

Switching to TNFi versus non-TNFi biologics in ulcerative colitis patients: Real-world outcomes from a German claims data analysis

Evi Zhuleku¹, Daniel Wirth², Riikka Nissinen³, Alun Passey⁴, Ivana Bravatà⁵, Despina Ziavra⁶, Andreas Duva⁴, Jennifer Lee⁷, Ulf Maywald⁸, Thomas Wilke⁹, Bernd Bokemeyer¹⁰

1. Cytel Inc., Berlin, Germany, 2. Janssen-Cilag GmbH, Neuss, Germany, 3. Janssen-Cilag Oy, Espoo, Finland, 4. Janssen-Cilag Ltd, High Wycombe, UK, 5. Janssen-Cilag S.P.A, Milan, Italy, 6. Janssen-Cilag S.A.C.I., Pefki, Greece, 7. Janssen-Cilag A/S Denmark, Birkerød, Denmark 8. AOK PLUS, Dresden, Germany, 9. Institut Für Pharmakoökonomie Und Arzneimittellogistik (IPAM) E.V, Wismar, Germany, 10. Interdisciplinary Crohn Colitis Centre Minden, Minden, Germany



Following failure on therapy with tumor necrosis factor inhibitors (TNFi), patients with ulcerative colitis exhibit more favorable real-world outcomes when switching outside-class to UST or VDZ compared to a different TNFi.

Background

The efficacy of biologic agents for treating patients with ulcerative colitis (UC) has been well proven, however loss of response remains a problem in clinical practice, leading to increased disease activity, decreased quality of life, as well as the onset of potential complications such as hospitalization or surgery¹⁻².

Objectives

With limited real-world data on preferential sequencing of advanced therapies, the objective of this study was to evaluate outcomes of patients with UC initiating tumor necrosis factor inhibitors (TNFis) and switching to another TNFi or non-TNFi biologic therapy following failure on first-line (1L) TNFis.

Results

PATIENT SELECTION

Overall, 166 patients with UC newly initiating TNFis and switching after failure were identified. In total, 84 and 82 were classified as WCS and OCS, switching to another TNFi, or UST/VDZ respectively (Figure 1).

Among the WCS, 37 (44.0%) switched to IFX, 27 (32.1%) switched to ADA, and the remaining 20 (23.8%) switched to GOL. In contrast, the OCS group comprised of 67 (81.7%) and 15 (18.3%) of patients switching to VDZ and UST, respectively.

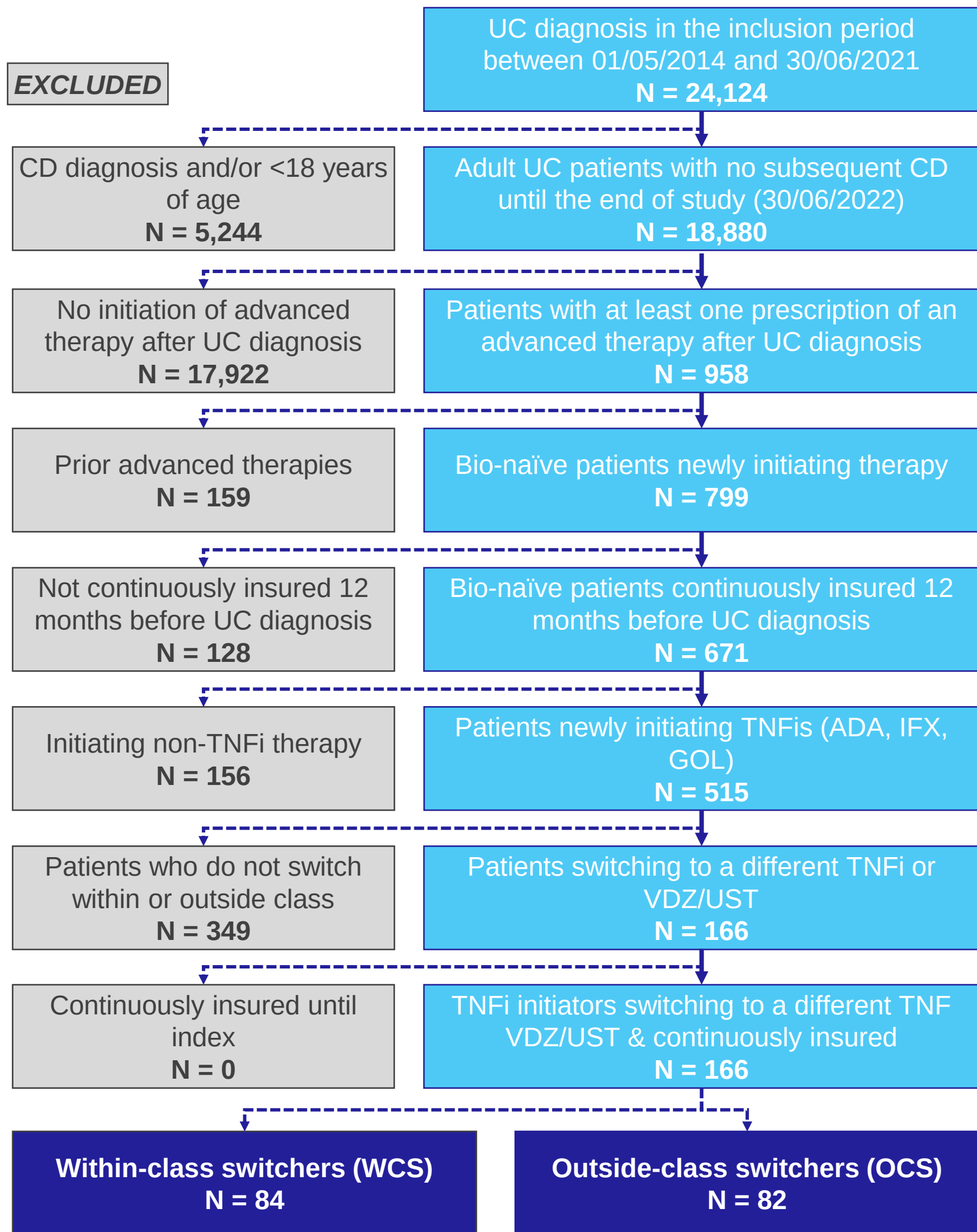


Figure 1. Patient attrition chart

PATIENT CHARACTERISTICS

Among the overall cohort prior to IPTW, patients had a mean age of 42.9 years, 49.4% were female and there was a mean 3.4 years of follow-up.

Between WCS and OCS, several baseline covariates were unbalanced prior to IPTW (absolute standardized mean difference, SMD >0.2), including the proportion of patients that were female, occurrence of cardiovascular diseases, occurrence of hypertension, number of gastroenterology visits and the proportion of patients with primary loss of response, defined as switch within 4 months of TNFi initiation (Table 1).

After IPTW, there were 71 and 76 patients remaining in the WCS and OCS groups (weighted N = 72.3 vs. 77.8), respectively. All baseline confounders were well balanced post-weighting.

Disclosures

This study was funded by Janssen-Cilag. DW, RN, AP, IB, DZ, AD, and JL are employees of Janssen-Cilag. EZ is an employee of Cytel Inc, whose work was funded by Janssen-Cilag. UM participated in this study as part of AOK PLUS. TW is a staff member of IPAM and has received honoraria from several pharmaceutical/consultancy firms e.g. NovoNordisk, Abbvie, Merck, GSK,BMS, LEO Pharma, Bayer, Boehringer Ingelheim. BB has received consultancy fees and grants from several pharmaceutical companies e.g. Abbvie, MSD, UCB, Takeda, Shield Therapeutics, Pfizer, Biogen, Janssen, and Boehringer Ingelheim.

Methods

PATIENT SELECTION

Adult patients with ≥1 inpatient and/or ≥2 confirmed outpatient UC diagnoses (ICD-10: K51.-) and no subsequent Crohn's disease diagnosis (ICD-10: K50.-) between 01/05/2014 and 30/06/2021 (inclusion period) were identified from the German AOK PLUS administrative claims dataset, covering >3.5 million insured individuals. Bio-naïve patients, defined as those with no prior prescriptions of advanced drugs, newly initiating TNFis (infliximab [IFX], adalimumab [ADA], golimumab [GOL]) in the inclusion period and switching to another agent after failure of the initial TNFi were selected (index = date of switch). Patients were classified as **within-class switchers (WCS)** if they switched to a different TNFi or **outside-class switchers (OCS)** if they switched to vedolizumab [VDZ] or ustekinumab [UST]. All patients were continuously insured from 12 months before their first observable UC diagnosis to the index date and followed from index to earliest of death, insurance end, or study end (30/06/2022).

ANALYSIS

WCS and OCS were adjusted using propensity score inverse probability of treatment weighting (IPTW) and characteristics were summarized before and after weighting. Cox regression models weighted using IPTW were utilized, comparing time to discontinuation (defined by a 60-day gap of no therapy after presumed end of drug supply), second treatment switch, and prolonged corticosteroid (CS) therapy, defined as 3 consecutive CS prescriptions including oral budesonide within 12-months.

Table 1. Baseline covariates in cohorts pre-/post-IPTW

	Unweighted			Weighted		
	WCS N=84	OCS N=82	SMD	WCS N=72.3	OCS N=77.8	SMD
Female (%)	54.76	43.90	0.217	47.89	50.16	-0.046
Age at index (mean)	43.11	42.63	0.035	41.96	42.68	-0.052
CCI (mean)	0.98	0.77	0.132	0.62	0.71	-0.065
Prior therapies at baseline, %						
5-ASA & similar agents	92.86	95.12	-0.095	94.96	91.06	0.171
Antibiotics	39.29	35.37	0.081	34.61	31.98	0.055
Corticosteroids (CS)	83.33	78.05	0.133	84.01	80.89	0.078
Concomitant CS*	13.10	17.07	-0.111	17.57	17.75	0.065
Immunosuppressants	36.90	29.27	0.162	38.23	34.33	0.083
UC-related surgeries	5.95	6.10	-0.006	4.32	5.66	0.055
Comorbidities at baseline, %						
Any cancer	3.57	3.66	-0.005	2.05	1.80	0.015
Colorectal cancer	0.00	0.00	-	-	-	-
Any cardiovascular disease	25.00	14.63	0.261	20.28	20.05	0.006
Diabetes	11.90	10.98	0.029	10.38	8.53	0.061
Hypertension	34.52	23.17	0.251	26.85	31.18	-0.097
Chronic kidney disease	2.38	7.32	-0.230	3.10	3.46	-0.018
Healthcare resource use at baseline, mean						
# of general practitioner visits	9.77	8.35	0.192	10.06	9.10	0.127
# of gastroenterology visits	5.02	7.55	-0.419	6.63	5.93	0.117
# of UC-related hosps.	0.62	0.54	0.092	0.60	0.57	0.024
Primary non-response ^b (%)	38.10	23.17	0.326	32.74	28.8	-0.086

OUTCOMES

WCS were significantly more likely to discontinue the index therapy (Hazard Ratio [HR] 1.82, 95% Confidence Interval [CI] 1.14 - 2.89, P = 0.012) and switch to a third therapy (HR 3.46, 95% CI 1.89 - 6.36, P < 0.001) (Figure 2 and Figure 3).

While WCS showed an increased likelihood to initiate prolonged CS therapy (HR 1.42, 95% CI 0.77 - 2.59, P = 0.260), results were not significant (Figure 4). When stratifying by patients with secondary loss of response, defined as switch after four months of TNFi initiation, the likelihood increased for WCS and differences were statistically significant, with an HR for WCS of 2.02 (95% CI 1.01 – 4.01, P = 0.046)

Figure 2. Time to treatment discontinuation

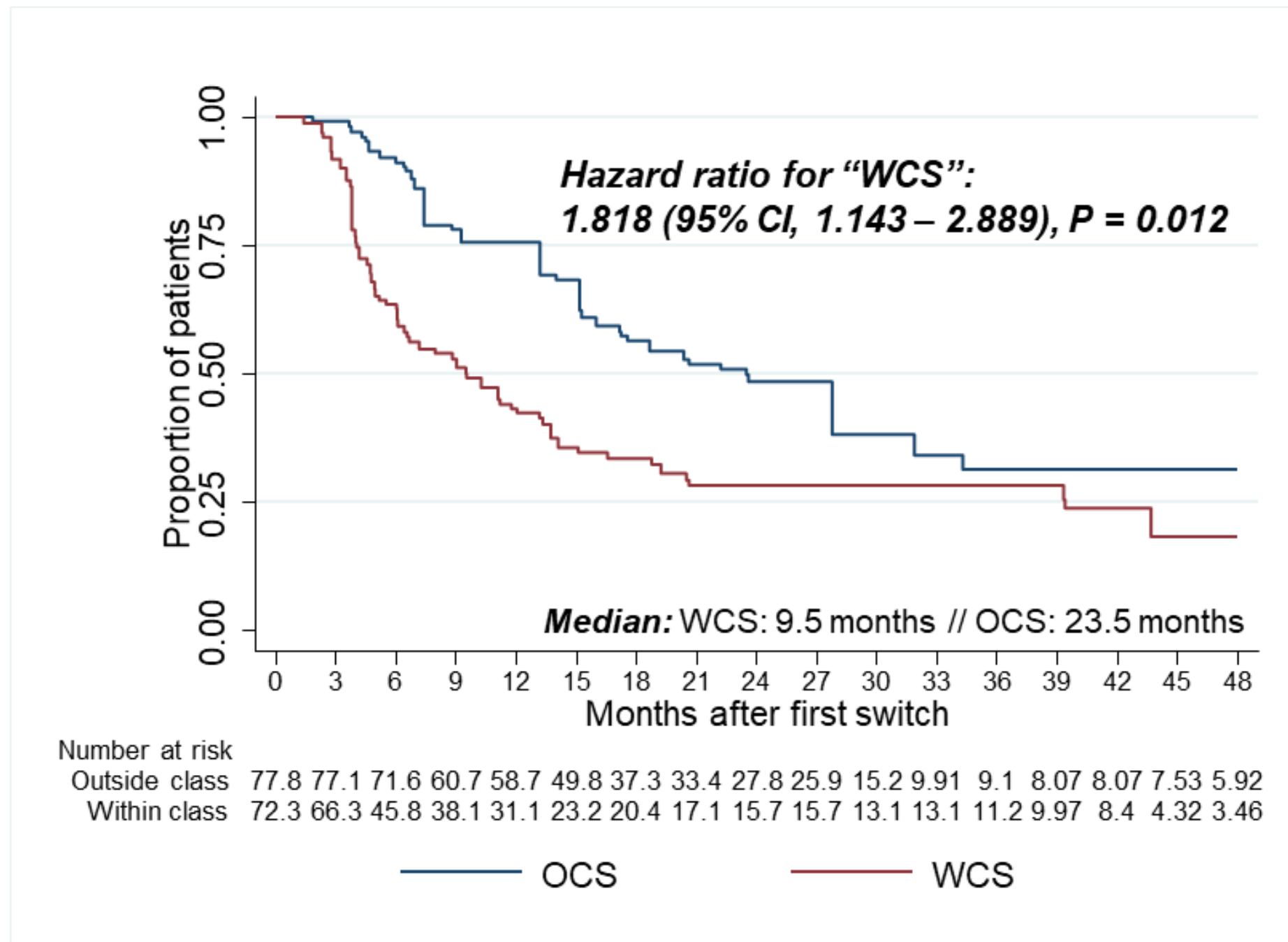


Figure 3. Time to second treatment switch

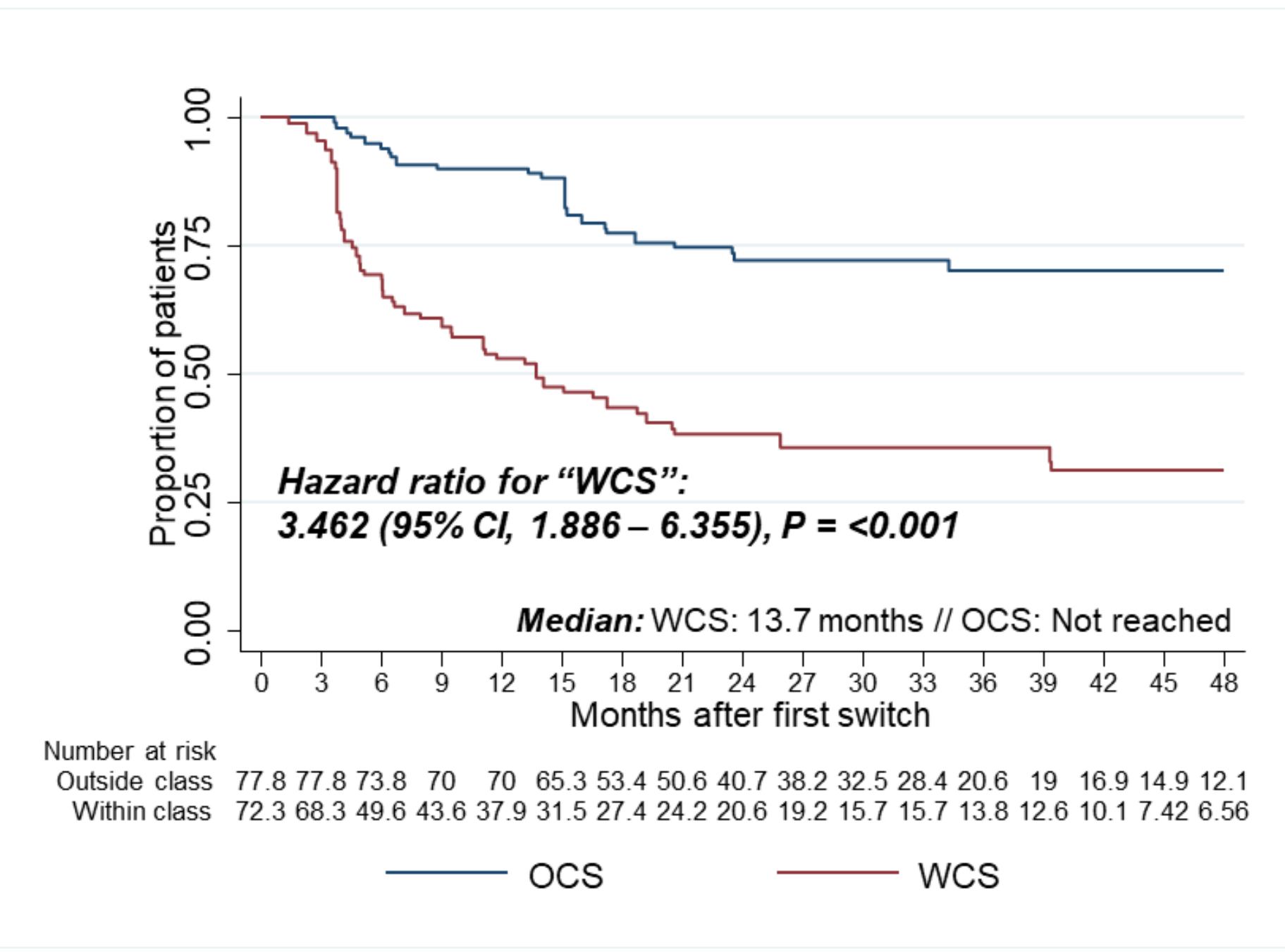
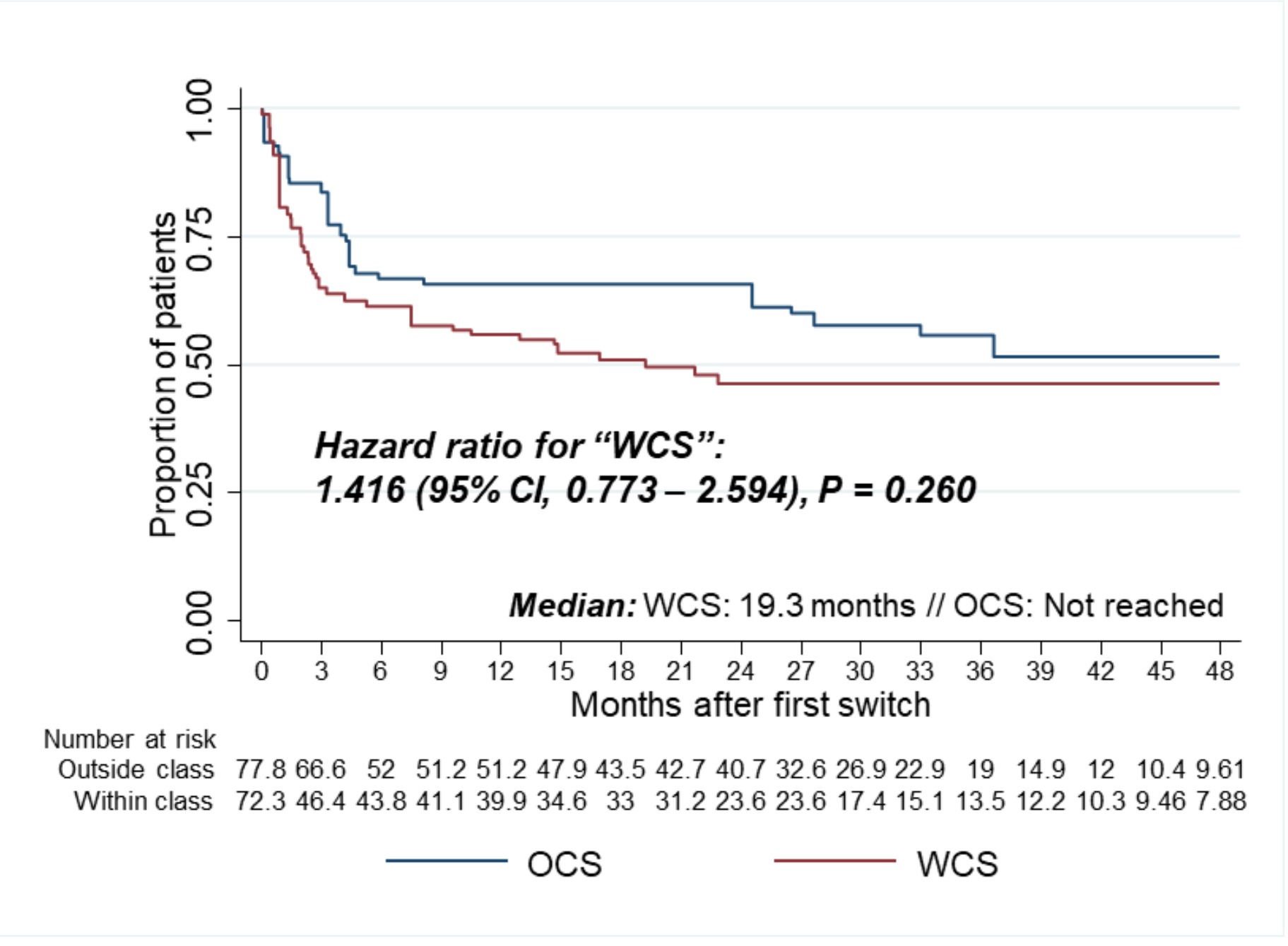


Figure 4. Time to prolonged corticosteroid therapy



Strengths & Limitations

We made use of a large population-based sickness fund. With uniform regulations and policies across Germany, a representative cohort of patient with UC was identified, free of study site/selection bias. Despite propensity score adjustment, potential unobserved confounders may still exist, particularly with respect to disease severity, dosing, and other clinical indicators. Moreover, the reason for discontinuation/switch is not directly available and a proxy-based definition for primary non-response/secondary loss of response was utilized.

Conclusions

This study suggests that following 1L TNFi failure, patients with UC exhibit more favorable real-world outcomes when switching outside-class to UST or VDZ compared to a different TNFi.

References

- [1] McDowell C, Farooq U, Haseeb M. Inflammatory Bowel Disease. [Updated 2023 Aug 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-.
- [2] Roda G, Jharap B, Neeraj N, Colombel JF. Loss of Response to Anti-TNFs: Definition, Epidemiology, and Management. Clin Transl Gastroenterol. 2016 Jan 7;7(1):e135. doi: 10.1038/ctg.2015.63. PMID: 26741065.