Theradiag

i-Tracker Infliximab

English

REF **CTI 002-100** Σ 100

INTENDED USE

i-Tracker Infliximab (Theradiag) is an automated assay intended for the quantitative measurement of Infliximab (anti-TNFα agent) in human serum or plasma samples.

DIAGNOSTIC VALUE

Anti-TNFα are therapeutic agents widely used to treat patients with various inflammatory diseases. Infliximab is one of the anti-TNFα recommended for the treatment of the rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, etc. This chimeric monoclonal antibody is able to bind TNFα. It blocks the action of TNFα responsible for the inflammatory state.

However, during the treatment, some patients can develop antibodies against Infliximab. Consequently, the plasmatic level of anti-TNFα decreases and simultaneous the disease symptoms reappear or increase.

Studies have shown that the trough level of a TNFα therapy (i.e. the circulating drug level just before the next injection) usually correlates clinical efficacy. This trough level is influenced by several factors, among them dosage and frequency of the injections, disease phenotype and activity, pharmacogenetic factors, co-medication and the formation of anti-drug antibodies.

Measurement of anti-TNFα drug level in combination with anti-drug antibodies quantification provides to the treating physician help for therapeutic guidance, hence maximizing treatment efficacy while minimizing to major cost savings.

i-Tracker Infliximab (Theradiag) assay is validated to monitor drug levels of any biological drug which contains the active substance Infliximab, that is the original drug Remicade®, and any biosimilar drug like CT-P13 (Remsima® or Inflectra®) and SB2 (Flixabi® or Renflexis®).

i-Tracker Infliximab (Theradiag) assay is calibrated with the NIBSC/WHO International Standard (cat:16/170) for Infliximab.

SPECIMEN COLLECTION

The specimen types appropriate to **i-Tracker Infliximab** are human sera and plasma.

Samples which are cloudy should be clarified by low-speed centrifugation.

To prevent erroneous results due to the presence of fibrin, ensure that complete clot formation has taken place prior to centrifugation of samples. Some samples, particularly those from patients receiving anticoagulant therapy, may require increased clotting time.

Freshly collected specimens could be tested after storage of at most 8 days kept in refrigerator (+2°C / +8°C) or 3 days at room temperature (+18°C / +25°C) and until 10 hours for onboard specimens.

5 freeze-thaw cycles for specimens do not affect the testing results.

METHOD PRINCIPLE

i-Tracker Infliximab assay is a two-step immunoassay using microparticles, acridinium-ester labeled chemiluminescent technology with the i-Track[10].

- In the first step, the TNFα coupled magnetic microparticles, and diluted human serum/plasma sample are mixed in an assay cuvette, which allows Infliximab to bind to the microparticles surface.
- After incubation, unbound reagent and sample matrix are removed by washing, and the microparticles-TNFα-Infliximab immunocomplex are kept with the help of a magnetic separator.
- Secondly, anti-Infliximab polyclonal antibodies conjugated to acridinium ester are added.
- After incubation, excess acridinium-ester conjugate is removed by washing and finally the light induced by acridinium-ester is detected by addition of triggers.
- The relative light unit (RLU) intensity is proportional to the amount of Infliximab.
- According to a certain specific Infliximab RLU-concentration standard curve, the RLU obtained can be interpreted to Infliximab concentration in the sample expressed as µg/mL.

For quantitation of Infliximab, the **i-Tracker Infliximab** assay uses a predefined lot specific Master Curve that is uploaded into the instrument through the reagent cartridge 2D barcode. The Master Curve is created during manufacturing by using in-house standards. Based on the Master Curve, and results obtained by running two Calibrators, an instrument specific Working Curve is created, which is used to calculate a concentration (µg/mL) from the RLU obtained for each sample.

KIT CONTENTS

Components are a matched set. **Barcode on the inside box are needed for the assay**.

Description	Volume
Cartridge reagents	
Microparticles : 1 vial of TNFα coupled microparticles in PBS with stabilizers. MP INF Preservatives: Sodium azide < 0.1% and Proclin 300 < 0.06% ***Ready to use***	3 mL*
Infliximab Buffer : 1 vial of PBS-Tween with stabilizer. BUF INF Preservative: Proclin 300 <0.06% ***Ready to use***	23 mL*
Specimen diluent : 1 vial of PBS-Tween with stabilizer. DIL INF Preservatives: Proclin 300 <0.06% ***Ready to use***	23 mL*
Immunoconjugate: 1 vial of acridinium-ester labeled polyclonal anti-Infliximab antibodies, containing PBS with stabilizers. IC INF Preservatives: Sodium azide < 0.1% and Proclin 300 < 0.06% ***Ready to use***	23 mL*
Control and Calibrators	
Infliximab Calibrator A: a calibrator tube containing Infliximab (low level) in stabilizers and preservatives. CALA INF **Target value for the calibrator is indicated on the 2D barcode localized in each kit.** Preservatives: Sodium azide < 0.1% and Proclin 300 < 0.06% ***Ready to use***	0.5 mL*
Infliximab Calibrator B: : a calibrator tube containing Infliximab (high level) in stabilizers and preservatives. CALB INF **Target value for the calibrator is indicated on the 2D barcode localized in each kit.** Preservatives: Sodium azide < 0.1% and Proclin 300 < 0.06% ***Ready to use***	0.5 mL*
Infliximab Control: a control tube containing Infliximab in stabilizers and preservatives. CTL1 INF **Acceptable range for the control is indicated on the 2D barcode localized in each kit.** Preservatives: Sodium azide < 0.1% and Proclin 300 < 0.06% ***Ready to use***	1mL*

*When loading a reagent, the i-Track[10] system indicates the remaining usable volume (dead volume is not taken into account).

MATERIALS REQUIRED BUT NOT PROVIDED

- i-Track[10] (Cat. No. TD 810400)
- Cartridge Checking System (CCS) (Cat. No. TD IS-6010)
- Cuvettes (Cat. No. TD IS-CC100)
- System Liquid (Syst.L) (Cat. No. TD IS-CS100)
- Trigger Set (Cat. No. TD IS-CT100)
- Wash Solution (Wash S) (Cat. No. TD CW100)
- Immunocleaner, (Cat. No. TD IS-IM100)
- D-Sorb Solution (Cat. No. TD IS-DS200)
- Disposable Waste Bags, (Cat No. TD IS-DW225)
- Barcode scanner
- XPrep

STABILITY AND STORAGE CONDITIONS

- The kit is stable until the expiration date when stored and handled as directed.
- Store the kit in refrigerator (+2°C / +8°C). Open reagents can be kept on board for a maximum of 30 days, or stored at +2°C / +8°C for a maximum of 60 days. When one of the two conditions is reached the reagents are no longer usable.
- The i-Track[10] software monitors the onboard (in-use) expiration of the reagent cartridge. The system will not allow use of a reagent which has expired.

PRECAUTIONS

1. The product is for in vitro diagnostic use only.
2. This assay is only for use on the i-Track[10].
3. Do not use the reagents beyond their expiration dates. Do not mix reagents from different lots.
4. Instructions must be carefully followed for reagent use and storage. Any modification in procedure may interferes with the results. The control, calibrators and contaminated vials must strictly follow safety guidelines or rules of biological hazards to ensure the users and environmental safety.
5. Reagents contain chemical and biological components. Avoid ingesting or splashing onto skin and mucous membrane. If direct contact with controls happens, rinse immediately the contact area with plenty of water and see a doctor if necessary.
6. Liquid waste and solid waste are temporarily stored on the i-Track[10] in separate containers. Waste management should also be handled in accordance with all federal, state and local environmental regulations when disposing of wastes.

7. Spilled reagents should be cleaned up immediately. Observe all federal, state and local environmental regulations when disposing of wastes.
8. Once opened, the reagent cartridge must be stored in the instrument's refrigerated reagent racks. Care should be taken to avoid spilling the reagents when the reagent cartridge is reloaded into the instrument.
9. Chemical contamination of the reagents can result from improper cleaning or rinsing of the instrument. Residues from common laboratory chemicals such as formalin, bleach, ethanol, or detergent can cause interference in the assay. Be sure to follow the recommended cleaning procedure of the instrument as outlined in the i-Track[10] user manual.
10. Reagents can contain Sodium azide < 0.1% and/or Proclin 300 <0.06%. Do not eat and avoid contact with skin and eyes. Azide can form explosive mixtures in copper or lead piping. Rinse thoroughly after flushing.
11. At this concentration, ProClin 300 is irritating to eyes and skin, and may be detrimental if enough quantity is ingested. It is a skin sensitizer; prolonged or repeated exposure may cause allergic reaction in certain sensitive individuals.
12. Avoid using reagents if signs of contamination or other visible changes occur.

ASSAY PROCEDURE

Place the reagent cartridge in the reagent compartment making sure that the barcode is read.

The calibrators and the control must be placed in the sample compartment and make sure that the barcode is read.

Select the appropriate assay protocol on the i-Track[10].

Note that for optimal performance, it is important to perform all routine maintenance procedures, such as routine cleaning, calibration and control procedures which are defined in the i-Track[10] User Manual.

See the i-Track[10] User Manual for preparation, setup, dilutions, adjustment, assay and quality control procedures.

Users should have the periodic calibration procedure for every 21 running days from last calibration, which will be reminded on the software interface. Besides, a calibration procedure should be carried out when a new batch of **i-Tracker Infliximab** kit is used.

The control procedure could be done before running the specimens every day. Users also can adjust the control procedure period according to their own lab frequency.

Sample Dilution

The specimens are diluted with Specimen Diluent prior to testing (dilution 1/10) by the i-Track[10] automatically.

ASSAY CHARACTERISTICS & PERFORMANCES

Lower Limit of Quantification (LLOQ) determination

A population of serum samples from healthy donors or untreated patients were valued by **i-Tracker Infliximab** assay.

Lower Limit of Quantification of Infliximab
0.3 µg/mL > 95th percentile

Dynamic range & Test Result Interpretation

With the help of the predicated two-point calibration master curve and a working curve for the instrument specified, the i-Track[10] will automatically calculate the Infliximab concentration of each specimen and interpret the results into µg/mL.

Measurement range Infliximab
0.3 µg/mL - 24 µg/mL

Results below the lower limit (< 0.3 µg/mL) will be reported as HDM-, while those above the upper limit (> 24 µg/mL) will be reported as HDM+.
Specimen with concentration < 0.3 µg/mL is unquantifiable.
Test results only reflect the sample collecting status and should be interpreted/analyzed for diagnosis in conjunction with other laboratory and clinical findings.

Interfering Substances studies

i-Tracker Infliximab (Theradiag) assay was evaluated to assess the impact of potential interfering molecules (bilirubin (0.2 mg/mL), hemoglobin (2 mg/mL), triglycerides (10 mg/mL), rheumatoid factors (1000 IU/mL) and biotin (2000 ng/mL)).
⇨ No interference is detected.

Cross Reactivity

i-Tracker Infliximab (Theradiag) assay was evaluated to assess the impact of potential cross reacting molecules (Adalimumab, Certolizumab, Etanercept, Golimumab, Ustekinumab, Vedolizumab, and anti-Adalimumab antibodies).

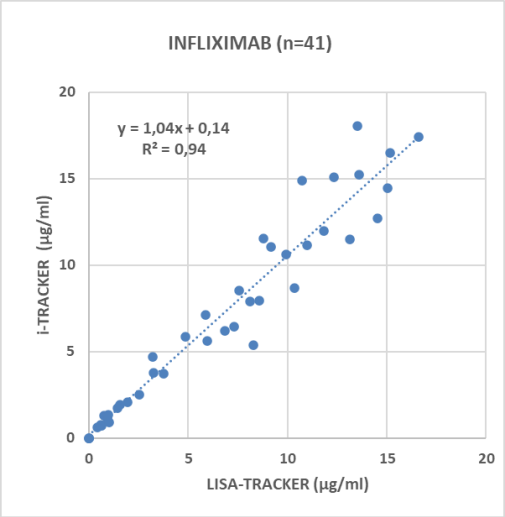
⇨ No cross reactivity is detected.

Precision

	Intra-run (10 tests in a same assay)		Inter-run (2 tests in 6 independent assay)	
Parameter	**Mean (µg/mL)**	**CV (%)**	**Mean (µg/mL)**	**CV (%)**
Infliximab	0.7	7.2	1.0	6.7
	7.5	5.1	7.8	5.1
	16.1	1.8	19.2	2.0

Correlation :

The quantification of Infliximab performed with **i-Tracker Infliximab** assay gave similar results than the quantification made with **LISA-TRACKER Infliximab** assay (Cat.n: LTI 002/LTI 005). A linear regression analysis, generated with 41 Infliximab samples, shown that both assays are equivalent (R^2 = 0.94 ; slope = 1.04).



LIMITATIONS

The effectiveness of this kit is only confirmed for human sera/plasma, the applicability of the other kinds of samples is not verified.

Reliable and reproducible results will be obtained when the assay procedure is carried out in accordance with the instructions and with adherence to good laboratory practice

Clinical diagnosis should not be made on the findings of a single test result but should integrate all clinical and laboratory findings.

QUALITY CONTROL

It is recommended to use internally and externally sourced control material. **IMMUNO-TROL i-Tracker Infliximab** control (Theradiag), (Cat.n: CTI 002-PC) contains **Infliximab**. This material is to be assayed in the same manner as the unknown sample.

REFERENCES

Ainsworth MA & al. Tumor necrosis factor-alpha binding capacity and anti-infliximab antibodies measured by fluidphase radioimmunoassays as predictors of clinical efficacy of infliximab in Crohn's disease. Am J Gastroenterol. 2008 Apr;103(4):944-8.

Afif W & al. Clinical Utility of Measuring Infliximab and Human Anti-Chimeric Antibody Concentrations in Patients With Inflammatory Bowel Disease. Am J Gastroenterol 2010; 105:1133–1139.

Arends S & al. The formation of autoantibodies and antibodies to TNF-α blocking agents in relation to clinical response in patients with ankylosing spondylitis. Clin Exp Rheumatol. 2010 Sep-Oct;28(5):661-8.

Attar A & al. Cost savings using a test-based de-escalation strategy for patients with Crohn's disease in remission on optimized infliximab: A discrete event model study. Dig Liver Dis. 2019 Jan;51(1):112-119

Avouac J & al. Systematic switch from innovator infliximab to biosimilar infliximab in inflammatory chronic diseases in daily clinical practice: The experience of Cochin University Hospital, Paris, France. Semin Arthritis Rheum. 2017 Oct 5.

Baert F & al. Influence of Immunogenicity on the Long-Term Efficacy of Infliximab in Crohn's Disease. N Engl J Med 2003;348:601-8.

Ben-Horin S & al. Undetectable anti-TNF drug levels in patients with long-term remission predict successful drug withdrawal.Aliment Pharmacol Ther. 2015 Aug;42(3):356-64.

Bendtzen K. Is There a Need for Immunopharmacologic Guidance of Anti–Tumor Necrosis Factor Therapies. ARTHRITIS & RHEUMATISM Vol. 63, No. 4, April 2011, pp 867–870.

Benucci M & al. Correlation between HLA haplotypes and the development of antidrug antibodies in a cohort of patients with rheumatic diseases. Biologics: Targets and Therapy 2018:12 37–41

Benucci M & al. Safety, efficacy and immunogenicity of switching from innovator to biosimilar infliximab in patients with spondyloarthritis: a 6-month real-life observational study. Immunol Res. 2016 Jul 23.

Bor R & al. Clinical role, optimal timing and frequency of serum infliximab and anti-infliximab antibody level measurements in patients with inflammatory bowel disease**.** PLoS One. 2017 Mar 31;12(3):e0172916

Bressler B & al. Clinical Practice Guidelines for the Medical Management of Nonhospitalized Ulcerative Colitis: The Toronto Consensus. Gastroenterology 2015;148:1035 – 1058.

Candon S & al. Clinical and biological consequences of immunization to infliximab in pediatric Crohn's disease. Clin Immunol. 2006 Jan;118(1):11-9.

Choon Jin Ooi & al. Best practices on immunomodulators and biologic agents for ulcerative colitis and Crohn's disease in Asia. Intest Res, May 31, 2019:1-26.

Choy & al. Efficacy of a novel PEGylated humanized anti-TNF (CDP870) in patients with rheumatoid arthritis : a phase II double-blinded, randomized, dose escalating trial. Rheumatology 2002;41:1133-1137.

Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517.

Coutzac C & al. Association Between Infliximab Trough Levels and the Occurrence of Paradoxical Manifestations in Patients with Inflammatory Bowel Disease: a Case-Control Study**.** J Crohns Colitis. 2015 Nov;9(11):982-7.

Desroches M & al. Treatment failure with antagonists of TNF-α: mechanisms and implications for the care of patients. Eur. Cytokine Netw., Vol. 21 n° 4, December 2010, 226-31.

DeVries & al. Inefficacy of infliximab in ankylosing spondylitis is correlated with antibody formation. Ann Rheum Dis. 2007 Jan;66(1):133-4.

Diagnostics Guidance [DG22] on Therapeutic monitoring of TNF-alpha Inhibitors in Crohn's Disease. https://www.nice.org.uk/guidance/dg22/chapter/1-Recommendations

ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications. Journal of Crohn's and Colitis, 2018, 1–32.

Edrees & al. Anti-tumor necrosis factor (TNF) therapy in rheumatoid arthritis: correlation of TNF-alpha serumlevel with clinical response and benefit from changing dose or frequency of infliximab infusions. Clin Exp Rheumatol. 2005 Jul-Aug;23(4):469-74.

Fay S & al.The Association Between Drug Levels and Endoscopic Recurrence in Postoperative Patients with Crohn's Disease Treated with Tumor Necrosis Factor Inhibitors. Inflamm Bowel Dis. 2017 Aug 22**.**

Fernandes SR & al. Proactive Infliximab Drug Monitoring Is Superior to Conventional Management in Inflammatory Bowel Disease. Inflamm Bowel Dis. 2019 Jun 27

Feuerstein J D. & al. Therapeutic Drug Monitoring in Inflammatory Bowel Disease. Gastroenterology. 2017:1-8.

Gecse KB, & al. Efficacy and Safety of the Biosimilar Infliximab CT-P13 Treatment in Inflammatory Bowel Diseases: A Prospective, Multicentre, Nationwide Cohort**.** J Crohns Colitis. 2016 Feb;10(2):133-40.

Gomollón F & al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease**.** J Crohns Colitis. 2016:1-23.

Gonczi L & al. Drug persistence and need for dose intensification to adalimumab therapy; the importance of therapeutic drug monitoring in inflammatory bowel diseases. BMC Gastroenterol. 2017 Aug 8;17(1):97

Gonczi L & al. Prediction of Short- and Medium-term Efficacy of Biosimilar Infliximab Therapy. Do Trough Levels and Antidrug Antibody Levels or Clinical And Biochemical Markers Play the More Important Role? J Crohns Colitis. 2016 Nov 12

Greuter T & al. Therapeutic Drug Monitoring to Guide Clinical Decision Making in Inflammatory Bowel Disease Patients with Loss of Response to Anti-TNF: A Delphi Technique-Based Consensus. Digestion. 2019 Aug 28:1-9.

Guidi L & al. Therapeutic drug monitoring is more cost-effective than a clinically-based approach in the management of loss of response to infliximab in inflammatory bowel disease: an observational multi-centre study. J Crohns Colitis. 2018 May 31

Jaminitski & al. The presence or absence of antibodies to infliximab or adalimumab determines the outcome of switching to etanercept. Rheum Dis. 2011 Feb;70(2):284-8.

Jentzer A & al. Short Communication: Evaluation of infliximab and anti-infliximab LISA-TRACKER immunoassays for the therapeutic drug monitoring of SB2 infliximab biosimilar. Ther Drug Monit. 2018 Sep 21**.**

Khan A & al. New Zealand Society of Gastroenterology Guidelines on Therapeutic Drug Monitoring in Inflammatory Bowel Disease. N Z Med J. 2019 Mar 8;132(1491):46-62.

Koren & al. Recommendation on risk-based strategies for detection and characterization of antibodies against biotechnology products. Journal of Immunological Methods, 333 (2008) 1-9.

Krzysiek R & al. Circulating Concentration of Infliximab and Response to Treatment in Ankylosing Spondylitis: Results From a Randomized Control Study. Arthritis & Rheumatism (Arthritis Care & Research) Vol. 61, No. 5, May 15, 2009, pp 569–57.

Lamb CA & al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut 2019;0:1–106.

Lee MW & al. Comparison of infliximab drug measurement across three commercially available ELISA kits**.** Pathology. 2016 Aug 23

Management of Paediatric Ulcerative Colitis, Part 1: Ambulatory Care—An Evidence-based Guideline. J Pediatr Gastroenterol Nutr. 2018 May 30.

Management of Paediatric Ulcerative Colitis, Part 2: Acute Severe Colitis—An Evidence-based Consensus Guideline. J Pediatr Gastroenterol Nutr. 2018 May 30.

Marcus Harbord & al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 2: Current Management. Journal of Crohn's and Colitis, 2017, 1–24.

Marotte & al. Circulating tumour necrosis factor-alpha bioactivity in rheumatoid arthritis patients treated with infliximab: link to clinical response. Arthritis Res Ther. 2005;7(1):R149-55.

Martelli L & al. Cost-effectiveness of drug monitoring of anti-TNF therapy in inflammatory bowel disease and rheumatoid arthritis: a systematic review**.** J Gastroenterol. 2017 Jan;52(1):19-25**.**

Mire-Sluis & al. Recommandation for the design and optimization of immunoassays used in the dectection of host antibodies against biotechnology products. Journal of Immunological Methods, 289 (2004) 1-16.

Mitrev N & al. Consensus statements on therapeutic drug monitoring of anti-tumour necrosis factor therapy in inflammatory bowel diseases. Aliment Pharmacol Ther. 2017 Dec;46(11-12):1037-1053.

Nasser Y & al. Comparison of Point-of-Care and Classical Immunoassays for the Monitoring Infliximab and Antibodies Against Infliximab in IBD. Dig Dis Sci. 2018 Jun 9

Papamichael K & al. Appropriate Therapeutic Drug Monitoring of Biologic Agents for Patients With Inflammatory Bowel Diseases. Clin. Gastroenterology and Hepatology, 24 March 2019.

Paul S & al. Letter: immunogenicity of anti-TNF in elderly IBD patients. Aliment Pharmacol Ther. 2019 Aug;50(3):336

Paul S & al. Letter: infliximab de-escalation based on trough levels in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2015 Oct;42(7):939-40.

Paul S & al. Therapeutic drug monitoring of infliximab and mucosal healing in inflammatory bowel disease: a prospective study. Inflamm Bowel Dis. 2013 Nov;19(12):2568-76

Peyrin-Biroulet L & al. French National Consensus Clinical Guidelines for the Management of Crohn's disease. Dig Liver Dis. 2016.

Peyrin-Biroulet L & al. French National Consensus Clinical Guidelines for the Management of Ulcerative Colitis. Dig Liver Dis. 2016; 48(7):726-33.

Poullenot F & al. Severe endoscopic lesions are not associated with more infliximab fecal loss in acute severe ulcerative colitis. Dig Liver Dis. 2018 Jul 10.

Radstake TRDJ & al. Formation of antibodies against infliximab and adalimumab strongly correlates with functional drug levels and clinical responses in rheumatoid arthritis. Ann Rheum Dis 2009;68:1739–1745.

Ram Raj Singh, & al. TNFα blockade in human diseases : mechanisms and future. Clin.Immunol., 2008 February ; 126(2):121-136.

Ruemmele F.M. & al. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. ournal of Crohn's and Colitis (2014).

Roblin X & al. Combination of C-reactive protein, infliximab trough levels, and stable but not transient antibodies to infliximab are associated with loss of response to infliximab in inflammatory bowel disease**.** J Crohns Colitis. 2015 Jul;9(7):525-31**.**

Roblin X & al. Cost savings of anti-TNF therapy using a test-based strategy versus an empirical dose escalation in Crohn's disease patients who lose response to infliximab. Journal of Market Access & Health Policy, [S.l.], v. 3, oct. 2015.

Roblin X & al. Development and Internal Validation of a Model Using Fecal Calprotectin in Combination with Infliximab Trough Levels to Predict Clinical Relapse in Crohn's Disease. Inflamm Bowel Dis. 2017 Jan;23(1):126-132.

Roblin X & al. Distinct Thresholds of Infliximab Trough Level Are Associated with Different Therapeutic Outcomes in Patients with Inflammatory Bowel Disease: A Prospective Observational Study. Inflamm Bowel Dis. 2017 Sep 22.

Schmitz EM & al. Therapeutic drug monitoring of infliximab: performance evaluation of three commercial ELISA kits. Clin Chem Lab Med. 2015 Nov 20.

Seow CH & al. Trough serum infliximab: a predictive factor of clinical outcome for infliximab treatment in acute ulcerative colitis. Gut. 2010 Jan;59(1):49-54.

Sparado A & al. Switching from infliximab or etanercept to adalimumab in resistant or intolerant patients with spondyloarthritis: a 4-year study. Rheumatology (Oxford). 2010 Jun;49(6):1107-11.

Steenholdt C, & al. Cut-off levels and diagnostic accuracy of infliximab trough levels and anti-infliximab antibodies in Crohn's disease. Scandinavian Journal of Gastroenterology, March 2011, Vol. 46, N°3, Pages 310-318.

Takeuchi & al. Baseline tumour necrosis factor alpha levels predict the necessity for dose escalation of infliximab therapy in patients with rheumatoid arthritis. Ann Rheum Dis. 2011 Jul;70(7):1208-15.

Ternant D & al. An enzyme-linked immunosorbent assay for therapeutic drug monitoring of Infliximab. Ther Drug Monit., 2006 April ; 28(2):169-174.

Therapeutic Drug Monitoring in Inflammatory Bowel Disease. Gastroenterology. 2017;153(3):835-857.

Therapeutic Drug Monitoring in Inflammatory Bowel Disease. Gastroenterology. 2017;153:858-859.

3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease. J Crohns Colitis. 2017; 11(1):3-25.

3rd European Evidence-based Consensus on the Diagnosis and Management of Ulcerative Colitis. J Crohns Colitis. 2017; 11(6):649-670.

Ungar B & al. Infliximab therapy intensification upon loss of response: Is there an optimal trough level? Dig Liver Dis. 2019 Mar 5.

Valido A & al. Efficacy, immunogenicity and cost analysis of a systematic switch from originator infliximab to biosimilar CT-P13 of all patients with inflammatory arthritis from a single center. Acta Reumatol Port. 2019 Nov 22

Van den Bemt BJF & al. Anti-infliximab antibodies are already detectable in most patients with rheumatoid arthritis halfway through an infusion cycle: an open-label pharmacokinetic cohort study. BMC Musculoskeletal Disorders 2011.

Vetterlein & al. No antibodies to PEG detected in patients treated with certolizumab pegol. Ann Rheum Dis 2008;67(Suppl II):236.

Vincent FB & al. Effect of serum anti-tumour necrosis factor (TNF) drug trough concentrations and antidrug antibodies (ADAb) to further anti-TNF short-term effectiveness after switching in rheumatoid arthritis and axial spondyloarthritis. Joint Bone Spine. 2016 Oct;83(5):595-7.

Wolbink GJ & al. Development of Anti-infliximab Antibodies and Relationship to Clinical Response in Patients With Rheumatoid Arthritis. ARTHRITIS & RHEUMATISM Vol. 54, No. 3, March 2006, pp711–715.

World Health Organization, WHO Expert Committee on Biological Standardization, Metcalfe, Clive, Bird, Chris, Dougall, Thomas. & al. (2017). Report on a collaborative study for proposed 1st international standard for Infliximab. WHO/BS/2017.2323.

Zufferey P & al. High level of anti-drug antibodies after intra-articular injection of anti-TNF**.** Rheumatology (Oxford). 2015 Dec;54(12):2291-2

SYMBOLS USED

CE	EC Declaration of conformity	IVD	*In Vitro* Diagnostic Medical Device
REF	Catalogue number		Manufacturer
LOT	Lot Number		Consult Instruction For Use
	Expiry Date		Temperature limitation
Σ	Number of tests		Biological hazard
	Warning		

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