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Key Literature – BÜHLMANN Therapeutic Drug Monitoring

BÜHLMANN Quantum Blue® Infliximab papers

- **Afonso, J. *et al.*, 2017, Therapeutic drug monitoring of CT-P13: a comparison of four different immunoassay, *Ther Adv Gastroenterol***

  "The Quantum Blue kit has the added advantage of being a bedside point-of-care solution, releasing results within 15 min of sampling, and therefore allowing an immediate adjustment of CT-P13 dosing."

- **Afonso, J. *et al.*, 2016, Proactive therapeutic drug monitoring of infliximab: a comparative study of a new point-of-care quantitative test with two established ELISA assays, *Aliment Pharmacol Ther***

  "The Quantum Blue IFX assay can successfully replace the commonly used ELISA-based IFX quantification kits…Moreover, it is a user-friendly desktop device that does not require specific laboratory facilities or highly specialised personnel."

- **Bodini, G., *et al.*, 2021, Therapeutic drug monitoring in Crohn's disease patients treated with anti-TNF: a comparison of two techniques, *European Journal of Gastroenterology & Hepatology***

  "(…) both POC and HMSA assays are techniques that are able to assess anti-TNF drug trough levels and reliably differentiate relapse and remission phases in Crohn's disease patients treated with either adalimumab or infliximab along the course of treatment."

- **Curci, D. *et al.*, 2019, Determination of Serum Infliximab Concentration by Point-of-care Devices in Children With Inflammatory Bowel Disease, *Gastroenterology: Inflammatory Bowel Disease***

  "Notably, POC IFX/QB has an upper quantification limit of 20mg/mL whereas the POC IFX/RQ up to 10mg/mL, and, whenever necessary, serum had to be diluted to quantify more precisely IFX concentrations above this limit."

- **Magro, F. *et al.*, 2018, The performance of Remicade®-optimized quantification assays in the assessment of Flixabi® levels, *Ther Adv Gastroenterol***

  "…, whereas the most accurate method to quantify Flixabi is the Buhlmann (with an ICC of 0.983)."

- **Magro, F. *et al.*, 2017, Clinical performance of an infliximab rapid quantification assay, *Ther Adv Gastroenterol***

  "Based on this study, we concluded that using the rapid IFX assessment system with a 3 µg/ml threshold is a reliable alternative to the time-consuming enzyme-linked immunosorbent assays in patients on the maintenance phase of IFX."

- **Nasser, Y. *et al.*, 2018, Comparison of Point-of-Care and Classical Immunoassays for the Monitoring Infliximab and Antibodies Against Infliximab in IBD, *Dig Dis and Sciences***

  "…the BÜHLMANN assay which has a broader linear range for trough determination up to 20 µg/mL."

- **Novakovic, V. *et al.*, 2019, Comparison of the Quantum Blue reader Point-of-Care system versus ELISA technique for therapeutic drug monitoring of Infliximab levels, *Clin Biochem***

  "When the samples were stratified according to the therapeutic interval, an almost perfect agreement between the methods was observed...In conclusion, our data demonstrate that QB is a suitable alternative to Promonitor IFX for TDM in patients treated with IFX for IBD."

- **Parra, S. *et al.*, 2018, Infliximab Trough Levels and Quality of Life in Patients with Inflammatory Bowel Disease in Maintenance Therapy, *Gastroenterol Res and Pract***

  "Quantitative determination of in serum was performed with the Quantum Blue® Infliximab assay… Satisfactory trough levels of infliximab were associated with higher rates of clinical remission, mucosal healing, and improved quality of life in inflammatory bowel disease patients maintenance therapy."

BÜHLMANN Quantum Blue® Infliximab posters

- **Afonso, J. *et al.*, 2021, Standardization of Quantum Blue® Rapid TDM Assays with WHO International Standards for Adalimumab and Infliximab , *ECCO 2021 P229***

  "The current standardizations of Quantum Blue® Adalimumab and Quantum Blue® Infliximab agree very well with the WHO international standards. Therefore, (they) are very well suited to accurately and reproducibly determine trough levels of anti-TNF-α biologics for efficient monitoring of immune therapies."

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- **Anchling, L. *et al.*, 2021, Serum levels of infliximab and adalimumab biosimilars can be measured equivalently to originator drugs by Quantum Blue® rapid testing as tool for therapeutic drug, *UEG Week 2021 P0342***

  "(…) equivalent quantification of infliximab and adalimumab originator drugs, as well as their biosimilars GP1111, SB2, CT-P13 and adalimumab-adaz allowing for identification of patients with suboptimal drug levels as part of their therapeutic drug monitoring."

- **Costa Santos, M. P. *et al.*, 2018, Point-of-care infliximab quantification in inflammatory bowel disease in daily practice, *ECCO 2018 P736***

  "Point-of-care IFX-TL measurement was easy to implement on a daily practice setting. IFX-TL considered to be within the therapeutic range were found in one-third of patients. In the remaining patients an immediate treatment adjustment could have been made, allowing for resources saving."

- **Lindsjø, I. *et al.*, 2016, Patient-near Infliximab trough-level testing by a novel quantitative rapid test: The Quantum Blue Infliximab test, *UEG Week 2016 P1379***

  "…, we have shown that such a test can accurately be performed by a nurse. This means that TDM now can be moved from a distant laboratory to the near patient facility…"

- **Rentsch, C.A. *et al.*, 2018, Pharmacist-led proactive therapeutic drug monitoring with infliximab (PROXIMO): utility of and cost-saving with the use of a rapid assay for assessing drug level, *ECCO 2018 P428***

  "Trough concentrations were assessed via the Bühlmann rapid test immediately prior toeach Infusion… The rapid test is accurate…Its application in the setting of maintenance therapy led to dose adjustment in 3 of 4 patients and higher rates of therapeutic levels, implying standard weight-based dosing is inadequate."

- **Schuster, T. B. et al., 2016, Performance of the BÜHLMANN Quantum Blue® Infliximab point-of-care assay dedicated for therapeutic drug monitoring of serum infliximab trough levels, *ECCO 2016 P242***

  "The BÜHLMANN Quantum Blue® Infliximab assay enables the quantitative determination of the infliximab trough level in serum within 15 minutes and exhibits an excellent correlation with existing ELISAs."

BÜHLMANN Quantum Blue® Adalimumab papers

- **Bodini, G., *et al.*, 2021, Therapeutic drug monitoring in Crohn's disease patients treated with anti-TNF: a comparison of two techniques, *European Journal of Gastroenterology & Hepatology***

  "(…) both POC and HMSA assays are techniques that are able to assess anti-TNF drug trough levels and reliably differentiate relapse and remission phases in Crohn's disease patients treated with either adalimumab or infliximab along the course of treatment."

- **Laserna-Mendieta, E. J. *et al.*, 2019, Comparison of a new rapid method for the determination of adalimumab serum levels with two established ELISA kits, *Clin Chem Lab Med***

  "The agreement among the three assays to identify patients with subtherapeutic concentrations of ADA (either below 5 µg/mL or 7.5 µg/mL) was high."

- **Rocha, C. *et al.*, 2019, Accuracy of the new rapid test for monitoring adalimumab levels, *Ther Adv Gastroenterol***

  "In conclusion, the Quantum Blue® Adalimumab is a reliable alternative to the commonly used ELISA-based ADL quantification kit. In fact, the rapid test allows a fast and accurate assessment of ADL levels, which in turn contributes towards proactive and cost-effective therapeutic management of IBD patients."

BÜHLMANN Quantum Blue® Adalimumab posters

- **Afonso, J. *et al.*, 2021, Standardization of Quantum Blue® Rapid TDM Assays with WHO International Standards for Adalimumab and Infliximab, *ECCO 2021 P229***

  "The current standardizations of Quantum Blue® Adalimumab and Quantum Blue® Infliximab agree very well with the WHO international standards. Therefore, (they) are very well suited to accurately and reproducibly determine trough levels of anti-TNF-α biologics for efficient monitoring of immune therapies."

- **Anchling, L. *et al.*, 2021, Serum levels of infliximab and adalimumab biosimilars can be measured equivalently to originator drugs by Quantum Blue® rapid testing as tool for therapeutic drug, *UEG Week 2021 P0342***

  "(…) equivalent quantification of infliximab and adalimumab originator drugs, as well as their biosimilars GP1111, SB2, CT-P13 and adalimumab-adaz allowing for identification of patients with suboptimal drug levels as part of their therapeutic drug monitoring."

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- **Bantleon, F. I. et al., 2017, Quantum Blue® Adalimumab: Development of the first point of care rapid test for therapeutic drug monitoring of serum adalimumab levels, *ECCO 2017 P283***

  "The BÜHLMANN Quantum Blue® Adalimumab assay enables the quantitative determination of adalimumab trough level in serum with a time to result of only 15 minutes."

- **Lindsjø, I. *et al.*, 2018, Patient-near Adalimumab trough-level testing by a novel quantitative rapid test: The Quantum Blue Adalimumab test, *UEG Week 2018 P1580***

  "In this investigation, we document a close correlation between a 15-minute rapid test for ADA trough-level with that of an standard laboratory assay. We have also shown the robustness of this test since a nurse can accurately perform it."

General TDM Literature

Infliximab trough level in IBD

- **Casteele, N. V. *et al.*, 2015, Trough Concentrations of Infliximab Guide Dosing for Patients With Inflammatory Bowel Disease, *Gastroenterology***

  "The predefined optimal interval of 3–7 µg/mL for infliximab TCs is applicable for responder patients treated with maintenance infliximab therapy."

- **Watterdal, S. S. *et al.*, 2021, Effect of Therapeutic Drug Monitoring vs Standard Therapy During Maintenance Infliximab Therapy on Disease Control in Patients With Immune-Mediated Inflammatory Diseases A Randomized Clinical Trial, *JAMA***

  "Among patients with immune-mediated inflammatory diseases undergoing maintenance therapy with infliximab, proactive TDM was more effective than treatment without TDM in sustaining disease control without disease worsening."

Anti-Infliximab antibodies in IBD

- **Imbrecht, M. *et al.*, 2019, Anti-infliximab antibodies: How to compare old and new data?, *Journal of Pharmaceutical and Biomedical Analysis***

  "From our ADA concentration comparison experiments, we deduced that the previously established cutoff of 8 µg/ml with the 1st generation ELISA has a similar impact as the cutoff of 374 ng/ml with the 2nd generation ELISA and a cutoff of 119 ng/ml in the ready-to-use ELISA kit."

- **Van Stappen, T. *et al.*, 2018, Clinical relevance of detecting anti-infliximab antibodies with a drug-tolerant assay: post hoc analysis of the TAXIT trial, *Gut***

  "Upon dose intensification, low concentration ADAs, not detectable using a drug-sensitive assay, disappear in more than half of the patients over time and are clinically non-relevant. In contrast, high concentration ADAs which are typically also detected in a drug-sensitive assay, persist over time and necessitate a higher cumulative dose and drug cost."

Adalimumab trough level in IBD

- **Roblin, X. *et al.*, 2014, Association Between Pharmacokinetics of Adalimumab and Mucosal Healing in patients With Inflammatory Bowel Disease, *Clin Gastroenterol and Hepatol***

  "An absence of mucosal healing was associated with trough levels of adalimumab less than 4.9 µg/mL…"

- **Ungar, B. *et al.*, 2016, Optimizing Anti-TNF-α Therapy: Serum Levels of Infliximab and Adalimumab Are Associated With Mucosal Healing in Patients With Inflammatory Bowel Diseases, *Clin Gastroenterol and Hepatol***

  "…the association between higher level of adalimumab and increased rate of mucosal healing reached a plateau at 12 µg/mL."

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General Recommendations for Therapeutic Drug Monitoring

- **Mitrev, N. *et al.*, 2017, Review article: consensus statements on therapeutic drug monitoring of ani-tumour necrosis factor therapy in inflammatory bowel disease, *Aliment Pharmacol Ther***

  "To achieve clinical remission in luminal IBD, infliximab and adalimumab trough concentrations in the range of 3-8 and 5-12 µg/mL, respectively, were deemed appropriate."

WHO Standardization Papers

- **Metcalfe, C. *et al.*, 2019, The first World Health Organization International Standard for infliximab products: A step towards maintaining harmonized biological activity, *MABS***

  "The results of this study showed that the candidate preparation, coded 16/170, is suitable as an IS for infliximab bioactivity. This infliximab IS from NIBSC, is intended to support in vitro bioassay calibration and validation by defining international units of bioactivity."

- **Wadhwa, M. *et al.*, 2021, The First WHO International Standard for Adalimumab: Dual Role in Bioactivity and Therapeutic Drug Monitoring, *Frontiers in Immunology***

  " (…) the recent establishment of the WHO IS for adalimumab based on the results of the international collaborative study allows it to be effectively used by stakeholders world-wide in several ways to promote not only product quality but also clinical monitoring in adalimumab treated patients."