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ORIGINAL RESEARCH ARTICLE

The Cost Effectiveness of Biologic Therapy for the Treatment of Chronic Plaque Psoriasis in Real Practice Settings in Italy

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Abstract

Background and Objectives Biologic therapies are considered to be cost effective by leading Health Technology Assessment (HTA) agencies and, therefore, eligible for reimbursement by public health services. However, biologic therapies entail sizable incremental costs and, besides, have a considerable financial impact that in Italy amounts to 13.7 % of the national health service's pharmaceutical expenditure. In the reimbursability decision process, an important role is played by both the drug efficacy data observed in pre-licensing RCTs and the economic modelling assumptions, as they give evidence on cost effectiveness. The administration of therapies in real practice settings is likely to produce a significant deviation from the results predicted by the models, theoretically outweighing the assumption on which the decision process is founded. This is a matter of concern for public health services and, consequently, an interesting topic to investigate.

Methods To overcome the lack of knowledge concerning the actual cost effectiveness of biologic therapies for the treatment of plaque psoriasis in the clinical practice setting in Italy, an observational study was conducted in 12 specialist centres on patients switching to biologic therapy within a 6-month enrolment window.

Results The study confirms in clinical practice the efficacy of the switch to biologic therapies, analysed using a number of clinical [Psoriasis Area and Severity Index (PASI), pain visual analogue scale (VAS) and itching VAS] and quality-of-life parameters. A general health-related quality of life (HR-QOL) improvement, with a 0.23

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quality-adjusted life-year (QALY) mean gain per patient, has been reported in the 6-month observation period. The direct medical costs to treat plaque psoriasis with biologic therapies amount to €15,073.7 per year (prior to their enrolment, the same patients cost €2,166.2 on an annual basis). After the switch to biologic agents, the cost per QALY during the first year of treatment amounts to €28,656.3.

Conclusion At least in the short-term, the clinical practice of the specialised Italian centres taking part in the study confirms that switching patients to a biologic drug produces an incremental cost-effectiveness ratio comparable with the values predicted by the HTA bodies.

1 Introduction

Psoriasis is one of the most common forms of chronic dermatitis, affecting 2–3 % of the population [1, 2]. It is a chronic, non-infectious inflammatory skin disease, with a relapsing–remitting course, meaning that psoriatic patients are never 'cured', rather they experience periods in which the effects of the illness are less obvious, alternating with periods in which they experience a flare-up [3]. The aetiology of psoriasis is still unclear and the data available at the current time suggest a multifactorial origin. Psoriasis is common amongst young individuals and is associated with a higher risk of cardiovascular events [4] and depressive symptoms [5].

The most common form of the condition is psoriasis vulgaris or plaque psoriasis, which accounts for 80 % of all cases [6]. In general, psoriasis is usually classified as mild, moderate or severe, depending on the surface area affected, redness, and the thickness and desquamation of the plaques. A number of instruments have been devised to define the severity of the disease and compare scores over time for the same patient and between patients [7].

Patients with forms of psoriasis refractory to topical treatments and with extensive lesions are usually switched to systemic oral or intravenous medications and UV light treatment. The systemic treatments used are immunomodulators cyclosporin (ciclosporine) and methotrexate, and the retinoid acitretin. Although administration is most commonly oral, these treatments must be administered under medical supervision and require regular monitoring to exclude the presence of infections. Patients with an inadequate response to systemic therapy or those presenting with contraindications to or who are intolerant to this kind of treatment are treated with biologic therapies. Biologic medications interfere in a selective way on various levels and with different actions on the pathological immunological processes that trigger and sustain psoriasis [8].

Given the high prevalence of psoriasis in the general population, its management in terms of medical and social costs is also of significant importance to society in general.

A comparative study conducted in 2004 [9] analysing the treatment of severe psoriasis (approximately 27–30 % of psoriasis patients) in seven European countries (France, Germany, Holland, Spain, Sweden, England and Italy), showed a large variability, with a mean annual cost per patient that ranged from €2,981 in France to €6,595 in Sweden, with a value of €3,712 in Italy. These figures underestimate the actual costs, as the study did not consider the costs sustained directly by patients, the costs of patients for whom psoriasis was a secondary diagnosis or the costs of treatment of any side effects of therapy. The cost-of-illness study conducted by Colombo et al. [10] estimated that moderate and severe psoriasis costs the Italian national health service (NHS) €2,403 million per year, equivalent to 1.8 % of total spending on health in 2007, and also confirmed that these costs were primarily for hospitalisation, followed by laboratory tests and systemic medication for a mean annual total of €8,372 per patient, of which 68 % (€5,690) were direct costs. In this analysis no patient was treated with biologic drugs.

CESAV (Centro di Economia Sanitaria A. e A. Valenti) [11], which assumed psoriasis has a prevalence of 3 % in the Italian population between 20 and 80 years of age, estimated the annual direct costs incurred by the Italian health service in 2008 for each patient with moderate or severe psoriasis to be €4,565.5 (of which 94.6 % was for drugs and 3.8 and 1.6 % was for outpatient clinical and hospital care, respectively). Consequently, the total cost of plaque psoriasis borne by the Italian health service, for moderate and severe patients only, would be €680 million.

The two studies show significant differences, both in the prevalence of moderate and severe psoriasis, and in costs for patients.

Biologic therapies are very expensive and, nowadays, their financial impact is relevant: in the Italian NHS biologic drugs amount to €30.1 per capita (13.7 % of the Italian NHS pharmaceutical expenditure). In particular, agents considered in this study represent 28.9 % of the expenditure for biologic drugs.

Despite the increasing costs implied, biologic drugs are reimbursed by most public health services, following evidence on their cost effectiveness as assessed by leading Health Technology Assessment (HTA) agencies.

In the decision process, efficacy data of drugs observed in pre-licensing randomised controlled trials (RCTs) and subsequent economic modelling play an important role. On the other side, possible deviations from model-predicted results, due to administration of therapies in a real population and in real practice settings, is an interesting topic and a potential matter of concern for public health services.

The aim of this study is to investigate the cost effectiveness of biologic therapy for the treatment of chronic plaque psoriasis in real practice settings for a caseload of Italian specialised centres.

The novel aspect of the study lies in the lack of studies considering the cost effectiveness of biologic therapy in clinical practice settings, as well as the shortage of information on the benefits of these agents in terms of quality of life in the Italian population.

2 Methods

2.1 Study Design

A prospective observational study was conducted to evaluate the direct medical costs and health-related quality of life (HR-QOL) of patients with chronic plaque psoriasis switching to treatment with biologics, with the aim of providing some economic insight, from the Italian NHS perspective, using a cost-utility approach.

The study enrolled all patients switching de novo to biologic therapy between 11 May and 31 December 2009 and all those who, during the same period, reverted to biologic treatment after at least 1 year's suspension. Eligibility to switch and the treatment administered was up to the physician's discretion. Enrolled patients were observed for 6 months.

The analysis was conducted in 12 specialised centres, members of the Psocare[1] network, located in different parts of Italy.

The significance of the differences in the mean values between the pre-enrolment and follow-up periods was assessed using the paired samples *t*-test, whereas the significance of the difference in mean values between the subgroups of patients taking the various biologics was evaluated using the one-sample *t*-test. More specifically, normality was analysed using the Kolmogorov–Smirnov test and the homogeneity of variance using Levene's test. When normality was refuted, non-parametric one-sample tests were performed.

[1] The Psocare project was launched as part of a programme promoted by the Italian Agency of Drugs (AIFA) and organised in association with dermatology societies and patient associations, under the technical coordination of the GISED (Gruppo Italiano Studi Epidemiologici in Dermatologia) research centre. Psocare was based on the philosophy that the psoriasis treatment strategies devised thus far have resulted in the consolidation of habits or behaviour amongst doctors rather than in clear outcomes in terms of efficacy. The aim of the project was therefore to evaluate the long-term efficacy and safety of the treatments available. The approach used is based on comparisons between different care strategies, with a view to obtaining a realistic estimate of their benefits and risks. The information collected in the Psocare project is therefore of great value when evaluating the outcomes of the treatments provided to psoriatic patients.

2.2 Data Collection

2.2.1 Demographics and Clinical Characteristics at Enrolment

Upon enrolment in the study, and before switching to biologic therapy, questionnaires were administered using the Computer-Assisted Personal Interviewing (CAPI) method to evaluate patients' HR-QOL and clinical conditions, including both subjective patient assessments and objective physician-assessed measures. Those completed by patients included general details and socioeconomic data, as well pain and itching visual analogue scales (VAS) and information on drugs used. Those completed by doctors involved the main elements of clinical evaluation [Psoriasis Area and Severity Index (PASI)].

At the end of the 6-month follow-up period, patients were asked to repeat the HR-QOL and clinical status questionnaires and information was collected about any treatment combinations and the reasons for withdrawal, where applicable; the objective severity of the condition was re-evaluated using the PASI score, and the pain and itching VAS scores were used to acquire a subjective evaluation.

2.2.2 Quality of Life and Cost Data

Direct medical costs included all costs used in connection with psoriasis: hospitalisation, day hospital and/or outpatient services, specialist appointments, laboratory tests, diagnostic procedures, phototherapy and drugs.

For the 6-month follow-up period, the actual costs of psoriasis treatment after switching to biologic therapy were collected prospectively, while utilisation of healthcare resources per patient in the 6 months[2] prior to the start of biologic therapy were calculated retrospectively. All costs were quantified in terms of burden on the Italian health service and were calculated using the applicable Italian health service list of charges.

HR-QOL was elicited using the European Quality of Life Questionnaire [12] at baseline (at the time of switch from systemic to biologic therapies) and quality-adjusted life-years (QALYs) were calculated after 6 months.

2.2.3 Cost Analysis

A cost-utility approach was used by comparing [using the incremental cost-effectiveness ratio (ICER)] the change in

[2] To avoid statistical bias due to patients' lack of memory regarding minute resource utilisation, data on laboratory services and visits were collected, asking for consumption in the previous 3 months, then assuming constant treatment.

HR-QOL attributed to treatment (expressing the benefits in terms of QALYs) with the increase in costs. The ICER was also calculated with alternative measurements of effectiveness obtained using the PASI and pain and itching VAS scores. The costs refer to year 2009.

3 Results

3.1 Baseline Data

A total of 185 patients were enrolled, with a minimum of seven and a maximum of 43 patients enrolled per centre. However, the analysis was performed on 178 patients as one centre withdrew before the end of the project. All patients completed the follow-up period.

Patients were between 18 and 79 years of age, with a median age of 49.5 years [mean 47.7 years ($\sigma^2 = 192.6$)]. The median age at diagnosis was 28.0 years [mean 30.6 years; range 1–70 years ($\sigma^2 = 211.7$)]. Although the literature suggests that prevalence is similar for both sexes [13], in this study males were more prevalent, accounting for 64.6 % of the total cohort (Table 1).

At enrolment, i.e. the switch to treatment with a biologic agent, 59.6 % of patients were prescribed etanercept, 32.0 % adalimumab and 8.4 % received infliximab.[3]

3.2 Efficacy Data

Between the start of treatment with a biologic and the end of the follow-up period, all subjective and objective measurements of clinical status improved. Patients' mean PASI scores dropped significantly from 21.6 to 9.0 ($p = 0.000$). More specifically, during the 6-month observation period, the number of patients with a PASI score <10 rose by 155.8 %, those with a PASI between 10 and 20 by 13.0 %, and patients with a PASI of between 20 and 30 and >30 dropped by 76.1 % and 86.0 %, respectively.

There was also a significant drop in the mean pain VAS score, which fell from 28.5 to 8.8 ($p = 0.000$). During the observation period, the proportion of patients with a pain VAS score <24 rose by 50.0 %, those with a score of 25–49 dropped by 47.1 %, those with a score of 50–74 dropped by 72.4 % and those with a score of 75–100 dropped by 82.1 %.

As regards the itching VAS, once again there was a significant reduction in the average score, which dropped from 31.7 to 7.7 ($p = 0.000$). During the observation period, patients with a pain VAS score <24 rose by 94.0 %, those with a score of 25–49 dropped by 86.0 %, those with a score of 50–74 dropped by 80.6 % and those with a score of 75–100 dropped by 75.0 %.

Table 1 Characteristics of the enrolled cohort

Variable	Value
N	178
Mean age, years (range)	47.7 (18–79)
Mean age at diagnosis, years	30.6
Males, %	64.6

3.2.1 *Differences Among the Biologics Used*

We noted that significant improvements in efficacy were observed for all three agents; however, differences between agents were not statistically significant. Patients who were prescribed etanercept at enrolment had a higher mean PASI than those prescribed adalimumab and infliximab (23.6, 18.0 and 21.0, respectively). During the 6-month observation period, there was a benefit in terms of a reduction in PASI of 14.4 for etanercept, 9.8 for adalimumab and 10.8 for infliximab (Fig. 1). Similarly for the pain VAS, the greatest benefit was observed for patients taking etanercept (from 31.5 to 7.7), followed by adalimumab (from 24.2 to 9.7) and infliximab (from 25.5 to 13.5) (Fig. 2).

For adalimumab and etanercept (the number of patients enrolled who received infliximab was lower) there was also a significant reduction in the itching VAS score, where once again the greatest benefit was observed for patients taking etanercept (from 34.0 to 7.2), followed by adalimumab (from 27.1 to 8.3) and infliximab (from 32.9 to 8.7) (Fig. 3).

In Figs. 1, 2 and 3, each box shows the maximum value, upper quartile, mean (red diamonds), lower quartile and minimum value, and eventual outliers.

3.3 Quality-of-Life Data

During the 6-month observation period there was a general improvement in HR-QOL, with a mean gain of 0.23 QALY per patient ($p = 0.000$). The number of patients with an HR-QOL <0.25 dropped by 76.3 %, those with an HR-QOL of 0.25–0.50 by 50.0 % and those with an HR-QOL of 0.50–0.75 by 44.9 %, with a consequential 125.9 % increase in those with an HR-QOL of 0.75.

For all three agents, the improvement in the quality of life measured using the EQ-5D questionnaire was statistically significant, with non-statistically significant differences between them; the greatest benefit was observed for

[3] Efalizumab, which was considered an alternative at the time the research protocol was devised, was not prescribed to any patient due to publication of a pharmacovigilance order by AIFA before enrolment started.

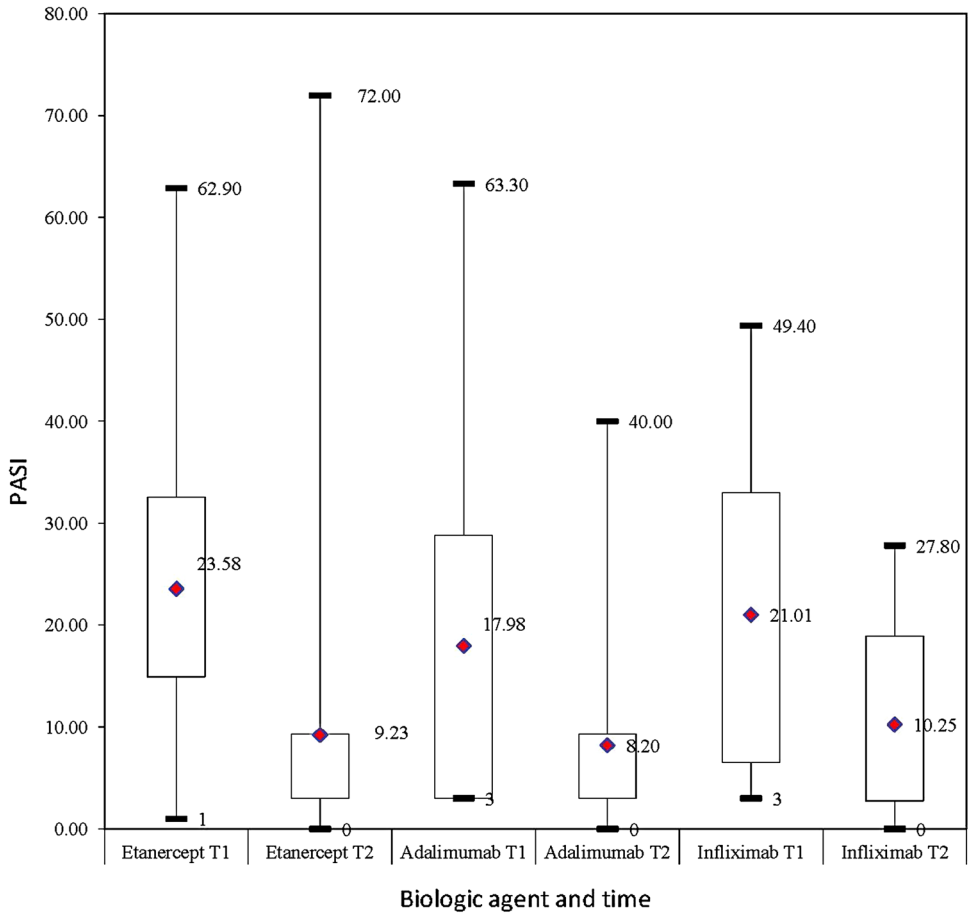

Fig. 1 Psoriasis Area and Severity Index (PASI) level

patients on etanercept (0.23 QALYs) versus 0.21 for adalimumab and infliximab (Tables 2 and 3).

3.4 Cost Analysis

Costs recorded for the 6-month period were annualised to permit easier comparison with other studies; we have assumed cost constancy over time, except in one case for drugs costs, because it seems appropriate to consider the intermittent administration of etanercept as provided in the technical file. In other words, for etanercept, which was the only drug approved in Italy for intermittent treatment [14], it was assumed that patients took 50 mg twice a week for 12 weeks, then 50 mg once a week for a further 12 weeks, before interrupting treatment for at least 3 months, the mean time for any recurrence. It should be noted that it was not possible to confirm this behaviour in clinical practice, due to the insufficient duration of the follow-up period. The assumption would appear to be fairly conservative, as it assumes that all patients continue with the treatment, whereas only 14 % of patients [15] experience a recurrence.

Before enrolment, the mean medical direct costs related to psoriasis were €2,166.2 on an annual basis: 38.8 % for hospitalisation, 18.0 % for day hospital services, 7.4 % for specialist visits, 23.6 % for laboratory tests, 4.5 % for diagnostic procedures and 7.8 % for psoriasis drugs.

Following the switch to biologic therapy, mean costs rose, due to the higher cost of the drugs (+8,003.5 %), whereas other costs dropped (−33.0 %), particularly, as expected, the cost of hospitalisation. The new cost breakdown at the end of the follow-up period is therefore 3.7 % for hospitalisation, 1.9 % for day hospital services, 0.8 % for specialist visits, 2.4 % for laboratory tests, 0.1 % for diagnostic procedures and 91.1 % for drugs. The mean total cost increase was €12,907.60 on an annual basis (Tables 4 and 5).

3.4.1 Incremental Cost-Effectiveness Ratio

The ICER of the switch to biologic therapies, from the perspective of the Italian health service, of patients with plaque psoriasis in real practice settings in the centres participating in the project is €28,656.3 per QALY gained, a value that would appear to be socially acceptable according to the most authoritative HTA agencies [16]. Although it refers to a very short observation period, this

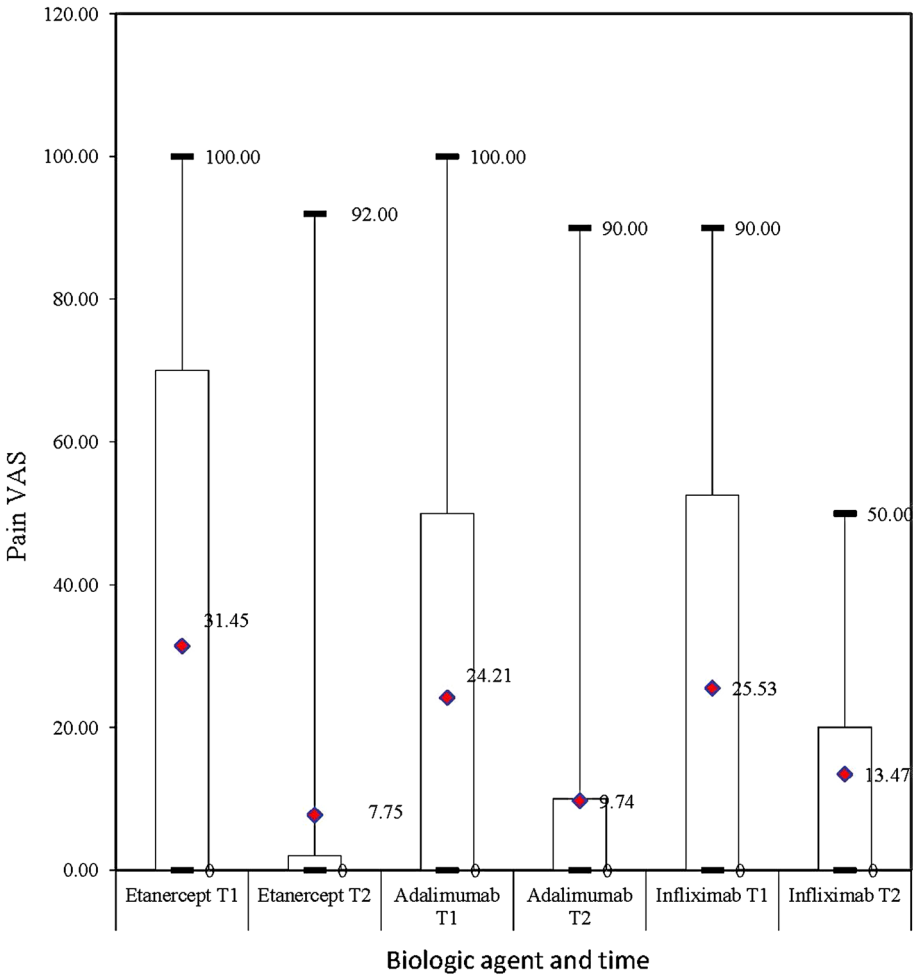

Fig. 2 Pain visual analogue scale (VAS) level

value is lower than that stated in the international literature [8, 17–19] for the single agents, as well as in the studies performed for their authorisation.

Although the differences in terms of benefit between the single compounds are not statistically significant,[4] for patients treated with etanercept[4] the incremental cost per QALY gained is €25,839.8, compared with €29,285.3 for adalimumab and €53,525.4 for infliximab (Table 6).

The incremental cost was €513.0 per PASI point, €328.8 per pain VAS point and €268.2 per itching VAS point. The incremental cost per PASI point gained was €504.3 with etanercept, €493.8 with adalimumab and €706.7 with infliximab. The cost per pain and itching VAS point gained was €270.8 and €250.1 with etanercept, €370.7 and €252.4 with adalimumab, and €983.2 and €523.9 with infliximab (Table 6).

3.5 Sensitivity Analyses

Univariate and probabilistic sensitivity analyses were performed. The results of the univariate sensitivity analysis are shown in the Tornado diagram (Fig. 4). Analysis focused, more specifically, on the change in HR-QOL benefits (for the whole sample) obtained by the limits of the confidence levels (95 % CI 0.21–0.23) and the 10 % change in the individual cost items (hospitalisation, specialist appointments, laboratory tests and diagnostic procedures). The results of the deterministic sensitivity analysis show that the ICER always remains below the €32,000 per QALY threshold, which suggests that the results are quite robust (Fig. 4).

Probabilistic sensitivity analysis has been performed, assuming gamma distributions for the cost, and beta for

[4] It should be noted that in real practice we observe switches between drugs, and that patients have been assigned to the drug group at enrolment (first biologic agent prescribed).

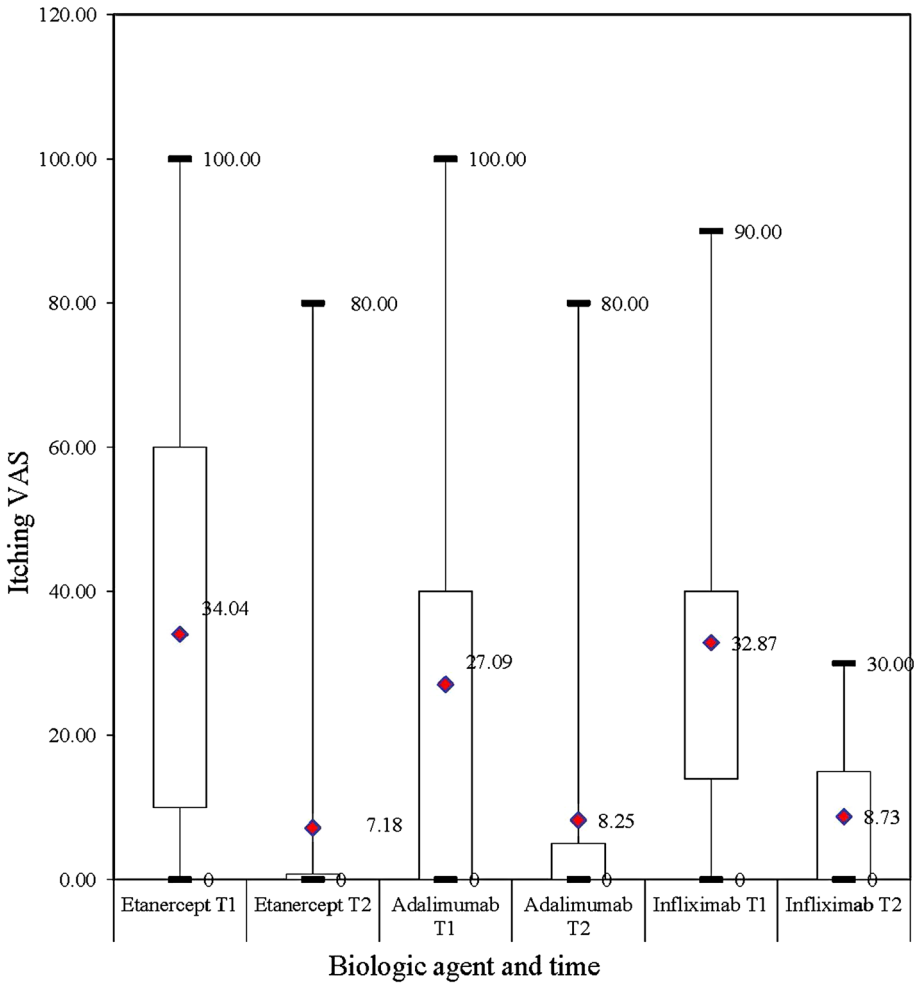

Fig. 3 Itching visual analogue scale (VAS) level

QALYs. The probabilistic sensitivity analysis indicates that biologic therapies for psoriasis are cost effective, with a €30,000 threshold[5] in 64.1 % of cases and a €40,000 threshold in 96.2 % of cases (Fig. 5).

4 Discussion

The cost of psoriasis patients in Italy is very high. As reported by Finzi et al. [20], hospitalisation constituted the largest component cost for the treatment of psoriasis in the past; but now, thanks to systemic and biologic agents, this cost is much lower [21].

The costs of treatment with biologics are significantly higher than those of conventional systemic therapy and vary from US$13,000 to US$30,000 [22]. Despite this, the cost effectiveness of biologic therapy has been extensively proven.

The UK National Institute for Health and Clinical Excellence (NICE) has published a number of technology appraisals on biologics using the evidence obtained in pre-approval studies [17, 19, 23, 24].

In the first report [17], NICE analysed the cost effectiveness of etanercept and efalizumab according to the authorised indications for the treatment of psoriasis, and concluded that efalizumab was more expensive and less efficacious than etanercept 25 mg × 2 per week as intermittent therapy: the ICER was found to be £24,346 and £15,297 per QALY gained, respectively. The ICERs for etanercept 25 mg × 2 as continuous therapy and etanercept 50 mg × 2 as intermittent therapy, on the other hand, were £23,905 and £43,395, respectively [17]. Consequently, on the basis of the clinical evidence available, etanercept was recommended by NICE for the treatment of adults with psoriasis with a PASI score of PASI ≥10 and Dermatology Life Quality Index (DLQI) score >10, and who are non-responders to, intolerant to, or have contraindications for systemic treatment with cyclosporin, methotrexate or psoralen and UVA phototherapy (PUVA) [17].

[5] Consider that the average cost-effectiveness analysis in Italy amounted to €28,000. In the literature this is reported as £30,000 (approximately €36,000) [26].

Table 2 Clinical benefits and quality of life

	Group (number of patients)			
	All (178)	Etanercept (106)	Adalimumab (57)	Infliximab (15)
HR-QOL				
Enrolment	0.58	0.62	0.52	0.60
Δ	0.23	0.23	0.21	0.21
p value*	0.000	0.000	0.000	0.001
VAS				
Enrolment	57.06	60.29	49.96	61.20
Δ	19.89	19.03	23.51	12.20
p value*	0.000	0.000	0.000	0.009
PASI				
Enrolment	21.57	23.58	17.98	21.01
Δ	12.58	14.35	9.77	10.76
p value*	0.000	0.000	0.000	0.006
Pain VAS				
Enrolment	28.43	31.45	24.21	25.53
Δ	19.63	23.70	14.47	12.07
p value*	0.000	0.000	0.000	0.142
Itching VAS				
Enrolment	31.71	34.04	27.09	32.87
Δ	24.06	26.86	18.84	24.13
p value*	0.000	0.000	0.000	0.009

HR-QOL health-related quality of life, *PASI* Psoriasis Area and Severity Index, *VAS* visual analogue scale

* Paired *T* test

Table 3 Differences in clinical and quality of life benefits between drugs

	Etanercept vs. infliximab	Etanercept vs. adalimumab	Infliximab vs. adalimumab
HR-QOL	0.03	0.02	0.00
p value	0.608[a]	0.657[b]	0.913[a]
VAS	6.83	−4.48	−11.31
p value	0.302[b]	0.280[b]	0.039[a]
PASI	1.82	2.81	0.99
p value	0.494[c]	0.121[c]	0.805[b]
Pain VAS	11.63	9.22	−2.41
p value	0.075[c]	0.187[c]	0.774[b]
Itching VAS	2.73	8.02	5.29
p value	0.751[b]	0.125[c]	0.405[c]

HR-QOL health-related quality of life, *PASI* Psoriasis Area and Severity Index, *VAS* visual analogue scale

[a] One simple *T* test, equal variances not assumed

[b] One simple *T* test, equal variances assumed

[c] Wilcoxon test

In 2008, NICE extended its evaluation to infliximab, which is recommended for the treatment of adults with severe psoriasis (PASI >20 and DLQI >18) who are non-responders to, intolerant to, or present with contraindications for systemic treatment [23]. Again in 2008, NICE also evaluated adalimumab, concluding that the ICER per QALY gained with adalimumab compared to supportive care is £30,500 and that adalimumab is superior to etanercept when administered as continuous treatment [19]. The same report states that the ICER for etanercept versus supportive care rises from £37,300 for continuous therapy to £27,600 for intermittent therapy [19]. In 2009, NICE also evaluated ustekinumab, comparing it to etanercept, adalimumab and infliximab [24].

Many subsequent studies have re-confirmed the cost-effectiveness of biologics for the treatment of psoriasis. Heinen-Kammerer et al. [18] conducted an analysis of the cost effectiveness of etanercept compared to systemic treatment, concluding that in patients with a baseline PASI and DLQI of >10, the ICER compared with systemic treatment is €45,491. Considering patients with a PASI >15 and DLQI >20, the ICER drops to €32,058 and €18,154, respectively [18].

In one American study conducted using a simulation model [25], the cost per patient was US$28,767 for etanercept 25 mg × 2, US$29,129 for etanercept with step-down treatment and US$37,959 for etanercept 50 mg × 2. Alefacept and efalizumab were found to be superior to etanercept 25 mg × 2.

Sizto et al. [8] performed a comparative cost-effectiveness analysis for biologics that concluded that adalimumab is the most cost-effective agent, with an ICER of £30,538 per QALY, followed by etanercept 25 and 50 mg (£37,284 and £37,676 per QALY, respectively), efalizumab (£40,000 per QALY) and infliximab (£42,492 per QALY).

The purpose of our analysis was to verify if values predicted with RCT evidence and economic modelling could be confirmed in real practice settings in Italy. The analysis not only applies to a real Italian population, but also aimed to confirm the HR-QOL benefit predicted by recording data directly for Italian patients.

Significant improvements were confirmed for all the objective and subjective clinical parameters considered. During the, albeit limited, duration of the follow-up period, the results appeared to be on average even better than those indicated in literature. The benefit in terms of HR-QOL were also significant.

The results obtained, although with some significant limitations (as previously mentioned and discussed below), seems to confirm the findings of social acceptability (in terms of cost per QALY) of biologic therapy predicted in the literature with models and the basis of trial evidence, hence on controlled populations, in the real practice of leading specialist centres in Italy also.

Table 4 Medical direct costs (€; year 2009), on an annual basis, borne by the Italian health service per patient

	Hospitalisation	Day hospital	Specialist appointments	Laboratory tests	Diagnostic procedures	Drugs	Total
Prior to enrolment	840.74	389.18	159.70	510.50	96.54	169.50	2,166.16
Observation period	560.50	279.20	126.74	363.56	8.34	13,735.40	15,073.74
Δ Costs	−280.24	−109.98	−32.96	−146.94	−88.20	13,565.90	12,907.58

The costs for patients who switched from one agent to another were calculated using the agent prescribed at enrolment if the patient switched treatment after 3 months and using the agent the patient switched to if the switch took place after less than 3 months from initial prescription

Table 5 Increase in the medical direct costs borne by the Italian health service (on an annual basis)

Group	Δ Costs (€)
All	12,907.58
Etanercept	12,129.10
Adalimumab	12,425.20
Infliximab	22,252.28

Table 6 Incremental cost-effectiveness ratio

Group	QALY	VAS	PASI	Pain VAS	Itching VAS
All	28,656.31	324.47	513.01	328.78	268.22
Etanercept	25,839.79	318.68	504.30	270.81	250.20
Adalimumab	29,285.34	264.25	493.77	370.68	252.39
Infliximab	53,525.38	911.98	706.07	983.24	523.95

PASI Psoriasis Area and Severity Index, *QALY* quality-adjusted life-year, *VAS* visual analogue scale

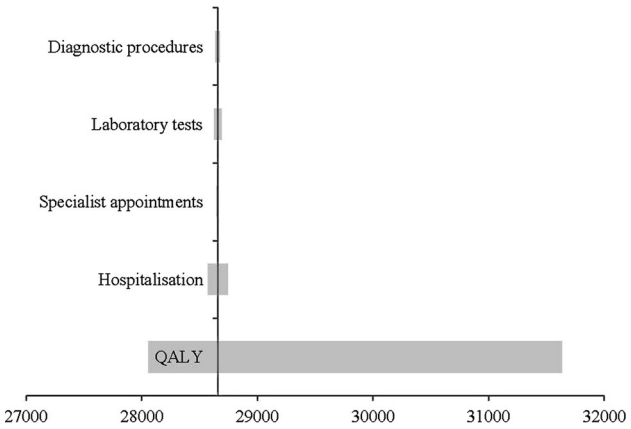

Fig. 4 Tornado diagram. *QALY* quality-adjusted life-year

4.1 Limitations of this Study

The main limit of our analysis was the short observation period which, for example, did not allow us to assess fully the impact of biologic treatment interruptions and use of intermittent therapies, as well as persistency of the treatment effect (and, consequently, constancy of costs). This would be of interest both in terms of clinician's behaviour and patient adherence and compliance, but would be appreciable only in the long term.

In addition, it is important to bear in mind that this is an observational study, with no control group: consequently, ICER calculation is not perfectly comparable with that of previous analyses based on RCT evidence: our calculation could be considered a conservative hypothesis, assuming that, without switching to biologic treatment, the patients' state of health and costs incurred would remain constant.

Also, despite certain differences between the agents used, the substantial cost effectiveness of all the agents prescribed by physicians was confirmed, but the size of the cohort enrolled did not make it possible to detect any statistically significant differences between the various drugs used.

5 Conclusions

Findings from our analysis, conducted by recording Italian data directly in real clinical practice settings, are in line with the predictions from models based on RCT and economic modelling, in terms of both efficacy and cost effectiveness.

The benefits of biologic therapy were found to be statistically significant according to a number of clinical (PASI, pain VAS and itching VAS) and HR-QOL-related parameters. More specifically, the study allowed for the validation, for the Italian population in particular, of the benefits in terms of quality of life, since the gain in QALYs was elicited directly from the patients enrolled.

The study also confirms that in the clinical practice of the participating Italian centres, the cost per QALY achieved, although from a short observation period, is

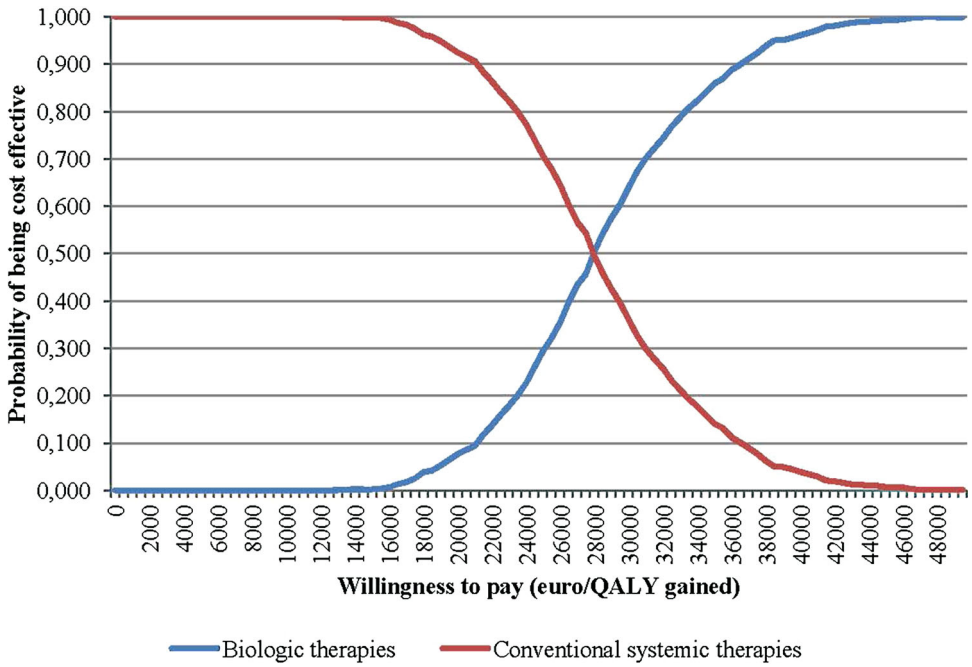

Fig. 5 Acceptability curve. *QALY* quality-adjusted life-year

comparable with results published in the most authoritative international HTA reports.

This analysis confirmed the substantial 'cost-utility' of the biologic therapies, as well as of all the compounds prescribed; although a number of differences were observed among the products used, the sample size made it impossible for any calculation of statistical significance.

The main limit of our analysis was the short observation period, which did not allow us to assess fully the impact of biologic treatment interruptions or intermittent etanercept therapy, as well as persistency of the treatment effect.

A certain degree of caution is required concerning the transferability of the results, since the participating centres are specialised facilities that are monitored as part of the Psocare project and are therefore presumably more attentive to the appropriateness of treatment choices: the study does, however, show that correct use of biologic therapy is also cost effective in clinical practice and therefore in 'real' patient populations.

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