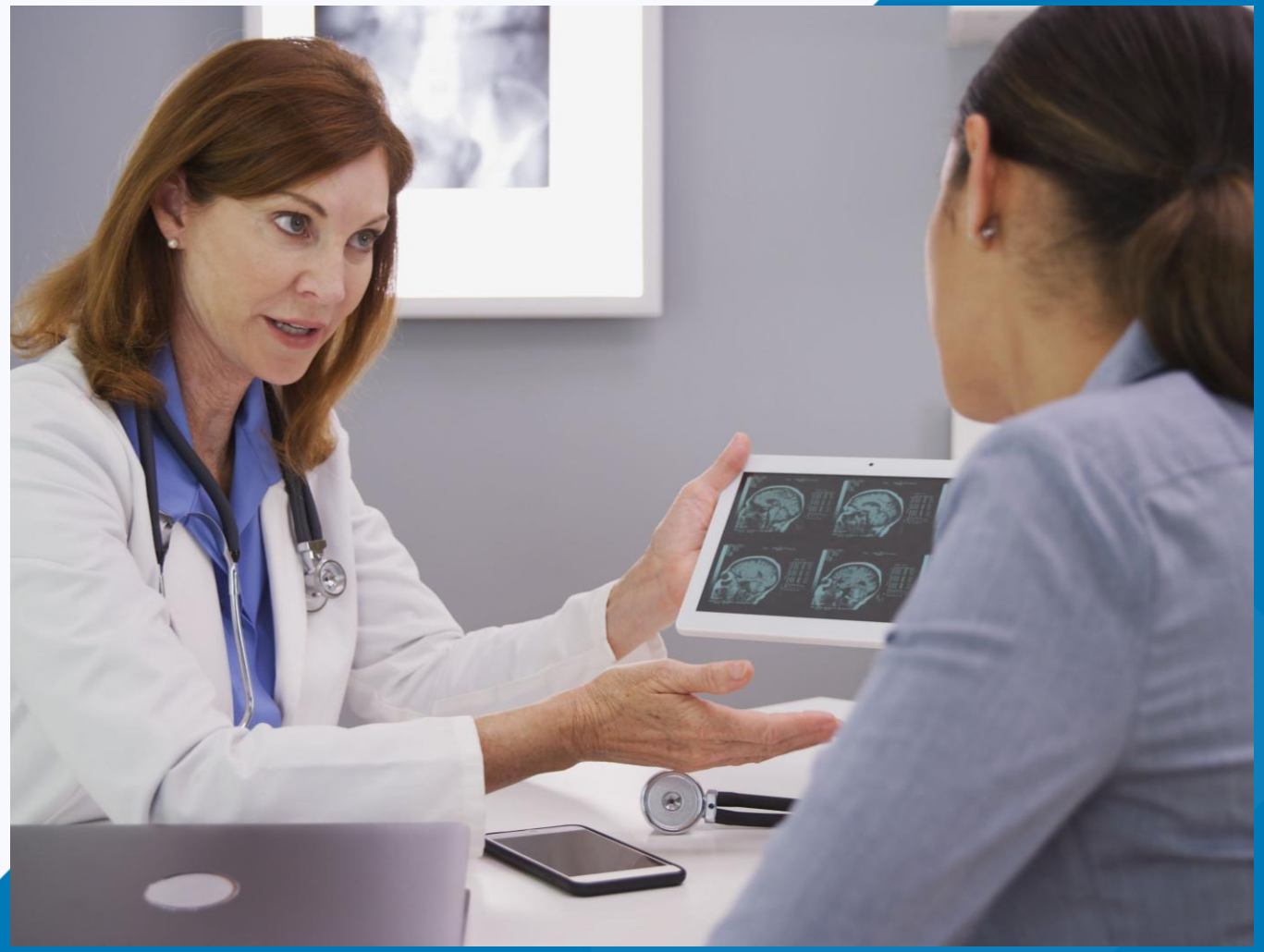
MONTH PROGRAMS

Tuesday, December 16
NEWLY DIAGNOSED MEETUP

Wednesday, January 14
WEBINAR
What the MS Disease Course Definitions Mean for You

Tuesday, January 27
YOUR QUESTIONS ANSWERED
Understanding MS Disease Courses



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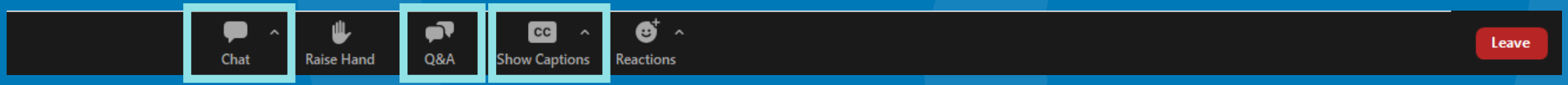
How to Ask Questions During the Webinar

Type in your questions using the Questions Box



Provide comments and engage with the speakers and audience using the **Chat Box**

NEW! Closed captioning

YOUR SPEAKERS

Kristin Galetta

Neurologist

California

Lauren Tardo

Neurologist

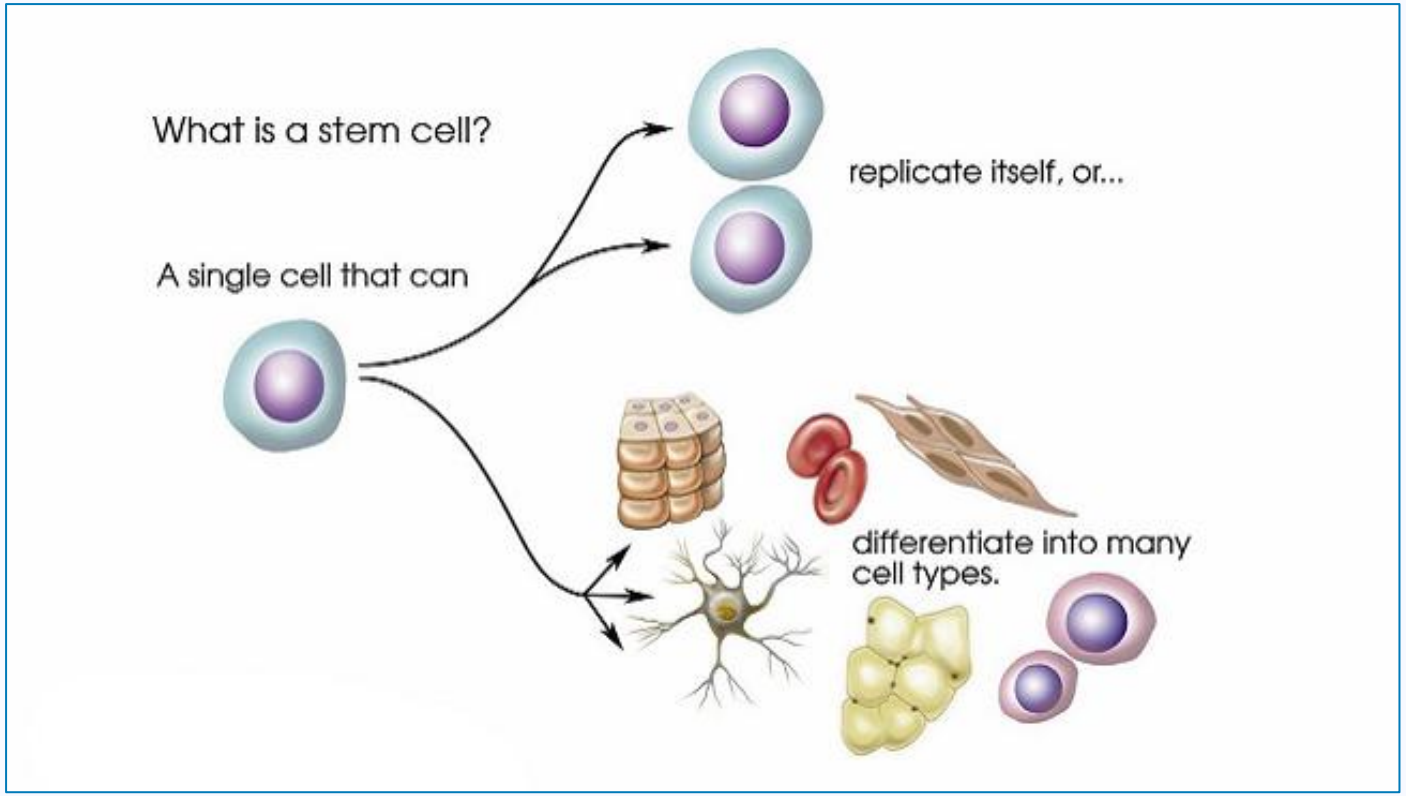
Texas

Learning Objectives

1. Stem Cell Therapies
2. Emerging Treatment Options
3. BTK Inhibitors for MS

Stem Cell Therapies

- Stem cells can differentiate into many different cell types
- Can serve many functions in MS
  - Reset the immune system
  - Restoration of damaged tissue



The National Academies of Science, Engineering, and Medicine

Types of Stem Cells

Mesenchymal

- Fat tissue
- Umbilical cord tissue
- Bone marrow

DO NOT TURN INTO OTHER TYPES OF CELLS

Hematopoietic

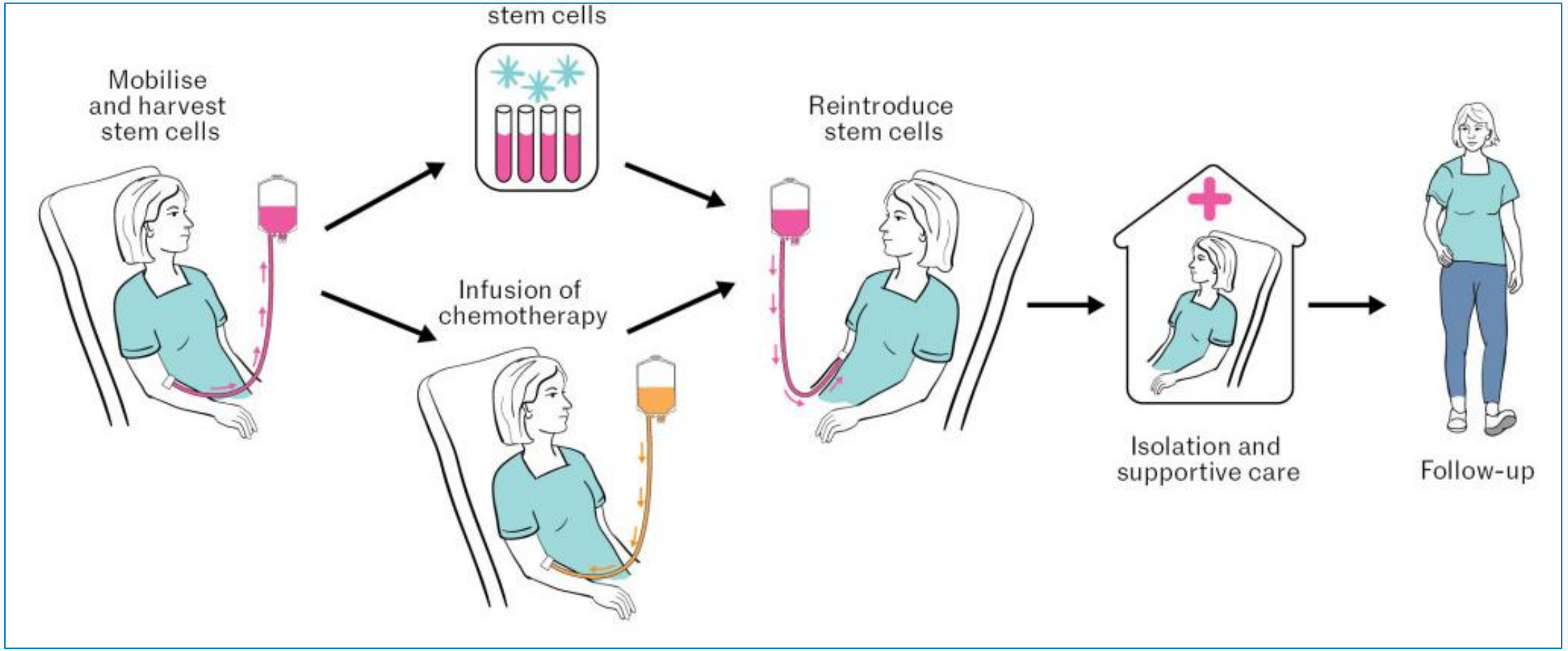
- Bone marrow
- Blood

Hematopoietic

- Resets the immune system
- Potential long-term remission for MS
- One time procedure
- Typically reserved for highly active disease
- Studies ongoing

Nabizadeh F, Pirahesh K, Rafiei N, Afrashteh F, Ahmadabad MA, Zabeti A, Mirmosayyeb O. Autologous Hematopoietic Stem-Cell Transplantation in Multiple Sclerosis: A Systematic Review and Meta-Analysis. Neurol Ther. 2022 Dec;11(4):1553-1569. doi: 10.1007/s40120-022-00389-x. Epub 2022 Jul 28. PMID: 35902484; PMCID: PMC9333355.

Hematopoietic

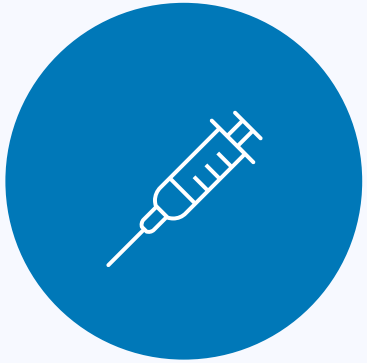


Nygaard GO, Holmøy T. Norwegian health service should offer stem cell therapy for multiple sclerosis. Tidsskr Nor Laegeforen. 2024 Feb 7;144(2). English, Norwegian. doi: 10.4045/tidsskr.23.0770. PMID: 38349100.

Risks

Infection

Infertility



Chemotherapy

Nausea, Hair Loss, Fatigue

Mesenchymal

May be beneficial as an adjunct for neuroprotection and slowing progression

Less invasive than hematopoietic

Less risk associated with this process

More information is needed, considered experimental and caution should be advised

Other Emerging Therapies

Numerous On The Horizon

- Frexalimab
- Forulumab
- CNM-AU8
- Biosimilars

Clinical Trial Phases

Phase	Focus	Participants
1 	Safety and dose testing Often in healthy volunteers	Small group
2 	Effectiveness and side effects	Slightly larger group
3 	Compare new vs existing treatment	Larger group
4 	Long-term follow-up after approval	Similar group followed over time

Frexalimab

- Monoclonal antibody targeting CD40-Ligand
  - Blocks interactions between different types of immune cells
- Given **subcutaneously**
- **Relapsing remitting** and **secondary progressive MS**
- Promising phase 2 results
- Phase 3 trial recruiting now

Vermersch P, Granziera C, Mao-Draayer Y, Cutter G, Kalbus O, Staikov I, Dufek M, Saubadu S, Bejuit R, Truffinet P, Djukic B, Wallstroem E, Giovannoni G; Frexalimab Phase 2 Trial Group. Inhibition of CD40L with Frexalimab in Multiple Sclerosis. N Engl J Med. 2024 Feb 15;390(7):589-600. doi: 10.1056/NEJMoa2309439. PMID: 38354138.

Foralumab

Foralumab

- Targets T-cells (CD3)
- Given intranasally
- For **non-active secondary progressive MS**
- Ongoing Phase 2 trial

Fast track designation by the FDA

Chitnis T, Singhal T, Zurawski J, Saraceno TJ, Gopalakrishnan N, Cain L, LaBarre B, King D, Bergmark RW, Maxfield AZ, Cicero S, Pan H, Dubey S, Vaquerano S, Hansel C, Healy B, Saxena S, Lokhande H, Baharnoori M, Madill E, Sheth M, Rodin R, Ye J, Clementi N, Clementi WA, Weiner HL. Nasal foralumab treatment of PIRA induces regulatory immunity, dampens microglial activation and stabilizes clinical progression in non-active secondary progressive MS. medRxiv [Preprint]. 2025 May 3:2025.04.30.25326602. doi: 10.1101/2025.04.30.25326602. PMID: 40657312; PMCID: PMC12248159.

CNM-AU8

- Gold nano-particles
- Oral suspension
- Does not interact with the immune system
- **Remyelination** and **neuroprotection**
- **Promising Phase 2 trial completed**

Barnett M, Beadnall H, Klistorner A, et al. VISIONARY-MS top-line results: a Phase 2, randomized, double-blind, parallel group, placebo-controlled study to assess the safety and efficacy of CNM-Au8, a catalytically active gold nanocrystal suspension in relapsing multiple sclerosis (PL5.005). *Neurology*. 2023;100:(17_supplement_2) **https://doi.org/10.1212/WNL.0000000000203858**.

Biosimilars

- Medication that is similar to a FDA approved medication
  - Same mechanism, dosing and route of administration
  - Similar effectiveness
  - Similar safety signals
- Typically cheaper
- Currently available – anti-CD20 (rituximab biosimilar), natalizumab biosimilar

BTK Inhibitors

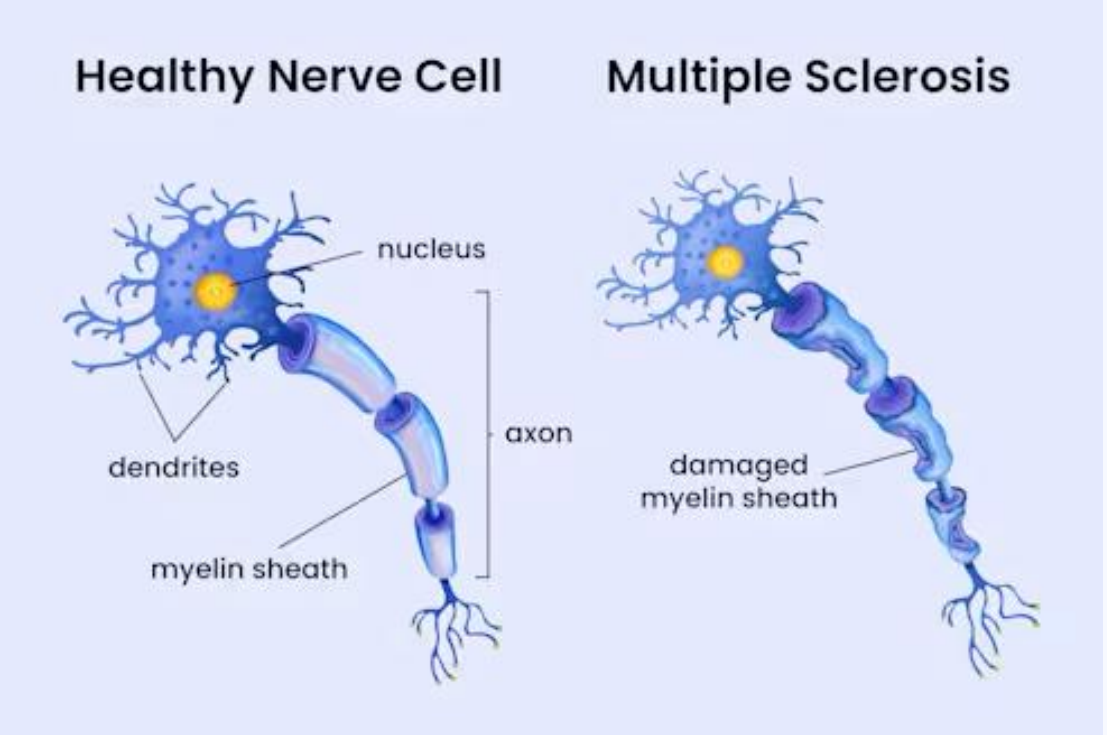
- What are BTK inhibitors?
- How would they work for MS?
- Why are there so many different types?
- How do they compare to B cell therapy?
- Where are we now with the BTK inhibitors for MS

BTK Inhibitors Background

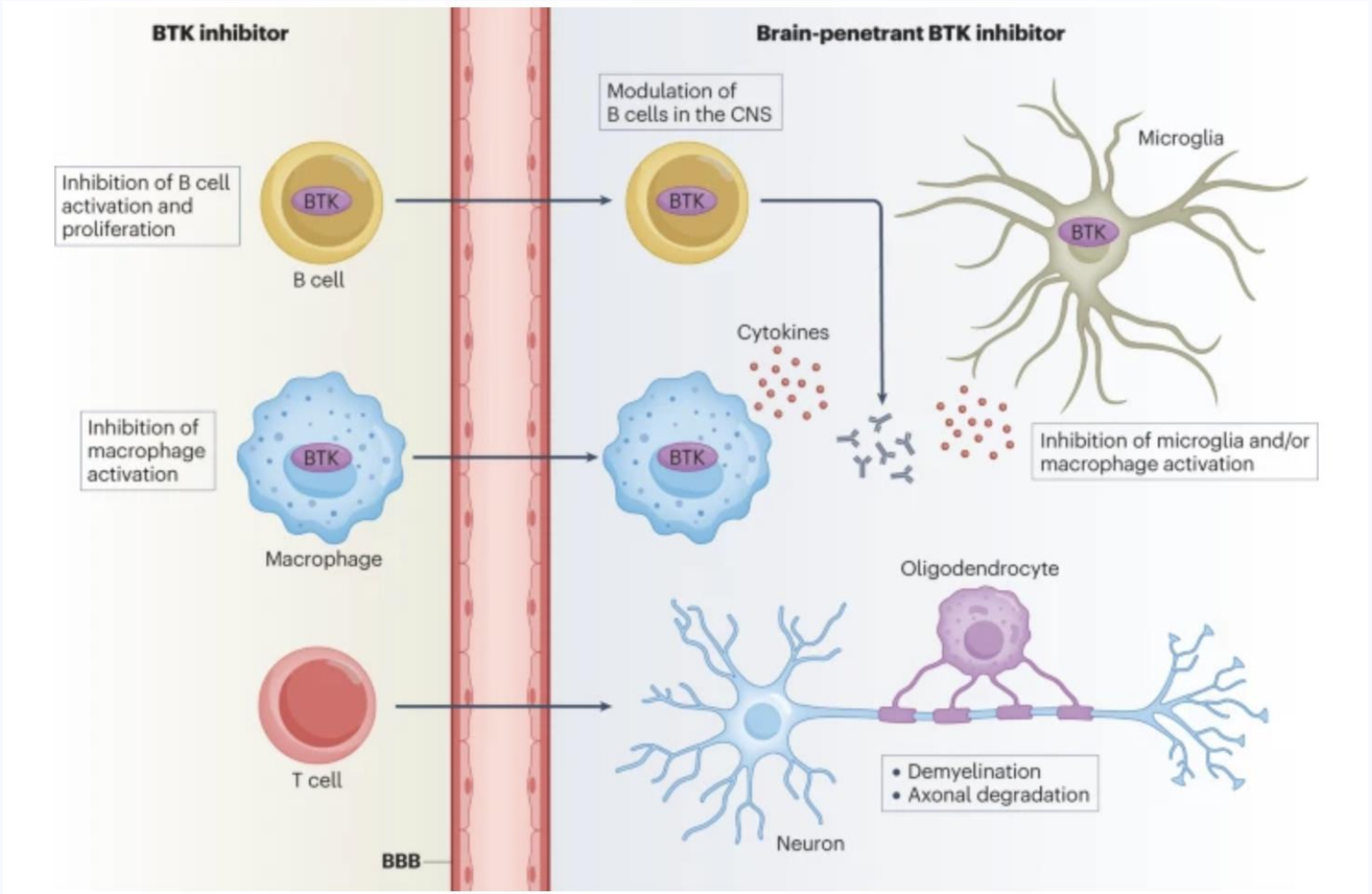
- BTK= Bruton Tyrosine Kinase
- BTKs are protein that activates certain immune cells (B cells and myeloid cells)
- BTK inhibitors are pills stop those immune cells from being activated
- These medications are already used in cancer and other autoimmune disease

BTK Inhibitors For MS

- MS involves B cells and innate immune cells mistakenly attacking myelin
- BTK is important in both cell types so blocking BTK might reduce inflammation



BTKs Work In The Blood But Also Get Into The Immune System Near The Brain

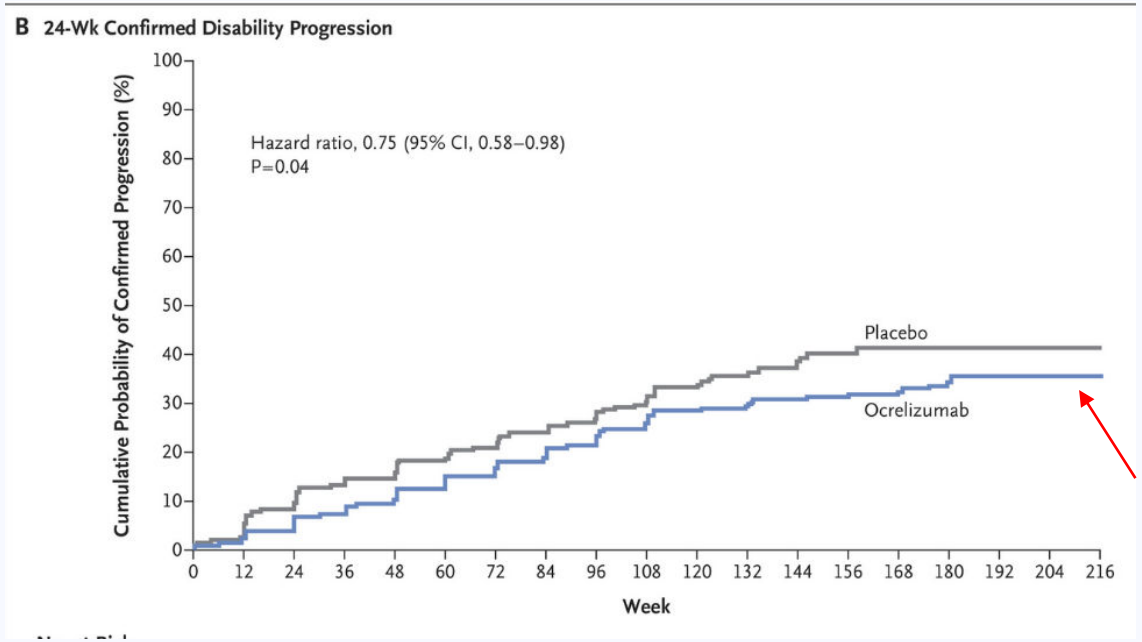


Relapsing disease= driven by B and T cells

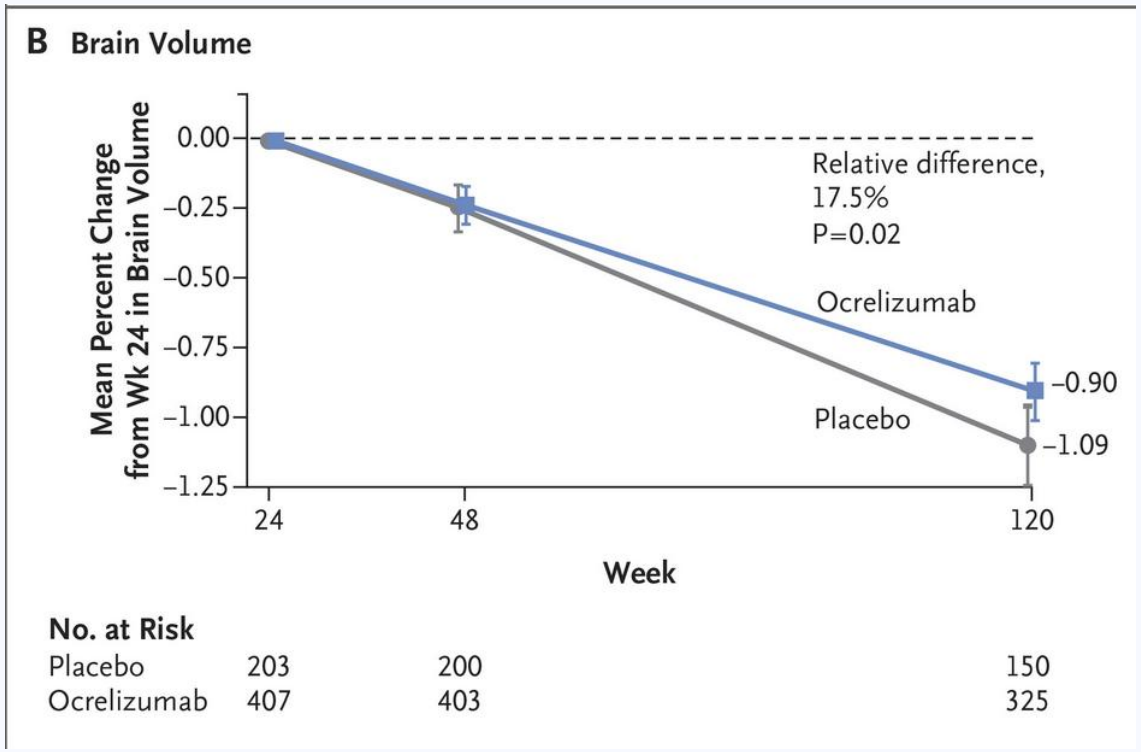
Progressive disease= B cells in the CNS and microglial

- Fighting inflammation in the privileged site of the CNS may be the key to reducing progression
- Many therapies show promise

For context- Ocrelizumab For PPMS



Less progression with Ocrelizumab at 24 weeks



Less brain volume loss

Comparing B Cell Therapy To BTK Inhibitors

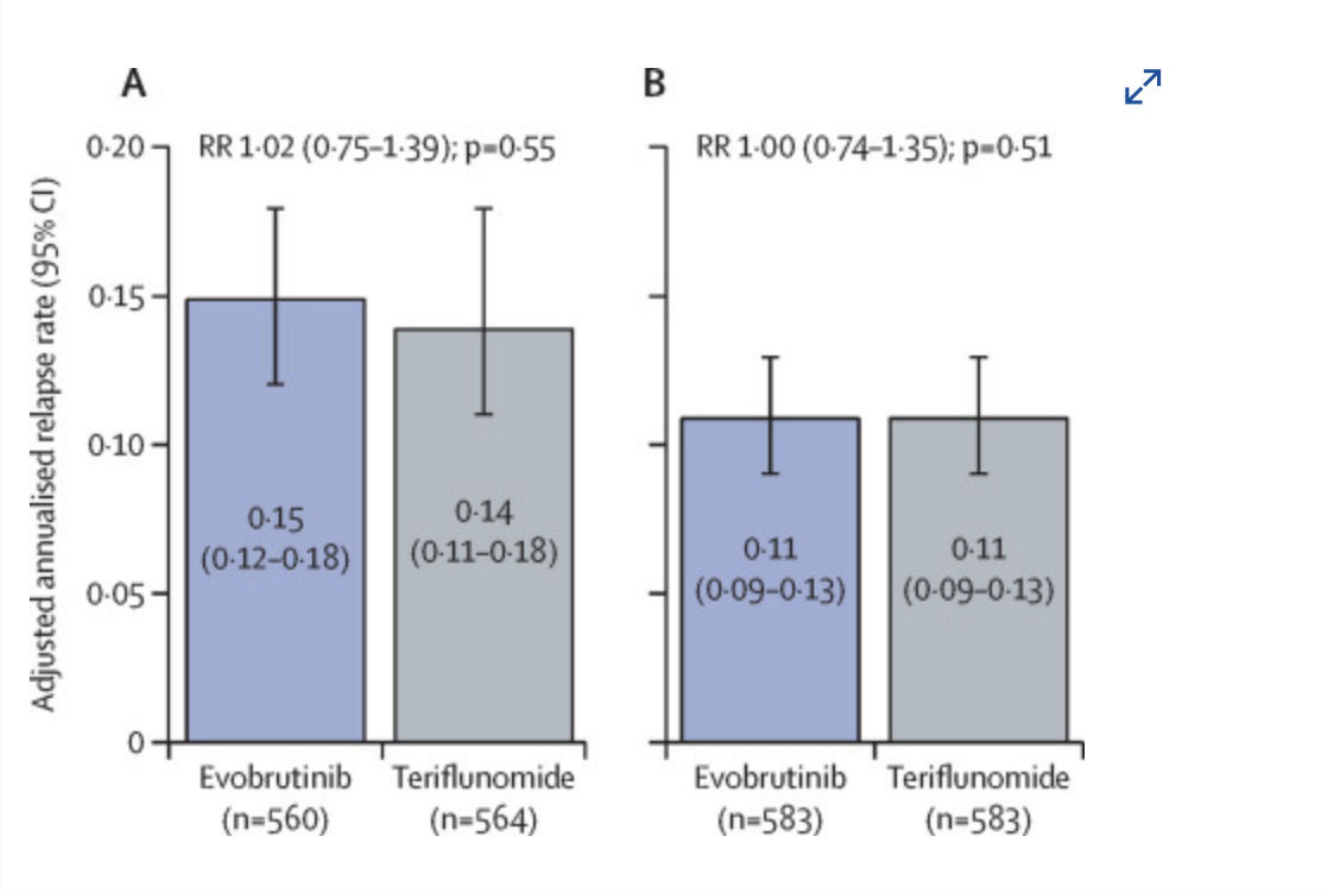
Feature	BTK inhibitors	Anti-CD 20
Form	Oral pill	Injection or infusion
Action	Dampens B cell and innate activity	Depletes B cells
Duration	Shorter	Longer lasting
Brain access	Crosses into CNS	Minimal concentrations in the brain
Trial state	Awaiting FDA approval for some, ongoing studies	FDA approved

BTK Inhibitors

BTK in MS	Status	Comment
Evobrutnib	Terminated	Did not meet primary endpoint= not superior to teriflunomide
Tolebrutinib	Phase 3 completed for RRMS and SPMS, Phase 3 ongoing for PPMS	FDA reviewing
Fenebrutnib	Reported outcomes in November!	
Remibrutnib, Orelebrunib	Phase 2	

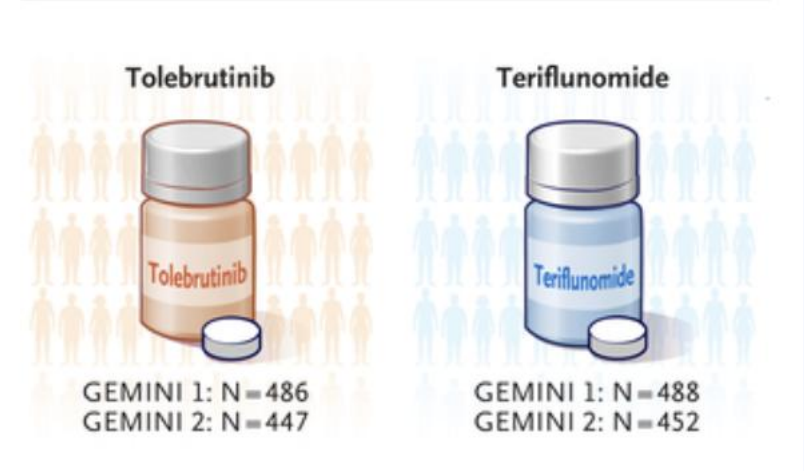
Evobrutinib

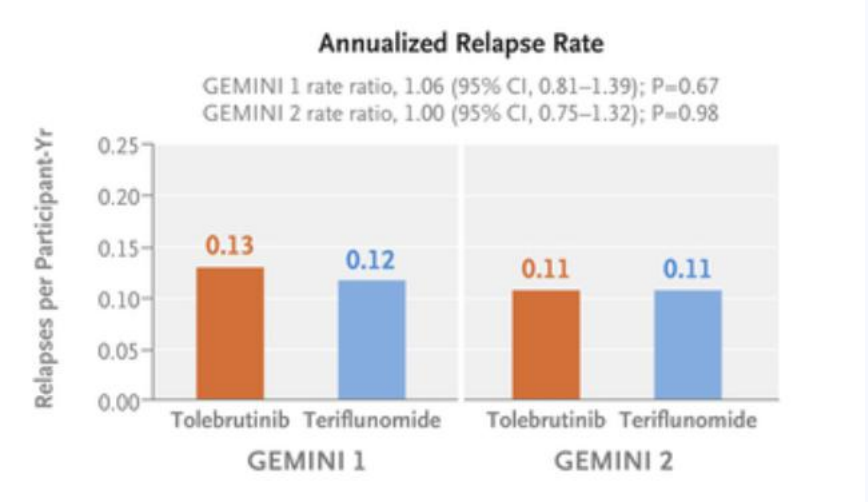
Evobrutinib was not better than Teriflunomide but it had more side effects most importantly in Liver enzymes



Tolebrutinib For Relapsing Multiple Sclerosis (GEMINI Trials)

- ~1800 people with relapsing MS were in these two trial
- ~ ½ got Teriflunomide and ½ got Tolebrutinib
- Annualized relapse rates were about the same
- BUT there was some benefit in progression

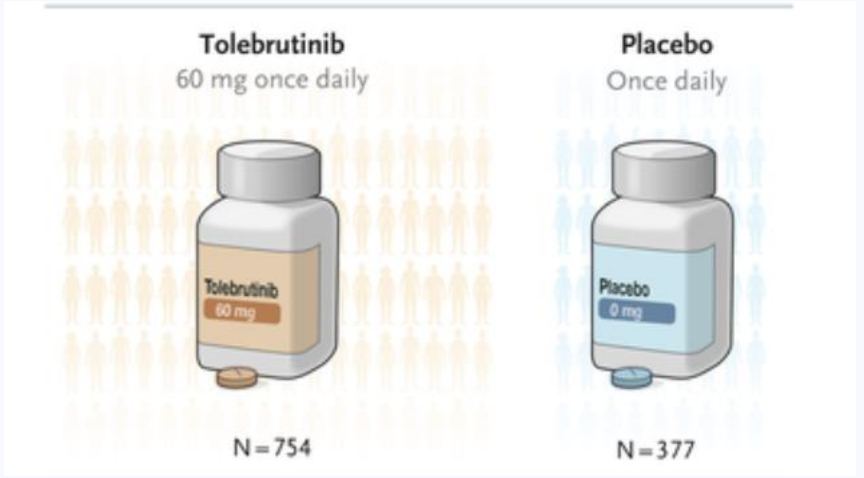


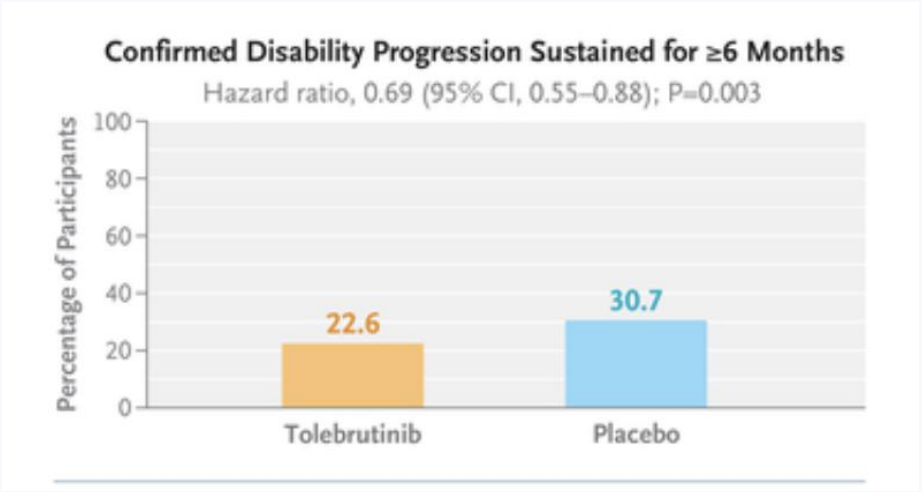


Tolebrutinib For Progressive MS (Hercules Trials)

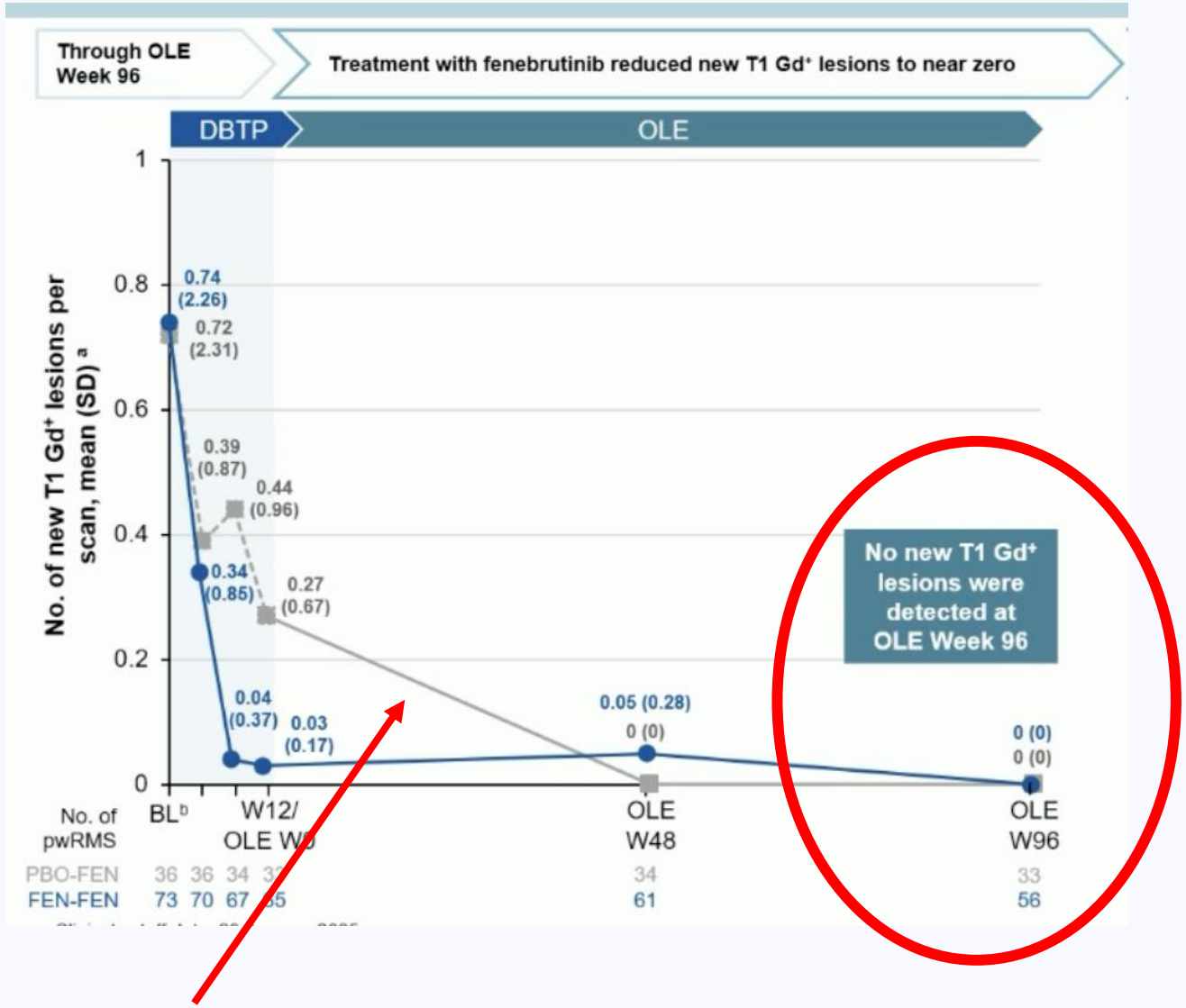
> 1000 patients with documented progression in prior 12 months no relapse in prior 24 months

- Delayed 6month confirmed disability progression: 31% decrease favoring Tolebrutinib
- 6month disability improvement: more on tolebrutinib





Fenebrutnib Phase 2(FENopta)- Relapsing MS

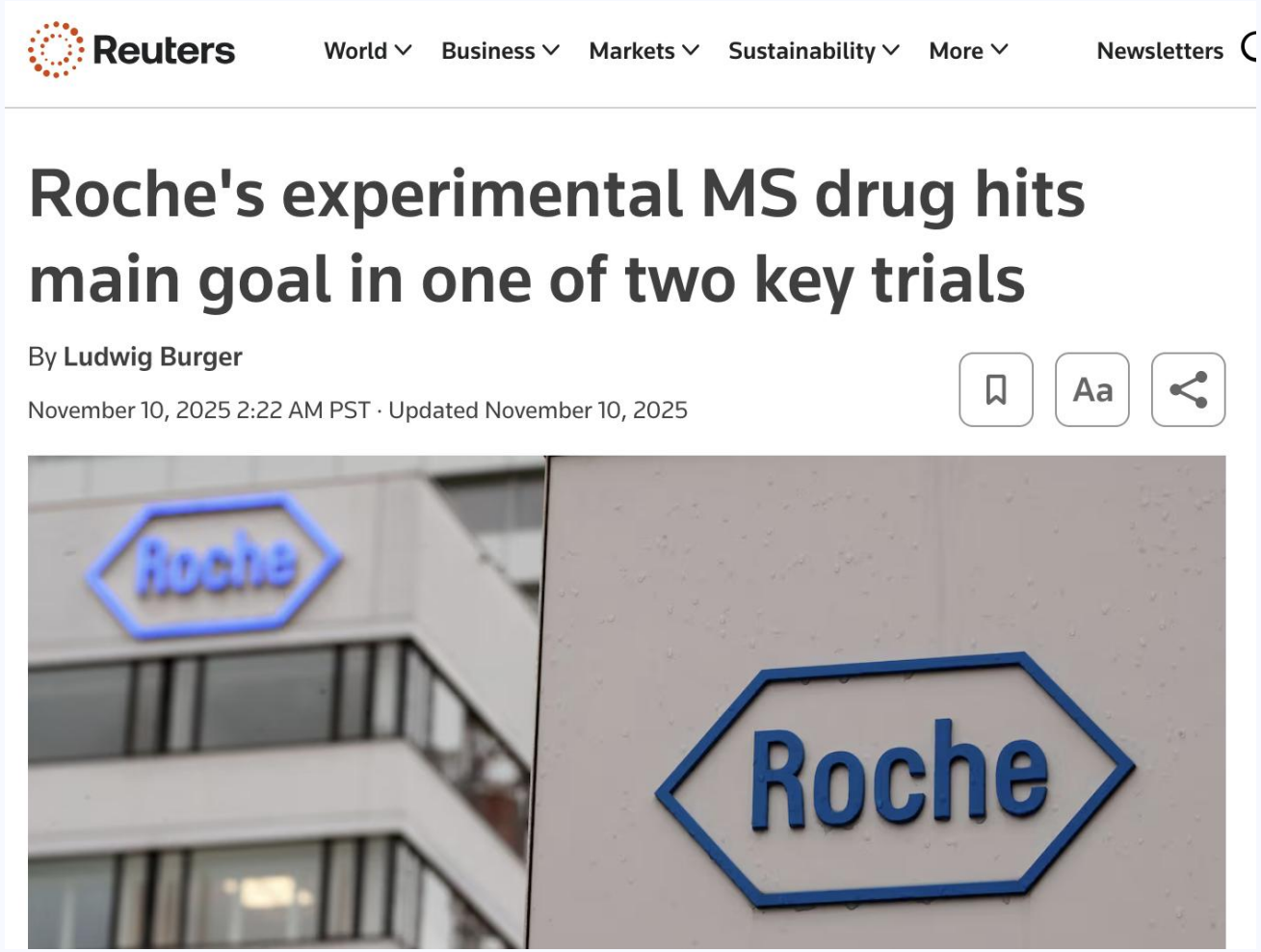


Near complete suppression of enhancing and T2 flair lesions

EDSS remained stable

- Almost 80 percent of people had NO disease activity at week 96
- ARR of 0.06
- Transient reversible hepatic enzyme elevations

Fenebrutnib



Reuters World Business Markets Sustainability More Newsletters

Roche's experimental MS drug hits main goal in one of two key trials

By **Ludwig Burger**

November 10, 2025 2:22 AM PST · Updated November 10, 2025

You may have seen the news last month!

Safety: Liver injury

No one really knows why liver injury occurs

Usually occurs within the first 3 months

Likely will need weekly labs for 3 months

However seems to be reversible with stopping the drug

Take Aways

- While in the same class, individual BTKs seem different
- Some promising results with Fenebrutinib for relapsing disease
- Whole class may be good at slowing progression
- Will need to watch liver function tests
- Will likely get FDA approval in the next months to year

Q+A

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What the New MS Disease Course Definitions Mean for You

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