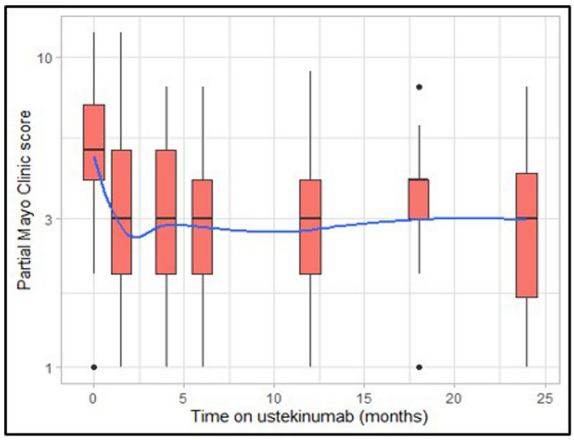

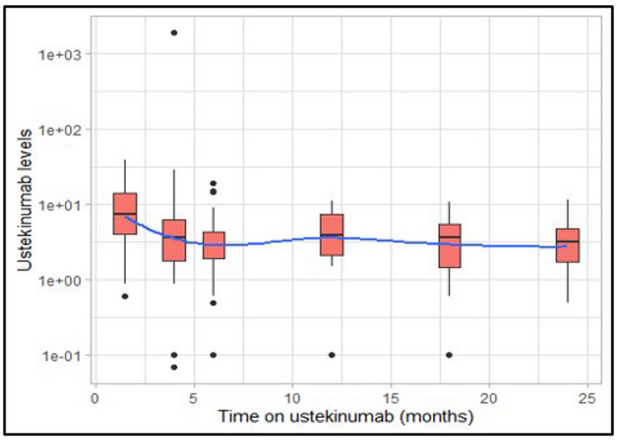

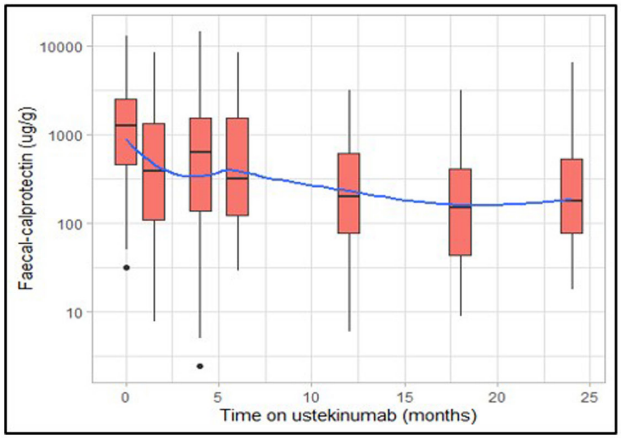

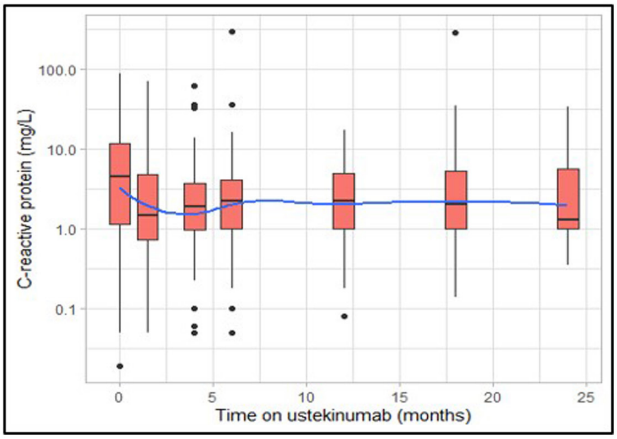

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P501

Safety of peri-operative biologics in patients with IBD undergoing resective bowel surgery: experiences of a single center cohort

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Background: Despite good safety data, the risk of peri-operative treatment with biologics in IBD is still discussed controversially. Recently, the prospective PUCCINI trial demonstrated that direct exposure to TNF-blockers within 12 wks. of abdominal surgery was not associated with more infectious complications. However, in daily clinical practice experiences on biological treatment peri-operatively are limited. In our current retrospective trial, we addressed the safety of different biologicals in a peri-operative setting.

Methods: Eligible pat. in this single center study were recruited from our IBD center between 2012 and 2022. Direct exposure to biologics was defined as exposure to biologics within 12 wks. before resective bowel surgery performed at our surgical department. To evaluate safety, the post-operative outcome focused on minor complications, defined as infectious complications, wound healing complications and major complications, defined as insufficiency of the anastomosis and abscess formation at surgery site post-operatively.

Results: A total of 447 IBD pat. (334 CD, 113 UC, 51.9% female) were included and followed for a median of 45 mo. [range 0-113]. Median age was 44 yrs. [19-89], median age at diagnosis was 24 yrs. [5-84] and median age at surgery was 41 yrs. [16/85]. Median disease duration until surgery was 11 yrs. [0-47]. 74.3% of pat. had moderate to severe disease activity at date of surgery. A total of 73.9% of pat. (326/447) had medical treatment at date of surgery, 61.5% of pat. (275/447) were treated with biologics within 3 mo. before surgery and 42.3% (189/447) had biologic treatment within 4 wks. before surgery. Overall, 36.9% of pat. (164/447) received infliximab, 13.0 % (58/447) adalimumab, 1.1% (6/447) golimumab, 5.8% (26/447) vedolizumab, and 6.5% (29/447) ustekinumab, peri-operatively. Most surgeries were planned electively (97.1%, 434/447) and performed laparoscopically (67.8%, 303/447). Minor and major post-operative complications occurred in 20.8% (93/447) of patients. Serious complications were observed in 9 pat., six had acute bleeding, one developed peritonitis and two died post-operatively (one with and one without biologics). Using logistic regression models, no significant differences regarding complications and safety were observed between pat. with versus without biologic treatment. Interestingly, CD pat. with direct exposure to biologics

within 4 wks. were more likely to undergo minimal-invasive surgery (68.6%, 107/156) than pat. with biologics within 3 mo. before surgery (48.28%, 28/58, p=0.02).

Conclusion: This retrospective single center study of 447 IBD patients could demonstrate that biologic treatment before surgery, even within 4 wks, is not associated with a higher risk of complications.

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P502

Application of an algorithm-based precision-dosing model to a real-world cohort of patients on infliximab maintenance therapy: implications for drug usage and cost

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Background: Infliximab is registered for use in patients with inflammatory bowel disease (IBD) at an intravenous maintenance dose of 5 mg/kg eight-weekly. Secondary loss of response during maintenance therapy occurs in up to 50% of patients. New precision dosing models, which forecast infliximab doses to achieve targeted trough levels, reduce non-response and improve patient outcomes. Aim: To compare standard 5 mg/kg eight-weekly infliximab dosing to the infliximab doses theoretically required to achieve predefined infliximab trough target levels, as determined by the iDOSE® precision dosing dashboard model.

Methods: IBD patients treated with eight-weekly maintenance infliximab therapy dosed at 5 mg/kg were included. A recorded infliximab dose was considered dose X if the following was available: three previous infliximab doses, albumin and C-reactive protein at time of dose X, trough infliximab level immediately preceding dose X and the patient's weight. The Baysient LLC iDOSE® software was then used to predict dose X to maintain therapeutic infliximab trough levels of ≥ either 5-10 or 3-7 µg/ml until the next eight-weekly dose. The predicted dose X was compared to the actual dose X given.

Results: 174 patients (56% male) were included with 417 dose X recordings. Of those, 135 had Crohn's disease, 31 ulcerative colitis and 8 IBD-unclassified. Median age was 36 (IQR 29-47) years with a disease duration of 5 (1-13) years. 76% of patients were receiving immunomodulators and 6% were smokers. Duration of infliximab therapy before dose X was 2 (0-4) years. Trough infliximab levels were 5.0 (2.5-7.6) µg/ml, serum albumin was 38 (35-40) g/L and C-reactive protein 3 (3-4) mg/L. Comparing actual dose X with predicted dose X, 52% and 32% of doses were subtherapeutic when aiming for trough levels of 5-10 and 3-7 µg/ml respectively. The underdosing occurred by 5.6 and 5.3 mg/kg per dose, respectively. Cost analysis showed total costs increased by 102% and 29% when aiming for trough levels 5-10 and 3-7 µg/ml. On multivariable regression analysis, significant associations with subtherapeutic infliximab levels were ulcerative colitis compared to Crohn's disease [OR: 9.81, 95% CI: 1.28-75.40, p = 0.028] and pre-dose X infliximab trough level [OR: 0.07, 95% CI: 0.03-0.15, p < 0.001].

Conclusion: More than half of maintenance infliximab drug doses given at our institution were too low to achieve therapeutic infliximab blood levels of at least 5 µg/ml. These patients would likely benefit from an increased dose or reduced dosing interval of infliximab. These findings need to be confirmed prospectively.

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P503

The risk of mild, moderate and severe infections in IBD patients: results from a prospective, multicentre, observational cohort study – PRIQ

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Background: Immunomodulators and biologicals are essential in current IBD management, but are associated with increased risk of infections. Considering the growing number of treatment options, the benefit-risk balance of drugs is becoming increasingly important in clinical decision making. To date, post-marketing surveillance studies mainly focus on severe infections. As a result, data on mild and moderate infections are scarce. These infections take longer to clear in immunosuppressed patients and can substantially impact quality of life. We aimed to assess the incidence of all infections and identify risk factors for the development of infections in IBD patients.

Methods: We previously developed and validated a Patient-Reported Infections Questionnaire (PRIQ), with excellent diagnostic accuracy, covering 15 infection categories with a 3-month recall period. The current prospective, multicentre, observational cohort study was performed between Jun, 1 2020 and Jul, 1 2021, enrolling consecutive IBD patients using the PRIQ implemented in myIBDcoach, an established telemedicine platform. Infection severity was defined as mild (self-limiting or topical treatment), moderate (oral antibiotics, antivirals or antifungals) or severe (hospitalization or IV treatment). Incidence rates (IR) were calculated for all infections, stratified for severity and subtype. Risk factors for infections were identified using multivariable logistic regression.

Results: In total, 629 IBD patients were included which completed 2391 PRIQs during 572 person-years (PY) of follow-up, resulting in 990 reported infections, corresponding to IRs of 17.3, 11.8, 5.1, and 0.4 per 10PY for all, mild, moderate, and severe infections, respectively (Tables 1-2). Upper respiratory tract (IR 26.9/100PY) and urinary tract infections (IR 14.8/100PY) were the most commonly