English

i-Tracker anti-Infliximab

REF **CTI 003-100** Σ 100

INTENDED USE

i-Tracker anti-Infliximab (Theradiag) is an automated assay intended for the quantitative measurement of Anti-Infliximab antibodies (anti-drug antibodies: ADAb) 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 anti-Infliximab (Theradiag) assay is validated to monitor anti-drug antibodies induced by 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®).

SPECIMEN COLLECTION

The specimen types appropriate to **i-Tracker anti-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 anti-Infliximab assay is a two-step immunoassay using microparticles, acridinium-ester labeled chemiluminescent technology with the i-Track[10].

- In the first step, the Infliximab coupled magnetic microparticles, and human serum/plasma sample are mixed in an assay cuvette, which allows Anti-Infliximab antibodies to bind to the microparticles surface.
- After incubation, unbound reagent and sample matrix are removed by washing, and the microparticles-Infliximab-Anti-Infliximab antibodies immunocomplex are kept with the help of a magnetic separator.
- Secondly, Infliximab conjugated to acridinium ester is 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 anti-Infliximab antibodies.
- According to a certain specific Anti-Infliximab antibodies RLU-concentration standard curve, the RLU obtained can be interpreted to Anti-Infliximab antibodies concentration in the sample expressed as ng/mL.

For quantitation of Anti-Infliximab antibodies, the **i-Tracker Anti-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 (ng/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 Infliximab coupled microparticles in PBS with stabilizers. MP AINF Preservatives: Sodium azide < 0.1% and Proclin 300 < 0.06% ***Ready to use***	3 mL*
anti-Infliximab Buffer : 1 vial of PBS-Tween with stabilizer. BUF AINF Preservative: Proclin 300 <0.06% ***Ready to use***	23 mL*
Immunoconjugate: 1 vial of acridinium-ester labeled Infliximab, containing PBS with stabilizers. IC AINF Preservatives: Sodium azide < 0.1% and Proclin 300 < 0.06% ***Ready to use***	23 mL*
Control and Calibrators	
anti-Infliximab Calibrator A: a calibrator tube containing Anti-Infliximab antibodies (low level) in stabilizers and preservatives. CALA AINF **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***	2 mL*
anti-Infliximab Calibrator B: : a calibrator tube containing Anti-Infliximab antibodies (high level) in stabilizers and preservatives. CALB AINF **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***	2 mL*
anti-Infliximab Control: a control tube containing Anti-Infliximab antibodies in stabilizers and preservatives. CTL1 AINF **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***	2 x 2 mL*

*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. The human derived material in this product was tested and found nonreactive for Hepatitis B Surface Antigen (HBsAg), Anti-HCV and HIV 1/2 antibodies. Handle as if potentially infectious. Avoid contact with skin and eyes. Do not empty into drains. Wear suitable protective clothing.
6. This product requires the handling of control, calibrators and human specimens which contain human sourced materials. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
7. 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.

8. 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 standards mention in the chapter Warnings and Precautions point No. 6.
9. Spilled reagents should be cleaned up immediately. Observe all federal, state and local environmental regulations when disposing of wastes.
10. 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.
11. 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.
12. 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.
13. 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.
14. 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 anti-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.

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 anti-Infliximab** assay.

Lower Limit of Quantification of anti-Infliximab
10 ng/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 Anti-Infliximab antibodies concentration of each specimen and interpret the results into ng/mL.

Measurement range anti-Infliximab
10 ng/mL - 2000 ng/mL

Results below the lower limit (< 10 ng/mL) will be reported as HDM-, while those above the upper limit (> 2000 ng/mL) will be reported as HDM+.
Specimen with concentration < 10 ng/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 anti-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 anti-Infliximab (Theradiag) assay was evaluated to assess the impact of potential cross reacting molecules (Adalimumab, Certolizumab, Etanercept, Golimumab, Ustekinumab, Vedolizumab and anti-Adalimumab antibodies).

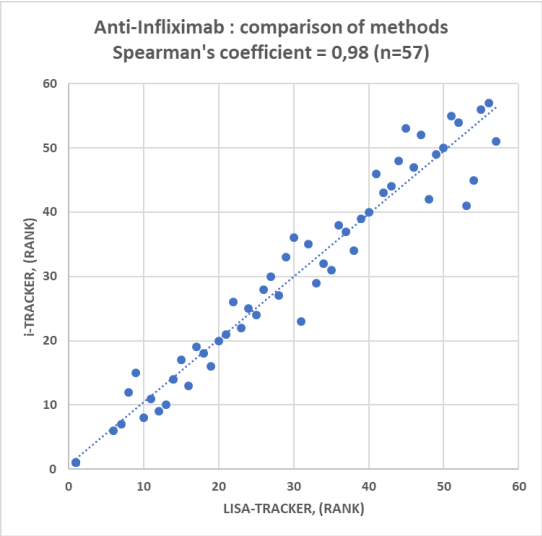
⇨ No cross reactivity is detected.

Precision

	Intra-run (10 tests in a same assay)		Inter-run (2 tests in 6 independent assay)	
Parameter	**Mean (ng/mL)**	**CV (%)**	**Mean (ng/mL)**	**CV (%)**
Anti-Infliximab	36	11.8	52	4.8
	164	1.8	184	2.3
	1462	3.2	1789	2.6

Correlation :

The quantification of Anti-Infliximab antibodies performed with i-Tracker **anti-Infliximab** assay gave similar results than the quantification made with **LISA-TRACKER anti-Infliximab** assay (Cat.n: LTI 003/LTI 005). Evaluation performed with 57 anti-Infliximab samples, shown that both assays are equivalent (Spearman's coefficient = 0.98).



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 anti-Infliximab** control (Theradiag), (Cat.n: CTI 003-PC) contains **anti-Infliximab antibodies**. This material is to be assayed in the same manner as the unknown sample.

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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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