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ORIGINAL ARTICLES
Economic Evaluation

Economic Evaluation of Tocilizumab Monotherapy Compared to Adalimumab Monotherapy in the Treatment of Severe Active Rheumatoid Arthritis

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ABSTRACT

Objectives: To estimate the cost-effectiveness of tocilizumab (TCZ) monotherapy (Mono) versus adalimumab (ADA) Mono from the US payer perspective in patients with rheumatoid arthritis for whom methotrexate is inappropriate. **Methods:** We compared TCZ Mono (8 mg/kg monthly) with ADA Mono (40 mg every other week), using efficacy results from a head-to-head study, ADalimumab ACTemrA (ADACTA). We calculated the incremental cost per responder (achievement of American College of Rheumatology [ACR] 20% improvement criteria, ACR 50% improvement criteria, ACR 70% improvement criteria, or low disease activity score) for TCZ versus ADA at 6 months. A patient-level simulation was used to estimate the lifetime incremental cost per quality-adjusted life-year (QALY) of initiating treatment with TCZ Mono versus ADA Mono. Both drugs are followed by an etanercept-certolizumab-palliative care sequence. Nonresponders discontinue at 6 months; responders experience a constant probability of discontinuation. Discontinuers move to the next treatment. ACR responses produce changes in the Health Assessment Questionnaire (HAQ) score. We mapped the HAQ score to utility to estimate QALYs. Costs include those related to hospitalization and those related to treatment (drug acquisition, administration, and monitoring). Probabilistic and one-way sensitivity analyses were conducted, along with several scenario analyses. **Results:** Compared with ADA, TCZ was more effective, with an estimated 6-month incremental cost ranging from $6,570 per additional low disease activity score achiever to $14,265 per additional ACR 70% improvement criteria responder. The lifetime incremental cost-effectiveness ratio was $36,944/QALY. **Conclusions:** TCZ Mono is projected to be cost-effective compared with ADA Mono in patients with severe rheumatoid arthritis for whom methotrexate is not appropriate, from a US payer perspective.

Keywords: anti-TNF-α, cost-effectiveness, rheumatoid arthritis, tocilizumab.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease leading to inflammation in joints and connective tissue, along with other systemic effects. It is associated with substantial economic and health-related quality-of-life impacts [1–3].

According to the American College of Rheumatology (ACR) guidelines, treatment for early RA should begin with the use of traditional (nonbiologic) disease-modifying antirheumatic drugs (DMARDs), most commonly methotrexate (MTX) [4]. For patients who do not tolerate MTX, alternate conventional DMARDs are often tried. For patients with established RA (≥6-month duration) and more severe disease, a biologic DMARD is often added [4]. Although many patients treated with a biologic agent continue to use traditional DMARDs in combination, studies have indicated that patients often discontinue these agents or have poor adherence because of intolerance, lack of efficacy, or other factors [5]. As a result, roughly 30% of the patients using a biologic DMARD receive it as monotherapy (Mono) [6,7]. In patients who are eligible to receive a biologic DMARD, antagonists to tumor necrosis factor alpha (anti–TNF-α) are generally started first. There is evidence to suggest, however, that other available biologic DMARDs, with different mechanisms of action, are similarly effective when used in combination with MTX after the failure of traditional DMARDs for the treatment of RA, with mean response rates around 60% to 70% [8]. Still, when used as

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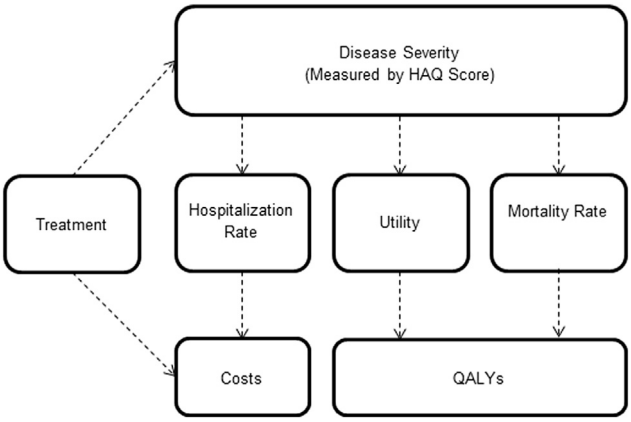

Fig. 1 – Use of HAQ Score in the lifetime model. The model captures changes in disease severity based on results from the HAQ, which then impacts utility, mortality rate and hospitalization rates in the model. HAQ, Health Assessment Questionnaire; QALY, quality-adjusted life year.

Mono, there may be differences in efficacy among biologic treatment options [9–11].

Tocilizumab (TCZ) is a humanized monoclonal antibody that inhibits the interleukin-6 receptor. Its safety and efficacy were demonstrated in three large phase III trials, for use in combination with MTX in patients with RA with inadequate response to traditional DMARDs [12–14]. More recently, a phase IV study, ADalimumab ACTemrA (ADACTA), compared monthly TCZ Mono head-to-head with a commonly used anti–TNF-α (adalimumab [ADA] Mono administered every other week [EOW]) in biologically naive patients with severe active RA who were intolerant to MTX or in whom continued MTX treatment was considered inappropriate. ADACTA was a 24-week, multicenter, randomized, double-blind, parallel-group study. Results indicated that TCZ Mono was superior to ADA Mono in reducing the signs and symptoms of RA within this patient population [10]. The cost-effectiveness of TCZ Mono relative to ADA Mono, however, has not been assessed. The objective of this study was to estimate the cost-effectiveness of monthly TCZ Mono versus ADA Mono EOW for biologically naive patients with severe active RA who are considering the use of a biologic and are not candidates for continued MTX, from the US payer perspective.

Methods

We determined the cost-effectiveness of treatment initiation with TCZ (8 mg/kg intravenously every 4 weeks) Mono compared with treatment initiation with ADA (40 mg subcutaneously EOW) Mono over two time horizons, 6 months and lifetime. The 6-month analysis was used to determine the incremental cost per additional clinical response with TCZ Mono versus ADA Mono over the treatment initiation phase, which aligns with the duration of the randomized, double-blind phase in ADACTA. Achievement of four RA clinical response levels was assessed: ACR 20% improvement criteria (ACR20), ACR 50% improvement criteria (ACR50), ACR 70% improvement criteria (ACR70) and low disease activity score (LDAS). The ACR response levels have been defined by the ACR and are widely used in RA clinical trials [15,16]. The ACR defines LDAS as having a 28-joint disease activity score of at least 2.6 but less than 3.2 [4]. Efficacy for TCZ and ADA was obtained directly from ADACTA [10].

A patient-level simulation model (10,000 patients) was used to estimate the incremental cost per quality-adjusted life-year (QALY) of initiating treatment with TCZ Mono or ADA Mono over a lifetime time horizon. Patient characteristics at entry into the model were based on baseline characteristics from ADACTA [10]. Patients enter the model after discontinuing MTX and begin treatment with either TCZ Mono or ADA Mono. In clinical practice, patients with RA generally progress through multiple treatments over time. Therefore, both TCZ and ADA are followed by an etanercept-certolizumab-palliative care treatment sequence in the model. Patients are reassessed every 6 months, at which point they can remain on current treatment, transition to the next treatment, or move to the absorbing state, death.

Treatment response is assessed at 6 months, and patients are categorized into one of four commonly used RA clinical response levels: ACR70, ACR50, ACR20, or nonresponder. These were chosen because they are commonly used and reported measures of treatment efficacy in clinical and cost-effectiveness studies in RA [17]. Responders continue on current treatment but experience a constant 16% probability of discontinuation because of intolerance or lack of efficacy thereafter. This rate is the average discontinuation rate observed in ADACTA (15% TCZ, 17% ADA) and is assumed to be the same for all treatments [10]. After discontinuation, either due to nonresponse at 6 months or later withdrawal, patients move on to the next treatment in the sequence. Response rates are treatment-specific and are derived from ADACTA for TCZ and ADA [10]. Because no head-to-head data were available for etanercept and certolizumab, response rates are estimated on the basis of results of a mixed treatment comparison (MTC) [18,19]. The available evidence for these agents, however, is from inadequate responders to traditional DMARDs, while in the model they are used after inadequate response to biologic DMARDs. Studies have shown that response rates are lower for patients with RA switching to a different anti–TNF-α, after a previous anti–TNF-α failure, than for those receiving their first anti–TNF-α [20]. Therefore, response rates for these agents were reduced in the model (assumed to be 84% of those from the MTC) [20]. The response rates for the palliative care group were assumed to equal the response rate for the placebo group from the MTC. Clinical trials generally report ACR response rates as cumulative categories, wherein ACR20/50/70 includes individuals achieving at least ACR20 and ACR50/70 includes individuals achieving at least ACR50. To derive mutually exclusive proportions for assigning patients to response categories, the rates were transformed as follows: 1) the ACR50/70 proportions

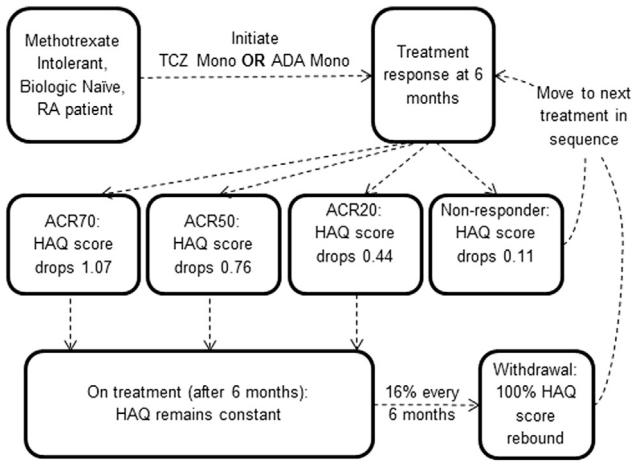

Fig. 2 – Lifetime model schematic. The schematic demonstrates how treatment influences HAQ score within the model. ACR, American College of Rheumatology; ADA, adalimumab; HAQ, Health Assessment Questionnaire; RA, rheumatoid arthritis; TCZ, tocilizumab.

were removed from the ACR20/50/70 group to create the ACR20 group, and 2) the ACR70 proportion was removed from the ACR50/70 group to create separate ACR50 and ACR70 groups. Those without an ACR20/50/70 response were nonresponders.

The model captures changes in disease severity on the basis of results from the Health Assessment Questionnaire (HAQ), a patient-reported outcome instrument that is commonly used in musculoskeletal disorders to measure functional status [21]. The HAQ Disability Index score then impacts patient utility, mortality rate, and hospitalization rate in the model (Fig. 1). The patient-level simulation approach allows the HAQ score to change over time as a function of baseline HAQ, treatment status, and time in the palliative care phase. The model schematic demonstrates how treatment influences the HAQ score within the model (Fig. 2). Each response level is linked to a change in the HAQ score, wherein a higher response leads to a greater reduction in the HAQ score (greater improvement). The relationship between response and the HAQ score was obtained

Table 1 – Key model parameters.

Input	Base	Low	High	Source
Population characteristics				
Age (y), mean	54	48	59	[12]
Body weight (kg)	77	70	85	–
Sex: female, %	80	72	89	[12]
Starting HAQ score, mean	1.65	1.49	1.82	[10]
Response, % of patients achieving ACR20, ACR50, ACR70				
Tocilizumab	18, 15, 33	17, 13, 29	20, 16, 36	[10]
Adalimumab EOW	22, 10, 18	19, 9, 16	23, 11, 20	[10]
Adalimumab weekly	13, 17, 27	12, 16, 24	15, 19, 29	[10,33]
Etanercept*	20, 24, 10	18, 22, 9	23, 26, 11	[18,19]
Certolizumab*	21, 17, 8	19, 15, 7	23, 19, 8	[18,19]
Palliative care	11, 5, 1	9, 5, 1	12, 6, 1	[18,19]
LDAS				
Tocilizumab	52	46	57	[10]
Adalimumab EOW	20	18	22	[10]
Adalimumab weekly	31	28	34	[10,33]
HAQ score change by state, mean				
Nonresponder, 6 mo	−0.11	−0.24	0.02	[10]
ACR20, 6 mo	−0.44	−0.55	−0.33	[10]
ACR50, 6 mo	−0.76	−0.94	−0.58	[10]
ACR70, 6 mo	−1.07	−1.22	−0.92	[10]
Palliative care (6 mo)	0.03	0.02	0.04	[22]
Hospital days per year by HAQ score, mean				
0.0–0.5	0.26	0	26	[29,30]
0.6–1.0	0.13	0	21	[29,30]
1.1–1.5	0.51	0	83	[29,30]
1.6–2.0	0.72	0	25	[29,30]
2.1–2.5	1.86	0	48	[29,30]
2.6–3.1	4.16	0	50	[29,30]
Unit costs ($)				
Hospitalization (DRG 547)	1251	875	1626	[28]
Treatment-related costs				
Tocilizumab (80-mg vial)	287	244	330	[27]
Etanercept (50-mg syringe)	603	513	693	[27]
Adalimumab (40-mg syringe)	1170	994	1345	[27]
Certolizumab (400-mg syringe)	2220	1887	2553	[27]
Infusion, 1-h (CPT 96413)	105	73	136	[28]
Outpatient visit (CPT 99202)	55	38	71	[28]
Outpatient visit (CPT 99212)	32	23	42	[28]
Chest x-ray (CPT 71034)	64	45	84	[28]
Other inputs				
Discontinuation rate (%), 6 mo	16	5	30	[10]
Ratio TNF-IR to DMARD-IR	0.84	0.75	0.92	[20]
Ratio ADA weekly to ADA EOW				
ACR20, ACR50, ACR70	1.16, 1.58, 1.48	1.04, 1.43, 1.34	1.28, 1.74, 1.63	[33]
Achievement of LDAS	1.55	1.39	1.70	[33]
HAQ mortality risk multiplier	1.33	1.10	1.61	[25,26]

ACR20, American College of Rheumatology 20% improvement criteria; ACR50, ACR 50% improvement criteria; ACR70, ACR 70% improvement criteria; ADA, adalimumab; CPT, Current Procedural Terminology; DMARD, disease-modifying antirheumatic drug; DRG, diagnosis related group; EOW, every other week; HAQ, Health Assessment Questionnaire; IR, inadequate response; LDAS, low disease activity score; TNF, tumor necrosis factor.

* Before adjustment for TNF-IR.

from ADACTA but is assumed to be the same for all treatments [10]. As a result, the impact of treatment on the HAQ score over the first 6 months is based entirely on the ACR 20/50/70 response level. After the first 6 months, the HAQ score is assumed to remain constant while on biologic treatment [22]. Patients who discontinue treatment experience a rebound in the HAQ score, returning to their starting HAQ score (i.e., the HAQ score before treatment initiation), until they begin their next treatment [23]. Patients who move through all treatment options and enter "palliative care" experience a constant increase in disease severity, modeled as an increase of 0.03 in the HAQ score every 6 months [22]. Table 1 presents the parameter inputs used in the economic model.

To generate preference-based quality-of-life estimates, the HAQ score was mapped to the EuroQol five-dimensional questionnaire (EQ-5D), using pooled data from TCZ clinical trials [12–14]. The utility mapping algorithm used in the model (Equation 1) has been published previously and assumes that improvements carry greater value at higher disease severities [24].

$$EQ\text{–}5D = 0.82 - (0.11 \times HAQ) - (0.07 \times HAQ^2) \quad (1)$$

Mortality rates were based on life table estimates, adjusted for RA-associated disability. The mortality risk adjustment (Equation 2) is dependent on the HAQ score and has been used in previous RA models [25,26].

$$\text{RA–specific mortality rate} = (\text{Mortality rate from life table})\,(1.33^{HAQ}) \quad (2)$$

Unit cost estimates are derived from published sources and are presented in Table 1 [27,28]. Costs are in 2013 US dollars. Modeled costs fell into two categories: treatment-related costs and hospitalization costs. Treatment-related costs included those for drug acquisition, administration, and monitoring. Drug acquisition cost was unique to each agent and was based on the wholesale acquisition cost [27]. The administration cost for TCZ included a 1-hour intravenous infusion (Current Procedural Terminology [CPT] 96413) for each dose (every 4 weeks) [28]. All other agents in the model are administered subcutaneously, and so the administration cost was based on an annual outpatient visit to obtain a new prescription (CPT 99202). Monitoring costs were considered to be the same across agents and included costs for physician visits (CPT 99202, 99212) and chest X-rays (CPT 71034), to check for signs of tuberculosis before treatment initiation. The number of inpatient hospital days (diagnosis-related group 547) was estimated on the basis of the HAQ score using the methods developed by Kobelt et al. and data from the Norfolk Arthritis Register, a large UK-based RA registry established in 1989 (Table 1) [29–32]. Overall, annual treatment-related costs were as follows: TCZ $30,547, ADA EOW $30,800, ADA weekly $61,234, etanercept $31,717, and certolizumab $29,226. Costs and QALYs were discounted at 3%.

Sensitivity Analyses

Sensitivity analyses were used to test the robustness of results for the lifetime model. First, overall parameter uncertainty was tested using one-way (inputs and ranges are provided in Table 1) and probabilistic sensitivity analyses (included 2,000 simulations of 10,000 patients; inputs and parameter distributions are provided in Appendix A in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2014.10.013). Then, several scenario analyses were conducted. The first compared treatment initiation with TCZ (8 mg/kg intravenously every 4 weeks) Mono to treatment initiation with ADA (40 mg subcutaneously weekly) Mono. Because weekly ADA dosing was not included as one of the randomized treatment groups in ADACTA, response rates for ADA weekly were estimated by increasing the ADA response observed in ADACTA, using a ratio derived from a study investigating the efficacy of both ADA dosage regimens (response to ADA weekly:response to ADA EOW) [33]. In addition, three scenarios were carried out within the lifetime model to further investigate the impact of specific parameters: 1) the cost of ADA was varied across a reasonable range (±15%), 2) the ratio of response of ADA weekly to ADA EOW was increased by 10%, and 3) TCZ Mono was compared with ADA Mono across a range of ADA dosing distributions (from 0% weekly/100% EOW to 100% weekly/0% EOW).

Results

The results of the model are presented in Table 2. When comparing TCZ Mono with ADA Mono EOW, TCZ was projected to be more effective but also more costly. Over 6 months, the proportion of patients achieving each response level (ACR 20/50/70 and LDAS) was higher for TCZ Mono than for ADA Mono, with incremental response proportions ranging from 15% for ACR70 to 32% for LDAS. Over the 6-month period, TCZ cost $2,083 more than did ADA ($15,636 vs. $13,553). As a result, the incremental cost-effectiveness ratio (ICER) for TCZ Mono over 6 months ranged from $6,570 per additional achievement of LDAS to $14,265 per additional achievement of ACR70 response. In the lifetime analysis, TCZ resulted in the incremental gain of 0.04 life-years (TCZ 15.93 vs. ADA 15.88) and 0.23 QALYs (TCZ 6.66 vs. ADA 6.43), while increasing cost by $8,532, compared with ADA (TCZ $178,643 vs. ADA $170,111). This produced an ICER of $36,944/QALY for TCZ Mono compared with ADA Mono.

Sensitivity Analyses

Results of the lifetime analysis were most sensitive to changes in drug acquisition cost, body weight, ACR response rates, and the discontinuation rate (Fig. 3). Scenario analyses further investigated the impact of ADA dosing frequency and uncertainty in ADA cost and other parameters of interest (Table 2). TCZ Mono was dominant compared with ADA Mono EOW when the cost of ADA was increased by 15%, while the ICER was $74,592/QALY when ADA cost was decreased by 15%. In the scenario comparing TCZ Mono with ADA Mono weekly, TCZ was more effective and less costly than ADA, in both the 6-month and lifetime analyses. TCZ Mono remained dominant compared with ADA Mono weekly when varying ADA costs and response rates in additional scenarios. When TCZ Mono was compared with ADA Mono, using a range of ADA Mono dosing distributions (weekly vs. EOW), TCZ remained dominant when at least 12% of ADA-treated patients were dosed weekly. Using the dosing distribution derived from a US health care claims analysis (94% EOW, 6% every week) resulted in an ICER of $18,895/QALY [34]. The results of the probabilistic sensitivity analyses demonstrate that there is a more than 50% probability that TCZ Mono is cost-effective compared with ADA Mono EOW if the willingness to pay is at least $40,000/QALY (Fig. 4). The probability that TCZ Mono is cost-effective compared with ADA Mono weekly is 100% at all levels of willingness to pay.

Discussion

ADACTA investigators found that TCZ Mono was superior to ADA Mono dosed EOW in reducing the signs and symptoms of RA in biologically naive patients with severe active RA in whom MTX treatment is considered inappropriate [10]. The present study expands on this finding by estimating the lifetime cost-effectiveness of TCZ Mono compared with

Table 2 – Model results.

	TCZ Mono	ADA Mono	Difference*	Incremental cost-effectiveness ratio
TCZ Mono vs. ADA Mono every other week (lifetime model)				
Costs ($)	178,643	170,111	8,532	
Life-years	15.93	15.88	0.04	
QALYs	6.66	6.43	0.23	$36,944/QALY
TCZ Mono vs. ADA Mono every other week (6-mo model)				
Costs ($)	15,863	13,780	2,083	
ACR20 (%)	65	49	16	$13,351/ACR20 response
ACR50 (%)	47	28	19	$10,735/ACR50 response
ACR70 (%)	33	18	15	$14,265/ACR70 response
LDAS (%)	52	20	32	$6,570/LDAS
TCZ Mono vs. ADA Mono weekly (lifetime model)				
Costs ($)	178,643	242,167	−63,525	
Life-years	15.93	15.91	0.02	
QALYs	6.66	6.57	0.09	TCZ dominates
TCZ Mono vs. ADA Mono weekly (6-mo model)				
Costs ($)	15,863	26,676	−10,813	
ACR20 (%)	65	57	8	
ACR50 (%)	47	44	3	TCZ dominates
ACR70 (%)	33	27	6	
LDAS (%)	52	31	21	
TCZ Mono vs. ADA Mono weekly (lifetime model scenarios)				
15% increase in cost of ADA				
Costs ($)	178,643	261,873	−83,230	
QALYs	6.66	6.57	0.09	TCZ dominates
15% decrease in cost of ADA				
Costs ($)	178,643	222,462	−44,820	
QALYs	6.66	6.57	0.09	TCZ dominates
10% increase in ratio of response rates for ADA weekly to ADA every other week				
Costs ($)	178,643	252,720	−74,077	
QALYs	6.66	6.64	0.02	TCZ dominates
TCZ Mono vs. ADA Mono every other week (lifetime model scenarios)				
15% increase in cost of ADA				
Costs ($)	178,643	178,805	−162	
QALYs	6.66	6.43	0.23	TCZ dominates
15% decrease in cost of ADA				
Costs ($)	178,643	161,416	17,226	
QALYs	6.66	6.43	0.23	$74,592/QALY
TCZ Mono vs. current dosing distribution for ADA Mono in the United States*				
Costs ($)	178,643	174,435	4,208	
QALYs	6.66	6.44	0.22	$18,895/QALY

ACR20, American College of Rheumatology 20% improvement criteria; ACR50, ACR 50% improvement criteria; ACR70, ACR 70% improvement criteria; ADA, adalimumab; LDAS, low disease activity score; Mono, monotherapy; QALY, quality-adjusted life-year; TCZ, tocilizumab.
* 94% ADA Mono 40 mg every other week, 6% ADA Mono 40 mg every week.

ADA Mono at $36,944 per QALY gained. The lifetime ICER and the short-term ICERs (e.g., $13,351/ACR20 response) are consistent with cost-effectiveness ratios reported for other biologic agents in similar populations [17,35]. In addition, in a scenario analysis comparing TCZ Mono with weekly ADA Mono, TCZ Mono is projected to be both more effective and less costly.

These results are noteworthy, given that anti-TNF-αs are generally used as first-line treatment in patients with RA eligible for biologic DMARDs. This study coupled with the results of the ADACTA trial and related clinical trials performed to date add to the growing literature demonstrating the positive clinical and economic impacts of the novel interleukin-6 receptor inhibitor, TCZ, in patients with severe RA.

In addition to our findings, the cost-effectiveness of TCZ in combination with MTX over a lifetime horizon has been previously demonstrated, from the Italian payer's perspective, when introduced before or substituted for anti–TNF-α's in patients with inadequate response to traditional DMARDs [24]. Although the main treatment comparator and sequencing were different than in the present study, TCZ was either dominant or considered cost-effective in all scenarios, and the probabilistic sensitivity analyses demonstrated roughly a 100% probability of TCZ being cost-effective at a willingness-to-pay value of €50,000/QALY. Although conducted in a different patient population and in a different country, the results of this study are in line with our findings.

The results of the lifetime model were most sensitive to changes in drug acquisition cost. Given that these costs vary among US payers, results may differ for individual payers. The wholesale acquisition cost, however, is a reasonable, and commonly used, unit cost estimate.

This study had several limitations, the greatest of which was the lack of head-to-head data for the entire treatment sequence. ADACTA is the only head-to-head trial to date that has tested the superiority of Mono with one biologic DMARD over another. ADA

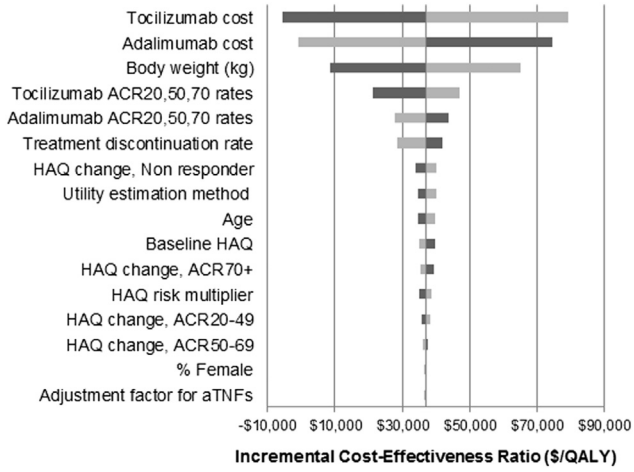

Fig. 3 – One-way sensitivity analysis (tocilizumab monotherapy vs. adalimumab monotherapy every other week). ACR, American College of Rheumatology; HAQ, Health Assessment Questionnaire; QALY, Quality Adjusted Life Years; TNF, tumor necrosis factor.

is a widely used first-line biologic DMARD, and is thus considered a good comparator. The lack of head-to-head data, however, also means that efficacy data for agents used later in the treatment sequence are based on the results of an MTC. As more head-to-head data become available, these results should be updated. The MTC also provided adjusted rates for TCZ and ADA. We chose to use the rates directly from ADACTA for our base case because these were considered the best data to inform the direct comparison. Using the rates from the MTC for TCZ and ADA provided similar results (ICER $38,375). Head-to-head data were also unavailable for comparing all dosage regimens of ADA and TCZ. Although ADA may be dosed weekly or EOW, only EOW dosing was used within ADACTA. Van de Putte et al. [33] demonstrated that weekly dosing of ADA Mono improves its efficacy [33]. In addition, the ADA package insert states that weekly dosing may be recommended in patients with RA receiving ADA Mono [36]. Therefore, we felt that it was important to include this dosing option as a scenario in the model. We were able to estimate ADA weekly efficacy by adjusting the results from ADACTA using data from van de Putte et al., who investigated the efficacy of both ADA doses [10,33]. In addition, we conducted an additional scenario analysis in which the ratio of response of ADA weekly to ADA EOW was increased by 10%, thus improving the effectiveness of ADA weekly. Results of all analyses demonstrated that TCZ Mono was dominant over ADA Mono weekly. In an additional scenario analysis using a range of ADA Mono dosing distributions, TCZ remained dominant when at least 12% of ADA-treated patients were dosed weekly. The availability of data was also limited for TCZ. The US label for TCZ recommends starting patients on 4 mg/kg and escalating the dose to 8 mg/kg on the basis of clinical response. Because the 4-mg/kg dose was not used in ADACTA and has not yet been evaluated in the Mono population, it could not be included in the model.

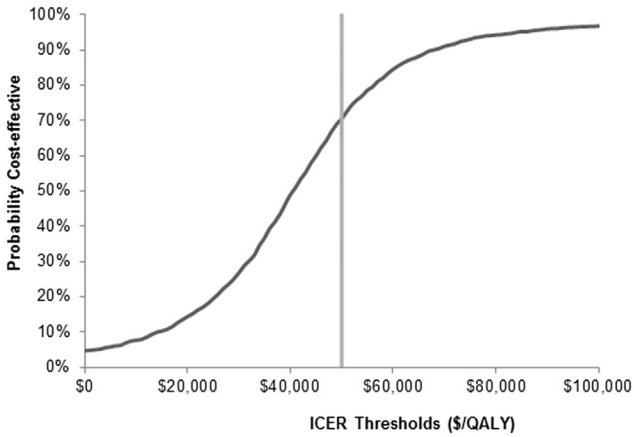

Fig. 4 – Cost-effectiveness acceptability curve (tocilizumab monotherapy vs. adalimumab monotherapy every other week). The probabilistic sensitivity analyses included 2,000 simulations of 10,000 patients. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life years.

Our model was also limited by its reliance on ACR rates and the associated mean change in the HAQ score from baseline. In this trial-based analysis, however, the two patient groups were relatively homogenous at baseline and we lacked data to inform an evaluation of the potential impact of patient heterogeneity at baseline. In addition, the HAQ may not fully capture disease severity. However, it is a psychometrically validated outcome measure that has been widely used in RA for many years [21]. Furthermore, using the HAQ to inform costs and outcomes is a common method in economic models of RA [37]. Finally, though the model predicts a greater decrease in the HAQ score on initiation with TCZ (vs. ADA), due to its superior ACR response rates, the ADACTA trial did not find a statistically significant difference in the HAQ scores between the two agents (−0.2; 95% confidence interval −0.3 to 0.0; $P = 0.0653$) [10]. This may be attributable to the fact that change in the HAQ score was a secondary outcome, and ADACTA was not powered to show a statistically significant difference in the HAQ score.

Finally, the model did not explicitly account for adverse effects. Because the safety profiles of biologic DMARDs are similar, it is not expected that their inclusion would significantly alter the results. In addition, costs of adverse effects are captured indirectly through treatment discontinuation, which leads to increases in the HAQ score and, therefore, increases in costs. Quality-of-life decrements are also incorporated indirectly, through changes in the HAQ score (mapped to the EQ-5D), on the basis of data derived from TCZ clinical trials.

Conclusions

From a US payer perspective, TCZ (8 mg/kg every 4 weeks) Mono is more effective and projected to be cost-effective compared with ADA Mono 40 mg EOW and dominant when compared with ADA Mono 40 mg weekly in patients with severe RA for whom MTX is not appropriate.

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Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.jval.2014.10.013 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

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