

Supplementary Table 2: Outcome variables and definitions

Outcome variable		Operational definition
Therapy sequence		Number of patients and frequency per sequence stratified by diagnosis (UC/CD) as well as first line index drug
Treatment line		Number of patients and frequency per line of advanced treatment stratified by diagnosis (UC/CD)
ToT		Number of days from 1L index date to start of 1L treatment or censoring date if no start of 2L treatment is observed in follow-up (either: death, end of observation, insurance switches or end of treatment line plus 60-day intake break) minus the number of days without treatment (e.g. between two prescriptions).
TTNT		Number of days from start of one treatment line to start of next treatment
TTIR		Outcomes are calculated according to Kaplan-Meier, i.e., the time until the first inadequate response event per patient occurs
Inadequate response event	Therapy discontinuation	>60-day prescription gap after end of previous prescription supply. (Date of discontinuation: End of the range of the last prescription before the 60-day gap)
	Therapy switch	Prescription of another advanced therapy without a concomitant refill prescription of the index therapy within a time frame of 180 days after consumption of defined daily dose [DDD] supply
	Dose escalation	In patients for whom a maintenance phase was observable, dose escalation was defined as a >1.5 time-increase of the recommended dose of index therapy (following European Summaries of Product Characteristics) across 3 consecutive index therapy prescriptions. When maintenance therapy started was defined specific to index drug: Maintenance therapy was assumed following the initiation phase, specified per drug: 4 weeks for ADA; 6 weeks for GOL; 14 weeks for IFX or VDZ; 8 weeks for TOFA; 12 weeks for UST.
	Prolonged use of corticosteroids	≥ 2 outpatient corticosteroid prescriptions during cohort's follow-up period with high dosing (>840mg/6 week time span threshold) (see supplementary Table 8 for relevant corticosteroids). Time to first prescription was measured
	Number of IBD-related hospitalizations per year	Inpatient admission with a primary diagnosis of UC/CD (Table 1) or IBD-related complications (supplementary Table 13)
	IBD-related surgeries per year	For included inpatient and outpatient service and procedure codes see supplementary Table 12
Mean normalized dosage factor during maintenance		For patients with maintenance phase the mean normalized dosage factor is calculated as the mean daily dosis per patients, which is divided by the recommended dosis and for this relation the mean is calculated over all applicable patients. The recommend dosage refers to European Summaries of Product Characteristics
Number of IBD-related hospitalizations per patient year		Inpatient patients with a main discharge diagnosis of UC/CD (supplementary table 1) or IBD-related complications (supplementary Table 13)
Duration of IBD-related hospital stays per patient year		Number of days from hospital admission to discharge with a primary diagnosis of UC/CD (supplementary table 1) or IBD-related complications (supplementary Table 13)
Number of IBD-related surgeries per patient year		For included inpatient and outpatient service and procedure codes see supplementary Table 12
Number of persons eligible for SHI sick pay		Number of persons eligible for SHI sick pay
Number IBD-related sick leave per patient year		Patients must have a sick leave notice with one diagnosis from supplementary table 1 (for patients eligible for sickness benefit only)

Duration of IBD-related sick leave	Number of sick days leave due to one diagnosis from supplementary table 1 (for patients eligible for sickness benefit only). Sick leave episodes that overlap with the start or end of the observation period are truncated accordingly.
Costs for IBD-specific hospitalizations	Mean (per patient) UC/CD-related inpatient costs incurred per year; assessment includes all costs incurred during an inpatient stay with a UC/CD main diagnosis, including diagnostics, medications and physician visits
Costs for IBD-specific medication per patient year (EUR)	Assessment of mean (per patient) UC/CD advanced therapy medication costs per year; includes the costs of the IBD advanced therapy drugs dispensed at the pharmacy
Costs for IBD-specific outpatient treatment per patient year (EUR)	Assessment of mean UC/CD-related (per patient) treatment costs per year of all outpatient treatments; costs include physician visits with UC/CD diagnosis attached to case, and diagnostic tests needed
IBD-related complementary and allied health services costs per patient year (EUR)	Assessment of UC/CD-related costs per patient year. We included incontinence aids (therapeutic appliance item numbers 152510*, 152517*, 152530*, 152531*, 152532*, 1599*) and stoma items (therapeutic appliance item number 29*)
Sick pay due to IBD per patient year (EUR)	Direct costs per year (SHI sick pay); related to UC/CD diagnoses for sick leave of ≥6 weeks duration (for patients eligible for sickness benefit only)
Total costs for IBD-specific treatment per patient year (EUR)	Direct IBD treatment cost display disease related costs from the SHI perspective including inpatient, outpatient, and medication costs as well as costs for complementary and allied health services and cost for sick pay*. IBD-related medication costs were corrected to the retail prices of 2022
Total costs for all-cause treatment per patient year (EUR)	Assessment of the overall mean (per patient) direct all-cause costs per year including medication, inpatient, outpatient, complementary and allied health service costs and sick pay*.
Concomitant treatment	Number of patients with concomitant treatment (as defined in supplementary Table 8) and/or conventional UC/CD treatment (as defined in supplementary Table 17) per year

ADA = adalimumab CD = Crohn's disease GOL = Golimumab IBD = Inflammatory bowel disease IFX = Infliximab SHI = statutory health insurance providers TOFA = Tofacitinib ToT = time on treatment TTIR = time to inadequate response TTNT = time to next treatment UC = Ulcerative Colitis UST = Ustekinumab VDZ = Vedolizumab

*sick pay was not included for comparative analysis