International Journal of Colorectal Disease (2019) 34:451–457
https://doi.org/10.1007/s00384-018-3212-6

ORIGINAL ARTICLE

Surgical outcomes of patients treated with ustekinumab vs. vedolizumab in inflammatory bowel disease: a matched case analysis

Matteo Novello[1] · Luca Stocchi[1] · Stefan Holubar[1] · Sherief Shawki[1] · Jeremy Lipman[1] · Emre Gorgun[1] · Tracy Hull[1] · Scott R. Steele[1]

Accepted: 30 November 2018 / Published online: 10 December 2018
© Springer-Verlag GmbH Germany, part of Springer Nature 2018

Abstract

Aim The association between preoperative use of monoclonal antibodies in inflammatory bowel disease (IBD) patients and postoperative complications is controversial, especially for the latest approved biologics, ustekinumab and vedolizumab, where data is limited. We hypothesized that ustekinumab-treated patients would have a similar overall postoperative complication rate as vedolizumab-treated patients. The aim of this study was to compare postoperative complications in patients receiving preoperative ustekinumab vs. vedolizumab.

Methods We queried our IRB-approved prospective database to identify Crohn's patients who underwent colorectal surgery and pretreatment with ustekinumab or vedolizumab within 12 weeks of surgery. Ustekinumab-treated patients were matched to vedolizumab-treated patients based on sex, age ± 5 years, date of operation ± 3 years, and type of surgery. Paired univariate analysis and conditional logistic regression of the matched pairs were performed. Our primary outcome was the short-term postoperative complication rate. Secondary outcomes included infectious complications, readmission, reoperation, and length of stay.

Results A total of 103 patients with Crohn's disease (CD) met the inclusion criteria (mean age 38.7 ± 13.4 years; male 51.2%). Overall, 30 patients received preoperative ustekinumab and 73 vedolizumab. In the univariate analysis, vedolizumab-treated patients had a higher postoperative complication rate ($p = 0.009$) and ileus rate ($p = 0.015$). After matching, 26 matched pairs were compared and logistic regression models demonstrated no significant difference in the primary outcome.

Conclusions For our limited experience, the choice of preoperative biologic treatment between ustekinumab and vedolizumab should not be influenced by fear of surgical complications.

It was presented as an E-poster at "The American Society of Colon and Rectal Surgeons 2018 Annual Scientific Meeting" in Nashville, TN, USA, May 19–23, 2018.

What does this paper add to the literature?
The association between preoperative use of ustekinumab and vedolizumab in inflammatory bowel disease patients and postoperative complications is controversial. Considering the little data available in literature and the increasing use of these biologics, we believe it is important to shed light on their preoperative use with respect to postoperative complications.

✉ Scott R. Steele
steeles3@ccf.org

Matteo Novello
matteo.novello@studio.unibo.it

Luca Stocchi
stocchl@ccf.org

Stefan Holubar
holubas@ccf.org

Sherief Shawki
shawkis@ccf.org

Jeremy Lipman
lipmanj@ccf.org

Emre Gorgun
gorgune@ccf.org

Tracy Hull
hullt@ccf.org

[1] Department of Colorectal Surgery, Digestive Disease & Surgery Institute, Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195, USA

Keywords Ustekinumab · Vedolizumab · Biologics · Colorectal surgery · Outcomes · Morbidity · Mortality · Comparison

Introduction

One of the most common indications of surgical intervention in IBD is refractoriness to medical treatment. Many biologic agents have been introduced sequentially to the medical armamentarium in managing ulcerative colitis (UC) and Crohn's disease (CD). Available in 2014, vedolizumab (VEDO) is a human monoclonal antibody that selectively inhibits leukocyte adhesion and migration into the gastrointestinal tract by binding to the α4β7 integrin. It was implemented in treating CD and UC as escalation therapy after failing other conventional medical treatments. Subsequently, ustekinumab (USTE), a human monoclonal antibody which binds to interleukin-12 and interleukin-23 preventing inflammatory cellular activation, was Food and Drug Administration–approved in 2016, though it is currently approved only for CD.

While these agents were shown to achieve remission in 53.1% [1] (USTE, CD) and 44.8% [2] (VEDO, CD) of patients respectively, some patients will not respond and progress to surgery. Usually, this happens in the context of refractory disease or progression while on medical therapy, indicating failure of medical management prompting surgical intervention. In this event, surgery is usually offered while the patient is still receiving the biologic agent. While the type of surgery needed depends on the disease and its sequelae, whether it is UC or CD, the impact of the preoperative biologic on the perioperative course and complications remains controversial.

After performing a study at our department, we noticed that preoperative VEDO is comparable to other biologics, such as infliximab and adalimumab, with respect to the postoperative complication rate. However, there are two other similar studies available in the literature regarding VEDO which present partially contradictory conclusions [3, 4]. Lightner and colleagues reported the link between the use of preoperative VEDO and risk of surgical site infection (SSI) in patients with IBD, while Yamada and colleagues stated that preoperative VEDO administration did not influence the postoperative morbidity rate. Additionally, the first study evaluating preoperative USTE was recently published and did not find a significant difference in terms of SSI when comparing it to preoperative anti-TNF-α exposure [5]. The administration of this new generation of biologics is increasing, and it is necessary to optimize the preoperative treatment of this patient population. To our knowledge, no study had compared the pattern of postop complications associated with preoperative treatment with USTE to VEDO.

Therefore, the aim of this study was to compare postoperative complications after colorectal surgical procedures for IBD in patients receiving VEDO vs. USTE. We hypothesized that USTE-treated patients would have a similar overall postoperative complication rate as compared to VEDO-treated patients.

Methods

We conducted a retrospective, single tertiary center, case-matched study of a prospectively maintained database. We queried our IRB-approved prospective database to identify patients with CD undergoing abdominal surgery from May 2014 until October 2017, corroborated by chart review. We stratified patients into two groups on the basis of monoclonal antibody treatment within 12 weeks from surgery: VEDO vs. USTE. Patients undergoing anorectal surgery alone and those who had treatment with anti-TNF-α agents within 12 weeks from surgery were excluded. The primary endpoint was overall morbidity occurring within the first 30 days after colorectal surgery for IBD. Secondary outcomes included 30-day infectious complications, readmission, reoperation, and postoperative length of stay.

Data abstracted included patient demographics, gender, age at the time of surgery, smoking history, comorbidities, duration of VEDO therapy, surgical procedure details, postoperative complications, postoperative packed red blood cell (PRBC) transfusion, postoperative length of hospital stay, reoperation, readmission, and mortality. Specific postoperative complications occurring within 30 days after surgery included surgical site infections (SSI, superficial or organ space), fascial dehiscence, perineal wound infection, anastomotic leak, other enteric leak, rectal stump leak, pneumonia, *Clostridium difficile* infection, sepsis, sterile fluid collection, stoma complication, small-bowel obstruction (SBO), ileus, bleeding, dehydration, and urinary tract infection (UTI). The variable "Any infection" was defined as the patient having at least one of the following considering the Center of Disease Control definitions [6]: superficial SSI and/or organ space SSI (intra-abdominal and/or pelvic abscess). Ileus was defined as the absence of bowel function on postoperative day 5 or the need for nasogastric tube insertion due to abdominal distension, nausea, or vomiting after initiating a liquid diet without evidence of mechanical bowel obstruction [7]. Dehydration was defined as ostomy output of 1500 mL over 24 h and a blood urea nitrogen/creatinine ratio ≥ 20 and/or physical findings of dehydration [8]. Hospital readmissions and reoperations were counted when occurring within 30 days from the date of hospital discharge. We collected data on preoperative medication use within 1 month from surgery for corticosteroids, opioid analgesics, and mesalamine (and derivatives). Preoperative immunomodulator use (azathioprine/6-

mercaptopurine, methotrexate) was considered positive when within 2 months from surgery. In addition, current or past use of biologic agents was carefully reported. The variable "Biologics tried any time before surgery" was not recorded for the vedolizumab group. Nutritional status was evaluated by collecting serum albumin within 30 days from the operation.

Case matching was performed to directly match USTE-treated patients to VEDO-treated patients on a 1:1 basis. The matching criteria were age ± 5 years, surgery date ± 2 years, gender, and procedure. The procedures selected were all elective and the three groups were defined as follows: group 1, completion proctectomy (CP) + end ileostomy (EI), total abdominal colectomy (TAC) + EI, proctectomy + EI, total proctocolectomy (TP) + EI, Hartmann's procedure, ostomy procedure, TAC with ileorectal anastomosis + ostomy; group 2, segmental resection, ileocolic resection, enterectomy; group 3, strictureplasty isolated; group 4, other pouch procedures. We selected these combinations so that in group 1, we could include major resections with stoma and in group 2 segmental resections. Group 4 was not densely populated and was excluded from the matching process because of no matching patients available in the VEDO group.

Statistical analysis

Univariate analyses were conducted to compare the demographics and preoperative variables of the USTE and VEDO groups. Pearson's chi-square test or Fisher's exact test was used for categorical factors, and ANOVA or the Kruskal-Wallis test was applied for continuous factors as appropriate. A descriptive paired univariate analysis was conducted on the matched sample to analyze the balance of other patient characteristics between treatment groups. Paired Student's *t* test or Wilcoxon signed-rank test was used for continuous factors, and McNemar's tests or Bowker's test of symmetry was used for categorical variables.

A conditional logistic regression model of the matched pairs was fit to assess readmission, reoperation, and overall and specific complications. Lastly, a linear mixed model treating the matched pairs as a random effect was fit to evaluate the impact of treatment on length of stay. p values < 0.05 were considered statistically significant. All analyses were performed using SAS (version 9.4, The SAS Institute, Cary, NC).

Results

A total of 103 patients with CD were included (mean age 38.7 ± 13.4 years; male 46.6%). Overall, 73 were treated with VEDO preoperatively and 30 received USTE (Table 1). Thirty-seven percent of cases in the USTE group were previously treated with VEDO; thus, the number of other biologics failed before surgery was significantly different between the cohorts ($p < 0.001$). Regarding differences in baseline and operative characteristics, the VEDO-treated patients presented more frequently with "Anemia/bleeding/preoperative transfusion required" (15.8% vs. 0%, $p = 0.0022$). The most common category of procedure was group 1 ($N = 35$, 48.6%). Baseline characteristics after matching are shown in Table 2. Overall, 26 matched pairs were successfully constructed and there was no difference in age, surgery date, gender, diagnosis, and procedures. Preoperative use of immunomodulators, corticosteroids, opioids, mesalamine, albuminemia, and comorbidities was all comparable among the groups in the matched paired univariate analysis. There was no significant difference among the matched pairs when comparing the number of patients who had other biologics than those who had USTE/VEDO respectively within 12 weeks ($p = 0.66$) and 1 year from surgery ($p = 0.56$).

With respect to the unmatched outcomes (Table 3), VEDO-treated patients had a higher overall postoperative complication rate (54.8% vs. 26.7%, $p = 0.009$) and an increased ileus rate (23.3% vs. 3.3%, $p = 0.015$). A total of 4 (5.5%) VEDO-treated patients required reoperation compared with zero in the USTE group ($p = 0.59$).

A linear mixed model showed that patients treated with USTE stayed 1.1 days less than patients who received VEDO; however, this was not statistically significant (95% confidence interval [CI] − 4.4, 2.3; $p = 0.52$). Eleven percent ($N = 3$) of the VEDO-treated patients vs. 59% ($N = 16$) of the USTE-treated patients had an open procedure performed ($p = 0.002$): ostomy procedures were more common in the USTE group (30.1%, $N = 8$) than in the VEDO group (11.1%, N = 3), even though this difference was not statistically significant. In addition, the increased ileus rate identified in the univariate unmatched analysis was not confirmed at the paired univariate analysis ($p = 0.21$).

For the paired analysis of outcomes, the conditional logistic regression model (Table 4) showed no significant difference among the matched pairs for overall complications, infectious complication, readmission rate, dehydration, enteric leak, intra-abdominal abscess, perineal wound infection, pneumonia, sepsis, organ space SSI, and superficial SSI.

Discussion and conclusion

This study demonstrated that IBD cases selected to undergo surgery following treatment with USTE had a similar risk of overall postoperative complications and perioperative outcomes as compared to VEDO administration. We designed our study to evaluate the introduction into our practice of two new biologic medications with very different pharmacodynamics from the most commonly used anti-TNF-α agents,

Table 1 Demographics and preoperative variables of unmatched retrospective cohorts

Factor	VEDO ($N = 73$)	USTE ($N = 30$)	p value
Male gender	36 (49.3)	12 (40.0)	0.39[c]
Age at surgery (years)	39.7 ± 13.3	36.3 ± 13.7	0.25[a]
Body mass index (kg/m^2)	24.9 ± 6.2	23.4 ± 7.1	0.29[a]
Race			0.32[d]
Hispanic	2 (2.7)	2 (6.7)	
Not Hispanic	70 (95.9)	28 (93.3)	
Duration of therapy before surgery (days)	208.6 ± 186.9	NA	NA
Time from last dose to surgery (days)	41.1 ± 23.8	50.9 ± 30.1	0.082[a]
Pulmonary comorbidity	4 (5)	0 (0)	0.35[c]
Cardiovascular comorbidity	8 (10.7)	4 (12.5)	0.75[c]
Renal comorbidity	1 (1.4)	0 (0)	1.0[c]
Anemia/bleeding/preoperative transfusion required	9 (15.8)	0 (0)	*0.022*[c]
Preoperative albumin (g/dL)	3.6 ± 0.6	3.7 ± 0.4	0.39[a]
Diabetes	3 (4.1)	0 (0)	0.99[d]
Number of other biologics failed before surgery	2.0 (0.00, 4.0)	3.0 (0.00, 4.0)	*< 0.001*[b]
Biologics tried any time before surgery			NA
Adalimumab	NA	27 (90.)	
Infliximab	NA	26 (86.7)	
Vedolizumab	NA	11 (36.7)	
Certolizumab	NA	12 (40)	
Procedure group			0.54[d]
Group 1	35 (48.6)	14 (46.7)	
Group 2	34 (47.2)	13 (43.3)	
Group 3	2 (2.8)	1 (3.3)	
Group 4	1 (1.4)	2 (6.7)	
Any new stoma	59 (80.8)	19 (63.)	0.07[c]
Other biologics within 3 months from surgery	3 (4.1)	4 (13.3)	0.66[c]
Other biologics within 1 year from surgery	33 (45.2)	15 (50.0)	0.70[c]
Preoperative immunomodulators	18 (24.7)	9 (30.0)	0.58[c]
Preoperative mesalamine (and derivatives)	13 (17.8)	2 (6.7)	0.15[c]
Preoperative corticosteroids	37 (50.7)	14 (46.7)	0.71[c]
Opioids within 1 month preoperatively	28 (38.4)	11 (36.7)	0.87[c]

Statistics are presented as mean ± SD, median (min, max), or N (column %)

p values: a = ANOVA, b = Kruskal-Wallis test, c = Pearson's chi-square test, d = Fisher's exact test. $P < 0.05$

but also concerning for leading to perioperative complications [3, 5]. VEDO was selected as the control group medication since it presents similar indications in the management of the patient with refractory CD with respect to USTE. In addition, they are both representatives of a new generation of non-anti-TNF biologics. When comparing the effects of biologic agents, it is important to take into account the half-life of the antibody since it might have a substantial impact on the patient's conditions. The medications must be both taken every 8 weeks, and their half-life is similar, being approximately 19 days for USTE [9] and 25 days for VEDO [10]. Additionally, the duration from last dose to the subsequent surgery date was comparable between our study groups and never exceeded 12 weeks, since this was an inclusion criterion based on previous reports from the Mayo Clinic [3, 5]. We believe that the time difference between the two half-lives is not large enough to justify a clinically significant influence on the postoperative outcomes.

The case-matched approach allowed us to carefully balance the two cohorts and compare patients with similar characteristics. We case-matched based on demographics, date of surgery, and specific procedures performed. We excluded individuals who underwent surgery without receiving biologics and those who had treatment with anti-TNF-α agents within 12 weeks from surgery since this would have triggered a further selection bias in an already diverse patient population. In fact, our results show that USTE and VEDO are typically used as fourth- or fifth-line biologic agents at our institution, and

Table 2 Demographics and preoperative variables of matched retrospective cohorts

Factor	VEDO ($N = 26$)	USTE ($N = 26$)	p value
Male gender	11 (42.3)	11(42.3)	–
Age at surgery (years)	38.5 ± 11.7	38.4 ± 13.2	0.96[a]
Body mass index (kg/m^2)	23.6 ± 5.6	23.7 ± 7.6	0.95[a]
Race			0.56[c]
Hispanic	1 (3.8)	2 (7.7)	
Not Hispanic	25 (96.2)	24 (92.3)	
Time from last dose to surgery (days)	40.3 ± 23.1	49.5 ± 30.1	0.29[a]
Number of other biologics failed before surgery	1.00 (0.00, 3.0)	3.0 (1.00, 4.0)	*< 0.001*[b]
Preoperative albumin (g/dL)	3.5 ± 0.7	3.7 ± 0.5	0.28[a]
Diabetes	2 (7.7)	0 (0.0)	0.24[c]
Biologics tried any time before surgery			NA
Adalimumab	NA	24 (92.3)	
Infliximab	NA	23 (88.5)	
Vedolizumab	NA	11 (42.3)	
Certolizumab	NA	12 (46.2)	
Procedure group			–
Group 1	14 (53.8)	14 (53.8)	
Group 2	11 (42.3)	11 (42.3)	
Group 3	1 (3.8)	1 (3.8)	
Any new stoma	24 (84.6)	17 (65.4)	0.13[d]
Other biologics within 3 months from surgery	3 (11.5)	4 (15.4)	0.66[c]
Other biologics within 1 year from surgery	16 (61.5)	14 (53.8)	0.56[c]
Preoperative immunomodulators	6 (23.1)	8 (30.8)	0.48[c]
Preoperative mesalamine (and derivatives)	3 (11.5)	2 (7.7)	0.65[c]
Preoperative corticosteroids	9 (34.6)	11 (42.3)	0.53[c]
Opioids within 1 month preoperatively	12 (46.2)	11 (42.3)	0.78[c]

Statistics are presented as mean ± SD, median (min, max), or N (column %)

p values: a = Paired t test, b = Wilcoxon signed-rank test, c = McNemar's test, d = Bowker's test of symmetry. $P < 0.05$

most of the patients received either medication after failing treatment with anti-TNF-α agents. The data that 40% of the USTE-treated patients were previously treated with VEDO frames USTE as a last therapeutic resource given the novelty that it represents and the consequent lack of data in the literature. Moreover, this fact is supported by the remarkable rates of preoperative administration of narcotics ($N = 55$, 32.0%) and corticosteroids ($N = 105$, 61.0%) which, besides suggesting a generalized advanced disease status, have also been shown to increase postoperative infections rates [11–16].

Our department showed in a case-matched study, not yet published, that preoperative VEDO is comparable to other biologics, such as infliximab and adalimumab, with respect to the postoperative complication rate. Thus, such results are closer to those reported by Yamada [4] and colleagues who demonstrated that preoperative VEDO administration did not influence the postoperative morbidity rate of patients undergoing surgery for IBD. To the best of our knowledge, there is only one study in the literature regarding the safety of preoperative USTE in colorectal surgery [5]. Lightner and colleagues concluded that USTE treatment within 12 weeks of surgery did not appear to increase the risk of infectious complications above that of CD patients treated with anti-TNF-α medications. In the univariate analysis, the USTE-treated patients had a significantly higher rate of return to the operating room; however, none of the examined variables were significant in the multivariate analysis. As stated by the authors, that study had several limitations. Data were obtained from six institutions, which might imply a variability of the overall patient management. It is striking that patients were enrolled during clinical trials, before the final FDA approval of USTE, thereby possibly assuming different doses/regimens than the officially approved ones [1]. In addition, the operations performed were grouped under the definition of "major abdominal procedure" which is rather non-specific and might as well refer to non-colorectal procedures. The specific surgery performed may be significantly associated with the risk of postoperative complications [17]. We therefore tried to avoid this confounding factor by

Table 3 Overall postoperative outcomes

Variable	VEDO ($N = 73$)	USTE ($N = 30$)	p value
Length of stay	8.4 ± 6.6	6.9 ± 5.3	0.27[a]
Any postoperative complication	40 (54.8)	8 (26.7)	*0.009*[c]
Overall infectious complications	11 (15.1)	7 (23.3)	0.32[c]
Sepsis	3 (4.1)	1 (3.3)	0.99[d]
Organ space SSI	4 (5.5)	1 (3.3)	0.99[d]
Superficial SSI	6 (8.2)	3 (10.0)	0.77[c]
Readmission	10 (13.7)	2 (6.7)	0.31[c]
Reoperation	4 (5.5)	0(0.0)	0.59[d]

Statistics are presented as mean ± SD, median [P25, P75], or N (column %)

p values: a = ANOVA, b = Kruskal-Wallis test, c = Pearson's chi-square test, d = Fisher's exact test. $P < 0.05$

enrolling only cases of elective abdominal colorectal procedures, which were case-matched according to the type of procedure performed.

Our study was limited by its single institution non-randomized retrospective nature. It is important to point out that VEDO is FDA-approved for both UC and CD, while USTE is only approved for CD. This indication might expand to include UC largely depending on the results of the UNIFI trial, the results of which should be available in November 2021 [18]. Nevertheless, we included only Crohn's patients and tried to address the heterogeneity of our patient sample by performing a case-matched analysis. As a tertiary care facility that has a more complex referral base, our results may not represent other institutions as a whole. Further, there is a small possibility that some of these patients may ultimately carry a diagnosis of indeterminate colitis and not CD. Since USTE was approved by the FDA in September 2016, our project includes just 12 months of data, thereby limiting the statistical power of the model. Our study may be underpowered to detect a difference or rather a failure to identify a true difference as seen in the univariate analysis, and there is the potential risk of bias given the heterogeneity of the grouped cohorts.

In addition, there was an association with an increased number of patients with anemia or bleeding in the VEDO group. At the present time, the authors feel this is not a true cause, and effect association and further evaluation with longer follow-up and larger experience will determine if this remains the same.

Table 4 Postoperative outcomes in the case-matched (1:1) logistic regression for ustekinumab vs. vedolizumab

Variable	Odds ratio (95% CI)	p value
Any postoperative complication	0.38 (0.10, 1.4)	0.15
Overall infectious complications	1.5 (0.42, 5.3)	0.53
Sepsis	1.00 (0.06, 16.0)	0.99
Organ space SSI	0.50 (0.05, 5.5)	0.57
Superficial SSI	1.00 (0.14, 7.1)	0.99
Readmission	0.25 (0.03, 2.2)	0.21

$N = 27$ patients in each group

Despite these limitations, this is the first study in the literature comparing USTE and VEDO from a surgical point of view. Considering the short study time frame, we were able to provide a first insight on these cases only thanks to the high volume and complexity level of cases managed at our unit. Based on the findings of this study, our department continues to look closely at results but considers surgery with a stoma not always mandatory. However, larger and more powerful study designs are necessary to generalize the results and clarify the relationship between surgical outcomes and the administration of this new generation of biologics.

In conclusion, our data indicate that the preoperative use of USTE in IBD patients, within 12 weeks from surgery, is associated with similar perioperative outcomes and overall postoperative complications when compared to VEDO. Thus, for our limited experience, the choice of preoperative biologic treatment between USTE and VEDO should not be influenced by fear of surgical complications.

Contribution of each author/coauthor

a. Substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data for the work: *Novello M.*, *Stocchi L.*, *Holubar S.D.*, *Shawki S.*, *Lipman J.M.*, *Gorgun E.*, *Hull T.*, *Steele S.R.*
b. Drafting the article or revising it critically for important intellectual content: *Novello M.*, *Stocchi L.*, *Holubar S.D.*, *Shawki S.*, *Lipman J.M.*, *Gorgun E.*, *Hull T.*, *Steele S.R.*
c. Final approval of the version to be published: *Novello M.*, *Stocchi L.*, *Holubar S.D.*, *Shawki S.*, *Lipman J.M.*, *Gorgun E.*, *Hull T.*, *Steele S.R.*
d. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: *Novello M.*, *Stocchi L.*, *Holubar S.D.*, *Shawki S.*, *Lipman J.M.*, *Gorgun E.*, *Hull T.*, *Steele S.R.*

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Feagan BG, Sandborn WJ, Gasink C, Jacobstein D, Lang Y, Friedman JR, et al. (2016) Ustekinumab as induction and maintenance therapy for Crohn's disease. N Engl J Med [Internet]. [cited 2018 Jan 21];375(20):1946–60. Available from: https://doi.org/10.1056/NEJMoa1602773
2. Sandborn WJ, Feagan BG, Rutgeerts P, Hanauer S, Colombel J-F, Sands BE, et al. (2013) Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med [Internet]. [cited 2018 Apr 5];369(8):711–21. Available from: https://doi.org/10.1056/NEJMoa1215739
3. Lightner AL, Raffals LE, Mathis KL, Cima RR, Tse CS, Pemberton JH, et al. (2016) Postoperative outcomes in vedolizumab-treated patients undergoing abdominal operations for inflammatory bowel disease. J Crohns Colitis [Internet]. [cited 2017 may 7];11(2):1–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27543504
4. Yamada A, Komaki Y, Patel N, Komaki F, Aelvoet AS, Tran AL, et al. (2017) Risk of postoperative complications among inflammatory bowel disease patients treated preoperatively with vedolizumab. Am J Gastroenterol [Internet]. [cited 2018 Jan 10];112(9):1423–9. Available from: https://doi.org/10.1038/ajg.2017.201
5. Lightner AL, McKenna NP, Tse CS, Hyman N, Smith R, Ovsepyan G, et al. (2017) Postoperative outcomes in ustekinumab-treated patients undergoing abdominal operations for Crohn's disease. J Crohn's Colitis [Internet]. Available from: https://doi.org/10.1093/ecco-jcc/jjx163/4694103
6. Centers for Disease Control and Prevention National Healthcare Safety Network. Surgical site infection (SSI) event. [Internet]. 2017 [cited 2017 Dec 27]. Available from: https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf
7. Gu J, Stocchi L, Remzi FH, Kiran RP. (2014) Total abdominal colectomy for severe ulcerative colitis: does the laparoscopic approach really have benefit? Surg Endosc [Internet]. [cited 2017 Dec 26];28(2):617–25. Available from: https://doi.org/10.1007/s00464-013-3218-7
8. Li W, Stocchi L, Cherla D, Liu G, Agostinelli A, Delaney CP, et al. (2017) Factors associated with hospital readmission following diverting ileostomy creation. Tech Coloproctol [Internet]. [cited 2017 Dec 28];21(8):641–8. Available from: https://doi.org/10.1007/s10151-017-1667-z
9. Food and Drug Administration. STELARA® (ustekinumab) injection, for subcutaneous or intravenous - FDA label [Internet]. 2016 [cited 2018 Apr 7]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/761044lbl.pdf
10. Food and Drug Administration, Center for Drug Evaluation and Research. ENTYVIO (vedolizumab) for injection, for intravenous use - FDA label [Internet]. 2017 [cited 2018 Apr 7]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125476s000lbl.pdf
11. Li Y, Stocchi L, Cherla D, Liu X, Remzi FH (2016) Association of preoperative narcotic use with postoperative complications and prolonged length of hospital stay in patients with Crohn disease. JAMA Surg [Internet]. [cited 2018 Jan 21];151(8):726–34. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26913479
12. Golub R, Golub RW, Cantu RJ, Stein HD (1997) A multivariate analysis of factors contributing to leakage of intestinal anastomoses. J Am Coll Surg 184(4):364–372
13. Post S, Betzler M, von Ditfurth B, Schürmann G, Küppers P, Herfarth C (1991) Risks of intestinal anastomoses in Crohn's disease. Ann Surg 213(1):37–42
14. Aberra FN, Lewis JD, Hass D, Rombeau JL, Osborne B, Lichtenstein GR (2003) Corticosteroids and immunomodulators: postoperative infectious complication risk in inflammatory bowel disease patients. Gastroenterology 125(2):320–327
15. Yamamoto T, Allan RN, Keighley MRB (2000) Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. Dis Colon Rectum [Internet] 43(8):1141–1145 Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00003453-200043080-00017
16. Nguyen GC, Elnahas A, Jackson TD (2014) The impact of preoperative steroid use on short-term outcomes following surgery for inflammatory bowel disease. J Crohns Colitis [Internet] 8(12):1661–1667 Available from: http://www.ncbi.nlm.nih.gov/pubmed/25107847
17. Varela JE, Wilson SE, Nguyen NT (2010) Laparoscopic surgery significantly reduces surgical-site infections compared with open surgery. Surg Endosc Other Interv Tech [Internet]. [cited 2016 Aug 7];24(2):270–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19533235
18. A study to evaluate the safety and efficacy of ustekinumab induction and maintenance therapy in participants with moderately to severely active ulcerative colitis (UNIFI) - ClinicalTrials.gov [Internet]. [cited 2018 Mar 11]. Available from: https://clinicaltrials.gov/ct2/show/study/NCT02407236