Sanquin Blood Supply

Licensing Opportunity

LIFE SCIENCES CENTER AMSTERDAM

Druglevel and Immunogenicity tests

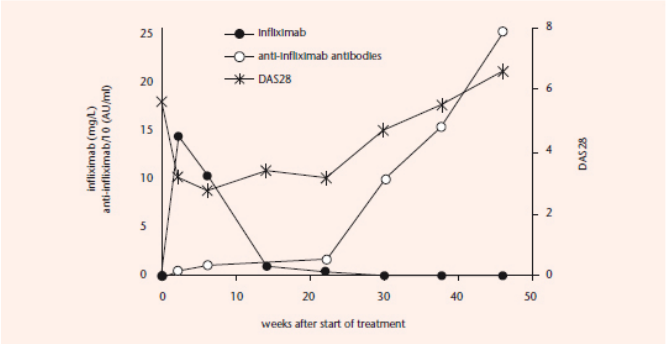
Sanquin developed druglevel and immunogenicity assays are characterised by:

- **standard platform (ELISA/RIA)**
- **high specificity / high sensitivity**
- **proven robustness and reliability**
- **capable of measuring in complexes**
- **IgG1 and IgG3 testing available**

Biological Therapeutics| *Monoclonal Antibodies* 2011

Background

Biological-derived proteins (biologicals) such as therapeutic antibodies elicit an unwanted antibody response in a substantial number of patients, resulting in a loss of efficacy of treatment. Sanquin Diagnostic Services introduces new tests for assessment of therapeutic antibodies and their immunogenicity. This enables fine tuning of drug dosage, early switch to other therapeutics and prevention of side-effects.



Trough levels of infliximab and antibodies against infliximab in serum and the Disease Activity Score in 28 joints (DAS28) in a rheumatoid arthritis patient treated with infliximab. After initial decrease of disease activity, the patient had a relapse of disease activity that coincided with a decrease in serum trough levels of infliximab and an increase in the anti-infliximab titre. AU= arbitrary units (after Wolbink, 2006).

The Technology

Sanquin Diagnostic Services has developed tests to determine levels of biologicals and antibodies directed against biologicals. HAHA and HACA are quantified using validated antigen-binding tests (RIA), while levels of therapeutic antibodies are assessed using validated ELISAs, both on a routine base. Serum samples are collected just prior to administration of the following drug dose, to prevent complex-formation of biological and antibody, which could lead to false-negative results.

Current Tests

Currently we perform tests to determine levels and immunogenicity of the following biologicals:

- infliximab
- adalimumab
- etanercept
- rituximab
- nataluzimab
- trastuzumab (on research base)

Immunogenicity tests in development

Our standard assay format allows for quick development of new tests. Currently we are developing tests for abatacept, abciximab and omalizumab. To inform yourself on the most recent assays in development, consult our website regularly: www.biologicals.sanquin.nl. Please contact Sanquin to evaluate possibilities for development of tests in which you are interested: biologicals@sanquin.nl.

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Key publications

1. Bartelds GM, Wijbrandts CA, Nurmohamed MT, Stapel S, Lems WF, Aarden L, Dijkmans BA, Tak PP and Wolbink GJ. Clinical response to adalimumab: relationship to anti-adalimumab antibodies and serum adalimumab concentrations in rheumatoid arthritis. Ann Rheum Dis 2007: 66(7):921-6.

2. Wolbink GJ, Vis M, Lems W, Voskuyl AE, de Groot E, Nurmohamed MT, Stapel S, Tak PP, Aarden L and Dijkmans B. Development of antiinfliximab antibodies and relationship to clinical response in patients with rheumatoid arthritis. Arthritis Rheum 2006; 54(3):711-5.

3. de Vries MK, Wolbink GJ, Stapel SO, de Vrieze H, van Denderen JC, Dijkmans BA, Aarden LA and van der Horst-Bruinsma IE. Decreased clinical response to infliximab in ankylosing spondylitis is correlated with anti-infliximab formation. Ann Rheum Dis 2007; 66(9):1252-4.

4. van der Laken CJ, Voskuyl AE, Roos JC, Stigter van Walsum M, de Groot ER, Wolbink G, Dijkmans BA and Aarden LA. Imaging and serum analysis of immune complex formation of radiolabelled infliximab and anti-infliximab in responders and non-responders to therapy for rheumatoid arthritis. Ann Rheum Dis 2007; 66(2):253-6.

5. Pijpe J, van Imhoff GW, Spijkervet FK, Roodenburg JL, Wolbink GJ, Mansour K, Vissink A, Kallenberg CG and Bootsma H. Rituximab treatment in patients with primary Sjogren's syndrome: an open-label phase II study. Arthritis Rheum 2005; 52(9):2740-50.

6. Bendtzen K, Geborek P, Svenson M, Larsson L, Kapetanovic MC, Saxne T. Individualized monitoring of drug bioavailability and immunogenicity in rheumatoid arthritis patients treated with the tumor necrosis factor alpha inhibitor infliximab. Arthritis Rheum 2006; 54(12):3782-9.

7. Baert F, Noman M, Vermeire S, Van Assche G, D' Haens G, Carbonez A, Rutgeerts P. Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. N Engl J Med 2003; 348(7):601-8.

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