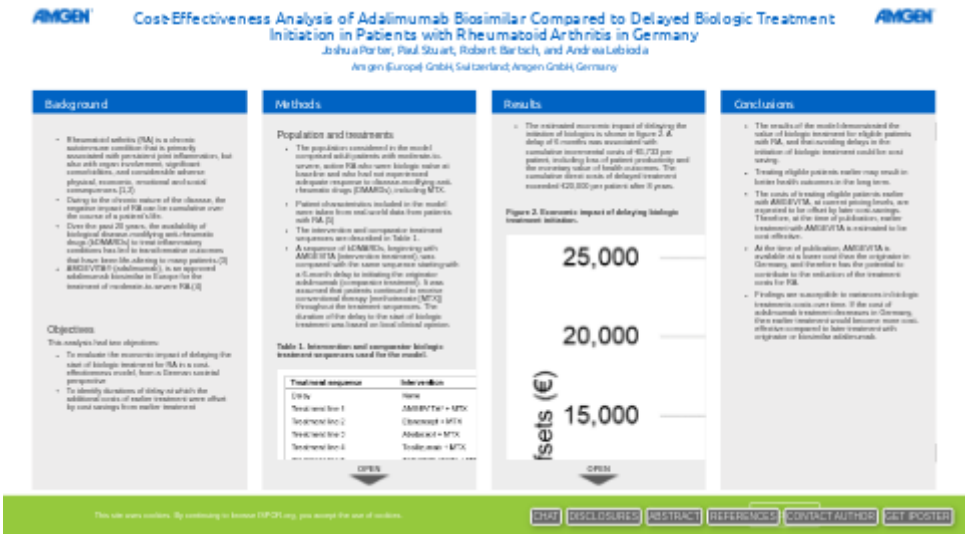
Cost-Effectiveness Analysis of Adalimumab Biosimilar Compared to Delayed Biologic Treatment Initiation in Patients with Rheumatoid Arthritis in Germany



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BACKGROUND

- Rheumatoid arthritis (RA) is a chronic autoimmune condition that is primarily associated with persistent joint inflammation, but also with organ involvement, significant comorbidities, and considerable adverse physical, economic, emotional and social consequences.(1,2)
- Owing to the chronic nature of the disease, the negative impact of RA can be cumulative over the course of a patient's life.
- Over the past 20 years, the availability of biological disease-modifying anti-rheumatic drugs (bDMARDs) to treat inflammatory conditions has led to transformative outcomes that have been life-altering to many patients. (3)
- AMGEVITA® (adalimumab), is an approved adalimumab biosimilar in Europe for the treatment of moderate-to-severe RA.(4)

Objectives

This analysis had two objectives:

- To evaluate the economic impact of delaying the start of biologic treatment for RA in a cost-effectiveness model, from a German societal perspective
- To identify durations of delay at which the additional costs of earlier treatment were offset by cost savings from earlier treatment

METHODS

Population and treatments

- The population considered in the model comprised adult patients with moderate-to-severe, active RA who were biologic naïve at baseline and who had not experienced adequate response to disease-modifying anti-rheumatic drugs (DMARDs), including methotrexate (MTX).

- Patient characteristics included in the model were taken from real-world data from patients with RA.(5)
- The intervention and comparator treatment sequences are described in Table 1.
- A sequence of bDMARDs, beginning with AMGEVITA (intervention treatment), was compared with the same sequence starting with a 6-month delay to initiating the originator adalimumab (comparator treatment). It was assumed that patients continued to receive conventional therapy (MTX) throughout the treatment sequences. The duration of the delay to the start of biologic treatment was based on local clinical opinion.

Table 1. Intervention and comparator biologic treatment sequences used for the model.

Treatment sequence	Intervention	Comparator
Delay	None	6 months
Treatment line 1	AMGEVITA[a] + MTX	Adalimumab[b] + MTX
Treatment line 2	Etanercept + MTX	Etanercept + MTX
Treatment line 3	Abatacept + MTX	Abatacept + MTX
Treatment line 4	Tocilizumab + MTX	Tocilizumab + MTX
Treatment line 5	Tofacitinib citrate + MTX	Tofacitinib citrate + MTX
Treatment line 6	Rituximab + MTX	Rituximab + MTX
Treatment line 7	NBT[b]	NBT[b]

[a]AMGEVITA was assigned equal efficacy to the originator, but with biosimilar price. [b]Originator. [c]Intervention and comparator treatment sequences both end with NBT, which patients are assumed to have continued.
MTX, methotrexate; NBT, non-biologic therapy.

Outcomes

- Cost inputs were taken from German cost databases, and comparative efficacy and utility were estimated from peer-reviewed literature.(5-7)

- The cost-effectiveness of AMGEVITA was assessed by comparing the additional cost of treating patients earlier, with the incremental monetary value of health outcomes, as measured by Quality Adjusted Life-Years.

- Health outcomes in the model were monetized using an assumed willingness to pay per Quality Adjusted Life Year. There is no accepted threshold used in Germany, but the World Health Organization (WHO) recommends a range of 1-3 times the Gross Domestic Product (GDP) per capita. To be conservative, the lower threshold of € 38,900 per incremental Quality Adjusted Life Year is used, equal to the GDP per capita for Germany. (8,9)

Model structure

- A semi-Markov cohort model was developed, based on previously published economic analyses in RA.(5,10)

- These previous models adopted a patient-level simulation approach to model the outcomes of individuals, then aggregated these to produce cohort-level estimates of the relevant outcomes. The semi-Markov model maintained a similar structure, but instead modelled patients on a cohort level.

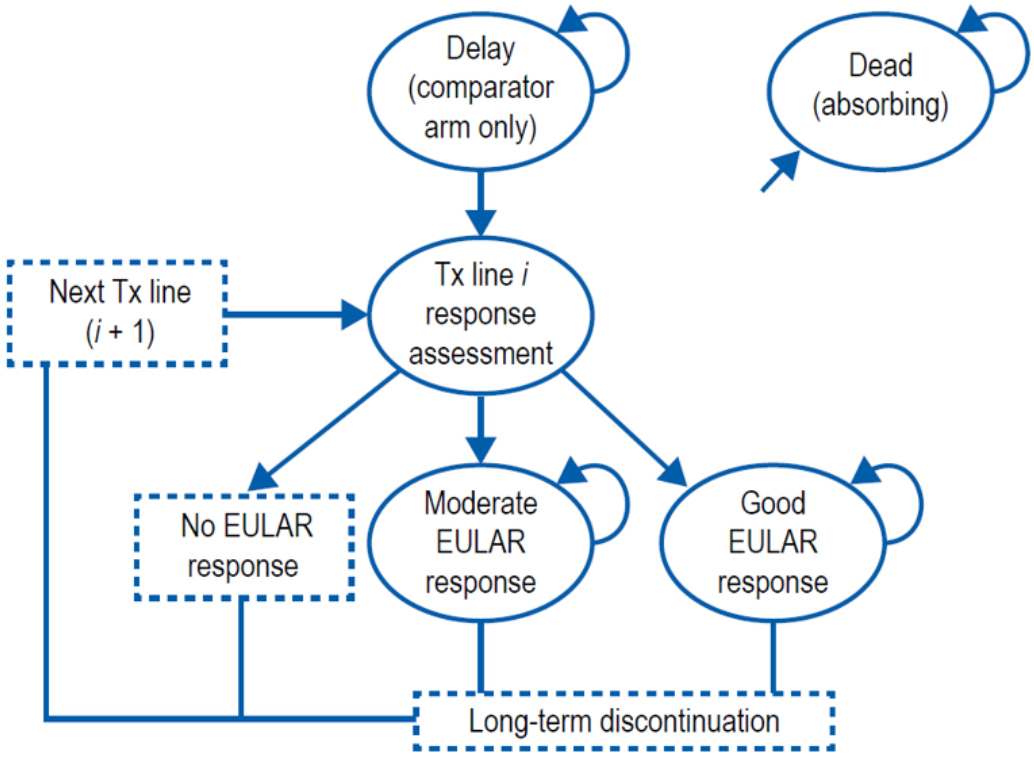
- Patients were assumed to be biologic naïve at baseline, but were eligible to receive biologic treatment (i.e. were moderate-severe and had not responded to conventional DMARDs including MTX) and progressed through a maximum of seven lines of treatment. Response to each treatment was categorised based on the European

League Against Rheumatism (EULAR) response criteria.(11) The EULAR responses were based on comparative efficacy data from a network meta-analysis that looked at American College of Rheumatology response categories.(10)

- The model adopted a cycle length of 6 months and a time horizon of 50 years. The model structure is summarized in Figure 1.

- Cost and outcomes were discounted at a rate of 5% per year, in line with standard practice for health economic models in Europe.(12)

Figure 1. Model summary.



EULAR, European League Against Rheumatism; *i*, treatment line number; Tx, treatment.

Solid ellipses indicate model health states, dashed boxes indicate immediate transitions

Model inputs

- Patient outcomes were based on Health Assessment Questionnaire (HAQ) scores.

- In the model, 5-dimension EuroQol questionnaire scores were determined by the HAQ score of patients in each treatment line, using a published analysis that has informed previous economic evaluations in RA.(5)

- The comparative treatment effects of the DMARDs, in terms of the proportions of patients with different EULAR response categories, were taken from a summary of efficacy data reported previously.(5)

- At the end of the 6-month response assessment period, patients could have a moderate EULAR response, a good EULAR response, or no EULAR response (derived as 1 minus the reported values for moderate and good response).(5)

- Response rates were stratified into first-line treatment and subsequent lines of treatment, to account for lower treatment efficacy following failure of the first line.

- Patients with no EULAR response discontinued biologic treatment at the end of the 6-month response assessment period.

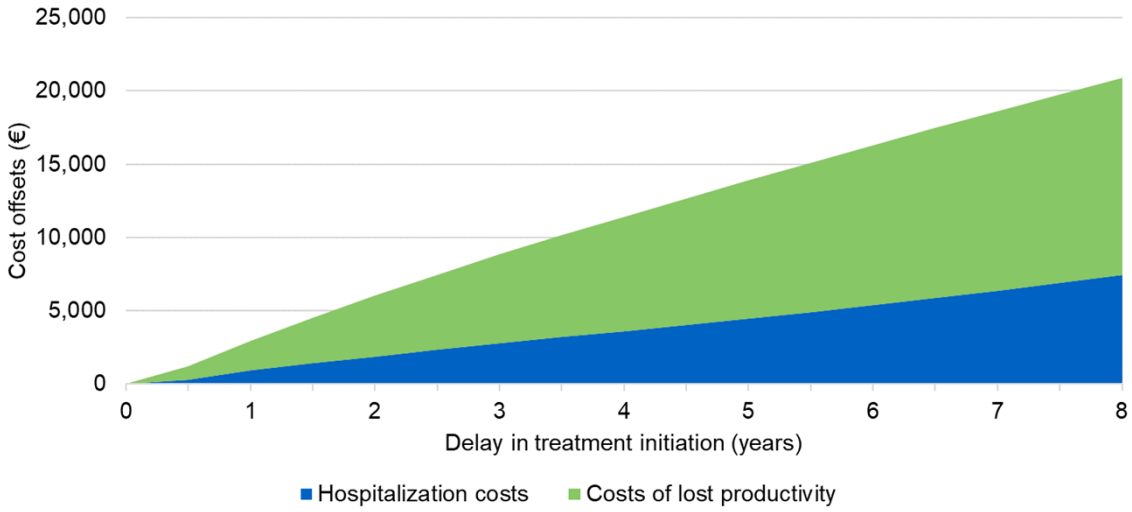
- Direct costs such as medication, administration, monitoring, tests, hospitalisation and adverse events were included in the model

- The cost to society resulting from lost patient productivity due to RA-related symptoms is also included in the model and represents the cost of patients needing to take time off work due to their illness.

RESULTS

- The estimated economic impact of delaying the initiation of biologics is shown in figure 2. A delay of 6 months was associated with cumulative incremental costs of €6,733 per patient, including loss of patient productivity and the monetary value of health outcomes. The cumulative direct costs of delayed treatment exceeded €20,000 per patient after 8 years.

Figure 2. Economic impact of delaying biologic treatment initiation.



- A summary of the results of the comparison of the intervention therapy sequence versus the comparator therapy sequence is presented in Table 2.

- Earlier intervention with lower-cost adalimumab is expected to be dominant compared to delayed treatment with adalimumab at current originator pricing, resulting in lower overall costs.

- In addition to the cost offsets of earlier intervention compared to a 6-month delay, lower-cost adalimumab compared with adalimumab at current originator pricing results in an overall lifetime reduction in costs of € 25,128 per patient, including the monetary value of health outcomes. This finding is consistent with similar analyses conducted in Brazil.(13)

Table 2. Amgevita versus later initiation with originator adalimumab.

	Drug Costs (incl. TEAE)	Medical Resource Use	Indirect Costs	Monetized Health Outcomes[a]	Total
AMGEVITA	164,240	13,676	46,211	-299,909	-75,782
Comparator	186,326	13,981	47,103	-298,064	-50,654
Incremental	**-22,085**	**-305**	**-891**	**-1,846**	**-25,128**

[a] Estimated by assigning an economic value to the monetized value of health outcomes (€38,900 per Quality Adjusted Life Year).
Assuming 6-month delay in comparator arm.
TEAE, treatment emergent adverse event.

- Excluding the monetary value of health outcomes, cost neutrality compared to later treatment with adalimumab at current originator pricing was estimated to be achieved treating 3 years earlier, assuming patients are eligible to receive biologic treatment at that time. If the monetized value of an improved health outcomes were included, earlier intervention is estimated to result in net savings for delay durations evaluated.

- Compared to later treatment with adalimumab at lower cost, the incremental treatment costs are expected to be partially offset by the economic value of possible improved health outcomes and medical and productivity cost offsets. Compared to a delay of 12 months in starting treatment, 27% of the incremental costs was offset by saved hospitalization and productivity costs, and 77% was offset if monetized health outcomes were included.

Table 3. Cost offsets of earlier treatment

Length of delay (years)	Comparison to	Incremental drug costs	Biosimilar savings	Medical resource use savings	Indirect cost savings	Monetized health outcomes	Total (proportion of incremental drug costs offset) - Health outcomes excluded		Total (proportion of incremental drug costs offset) - Health outcomes included	
3	Originator adalimumab	40,812	31,536	2,783	6,051	19,648	443	99%	-19,205	147%
1	Biosimilar adalimumab	11,027	0	944	2,018	5,504	8,065	27%	2,561	77%

CONCLUSIONS

- The results of the model demonstrated the value of biologic treatment for eligible patients with RA, and that avoiding delays in the initiation of biologic treatment could be cost saving.

- Treating eligible patients earlier may result in better health outcomes in the long term.

- The costs of treating eligible patients earlier with AMGEVITA, at current pricing levels, are expected to be offset by later cost-savings. Therefore, at the time of publication, earlier treatment with AMGEVITA is estimated to be cost effective.

- At the time of publication, AMGEVITA is available at a lower cost than the originator in Germany, and therefore has the potential to contribute to the reduction of the treatment costs for RA.

- Findings are susceptible to variances in biologic treatments costs over time. If the cost of adalimumab treatment decreases in Germany, then earlier treatment would become more cost-effective compared to later treatment with originator or biosimilar adalimumab.

DISCLOSURES

Conflicts of interests

JP, PS, RB and AL are Amgen employees and hold Amgen stock.

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ABSTRACT

OBJECTIVES

The progression of moderate and severe rheumatoid arthritis (RA) is controlled for many patients by biologic disease modifying anti-rheumatic drugs (bDMARDs). However, once patients become eligible for these therapies, they often face a delay in starting treatment, largely due to cost concerns. This analysis aimed to evaluate the economic impact of these delays in biologic treatment, adapting a published cost-effectiveness framework to a German societal perspective.

METHODS

A semi-Markov cohort model was developed, with a cycle length of 6 months and a time horizon of 50 years. Cost and Quality Adjusted Life-Years (QALYs) were discounted at an annual rate of 5%. A sequence of bDMARDs beginning with immediate initiation of AMGEVITA (adalimumab) was compared to the same sequence in the comparator arm starting with a 6-month delay of originator adalimumab. During the delay, patients are assumed to continue conventional therapy. Treatment effects were modeled on patients' Health Assessment Questionnaire (HAQ) scores, which in turn determined economic and quality of life outcomes. Cost inputs were taken from local sources, and comparative effcacy and utility estimates were collected from peer-reviewed literature. For each arm, the model estimates the total direct costs, life-years (LYs) and QALYs. The results of the model were used to derive the incremental cost-effectiveness ratio (ICER).

RESULTS

The comparator arm, including the treatment delay, resulted in total discounted costs of €247,409, together with 20.590 LYs and 7.662 discounted QALY. Earlier intervention with AMGEVITA resulted in total discounted costs of €224,127, together with 20.619 LYs and 7.710 discounted QALYs. With a cost reduction of €23,282 and incremental QALYs and LYs of 0.047 and 0.029, respectively, earlier intervention with AMGEVITA dominated later intervention with originator adalimumab.

CONCLUSIONS

The availability of AMGEVITA allows eligible RA patients to be treated earlier with biologics, whilst simultaneously reducing the costs of treating RA versus the originator.

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