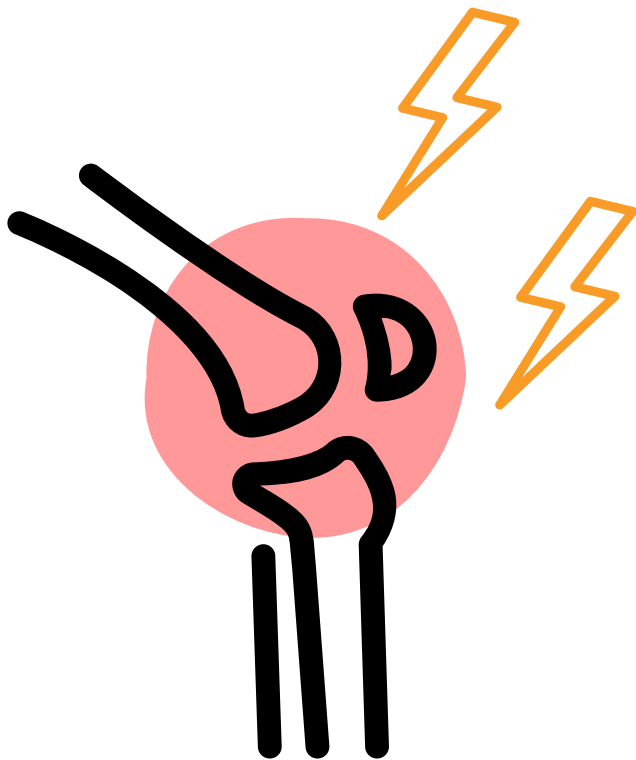


Allowing Rheumatoid Arthritis patients to live a normal life with biologics



CASE OUTLINE

- I. **Case for change**
 - *Situation*
 - *Challenge*
 - *Paradigm shift*
 - *Patient population*
- II. **Value to patients**
- III. **Value to the healthcare system**
- IV. **Value to society**
- V. **Annex**
 - *Key assumptions*
 - *Reference list*

Case summary | Rheumatoid Arthritis

Allowing RA patients to live a normal life with biologics

CASE FOR CHANGE



- **Situation** – Rheumatoid Arthritis (RA) is a chronic, destructive autoimmune disease for which 32% of patients did not have access to effective treatments before 1998
- **Challenge** – Standard of care (SoC) treatment is conventional disease modifying antirheumatic drugs (cDMARDs), most often starting with methotrexate. These treatments work insufficiently for 32% of patients who remain in need for a better working treatment
- **Paradigm shift** – In 1998, the first biological DMARD (bDMARD) entered the market, providing these patients with a new treatment option
- **Population** – The prevalence of Rheumatoid Arthritis is 0.5%–1.0%, meaning there are 2,236,037–4,472,075 patients with RA in EU27 in 2021

VALUE FOR PATIENTS



- **Reduced RA symptoms** – Biological DMARDs are effective in improving disease activity which leads to symptom reduction: less pain, less joint damage, and better overall health
- **Radical change of patient experience** – bDMARDs are significantly more effective at reducing DAS28 to <2.6 compared with cDMARDs, drastically improving patient experience
- **Slowed disease progression** – Treatment with bDMARDs does not only lead to symptom reduction but also better disease control, showing less progression of joint damage
- **Improved Quality of Life** – Patients are more mobile and less affected by the symptoms of their disease, causing an improved Quality of Life (QoL)

VALUE TO THE HEALTHCARE SYSTEM



- **Preventable resource use** – More effective disease management due to bDMARD treatment, as well as reduction in resource utilisation.

VALUE TO SOCIETY



- **Economic gains** – bDMARD use results in reduced absenteeism and presenteeism in EU27 RA patients, resulting in increased productivity
- **Enjoying life again** – Because patients are less troubled by their disease, they can enjoy time with their family and friends again

TOWARDS THE FUTURE



- The innovation that bDMARDs have brought to RA patients is life changing, but there remain unmet needs in this therapy area

Rheumatoid Arthritis is a chronic, destructive autoimmune disease for which 32% of patients did not have access to effective treatments until 1998



Rheumatoid Arthritis



Rheumatoid Arthritis (RA) is a chronic, destructive **autoimmune** disease that causes **inflammation** of the **joints and other systemic issues**¹



RA can develop at all ages, but is mostly diagnosed between 30 and 60 years of age, and is twice as common in women as in men¹



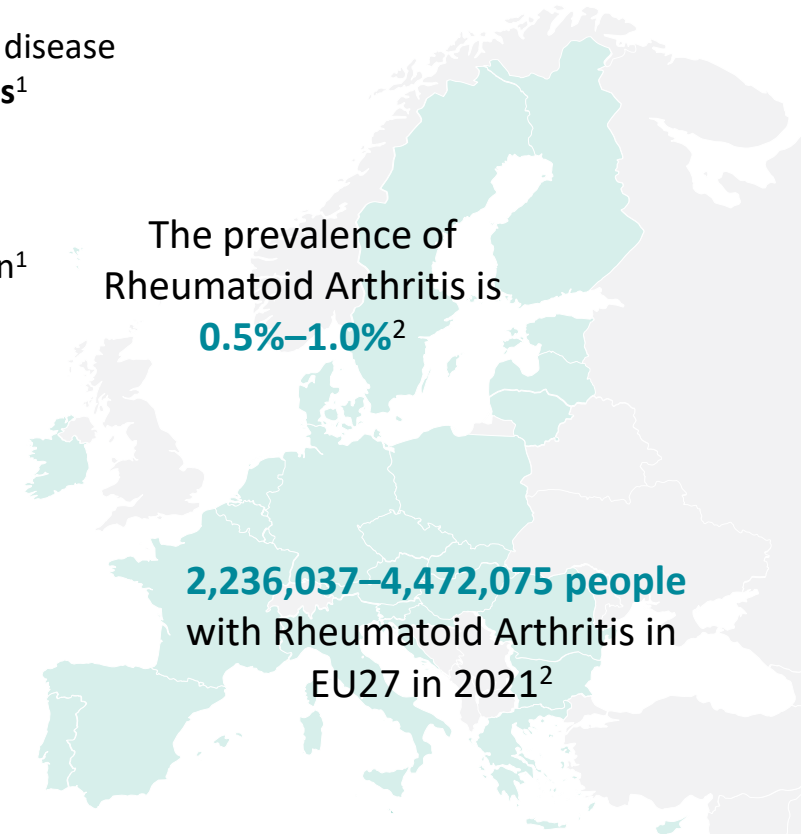
Standard of care (SoC) treatment is conventional disease modifying antirheumatic drugs (cDMARDs), most often starting with methotrexate³



These treatments **work insufficiently for 32% of patients**, who remain in need for a better working treatment³



In 1998 the first **biological DMARD** (bDMARD) entered the market, providing these patients with a **new treatment option**³



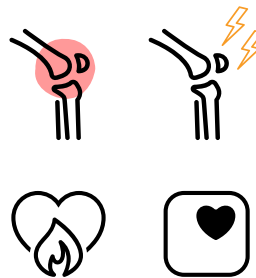
1. HEALTHLINE, ACCESSED JULY '22
2. MINICHELLO, ET AL. 2016
3. KALÓ, ET AL. 2017

Biological DMARDs are effective in improving disease activity, leading to symptom reduction: less pain, less joint damage, and better overall health

Inflammatory activity cannot be measured using one single variable. The Disease Activity Score (DAS) was developed to measure disease activity¹

DAS28 score is calculated on the basis of:²

- Number of swollen joints (out of the 28)
- Number of tender joints (out of the 28)
- Inflammation values in the blood (C reactive protein (CRP) or erythrocyte sedimentation rate (ESR))
- Answers to a patient health assessment questionnaire



| DAS28 score 0–9.4 | Translation into disease activity ² |
|----------------------|---|
| <2.6 | Disease remission |
| 2.6–3.2 | Low disease activity |
| 3.2–5.1 | Moderate disease activity |
| >5.1 | High disease activity |

Many studies have investigated the efficacy of bDMARDs³



Different treatment groups

- bDMARD monotherapy vs. cDMARDs +/- placebo
- bDMARDs + cDMARDs vs. cDMARDs +/- placebo



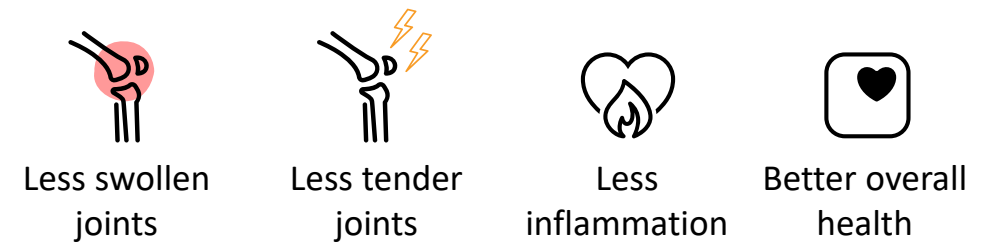
Different patient populations

- Treatment naïve patients
- Patients previously treated with cDMARDs



These studies prove that a bigger % of patients on bDMARDs scored <2.6 or 2.6–3.2 on DAS28 than patients on cDMARDs³

...meaning:

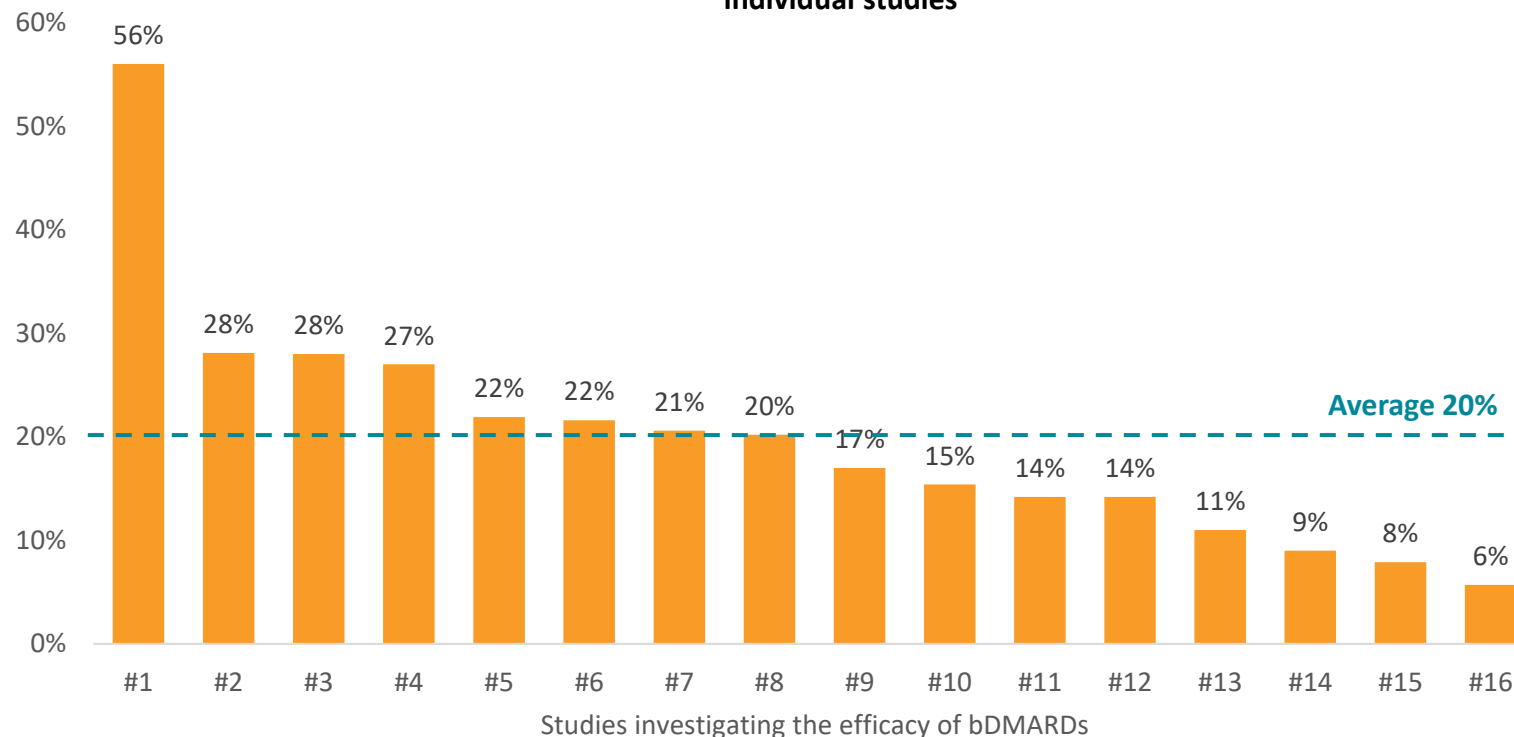


1. VAN RIEL & RENSKERS 2016
 2. ARTHRITIS HEALTH, ACCESSED JULY '22
 3. NICE TECHNOLOGY ASSESSMENT REPORT TA375 P.101-102

bDMARDS are significantly more effective at reducing DAS28 to <2.6 compared with cDMARDS, drastically improving patient experience



Absolute improvement of patients scoring DAS28 score <2.6 for patients using bDMARDS vs cDMARDS across 15 individual studies



Treatment with bDMARDS changes the patient's experience of their disease²

- "After the treatment, I feel like I can do things that everyone else can do"
- "I was mostly just thankful to get back to being self-sufficient"
- "I didn't want him to remember me as the mum who was always in pain and crying. And I'm not that mum anymore"
- "It's significant when you do something that's very normal, and you realize five minutes into it that you're able to do it"
- "Before my current medication, I would have been happy selling the business and living a lifestyle where I didn't have to do much. But now, I want to do better in business and life."

Patients receiving bDMARDs instead of cDMARDs are experiencing fewer RA symptoms, drastically improving patient experience



Disease activity of patients is scored after treatment

| | | | | |
|------------------|-----------|---------|----------|------|
| DAS28 score | <2.6 | 2.6–3.2 | 3.2–5.1 | >5.1 |
| Disease activity | Remission | Low | Moderate | High |

+20%
more patients in
the bDMARDs
treatment group
vs. cDMARDs
treatment group¹

Disease remission: signs and symptoms are relieved for an extended period of time³

Treatment with bDMARDs changes the patient's experience of their disease²

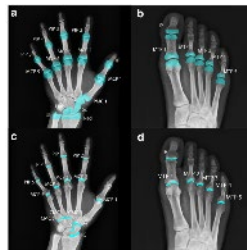
- "After the treatment, I feel like I can do things that everyone else can do"
- "I was mostly just thankful to get back to being self-sufficient"
- "I didn't want him to remember me as the mum who was always in pain and crying. And I'm not that mum anymore"
- "It's significant when you do something that's very normal, and you realize five minutes into it that you're able to do it"
- "Before my current medication, I would have been happy selling the business and living a lifestyle where I didn't have to do much. But now, I want to do better in business and life."

Treatment with bDMARDs does not only lead to symptom reduction but also greater disease control and less progression of joint damage

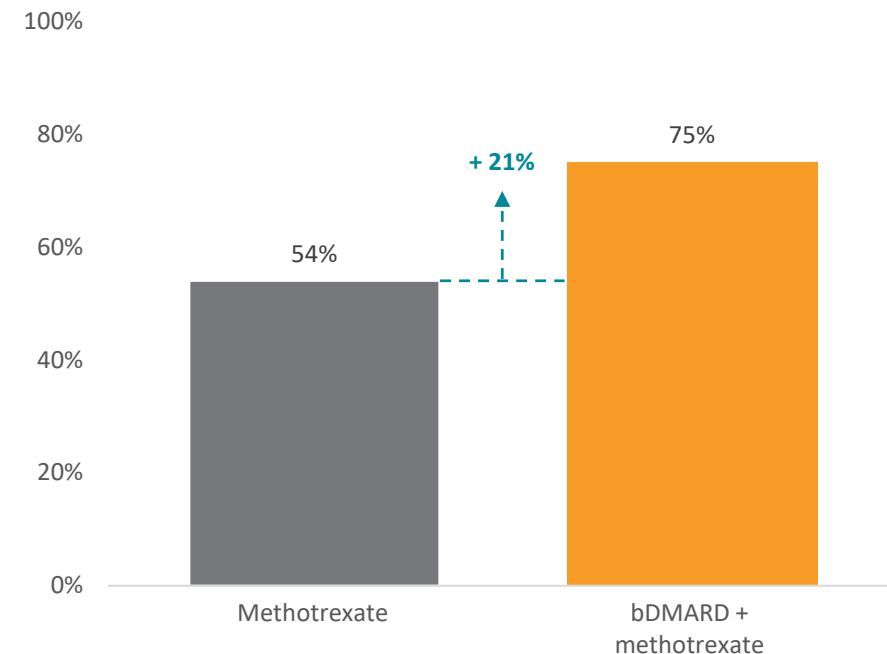
75% of patient showed no signs of disease progression and joint damage 1 year after treatment initiation with bDMARDs¹

+21% compared with the proportion of patients showing no disease progression 1 year after treatment initiation with methotrexate¹

Structural changes of bone and cartilage are the hallmarks of rheumatoid arthritis. Disease progression is measured by scoring joint erosion and joint space narrowing in radiographs of hands and feet^{2,3}



Proportion of patients with radiographic non-progression 52 weeks after start of treatment (%)¹



Patients taking bDMARDs are more mobile and less affected by the symptoms of their disease, causing an improved Quality of Life (QoL)

+44% improvement in quality of life is experienced by female patients one year after switching their treatment to bDMARDs¹

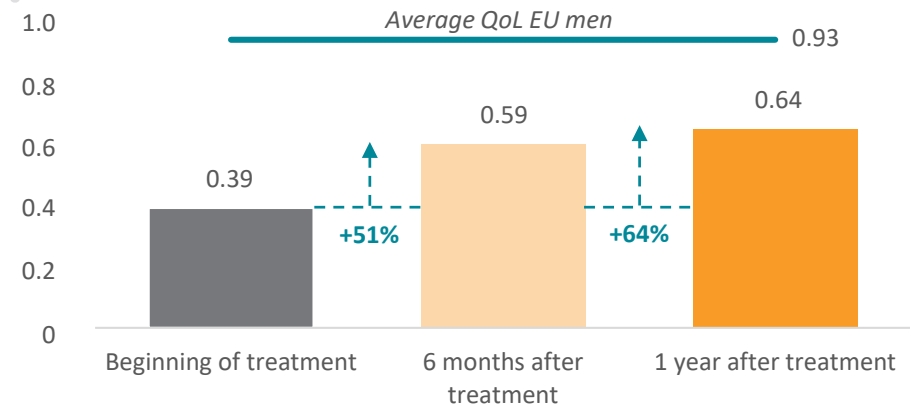
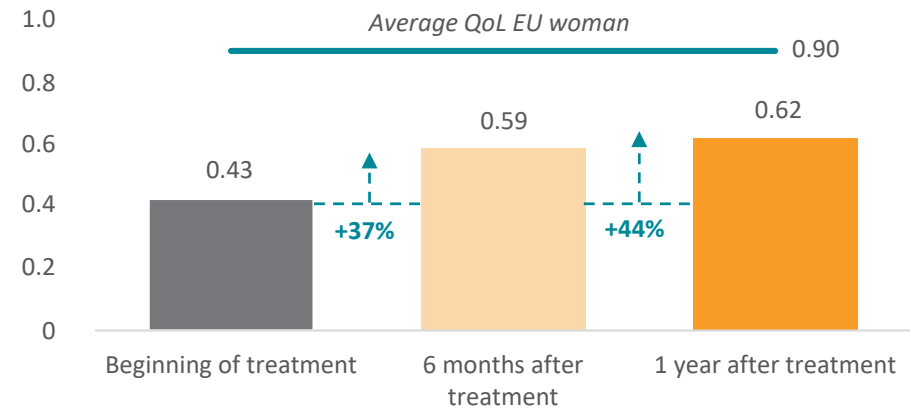
+64% improvement in quality of life is experienced by male patients one year after switching their treatment to bDMARDs¹

"It is revolutionary what biologics brought to patients"
– Patient Expert

Quality of Life (QoL) can be measured with various instruments, of which EQ5D is globally accepted. EQ5D calculates a score ranging from 0 to 1²



Improvement in QoL* with treatment switch to bDMARDs¹



*MEASURED BY EQ5D
1. BOYADZIEVA, ET AL. 2018
2. EUROQOL, ACCESSED AUGUST '22

Because patients are less troubled by their disease, they feel self-sufficient and can enjoy time with their family and friends again



70-80% more time able to perform household work

Treatment with bDMARDs gives patients their life back

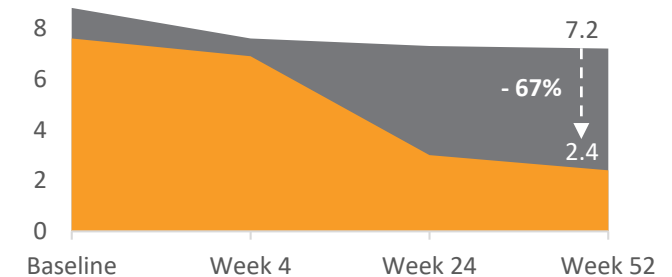


40-60% more time able to spend with family and friends

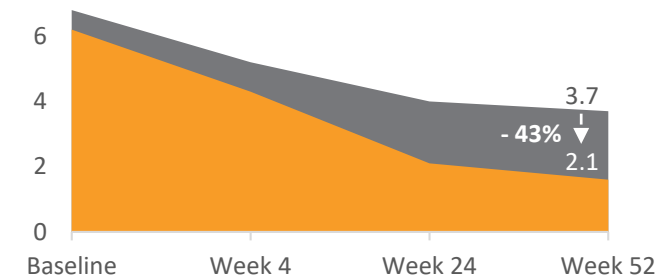
“People were stuck at home, feeling depressed because people are human beings and should be able to socialize. Now you can contribute again to your family, to the society, travel and see your friends again”

– Patient Expert

Lost days of household work per month¹



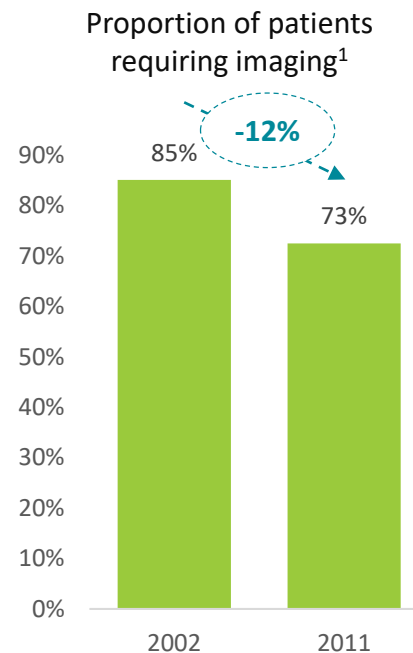
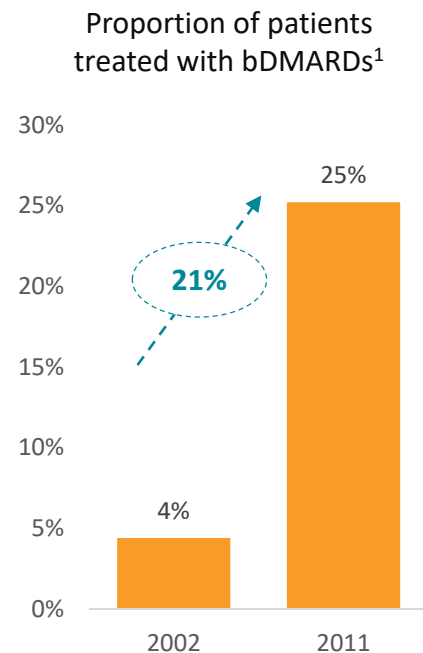
Lost days of family, social, and leisure activity per month¹



Treatment Placebo + methotrexate bDMARDs + methotrexate

bDMARD treatment leads not only to more effective disease management, but to a reduction in resource utilisation as well

 Analysis of National Database of the German Collaborative Arthritis Centres from 2002 to 2011



"I always tell my students that in the past my waiting room was full of wheelchairs. Now we only see patients in a wheelchair when they had a normal accident because they can live a normal life again"
– Healthcare Professional



"We used to have a special clinic for the care of Rheumatoid Arthritis patients who had severe pain and serious damage to their joints. This clinic closed in 1997 because we can help patients much better"
– Healthcare Professional²

bDMARD use results in reduced absenteeism and presenteeism in EU27 RA patients, resulting in increased productivity

132M workdays

gained per year for the entire RA population (absenteeism)

+87M workdays

gained with full productivity per year for the entire RA population (presenteeism)

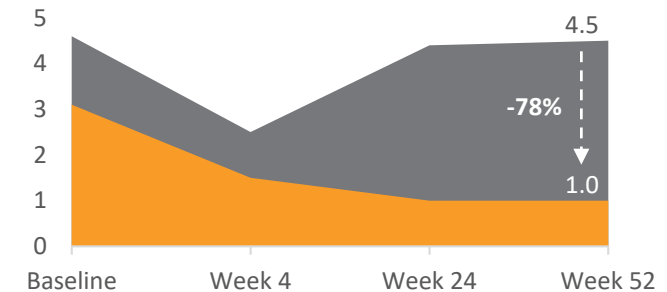
“bDMARDs provided patients with the ability to keep their normal life. Work life but also personal life... First, they had lower productivity but now they can contribute and maintain jobs”

– Healthcare Professional

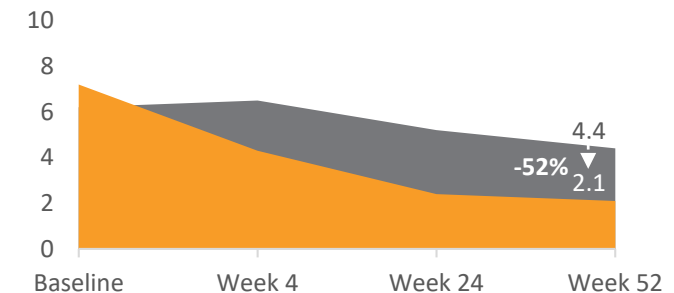
“You feel useful again”

– Patient Expert

Workdays missed per month (absenteeism)¹



Workdays with reduced productivity by ≥50% per month (presenteeism)¹



Treatment Placebo + methotrexate bDMARDs + methotrexate

The innovation that bDMARDs brought to RA patients is life changing, but there are remaining unmet needs in this patient population

bDMARDs bring great benefits to RA patients and allow them to participate in life again.

However, these patients are still chronic patients and there **are remaining unmet needs**



Early diagnosis

“My dream for the future is that we have no disability caused by rheumatoid disease anymore. To reach that, we should raise awareness so that people have the right diagnosis and treatment as soon as possible.”

– Patient Expert

“People should recognize when they should visit the doctors with their symptoms and the GP should recognize when to refer the patient to the rheumatologist.”

– Patient Expert

“All stakeholders should collaborate to ensure that patients are identified as early as possible: patients, doctors, specialists.”

– Patient Expert



New targets for treatment & diagnoses

“There are 3 types of patients: patients doing very well, patients doing very badly, and the rest of patients. For the first group, we don’t have an unmet need. For the second group, we need new treatments. This can be new therapies for targets currently in clinical development or new combination between bDMARDs and add-on safe therapies. For the last group, we will not change their treatment because they are responding but there is room for improvement. This can be done by having a holistic treatment approach, including physical activity, psychotherapy and diet counselling.”

– Healthcare Professional



Cure or prevention

“Currently patients are still suffering from their disease. We should not forget how impactful it is to hear that you have a chronic disease.”

– Healthcare Professional

“My dream is that we can cure Rheumatoid Arthritis and other rheumatic diseases.”

– Healthcare Professional

Assumptions

To quantify the treatment effect of bDMARDs and the associated patient experience, we used the following **assumptions**:

1. All bDMARDs cause improvement of the DAS28 score, and this can be considered to be a class effect
2. Improvements in DAS score represent symptom reduction and improved patient-reported health. These improvements cascade into additional benefits, such as better physical functioning, improvement quality of life, etc.
3. The additional benefits of bDMARDs are also considered to be a class effect

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- Lavender, 2021. <https://www.self.com/story/rheumatoid-arthritis-medication-changes> Accessed July '22
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Interviews

Interviews conducted in July and August 2022 with 1 Patient Advocate and 2 Healthcare Professionals (KOLs)