a slightly higher relative prevalence in UC. Patients with CD tended to have a higher probability of ACI, either alone or in combination with IDA. Besides effective iron therapy, inflammation management is therefore an important prerequisite for effective anaemia therapy in patients with IBD and iron-related anaemia.

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Surgery management of Crohn's disease in children: our experience

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Background: Classically, surgical treatment in paediatric Crohn's disease (CD) was the last option after the failure of available medical treatments. Currently, surgery is offered in patients with localised inflammatory activity despite optimised medical treatment or in patients with complications of the disease in early stages. The aim of our study is to review our experience to know the phenotype of patients who need surgery, surgical technique used and short- and medium-term results.
Methods: Retrospective cohort study of patients with paediatric CD who underwent surgery (excluding surgery of perianal disease) between 2012 and 2017 in a tertiary paediatric hospital. Epidemiological, clinical, analytical, radiological, endoscopic and surgical variables were collected and analysed.
Results: Twenty-five patients had required surgical treatment (52% males). Mean age at diagnosis was 11.6 ± 2.5 years, with a median (IQR) from the onset of symptoms to diagnosis of 0.74 (1) years. Mean time from diagnosis to the date of surgery was 2.5 ± 2 years. Forty per cent had a structuring behaviour at debut, 4% penetrating and 12% both of them. The most frequent location was ileocolonic (60%). Regarding the treatments received before surgery, 68% had received exclusive enteral nutrition and immunosuppressives, 20% corticosteroids and immunosuppressives, 20% anti-TNF-α treatment in monotherapy and 84% biological treatment (anti-TNFα/vedolizumab/ustekinumab) with immunosuppressives. The most frequent surgical indication was recurrent intestinal obstruction (84%). All interventions were initiated by laparoscopy although 12% were converted to laparotomy. Eighty-four per cent of the patients had a single resection, 8% multiple resections, and in the remaining an ileostomy without resection was performed. Ileocaecal area was resected in 78.3% of the patients and in 2 patients a single strictureplasty was performed. Mean surgical time was 3.8 ± 1.2 h and the average number of days of admission was 8.2 ± 3.3. There were no cases of surgical wound infection or postoperative ileus. For prevention of postoperative recurrence, 96% of patients received biological treatment (anti-TNF-α, ustekinumab) ± immunosuppressives. To date, endoscopic control has been performed in 13 patients (between 6 and 12 months after surgery) with the following Rutgeerts index: i0 46.1%; i1 30.8%; i2 15.4%; i4 7.7%. At follow-up, one patient required surgical re-intervention.
Conclusions: Although new biological treatments has reduced the need of surgery in paediatric Crohn's disease, a surgical approach by experienced teams, could be an effective and safe alternative in selected cases with complicated disease or unresponsive to medical treatment.

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Rapidity of symptomatic and inflammatory biomarker improvements following upadacitinib induction treatment: data from the U-ACHIEVE study

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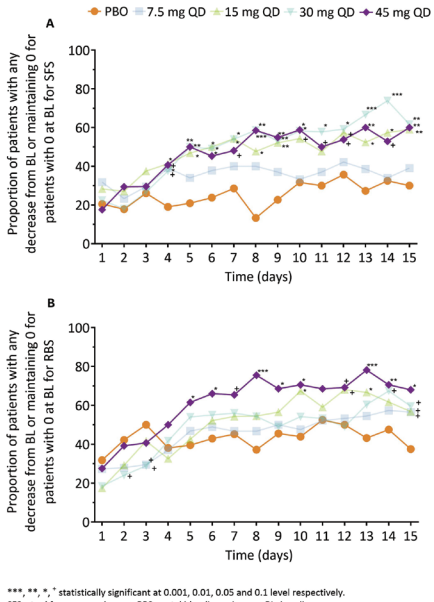
Background: Upadacitinib (UPA), an oral, selective Janus Kinase 1 inhibitor, demonstrated improved efficacy compared with placebo (PBO) in a Phase 2b induction study in patients with moderately-to-severely active ulcerative colitis (UC).[1] This analysis assessed the time to onset of symptomatic improvement, clinical response, and improvement in biomarkers during the induction phase of U-ACHIEVE.
Methods: Adult patients with moderately to severely active UC were randomised to double-blind therapy with extended-release UPA 7.5, 15, 30, 45 mg once daily (QD) or PBO for 8 weeks. Data from patient daily diary (as observed) on Mayo stool frequency subscore (SFS, 0–3) and rectal bleeding subscore (RBS, 0–3), as well as bowel urgency (BU, Y/N) and abdominal pain (AP, 0–3) were examined daily in the first 15 days of therapy. The proportion of patients with clinical response per partial Mayo score (decrease from baseline [BL] in Partial Mayo score ≥ 2 points and ≥ 30%, PLUS a decrease in RBS ≥ 1 or an absolute RBS ≤ 1), and the change from BL in high-sensitivity C-reactive protein (hs-CRP) and faecal calprotectin (FC) were evaluated at Week 2. Comparisons between each UPA dose with PBO for proportions was assessed by Cochran–Mantel–Haenszel tests and mean change from BL by analysis of covariance with treatment and randomisation factors as covariate.
Results: A total of 250 patients were randomised. The mean SFS was 2.7 and RBS was 1.7 at BL. Trends of higher proportion of patients achieving symptom improvement in SFS and RBS were observed in the UPA 45 mg group than PBO as early as Day 4 (figure) and reached statistical significance ($p < 0.05$) by Day 8 in SFS, RBS, BU, and AP (Table 1).

Figure. Proportion of patients with (A) any decrease from baseline or maintaining 0 for patients with 0 at baseline for SFS and (B) any decrease from baseline or maintaining 0 for patients with 0 at baseline for RBS.



***, **, *, ˚ statistically significant at 0.001, 0.01, 0.05 and 0.1 level respectively.
SFS: stool frequency subscore; RBS: rectal bleeding subscore; BL: baseline.

Table 1. Proportion of patients with SFS =1, RBS = 0, AP =1, and no BU at Day 8.

	PBO	UPA 7.5 mg QD	UPA 15 mg QD	UPA 30 mg QD	UPA 45 mg QD
Proportion of patients with SFS ≤1	6/43 (14.0)	14/45 (31.1)$^{+}$	12/44 (27.3)	15/46 (32.6)*	21/53 (39.6)**
Proportion of patients with RBS = 0	9/43 (20.9)	16/45 (35.6)	19/44 (43.2)*	21/46 (45.7)*	33/53 (62.3)***
Proportion of patients with no BU	2/41 (4.9)	6/40 (15.0)	11/40 (27.5)**	9/42 (21.4)*	19/50 (38.0)***
Proportion of patients with AP ≤ 1 [a]	11/20 (55.0)	11/23 (47.8)	8/21 (38.1)	15/23 (65.2)	23/28 (82.1)*

***, **, *, $^{+}$ statistically significant at 0.001, 0.01, 0.05 and 0.1 level respectively.
PBO: placebo; UPA: upadacitinib; QD: once daily; SFS: stool frequency subscore; RBS: rectal bleeding subscore; BU: bowel urgency; AP: abdominal pain.
[a] The analyses were conducted among patients with AP >1 at BL.

At Week 2, the proportion of patients with clinical response and the median change from BL in hs-CRP was statistically significantly greater in the UPA 15, 30, and 45 mg QD groups vs. the PBO group (Table 2).

Table 2. Clinical and biomarker outcomes at Week 2.

Endpoints	Placebo n=46	UPA 7.5 mg QD n=47	UPA 15 mg QD n=49	UPA 30 mg QD n=52	UPA 45 mg QD n=56
Clinical response per partial Mayo score[a], n (%)	7 (15.2)	11 (23.4)	18 (36.7)*	19 (36.5)*	31 (55.4)***
Mean change from baseline in hs-CRP (mg/L)[b] Median (range)	0.095 (-15.98, 30.10)	-2.150*** (-20.58, 4.30)	-5.275** (-115.37, 36.84)	-4.950*** (-45.00, 2.93)	-3.090*** (-61.73, 19.69)
Mean change from baseline in FC (mcg/g)[b] Median (range)	-365.0 (-11820, 8522)	-382.5 (-6593, 13420)	-662.0 (-15174, 25639)	132.0 (-17838, 5341)	-659.0 (-16528, 11610)

***, **, * statistically significant at 0.001, 0.01, and 0.05 levels, respectively.
[a] non-responder imputation analysis; [b] last observation carried forward analysis.
UPA: upadacitinib; QD: once daily; hs-CRP: high sensitivity C-reactive protein; FC: faecal calprotectin.

Conclusions: Early symptomatic improvement, as early as Day 4, was observed with UPA treatment in patients with active UC, concurrent with a rapid decrease in markers of inflammation.

Reference

1. Sandborn WJ, Ghosh S, Pans J, *et al*. Efficacy and safety of upadacitinib as an induction therapy for patients with moderately-to-severely active ulcerative colitis: data from the phase 2b study U-ACHIEVE. In: United European Gastroenterology (UEG) Week, Presentation #OP195, 20–24 October 2018, Austria Center Vienna, Vienna, Austria.

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Darvadstrocel treatment outcomes in Crohn's disease patients with complex perianal fistulas: the role of TNFi co-treatment in ADMIRE CD

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Background: Darvadstrocel (DVS) is an expanded, allogeneic, adipose-derived, mesenchymal stem cell therapy indicated in the treatment of complex perianal fistulas (CPAF) in patients with Crohn's disease (CD).[1,2] In ADMIRE CD (NCT01541579), a pivotal Phase 3, double-blind, randomised study, more patients who received DVS in addition to standard of care achieved combined remission at Weeks 24 and 52 compared with standard of care with placebo (PBO).[1,2] This post-hoc analysis assessed the role of co-treatment with tumour necrosis factor inhibitors (TNFi) on the outcomes for DVS therapy in treatment-refractory patients with CPAF in CD.

Methods: In ADMIRE CD patients were randomised to receive DVS or PBO. Allowed co-treatments were TNFi or immunomodulators (IMM). Randomisation was stratified by co-treatment received at baseline. This analysis was performed on the modified intent-to-treat population (mITT) (received study treatment and had at least one post-baseline efficacy assessment). Two subgroups were examined: TNFi co-treatment (with or without IMM); and no co-treatment. The outcomes examined were combined remission (clinical assessment of closure of all treated external openings draining at baseline, and the absence of collections >2 cm confirmed by MRI) and clinical remission (closure of all treated external openings that were draining at baseline despite gentle finger compression) at Weeks 24 and 52.

Results: In both subgroups at Weeks 24 and 52, the proportion of patients achieving combined and clinical remission in the DVS arm was greater than with PBO. TNFi with DVS achieved and sustained greater clinical remission compared with TNFi with PBO at Week 24 (58.7% vs. 50.0%) and Week 52 (61.9% vs. 43.5%). In the TNFi subgroup, the number of treatment-emergent adverse events related to study treatment was greater in the PBO arm than in the DVS arm, the most frequent being anal abscess.

Conclusions: In patients not receiving TNFi co-treatment, at Week 52 DVS compared with PBO had a benefit of similar magnitude compared with patients receiving concomitant TNFi. At Week 52, only the DVS groups achieved >60% clinical remission regardless of TNFi use. In summary, with or without TNFi, DVS consistently provided greater benefit than PBO alone. Further studies with larger cohorts are needed to confirm these post-hoc observations.

Table 1. Combined and clinical remission at Week 24 by TNFi co-treatment (mITT population). *LOCF rules applied. **No TNFi or IMM co-treatment at baseline. ***Patients co-treated with IMM only.

	Combined remission,* 24 weeks			Clinical remission,* 24 weeks		
Co-treatment	DVS *n*, % (95% CI)	PBO *n*, % (95% CI)	Treatment difference (p.p.) (95% CI)	DVS n, % (95% CI)	PBO n, % (95% CI)	Treatment difference (p.p.) (95% CI)
TNFi (with or without IMM) *n* = 125	35, 55.6 (43.3 to 67.8)	26, 41.9 (29.7 to 54.2)	13.6 (–3.7 to 31.0)	37, 58.7 (46.6 to 70.9)	31, 50.0 (37.6 to 62.4)	8.7 (–8.7 to 26.1)
No co-treatment** *n* = 43	13, 54.2 (34.2 to 74.1)	4, 21.1 (2.7 to 39.4)	33.1 (6.0 to 60.2)	14, 58.3 (38.6 to 78.1)	5, 26.3 (6.5 to 46.1)	32.0 (4.1 to 60.0)
Full mITT population*** *n* = 204	53, 51.5 (41.8 to 61.1)	36, 35.6 (26.3 to 45.0)	15.8 (2.4 to 29.2)	57, 55.3 (45.7 to 64.9)	43, 42.6 (32.9 to 52.2)	12.8 (–0.8 to 26.4)
Confidence interval [CI]	Percentage points (p.p.)					