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LISA TRACKER kits

A diagnostic tool allowing the individual or simultaneous dosage of:

- the prescribed drug (original biological and biosimilar),
- Anti-Drug Antibodies (ADAb).

- Infliximab (Anti TNFα)
- Adalimumab (Anti TNFα)
- Etanercept (Anti TNFα)
- Certolizumab (Anti TNFα)
- Golimumab (Anti TNFα)
- Tocilizumab (Anti IL6R)
- Rituximab (Anti CD20)
- Bevacizumab (Anti VEGF)
- Trastuzumab (Anti HER2)
- Ustekinumab (Anti IL12, IL23)
- NEW Vedolizumab (Anti integrin α4β7)

	Reference	Designation	Packaging
3 parameters: **TNFα + Drug + ADAb**	LTx 001	LISA TRACKER Premium	3 x 32 tests
2 parameters: **Drug + ADAb**	LTx 005	LISA TRACKER Duo Drug + ADAb	2 x 48 tests
1 parameter: **Drug**	LTx 002-48	LISA TRACKER Drug	48 tests
1 parameter: **ADAb**	LTx 003-48	LISA- TRACKER anti-Drug	48 tests
1 parameter: **TNFα**	LTT 004-48	LISA- TRACKER TNFα	48 tests

(x= Infliximab / Adalimumab / Etanercept / Certolizumab Pegol / Golimumab / Rituximab / Tocilizumab / Bevacizumab / TRastuzumab / Ustekinumab / Vedolizumab)

The advantages of the LISA TRACKER range

- A complete range of assays
- ELISA format for an easy use in routine
- Standardized protocols
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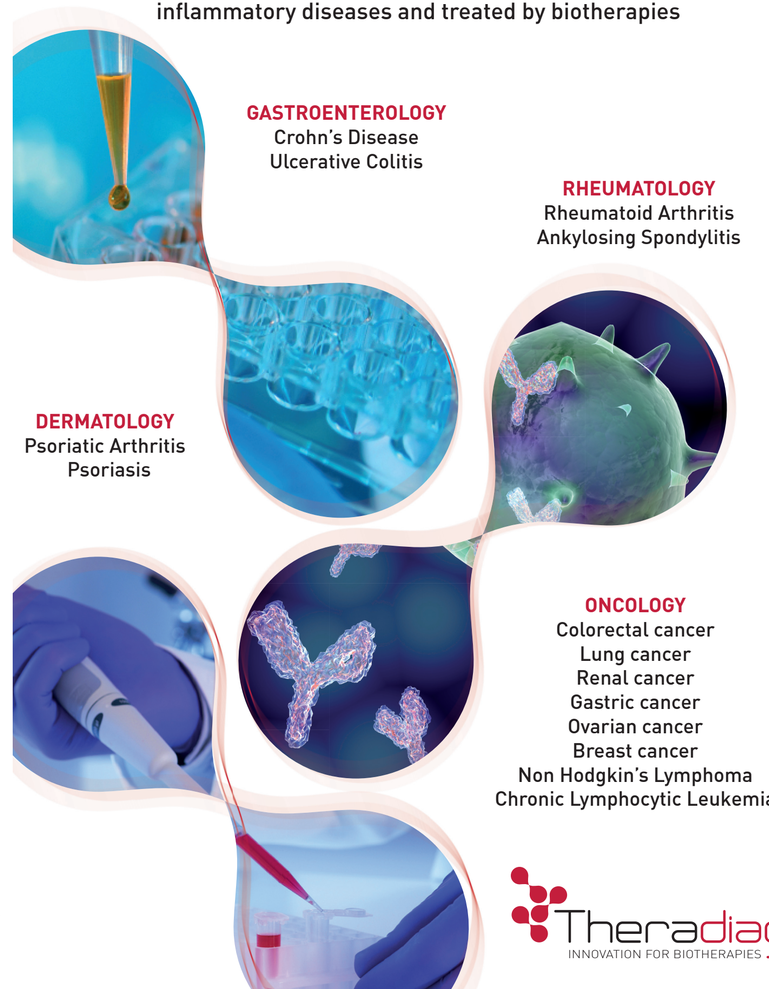
LISA TRACKER

Monitoring of patients under biotherapies

ANTICIPATION, OPTIMIZATION and **ORIENTATION**
For the treatment of patients with cancer or chronic inflammatory diseases and treated by biotherapies



GASTROENTEROLOGY
Crohn's Disease
Ulcerative Colitis

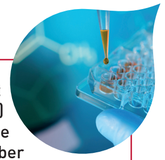
RHEUMATOLOGY
Rheumatoid Arthritis
Ankylosing Spondylitis

DERMATOLOGY
Psoriatic Arthritis
Psoriasis

ONCOLOGY
Colorectal cancer
Lung cancer
Renal cancer
Gastric cancer
Ovarian cancer
Breast cancer
Non Hodgkin's Lymphoma
Chronic Lymphocytic Leukemia

Theradiag
INNOVATION FOR BIOTHERAPIES

Biotherapies in chronic inflammatory diseases and cancers



Biotherapies (original products and biosimilars) have revolutionized the treatment of chronic inflammatory diseases in their rheumatic (RA, AS, RF), cutaneous (PS) and digestive (CD, UC) forms as well as the treatment of some cancers. Despite the initial 60 to 70% response rate in various pathologies, there is still a significant number of patients that are non-responders (primary non-responders), experience loss of response to the treatment (secondary resistance) or suffer from adverse effects [1].

Biologic	Structure	Pathologies
Infliximab	Chimeric	RA, AS, PA, PS, CD, UC
Adalimumab	Human	RA, AS, PA, PS, CD, UC
Etanercept	Fusion protein	RA, AS, PA, PS
Certolizumab Pegol	Humanized	RA, AS, PA, CD (USA)
Golimumab	Human	RA, AS, PA, PS, UC
Rituximab	Chimeric	RA, NHL, CLL
Tocilizumab	Humanised	RA
Bevacizumab	Humanised	mC (breast, lung, renal, ovarian, colon, rectal)
Trastuzumab	Humanised	Breast cancer, mC (breast, gastric)
Ustekinumab	Human	PA, PS
Vedolizumab	Humanised	CD, UC

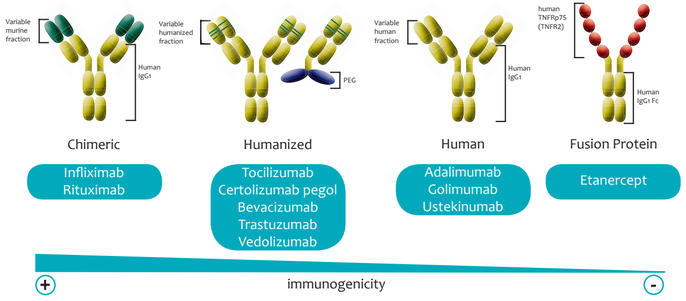
The loss of clinical response can be linked to the immunogenicity of these molecules and/or to their bioavailability [1,2,3,4].

RA: Rheumatoid Arthritis, AS: Ankylosing Spondylitis, RF: Rheumatic Fever, PA: Psoriatic Arthritis, PS: Psoriasis, CD: Crohn's Disease, UC: Ulcerative Colitis, NHL: Non Hodgkin's Lymphoma, CLL: Chronic Lymphocytic Leukemia, mC: metastatic Cancer.

Immunogenicity

Biotherapies are immunogenic and trigger the production of ADAb (Anti-Drug Antibodies). Studies show variability in ADAb incidence and can reach 60% for Infliximab [1]. The frequency of ADAb incidence varies according to the molecules and depends on:

- the dose administered,
- the treatment scheme,
- the immunogenicity of each molecule, linked to their structure,
- the individual pharmacokinetic variability.

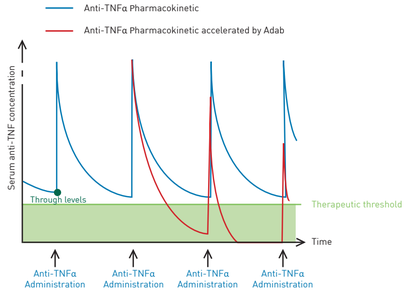


Pharmacokinetic (PK) of biotherapies

Various factors affect the pharmacokinetic of the biotherapies, in particular heterogeneity of patients, their pathology, the use of other medications, and more importantly ADAb appearance.

The presence of ADAb has a direct impact on the treatment efficacy by blocking the action of the drug.

Futhermore, ADAb increase the clearance and reduce the drug concentration, leading to loss of clinical efficacy [5,6].



Factors that influence PK of biotherapies	Impact
Presence of ADAb	Decreases drug concentration Increases clearance Worse clinical outcomes
Concomitant use of immunosuppresives	Reduces ADAb formation Increases drug concentration Decreases drug clearance Better clinical outcomes
Low serum albumin concentration	Increases drug clearance Worse clinical outcome
High baseline CRP concentration	Increases drug clearance
High baseline TNF concentration	May decrease drug concentration by increasing clearance
High body size	May increase drug clearance
Sex	Males have higher clearance

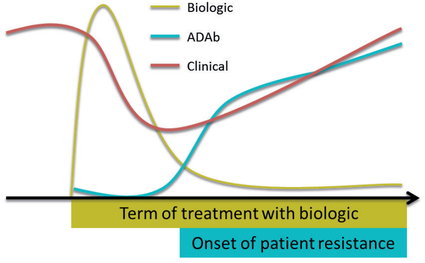
Adapted from: [23]

Bioavailability and clinical consequences

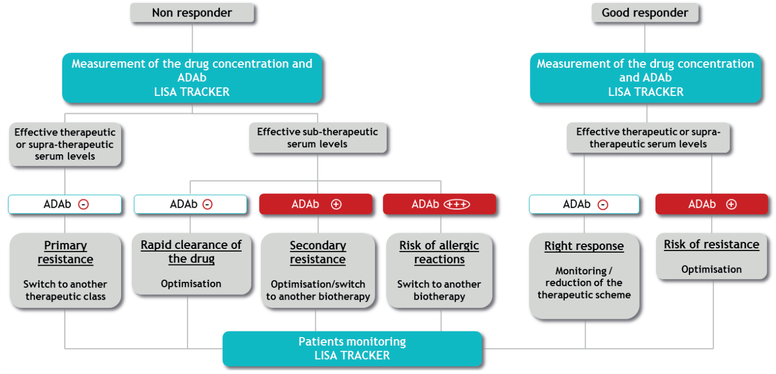
Published data indicate that trough drug concentration and clinical response to the treatment are closely linked [1,7,8,10,11,12,14,15,16,17].

Lower trough levels than the therapeutic threshold is associated with a loss or a partial response to the treatment and a reappearance of the clinical symptoms.

Trough levels concentrations higher than the therapeutic window do not bring additional clinical benefits and increase risks of iatrogenic effects and costs of treatment [1,7,8,10,11,12,14,15,16, 17,18,19,20].



Personalized optimization of treatment by biotherapy



Adapted from: [1,2,3,4,7,8,10,11,12,14,15,16,17]

Serum dosages and benefits

Drug trough levels and ADAb production appear to be two parameters that enable, based on patient's clinical status, to make rational therapeutic decisions in different clinical situations:

- Predict clinical response [1,7,10,11,12,16,17, 25].
- Guide therapy after a treatment failure [8,14,16].
- Therapeutic switch follow-up [9].
- Predict postoperative complications [22].
- Guide treatment downscaling for patients in remission [21, 24].
- Reduce treatment costs by implementing a rational decision-making patient care management [18,19,20].
- Decrease the risk of allergic reactions during the infusion or other adverse effects.