CLINICAL DIAGNOSTICS

PROmonitor

Step forward in monitoring biological therapies

Efficient and high-quality testing for drug levels and immunogenicity

DRUG MONITORING

GRIFOLS

PROmonitor

Therapeutic drug monitoring: a real need

Therapeutic drug monitoring is being increasingly adopted to try to optimize patients outcomes, particularly during maintenance treatment.[41]

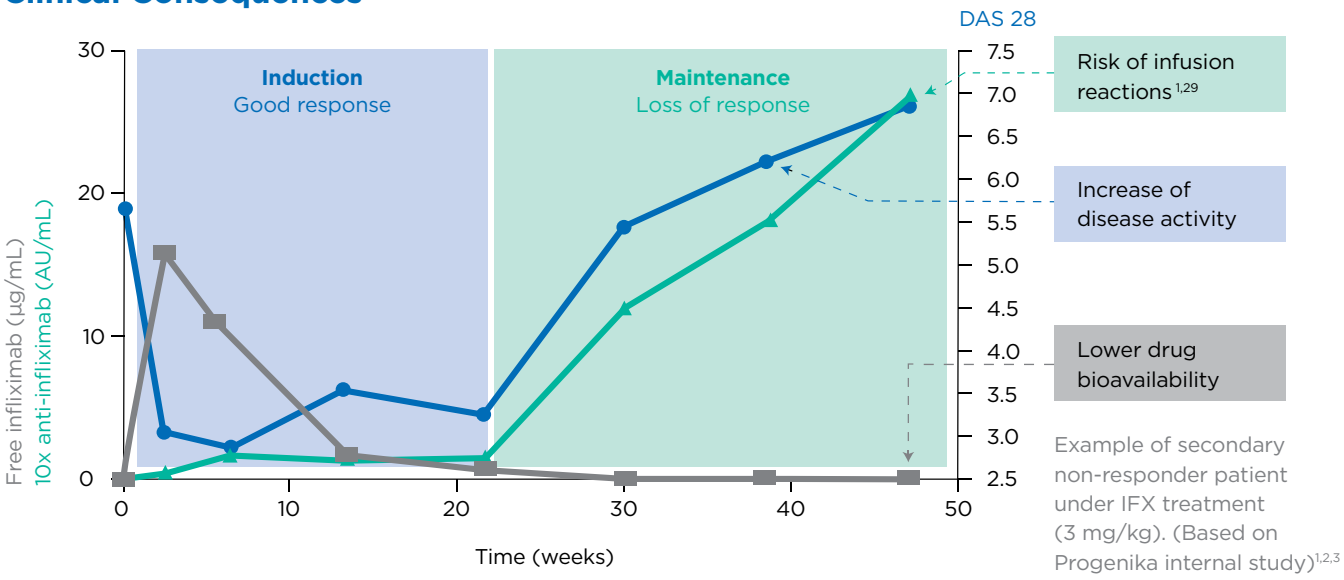
Correlation between DL/ADA levels and clinical response[3,27,28,33,37]

Drug and anti-drug antibodies levels strongly correlate with clinical response

Positive antibodies to TNF inhibitors correlate to null or sub-therapeutic levels of the drug and poor clinical response

Therapeutic levels of TNF inhibitors correlate to low or null titer of anti-drug antibodies and good or moderate clinical response

Clinical Consequences



Example of secondary non-responder patient under IFX treatment (3 mg/kg). (Based on Progenika internal study)[1,2,3]

Testing for drug levels and immunogenicity

Easy-to-use ELISA kits for routine use in clinical laboratories.

Quantitative determination of drug levels and anti-drug antibodies levels for the main biological treatments in different therapy areas

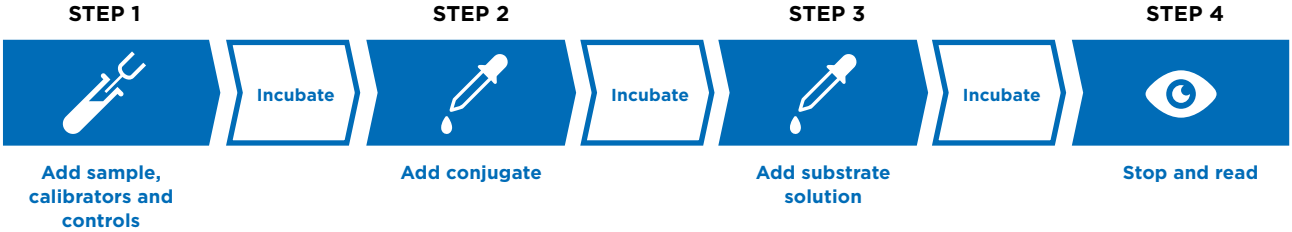
Optimized methodology

- Multiple configurations. Removable strips
- Manual or automated mode
- Quick procedure: 2 hr 30 min
- Microplate precoated and ready-to-use reagents

High quality for reliable results

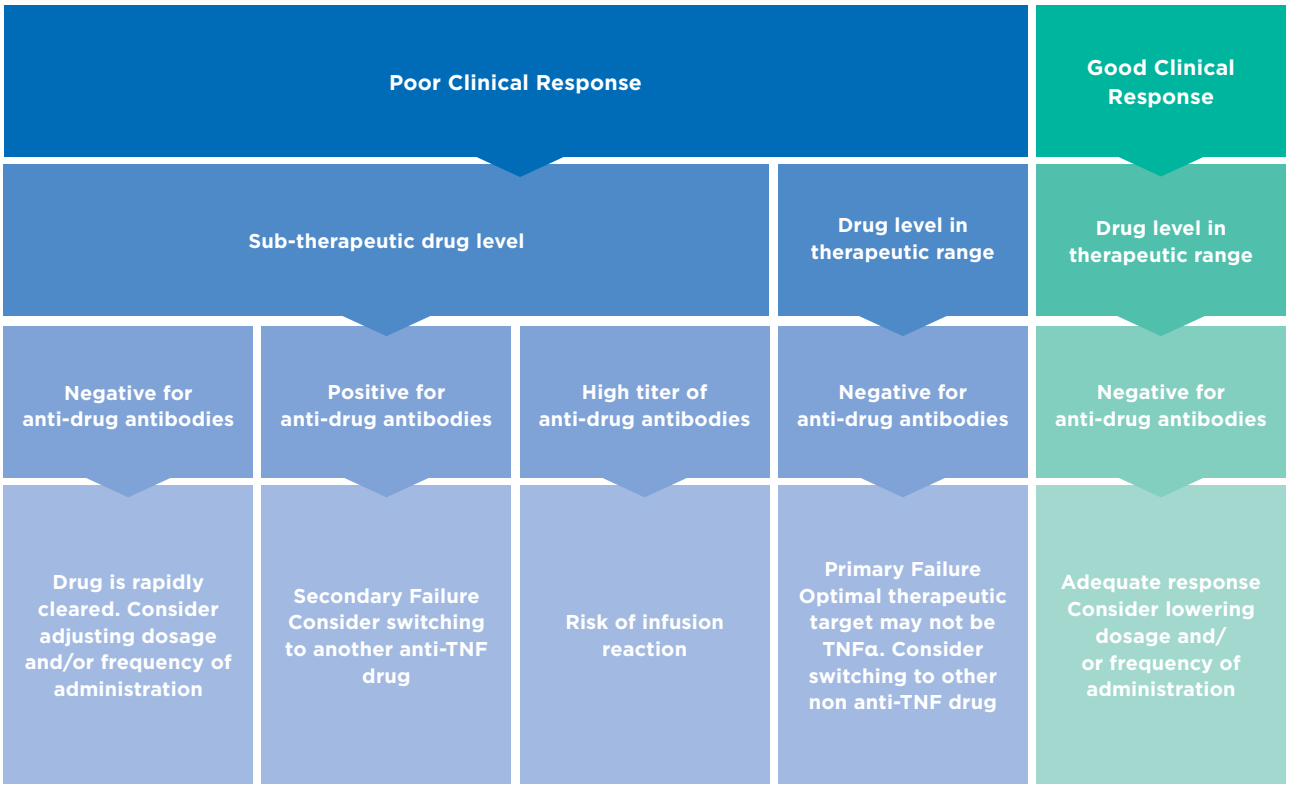
- Highly qualified professionals
- Supported by a large number of peer-reviewed articles
- High specificity and sensitivity
- Easy data interpretation

Simple Procedure



Quick procedure: 2 hours 30 minutes
Hands-on time: 30 minutes
4 simple steps

Algorithm for Patient Management



Illustrative internal algorithm for patient management using drug levels and immunogenicity testing. Not for use as sole input in clinical decisions. Based on published literature[1,3,35,36,39]

Main benefits of therapeutic drug monitoring

By providing TDM tools, clinicians may improve patient treatment strategy, reducing the risk of inadequate treatments, inappropriate dosages and side effects.[7,31,35,36,40,42]

It is widely accepted that there is a correlation between drug levels and therapeutic response. In consequence, drug monitoring and, if appropriate, tests for antibodies, may provide a more accurate analysis and help to adjust dosage in a personalized therapy strategy.[7,35,42]

TDM may shed light on the main situations encountered in the clinical practice: primary treatment failure, inadequate treatment response, adverse reaction to the injection, or secondary loss of response.[31,36,40,42]

Working together to administer the proper dose for the optimal treatment, resulting in efficient use of money[15,30,32,34,38]

A lack of information about serum drug levels and ADA can lead to non-optimal clinical treatment decisions and lead to unnecessary costs.[15]

In consequence, a test-based strategy with TDM of anti-TNF is more cost-effective than an empirical strategy in both IBD and RA patients, with no negative impact on efficacy.[30,34,38]

TDM should be taken into consideration by physicians and healthcare authorities to guide decision-making in clinical practice and to reduce the costs of healthcare.[38]

Main peer-reviewed articles using Promonitor kits

1. Pascual-Salcedo D, et al. Influence of immunogenicity on the efficacy of long-term treatment with infliximab in rheumatoid arthritis. Rheumatology 2011; 50:1445-1452.
2. Plasencia C, et al. Influence of immunogenicity on the efficacy of longterm treatment of spondyloarthritis with infliximab. Ann Rheum Dis. 2012;71(12):1955-60.
3. Rosas J, et al. Clinical relevance of monitoring serum levels of adalimumab in patients with rheumatoid arthritis in daily practice. Clin Exp Rheumatol. 2014;32(6):942-8.
4. Sanmarti R, et al. Towards optimal cut-off trough levels of adalimumab and etanercept for a good therapeutic response in rheumatoid arthritis. Results of the INMUNOREMAR study. Ann Rheum Dis. 2015;74(8):e42.
5. Jani M, et al. Clinical utility of random anti-tumour necrosis factor drug testing and measurement of anti-drug antibodies on long-term treatment response in rheumatoid arthritis. Lancet. 2015;385 Suppl 1:S48.
6. Chen DY, et al. Drug trough levels predict therapeutic responses to dose reduction of adalimumab for rheumatoid arthritis patients during 24 weeks of follow-up. Rheumatology (Oxford). 2016 ;55(1):143-8.
7. Chen DY, et al. Immunogenicity, drug trough levels and therapeutic response in patients with rheumatoid arthritis or ankylosing spondylitis after 24-week golimumab treatment. Ann Rheum Dis. 2015;74(12):2261-4.
8. Schmitz EM, et al. Therapeutic drug monitoring of infliximab: performance evaluation of three commercial ELISA kits. Clin Chem Lab Med. 2016;54(7):1211-9.
9. Llinares-Tello F, et al. Analytical and clinical evaluation of a new immunoassay for therapeutic drug monitoring of etanercept. Clin Chem Lab Med. 2015;53(10):e279-82.
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12. Zisapel M, et al. Prevalence of TNF-α blocker immunogenicity in psoriatic arthritis. J Rheumatol. 2015;42(1):73-8.
13. Almirall M, et al. Drug levels, immunogenicity and assessment of active sacroiliitis in patients with axial spondyloarthritis under biologic tapering strategy. Rheumatol Int. 2016;36(4):575-8.
14. Sieczkowska J, et al. Switching Between Infliximab Originator and Biosimilar in Paediatric Patients with Inflammatory Bowel Disease. Preliminary Observations. J Crohns Colitis. 2016;10(2):127-32.
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18. Ghia C, et al. Analytical and Clinical Evaluation of an Immunoassay for Estimating Immunogenicity of Infliximab and Etanercept in Indian Population. J Assoc Physicians India. 2016;64(9):14-17.
19. Chimenti MS, et al. Long-term treatment with adalimumab in psoriatic arthritis: serum adalimumab concentration, immunogenicity and the link with clinical response. J Int Med Res. 2016;44(1 suppl):48-52.
20. Burmester GR, et al. Low immunogenicity of tocilizumab in patients with rheumatoid arthritis. Ann Rheum Dis. 2017;76(6):1078-1085.
21. Ruiz-Argüello MB, et al. Antibodies to infliximab in Remicade-treated rheumatic patients show identical reactivity towards biosimilars. Ann Rheum Dis. 2016;75(9):1693-6.
22. Cordero-Coma M, et al. Adalimumab for Treatment of Noninfectious Uveitis: Immunogenicity and Clinical Relevance of Measuring Serum Drug Levels and Antidrug Antibodies. Ophthalmology. 2016 ;123(12):2618-2625.
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Other peer-reviewed articles mentioned in this brochure

28. Radstake TR, et 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(11):1739-45.
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33. Nanda KS, et al. Impact of antibodies to infliximab on clinical outcomes and serum infliximab levels in patients with inflammatory bowel disease (IBD): a meta-analysis. Am J Gastroenterol. 2013;108(1):40-7.
34. Steenholdt C, 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. 2014;63(6):919-27.
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Manual or Automated Mode

- Promonitor kits can be fully automated in any open ELISA processor, leading to an increase in productivity and reliability
- Grifols provides adapted protocols for Triturus and is continuously working on the adaptation to other instruments
- Tests can also be performed manually (2 hours 30 min or 1 hour 45 min) with minimal hands-on time (30 min) and the only platform required is a microplate reader

Tests can be fully automated in Triturus, SQII or any ELISA open processor

Biosimilars

Evaluation studies have demonstrated that Promonitor kits are able to quantify the following biosimilars and the corresponding anti-biosimilar antibodies [21, 24, 25, 26, 43, 44]:

Infliximab	Remsima/Inflectra (CT-P13) Flixabi (SB2)
Adalimumab	Amgevita (ABP 501) Imraldi (SB5) Hyrimoz (GP 2017)
Etanercept	Benepali (SB4) Erelzi (GP 2015)
Rituximab	Truxima (CT-P10)

Diagnostic Service

Grifols is offering TDM testing services in its facilities in Europe and North America. An easy-to-use sample collection and shipping service is provided (available in US). Physicians receive a complete report detailing results and reference values.

San Marcos, TX, US

Derio, Spain

Current portfolio

- Promonitor Infliximab
- Promonitor anti-Infliximab
- Promonitor Adalimumab
- Promonitor anti-Adalimumab
- Promonitor Etanercept
- Promonitor anti-Etanercept
- Promonitor Rituximab
- Promonitor anti-Rituximab
- Promonitor Golimumab
- Promonitor anti-Golimumab
- Promonitor Vedolizumab
- Promonitor anti-Vedolizumab
- Promonitor Ustekinumab
- Promonitor anti-Ustekinumab

Under development

- Promonitor Tocilizumab*
- Promonitor anti-Tocilizumab*

*Already available for sale for RUO

Product registration and availability vary by country. Ask your local Grifols representative for more information.

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