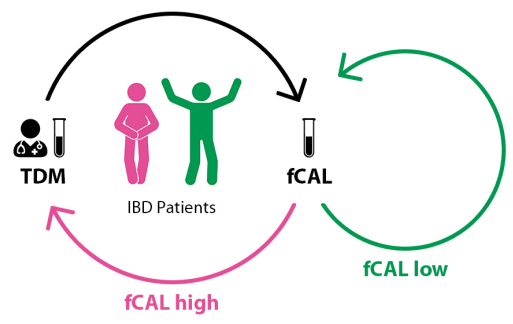
BÜHLMANN Fecal Calprotectin & Therapeutic Drug Monitoring in IBD

BÜHLMANN

MFMO001-03E

Inflammatory Bowel Disease (**IBD**) encompasses two main diseases, Crohn's Disease (CD) and Ulcerative Colitis (UC). They are chronic life-long autoinflammatory diseases mainly affecting the gastrointestinal tract. According to the European Federation of Crohn's and Ulcerative Colitis associations, there are currently over 10 million IBD patients worldwide. The disease course is characterized by periods of remission and flares that heavily impact quality of life of patients and increase the risk of irreversible organ damage and disability. Therefore, the main objective of disease management is to achieve long term remission, prevention of complication and improve quality of life. Among other clinical assessments disease management includes repeated measurements of calprotectin in stool (**fCAL**) as non-invasive marker of mucosal inflammation as well as the measurement of drug concentration as part of the therapeutic drug monitoring (**TDM**).



Adapted from Mitrev et al. 2017

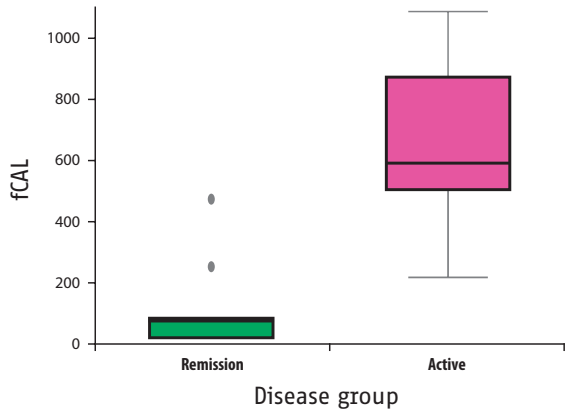
Figure 1: Simplified IBD monitoring pathway

Published data show the value of BÜHLMANN Calprotectin

BÜHLMANN Calprotectin reflects the degree of Mucosal Healing

Fecal calprotectin is an excellent non-invasive surrogate marker for mucosal healing. Using it as a target in a treat to target (**T2T**) disease monitoring is recommended by all major disease management guidelines such as ECCO-ESGAR [1], STRIDE II [2], and AGA guidelines [3]. With the advent of smartphone-based fCAL home tests, IBD monitoring is increasingly included in T2T virtual clinics[4]. Walsh et al. from Oxford show that fCAL levels tested by patients with the BÜHLMANN IB*Doc*® Home Test, highly correlated with histological remission cut-off of 147 µg/g (**Fig. 2**) [5]. This cut-off corresponds to Guardiola et al. and Lobaton et al. who established a calprotectin value, measured in the lab with BÜHLMANN fCAL® ELISA above 155 µg/g [6] and Quantum Blue® rapid tests above 272 µg/g [7,8], as reliable indicator for histological inflammation and clinical and endoscopic remission in UC patients and CD patients, respectively.

Benefit: BÜHLMANN fCAL® ELISA, IB*Doc*® and Quantum Blue® highly correlate with histologic healing and accurately predict remission.



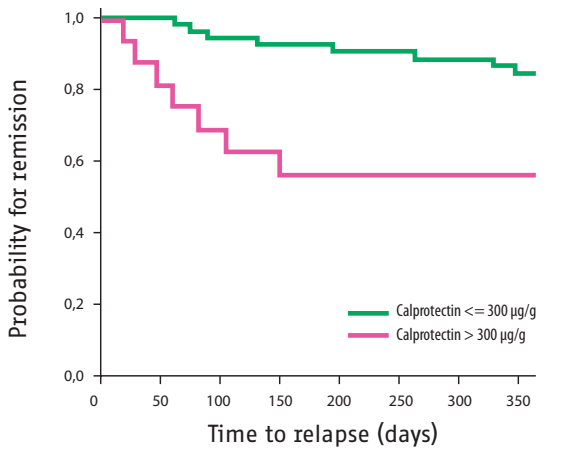
adapted from Walsh et al., 2018

Figure 2: Correlation of IB*Doc*® Calprotectin to distinguish between active and UC in remission

BÜHLMANN Calprotectin predicts increased risk of relapse

Theede et al. followed 70 UC patients in remission over 12 months [9]. A cut-off value of >321 µg/g with BÜHLMANN fCAL® ELISA was able to predict a relapse at 6 months (ROC AUC of 0.775) and showed a significant increase in relapse rate after 12 months for patients at measured levels of above 300 µg/g (**Fig. 3**). Fecal calprotectin was also measured with Quantum Blue® rapid test in 4 months intervals by Ferreiro-Iglesias et al. in 71 CD and 24 UC patients under anti-TNF therapy [10]. The study revealed that two consecutive calprotectin measurements above 300 µg/g predict relapse over the following 4 months with high significance.

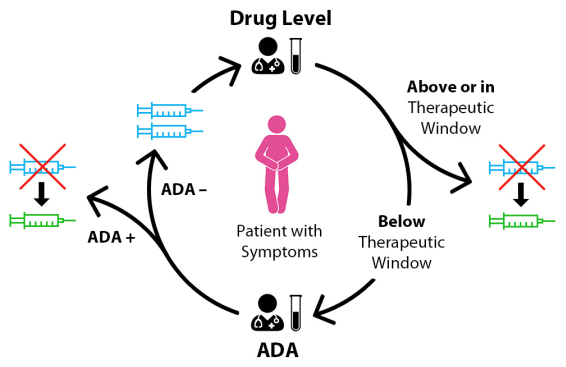
Benefit: BÜHLMANN Calprotectin supports relapse prediction in IBD patients without symptoms within 6 months.



adapted from Theede et al., 2016

Figure 3: Kaplan-Meier plot showing relapse rates during a one-year follow-up at a calprotectin cut-off of 300 µg/g

The advent of Tumor Necrosis Factor (TNF) inhibitors has improved outcomes of IBD. However, treatment failures of TNF inhibitors are common, and 30% to 50% of patients who initially respond, become nonresponsive to TNF inhibitors within the first years of therapy[11]. For some patients, anti-drug antibodies (**ADA**) may be a reason to change their treatment. The drug level in the patient blood and the potential presence of ADA can easily be checked by therapeutic drug monitoring (**TDM**). In addition to fCAL monitoring, TDM in IBD patients receiving anti-TNF agents can help to optimize treatment and outcomes.



Adapted from Mitrev et al. 2017

Figure 4: Simplified TDM pathway for symptomatic IBD patients

Published data show the value of BÜHLMANN TDM

Quantum Blue® TDM tests detect loss of response and correlate with mucosal healing

Parra et al. investigated the association between infliximab trough levels and quality of life in IBD patients in maintenance therapy[12]. 71 patients were included in the study (55 with CD and 16 with UC). Drug levels were measured with the Quantum Blue® Infliximab assay and defined as satisfactory (≥3 µg/mL) or unsatisfactory (≤3 µg/mL) in comparison to mucosal healing (MH), clinical remission (CR) and quality of life (QoL). The study showed that IBD patients with adequate serum IFX levels have higher rates of CR, MH and improved quality of life (**Fig. 5**).

Benefit: The Quantum Blue® Infliximab is useful to detect loss of response and consequently helps to improve quality of life.

Disease control	Clinical remission	Mucosal healing	Global Quality of Life
TL ≥ 3 µg/mL	85.7 %	85.7 %	183/224
TL < 3 µg/mL	27.9 %	18.6 %	161.9/224

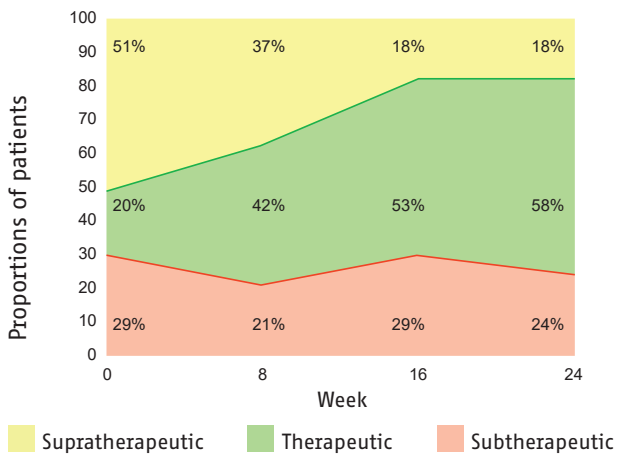
Adapted from Parra et al. 2018

Figure 5: Clinical remission, mucosal healing, and quality of life scores according to infliximab levels

Quantum Blue® TDM tests increase the number of patients within the therapeutic range

Rentsch et al. evaluated the benefit of immediate dose adjustment following Quantum Blue® TDM assay performed the same day[13]. 48 IBD patients under infliximab maintenance treatment (5 mg/kg every 8 weeks) were included in the study. Among the 45 patients studied over 24 weeks, the proportion within the therapeutic range of 3 to 7 mg/kg (the primary end point) increased from 20% to 58% ($P < 0.001$; Fisher exact test) (**Fig. 6**). Among the 33 patients studied over 48 weeks, the proportion within the therapeutic range increased from 24% to 64% ($P < 0.001$) and the total infliximab cost was reduced by 4%.

Benefit: Immediate dose adjustment at trough levels based on BÜHLMANN Quantum Blue® TDM increases the proportion of patients in the infliximab therapeutic window.



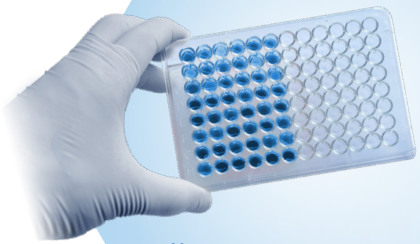
Adapted from Rentsch et al. 2023

Figure 6: Proportion of patients with infliximab levels over, within, or below the therapeutic range over 24 weeks of observation

The BÜHLMANN IBD Monitoring Portfolio

Quantum Blue®
fCAL and TDM
Rapid Tests

IB*Doc*®
fCAL Home Test



BÜHLMANN fCAL® ELISA
The Gold Standard

BÜHLMANN fCAL® turbo
For Lab Automation

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Quantum Blue® fCAL	LF-CHR25 / LF-CALE25
Quantum Blue® Adalimumab	LF-TLAD10 / LF-TLAD25
Quantum Blue® Infliximab	LF-TLIF10 / LF-TLIF25
Quantum Blue® Anti-Adalimumab	LF-ADAD10 / LF-ADAD25
Quantum Blue® Anti-Infliximab	LF-ADIF10 / LF-ADIF25
IB*Doc*® Calprotectin Kit	LF-IBDOC8 / BI-IBDOC
BÜHLMANN fCAL® ELISA	EK-CAL / EK-CAL2 / EK-CAL2-WEX
BÜHLMANN fCAL® turbo	KK-CAL (Kit)

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