Therapeutic drug monitoring (TDM) is a safe method to early measure drug level and detect anti-drug antibodies, guide the therapeutic procedure and optimize treatment efficacy

UNIQUE TDM MENU

- Comprehensive menu in inflammatory diseases and oncology
- CE-IVD validation on serum and plasma samples
- Validation in accordance with the 1st WHO international standards (Infliximab and Adalimumab)
- Validation with Princeps and Biosimilars
- Continuous development on new parameters

CLINICALLY VALIDATED

- Routine use tailored to your clinical practice
- Measurement ranges tailored to induction and maintenance treatment phases

EASY-TO-USE

- Ready-to-use reagents
- Standardized protocols from sample collection to results interpretation
- Validated on automated platforms (DS2, DSX, Evolis, etc.)
- Validated with IMMUNO-TROL INTERNAL CONTROL

LISA TRACKER is a solution validated and supported by pharmaceutical companies to adapt patient treatment

A **COMPLETE SOLUTION** TAILORED TO YOUR MONITORING TESTING NEEDS

Measurement range	
Infliximab 0,3-20 µg/mL	**Anti-Infliximab** 10-200 ng/mL
Adalimumab 0,3-20 µg/ml	**Anti-Adalimumab** 10-160 ng/mL
Certolizumab Pegol 3-84 µg/mL	**Anti-Certolizumab Pegol** 5-160 UA/mL
Etanercept 0,2-5 µg/ml	**Anti-Etanercept** 10-100 ng/ml
Vedolizumab 2-60 µg/mL	**Anti-Vedolizumab** 35-500 ng/mL
Ustekinumab 40-1000 ng/mL & 0,4-10 µg/mL	**Anti-Ustekinumab** 3-100 UA/mL
Golimumab 0,1-8µg/mL	**Anti-Golimumab** 5-80 ng/mL
Secukinumab 4-120 µg/ml	**Anti-Secukinumab** 50-1000 ng/mL
Rituximab 2-50 µg/ml	**Anti-Rituximab** 5-100 µg/ml
Bevacizumab 10-300 µg/ml	**Anti-Bevacizumab** 3-60 ng/mL
Trastuzumab 10-200 µg/ml	**Anti-Trastuzumab** 10-120 ng/mL
Tocilizumab 1-50 µg/ml	**Anti-Tocilizumab** 5-100 ng/mL

Tracker

Reference	Designation	Packaging
LTx 005	LISA TRACKER Duo Drug + ADAb	2 x 48 tests
LTx 002-48	LISA TRACKER Drug	48 tests
LTx 003-48	LISA TRACKER Anti-Drug	48 tests
LTT 004-96	LISA TRACKER TNF	96 tests

x = Infliximab / Adalimumab / Etanercept / Certolizumab Pegol / Golimumab / Rituximab / Secukinumab / Tocilizumab / Bevacizumab / TRAstuzumab / Ustekinumab / Vedolizumab

IMMUNO-TROL Internal Quality Control

A range of ready-to-use, internal Quality Control sera, CE marked, dedicated to the pharmacological dosage of biotherapies

Reference	Designation	Control
LTx 002-PC	Immuno-Trol Drug: Positive control two levels	2 x 250 µl
LTx 003-PC	Immuno-Trol anti-Drug: Positive control two levels	2 x 1 ml

CE Read carefully the instructions for use of the product insert before use. Pictures may differ from actual products.

Tracker 8p - V.03/2019 - UK

Theradiag INNOVATION FOR BIOTHERAPIES

Distributed by Abacus dx
1800 ABACUS (AUS) 0800 222 170 (NZ) | info@abacusdx.com | www.abacusdx.com
abacus dx

Tracker

THERAPEUTIC DRUG MONITORING IN INFLAMMATORY BOWEL DISEASES

MEASUREMENT OF **BIOLOGICAL DRUG** AND **FREE ANTI-DRUG** ANTIBODIES

EXTEND TREATMENT RESPONSE WHILE **MINIMIZING COSTS** AND **SIDE EFFECTS**

LISA TRACKER is your clinical decision-making tool for Inflammatory Bowel Diseases

CLINICALLY RELEVANT

- Numerous publications with LISA TRACKER in peer-reviewed journals
- International decision algorithms validated with LISA TRACKER

COST-EFFECTIVE

TDM strategy leads to major cost savings (28 to 50%) related to a biologic treatment[24]

- in Ulcerative Colitis (UC) and Crohn's Disease (CD)
- in patients in remission for treatment de-escalation[25]
- in patients with loss of response[26]

ACCURATE

- Accurate quantitative measurement of drugs and anti-drug antibodies
- Detection of free anti-drug antibodies as recommended by international guidelines to fit patient's status
- Performance validated with both Originators and Biosimilars

Therapeutic Drug Monitoring strategy leads to major cost savings in IBD patients while maintaining appropriate efficacy[6]

THERAPEUTIC DRUG MONITORING TO MAINTAIN PATIENT UNDER TREATMENT AND SUPPORT THE PROPER USE OF DRUGS

NEARLY 20-30%

of patients do not respond to an anti-TNFα treatment[1]

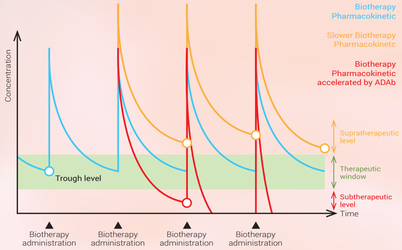
50% OF IBD PATIENTS

experience relapse in disease activity during maintenance therapy[2,3]

Pharmacokinetics and pharmacodynamics of biological therapies are highly variable among patients.

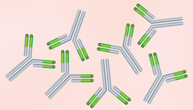
Patients with higher dose of drug or slower pharmacokinetics may have drug trough level above the therapeutic window (supratherapeutic). Higher trough levels may increase side effects.

Patients with lower dose due to the presence of anti-drug antibodies or with low serum albumin concentration or high baseline CRP concentration may have drug trough levels below the therapeutic window (subtherapeutic), leading to reduced drug efficacy.



Therapeutic Drug Monitoring helps physicians **to make rational treatment decisions during the course of IBD**

Immunogenicity of Biologics	Crohn's Disease	Ulcerative Colitis
Infliximab & Infliximab Biosimilar (CT-P13)	up to 83%[4]	up to 46%[4]
Adalimumab	up to 35%[4]	up to 5%[4]
Certolizumab Pegol	up to 25%[4]	up to 25%[4]
Vedolizumab	up to 3.7%[4]	up to 3.7%[4]
Ustekinumab	up to 1%[4,27]	up to 1%[4,22]
Golimumab	-	up to 19%[5]

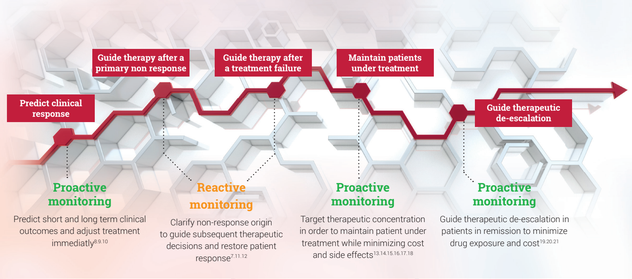


Anti-drug antibodies rates vary widely among biologics regardless of the disease.

Assessment of the immunogenicity of these agents is an important consideration in the treatment decision making process.

1. E. Zittan, B. Kabakchiev, c R. Milgrom, c G. C. Nguyen, a K. Croitoru, a A. H. Steinhart, a and M. G. Silverberg Higher Adalimumab Drug Levels are Associated with Mucosal Healing in Patients with Crohn's Disease ,c Crohns Colitis. 2016 May; 10(5): 513–519.
2. N. Vande Casteele, M. Ferrante, G. van Assche et al., "vol. 148, no. 7, pp. 1320–1329.e3, 2015. Trough concentrations of infliximab guide dosing for patients with inflammatory bowel disease," Gastroenterology.
3. C. Steenholdt, J. Brynskov, O. Ø. Thomsen et al., "Individualised therapy is more cost-effective than dose intensification in patients with Crohn's disease who lose response to anti-TNF treatment: a randomised, controlled trial," Gut, vol. 63, no. 6, pp. 919–927, 2014.
4. Strand V, Balsa A, Al-Saleh J, Barile-Fabris L, Horiuchi T, Takeuchi T, Lula S, Hawes C, Kola B, Marshall L.Immunogenicity of Biologics in Chronic Inflammatory Bowel diseases- BioDrugs. 2017 Aug;31(4):299-316.
5. Omoniyi J. Adedokun, Zhenhua Xu, a Colleen W. Marano, b Richard Strauss, c Hongwei Zhang, a Jewel Johanns, d Honghui Zhou, a Hugh M. Davis, e Walter Reinisch, f Brian G. Feagan, g Paul Rutgeerts, h and William J. Sandborn i Pharmacokinetics and Exposure-response Relationship of Golimumab in Patients with Moderately-to-Severely Active Ulcerative Colitis: Results from Phase 2/3 PURSUIT Induction and Maintenance Studies.J Crohns Colitis. 2017 Jan; 11(1): 38–48.
6. Martinelli L, Martelli L, Olivera P, Roblin X, Attar A, Peyrin-Biroulet L. 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.
7. Papamichael K, Vande Casteele N, Ferrante M, Gils A, Cheifetz AS.Therapeutic Drug Monitoring During Induction of Anti-Tumor Necrosis Factor Therapy in Inflammatory Bowel Disease: Defining a Therapeutic Drug Window. Inflamm Bowel Dis. 2017 Sep;23(9):1510-1515.
8. Papamichael K et al. Improved Long-term Outcomes of Patients With Inflammatory Bowel Disease Receiving Proactive Compared With Reactive Monitoring of Serum Concentrations of Infliximab. Clin Gastroenterol Hepatol. 2017 Oct;15(10):1580-1588.e3
9. Papamichael K et al. Improved Long-term Outcomes of Patients With Inflammatory Bowel Disease Receiving Proactive Compared With Reactive Monitoring of Serum Concentrations of Infliximab. Clin Gastroenterol Hepatol. 2017 Oct;15(10):1580-1588.e3
10. Wright EK, Kamm MA, De Cruz P, Hamilton AL, Selvaraj P, Princen F, Gorelik A, Liew D, Prideaux L, Lawrance IC, Andrews JM, Bampton PA, Jakobovits SL, Florin TH, Gibson PR, Debinski H, Macrae FA, Samuel D, Kronborg I, Radford-Smith G, Geary RB, Selby W, Bell SJ, Brown SJ, Connell WR.Anti-TNF Therapeutic Drug Monitoring in Postoperative Crohn's Disease. J Crohns Colitis. 2018 May 26;12(6):663-661. doi: 10.1093/ecco-jcc/jjy033
11. Roblin X, Rinaudo M, Del Tedesco E, Phelip JM, Genin C, Peyrin-Biroulet L, Paul S. et al. Development of an algorithm incorporating pharmacokinetics of adalimumab in inflammatory bowel diseases. Am J Gastroenterol. 2014 Aug;109(8):1250-6. doi: 10.1038/ajg.2014.146.
12. Roblin X, Vinet C, Paul S, Duru G, Willet N, Boschetti G, Del Tedesco E, Peyrin-Biroulet L, Marc Phelip J, Nancey S, Flourie B; Is the Pharmacokinetic Profile of a First Anti-TNF Predictive of the Clinical Outcome and Pharmacokinetics of a Second Anti-TNF? Inflamm Bowel Dis. 2018 Apr 26.
13. Papamichael K et al. Improved Long-term Outcomes of Patients With Inflammatory Bowel Disease Receiving Proactive Compared With Reactive Monitoring of Serum Concentrations of Infliximab. Clin Gastroenterol Hepatol. 2017 Oct;15(10):1580-1588.e3
14. Papamichael K, Vajravelu RK, Osterman MT, Cheifetz AS. Long-Term Outcome of Infliximab Optimization for Overcoming Immunogenicity in Patients with Inflammatory Bowel Disease. Dig Dis Sci. 2018 Mar;63(3):761-767. doi: 10.1007/s10620-018-4917-7.
15. Papamichael K, Vajravelu RK, Osterman MT, Cheifetz AS. Long-Term Outcome of Infliximab Optimization for Overcoming Immunogenicity in Patients with Inflammatory Bowel Disease. Dig Dis Sci. 2018 Mar;63(3):761-767. doi: 10.1007/s10620-018-4917-7.
16. 3rd European Evidence-based Consensus on the Diagnosis and Management of Ulcerative Colitis-J Crohns Colitis. 2017; 11(6):649-670.
17. Afif W et al. Clinical utility of measuring infliximab and human anti-chimeric antibody concentrations in patients with inflammatory bowel disease. Am J Gastroenterol. 2010 May;105(5):1133-9.
18. Roblin X et al. Development of an algorithm incorporating pharmacokinetics of adalimumab in inflammatory bowel diseases Am J Gastroenterol. 2014 Aug;109(8):1250-6.
19. Ungaro M.J. et al. : Successful reduction of overexposure in patients with rheumatoid arthritis with high serum adalimumab concentrations: an open-label, non-inferiority, randomized clinical trial-Ann Rheum Dis. 2018 Apr;77(4):484-487
20. Arnott A et al. Therapeutic drug monitoring is predictive of loss of response after de-escalation of infliximab therapy in patients with inflammatory bowel disease in clinical remission. Clin Res Hepatol Gastroenterol. 2016 Feb;40(1):90-8.
21. Paul S et al. Infliximab de-escalation based on trough levels in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2015 Oct;42(7):939-40.
22. Therapeutic Drug Monitoring in Inflammatory Bowel Disease too little too early?-comments on the American Gastroenterology Association Guideline Transl Gastroenterol Hepatol. 2017;2:113
23. Papamichael K , Cheifetz AS. Therapeutic drug monitoring in inflammatory bowel disease : for every patient and every drug? co-gastroenterology vol. 35 2019
24. L. Martelli L, Olivera P, Roblin X, Attar A, Peyrin-Biroulet L. 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.
25. Velayos FS, Kahn JG, Sandborn WJ, Feagan BG A test-based strategy is more cost effective than empiric dose escalation for patients with Crohn's disease who lose responsiveness to infliximab, Clin Gastroenterol Hepatol. 2013 Jun;11(6):664-66. doi: 10.1016/j.cgh.2012.12.035. Epub 2013 Jan 26
26. Guidi L et al. 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.

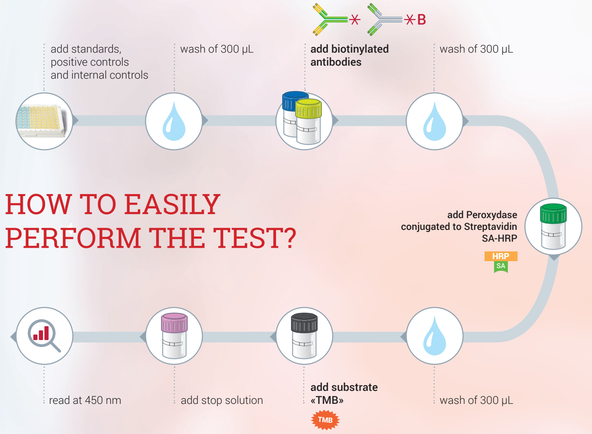
WHEN TO PERFORM TDM?



THERAPEUTIC THRESHOLDS

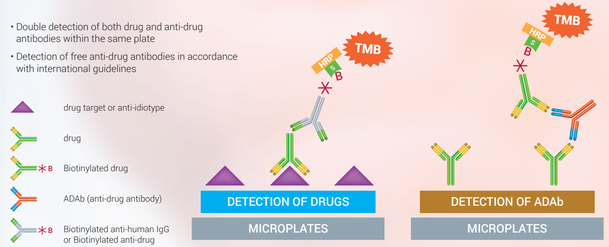
		SUGGESTED DRUG CONCENTRATION THRESHOLD FOR CLINICAL RESPONSE/REMISSION[23] (µG/ML)	SUGGESTED DRUG CONCENTRATION THRESHOLD FOR MUCOSAL HEALING[23] (µG/ML)
Infliximab	Induction (week 2)	≥ 20	≥ 25
	Induction (week 6)	≥ 10	N/A
	Postinduction (week 14)	≥ 3	≥ 7
	Maintenance	≥ 3	≥ 7
Adalimumab	Postinduction (week 14)	≥ 5	≥ 7
	Maintenance	≥ 3	≥ 8
Certolizumab Pegol	Postinduction (week 6)	≥ 32	N/A
	Maintenance	≥ 15	N/A
Golimumab	Postinduction (week 6)	≥ 2.5	N/A
	Maintenance	≥ 1	N/A
Vedolizumab	Induction (week 2)	≥ 28	N/A
	Induction (week 6)	≥ 24	N/A
	Postinduction (week 14)	≥ 15	≥ 17
	Maintenance	≥ 12	≥ 14
Ustekinumab	Postinduction (week 8)	≥ 3.5	N/A
	Maintenance	≥ 1	≥ 4.5

N/A, not applicable, due to paucity of data.
These target ranges were those used in landmark studies or international guidelines and do not necessarily translate into general recommendations for individual patients.
The target ranges may vary with newly published studies.



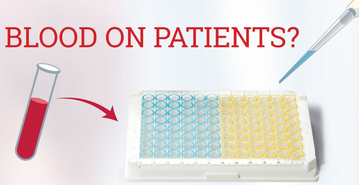
HOW TO EASILY PERFORM THE TEST?

- Double detection of both drug and anti-drug antibodies within the same plate
- Detection of free anti-drug antibodies in accordance with international guidelines



WHEN TO COLLECT BLOOD ON PATIENTS?

- Timing of samples collection is key to interpret the result as the drug concentration varies during the interval between two injections
- Drug and anti-drug measurement is recommended to be performed at Trough Concentration (TC), just before the next dose, both during induction and mainenance:
  - Target ranges are defined using TC
  - Free anti-drug antibodies are mostly detectable at TC

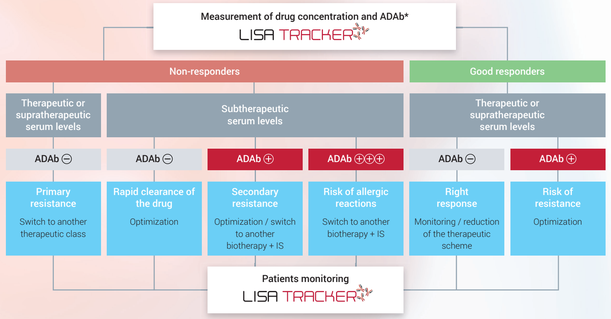


INTERPRET DOSING INFORMATION

- Drug levels required to improve clinical outcomes may vary between patients and depend on the desired therapeutic endpoint
- In patients with undetectable drug levels, anti-drug antibody (ADAb) quantification helps to identify how to improve patient response
- If your patients are good responders with higher drug trough levels, dose excalation may be possible without affecting clinical outcomes
- In patients with high anti-drug antibodies levels, a switch in-class may be necessary
- In patients with low anti-drug antibodies levels, the addition of an immunosuppressive drug may improve clinical outcomes

Example of therapeutic decision algorithm in patient with loss of response

	Negative Anti-drug Antibodies	Positive Anti-drug Antibodies
Therapeutic level of Drug	Switch out of therapeutic class	Retest
Subtherapeutic level of Drug	Treatment Optimization	Switch in-class



IS = immunosuppressant

* These findings do not constitute a diagnosis in any case. They reflect information available in published peer-reviewed literature and guidelines and should be independently evaluated by the treating clinician and used to complete other clinical and biological information in accordance with clinician's independent medical judgment.