



# SERUM CONTROL FOR THERAPEUTIC ANTIBODY AND IGE DURING TREATMENT WITH OMALIZUMAB

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## Introduction

Therapeutic Antibodies (TAB), e.g. Omalizumab or Adalimumab, have an increasing meaning in clinical use. More than 1000 clinical studies on TAB are listed. The common unique speciality is, that all of these TAB are antibodies against a human Antigen, i.e. Protein, which is responsible for a disease or severity of a disease. One more common speciality is, that all of these TAB and their target cannot be monitored furthermore after beginning of the therapy with TAB.

Reasons are:

- Components of the test system are already in the sample – (the TAB binds the same epitope as the capture antibody or the signal antibody of the test system)
- The TAB binds to other epitopes than the antibodies of the test kit. The assay cannot differentiate between the target and the target TAB complex.
- The different kinetic of the reaction between the TAB, the capture antibody and the target TAB complex disturbs a sufficient result of the test.

## Methods

The aim of the study was to develop an in vitro test by which can be measured Tab as well as target protein in serum samples. The test is based on a traditional modified sandwich assay. By standard addition was tested the influence of the TAB on the antigen (target) standard calibration curves. The concentration of the free available antigen and the TAB were calculated by a special fitted mathematical axiom. The *recovery*ELISA was already adapted for different therapeutic antibodies.

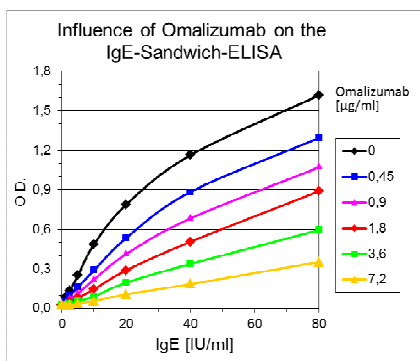


Fig. 1: Influence of different concentrations of Omalizumab on the calibration curve of a conventional IgE-ELISA

## Results

The principle of the *recovery*ELISA was proved in different clinical samples and observatory studies on patients treated with Omalizumab and Adalimumab. It was shown that the TAB and the target can be measured in therapeutic concentrations in patient serum during treatment with TAB.

Allergic Asthma (n=7)	IgE (IU/ml)	IgE Recovery (%)	Omalizumab (µg/ml)
before treatment	783 ± 864	100 ± 0	0 ± 0
4 weeks after	14 ± 23	3 ± 2	32 ± 26

Tab. 1: Results of a first preliminary proof of concept, the study for validation of the *recovery*ELISA.

The comparison of IgE determinations during Omalizumab therapy with two other commercial IgE-ELISA kits was performed. In the presence of therapeutic antibody, conventional Sandwich ELISA systematically measures very high levels of IgE. The use of a conventional ELISA kit is obsolete during a TAB treatment.

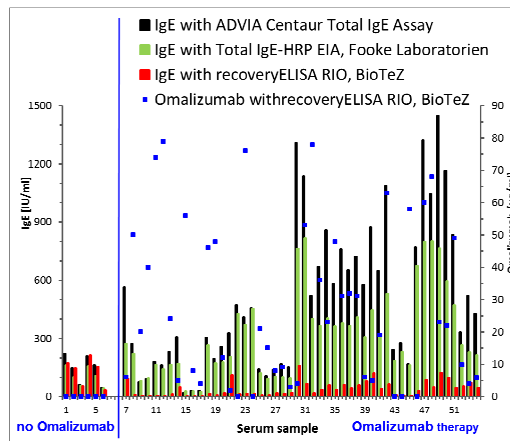


Fig. 2: Comparison of the analytical results with two other commercial IgE ELISA kits

## References:

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## Discussion

The *recovery*ELISA enables the monitoring of the treatment with therapeutic antibodies, due to actual concentrations of the antigen and the antibody in serum. The method can be adapted for all newly developed therapeutic antibodies.

It was shown, that during treatment significant active concentrations of the TAB are detectable. The target antigen was significantly reduced in a range, described in the treatment guidelines.

It seems possible, that a remaining or increasing accumulation of the TAB may occur during long-term treatment.

The *recovery*ELISA gives the possibility to monitor an antibody therapy during treatment, particularly interesting at the beginning. In our view traditional ELISA's are not suitable for laboratory controls during TAB therapy.

The *recovery*ELISA may be adapted for all these drugs.

Possible therapeutic decisions should be focus in further studies.

The *recovery*ELISA is also an interesting tool during early-stage development of new therapeutic antibodies.

In Table 2 some more therapeutic antibodies are listed, already on the market or in pre-clinical studies.

Target (Antigen)	Biopharmaceutical
IgE	Omalizumab
TNF-alpha	Adalimumab
TNF-alpha	Infliximab
TNF-alpha	Etanercept
Her2	Trastuzumab
VEGF	Bevacizumab

Tab. 2: The exemplary list of therapeutic antibodies, for which the test system should be adapted.

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