Therapeutic drug monitoring (TDM)

- ELISAs and rapid assays
- 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, golimumab, vedolizumab and ustekinumab are biologic agents used for the treatment of inflammatory diseases such as Crohn's disease and ulcerative colitis. **Infliximab** (IFX), **adalimumab** (ADM) and **golimumab** (GLM) belong to the group of TNFα blockers. **Vedolizumab** (VDZ) instead is an α4β7-integrin antagonist. **Ustekinumab** is an antibody against the cytokines interleukin-12 (IL-12) and interleukin-23 (IL-23)

How do therapeutic monoclonal antibodies work?

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.

IL-12/IL-23 blocker Ustekinumab (UST) is a fully human monoclonal antibody that binds to the p40 subunit common to IL-12 and IL-23 thereby preventing the interaction with the cytokine receptors on T cells, natural killer cells and antigen-presenting cells. The further inflammatory reaction is stopped.

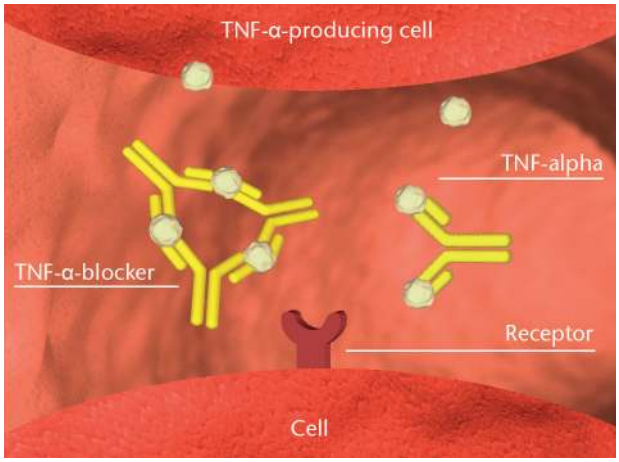

Figure 1: Example of the function of TNFα blockers. TNFα blockers scavenge TNFα, which as a result, can no longer bind to the receptor. The pathway leading to disease is interrupted, because the receptor is not activated anymore. Therefore, no pro-inflammatory signal is transmitted.

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. 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.

TDM 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
- ELISAs and the corresponding rapid assays correlate very well due to identical monoclonal antibodies
- RIDASCREEN® IFX Monitoring and RIDA®QUICK IFX Monitoring quantify infliximab and its biosimilars. RIDASCREEN® ADM Monitoring and RIDA®QUICK ADM Monitoring quantify adalimumab
- The rapid assays RIDA®QUICK IFX Monitoring and RIDA®QUICK ADM Monitoring allow the determination of trough level concentrations of infliximab and its biosimilars and adalimumab, respectively within 20 minutes
- All ELISAs are validated on automated ELISA readers such as DSX® and have breakable microwell plates

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 is usefull 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.

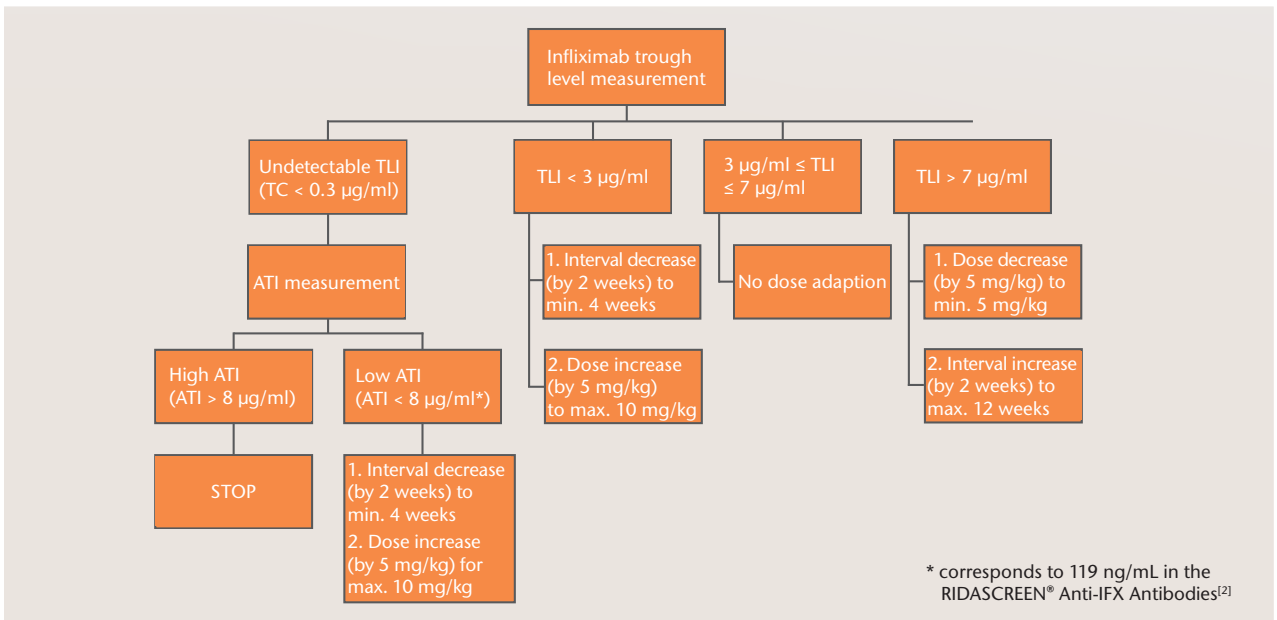

Figure 3: TAXIT-Algorithm based on TLI and ATI (*Niels Vande Casteele et. al.* 2015)
TLI = Trough Level Infliximab, ATI = Antibodies Towards Infliximab

Referenzen:

[1] *Vande Casteele N* et al. Trough concentrations of infliximab guide dosing for patients with inflammatory bowel disease. Gastroenterology 2015;148:1320-1329.e3

[2] *Imbrechts M* et al. Anti-infliximab antibodies: How to compare old and new data? J Pharm Biomed Anal 2020;177:112842

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 quantitative determination of infliximab (IFX) and its biosimilars	96	Serum/ plasma	G09041
RIDASCREEN® Anti-IFX Antibodies	Enzyme immunoassay for the quantitative determination of antibodies to infliximab (IFX) and its biosimilars	96	Serum/ plasma	G09042
RIDASCREEN® ADM Monitoring	Enzyme immunoassay for the quantitative determination of adalimumab (ADM)	96	Serum/ plasma	G09043
RIDASCREEN® Anti-ADM Antibodies	Enzyme immunoassay for the quantitative determination of antibodies to adalimumab (ADM)	96	Serum/ plasma	G09044
RIDASCREEN® VDZ Monitoring	Enzyme immunoassay for the quantitative determination of vedolizumab (VDZ)	96	Serum/ plasma	G09045
RIDASCREEN® GLM Monitoring	Enzyme immunoassay for the quantitative determination of golimumab (GLM)	96	Serum/ plasma	G09047
New RIDASCREEN® UST Monitoring	Enzyme immunoassay for the quantitative determination of ustekinumab (UST)	96	Serum/ plasma	G09049
RIDA®QUICK IFX Monitoring	Immunochromatographic lateral flow assay for the quantitative determination of infliximab (IFX) and its biosimilars	25	Serum/ plasma	GN3041
RIDA®QUICK ADM Monitoring	Immunochromatographic lateral flow assay for the quantitative determination of adalimumab (ADM)	25	Serum/ plasma	GN3043

Also available:
For IBD and IBS diagnostics

	Enzyme immunoassay			
RIDASCREEN® Calprotectin	Enzyme immunoassay for the quantitative determination of calprotectin	96	Stool	G09036

Accessories

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 - IVD SET	Lateral flow reader (CE-IVD) and 2D barcode scanner • for read out of GN3041 and GN3043			ZRQS2-KD-SET
RIDA®QUICK IFX Monitoring Control Set	Positive controls • accessory for GN3041			GP3041
RIDA®QUICK ADM Monitoring Control Set	Positive controls • accessory for GN3043			GP3043

For further details and information visit our website www.r-biopharm.com, contact your local distributor or Clinical Sales International.

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