



MEDIA BACKGROUNDER

ABOUT RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a type of arthritis (chronic inflammatory polyarthritis) that typically affects hands and feet, although any joint in the body may be affected such as wrists, knees, hips and shoulders.¹ Over time, joint destruction can occur resulting in permanent damage, bone destruction and deformity.¹

What causes rheumatoid arthritis?

The cause of RA is not known.¹ However, it is thought that some people inherit genes that affect the way the immune system works making them more susceptible to the disease than others.¹ Environmental factors such as an infection may also trigger RA and generate an immune response.

In RA, synovial cells found in the joint lining grow and increase in numbers and size, thereby invading and destroying the joint's articular cartilage.¹ This process is driven by a cytokine called tumor necrosis factor (TNF). In healthy people, TNF levels are maintained at normal levels by a variety of anti-inflammatory cytokines. But people with an immune disease such as RA have too much TNF in their bodies.² This excess of TNF-alpha leads to inflammation in joints of people with RA.

What are the symptoms of rheumatoid arthritis?

In most cases of RA, symptoms are intermittent, with regular flare-ups.² In severe cases of RA, these flare-ups may last several years or a lifetime. Repeated or continual flare-ups are a marker of continuous inflammation or disease activity that can lead to serious joint damage and disability.¹

Clinical symptoms include:

- Stiffness, commonly in the morning.
- Joint swelling that can occur in any joint but most often occurs in small joints of the hands and feet and often symmetrically.
- Tiredness, fever, weight loss and depression.



What is the impact on patients?

RA reduces a patient's lifespan by about 10 years if only the symptoms are treated.² It is also associated with the following co-morbidities:

- Increased risk of heart disease³ and infection leading to premature death.⁴
- Permanent joint damage which may lead to loss of function.²

An accurate diagnosis of RA can be difficult as there is no single test for the condition and the symptoms develop over time. Diagnosis is normally based on a number of symptoms including the pattern of affected joints, x-ray or scan results and/or high levels of an antibody called rheumatoid factor (RF) in the blood.¹

Who does rheumatoid arthritis affect?

RA affects between 0.5 to 1 per cent of the adult population worldwide. Two to three times as many women as men suffer from the disease. RA can start at any age, but the peak age of onset is between 30 and 55 years.¹

What is the economic impact of rheumatoid arthritis?

The World Health Organization assesses the economic burden of RA on three levels—direct, indirect and psychosocial costs.⁵ Direct costs to governments can be substantial. For example, in the United States, a systematic review revealed that the average annual medical cost associated with RA is US\$5,720 per patient of which in-patient cost is the largest component.⁶ Across Asia-Pacific, the costs are equally high. For instance:

- In Korea, the economic burden of RA is estimated to be US\$624.9 million, equivalent to 0.11 per cent of the GNP.⁷
- In China, Japan and Taiwan RA affects 0.3 per cent of the population in each country—or 4 million, 380,000 and 69,000 people respectively.^{8, 9, 10}
- In Australia, arthritis costs A\$24 billion each year in healthcare, lost time at work, shortened lives and years spent with disability.¹¹
- In Thailand, the average societal cost of RA is estimated to be US\$2,682, 41.4 per cent of a patient's average annual income. Direct and indirect costs are estimated to be US\$2,135 and US\$547 per patient per year, respectively.¹²
- In Malaysia, RA affects about 0.5 per cent of adults between the ages of 25 and 50.¹³



What treatment options are available?

The treatment of RA has changed considerably in the past decade, moving from a conservative approach designed to control clinical symptoms to a more progressive approach designed to limit joint destruction.¹

Historically, RA was typically treated with non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and simple analgesics to relieve pain and symptoms. However, NSAIDs have been replaced by disease modifying anti-rheumatic drugs (DMARDs) which are more effective at preventing long-term structural damage. These include: methotrexate, sulfasalazine, cyclosporine, leflunomide and gold. While methotrexate is the most commonly used treatment, it has been associated with considerable toxicities including bone marrow suppression, hepatotoxicity and idiopathic lung reactions.¹

In addition to DMARDs, newer treatments such as biological (Tumor Necrosis Factor/TNF inhibitors) therapies are also routinely used to treat RA. These drugs selectively target mediators believed to be involved in the pathogenesis of RA, specifically IL-1 and TNF.² The biologics include ENBREL® (etanercept), REMICADE® (infliximab) and HUMIRA® (adalimumab).

TNF inhibitors have been shown to slow the progression of joint damage, or even inhibit progression altogether (achieve remission), as measured by x-ray assessed by radiography and magnetic resonance imaging (MRI). TNF inhibitors have also been shown to decrease the disability assessed by Health Assessment Questionnaires (HAQs) which demonstrates highly positive effects for patients. The B-cell inhibitor MABTHERA® is also available for treatment of RA.

Early effective treatment may not only postpone, slow, or even stop disease progression, thereby improving quality of life, but also decrease costs by preserving productivity and reducing the need for surgery, admission to acute-care and extended-care hospitals, and reliance on social services.²

Safety and Tolerability of TNF Inhibitors

Although TNF inhibitors have a well-established safety profile spanning more than a decade, there have been rare reports of opportunistic infections including tuberculosis (TB) and worsening pre-existing heart failure in patients treated with TNF inhibitors. Increased risks for lymphoma and skin cancer, as well as occurrences of demyelinating diseases, were also reported albeit rare.¹⁴

Are biologics cost-effective?

The cost of biological therapy for inflammatory conditions such as RA could be considered high when directly compared to other treatments, but the improvement in patients' quality of life and minimalisation



of co-morbidities can significantly impact the indirect costs associated with RA, making their use more cost-effective.¹⁴

Why is there a need for early treatment?

Reaching remission is a key goal for patients with RA. In addition to the associated substantial economic burden, RA when left untreated may cause permanent joint damage leading to loss of function and eventually, premature death.^{2, 6} Benefits associated with early disease intervention in RA have been previously demonstrated.

- Results from the COMET (COmbination of Methotrexate and ETanercept in Active Early Rheumatoid Arthritis) Study demonstrate that early treatment of RA with methotrexate and etanercept can allow a patient to achieve clinical, radiographic and functional remission.¹⁵ Further data from the COMET trial show that the number of lost work days in patients treated with the etanercept combination was significantly less than that of patients receiving methotrexate alone.¹⁶
- In the PREMIER Study, combination therapy with adalimumab and methotrexate showed significantly improved signs and symptoms of RA. It also effected remissions in patients with early and aggressive RA who had not had previous methotrexate treatment compared to methotrexate or adalimumab alone.¹⁷
- A study by Durez et al revealed that the combination therapy of methotrexate plus infliximab versus methotrexate alone was superior in reducing MRI-detected signs of synovitis and bone edema in patients with early RA. In this study, 70 per cent of the patients treated with the combination experienced remission after a year of treatment.¹⁸

—Ends—



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