Serum Calprotectin (MRP8/14; S100A8/S100A9)

Monitoring Rheumatoid Arthritis

**MRP8/14 ELISA**

- Ready to use Reagents
- Premeasured Calibrators Covering a dynamic range from 0.4 to 24 mg/mL
- Short Time to Result

**Quantum Blue® MRP8/14**

- **Rapid**: Results within minutes
- **Quantitative**: quantitative results from 0.5 to 10 mg/mL
- **Ease of Use**: RFID chip card recognizes both, parameter and lot number.
Rheumatoid Arthritis

Rheumatoid Arthritis is a common chronic inflammatory autoimmune disease which is characterized by persistent synovitis, development of joint deformities, presence of autoantibodies, and an increased risk of cardiovascular comorbidities.

Treatment to target (T2T) is an acknowledged and optimal treatment strategy providing the best results for suppressing the inflammation and thus avoiding irreversible joint damage. In daily clinical practice, regular and systematic monitoring of inflammatory activity is useful to:

- Understand if the therapy is needed and effective
- Assure that rheumatoid inflammation is under control
- Make sure that overtreatment is avoided
- Identify rapidly advancing disease with high levels of inflammatory activity over time and fast radiographic progression
- Support the choice of specific disease modifying anti-rheumatic drugs (DMARDs)
- Adjust DMARD dosage in the titration of disease activity
- Support treatment expectations

Serum calprotectin has some superior, predominant and unmet properties over currently used biological measures.

Serum Calprotectin

Calprotectin is also known as myeloid-related protein 8/14 (MRP8/14) or S100A8/S100A9. Calprotectin is released from activated granulocytes and monocytes/macrophages in the synovium and synovial fluid during inflammation (1, 2, 3). Several reports have demonstrated, that calprotectin levels correlate with disease activity in various inflammatory diseases such as Rheumatoid Arthritis (4, 5), Juvenile Rheumatoid Arthritis (6), Psoriatic Arthritis (7) or Systemic Lupus Erythematosus (8).

Calprotectin levels correlate with ultra-sonographic scores of Synovitis (9) and predict radiographic joint damage in Rheumatoid Arthritis (10, 11) or ultrasound Synovitis (12). Unlike conventional acute-phase proteins (such as e.g. erythrocyte sedimentation rate, ESR), calprotectin directly reflects the leukocytes in the inflamed joints rather than systemic inflammatory activity. Circulating calprotectin levels decrease with effective treatment (13, 14). Initiation of conventional treatment in patients naïve for disease modifying anti-rheumatic drugs results in the near normalization of calprotectin levels (15). Decreases in calprotectin are associated with improvements in the total number of swollen joints over time (16).

Thus, calprotectin in serum is a considerable, very sensitive marker of local disease activity (17, 18, 19, 20, 21).

1. Niki Y et al., J Clin Invest, 2001
2. Foell D et al., Arthritis Rheum, 2004
3. Foell D et al., JAMA, 2010
6. Frosch M et al., Arthritis Rheum, 2000
8. Haga HJ et al., Lupus, 1993
11. Hammer HB et al., Ann Rheum Dis, 2010
13. Brun JG et al., J Rheumatol, 1994
17. Frosch M et al., Arthritis Rheum, 2000
Elevated Baseline Serum Calprotectin Levels (Fig.1)
Serum calprotectin levels are elevated in recent onset DMARD\(^1\) / GC\(^2\) naïve Rheumatoid Arthritis and are normalized, once patients achieved remission after conventional treatment. Decreases of serum calprotectin levels are associated with improvements in the number of affected joints.
*Cerezo A L et al., Arthritis Res. and Ther., 2011*

Serum Calprotectin Levels Decrease in Response to Treatment (Fig.2)
Serum calprotectin and disease activity measured by a disease activity score based on a 28-joint count (DAS28) in a cohort of 60 patients with Rheumatoid Arthritis treated with biological agents or DMARDs. Serum calprotectin levels strongly correlate with clinical and laboratory assessments of joint inflammation and also decrease in response to treatment.
*Garcia-Arias M et al., Mol Diagn. Ther., 2013*

**Discrimination between Responders and Non-Responders**
Baseline serum calprotectin levels are higher in responders to biological treatment vs non-responders to infliximab.
Serum calprotectin levels are also higher in good and moderate responders of other biological treatments such as adalimumab and/or rituximab. Thus serum calprotectin before treatment is consistently higher in responders to targeted treatment irrespective of the specific mechanism of action (Fig.3).
*Choi Y et al., Ann Rheum Dis, 2013*

Changes of serum calprotectin levels after 4 and 16 weeks of treatment with infliximab. Serum calprotectin levels in good and moderate responders according to EULAR criteria to infliximab decrease after 4 and 16 weeks of therapy. Serum calprotectin in non responders (EULAR) are not significantly different after the same time of treatment (1 dot represents 1 patient) (Fig.4 and 5).
*Choi Y et al., Ann Rheum Dis, 2013*
**Test Principle**

**Monoclonal Antibody**

The MRP8/14 ELISA and Quantum Blue® MRP8/14 lateral flow assay by BÜHLMANN are based on the application of a highly sensitive and specific monoclonal antibody to the active form of calprotectin. This provides the tool for high clinical accuracy in the test portfolio, thus covering all levels of calprotectin measurements from central laboratory to the doctor’s office.

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- **Quantitative**
  - Quantum Blue® MRP8/14 test provides quantitative results from 0.5 to 10 mg/mL.
- **Ease of Use**
  - RFID chip card of Quantum Blue® contains entire test methods incl. lot-specific curve parameters and batch information.
- **Excellent comparison to MRP8/14 ELISA**