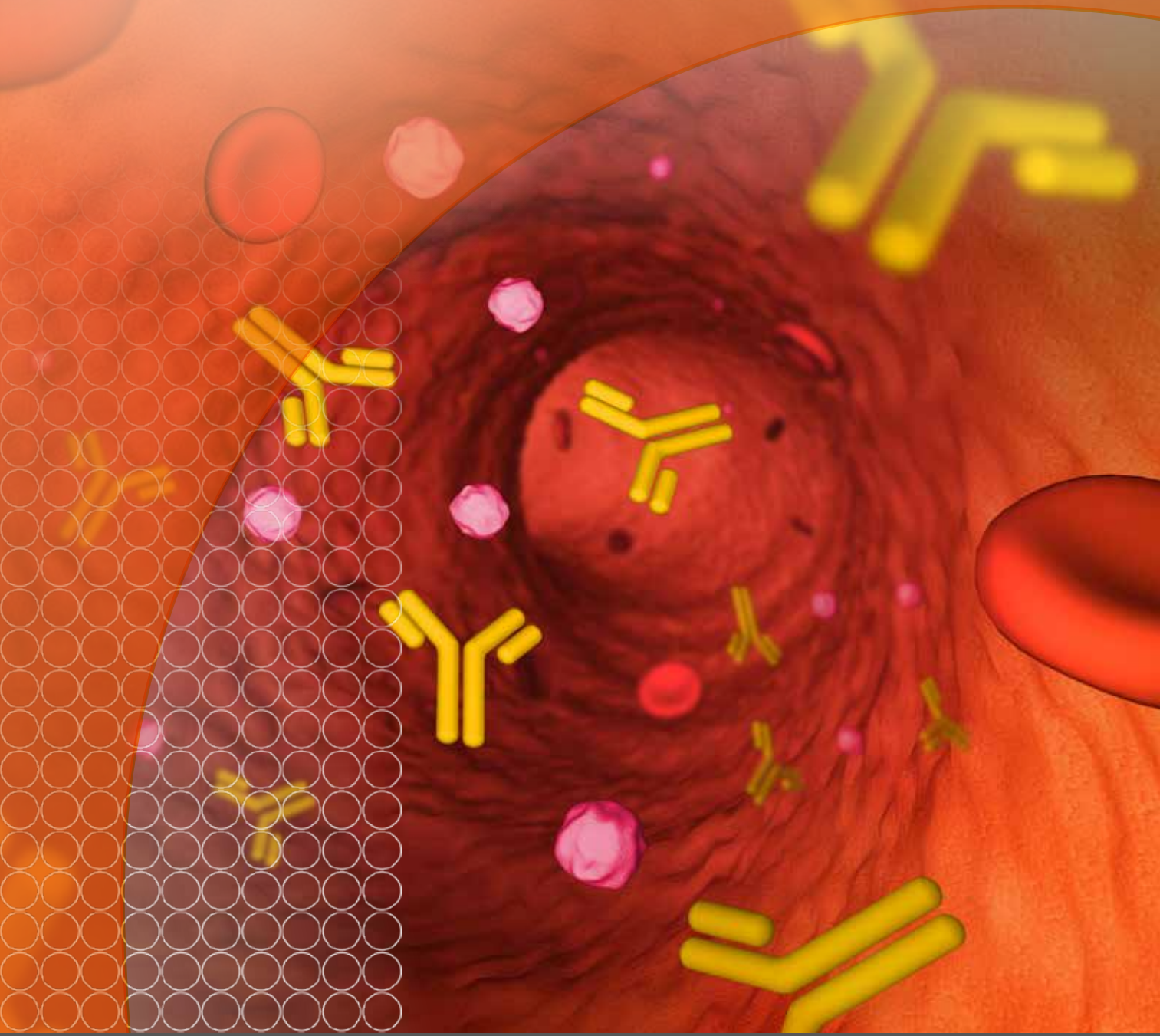
Therapeutic drug monitoring (TDM)

- ELISA and rapid assay
- Quantification of drug concentrations and anti-drug antibodies
- Validated by KU Leuven, Belgium
- Ready to use reagents
- Validated on automated ELISA systems



Therapeutic monoclonal antibodies

Therapeutic monoclonal antibodies, such as infliximab, adalimumab and vedolizumab, are biologic agents used for the treatment of inflammatory diseases such as Crohn's disease and ulcerative colitis. **Infliximab** and **adalimumab** (ADM) belong to the group of TNFα blockers. Vedolizumab instead is an α4β7-integrin antagonist.

How do therapeutic monoclonal antibodies function?

TNFα blockers

In healthy individuals, TNFα plays an essential role in the regulation of inflammation via binding to specific receptors.

In patients with Crohn's disease and ulcerative colitis, the immune cells are continously triggered to produce TNFα, so that the inflammation does not cease and becomes chronic.

TNFα blockers bind to TNFα (see Figure 1), hereby blocking the pro-inflammatory signaling pathway that inflicts damage to the gut tissue.
As a result, gut inflammation and symptoms in patients with inflammatory bowel diseases resolve.

α4β7-integrin antagonists

The α4β7-integrin antagonist vedolizumab is a gut-specific, humanized monoclonal antibody targeting the α4β7-integrin protein. This protein is involved in the migration of lymphocytes to the gut.

By binding to the α4β7-integrin the lymphocytes are prevented from migrating into the gut lumen so that they cannot exert their pro-inflammatory effect.

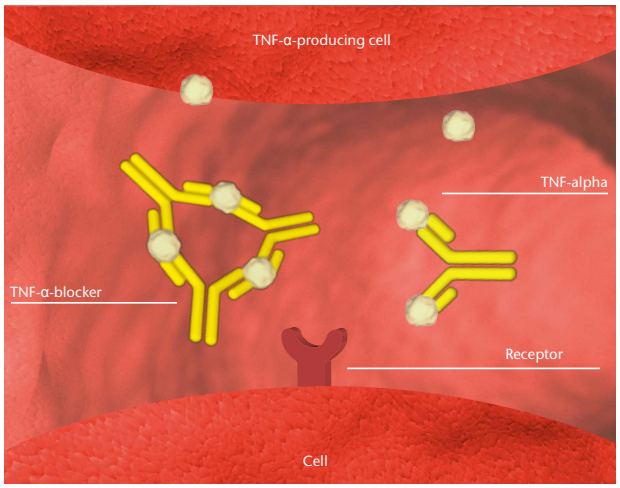


Figure 1: Example of the function of TNFα blockers. TNFα blockers scavenge TNFα, which as a result can no longer bind to the receptor. The pathway leading to disease is interrupted, because the receptor is not activated anymore. Therefore, no pro-inflammatory signal is transmitted.

Individual dose adjustment by measuring drug levels and immunogenicity

In order for biological drugs to work optimally, the drug concentration needs to be sufficiently high. Therefore, regular drug concentration monitoring is advised. The trough concentration (TC) is defined as the drug concentration in the blood measured right before the next infusion (see Figure 2).

Immunogenicity may have an impact on the efficacy of the drug. Anti-drug antibodies (ADA) may bind to the drug and lead to a decrease in drug availability and allergy-like reactions.

Monitoring of drug- and anti-drug-antibody-concentrations of biologic agents helps to optimally adjust the therapy to the individual needs of the patient.

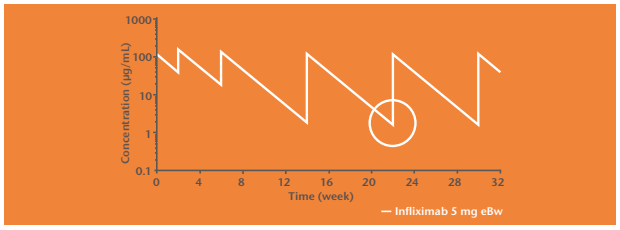


Figure 2: Pharmacokinetic profile of IFX. The white circle marks an example of a trough concentration.
(Adapted from *Tracey D. et al.*, Pharm & Ther 2008)

TDM of TNFα blockers and anti-integrins using RIDASCREEN® and RIDA®QUICK assays

Key features of R-Biopharm's TDM assays

- All TDM assays of R-Biopharm AG are validated by KU Leuven, Belgium
- ELISA assays and the rapid assays correlate very well due to identical monoclonal antibodies
- ELISA assays are validated on automated ELISA readers such as DSX®
- RIDASCREEN® IFX Monitoring and RIDA®QUICK IFX Monitoring quantify infliximab and its biosimilars
- RIDA®QUICK IFX Monitoring is a rapid point-of-care assay, which allows for the quantitative determination of infliximab within 20 minutes.

Therapy adjustment based on therapeutic drug monitoring

The TAXIT-Algorithm (TAXIT = Trough Concentration Adapted Infliximab Treatment, Figure 3) is a recommendation for therapy adaptation based on the results of trough- and anti-drug-antibody-concentrations of infliximab. It is a result of the study[1] by *Niels Vande Casteele et al.* (KU Leuven, Belgium) which investigated the effect of drug monitoring on the outcome of TNFα-treatment. The study shows the positive effect of TDM for **therapy optimization** and **treatment cost reduction**. Moreover, it indicates that testing for anti-drug-antibodies does not have to be performed on a standard basis but only in patients with undetectable trough concentrations of infliximab (see Figure 3). RIDASCREEN® IFX Monitoring and RIDASCREEN® Anti-IFX Antibodies are based on the assays used in this study.

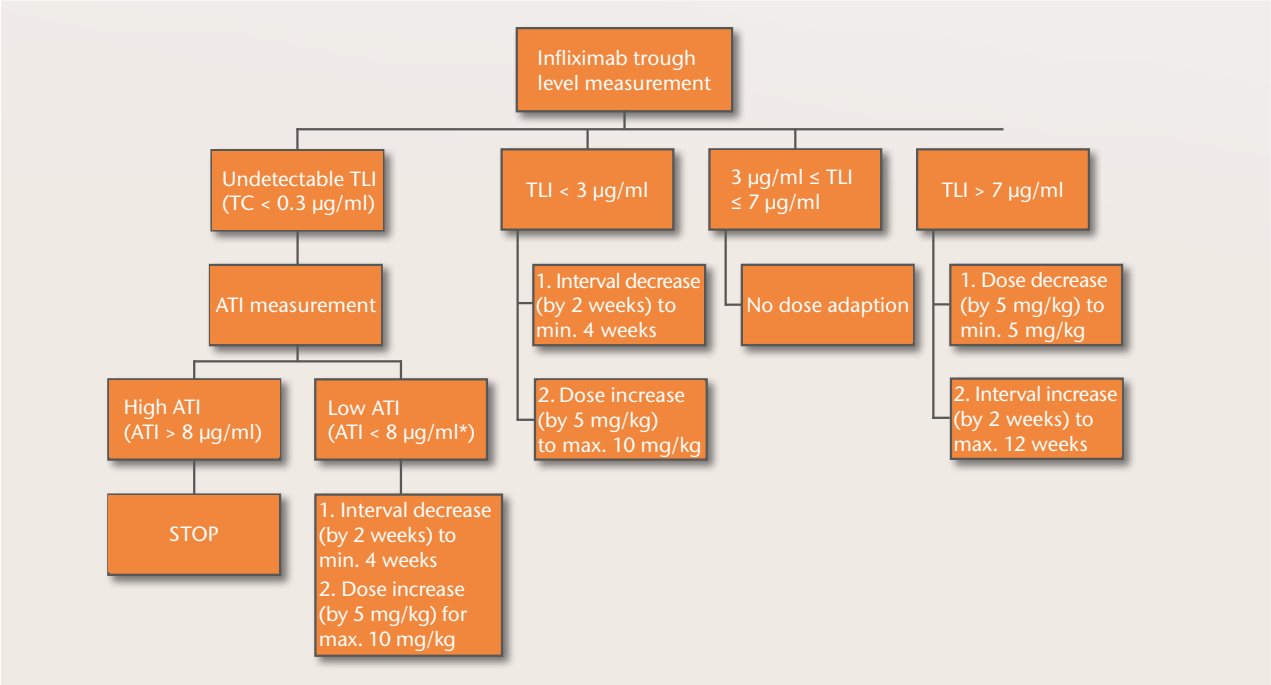


Figure 3:
TAXIT-Algorithm based on TLI and ATI (*Niels Vande Casteele et. al.* 2015)
TLI = Trough Level Infliximab, ATI = Antibodies Towards Infliximab

References:
[1] *Vande Casteele N. et al.*, Trough Concentrations of Infliximab Guide Dosing for Patients with Inflammatory Bowel Disease. Gastroenterology 2015; 148(7):1320-9.

R-Biopharm therapeutic drug monitoring (TDM) at a glance

Product	Description	Tests	Matrix	Art. No.
	Enzyme immunoassays and lateral flow assay			
RIDASCREEN® IFX Monitoring	Enzyme immunoassay for the quantification of infliximab and its biosimilars	96	Serum/ plasma	G09041
RIDASCREEN® Anti-IFX Antibodies	Enzyme immunoassay for the quantification of antibodies to infliximab and its biosimilars	96	Serum/ plasma	G09042
RIDASCREEN® ADM Monitoring	Enzyme immunoassay for the quantification of adalimumab	96	Serum/ plasma	G09043
RIDASCREEN® Anti-ADM Antibodies	Enzyme immunoassay for the quantification of antibodies to adalimumab	96	Serum/ plasma	G09044
New RIDASCREEN® VDZ Monitoring	Enzyme immunoassay for the quantification of vedolizumab	96	Serum/ Plasma	G09045
RIDA®QUICK IFX Monitoring	Immunochromatographic lateral flow assay for the quantification of infliximab and its biosimilars	25	Serum/ plasma	GN3041

Also available:
For IBD and IBS diagnostics

Product	Description	Tests	Matrix	Art. No.
	Enzyme immunoassay			
RIDASCREEN® Calprotectin	Enzyme immunoassay for the quantification of calprotectin	96	Stool	G09036

Accessory

Product	Description	Tests	Matrix	Art. No.
RIDA®TUBE Calprotectin	For collection and preparation of stool samples • only use with RIDASCREEN® Calprotectin G09036	50		GZ3016
RIDA®TUBE	For collection and preparation of stool samples • unfilled; to use after internal validation	50		GZ3013
RIDA®QUICK SCAN II	Lateral flow reader – for read out of GN3041			ZRQS2-KD
RIDA®QUICK IFX Monitoring Control Set	Positive controls – accessory for GN3041			GP3041

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