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ORIGINAL RESEARCH

Cost per responder of Adalimumab biosimilars MSB11022 and ABP 501 versus the originator and methotrexate in chronic plaque psoriasis

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ABSTRACT

Background: Pharmacoeconomic studies comparing the cost of adalimumab biosimilars versus the originator and conventional drugs in psoriasis are lacking.

Research design and methods: To assess the cost per responder of adalimumab biosimilars versus the originator and methotrexate for psoriasis treatment. A cost per responder analysis comparing adalimumab biosimilars MSB11022 (Idacio®) and ABP 501 (Amgevita®), and methotrexate to the originator (Humira®) was performed. The incremental cost per responder was calculated by multiplying the cost of treatment based on the perspective of the National Healthcare System and number needed to treat for each therapy.

Results: Considering the PASI75 response rate at 16 weeks, the cost per responder for MSB11022 and ABP 501 compared to the originator was € 500 versus 1,831 and € 968 versus 1,949, respectively. For the same endpoint, the cost per responder for subcutaneous or oral methotrexate was € 543 or 34 compared to 2,117 for adalimumab originator. At an indirect comparison among methotrexate, MSB11022 and ABP 501, the costs per PASI75 responder at week 16 were 2%, 26%, 27% and 50% of that of the originator, respectively.

Conclusions: The use of biosimilars was confirmed as a valuable pharmacoeconomic strategy to lower healthcare cost in patients with psoriasis.

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Psoriasis; cost per responder; methotrexate; adalimumab; biosimilar

1. Introduction

Psoriasis is a common, chronic, inflammatory, debilitating, systemic disease with a great impact on healthcare systems worldwide that affects 1–4% of the population worldwide, and about 14 million people in Europe [1]. About 20%–30% of patients with chronic plaque psoriasis have a moderate-to-severe disease [2], and they are candidate to systemic treatment including phototherapy, conventional systemic agents (acitretin, ciclosporin, methotrexate, fumarates) and targeted therapies (biologics and small molecules) [3]. Treatment of moderate-to-severe psoriasis with biologic drugs poses a significant economic burden to the health systems [4]. Loss of response, lack of response, or discontinuation due to adverse events represent a concrete therapeutic challenge for dermatologists that have to switch patients to other treatments [5]. At the Multinational Assessment of Psoriasis and Psoriatic Arthritis survey, dermatologists replied that the reasons for not initiating or maintaining systemic therapy with biologics were related to concerns about their costs [6]. Over the last few years, the expiration of some biologic patents has made possible the development of biosimilar versions of biologics with a reduced cost compared to their originator. There are discernible tendencies across European countries with regard to policy measures targeting the price and uptake of biosimilars [7]. As of now, the economic advantage of biosimilars compared to both the originator and conventional systemic drugs (such as methotrexate) has not yet been quantified. Hence, the aim of the present study was to assess the cost per responder of adalimumab biosimilars MSB11022 (Idacio®), ABP 501 (Amgevita®) and methotrexate (either subcutaneous or oral) versus the originator (Humira®) for the treatment of moderate-to-severe plaque psoriasis from the perspective of the Italian National Health System.

2. Patients and methods

A cost per responder analysis of MSB11022 (Idacio®), ABP 501 (Amgevita®) biosimilars versus adalimumab originator (Humira®) and methotrexate (either subcutaneous or oral) was developed based on efficacy data from three head-to-head randomized controlled trials [8–10]. In particular, data on efficacy of MSB11022, ABP 501 biosimilars versus adalimumab originator were derived from AURIEL-PsO [8] and NCT01970488 [9] clinical trials, respectively (Table 1). Data on efficacy of methotrexate versus adalimumab originator were derived from the CHAMPION clinical trial (Table 1) [10]. These three clinical trials were selected because of the head-to-head comparison between MSB11022, ABP 501, methotrexate and the adalimumab originator, respectively. The other adalimumab biosimilars available were not selected because there are

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Supplemental data for this article can be accessed here.

Table 1. Efficacy data of Adalimumab biosimilars MSB11022, ABP 501 versus the originator and methotrexate from head-to-head phase 3 randomized controlled clinical trials.

Head-to-head trials	PASI75 week 16 (%)	PASI90 week 16 (%)	PASI100 week 16 (%)	PASI75 week 50–52 (%)	PASI90 week 50–52 (%)	PASI100 week 50–52 (%)	Reference
MSB11022 vs adalimumab originator	89.7 vs 91.6	64.0 vs 66.0	33.0 vs 37.2	90.9 vs 92.9	76.3 vs 78.8	53.8 vs 54.1	Hercogová J et al. [8]
ABP 501 vs adalimumab originator	81.6 vs 86.1	52.6 vs 53.2	19.1 vs 20.3	85.1 vs 87.1	59.0 vs 64.3	32.8 vs 35.7	Papp K et al. [9]
Methotrexate vs adalimumab originator	35.5 vs 79.6	13.6 vs 51.9	7.3 vs 16.7	-	-	-	Saurat JH et al. [10]

no head-to-head comparative studies with the originator in psoriasis, or the PASI90/100 data is not reported such as in the case of GP2017 [11]. The study population of the trials included adult patients with moderate-to-severe chronic plaque psoriasis. The clinical efficacy measures were defined as an improvement in PASI equal to or greater than 75%, 90% or 100% from baseline, i.e. PASI75, 90 and 100, respectively [12]. The time points selected for the pharmacoeconomic assessments were 16 and 52 weeks, consistently with the primary and secondary end points of the trials.

2.1. Drug administration scheme

Dosing regimens for adalimumab originator and biosimilars were those labeled for moderate-to-severe chronic plaque psoriasis in adults [13], i.e. 80 mg at week 0, then 40 mg every other week starting at week 1 (Table S1). Methotrexate in the CHAMPION trial was initiated at 7.5 mg per week at week 0, increased to 10 mg per week at week 2, and increased to 15 mg per week at week 4 for all patients. From week 8 onward, patients who achieved PASI 50 maintained their current dosages for the duration of the study, while those who did not achieve PASI 50 had their dosage increased to 20 mg per week. By week 12, only patients not achieving a PASI 50 response and who had a response < PASI 50 at week 8 underwent further dosage increase to 25 mg per week for the duration of the study (Table S1). The mean ± standard deviation weekly dosages of methotrexate were 14.2 ± 3.0 mg at week 4, 16.8 ± 3.0 mg at week 8, 18.8 ± 4.8 mg at week 12 and 19.2 ± 4.9 mg at week 15. To calculate drug costs, methotrexate was assumed to be started at 7.5 mg/week and escalated to 10 mg in weeks 2–3, to 15 mg in weeks 4–6 and to 20 mg onwards. Costs of both subcutaneous and oral formulations were considered. The costs of folic acid, at the guideline recommended weekly dose of 5 mg, were also added to the costs of methotrexate treatment (Table 2).

2.2. Cost per responder model

The cost per responder model was based on the perspective of the Italian public healthcare system. Regarding cost of biologic drugs, ex-factory wholesale purchase prices were used, including the mandatory discounts according to the national legislation (5% discount, plus a further 5% reduction on the discount result) and the additional discounts determined by the current framework agreement of the Veneto region (Table 2) [14–21]. For methotrexate and folic acid, official retail prices were used. All costs were reported in 2022 Euros. Only drug acquisition costs were considered, while other costs including treatment administration and monitoring were excluded. The incremental cost per responder was calculated by multiplying the cost of treatment and number needed to treat (NNT) for each of the therapies. Different scenario analyses were undertaken assuming alternative drug acquisition discounts (−40%; −60%; −80%), (Table S2). Because a *direct* comparison of the cost per responder of MSB11022 or ABP 501 biosimilars versus methotrexate was not possible due to the absence of head-to-head studies, an *indirect* comparison was performed. The indirect comparison was expressed as a percentage of the cost per PASI75/90/100 responder at week 16 relative to the originator. This value was calculated by dividing the cost per responder of methotrexate (oral and subcutaneous) and the two biosimilars by the cost per responder of the originator.

Table 2. Drug costs of Adalimumab originator, its biosimilars, methotrexate and folin (in Euro).

Drug (trade name)	Original price per package	Discount*	Discounted price per package	Reference
Adalimumab originator (Humira®) 40 mg, 2 syringes	1.068.56	70.05%	320.00	[14]
ABP 501 (Amgevita®) 40 mg, 2 syringes	854.84	82.31%	151.2	[15]
MSB11022 (Idacio®) 40 mg, 2 syringes	758.68	88.69%	85.80	[16]
Methotrexate 2.5 mg, 30 tablets	4.43	-	4.43	[17]
Methotrexate 7.5 mg, 4 syringes^	23.81	-	23.81	[18]
Methotrexate 10 mg, 4 syringes^	30.76	-	30.76	[19]
Methotrexate 15 mg, 4 syringes^	44.89	-	44.89	[19]
Methotrexate 20 mg, 4 syringes^	59.39	-	59.39	[19]
Folin 5 mg, 120 tablets	12.45	-	12.45	[20]

*Discounted prices were derived from [21].
^ for subcutaneous injection

2.3. Direct costs analysis

Direct costs relative to the dermatologic visits and lab workup related to a 52-week treatment with methotrexate or adalimumab have been estimated. The cost of dermatological visits (baseline and follow up visits) and that of lab workup were estimated according to the tariffs of the Veneto region [22]. The frequency of the follow-up visits and the lab workup

considered for the costs analysis was consistent with the recommendations of Euroguiderm psoriasis guideline [13].

3. Results

The cost per responder of adalimumab biosimilars MSB11022, ABP 501 and methotrexate (either subcutaneous or oral) was considerably lower compared to the originator across all responder definitions and time points.

3.1. Adalimumab biosimilars versus originator

The cost per PASI75 responder at 16 weeks for MSB11022 and ABP 501 compared to the originator was € 500 versus € 1,831 and € 968 versus € 1,949, respectively (Figure 1A, B). The cost per PASI75 responder at 52 weeks for MSB11022 and ABP 501 compared to the originator was € 1,345 versus € 4,925 and € 2,542 versus € 5,244, respectively (Figure 2A, B). The cost per PASI90 responder at 16 weeks for MSB11022 and ABP 501 compared to the originator was € 703 versus € 2,554 and € 1,508 versus € 3,158, respectively (Figure 1A, B). The cost per PASI90 responder at 52 weeks for MSB11022 and ABP 501 compared to the originator was € 1,602 versus € 5,791 and € 3,641 versus € 7,114, respectively (Figure 2A, B).

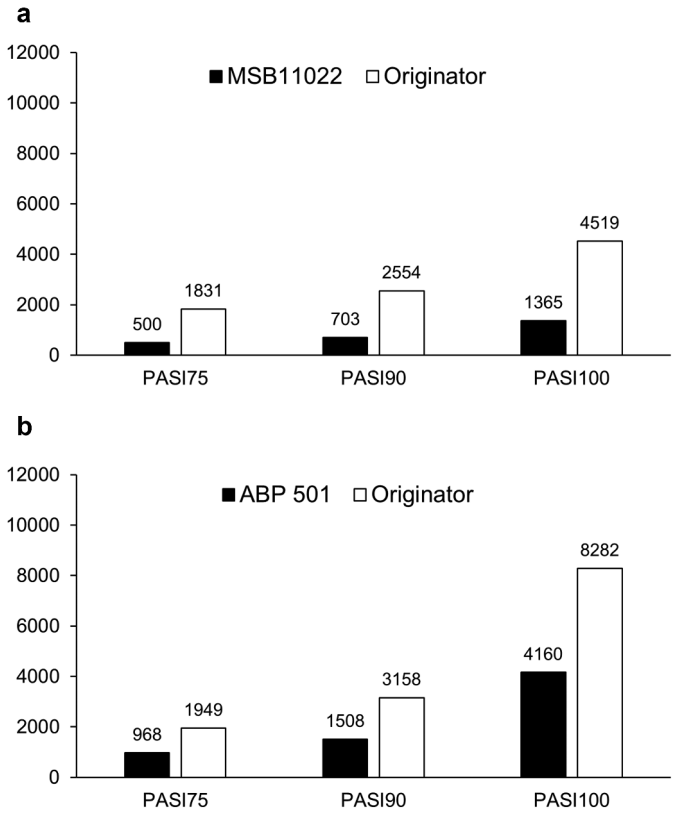

Figure 1. Cost per PASI75/90/100 responder analysis at week 16 (in Euro). MSB11022 (black histogram) versus Adalimumab originator (white histogram) in panel A. ABP 501 (black histogram) versus Adalimumab originator (white histogram) in panel B.

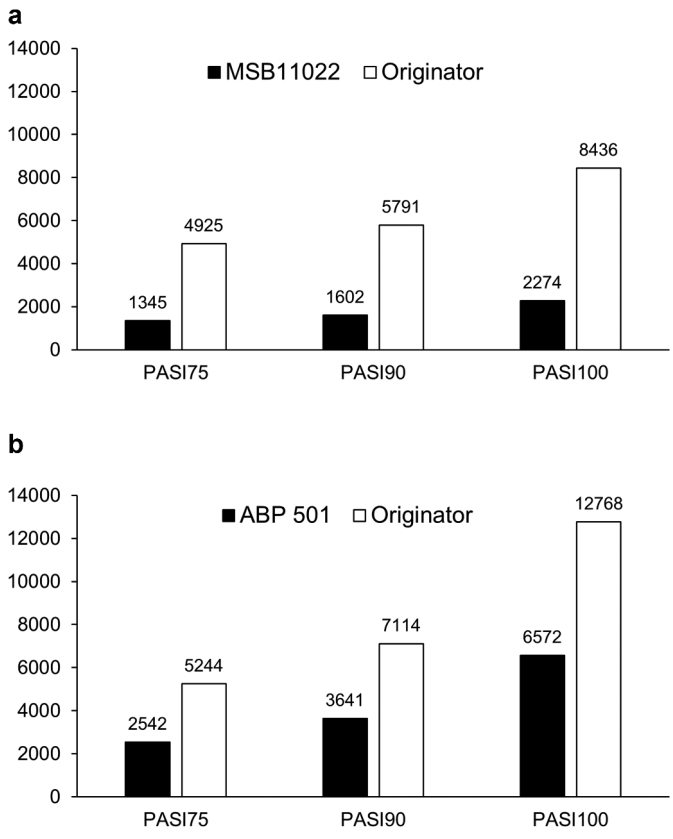

Figure 2. Cost per PASI75/90/100 responder analysis at week 52 (in Euro). MSB11022 (black histogram) versus Adalimumab originator (white histogram) at 52 weeks in panel A. ABP 501 (black histogram) versus Adalimumab originator (white histogram) at 52 weeks in panel B.

3.2. Methotrexate versus Adalimumab originator

The cost per PASI75 responder at 16 weeks for subcutaneous or oral methotrexate was € 543 or € 34 compared to € 2,117 for adalimumab originator (Figure 3A) and the cost per PASI90 responder at 16 weeks for subcutaneous or oral methotrexate was € 1416 or € 88 compared to € 3,242 for adalimumab originator, respectively (Figure 3A). At an indirect comparison of the different agents, the costs per PASI75 responder at week 16 of oral and subcutaneous methotrexate, MSB11022 and ABP 501, were respectively 2%, 26%, 27% and 50% of that of the originator (Figure 3B). Overall, the differences in the mean cost per responder between originator adalimumab and the other drugs even increased with PASI90 and PASI100 response. Scenario analysis showed that results were consistent across different drug acquisition discount models (Tables S2 and S3).

3.3. Costs relative to the dermatologic visits and lab workup

Costs relative to the dermatologic visits and lab workup related to a 52-week treatment with methotrexate or adalimumab are reported in Table S4. The cost of dermatological visits (baseline and three follow-up visits) was the same between patients receiving methotrexate and adalimumab (i.e. € 63.25). As to the lab workup, screening tests were less expensive for

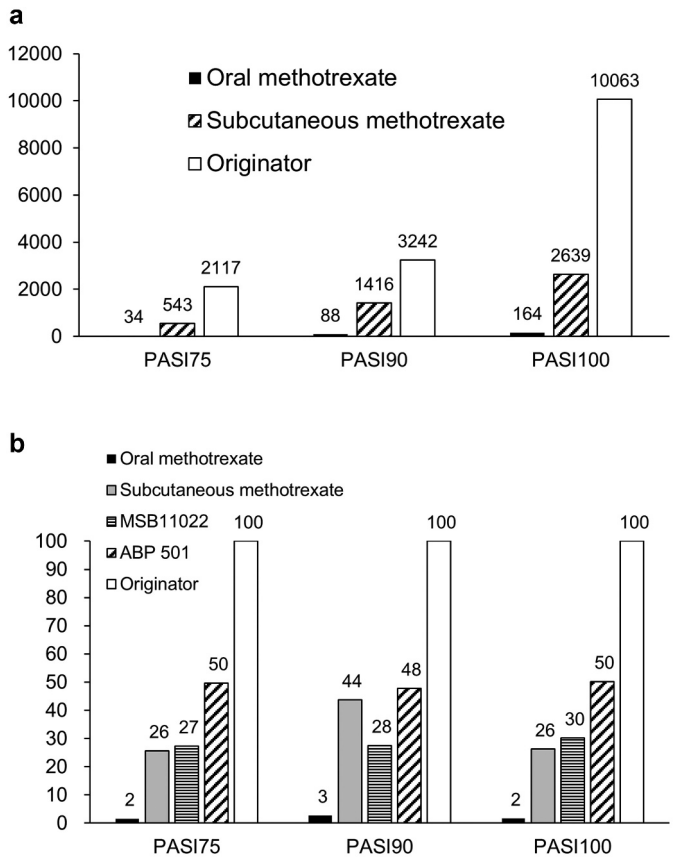

Figure 3. Cost per PASI75/90/100 responder analysis at week 16 (in Euro) of oral methotrexate (black histogram) and subcutaneous methotrexate (dashed histogram) versus Adalimumab originator (white histogram) in panel A. Indirect comparison of the costs per responder at 16 weeks of methotrexate (oral and subcutaneous), MSB11022 and ABP 501 (panel B), expressed as percentages of the cost per responder of Adalimumab originator.

methotrexate than adalimumab (€ 60.85 vs € 97.20) because interferon gamma release assay (QuantiFERON TB gold) is required only for patients who are candidate to the TNF-α inhibitor. In contrast, lab monitoring tests during the treatment was more expensive for methotrexate compared to adalimumab (€ 49.40 vs € 26.10) because of more frequent repetition of full blood count, serum creatinine and liver blood tests required in those receiving methotrexate. Summing up all items of expenditure, the annual direct costs of the dermatologic visits and lab workup were € 173.50 and € 186.55 for patients treated with methotrexate or adalimumab, respectively.

4. Discussion

The major finding of the study is that the costs per responder of adalimumab biosimilars MSB11022 or ABP 501 and methotrexate (either oral or subcutaneous) were considerably lower compared to the originator across all responder definitions and time points. Interestingly, the cost per responder of MSB11022 was approximately similar to subcutaneous methotrexate both for PASI75 and PASI100, while even more convenient for PASI90, due to the current discount of adalimumab biosimilars in Italy.

These findings are novel because of the lack of pharmacoeconomic analysis comparing adalimumab biosimilars to the originator and methotrexate, which represent the main reference drugs among TNF- inhibitors and conventional agents for the systemic therapy of psoriasis, respectively. Given the lower cost of adalimumab biosimilars compared to the originator, it is likely that their use will be progressively implemented in the future [23]. This is consistent with a recent cost-effectiveness analysis that found adalimumab biosimilars as the optimal first-line biologic treatment in the UK [24]. In this regard, the better cost-effectiveness of biosimilars may allow a higher number of patients with moderate-to-severe to receive biological treatment, especially in countries with constrained health expenditure, thus helping address undertreatment. Indeed, a significant proportion of patients with moderate-to-severe psoriasis is not receiving an adequate treatment in part because of the high cost of drugs [25]. Even among those who receive treatment, around a quarter of patients with moderate–severe psoriasis is only managed with topical agents [25]. In a systematic review that included studies from five European countries, the total annual cost per psoriasis patient ranged from US $2,077 to US $13,132 [26] and the introduction of biologics for the treatment of moderate-to-severe psoriasis has led to a 3-fold to 5-fold increase in direct costs [26].

The considerable reduction in the cost gap between adalimumab biosimilars and methotrexate may prompt their early use, for example in patients with a higher psychological impact and comorbidities that represent contraindications to conventional agents. Indeed, psoriasis is associated with a negative impact on psychosocial well-being, social stigmatization and reduction in the quality of life [27–29]. Furthermore, work productivity loss was shown to be correlated with the body surface area involvement, confirming a direct relationship between psoriasis severity and its economic burden [30]. Besides, adalimumab is not only more effective than methotrexate, but it is usually better tolerated [31]. Indeed, in a large multicenter study methotrexate drug survival rate at 5 years was 8%, the main reason for discontinuation was adverse effects (32.2%) such as nausea and vomiting [32], that are uncommon in patients treated with adalimumab [33]. Furthermore, methotrexate – unlike adalimumab – is associated with a significant risk of hepatotoxicity, possibly because fatty liver disease is quite common in patients with plaque psoriasis [34–36]. In a population-based cohort study, mild liver disease and cirrhosis-related hospitalization had an incidence rate per 1000 person-years of 4.22 (95% confidence interval [CI] 3.61–4.91) and 0.73 (95% CI 0.49–1.05) in psoriatic patients treated with methotrexate, respectively [37]. Ultimately, to what extent the early treatment with biologic disease modifying anti-rheumatic drugs including adalimumab could modify the disease course in terms of prevention of psoriatic arthritis and/or cumulative quality of life impairment is currently under investigation [38–41].

We acknowledge the limitations of this study. Firstly, the discount percentages of biosimilars are those of the Italian market and we do not know to what extent they are applicable in other countries. To overcome this issue, we included a scenario

analysis with discount percentages of 40%, 60% and 80% which, however, provide consistent results. Another limitation is that the cost per responder of adalimumab originator varies considerably across the comparisons with the different biosimilars due to the fact that efficacy data were derived from different clinical trials. Furthermore, in the absence of a direct comparison between methotrexate and adalimumab biosimilars we had to make an indirect comparison. Conversely, the comparison between biosimilars MSB11022 and ABP 501 and adalimumab originator was based on controlled, randomized clinical trials. Ultimately, only two adalimumab biosimilars were included in this pharmacoeconomic analysis because the other biosimilars approved either do not have studies in psoriasis or the PASI90/100 response rate is not reported, such as in the case of GP2017 [11].

5. Conclusions

The present study highlighted the favorable economic profile of adalimumab biosimilars and methotrexate over adalimumab originator from the perspective of the Italian National Health Service. Future research employing clinical investigations, artificial network analysis and nanodermatology-based solutions would allow to predict drug efficacy and select the most cost-effective agent in patients with plaque psoriasis [42,43].

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Declaration of interests

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Author contributions

P Gisondi and P Armeni, conceived and designed the study; P Gisondi, P Armeni, D Geat, F Bellinato and M Maurelli were involved in the analysis and interpretation of the data; all the authors contributed to drafting the paper and revising it critically for intellectual content. All the authors have read and agreed to the published version of the manuscript.

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