Presence of risk factors associated with colectomy among patients with colectomy in the tofacitinib OCTAVE ulcerative colitis clinical program

B0370

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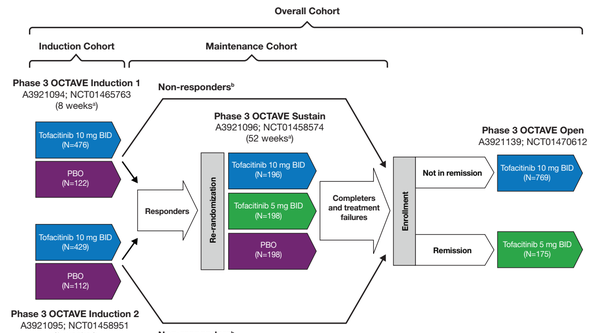
Introduction

- Tofacitinib is an oral small molecule Janus kinase inhibitor for the treatment of UC
- Avoidance of colectomy remains an important goal of UC therapy, as there are known factors associated with increased risk of colectomy[1]

Objective

- To assess baseline characteristics and the presence of previously identified risk factors for colectomy[1] among patients who underwent colectomy in the tofacitinib OCTAVE UC clinical program through post hoc analysis

Figure 1. Overview of the tofacitinib OCTAVE UC clinical program



[a]Final complete efficacy assessment at Week 8/52. Treatment continued up to Week 9/53
[b]Non-responders from OCTAVE Induction 1 and 2 received tofacitinib 10 mg BID in OCTAVE Open
N, number of patients in the treatment group

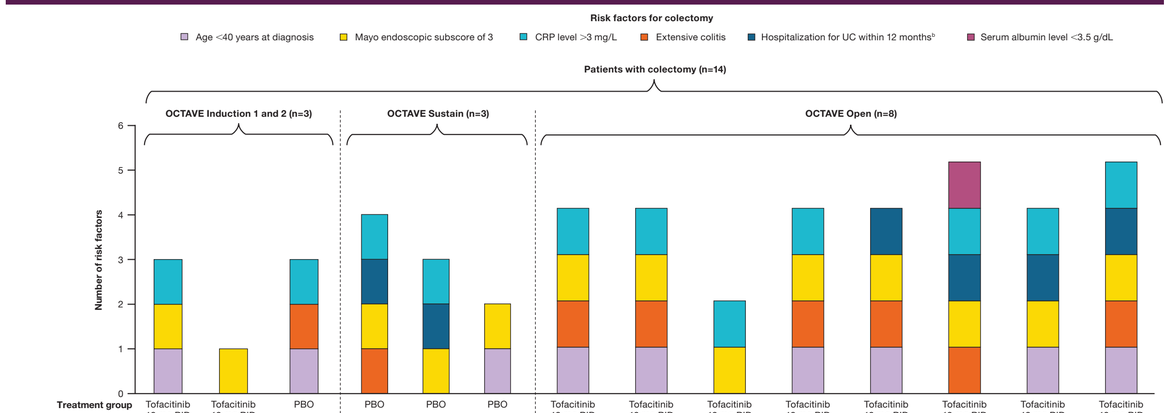
Methods

- IRs were assessed in three cohorts (**Figure 1**): Induction (PBO or tofacitinib 10 mg BID), Maintenance (PBO, tofacitinib 5 or 10 mg BID), and Overall (patients who received ≥1 dose of tofacitinib 5 or 10 mg BID in the Phase 3 or OLE studies)
- Risk factors[1] assessed at baseline were:
  - Age <40 years at diagnosis
  - Extensive colitis
  - Severe endoscopic disease (Mayo endoscopic subscore of 3)
  - Hospitalization for UC within 12 months
  - CRP level >3 mg/L
  - Serum albumin level <3.5 g/dL

Results

- In total, over a maximum period of 7.8 years of tofacitinib exposure, 14 patients underwent colectomy:
  - Three patients in OCTAVE Induction 1 and 2: tofacitinib 10 mg BID: n=2; PBO: n=1
  - Three patients in OCTAVE Sustain: PBO: n=3
  - Eight patients in OCTAVE Open: tofacitinib 10 mg BID: n=8; per protocol patients were not in remission at baseline
- Patients with colectomy in the tofacitinib OCTAVE UC clinical program had multiple complex risk factors, including those associated with increased risk of colectomy; all patients had ≥1 risk factor and had experienced prior TNFi failure (**Figure 2**)
- IRs for colectomy were numerically higher for patients receiving PBO vs tofacitinib 5 or 10 mg BID in the Induction and Maintenance Cohorts (**Figure 3**)

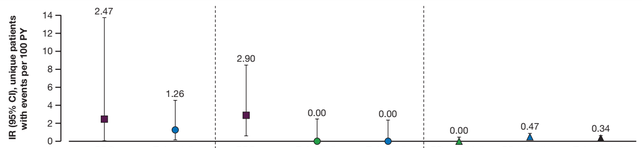
Figure 2. Risk factors[a] for colectomy, baseline demographics, and clinical characteristics in each patient with colectomy



Treatment group	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	PBO	PBO	PBO	PBO	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID
Subpopulation	-	-	-	-	-	-	Maintenance treatment failure[c]	Maintenance treatment failure[c]	Maintenance treatment failure[c]	Induction non-responder[d]	Induction non-responder[d]	Maintenance treatment failure[c]	Induction non-responder[d]	Induction non-responder[d]
Induction/ maintenance treatment group[e]	-	-	-	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	PBO	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	PBO	Tofacitinib 10 mg BID	Tofacitinib 10 mg BID	PBO	Tofacitinib 10 mg BID
Sex	Male	Male	Female	Female	Female	Female	Female	Female	Male	Female	Male	Male	Female	Female
Disease duration (years)[f]	⩾6	<6	<6	⩾6	<6	⩾6	⩾6	⩾6	<6	⩾6	<6	⩾6	⩾6	<6
Baseline CRP (mg/L)	53.53	1.9	4.36	4.65	19.59	1.08	13.42	4.02	4.5	36.8	1.71	40.53	4.34	7.5
Baseline albumin (g/dL)	4	4.3	3.6	4	3.9	4.5	4.1	4.2	3.7	4.2	4.3	3.2	4.1	4
Smoking history	Ex-smoker	Never smoked	Never smoked	Ex-smoker	Ex-smoker	Never smoked	Never smoked	Never smoked	Ex-smoker	Never smoked	Current smoker	Ex-smoker	Never smoked	Never smoked
Baseline corticosteroid use[a]	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes
Prior TNFi failure[a]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Days of treatment prior to colectomy[f]	21	38	58	126	143	63	62	132	44	92	56	375	47	174
Total Mayo score at last visit prior to colectomy	11	11	9	6	10	4	12	6	11	4	8	11	11	6

Individual patients are shown along the x-axis
[a]Risk factor data are from baseline of OCTAVE Induction 1 and 2
[b]Hospitalization for UC was considered a risk factor if it occurred within 12 months prior to enrollment into the induction studies
[c]Maintenance treatment failures comprised induction responders who experienced treatment failure in OCTAVE Sustain and received tofacitinib 10 mg BID in OCTAVE Open
[d]Induction non-responders comprised patients who did not achieve a clinical response after 8 weeks of induction treatment with tofacitinib 10 mg BID or PBO and received tofacitinib 10 mg BID in OCTAVE Open
[e]Induction treatment group allocations are presented for induction non-responders. Maintenance treatment group allocations are presented for maintenance treatment failures
[f]Data were taken from baseline of the respective studies in which the colectomy occurred
n, number of patients with colectomy

Figure 3. IRs for colectomy in the UC clinical program



n/N (%)	1/234 (0.4)	2/905 (0.2)	3/198 (1.5)	0/198 (0.0)	0/196 (0.0)	0/201 (0.0)	10/923 (1.1)	10/1124 (0.9)
PY	40.6	158.7	103.5	148.8	157.3	798.7	2117.2	2916.0

All events, including those that are outside the 28-day risk period (defined as the period up to 28 days beyond the last dose of the study drug), are included
Tofacitinib doses in the Overall Cohort were categorized based on the average daily tofacitinib dose and defined as follows: PD tofacitinib 5 mg BID, average total daily dose of tofacitinib <15 mg, and PD tofacitinib 10 mg BID, average total daily dose of tofacitinib ≥15 mg
n, number of patients with the event; N, number of patients evaluable for colectomy

Limitations

- This analysis was limited by:
  - The low number of colectomies
  - Identification of colectomies via case report form and not via electronic medical record review, which may have resulted in underestimation of events
  - Specific reasons for colectomy were not collected during the studies included in this analysis

Conclusions

- **Colectomies were infrequent in the tofacitinib OCTAVE UC clinical program**
- **All colectomies were in patients with prior TNFi failure and most had multiple risk factors**
- **For induction responders, colectomies only occurred in patients who received PBO and not tofacitinib in OCTAVE Sustain, which supports the importance of patients with moderate to severe UC remaining on active therapy**
- **No colectomies were reported among patients who received tofacitinib 5 mg BID in OCTAVE Open (patients in remission at the conclusion of OCTAVE Sustain), supporting the importance of remission as a treatment goal**

Abbreviations

–, not applicable; **BID**, twice daily; **CI**, confidence interval; **CRP**, C-reactive protein; **IR**, incidence rate (unique patients with events per 100 PY of exposure); **OLE**, open-label, long-term extension; **PBO**, placebo; **PD**, predominant dose; **PY**, patient-years; **RBS**, rectal bleeding subscore; **TNFi**, tumor necrosis factor inhibitor; **UC**, ulcerative colitis.

References

1. Rubin DT et al. Am J Gastroenterol 2019; 114: 384-413.
2. DeTora LM et al. Ann Intern Med 2022; 175: 1298-1304.

Endpoint definitions

Clinical response in OCTAVE Induction 1 and 2 was defined as a decrease from induction study baseline total Mayo score of ≥3 points and ≥30%, plus a decrease in RBS of ≥1 point or an absolute RBS of 0 or 1.

Remission was defined as a total Mayo score of ≤2 with no individual subscore >1, and an RBS of 0.

Treatment failure was defined as a ≥3-point increase from OCTAVE Sustain baseline total Mayo score plus a ≥1-point increase in RBS and endoscopic subscore, and an absolute endoscopic subscore of ≥2 points after ≥6 weeks of treatment.

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Disclosures

DT Rubin has received consulting fees from Pfizer Inc. L Salese is a stockholder of Pfizer Inc and was an employee of Pfizer Inc at the time of this analysis. PG Kotze has received consulting fees, speaker fees, and research grants from Pfizer Inc. JC Woolcott, C Su, and R Mundayat are employees and stockholders of Pfizer Inc. J Paulissen is an employee of Syneos Health, which was a paid contractor to Pfizer in connection with the development of this poster and the related statistical analysis. J Torres has received advisory board and speaker fees from Pfizer Inc. MD Long has received consulting fees and research grants from Pfizer Inc.

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