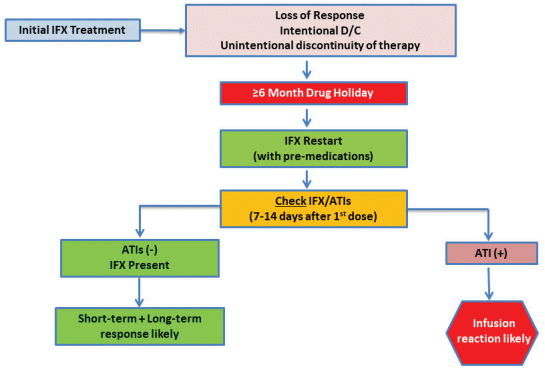
	No immunosuppression (n=24)	Thiopurines (n=12)	Anti-TNF therapy (n=12)	Combination therapy (n=12)	Healthy Controls age 50-59 (n=12)	p - value
Age (range)	44 (32-49)	39.5 (35-49)	40.5 (35-46)	42 (35-48)	51.5(50-59)	<0.001
Sex, male (%)	10 (42%)	6 (50%)	6 (50%)	7 (58%)	6 (50%)	0.86
Crohn	8	7	9	10	–	0.014
Active disease (HBI >8)	2	2	1	1	–	
Ulcerative colitis	16	5	3	2	–	
Active disease (partial Mayo >2)	2	1	0	1	–	
Length of IBD Diagnosis, months (median(range))	154.5 (73-217)	62 (11-432)	144 (12-324)	136.5 (22-432)	–	0.96
Thiopurine dose, milligrams (median (range))	–	150 (50-200)	–	150* (50-250)	–	–
Interferon gamma secreting cells						
Tetanus toxoid (median (range))	29 (1-117)	30 (1-76)	43 (11-135)	61 (1-137)	36 (4-99)	0.26
Varicella zoster virus (median (range))	43 (2-295)	27 (5-235)	40 (18-138)	60 (6-181)	43 (11-178)	0.70
* one patient on methotrexate 15mg/week						

Mo1890

USING THERAPEUTIC DRUG MONITORING TO PREDICT SUCCESS OF RESTARTING INFLIXIMAB THERAPY AFTER A DRUG HOLIDAY IN INFLAMMATORY BOWEL DISEASE

Inessa Normatov, Jingzhou D. Wang, George E. Gulotta, Shivani Patel, David T. Rubin

Background: Previous studies in inflammatory bowel disease (IBD) demonstrate that episodic exposure to infliximab (IFX) is associated with a high rate of infusion reactions and loss of response. These findings led to general recommendations regarding persistency of therapy and the perception that after a drug holiday, resuming therapy was high risk and should not be attempted. More recently, several studies have demonstrated that reinitiating IFX in select patients can be safe and effective (1). We report the results of our "restart protocol" which utilizes therapeutic drug monitoring (TDM). **Methods:** This was a prospective observational trial of a restart protocol for IBD patients who were previously treated with IFX, but have been off IFX for ≥6 months, and are currently actively inflamed (Fig 1). Pre-meds of acetaminophen 650mg, diphenhydramine 25mg IV and solumedrol 40mg IV were administered prior to the first re-infusion. 7 to 14 days post infusion, we measured serum IFX level and antibodies to infliximab (ATI). Patient demographics, medical history, reason for discontinuing IFX and duration of drug holiday were identified through the electronic medical record. Outcomes of interest include results of TDM, infusion reactions, and medication persistence at 14 weeks and 1 year. **Results:** 18 patients (mean age 41.3±16.5y; 11 (61%) female; 12 (67%) with Crohn's disease) between Jan 1, 2014 and June 1, 2018 restarted IFX using this protocol. Reasons for being off IFX included: primary non-response (4), loss of response (6), patient preference (4), surgery-related interruption (3), and loss of follow-up (1). The mean duration of drug holiday was 55.2 months (95% CI: 32.0-78.5). The median post-infusion IFX level was 21.6 ćg/mL (range 0-65.6). ATI were present in 6/18 (35%) of patients. 2 patients had undetectable IFX levels and both had detectable ATI. One patient had an immediate hypersensitivity reaction with the first infusion. Four patients had an infusion reaction with subsequent treatment, 2 of whom had ATI with the first infusion. There were no cases of anaphylaxis. Of the 12 patients without ATI who proceeded with their additional loading doses and maintenance doses, 10/12 had a clinical response at week 14 and 6/10 remained on IFX at 1 year. The likelihood of 1 year response after reintroduction was associated with shorter duration of drug holiday (responder 19.7±13.7m vs non-responder 68.6±15.0m; p=0.039). **Conclusion:** We describe our restart protocol for IFX after drug holiday and show that IFX can be safely restarted. Post-infusion TDM is predictive of 14 week and 1 year outcomes. 1. Baert, et al. CGH 2014;12:1474-1481.



Chicago Algorithm for Restarting IFX

Mo1891

POST-MARKETING SAFETY EXPERIENCE OF VEDOLIZUMAB IN PATIENTS RECEIVING CONCOMITANT TREATMENT WITH OTHER BIOLOGICS

Russell D. Cohen, Fatima Bhayat, Aimee Blake, Simon P. Travis

Background: Vedolizumab (VDZ) is a gut-selective antibody to α4β7 integrin approved to treat moderate to severe Crohn's disease and ulcerative colitis in adults. Concomitant treatment with VDZ and other biologics is not recommended in the VDZ prescribing information and has not been evaluated in clinical trials, meaning that safety data are limited on patients receiving this combination. We compared 4 years of post-marketing safety data reported to Takeda Pharmaceutical Company Ltd (Takeda) on patients receiving VDZ and concomitant treatment including other biologics ('with CB') with patients receiving VDZ and concomitant therapy excluding other biologics ('without CB'). **Methods:** The VDZ Global Safety Database contains all adverse event (AE) reports received by Takeda, including concomitant medication data if available, since VDZ approval on May 20, 2014. Reports received between approval and May 19, 2018 with concomitant medication data were identified for review using Medical Dictionary for Regulatory Activities version 21.0. VDZ exposure was estimated using the number of vials shipped globally, assuming 8–week dosing intervals. **Results:** In approximately 208 050 patient-years of VDZ exposure, 80 218 AEs were reported in 32 752 patients. Of these AEs, 2847 (4%) were in 1112 (3%) patients with CB and 54 855 (68%) were in 20 201 (62%) patients without CB (other AEs were in patients with no concomitant medication reported; Table 1). There were 1003 patients with Crohn's disease or ulcerative colitis with CB and 18 974 without CB. Infections accounted for 202 AEs (7%) in patients with CB and 4414 (8%) without CB, of which 21% and 18% were serious, respectively. There were 7 post-operative complications and 16 infusion-site reactions in patients with CB compared with 186 and 453, respectively, in those without CB (< 1% and 1% of AEs in each group). A total of 2 malignancies and 7 fatal AEs (both < 1%) occurred in patients with CB, versus 176 malignancies and 140 fatal AEs (both < 1%) in patients without CB. **Conclusion:** This analysis provides information on VDZ safety with and without CB in the real-world setting. Limitations of post-marketing safety reports should be considered when interpreting these results, including that duration of VDZ with CB was not included in reports. Additionally, the numbers of AEs reported in patients receiving VDZ with CB were small, and the number of patients receiving VDZ with CB was much lower than those without CB. These data do not suggest an increased risk of AEs in patients receiving VDZ with CB versus VDZ without CB.

Table 1. Patient characteristics, vedolizumab continuation and adverse events in patients receiving vedolizumab with and without concomitant treatment with other biologics.

Characteristic, n (%)	Patients receiving vedolizumab with concomitant biologic treatment			Patients receiving vedolizumab without concomitant biologic treatment		
n= number of patients	Crohn's disease n = 460	Ulcerative colitis n = 543	Other indications[a] n = 109	Crohn's disease n = 8861	Ulcerative colitis n = 10 113	Other indications[a] n = 1227
Sex						
Female	279 (61)	240 (44)	69 (63)	5499 (62)	5130 (51)	723 (59)
Male	178 (39)	301 (55)	35 (32)	3341 (38)	4954 (49)	473 (39)
Not reported	3 (1)	2 (< 1)	5 (5)	21 (< 1)	29 (< 1)	31 (3)
Age, years[b]						
< 18 years	7 (2)	5 (1)	2 (2)	118 (1)	231 (2)	28 (2)
18–64 years	406 (88)	481 (89)	73 (67)	7889 (89)	8025 (79)	653 (53)
≥ 65 years	39 (8)	48 (9)	4 (4)	1464 (17)	1702 (17)	195 (16)
Not reported	8 (2)	8 (1)	28 (26)	179 (2)	155 (2)	351 (29)
Concomitant biologics[c]						
Concomitant anti-TNFs therapy	339 (74)	520 (96)	73 (67)			
Other concomitant biologic therapy	117 (25)	22 (4)	34 (31)	N/A	N/A	N/A
Concomitant anti-TNFs and other biologics	4 (1)	1 (< 1)	2 (2)			
Other concomitant immunosupressant						
Yes	133 (29)	167 (31)	32 (29)	2110 (24)	2399 (24)	278 (22)
No	327 (71)	376 (69)	77 (71)	6751 (76)	7714 (76)	951 (78)
Concomitant corticosteroid						
Yes	180 (39)	261 (48)	49 (45)	3763 (42)	5697 (56)	432 (35)
No	280 (61)	282 (52)	60 (55)	5098 (58)	4416 (44)	795 (65)
Category of ad verse event, n (%)						
n= number of events						
	Crohn's disease n = 1285	Ulcerative colitis n = 1363	Other indications[a] n = 199	Crohn's disease n = 25 929	Ulcerative colitis n = 26 272	Other indications[a] n = 2654
Infections[d]	98 (8)	104 (8)	40 (20)	2291 (9)	2213 (8)	438 (17)
Serious infections	22 (2)	21 (2)	18 (9)	480 (2)	324 (1)	121 (5)
Malignancies[e]	1 (< 1)	1 (< 1)	2 (1)	82 (< 1)	84 (< 1)	12 (1)
Infusion-site reactions	10 (1)	6 (< 1)	0 (0)	235 (1)	218 (1)	7 (< 1)
Fatal events[f]	4 (< 1)	3 (< 1)	1 (1)	80 (< 1)	60 (< 1)	32 (1)
Post-operative complications	4 (< 1)	3 (< 1)	2 (1)	135 (1)	51 (< 1)	23 (1)
Vedolizumab continuation following adverse event, n (%)						
n= number of patients						
	Crohn's disease n = 460	Ulcerative colitis n = 543	Other indications[a] n = 109	Crohn's disease n = 8861	Ulcerative colitis n = 10 113	Other indications[a] n = 1227
Treatment continued	352 (77)	446 (82)	33 (30)	7301 (82)	8586 (85)	814 (66)
Treatment discontinued	87 (19)	79 (15)	57 (52)	1143 (13)	1232 (12)	224 (18)
Not applicable	5 (1)	2 (< 1)	2 (2)	59 (1)	47 (< 1)	24 (2)
Not reported/unknown	16 (3)	16 (3)	17 (16)	359 (4)	268 (3)	165 (13)

[a]Including patients with unspecified inflammatory bowel disease, off-label use and unreported indications.
[b]Vedolizumab is not approved for use in patients < 18 years of age.
[c]Receipt of vedolizumab therapy concomitantly with other biologics is not recommended in the vedolizumab prescribing information.
[d]The most frequently reported serious infections for patients receiving vedolizumab with CB were intestinal abscess, anal abscess and pneumonia (2 patients [9%] each) in Crohn's disease and *Clostridium difficile* infection/colitis (3 patients [14%]), pneumonia and cytomegaloviral infection/colitis (2 patients each [14%]) in ulcerative colitis.
[e]Malignancy events in both groups excluded colon adenomas, benign events and non-melanoma skin cancer, as well as malignancies in patients experiencing an event before initiation of vedolizumab therapy. Of the four malignancies in the group with CB, there was one lower GI malignancy (Crohn's disease), two hematological malignancies (1 ulcerative colitis, 1 other indication) and one neuroendocrine malignancy (1 other indication).
[f]Of the fatal events in the group with CB, 3 reports contained the term 'death' with no further detail (all in patients with Crohn's disease), 1 event was listed as adenocarcinoma (Crohn's disease), 1 was leukemia (off-label use for graft-versus-host disease) and 1 patient had 3 fatal events (ulcerative colitis, multiple organ dysfunction syndrome and drug ineffective).
AE, adverse event; N/A, not applicable; TNF, tumor necrosis factor.

Mo1892

NON-MEDICAL REVERSE SWITCH BETWEEN THE ORIGINATOR INFLIXIMAB AND ITS BIOSIMILAR IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: CLINICAL OUTCOMES AND THERAPEUTIC DRUG MONITORING

Lorant Gonczi, Akos Ilias, Kata Szanto, Zsuzsanna Kurti, Petra Anna Golovics, Klaudia Farkas, Eszter Schafer, Zoltán Szepes, Balazs Szalay, Aron Vincze, Tamas Szamosi, Tamas Molnar, Peter L. Lakatos

Background: Switching from the originator to a biosimilar infliximab (IFX) in patients with inflammatory bowel disease (IBD) has proven to be successful, although clinical evidence is lacking on reverse and/or multiple switching. The aim of the present study was to evaluate medium-term drug sustainability, safety and immunogenicity profile of reverse switching from a biosimilar to the originator IFX in a consecutive multicenter real-life cohort. **Methods**: We performed a prospective observational study of 174 consecutive patients with IBD (136 with Crohn's disease [CD] and 38 with ulcerative colitis [UC]) who were switched from the biosimilar infliximab CT-P13 to the originator Remicade during maintenance therapy. Previous exposure to the originator was 8% (n=14). In September 2017, a non-medical reverse switch took place in all Hungarian patients from the biosimilar to the originator infliximab due to change in reimbursement policies. We collected clinical and biochemical information from patients at baseline (time of the switch) and 8, 16 and 24 weeks thereafter. Serum drug trough levels and anti-drug antibodies were measured at baseline and week 16. **Results:** Complicated disease behavior and perianal manifestation was present in 39.7% and 48.5% of CD patients. 54.1% of UC patients had extensive colitis. Previous exposure to the originator was 8.0% (n=14). There was no significant difference between the proportion of patients in clinical remission (based on Crohn's Disease Activity Index <150 points or no fistula drainage; partial Mayo score <3) at week 8 before switch, at switch/baseline and at week 16 and 24 (CD: 82.6/80.6/77.5/76.3%, p=0.60; UC: 82.9/81.6/83.7/84.8%, p= 0.98). In all IBD patients, mean serum IFX trough levels were 5.33 µg/ml (SD: 4.70) at