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New Development... New Development...

Anti-natalizumab antibody assay

Since 15 March 2009, we have been offering assays of anti-natalizumab antibodies.

These antibodies can appear during treatment with natalizumab (Tysabri®), a drug indicated in highly active forms of relapsing-remitting multiple sclerosis (MS) in adult patients.

Natalizumab is a humanised monoclonal antibody directed against integrin $\alpha 4$, a selective inhibitor of adhesion molecules in MS, and has been marketed by Biogen Idec France since April 2007. It is administered in a slow intravenous infusion every 4 weeks.

Some patients may develop anti-natalizumab antibodies during the course of treatment. The presence of *persistent* anti-natalizumab antibodies (as confirmed by 2 positive assays at an interval of 6 weeks) is seen in 6% of patients on treatment and could account for the adverse reactions associated with infusion (shivers, nausea, vomiting, dizziness, vasomotor flush) and for diminishing therapeutic efficacy.

In accordance with the French Health Products Safety Agency's recommendations, screening for natalizumab immunogenicity should be carried out:

- after approximately 6 months of treatment in the event of infusion-related reactions or treatment inefficacy,
- by routine assay after prolonged discontinuation of treatment.

If an initial sample proves positive, testing should be repeated after 6 weeks and Tysabri® should be definitively discontinued if persistent anti-natalizumab antibodies are confirmed.

This analysis is prescribed by neurologists by completing a specific form that includes information concerning the reason for assay as well as the number of infusions given.

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- IN PRACTICE -

- Sample type: 1 to 2 ml of serum, frozen or at ambient temperature
- Assay method: ELISA
- Run frequency: 1/week
- Technical turnaround time: 1 day



Note

2009 CATALOGUE of Analyses

The 2009 catalogue is now available and includes the latest changes in nomenclature and methods as well as all updates concerning other items for the same analysis and all parameters developed over the last 12 months, i.e. since the last edition was released.

Please discard all 2008 catalogues on receipt of your 2009 catalogue in order to avoid confusion.

We would like to remind you that our entire catalogue is available on our website:

<http://www.pasteur-cerba.com>

(Section: *catalogue*), which is updated in real time.

Furthermore, the 2009 analytical catalogue can be downloaded from: **CATANACERBA**.

PUBLIC HOLIDAYS

Monday 13 April 2009

Friday 1 May 2009

Friday 8 May 2009

Thursday 21 May 2009

Please note that our medical secretariat will be closed on the above dates and that there will be no sample reception.

Please do not carry out sampling on the days before the above holidays for any of the following analyses:

HLA Class I, lymphocyte sub-populations, cellular allergy tests,

CMV blood antigens, lysosomal enzymes, constitutional karyotypes and all bone marrow analyses.

Analysis info ... Analysis info ... Analysis info ... Analysis info ...

Haemoglobin testing and molecular identification of rare variants

- Biologists are increasingly called upon to diagnose haemoglobin diseases.

There are many clinical and laboratory reasons for prescription of this type of test:

- prevention: screening of patients with risk factors (ethnic origin, familial survey) in specific situations (pregnancy, surgery);
- aetiological screening of blood test abnormalities (anaemia, microcytosis, polyglobulinaemia, haemolysis);
- fortuitous discovery of an abnormal profile during HbA1c assay.)

Interpretation of the results always requires knowledge of the clinical and laboratory circumstances in which the prescription is made (WBC count, RBC count, haemolysis analysis, details of any transfusions) and of the patient's ethnic background.

- If the observed profile is normal, haemoglobin (Hb) testing involves precise determination of levels of HbA2 and F allowing diagnosis of thalassaemia syndrome. The nomenclature of medical laboratory procedures allows for the use of molecular biology techniques in genetic counselling and prenatal diagnosis.
- If the profile observed is abnormal and exhibits one or more Hb variants, diagnosis of haemoglobin disease is based on identification and precise quantitation of the abnormal fractions. More than 1000 variants have been identified to date in the HbVar databank accessible online (<http://globin.cse.edu/globin/hbvar/menu.html>). These may be classified into four groups:
 - Mutants responsible for major public health problems. The main issues are HbS in the African population and HbE in South-East Asian populations.
 - Rarer variants, present in populations with a high prevalence of HbS. This is the case for instance for HbC, O-Arab and D-Los Angeles (D-Punjab), which in themselves exert only minimal pathogenic effects, but which when associated with HbS result in major drepanocytic syndromes.
 - Rare variants responsible for a variety of haematological disorders: unstable Hb (the cause of chronic haemolytic anaemia), high oxygen affinity Hb (responsible for polyglobulinaemia), low oxygen affinity Hb (responsible for anaemia with cyanosis), and HbM (responsible for methaemoglobinaemia).
 - Mild polymorphism or mutations, normally completely clinically silent. These mutants must be characterised and registered in databases in order to avoid confusion with mutants having severe clinical consequences

In view of their frequency, identification of certain variants (HbS, C, E, Lepore, H) may be made by examining their biochemical behaviour (electrophoresis, chromatography, etc) in relation to the patient's CBC, iron status and ethnic origin. However, detailed identification of other rarer variants requires the use of different methods, including gene sequencing methods for globin α and β , which are beginning to play an increasingly important role.

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- IN PRACTICE -

- Sample type: 5 ml whole blood on EDTA
- Assay method: capillary electrophoresis + HPLC +/- sequencing
- Run frequency: 6/7 d and 1/week (rare variants)
- Technical turnaround time: 3 to 15 days

You must enclose a “Haemoglobin study” application/information form and a “Consultation certificate and consent form”* (this is a legal obligation for genomic molecular biology tests)

*available from www.pasteur-cerba.com