

Striving for innovation

The burden of rheumatoid arthritis and the pursuit for remission

By Selina McKee

The outlook for patients with rheumatoid arthritis (RA) has improved drastically in the last few decades, driven by the emergence of disease-modifying anti-rheumatic drugs (DMARDs), biologic medicines and JAK inhibitors.^{1,2} However, despite considerable progress in the field, there remains significant unmet need for patients – particularly with regard to achieving clinical remission – which pharma companies, in collaboration with the research community, are now striving to address.^{3,4}

RA is a chronic, destructive disease thought to affect around 1% of European and US populations.⁵ It falls within the top 15% of 291 conditions studied causing disability globally and tends to emerge during the most productive years of adulthood, between the ages of 20 and 40, impacting both individual patients and society as a whole.^{6,7}

RA is classified as an autoimmune disease in that the body's immune system mistakenly focuses its attack on cells lining the joints.⁸ This causes the synovium to become inflamed, leaving joints swollen, stiff and painful.⁸ As Dr Louis Bessette, Assistant Professor, Faculty of Medicine, at Université Laval, explains: "The main symptoms of RA are joint pain and joint swelling, but as it is a systemic disease, patients can also experience fatigue, lack of energy, fever and loss of appetite."

"RA often hits patients in the joints that matter in terms of daily living and work," says Dr Aileen Pangan, rheumatologist and executive medical director, Immunology Clinical Development, at AbbVie. "Sometimes patients can't take care of themselves, they are unable to comb their hair or button their coats. It is emotionally distressing for patients to not be able to perform what is expected of them, as a parent, a partner, or an employee."

Because there is still no cure for RA, the primary goal of treatment is to help patients reach clinical remission, or a state where the signs and symptoms of the disease are nearly completely absent, allowing patients to return to a more normal life.^{3,9} However, if left untreated, or if people fail to respond fully to existing therapy, "the consequences are disability, deformity and even early death," said Dr Bessette.

Further highlighting the burden of the disease, Dr Bessette said that 50%-70% of patients he sees for the first time in his clinic are disabled and not able to work. "And even with treatment not all patients can return to employment, which has a major impact on society as well as individuals."

That's because, despite improvements in therapy, many patients are unable to reach remission.³ For example, a recent targeted

literature review found DAS28<2.6 remission rates ranging from just 14.7% to 26.4% over six–12 months and 10.2% to 53.4% over three–20 months for patients treated with conventional DMARD monotherapies and biologic monotherapies, respectively, shedding further light on the current picture of treatment outcomes.¹⁰ Even when disease activity is considered low, some patients may still be suffering with pain, fatigue and morning joint stiffness, signalling room for improvement across the RA population.^{11,12}

Another study led by researchers at the University of Oxford, UK, and published in RMD Open, found that over a quarter (27%) of RA patients from France, Germany, Italy, Spain, and the UK had inadequate disease control (in 2014).¹³ This was linked to negative outcomes, as those with inadequately controlled disease had significantly worse pain scores, and higher rates of depression and flares.¹³

'Despite all currently available treatments, we're not seeing anything near 100% of patients in remission'

"Every time I see a new patient with RA – it's friends for life. I'll see that patient every three or six months for the rest of his or her life," said Dr Bessette, emphasising the level of life-long care patients need. "This disease has a major impact on patients' quality of life, as it affects their ability to work, their wellbeing and their social lives, but the cost to society is also very important," he stressed, noting that in Europe alone the indirect and direct costs of living with RA is about 45 billion euros (in 2006).⁵

This is particularly pertinent considering the expected rise in cases; according to a forecast by GlobalData, the total prevalent cases of RA across the world's eight major markets (including the US, Europe and Japan) will jump to 6,971,304 by 2025, representing a rise of 12% since 2015.¹⁴ The future economic burden will likely increase as a result due to managing symptoms, loss of productivity, and hospitalisation, underscoring the need for new approaches to managing the condition.¹⁴

Dr Pangan says that while AbbVie is proud of its legacy in RA and contribution to the field, there's still a lot of work to be done.



“Despite all currently available treatments, we’re not seeing anything near 100% of patients in remission. As uncontrolled RA causes long term disability it’s very important not just to achieve a good response but achieve clinical remission or low disease activity.”

Looking forward, it is widely recognised that more treatment options are essential if more patients are to achieve clinical remission.³ This will likely require a deeper understanding of the drivers of chronic inflammation and which combination of compounds can effectively target these pathways.³

“The combined efforts of both academic and industry researchers have brought a lot of new insight about the disease and that there are multiple pathways involved in immune mediated inflammatory diseases like RA,” Dr Pangan said. “It’s not a simple disease. Because of that, we’re really excited about exploring new targets, new mechanism of actions, and new treatment approaches.”

One of AbbVie’s research priorities is to gain deeper understanding of whether a combination of therapies will get more patients closer to clinical remission.⁴ The firm is exploring ways to inhibit multiple disease pathways and also the potential for greater precision

through use of technologies such as antibody drug conjugates (ADCs), which could deliver an anti-inflammatory medicine directly to its target.⁴

Making headway in the treatment of RA remains a key focus for AbbVie.⁴ “The breadth of our experience in RA research continues to drive our current and future programmes to develop innovative medicines that could have life-changing impact for patients around the world,” said Dr Pangan.

However, other factors also play an important role in treatment outcomes.¹⁵ According to Dr Bessette, the earlier patients start treatment the better chance they have at achieving remission, but this can be delayed for a number of reasons. Receiving a timely diagnosis can be hampered by a lack of adequate training on RA in primary care and the absence of a single test able to determine its presence.¹⁵ Also, depending on where you live, getting access to a rheumatologist can be problematic.¹⁶

“New treatments, improved access and a better model of care, that addresses current gaps in healthcare systems’ infrastructures, would be of benefit to both patients and society,” he stressed. ▲

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