Safety of Ustekinumab in patients 65 years or older with Inflammatory Bowel Disease: A propensity-matched analysis

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BACKGROUND

- Ustekinumab (UST), a monoclonal antibody targeting both IL-12 and IL-23 receptors is used to treat moderate to severe Crohn's disease (CD) or Ulcerative colitis (UC)
- Owing to its mechanism, there is always a concern for adverse effects, like malignancy and opportunistic infections (OI)
- Studies have not shown an increased risk of adverse events however, there is limited data on the long-term effects on the elderly patients
- Our aim was to assess the risk of malignancy and opportunistic infections (OI) in patients with IBD, 65 years or older who were treated with UST compared to other biologic medications and small molecule therapy

METHODS

- Real-time search and analysis of the U.S Collaborative Network in the TriNetX platform containing ~ 85 million patients from 52 health care organizations
- Inclusion criteria: Patients with ICD-10 codes for UC or CD who were prescribed UST
- Exclusion criteria: Patients on azathioprine, mercaptopurine and methotrexate or on UST for less than 6 months
- Study outcomes: Malignancy and OI within 3 years of UST
  - Malignancy → Any solid organ or blood related malignancy
  - OI → influenza, tuberculosis, nocardiosis, clostridium difficile, legionnaires disease, listeriosis, pneumocystosis, candidiasis, aspergillosis, strongyloidiasis

Table 1: Risk of malignancy and opportunistic infections in patients with IBD on UST compared to other biologic or small molecule therapy and 5-ASA agents expressed as adjusted odds ratio (aOR) with 95% confidence interval (CI)

Adverse event	Medication	N (%)	aOR	95% CI
Malignancy	UST	16 (13.9%)	0.58	0.29 – 1.15
	5-ASA	25 (21.7%)		
OI	UST	17 (16.6%)	1.04	0.50 – 2.1
	5-ASA	19 (16.1%)		
Malignancy	TNFi	12 (9.6%)	0.73	0.32 – 1.64
	UST	15 (12.7%)		
OI	TNFi	20 (17.6%)	1.12	0.55 – 2.28
	UST	17 (16%)		
Malignancy	UST	15 (13.7%)	1.31	0.58 – 2.95
	Vedolizumab	12 (10.8%)		
OI	UST	16 (16.3%)	0.85	0.41 – 1.76
	Vedolizumab	20 (18.5%)		
Malignancy	UST	10 (20.4%)	1.07	0.40 – 2.86
	Tofacitinib	10 (19.2%)		
OI	UST	10 (23.8%)	0.80	0.31 – 2.05
	Tofacitinib	14 (28%)		

METHODS

- Risk expressed as adjusted odds ratio (aOR) with 95% confidence interval (CI)
- Propensity score matching was performed for age, gender, race, ethnicity, diabetes mellitus, nicotine dependence, BMI ≥ 30, history of oral or intravenous steroids and mean hemoglobin, C-reactive protein, albumin and calprotectin within 1 year of UST

Results

- We identified 147 patients with IBD age greater than 65 years who were on UST, 1493 patients were on anti-tumor necrosis factor alpha (TNFi), 494 were on vedolizumab, 92 were on tofacitinib and 6040 patients were on 5-ASA therapy
- There was no difference in the risk of malignancy (aOR 0.58, 95% CI 0.29-1.15) and OI (aOR, 1.04, 95% CI 0.50-2.1) in patients 65 years or older when treated with UST compared to 5-ASA therapy in patients with IBD
- There was no difference in the risk of malignancy and OI in patients 65 years or older when treated with UST compared to TNFi, vedolizumab and tofacitinib (Table 1)

Conclusion

- Ustekinumab appears to be safe in patients with IBD who are 65 years or older compared to other biologic or small molecule therapy and in patients who are not on immunosuppressive therapy