ONE-YEAR COMPARATIVE EFFECTIVENESS OF UPADACITINIB VERSUS TOFACITINIB FOR ULCERATIVE COLITIS: A MULTICENTER COHORT STUDY

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Background: We compared real-world outcomes of upadacitinib vs tofacitinib for ulcerative colitis (UC) through 52 weeks.

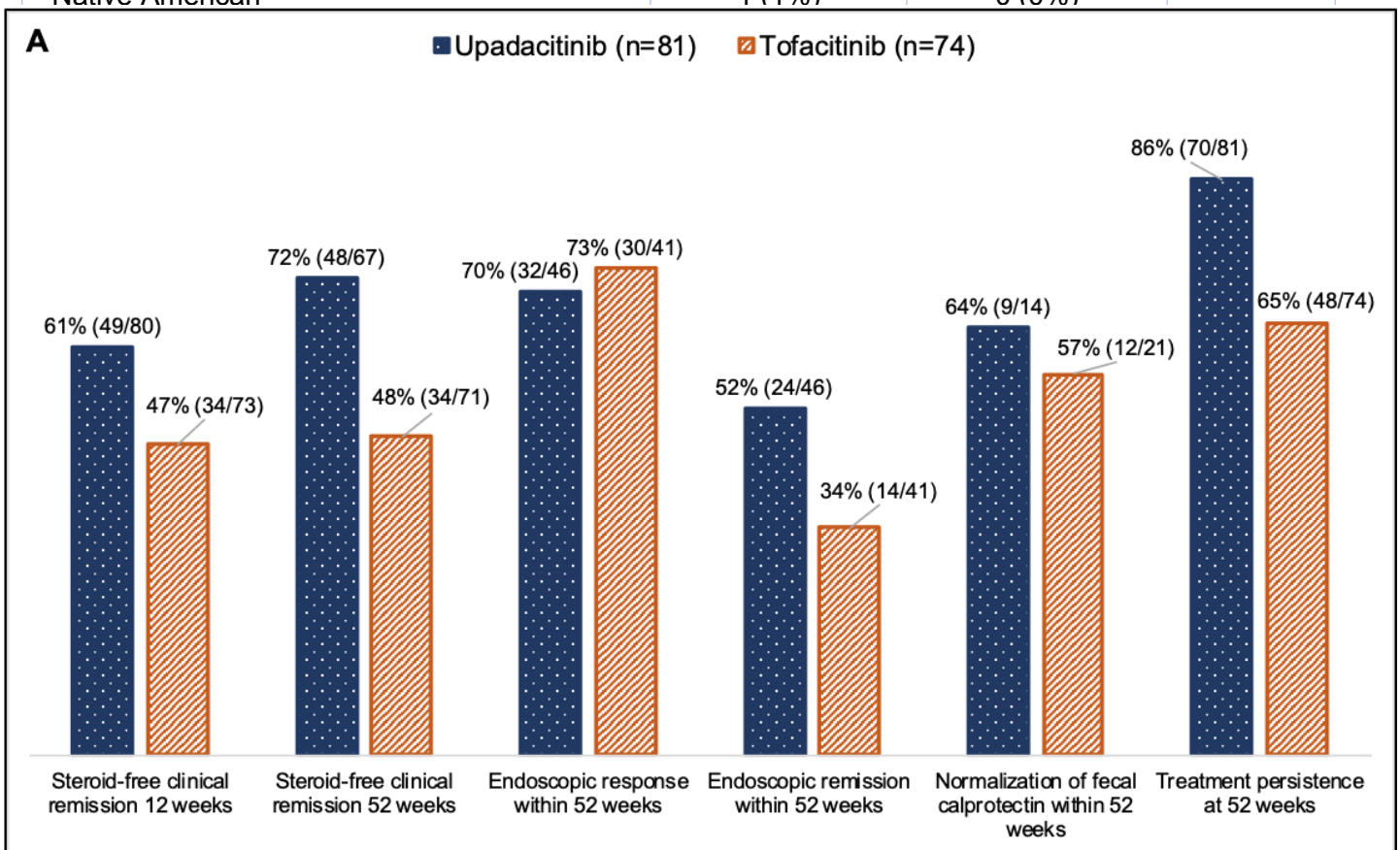
Methods: In this retrospective cohort study, adults initiated upadacitinib or tofacitinib for UC between 1/1/2020-2/1/2023 at two US academic centers. Electronic records were manually reviewed. The primary outcome was steroid-free clinical remission at 52 (+/-4) weeks, defined using the following tiered criteria based on available documentation: A. Simple clinical colitis activity index (SCCAI) ≤2 points B. Partial Mayo ≤2 points C. Provider global assessment of clinical remission and no use of oral corticosteroids at assessment. Secondary outcomes were SFCR at 12 (+/-4) weeks, endoscopic response (improvement in Mayo endoscopic subscore [MES] by ≥1 point), and endoscopic remission (MES=0) within 52 weeks. Other outcomes were normalization of fecal calprotectin (<250 ug/g), treatment persistence, and adverse events (AEs). Inverse probability of treatment-weighted (IPTW) logistic regression was performed to compare upadacitinib vs tofacitinib for primary/secondary outcomes.

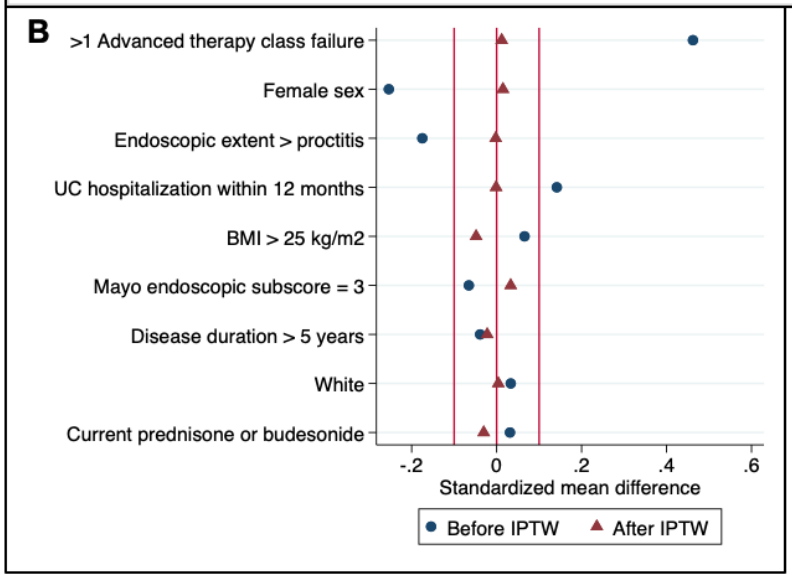
Results: 155 patients initiated upadacitinib (n=81) and tofacitinib (n=74). Baseline characteristics (**Table 1**) were similar, however upadacitinib patients had more prior vedolizumab and ustekinumab failures. A higher proportion of upadacitinib patients met all outcomes except for endoscopic response (similar between groups) (**Figure 1A**). AEs for upadacitinib (n=14) included peripheral edema, shingles, rash (n=2), pneumonia, diverticulitis, streptococcal pharyngitis, cellulitis, acne, chest pain, bacteremia, elevated liver enzymes, nausea, and neutropenia and for tofacitinib (n= 12) included *Clostridioides difficile* infection, pneumonia, chemical pregnancy / miscarriage (n=2), skin abscess, dental abscess, elevated liver enzymes, ankle swelling, norovirus infection, shingles (n=2), and DVT. After IPTW, which successfully balanced covariates (**Figure 1B**), upadacitinib was associated with significantly higher odds of SFCR at 12 weeks (OR 2.3, 95% CI 1.1-4.6) and 52 weeks (OR 3.0, 95% CI 1.4-6.6) and non-significantly higher odds of endoscopic response (OR 1.2) and endoscopic remission (OR 2.2) vs tofacitinib (**Figure 1C**). Results were similar in a sensitivity analysis that excluded upadacitinib patients with prior tofacitinib exposure.

Conclusion: Upadacitinib was associated with significantly higher odds of SFCR at 12 and 52 weeks and non-significantly higher odds of endoscopic response and remission vs tofacitinib for UC.

Table 1. Baseline characteristics

Characteristics*	Updacitinib (n=81)	Tofacitinibcitinib (n=74)	P-value
Demographics			
Female, n (%)	38 (47%)	43 (58%)	0.16
Age at initiation, y, median (IQR)	40 (29, 49)	39 (27, 54)	0.80
Disease duration, y, median (IQR)	9 (3, 14)	7 (3, 14)	0.68
Race, n (%)			0.52
White	71 (88%)	65 (88%)	
Black	3 (4%)	2 (3%)	
Asian	6 (7%)	5 (7%)	
Native American	1 (1%)	0 (0%)	





C Primary analysis	OR	95% LCL	95% UCL
SFCR 12 weeks (upa vs tofa)	2.28	1.13	4.59
SFCR 52 weeks (upa vs tofa)	3.01	1.39	6.55
Endoscopic response (upa vs tofa)	1.24	0.45	3.43
Endoscopic remission (upa vs tofa)	2.19	0.83	5.80
Sensitivity analysis (exclusion of patients with prior tofa exposure)	**OR**	**95% LCL**	**95% UCL**
SFCR 12 weeks (upa vs tofa)	2.92	1.31	6.50
SFCR 52 weeks (upa vs tofa)	3.36	1.39	8.14

Figure 1. A. Unadjusted outcomes. There is variability in fraction denominators due to missing data. B. Successful covariate balance after IPTW with <10% absolute standardized differences. C. IPTW logistic regression results.
Abbreviations: UC= ulcerative colitis, BMI = body mass index, IPTW = inverse probability of treatment weighting, SFCR = steroid-free clinical remission, OR = odds ratio, LCL = lower confidence limit, UCL = upper confidence limit