Elecsys® anti-CCP (anti-cyclic citrullinated peptides),
- an automated assay for aid in the diagnosis of rheumatoid arthritis

Sponsor: Roche Diagnostics GmbH, Penzberg, Germany

Introduction
Rheumatoid arthritis (RA) is an inflammatory rheumatic disorder with a worldwide prevalence of about 0.5-1.0 %. Although the course of RA varies widely among affected individuals, for a significant number of patients RA presents with persistent pain and stiffness, progressive joint destruction, functional decline and premature mortality. The typical clinical picture of RA is that of a symmetric polyarthritis preferentially but not exclusively affecting the small joints of hands and feet.

Despite this typical clinical picture of RA is often hampered by the unspecific onset of the disease and the lack of diagnostic criteria for RA. Thus, RA is currently still mainly based on clinical symptoms, preferably but not exclusively affecting the small joints of hands and feet.

In recent years, however, testing for auto-antibodies against cyclic citrullinated peptides (CCP) in suspected RA patients has gained increasing acceptance among specialists. The occurrence of these auto-antibodies seems to be highly specific for the presence of CCP in suspected RA patients has gained increasing acceptance among specialists. The occurrence of these auto-antibodies seems to be highly specific for the diagnosis of RA. However, the assay is currently still mainly based on clinical symptoms.

The Elecsys® anti-CCP is an immunoassay based on the biotin-streptavidin coupling technology employing an IgG-capture assay format. The format uses biotinylated peptides that are recognized by anti-CCP antibodies from patient samples and a ruthenium labeled monoclonal antibody that recognizes aggregated human IgG. The resulting immunocomplexes immobilize at the streptavidin coated magnetic microbeads. The measured electrochemiluminescence (ECLIA technology) signal is proportional to the anti-CCP-IgG antibody concentration in the sample.

Elecsys® anti-CCP assay principle

The Elecsys® anti-CCP assay is an immunoassay based on the biotin-streptavidin technology employing an IgG-capture assay format. The format uses biotinylated peptides that are recognized by anti-CCP antibodies from patient samples and a ruthenium labeled monoclonal antibody that recognizes aggregated human IgG. The resulting immunocomplexes immobilize at the streptavidin coated magnetic microbeads. The measured electrochemiluminescence (ECLIA technology) signal is proportional to the anti-CCP-IgG antibody concentration in the sample.

Elecsys® anti-CCP evaluation study

The technical and clinical performance of the Elecsys® anti-CCP assay was assessed under routine laboratory conditions and compared to other commercially available anti-CCP assays.

The evaluation study involved 5 European study sites:
• France: Hospital Cochin Paris
• Spain: Hospital Universitario de Salamanca
• Switzerland: ACR Labor Chur
• Italy: University Hospital of Padova
• Germany: Klinikum der Johannes Gutenberg Universität Mainz

The clinical study collective consisted of the following 2269 patient samples:
• 792 samples of rheumatoid arthritis (RA) patients
• 907 samples of non-RA patients (non RA-rheumatic and non-rheumatic disorders)
• 420 healthy samples

Elecsys® anti-CCP assay within-run/total precision

Both the within-run as well as the total precision of the Elecsys® anti-CCP assay under routine laboratory conditions were very good (within-run precision: CV between 0.4% and 1.8%; total precision: CV between 1.5% and 9.9%).

<table>
<thead>
<tr>
<th>Country</th>
<th>Mean CV (%)</th>
<th>CV (%)</th>
<th>Within-run CV (%)</th>
<th>Total CV (%)</th>
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<tr>
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ROC analysis

The area under the ROC curve (receiver operating characteristics) curve was 0.85 (95% confidence interval: 0.83 – 0.87) for the Elecsys® anti-CCP assay and 0.82 (95% confidence interval: 0.80 – 0.84) for the Eurodiagnostica Immunoscan RA Anti-CCP assay.

From the ROC analysis the optimal cut-off for the Elecsys® anti-CCP assay was determined at 17 U/mL.

Sensitivity/Specificity

The technical and clinical performance of the Elecsys® anti-CCP assay was comparable to that of other commercially available anti-CCP assays. The assay is excellently suited for use as an aid in the diagnosis of RA.

Method comparisons

Comparison of the Elecsys® anti-CCP assay with the Eurodiagnostica Immunoscan RA Anti-CCP assay by use of contingency tables showed a good overall agreement of 96.7 % for the two assays.

Conclusions

The Elecsys® anti-CCP assay - one of the first fully automated anti-CCP assays on the market – possesses a high precision as well as a clinical performance comparable to that of other commercially available anti-CCP assays. The assay is thus excellently suited for use as an aid in the diagnosis of RA.