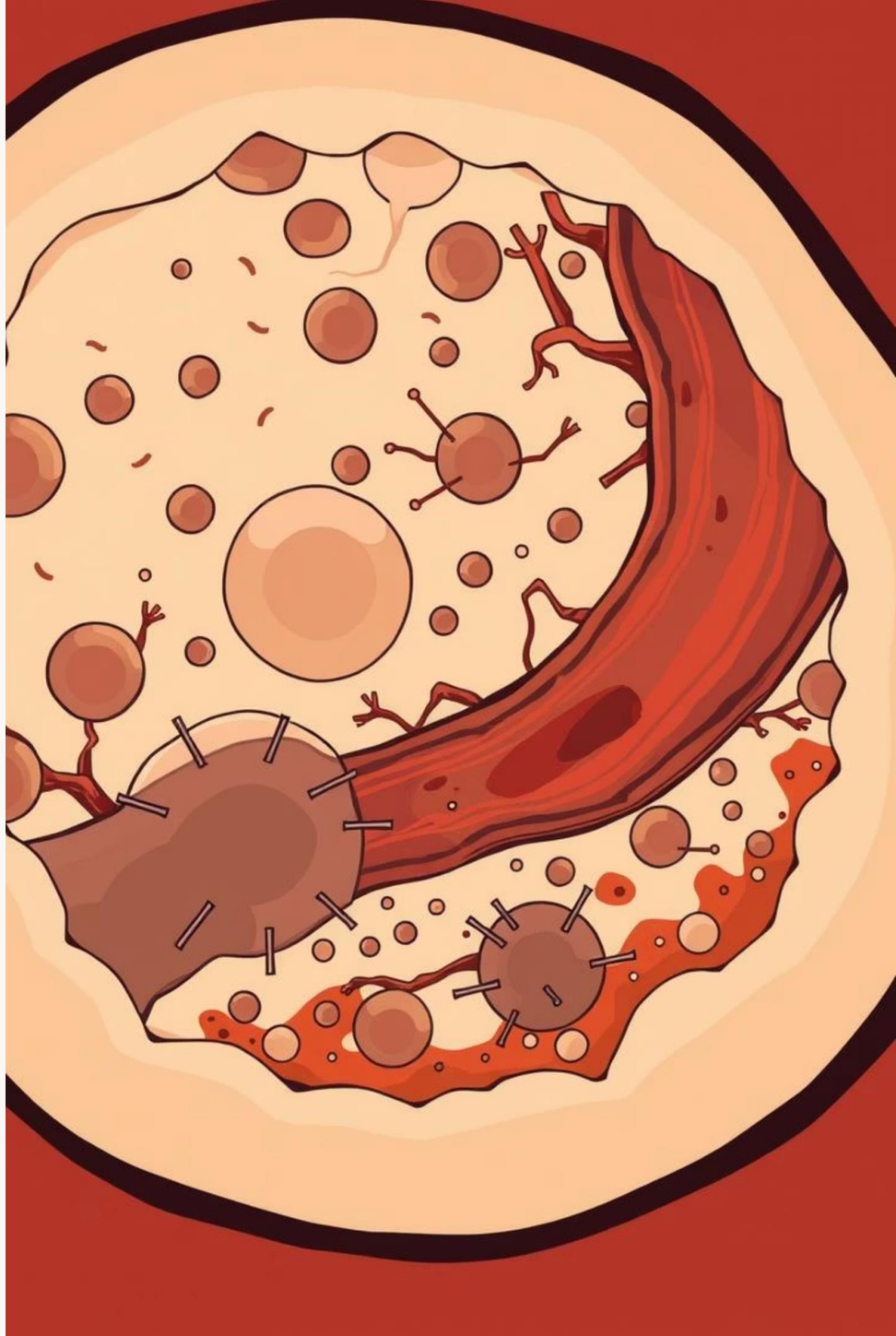
Upadacitinib for Giant-Cell Arteritis

A Phase 3 Trial of Upadacitinib for Giant-Cell Arteritis, published in the New England Journal of Medicine.



Understanding Giant-Cell Arteritis (GCA)

Giant-cell arteritis is a systemic vasculitis primarily affecting large and medium-sized arteries, common in adults over 50.

Key Symptoms

- Headaches
- Scalp/temple pain
- Jaw claudication
- Vision impairment

Current Treatment

Glucocorticoids are the primary treatment, but 50-80% of patients relapse during tapering.

Unmet Need

There is a significant need for effective, glucocorticoid-sparing treatments.

Introducing Upadacitinib

Upadacitinib is a selective Janus kinase (JAK) inhibitor that blocks signaling of cytokines like interleukin-6 and interferon-γ, which play key roles in GCA pathogenesis.

Mechanism of Action

Targets the JAK-STAT pathway to block multiple pathogenic pathways in GCA.

Potential Benefits

Offers a potential oral, targeted therapy for GCA, allowing for more rapid glucocorticoid tapering.

SELECT-GCA Trial Design

A randomized, double-blind, placebo-controlled Phase 3 trial conducted at 100 sites in 24 countries.

1

Patient Cohort

Adults ≥50 with new-onset or relapsing GCA, active within 8 weeks of baseline.

2

Randomization

Patients assigned 2:1:1 to Upadacitinib 15 mg, 7.5 mg (both with 26-week GC taper), or Placebo (52-week GC taper).

3

Primary End Point

Sustained remission at week 52 (absence of GCA signs/symptoms from week 12-52 + adherence to GC taper).

Trial Participants

A total of 428 patients were randomized and treated across the study groups.

Female sex	68.8%	74.6%
Mean Age	71.6 years	70.8 years
New-onset GCA	67.9%	70.8%
Relapsing GCA	32.1%	29.2%

Baseline demographics and disease characteristics were balanced across all trial groups.

Key Efficacy Results: Upadacitinib 15 mg

Upadacitinib 15 mg showed superiority over placebo in achieving sustained remission.

Sustained Remission

Upadacitinib 15 mg vs. Placebo (29.0%)

Sustained Complete Remission

Upadacitinib 15 mg vs. Placebo (16.1%)

The 7.5 mg dose was not superior to placebo for the primary end point.

Additional Efficacy Outcomes

Upadacitinib 15 mg demonstrated significant benefits beyond primary remission.

Reduced Glucocorticoid Exposure

Median cumulative exposure: 1615 mg (Upadacitinib 15 mg) vs. 2882 mg (Placebo).

Fewer Disease Flares

34.3% of patients on Upadacitinib 15 mg had ≥1 flare vs. 55.6% on placebo.

Improved Patient Outcomes

Significantly reduced fatigue and improved quality of life with Upadacitinib 15 mg.

Safety Profile

Safety outcomes were generally similar between upadacitinib and placebo groups over 52 weeks.

Common Adverse Events (15 mg group)

- Headache (16.3%)
- Arthralgia (13.9%)
- Hypertension (13.4%)
- COVID-19 (13.4%)

Key Safety Findings

- Lower discontinuation rates with Upadacitinib.
- Higher incidence of herpes zoster and creatine kinase elevation with 15 mg dose.
- No major adverse cardiovascular events in Upadacitinib groups.

Trial Strengths

The SELECT-GCA trial demonstrated robust methodology and broad applicability.

Rigorous Design

Placebo-controlled with blinded glucocorticoid taper and multiplicity-adjusted analyses.

Large Sample Size

Over 400 patients enrolled for a relatively rare disease.

Global Generalizability

Inclusion of patients from 24 countries across four continents.

Patient-Reported Outcomes

Included domains important to GCA patients, enhancing relevance.

Conclusion & Next Steps

Upadacitinib 15 mg offers a promising new treatment option for Giant-Cell Arteritis.

Efficacy Confirmed

Upadacitinib 15 mg showed superior efficacy and lower glucocorticoid use compared to placebo.

Consistent Safety

Overall safety profile aligns with known Upadacitinib safety data, with no new significant risks identified.

Long-Term Assessment

Longer follow-up is needed to assess cardiovascular risk and overall safety beyond 2 years.