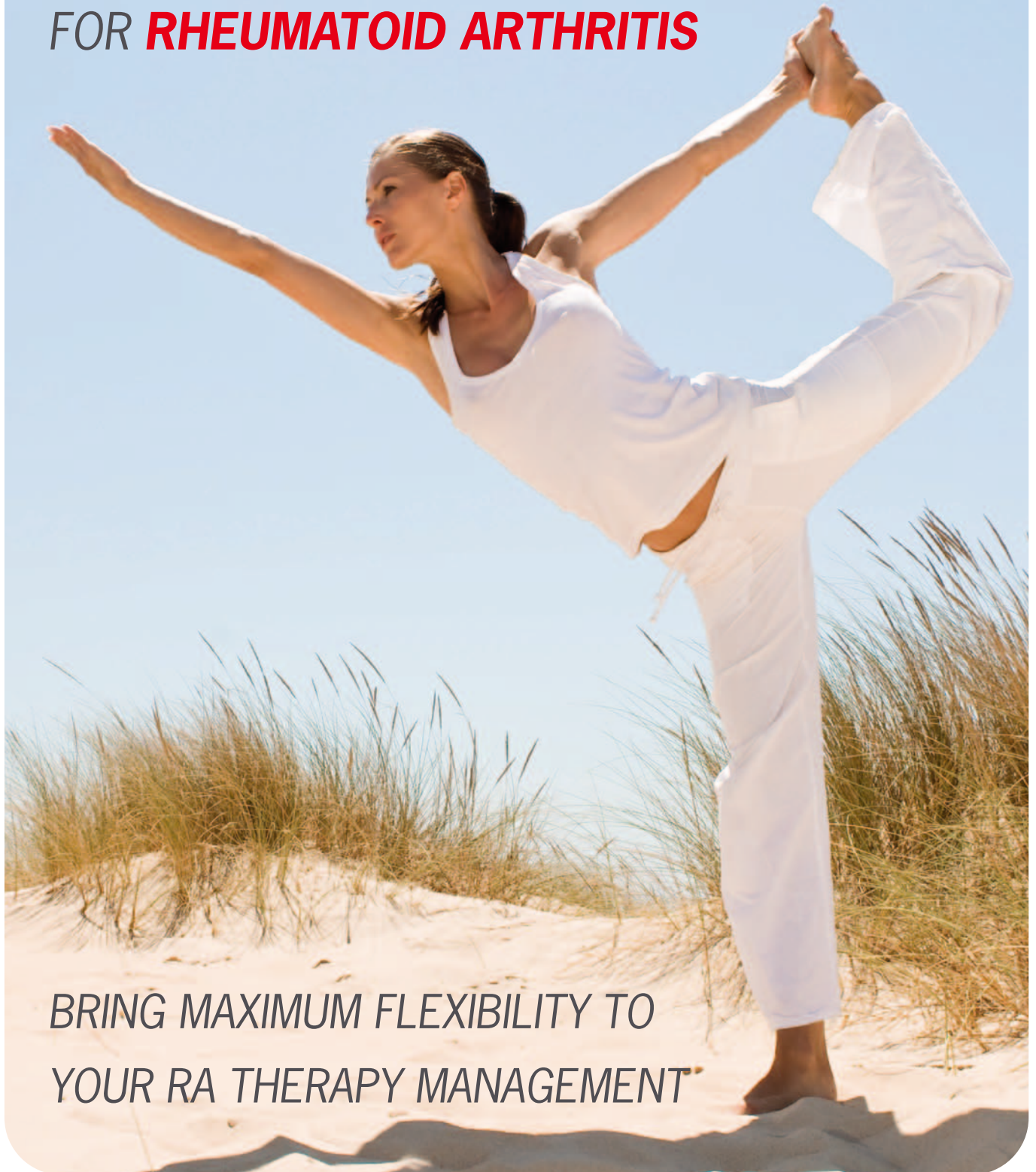


A **PROGNOSTIC AND ACTIVITY MARKER**  
FOR **RHEUMATOID ARTHRITIS**



BRING MAXIMUM FLEXIBILITY TO  
YOUR RA THERAPY MANAGEMENT\*

**AESKULISA**<sup>®</sup> **MMP-3**

 **AESKU GROUP**  
WE TAKE CARE OF YOUR HEALTH



## AESKULISA® MMP-3: Rheumatoid Arthritis – A Therapeutic Challenge

**Early diagnosis** of rheumatoid arthritis (RA), **prognosis of progression** and **disease activity control** are crucial to therapy success. The aim of RA treatment is to reduce synovial inflammation and to prevent joint destruction. Therefore, the major therapeutic strategies in RA management are early introduction of anti-rheumatic drugs and strict control of disease activity and therapy success. While some RA patients may remit with basic rheumatic therapy, others may need a more aggressive treatment. To improve the decision-making of the appropriate therapy, specific markers are needed that reflect inflammation and disease activity and provide additional long-term prognostic information for patients with RA. Additionally, these should also be applied as a means of monitoring therapeutic success.

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

### AESKULISA® MMP-3 – A Novel Activity Marker

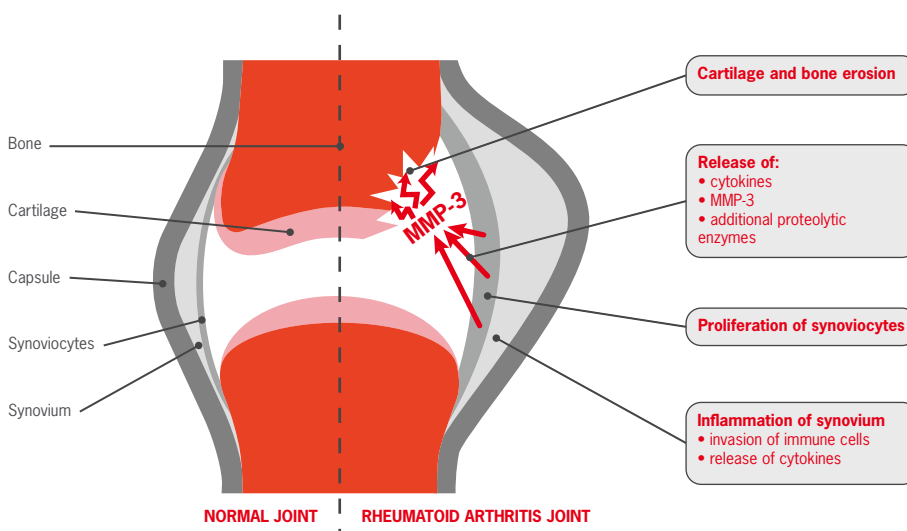
Matrix metalloproteinase (MMP)-3 is thought to be a **key player in cartilage and bone destruction**. Due to its broad substrate specificity MMP-3 is capable of degrading connective tissue matrix components and activating other destructive enzymes. Its expression is considerably enhanced in rheumatoid arthritis, even in the early phase.

MMP-3 is a serological marker that can identify patients with a high and imminent risk of developing bone erosions even in an early phase of the disease. In contrast to other inflammation markers it is locally produced in the inflamed joint and released into the blood stream. Serum MMP-3 levels correlate with MMP-3 levels produced by the synovium, thus **reflecting disease activity** and **enabling prognosis of progression**. Moreover, MMP-3 levels drop as a consequence of efficient therapy and therefore, it is an **excellent marker of successful therapy**.

Due to its multifaceted informative value, MMP-3 helps 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 aligning 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® 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® MMP-3: A NEW PROGNOSTIC AND ACTIVITY MARKER FOR RA**

### **Predicting joint damage:**

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."*<sup>2</sup>

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

*"... determination of baseline MMP-3, in conjunction with traditional serologic markers, may provide additional prognostic information for patients with RA."*<sup>9</sup>

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

*"... dynamic monitoring of serum MMP-3 may be helpful for predicting radiographic progression in RA and continuously elevated serum MMP-3 for 3~6 months may be a significant predictor of one-year radiographic progression."*<sup>11</sup>

### **Assessing inflammatory activity:**

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."*<sup>5</sup>

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

*"... synovial MMP-3 was elevated in RA synovium and positively correlated with synovitis ... . Serum MMP-3 was significantly correlated with synovial MMP-3 ... and had the ability to distinguish high grade from low grade synovitis in RA ... . Serum MMP-3 may be an alternative noninvasive biomarker of histological synovitis."*<sup>12</sup>

### **Monitoring therapy success:**

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."*<sup>3</sup>

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

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

*"... normalisation of MMP-3 levels at cessation of TCZ (tocilizumab) as independent predictive markers for longer duration of LDA (low disease activity)."*<sup>10</sup>

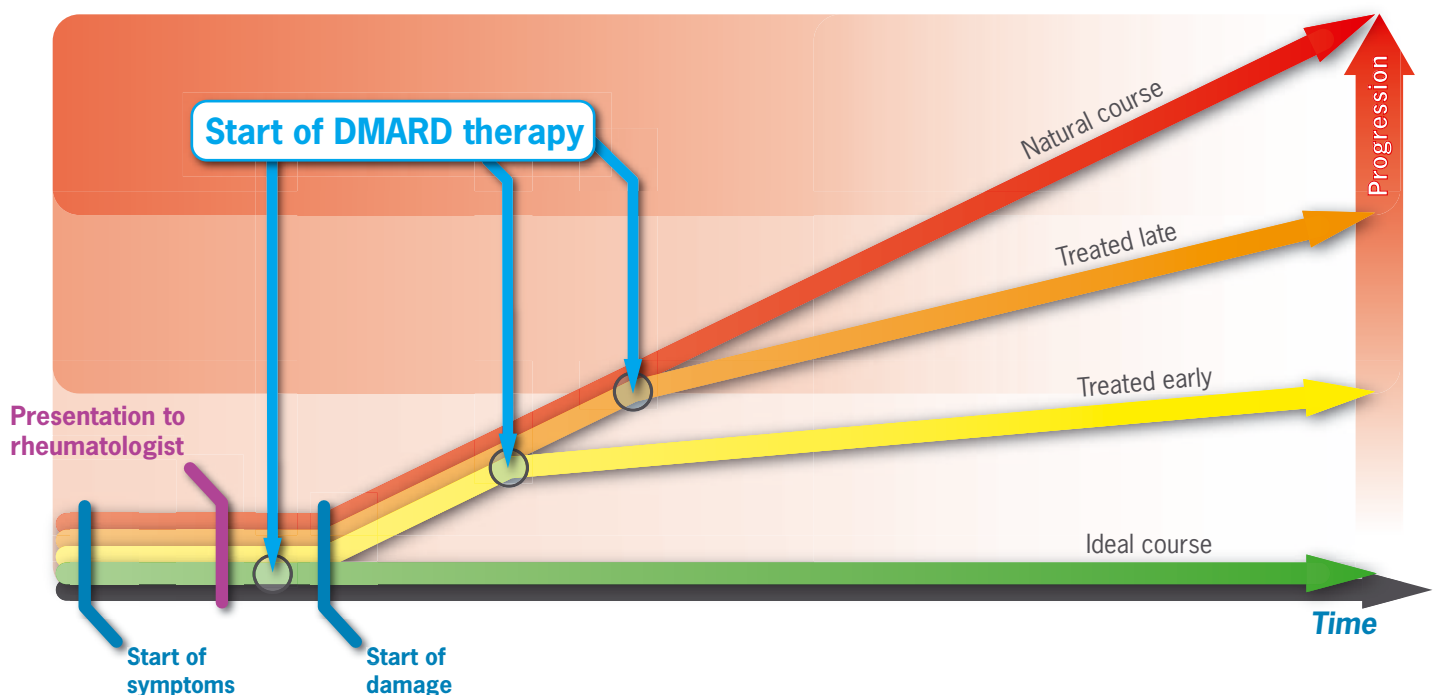
## **AESKULISA® MMP-3: A NEW PROGNOSTIC AND ACTIVITY MARKER FOR RA**

**AESKULISA® 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

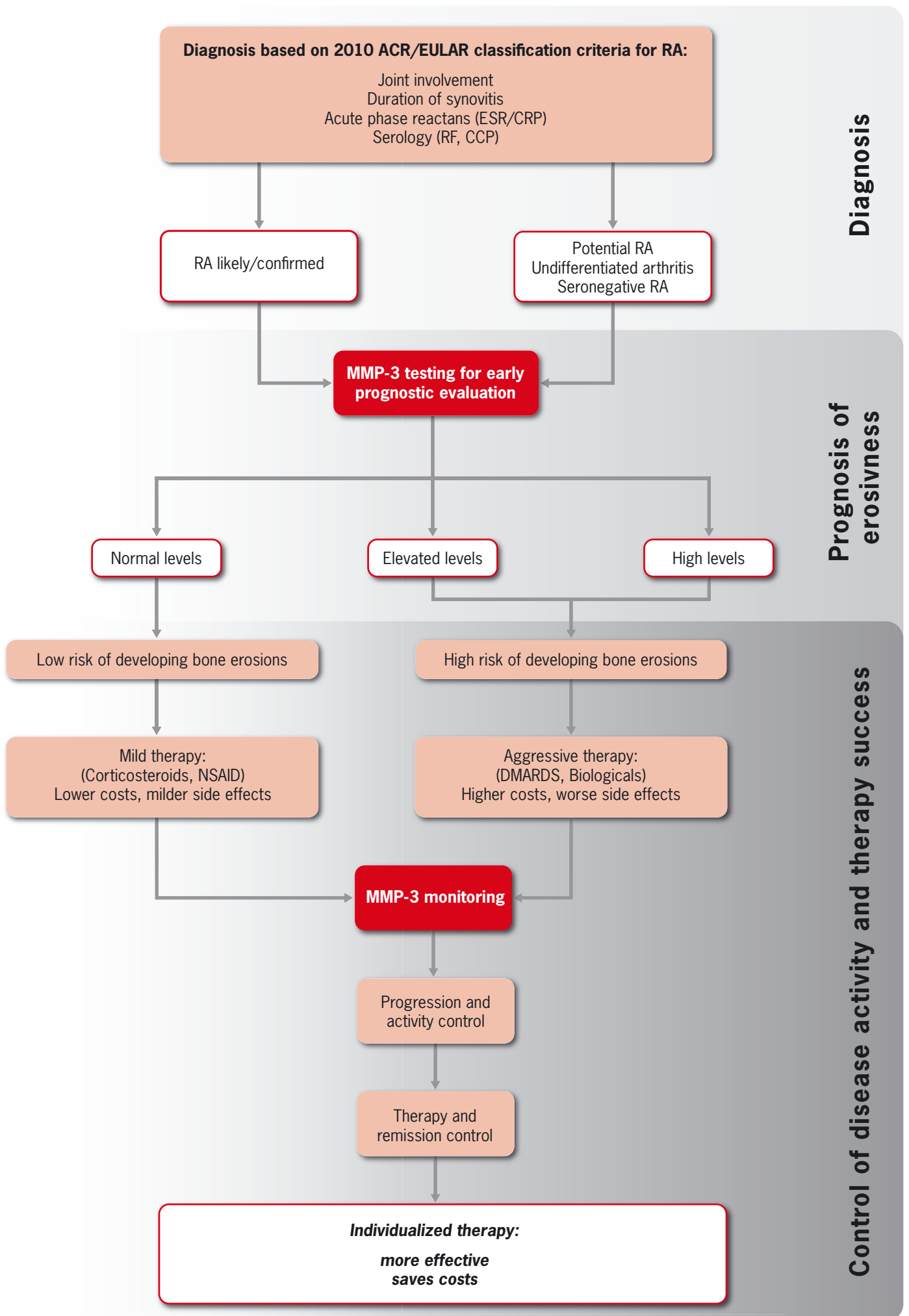
In addition to the personal restraints of each patient, RA is generating high costs for the health-care system (diagnostics, anti-rheumatic drugs, physical therapies, etc.) and for the economy (loss of working ability).

### **ALTERING THE COURSE OF RA**



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

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



A definite clinical diagnosis should not be based on the results of the performed tests alone, 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.



**Conjugate:**  
mAb anti-human  
MMP-3-HRP

**Standard Range:**  
0 - 200 ng/ml

**Kit Configuration:**  
Single

**Antigens coated:**  
mAb anti-human MMP-3

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

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