## OP17

### Maintenance phase propensity score adjusted effectiveness and persistence at week-52 in biologic-naïve Ulcerative Colitis patients treated with vedolizumab or anti-TNF (VEDO IBD-study)

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**Background:** In this real-world-evidence (RWE) study we aimed to analyse the persistence of biologic therapy in biologic-naïve ulcerative colitis (UC) patients and to compare 1-year effectiveness of vedolizumab (VDZ) and anti-TNF.

**Methods:** Between 2017 and 2020, 1200 consecutively enrolled biologic-naïve and biologic- experienced patients with UC and Crohn´s disease (CD) were prospectively included in the $VEDO_{IBD}$-Registry from 45 IBD-experienced centres across Germany. After exclusion of bio-experienced patients, CD and missing outcomes, the final sample consisted of 274 biologic-naïve UC-patients with 1-year follow-up data. Switchers of a drug were considered as treatment failure (modified intention-to-treat analysis; mITT) while switchers were excluded from per protocol analysis (PP). Clinical response modified (reduction of partial Mayo score (pMayo) from baseline to 1-year by >3 points or a reduction of at least 30% compared to baseline or reaching remission at 1-year) and (steroid-free) remission rates (pMayo ≤1 plus a bleeding subscore=0 (and no systemic use of steroids or budesonide at 1-year)) were predefined as outcomes. To reduce the effect of confounders, PS adjustment with inverse probability of treatment weighting (IPTW) was implemented. A weighted logistic regression was used, and the results were reported as odds ratio (OR) and 95% confidence interval (CI).

**Results:** 158 VDZ and 116 anti-TNF (ADA: 27.6%, IFX: 57.8%, GOL: 14.7%) biologic-naïve UC-patients were included in this prospective RWE comparing the effectiveness of VDZ vs anti-TNF. Until week 52 significantly more patients switched to another biologic-drug in the anti-TNF group than in the VDZ group (40.5% vs 16.5%; p<0.001) (Fig. 1). In mITT, clinical response at 1-year was significantly higher in VDZ than in anti-TNF treated patients (61.7% vs. 40.3%; OR 2.39 (95% CI 1.39–4.10)). VDZ also tended to be superior to anti-TNF for (steroid-free) remission (Tab. 1; p=0.058 (p=0.051)). In the PP-analysis, VDZ showed numerically higher 1-year effectiveness, but this did not reach statistical significance (Tab. 1). Analysing week-14 induction phase responders (Tab. 2), VDZ had numerically higher effectiveness rates compared to anti-TNF but without significant difference.

**Conclusion:** The 1-year maintenance findings suggested, in line with our previous induction phase data, only moderate long-term effectiveness in both groups. However, besides the significant response data, VDZ showed numerically higher remission rates compared to anti-TNF though only borderline significant. The higher treatment persistence of VDZ vs anti-TNF, along with the higher effectiveness, may suggest VDZ as a first-line biologic therapy option in UC patients.

**Figure 1**. Kaplan-Meier curve showing the percentage of vedolizumab and anti-TNF-users maintaining or switching drug over time

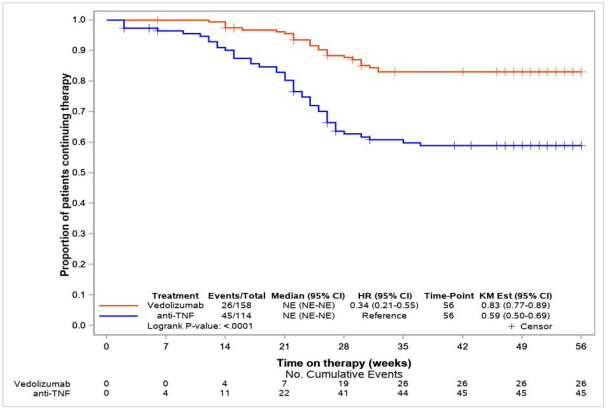


**Table 1**. 1-year effectiveness from baseline to week-52 of vedolizumab vs anti-TNF in bio-naïve UC-patients in the PS-weighted $VEDO_{IBD}$ study

| Outcome | Vedolizumab | Anti-TNF | Vedolizumab | Anti-TNF |
|---|---|---|---|---|
| | % | % | OR 95%(CI) | |
| **modified intention-to-treat analysis** (n) | 158 | 116 | 158 | 116 |
| *Clinical response* | 61.7 | 40.3 | 2.39 (1.39-4.10) | Ref |
| *Clinical remission* | 38.2 | 26.0 | 1.76 (0.98-3.18) | Ref |
| *Steroid-free remission* | 36.5 | 24.0 | 1.82 (1.00-3.34) | Ref |
| **Per protocol analysis** (n) | 132 | 69 | 132 | 69 |
| *Clinical response* | 73.5 | 64.4 | 1.53 (0.71-3.28) | Ref |
| *Clinical remission* | 45.1 | 41.0 | 1.18 (0.61-2.30) | Ref |
| *Steroid-free remission* | 43.1 | 37.8 | 1.25 (0.64-2.44) | Ref |

modified intention-to-treat analysis (mITT): switchers = outcome failure
per protocol analysis (PP): switchers are excluded

**Table 2**. 1-year effectiveness of week-14 responders of vedolizumab vs anti-TNF in bio-naïve UC-patients after induction phase in the PS-weighted $VEDO_{IBD}$ study

| Outcome | Vedolizumab | Anti-TNF | Vedolizumab | Anti-TNF |
|---|---|---|---|---|
| | % | % | OR 95%(CI) | |
| **Modified intention-to-treat analysis (n)** | 74 | 54 | 74 | 54 |
| *Clinical response* | 68.7 | 56.6 | 1.68 (0.55-5.10) | Ref |
| *Clinical remission* | 46.9 | 40.0 | 1.33 (0.49-3.58) | Ref |
| *Steroid-free remission* | 46.0 | 39.0 | 1.33 (0.49-3.60) | Ref |
| **Per protocol analysis (n)** | 64 | 37 | 64 | 37 |
| *Clinical response* | 80.8 | 76.7 | 1.28 (0.30-5.55) | Ref |
| *Clinical remission* | 57.4 | 53.4 | 1.18 (0.42-3.29) | Ref |
| *Steroid-free remission* | 56.2 | 52.0 | 1.19 (0.43-3.30) | Ref |

modified intention-to-treat analysis (mITT): switchers = outcome failure
per protocol analysis (PP): switchers are excluded

## Scientific Session 6: Do we see light at the end of the fistula track?

## OP18

### Efficacy and safety of filgotinib for the treatment of perianal fistulizing Crohn's Disease: Results from the phase 2 DIVERGENCE 2 study

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**Background:** Treatment of perianal fistulizing Crohn's disease (PFCD) is a major unmet need. Filgotinib (FIL) is a once-daily, oral, preferential Janus kinase 1 inhibitor in development for the treatment of

inflammatory bowel diseases. The efficacy and safety of FIL for the treatment of PFCD was evaluated in the phase 2, double-blind, randomized, placebo (PBO)-controlled DIVERGENCE 2 study (NCT03077412).

**Methods:** Patients (18–75 years old) with PFCD (documented diagnosis of CD for at least 3 months and 1–3 external openings [EOs] with drainage [spontaneous or on compression] for ≥ 4 weeks before screening) previously treated with antibiotics, immunomodulators and/or tumour necrosis factor inhibitors (TNFi) were randomized (2:2:1) to receive FIL 200 mg, FIL 100 mg or PBO once daily for up to 24 weeks. Active luminal CD was permitted providing that the Crohn's Disease Activity Index score was ≤ 300 at screening. The primary endpoint was combined fistula response (reduction of ≥ 1 from baseline in the number of draining EOs determined by investigator assessment and no fluid collections > 1 cm on centrally read pelvic magnetic resonance imaging [MRI]) at Week 24. Combined fistula remission (closure of all draining EOs present at baseline and no fluid collections > 1 cm) at Week 24 was a key secondary endpoint. The study was not powered for statistical comparisons and was prematurely terminated owing to low recruitment rates during the COVID-19 pandemic.

**Results:** Baseline characteristics were broadly similar across the treatment groups (Table 1). Overall, 91.2% of patients had complex perianal fistulae and TNFi treatment had previously failed in 64.9% of patients. A lower proportion of patients randomized to receive FIL 200 mg discontinued the study compared with those who received PBO (Table 2). The proportion of patients who achieved a combined fistula response at Week 24 was numerically higher in the FIL 200 mg group (47.1%; 90% confidence interval [CI]: 26.0–68.9) than in the PBO group (25.0%; 90% CI: 7.2–52.7) (Figure 1), with similar results observed for combined fistula remission (FIL 200 mg [47.1%; CI: 26.0–68.9] versus PBO [16.7%; CI: 3.0–43.8]) (Figure 2). Treatment-emergent severe adverse events were highest in the FIL 200 mg group (Table 2). Adverse event rates were otherwise similar across treatment groups.

**Table 1.** Baseline demographics and clinical characteristics

| Baseline characteristic | PBO (n=15) | FIL 100 mg (n=25) | FIL 200 mg (n=17) |
|---|---|---|---|
| Mean age, years (SD) | 39 (11.8) | 41 (14.0) | 39 (11.2) |
| Female, n (%) | 4 (26.7) | 10 (40.0) | 9 (52.9) |
| Mean duration of perianal fistulizing CD, years (SD) | 7.5 (7.94) | 11.9 (11.06) | 10.3 (8.29) |
| Mean CDAI Score (SD) | 190 (57.9) | 194 (67.1) | 190 (62.4) |
| Active luminal disease[a], n (%) | 11 (73.3) | 17 (68.0) | 13 (76.5) |
| Moderately active luminal disease[b], n (%) | 4 (26.7) | 10 (40.0) | 7 (41.2) |
| Mean PDAI Score, (SD) | 7 (3.1) | 8 (3.4) | 9 (3.1) |
| Complex perianal fistulae by MRI[c], n (%) | 13 (86.7) | 22 (88.0) | 17 (100.0) |
| Original Van Assche Score, mean (SD) | 11.4 (4.26) | 12.3 (3.84) | 14.9 (4.74) |
| Modified Van Assche Score, mean (SD) | 10.5 (3.44) | 11.5 (3.03) | 13.6 (3.69) |
| Prior failure of antibiotics for perianal fistulae, n (%) | 8 (53.3) | 12 (48.0) | 9 (52.9) |
| Prior failure of immunomodulators for perianal fistulae, n (%) | 6 (40.0) | 19 (76.0) | 12 (70.6) |
| Prior biologics used ≥3, n (%) | 4 (26.7) | 12 (48.0) | 6 (35.3) |
| Prior failure of TNFi therapy for perianal fistulae, n (%) | 9 (60.0) | 16 (64.0) | 12 (70.6) |
| Prior failure of vedolizumab, n (%) | 2 (13.3) | 4 (16.0) | 5 (29.4) |
| Prior failure of ustekinumab, n (%) | 3 (20.0) | 10 (40.0) | 3 (17.6) |

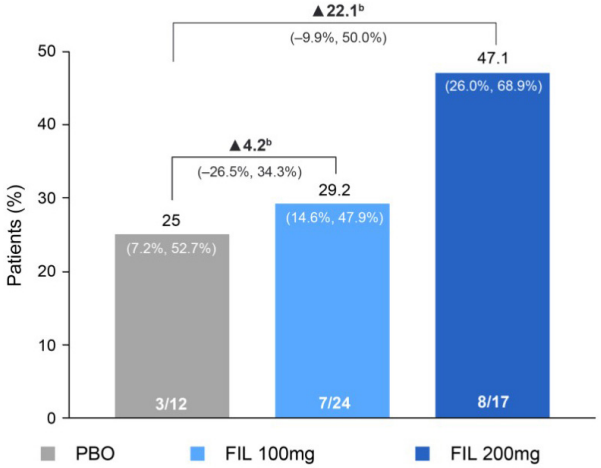
[a]Active luminal disease: CDAI ≥ 150
[b]Moderately active luminal disease: CDAI ≥ 220
[c]Complex perianal fistulae: multiple simple fistulae or single branched (multiple EOs arising from one fistula tract), trans-, extra- or suprasphincteric fistulae tracts, possible extensions and/or focal to small collections
CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; EO, external opening; FIL, filgotinib; MRI, magnetic resonance imaging; PBO, placebo; PDAI, Perianal Disease Activity Index; SD, standard deviation; TNFi, tumour necrosis factor inhibitor

**Table 2.** Adverse events and study discontinuation

| AEs and discontinuation, n (%) | PBO (n=15) | FIL 100 mg (n=25) | FIL 200 mg (n=17) |
|---|---|---|---|
| **Any TEAE** (%) | 11 (73.3) | 18 (72.0) | 14 (82.4) |
| **TESAE** (%) | 1 (6.7) | 2 (8.0) | 5[a] (29.4) |
| **Death** | 0 | 0 | 0 |
| **AEs of interest** | | | |
| Infections (%) | 8 (53.3) | 9 (36.0) | 11 (64.7) |
| Serious infections (%) | 1[b] (6.7) | 0 | 2[a] (11.8) |
| Herpes zoster (%) | 0 | 0 | 0 |
| Opportunistic infections (%) | 0 | 0 | 0 |
| Pulmonary embolism (%) | 0 | 0 | 0 |
| Venous thrombosis excluding PE (%) | 0 | 0 | 0 |
| **Discontinuation** | | | |
| All (%) | 9 (60.0) | 13 (52.0) | 3 (17.6) |
| TEAE (%) | 2 (13.3) | 2 (8.0) | 1 (5.9) |
| Non-responder (CD or PFD) at Week 10[c] (%) | 3 (20.0) | 5 (20.0) | 1 (5.9) |
| Protocol-specified disease worsening[d] (%) | 3 (20.0) | 3 (12.0) | 1 (5.9) |
| Investigator's discretion (%) | 1 (6.7) | 1 (4.0) | 0 |
| Withdrew consent (%) | 0 | 2 (8.0) | 0 |

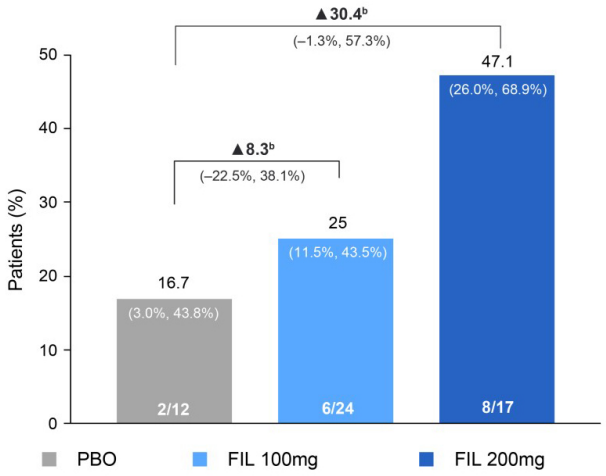
[a]One patient reported severe bronchitis, one patient reported suspected COVID-19
[b]One patient reported a vulval abscess
[c]Luminal disease non-responders were defined as patients who either had a baseline CDAI score ≥ 220 and never achieved a ≥ 70-point CDAI reduction from baseline at any point up to and including Week 10 or had a baseline CDAI score < 220 and had an increase in CDAI of ≥ 100 points from baseline, with CDAI ≥ 220 at Week 10. PFD non-responders were defined as patients who met the following PDAI symptom subscore criteria: 'Discharge' subscore > 1 and a ≥ 1-point increase from baseline, at Weeks 6 and 10 or 'Pain/restriction of activities' subscore > 1, and a ≥ 1-point increase from baseline, at Weeks 6 and 10
[d]Protocol-specified disease worsening was defined as a ≥ 100-point increase in CDAI score from the Week 10 value and CDAI score ≥ 220 points at two consecutive visits
AEs, adverse events; CD, Crohn's disease; FIL, filgotinib; PBO, placebo; PE, pulmonary embolism; PFD, perianal fistulizing disease; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event

**Figure 1.** Combined fistula response[a] at Week 24




[a]Combined fistula response was defined as the reduction of ≥ 1 from baseline in the number of draining external perianal fistula openings and absence of fluid collections of > 1 cm on MRI
[b]Risk difference in proportions (90% CI); non-responder imputation
CI, confidence interval; FIL, filgotinib; MRI, magnetic resonance imaging; PBO, placebo

**Figure 2.** Combined fistula remission[a] at Week 24




[a]Combined fistula remission was defined as perianal fistula closure of all EOs that were draining at baseline and absence of fluid collections > 1 cm on MRI
[b]Risk difference in proportions (90% CI); non-responder imputation
CI, confidence interval; EO, external opening; FIL, filgotinib; MRI, magnetic resonance imaging; PBO, placebo

**Conclusion:** In this phase 2 study, numerically higher fistula response and remission rates were observed after 24 weeks of treatment with FIL 200 mg versus PBO in patients with active PFCD and a history of multiple medical treatment failures. FIL was well tolerated overall. Further studies of FIL for the treatment of PFCD are warranted.

## OP19

## Classifying perianal fistulising Crohn's Disease: An expert-consensus to guide decision-making in daily practice and clinical trials

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**Background:** Perianal fistulising Crohn's disease (CD) is an aggressive disease phenotype that can have a significant impact on patients' quality of life. Current biological understanding of perianal fistulising CD remains inadequate and previous classification systems have not provided clear guidance on therapy in clinical practice nor on defining patient cohorts within clinical trials. To counter this unmet need, we propose a new classification system for perianal fistulising CD.
**Methods:** The proposed classification system was developed through a modified nominal group technique expert consensus process involving open discussion and formal voting on previously defined statements. Consensus agreement was defined a priori as 80% voting "strongly agree" or "agree with minor reservation". Participants included gastroenterologists, radiologists, surgeons active in a tertiary IBD centre and a patient representative.
**Results:** The classification identifies four groups of patients with perianal fistulising CD. Key elements include stratification according to disease severity as well as disease outcome; synchronisation of patient and clinician goals in decision making, with a proactive, combined medical and surgical approach, on a 'treat to patient goal' basis; and identification of indications for curative fistula treatment, diverting ostomy and proctectomy. The new classification retains an element of