

A **PROGNOSTIC AND ACTIVITY MARKER**
FOR **RHEUMATOID ARTHRITIS**

BRING MAXIMUM
FLEXIBILITY TO YOUR RA
THERAPY MANAGEMENT

AESKULISA[®] DF MMP-3

AESKULISA® DF MMP-3: FOR AN IMPROVED THERAPY MANAGEMENT OF RHEUMATOID ARTHRITIS

Early diagnosis of rheumatoid arthritis (RA), **prognosis of progression** and **disease activity control** are crucial to therapy success, because joint destruction can be stopped and in some cases even be completely avoided when appropriate drug therapy is given at an early stage.

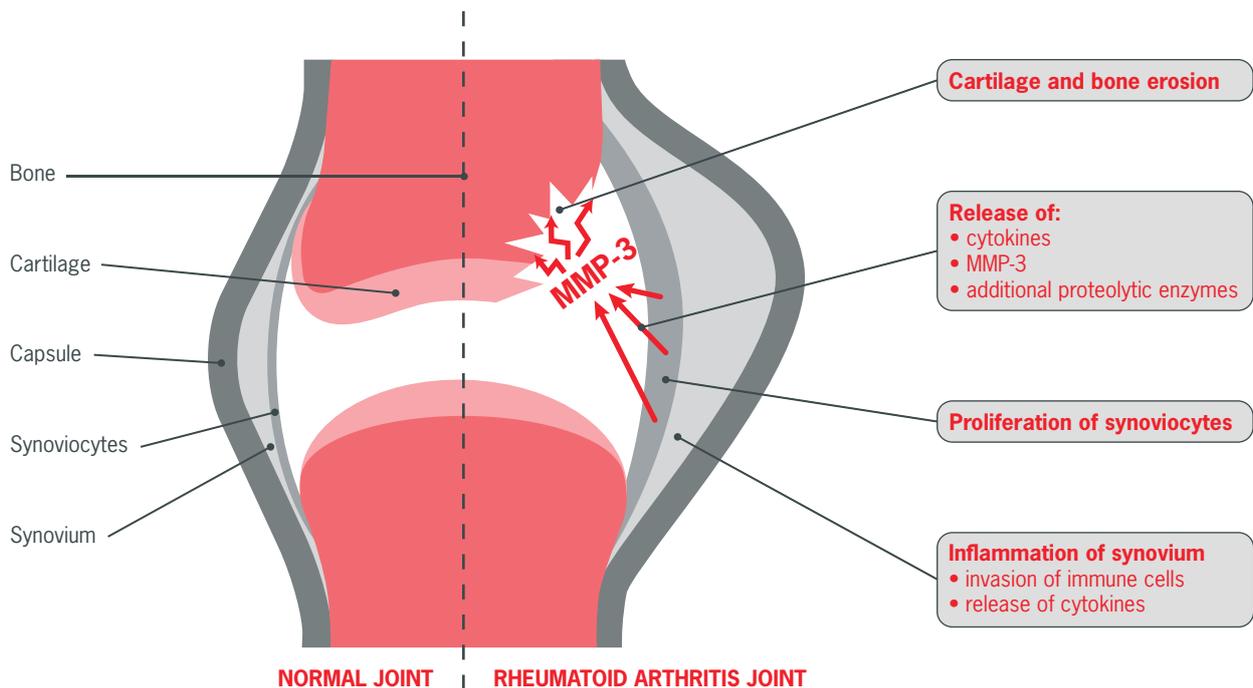
Not all RA patients would benefit from aggressive drug therapy due to severe side effects, high costs and individually differing disease progression.

Therefore it is very important for the therapy management of RA to differentiate those patients with fast progression and / or high risk of bone erosions from those patients with a mild disease course.

“Undoubtedly, treating patients at a stage at which evolution of joint damage can still be prevented would be ideal.”¹

MMP-3 is an outstanding serological marker that can identify patients with a high and imminent risk of developing bone erosions even in an early phase of the disease. Furthermore, due to its direct implication in the joint destruction process, MMP-3 can also be used to monitor disease activity and therapy success, thereby helping physicians to create and adapt an individualized drug therapy for each patient.

WHAT HAS MMP-3 GOT TO DO WITH RHEUMATOID ARTHRITIS?



Due to massive inflammation of the synovium and vast proliferation of the alining synoviocytes, there is an increased expression of MMP-3 in RA patients which is released into the synovial fluid.

MMP-3 is a key player in cartilage and bone destruction. On the one hand it degrades a broad range of matrix molecules by itself and on the other hand it activates further degrading enzymes.

AESKULISA® DF MMP-3 measures the MMP-3 concentration in serum which reflects the degree of inflammation and degradation activity in the joints of RA patients.

AESKULISA® DF MMP-3: A NEW PROGNOSTIC AND ACTIVITY MARKER FOR RA

AESKULISA® DF MMP-3: Predicting joint damage, assessing inflammatory activity and monitoring therapy success.

Serum concentration of MMP-3 is a useful marker to predict bone damage in the early stage of RA and helps to identify patients that benefit from aggressive drug therapy.

*"In conclusion, serum MMP-3 is a good indicator for assessing the progression of joint damage in the subsequent 6-12 month of disease in early RA. Thus patients with early RA who have continuous elevation of serum MMP-3 should be considered candidates for a more aggressive therapeutic strategy."*²

*"... baseline levels of pro-MMP-3 predict the loss of articular cartilage and total joint damage progression."*³

*"...[MMP-3] may have a particular value in predicting the progression of erosive disease in patients who are not erosive at presentation."*⁴

MMP-3 reflects inflammatory activity in joints of RA patients because MMP-3 serum levels correlate with inflammation markers like CRP and joint destruction.

*"... levels of MMP-3 ... in RA patient sera are increased in association with inflammation. Furthermore, the level of MMP-3 in serum provides a particularly useful marker of inflammatory activity in the joints of patients with RA."*⁵

*"Thus, elevation of serum MMP-3 level represents the disease activity of RA patients regardless of age or the disease duration."*⁶

MMP-3 is a specific and useful marker to monitor therapy success because MMP-3 is produced in the affected joint where it is directly involved in tissue degradation.

*"Taken together, these results indicate that MMP-3 may be seen as a constitutive marker of the pathological process underlying joint tissue degradation in RA."*³

*"Therapy with MTX resulted in clinical improvement and reduced serum MMP levels in patient with RA, ..."*⁷

*"Serum MMP-3 levels decrease in patients with early RA who respond to SSZ or to the combination of MTX and SSZ."*⁸

AESKULISA® DF MMP-3: A NEW PROGNOSTIC AND ACTIVITY MARKER FOR RA

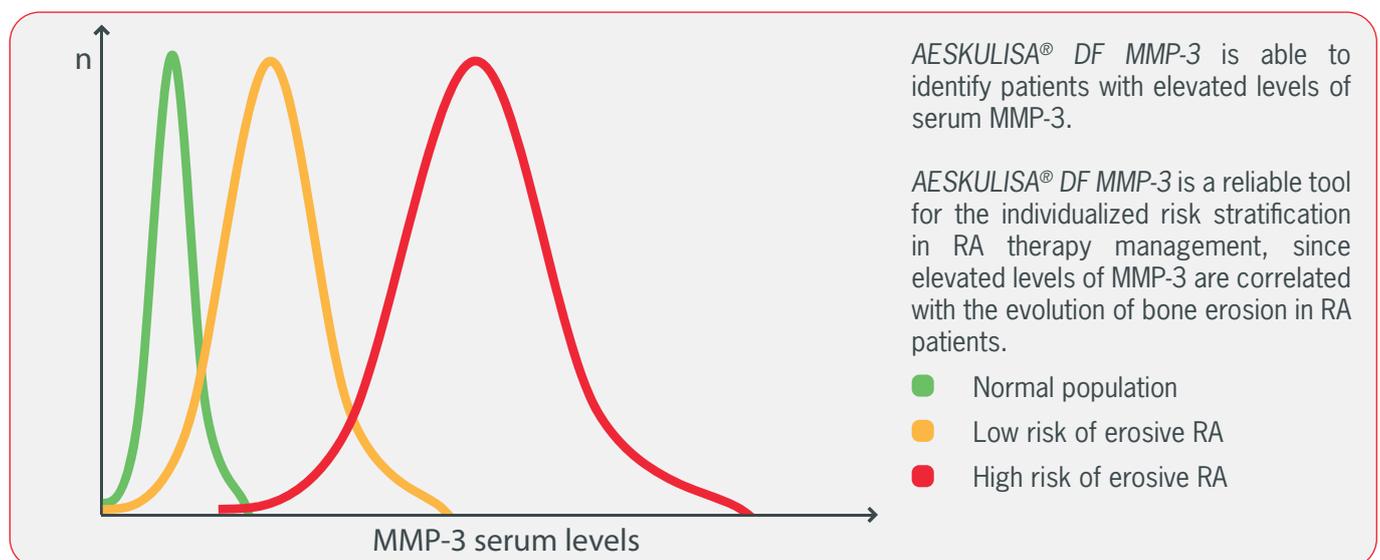
AESKULISA® DF MMP-3 offers the following benefits:

- Prediction of bone erosion even in the early phase of the disease
- Identification of patients that benefit from aggressive drug therapy
- Faster and cheaper monitoring of disease activity in comparison to the assessment of clinical activity by using activity scores like DAS, DAS28, SDAI or CDAI
- Reducing the time until patients can receive the appropriate therapy

In addition to the personal restraints of each patient, RA is generating high costs for the health-care system (diagnostics, anti-rheumatic drugs, physical therapies, etc.) and for the economy (loss of working ability).

MMP-3 helps to reduce costs by optimizing RA therapy:

- Patients will receive drugs which fit individually to their state of health
- Patients will show faster and longer remission thereby reducing amount of drugs needed
- Side effects and secondary disease manifestations will be reduced
- Maintenance of joint function and working ability will relieve the health care system and economy



¹ Aletaha, D. et al. (2010) 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum.* 62, 2569-2581

² Yamanaka, H. et al. (2000) Serum matrix metalloproteinase 3 as a predictor of the degree of joint destruction during the six months after measurement, in patients with early rheumatoid arthritis. *Arthritis Rheum.* 43, 852-858

³ Tchetverikov, I. et al. (2003) Matrix metalloproteinases-3, -8, -9 as markers of disease activity and joint damage progression in early rheumatoid arthritis. *Ann. Rheum. Dis.* 62, 1094-1099

⁴ Green, M.J. et al. (2003) Serum MMP-3 and MMP-1 and progression of joint damage in early rheumatoid arthritis. *Rheumatology. (Oxford)* 42, 83-88

⁵ Yoshihara, Y. et al. (1995) Increased levels of stromelysin-1 and tissue inhibitor of metalloproteinases-1 in sera from patients with rheumatoid arthritis. *Arthritis Rheum.* 38, 969-975

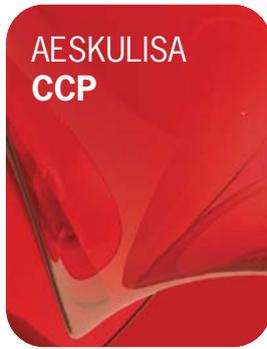
⁶ Shinozaki, M. et al. (2007) Elevation of serum matrix metalloproteinase-3 as a predictive marker for the long-term disability of rheumatoid arthritis patients in a prospective observational cohort IORRA. *Mod. Rheumatol.* 17, 403-408

⁷ Fiedorczyk, M. et al. (2006) Serum matrix metalloproteinases and tissue inhibitors of metalloproteinases in patients with early rheumatoid arthritis. *J. Rheumatol.* 33, 1523-1529

⁸ Posthumus, M.D. et al. (2002) Serum matrix metalloproteinase 3 levels during treatment with sulfasalazine or combination of methotrexate and sulfasalazine in patients with early rheumatoid arthritis. *J. Rheumatol.* 29, 883-889

REF 3166

**AESKULISA
CCP**



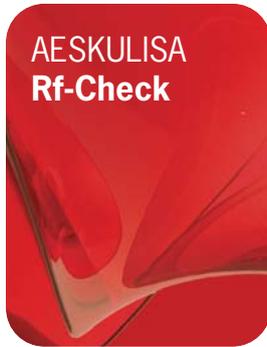
Conjugate:
anti-human IgG-HRP
Equivocal Zone:
12 - 18 U/ml
Standard Range:
0 - 300 U/ml
Kit Configuration:
Single-G

Antigens coated:
Specific cyclic citrullinated peptides

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgG autoantibodies to specific cyclic citrullinated peptides in human serum

REF 3160

**AESKULISA
Rf-Check**



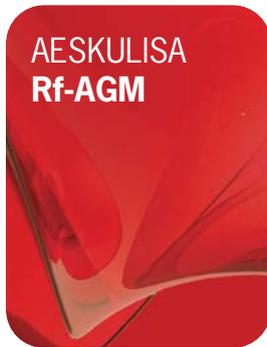
Conjugate:
anti-human IgA/M/G-HRP
Equivocal Zone:
16 - 24 U/ml
Standard Range:
0 - 300 U/ml
Kit Configuration:
Single-Check

Antigens coated:
Fc fragments of native human immunoglobulins (IgG)

Enzyme-linked immunoassay (ELISA) for the combined quantitative and qualitative determination of IgA, IgG and IgM rheumatoid factors in human serum

REF 3161

**AESKULISA
Rf-AGM**



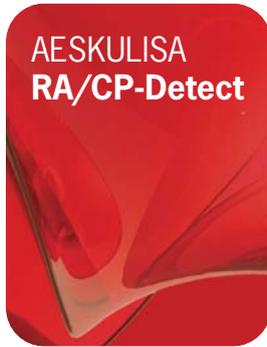
Conjugate:
anti-human IgA+IgG+IgM-HRP
Equivocal Zone:
12 - 18 U/ml
Standard Range:
0 - 300 U/ml
Kit Configuration:
Single-AGM

Antigens coated:
Fc fragments of native human immunoglobulins (IgG)

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgA, IgG and/or IgM rheumatoid factors in human serum

REF 3165

**AESKULISA
RA/CP-Detect**



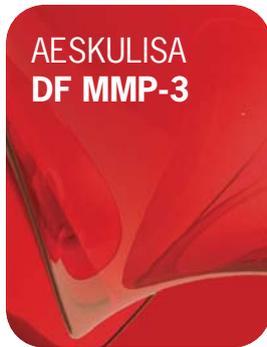
Conjugate:
anti-human IgG-HRP
Equivocal Zone:
12 - 18 U/ml
Standard Range:
0 - 300 U/ml
Kit Configuration:
Single-G

Antigens coated:
Synthetic citrullinated peptides

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgG autoantibodies to synthetic citrullinated peptides in human serum

REF 3167

**AESKULISA
DF MMP-3**



Conjugate:
mAb anti-human MMP-3-HRP
Standard Range:
0 - 800 ng/ml

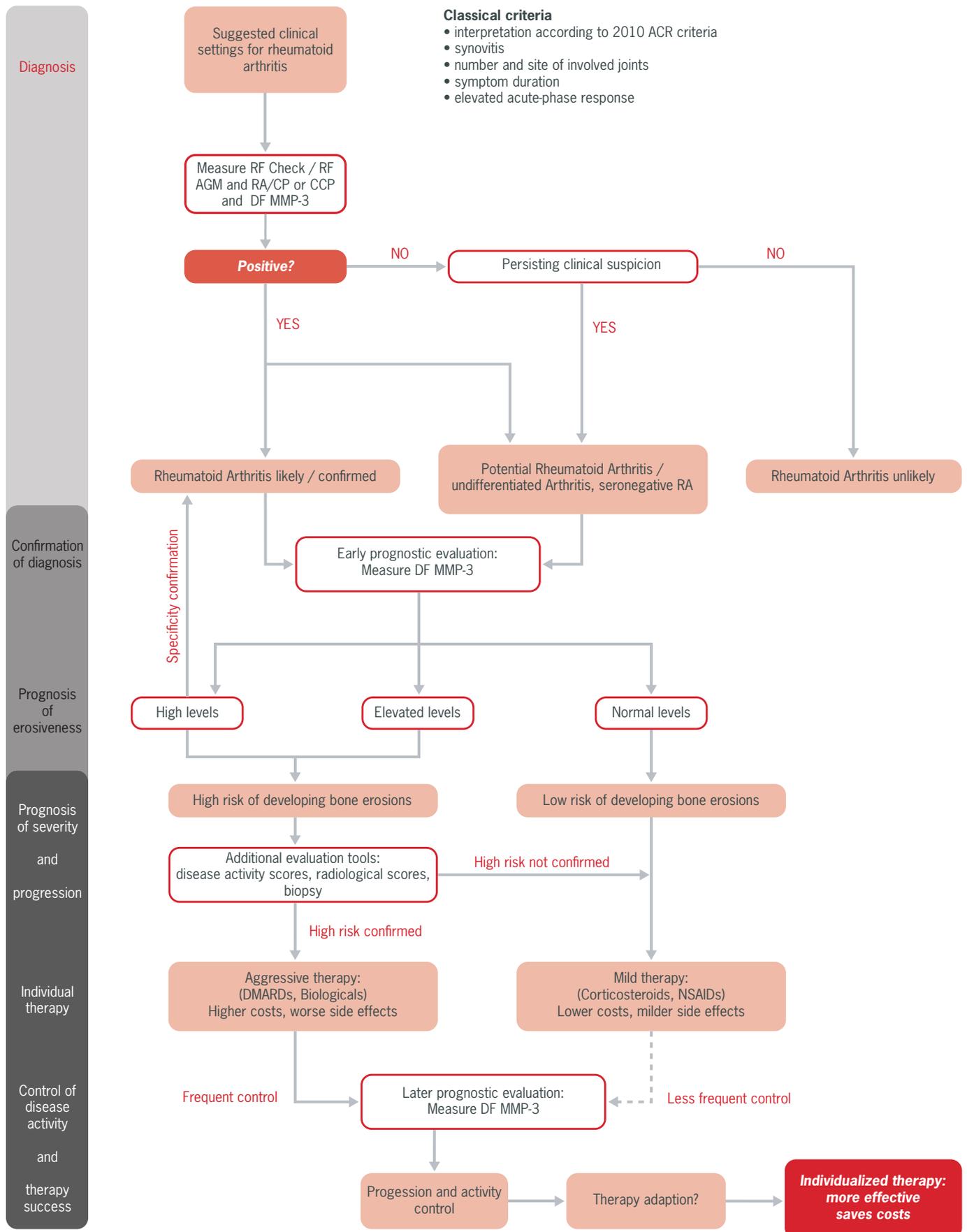
Antigens coated:
mAb anti-human MMP-3

Enzyme-linked immunoassay (ELISA) for the quantitative determination of matrix metalloproteinase-3 (MMP-3) in human serum

First CE certified IVD for MMP-3 determination in serum samples.

AESKULISA DF MMP-3: A NEW PROGNOSTIC AND ACTIVITY MARKER

SUGGESTED APPROACH TO RHEUMATOID ARTHRITIS DIAGNOSIS AND PROGNOSIS



A definite clinical diagnosis should not be based on the results of the performed tests only but should be made by the physician after all clinical and laboratory findings have been evaluated. The diagnosis is to be verified using different diagnostic methods.