



# Rapid Recurrence of Stroke After Tofacitinib Initiation:

Composite Outcomes Challenge Informed Decisionmaking in Ulcerative Colitis Management

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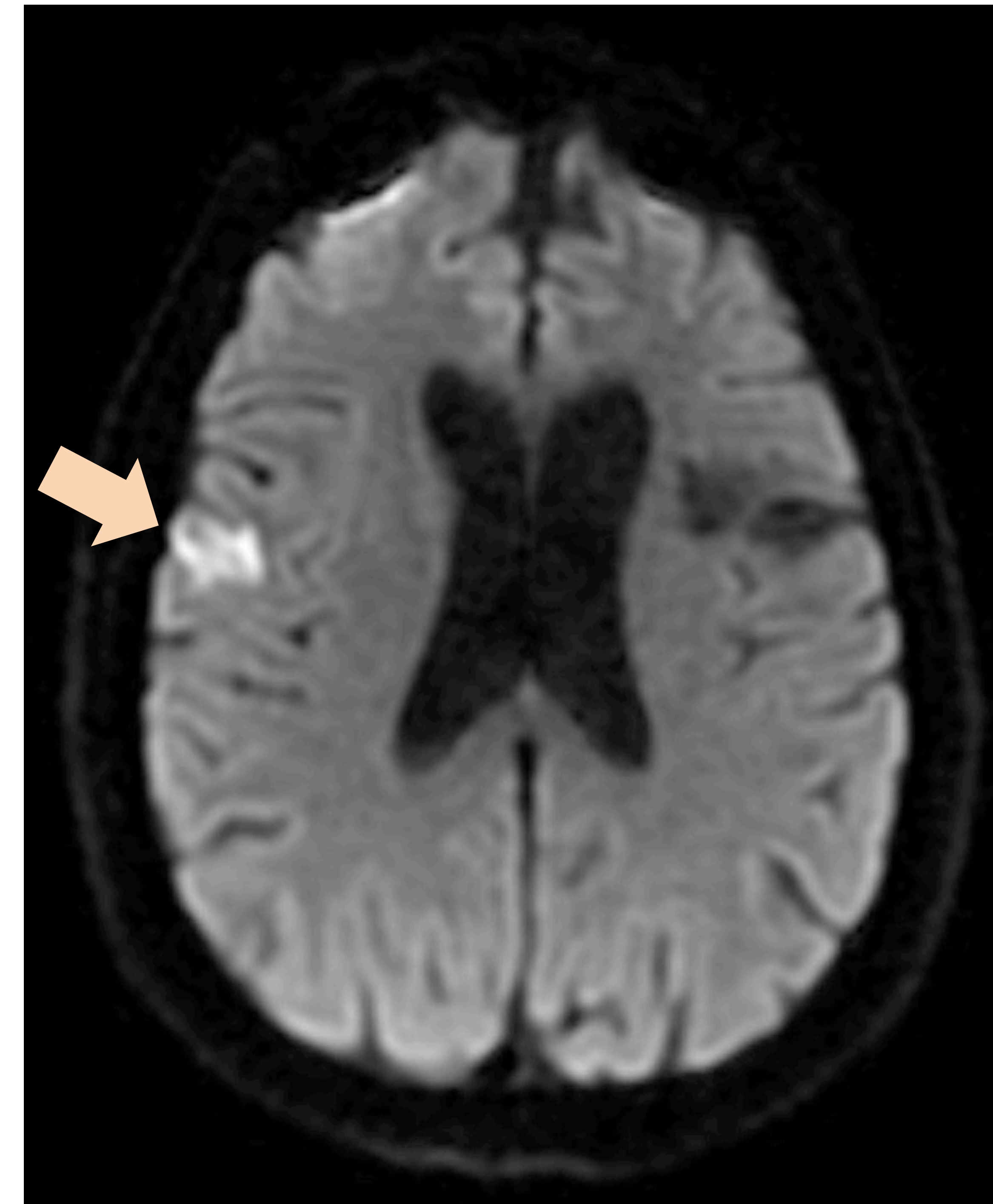
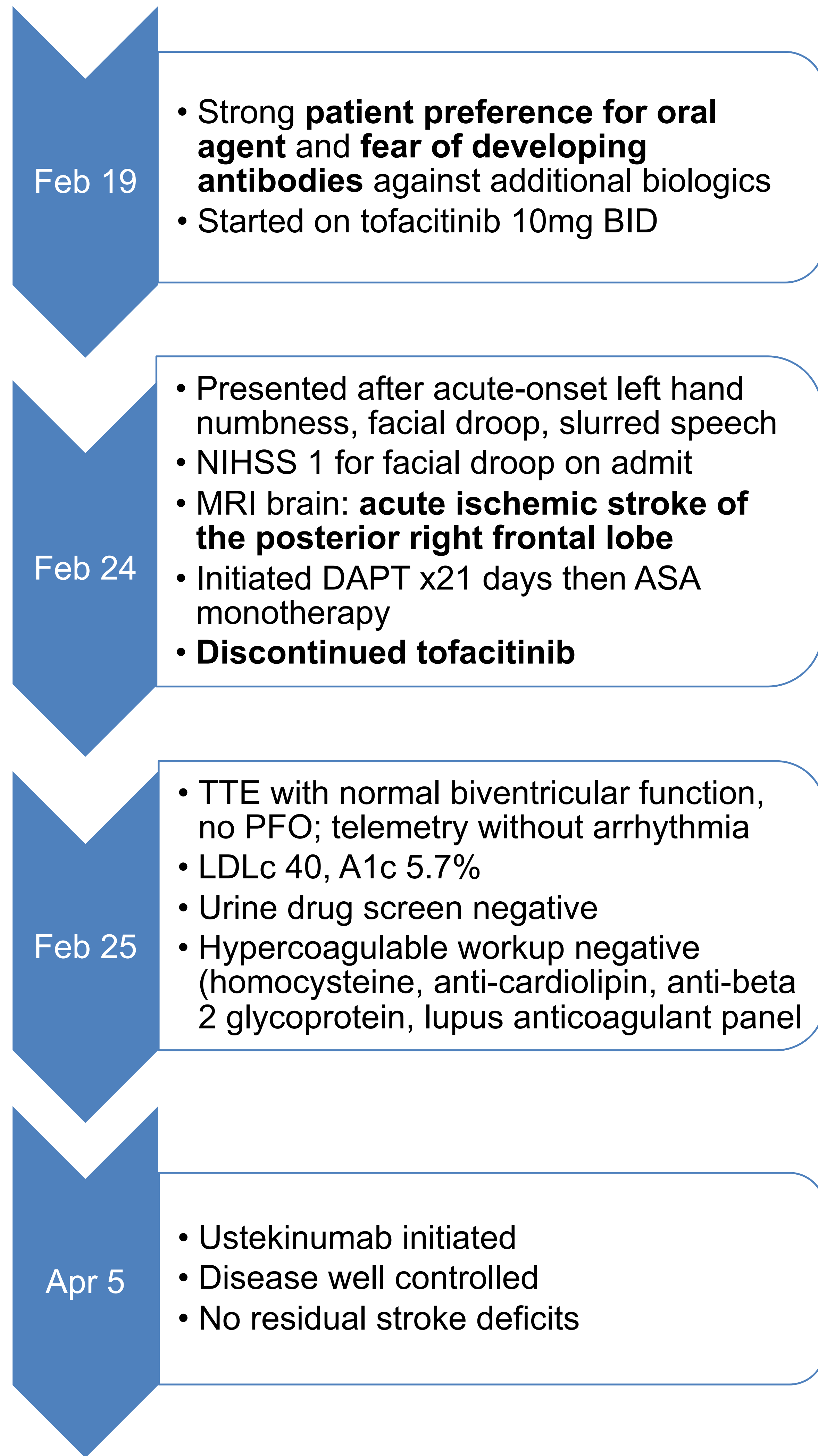
## BACKGROUND

- Tofacitinib (Xeljanz) is an oral small molecule Janus kinase (JAK) inhibitor approved for the treatment of ulcerative colitis with incomplete response or intolerance to tumor necrosis factor (TNF) inhibitors.
- In the United States and Canada, tofacitinib carries a boxed warning for major adverse cardiovascular events (MACE) based on randomized, open-label study of cardiovascular risk-enriched adults.<sup>1</sup>
- We present a case of recurrent stroke within days of tofacitinib initiation in a patient with ulcerative colitis.

## THE PATIENT

- 59 year old man with ulcerative colitis
- UC diagnosed 8 months prior to presentation after surveillance colonoscopy with history of previous nonadvanced adenoma and incidental rectal bleeding x2 months
  - Multiple hospitalizations with inadequate response to oral mesalamine, IV steroids, and prednisone tapers
  - Initiated infliximab but after 3 doses developed undetectable drug trough and high anti-drug antibody (>100 U/mL)
- Prior ischemic stroke of the left frontal lobe 3 years ago attributed to cocaine use
  - Since then, completely abstinent from cocaine
  - Remote 4 pack-year smoking history
  - Workup unrevealing for other causes
  - Continues on statin and ASA

## TIMELINE



**Image 1. Recurrent acute ischemic stroke within one week of tofacitinib initiation.** Magnetic resonance imaging reveals a focus of acute restricted diffusion (approximately 1.4 x 1.8 cm) within the posterior right frontal lobe (middle cerebral artery territory).

## DISCUSSION

- While tofacitinib has shown elevated MACE risk compared to TNF inhibitors in rheumatoid arthritis,<sup>1</sup> no studies have yet examined these outcomes in ulcerative colitis or parsed risk of stroke from composite cardiovascular events.
- Stroke can occur within days after tofacitinib initiation in ulcerative colitis in a patient with underlying risk factors.
- Risk of MACE appears to be higher with 10mg BID than 5mg BID dosing (respective HR 1.41 and 1.16 versus TNF inhibitor).<sup>1</sup>
- Non-composite outcome data -- separating risks of stroke and myocardial infarction -- are essential to guide shared decisionmaking using patient-specific risk factors.
- Evolving safety profiles must be carefully balanced alongside patient preferences, including preferences for oral therapies.

<sup>1</sup> Ytterberg SR et al. NEJM 2022; 386(4):316-326).

## CONTACT INFORMATION

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### FDA Boxed Warning:

“RA patients 50 years of age and older with at least one cardiovascular risk factor, treated with XELJANZ 5 mg twice daily or XELJANZ 10 mg twice daily, had a **higher rate of major adverse cardiovascular events (MACE)** (defined as cardiovascular death, myocardial infarction, and stroke), compared to those treated with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue XELJANZ/XELJANZ XR/XELJANZ Oral Solution in patients that have experienced a myocardial infarction or stroke.”