

The Cost of Psoriasis in Patients under Conventional Systemic Therapy or Biologic: The Results of a Retrospective Analysis Carried out in an Italian Center

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Received date: July 16, 2018; Accepted date: August 09, 2018; Published date: August 15, 2018

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Abstract

Objective: To present an update of the cost profile of psoriasis in patients with conventional systemic therapy or biologic referring to a Center of the Piedmont Region.

Methods: A retrospective, observational cohort study was conducted to estimate the cost of the treatment with conventional systemic therapy or biologic of adult patients with psoriasis referring to an Italian Center. The enrollment window started on July 1, 2017 and ended on January 31, 2018. Each patient identified was followed-up retrospectively for six months. The database collected the main details on demographics, clinical data and resource consumption (treatments administered, visits, blood tests and instrumental examinations, etc.) for each patient enrolled. The PASI index was evaluated to reconstruct the evolution over time of the seriousness of psoriasis for each patient enrolled.

Results: 181 patients were considered, 45.9% treated with a biologic and 54.1% with a conventional systemic therapy. During the 6 months follow-up, 2.4% patients with biologic and 11.2% with conventional systemic therapy discontinued the treatment ($p=0.0233$). At the beginning (baseline) a more compromised disease activity (PASI score) in patients with the biologic emerged (19.8 vs. 13.9; $p=0.0005$). Twelve months before enrolment the average PASI score showed a substantial overlap (5.9 vs. 5.8; $p=0.9375$). Upon enrollment patients treated with the biologic reported the lowest mean PASI score (2.7 vs. 3.8; $p=0.1127$). The 6 months cost of treatment was € 5,675 for biologic and € 321 for conventional systemic therapy ($p<0.0001$). The cost for the management of psoriasis was significantly higher in patients with moderate-to-severe PASI.

Conclusions: The data collected seem to be sufficient to state that psoriasis is a disease with a quite high overall cost for the NHS and/or society, and that, due to its chronicity, such cost is likely to increase with the progression of severity.

Keywords: Psoriasis; Cost; Biologic; Conventional systemic therapy; PASI score; QALY

Introduction

According to the data from a recent review of the literature in the adult population, the prevalence of psoriasis varies from 0.91% (United States) to 8.5% (Norway), while incidence is between 78.9/100.000 person-years (United States) and 230/100.000 person-years (Italy) [1,2]. The data also show that the onset of psoriasis changes depending on age and geographic area (being more common in Countries further away from the equator) [1]. In about three-quarters of patients, psoriasis occurs before age 40, hitting males and females equally [2,3].

Psoriasis is a chronic inflammatory disease of the skin, clinically characterized by redness (erythema), thickening, desquamation (scaling) and by the alternation of remission and relapse phases of variable duration [4-6]. The etiology of psoriasis is not yet well known, and the information currently available suggests a multifactorial origin

(autoimmune, genetic and environmental factors) [2]. In addition to the typical clinical manifestations of the disease itself, psoriasis is associated with depressive symptoms and with a high risk for cardiovascular events [7,8].

With approximately 80% of all cases, plaque psoriasis is the most common form [9,10]. Generally, the severity degree of psoriasis is classified into mild, moderate or severe, depending on the area of the body involved and on the lesions (erythema, infiltration and desquamation). Over the years, different clinometric indexes were developed to assess its seriousness, such as PASI (Psoriasis Area and Severity Index), BSA (Body Surface Area) and PGA (Physician Global Assessment) [11].

Patients with forms of psoriasis refractory to topical therapies and with extensive lesions are usually treated with conventional systemic therapy and phototherapy. The main conventional systemic therapies consist of immunomodulators (eg. methotrexate and cyclosporine) or retinoids (eg. acitretin) [12]. Although administration is

predominantly oral, conventional systemic therapies require the constant supervision of a physician and a regular monitoring, for the management of any related adverse events [11]. Patients with an inadequate response or who have a contraindication or are intolerant to the conventional systemic therapy are treated instead with a biologic (eg. etanercept, infliximab, ustekinumab) although treatment with some biologics (eg. adalimumab, secukinumab) is already possible when patients are candidates for systemic therapy [11].

Given the high prevalence of psoriasis among the general population, in addition to the clinical aspects, it becomes important to also investigate its management, in terms of costs borne by the Healthcare Service (direct costs) or by society (direct and indirect costs). A comparative study conducted in 2004 compared the treatment cost of patients with severe psoriasis (approximately 27%-30% of total patients) in seven European Countries (France, Germany, Netherlands, Spain, Sweden, Belgium, England and Italy) [13]. The study identified a wide variability in the average annual cost of treatment, from the estimated € 2,981 for France to the € 6,595 for Sweden (and € 3,712 for Italy) [13]. A subsequent disease cost analysis, conducted in Italy by Colombo et al., estimated an average annual cost per patient diagnosed with moderate to severe psoriasis of € 8,371.61, of which € 5,690.10 for direct costs and € 2,681.51 for indirect costs [14].

The objective of this analysis is to present-with the aid of Real World Data (RWD) an update of the cost profile of psoriasis in patients under conventional systemic therapy or biologic referring to a center of the Piedmont Region and, when possible, to examine this cost compared to some clinical variables.

Methods

Study design

A retrospective, observational, non-interventional cohort study was conducted to estimate the (direct and indirect) cost of the treatment with conventional systemic therapy or biologic of adult patients diagnosed with psoriasis referring to the “University Dermatology Department Dermo II-Città della Salute e della Scienza di Torino” (henceforth the “Center”), the reference site of the Piedmont Region for the treatment of psoriasis.

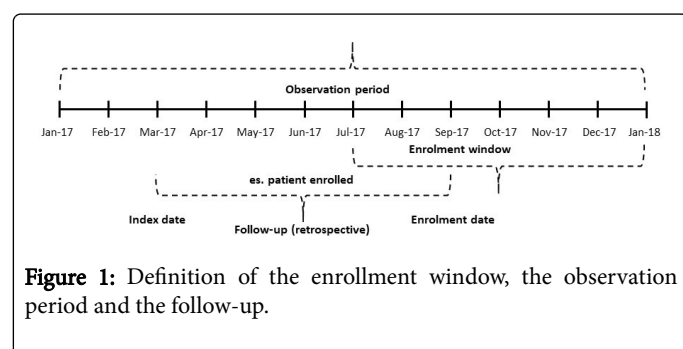


Figure 1: Definition of the enrollment window, the observation period and the follow-up.

The enrollment window-defined as the period of time needed to recruit the first 200 patients who were referred to the Center with a diagnosis of psoriasis (see next paragraph, “Population”) started on July 1, 2017 and ended on January 31, 2018 (Figure 1). Each patient identified was then followed up retrospectively for six months. This period, as shown in Figure 1, is defined by the date of enrollment and the index date, whereas the latter corresponds retrospectively to the

beginning of the follow-up for each patient. Based on the enrollment window, in order to ensure to each patient a six-month retrospective follow-up, the study observation period spanned from January 1, 2017 to January 31, 2018 (Figure 1).

Population

The population subject of the analysis was selected among the 200 patients who, with a diagnosis of psoriasis, referred to the Center during the enrollment period. From these, the patients who had not been treated for at least six months (follow-up) with a conventional systemic therapy or biologic were subsequently excluded. The patients’ selection flowchart was shown in Figure 2.

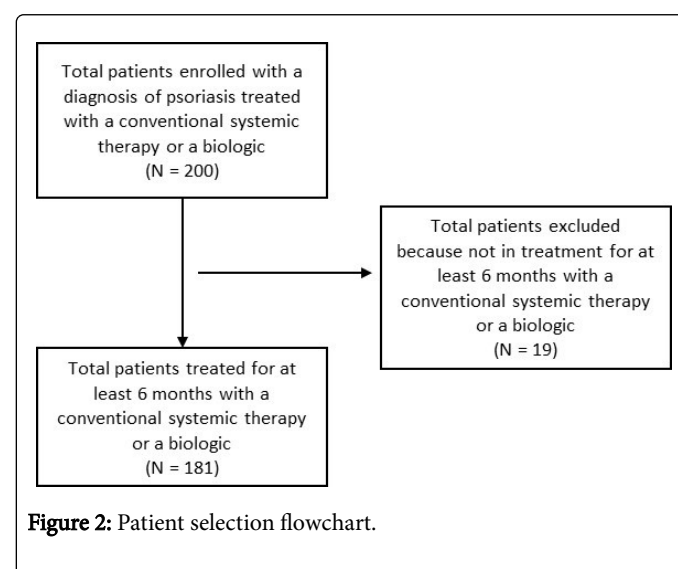


Figure 2: Patient selection flowchart.

Since-in view of a relative variability of the average cost of treatment of about 50% (coefficient of variation)-a number of patients not lower than approximately 100 would have been sufficient to allow an estimate accuracy (in terms of relative estimate error) not lower than 10% (with a 95% Confidence Interval), an initial sample of 200 patients was considered adequate to allow the determination of a reliable estimate of the average cost of treatment.

Data collection

The data, extracted from the medical records of the Center, were anonymized and reorganized into a database that collected the main details on demographics, clinical data and resource consumption for each patient enrolled. Specifically, the database included variables such as age, gender, diagnosis, time to diagnosis and presence of concomitant therapies. Thanks to the PASI index, it was possible to reconstruct the evolution over time of the seriousness of psoriasis for each patient enrolled. HRQL (Health-Related Quality of Life) was investigated by administering the EuroQol 5-Dimension (EQ-5D) questionnaire [15,16].

The database also included the consumption associated with the conventional systemic therapies and biologics administered, visits (Psicare, specialist or general medicine), blood tests and instrumental examinations, accesses as outpatients and hospital admissions paid for. For each patient, the duration of the therapy ongoing at the time of enrollment was defined retrospectively, the presence of induction (if the first administration of the conventional systemic therapy or the

biologic had occurred in concomitance with the index date) and/or the suspension/discontinuation of the treatment administered during the follow-up were identified. In addition to the healthcare consumption, the database also gathered information on the number of working days lost (indirect cost) by the patient and/or any caregiver due to psoriasis.

Definitions and outcomes

The diagnosis of psoriasis was clinically confirmed on the basis of what indicated in the medical records. The time to diagnosis was defined as the number of years between the date of enrolment and the date on which the psoriasis was clinically confirmed.

The index date, as shown in Figure 1, represents the beginning of the follow-up period for each patient enrolled, and was calculated retrospectively at six months before the date of enrollment. In accordance with what indicated in the medical records on the index date, for each patient the ongoing treatment (conventional systemic therapy or biologic) was identified. The change of therapy-or switch- was defined as the prescription, during the follow-up, of a treatment (conventional systemic therapy or biologic) different from the one ongoing on the index date. The presence of treatment induction, evaluated with respect to the index date, was confirmed with regard to what indicated in the medical record. The duration of the drug therapy already ongoing on the index date was calculated as the difference between the date of enrollment and the date at baseline, where the latter corresponds to the moment when the therapy ongoing on the index date is administered for the first time. The date at baseline can therefore go back retrospectively to a time longer than that covered by the period of observation.

The PASI index provides an overall score of the disease state by combining the assessment of the severity of the lesions (such as erythema, infiltration and desquamation) with that of the body area affected by the disease. The relevant score can vary from a minimum of 0-absence of disease-to a maximum of 72-highest degree of disease [15]. The PASI index was evaluated both as average score and as the number of patients distributed per severity class (absent disease if PASI=0, mild disease if $0 < \text{PASI} < 10$, moderate disease if $10 \leq \text{PASI} \leq 20$ and severe disease if $\text{PASI} > 20$). Thanks to the data collected in the clinical records of the Center, four temporal evaluations of the PASI index could be determined for each patient: at the time of enrollment, on the index date (i.e. six months before enrollment), 12 months before enrollment and on the baseline date (Figure 3).

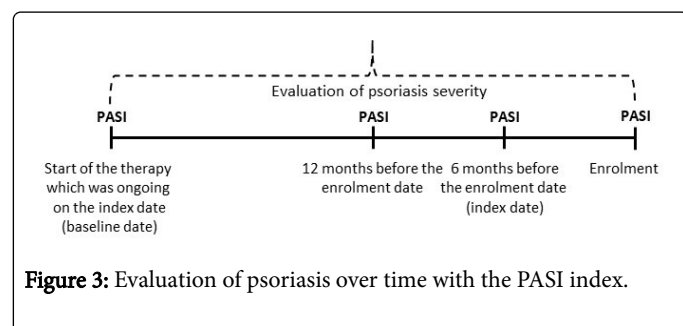


Figure 3: Evaluation of psoriasis over time with the PASI index.

With the objective to finally assess the health-related quality of life, patients were asked to complete the EQ-5D questionnaire at two different times: on the index date and on enrollment. EQ-5D is a standardized instrument that allows measuring the quality of life of respondents [16]. The questionnaire consists of two distinct sections. The first one asks a subjective evaluation for five domains (mobility,

self-care, daily activities, pain/discomfort and anxiety/depression) which, thanks to an algorithm, is translated into a succinct index of the patient-perceived health status, called Quality-Adjusted Life Year (QALY), where the value 0 corresponds to the state of death and value 1 to a perfect health status [16]. The second section of EQ-5D includes a Visual Analogic Assessment (VAS), graphically represented by a scale ranging from 0 (worst possible health status) to 100 (best possible health status), on which respondents indicates their perceived level of health [16].

Treatment costs

The cost analysis was carried out by adopting the dual perspective of the National Health Service (NHS) and that of society. In the first case, only direct medical costs were considered (eg. conventional systemic therapy, biologic, visits, etc), while in the second case the indirect costs generated by the loss of working days by patients and/or caregiver due to psoriasis have been added to the direct costs.

The definition of the cost of the conventional systemic therapy or the biologic occurred by detecting for each individual patient the actual cost incurred by the hospital pharmacy of the Center during the follow-up period. For each drug, the relevant purchase price-net of all discounts (mandatory and not) was then considered. Visits (Psocare, specialist or general medicine), blood tests and instrumental examinations, outpatient accesses and hospitalizations were instead valued on the basis of the regional fees paid by the Piedmont Region. To estimate the loss of productivity caused by psoriasis, the human capital method was used. Therefore, the lost workday was valued assuming a daily income of € 131.37, obtained by dividing the average annual gross salary of € 28,900 (source: ISTAT) by 220 annual working days [17].

Data analysis

The quantitative variables were described as a mean value (\pm standard deviation), while the categorical ones as a numerical value (percentage). The significance of the differences between the collected/processed data has been verified using the Student's (two-tailed) t-test. The analysis was supported by the software Microsoft® Excel® for Windows (Microsoft Corporation, Seattle, WA, USA) and SPSS® version 13.0 for Windows (SPSS Inc., Chicago, IL, USA).

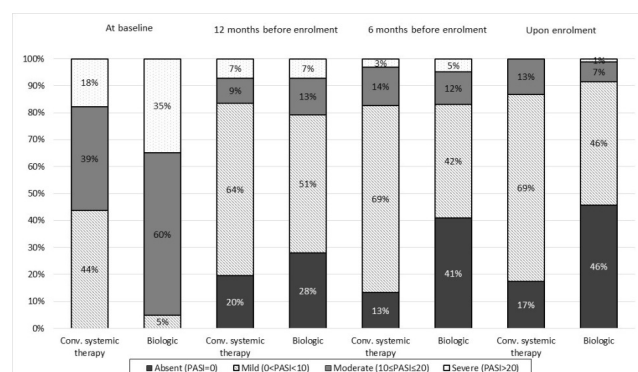


Figure 4: Evolution of patient distribution by PASI class.

Code of ethics

The study was designed by the sponsor, Novartis Italia, by an academic group of the Center, which includes authors who are not employees of Novartis Italia, and by Health and Publishing Services. The study was conducted in accordance with the indications specified by the GPPs (Guidelines for Good Pharmacoepidemiology Practices) of ISPE (International Society for Pharmacoepidemiology), by STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) and in accordance with the principles of the Declaration of Helsinki [16,17]. The study was approved by the Center's own Ethics Committee. All patients provided their informed consent.

Results

Sample characteristics

During the enrollment window, 200 patients with a diagnosis of psoriasis were referred to the Center. Of these, 19 did not meet the inclusion criteria, since they were not under treatment for at least 6 months (index date) with a conventional systemic therapy or with a

biologic (Figure 2). Overall, 181 patients were therefore considered, of whom 83 (45.9%) treated with a biologic and 98 (54.1%) with a conventional systemic therapy. The subjects taking a biologic were younger than those under conventional systemic therapy (55.2 years (\pm 14.0) vs. 61.1 years (\pm 15.2); $p=0.005$) (Table 1). Consequently, the percentage of pensioners was higher in the group treated with conventional systemic therapy (26.5% vs. 45.9%; $p=0.008$). The median time to diagnosis was 16.8 years (\pm 11.3) for patients treated with biological and 13.4 years (\pm 11.9) for those with conventional systemic therapy ($p=0.050$), while the average duration of the ongoing pharmacological therapy was 3.5 years (\pm 3.4) for the biologic and 2.3 years (\pm 2.4) for the conventional systemic therapy ($p=0.008$) (Table 1). On the index date, induction was more frequent in patients treated with the biologic (13.3% vs. 3.1%; $p=0.012$). No significant differences were however found in the mean number of concomitant therapies, or of patients taking medicinal products for hypertension, diabetes, high cholesterol or joint pain (Table 1). On the index date, 52 (28.7%) patients were being treated with methotrexate, 29 (16.0%) with adalimumab, 27 (14.9%) with ustekinumab, 24 (13.3%) with acitretin, 22 (12.2%) with etanercept, 22 (12.2%) with cyclosporine, 3 (1.7%) with infliximab and 2 (1.1%) with secukinumab.

Parameters	Biological treatment	Conventional systemic treatment	Total	p value
Patient no. (%)	83 (45.9)	98 (54.1)	181 (100)	
Males no. (%)	60 (72.3)	58 (59.2)	118 (65.2)	$p=0.067$
Mean age, years (\pm std. dev.)	55.2 (\pm 14.0)	61.1 (\pm 15.2)	58.4 (\pm 14.9)	$p=0.005$
Working, no. (%)				
Worker	45 (54.2)	41 (41.8)	86 (47.5)	$p=0.098$
Pensioner	22 (26.5)	45 (45.9)	67 (37.0)	$p=0.008$
Unemployed	6 (7.2)	4 (4.1)	10 (5.5)	$p=0.364$
Housewife	4 (4.8)	6 (6.1)	10 (5.5)	$p=0.703$
Student	6 (7.2)	2 (2.0)	8 (4.4)	$p=0.090$
Time to diagnosis, years (\pm std. dev.)	16.8 (\pm 11.3)	13.4 (\pm 11.9)	15.0 (\pm 11.7)	$p=0.050$
Induction, no. (%)	11 (13.3)	3 (3.1)	14 (7.7)	$p=0.012$
Duration of pharmacological therapy, years (\pm std. dev.)	3.5 (\pm 3.4)	2.3 (\pm 2.4)	2.9 (\pm 2.9)	$p=0.008$
Concomitant treatments, no. (\pm std. dev.)	0.7 (\pm 0.8)	0.8 (\pm 0.9)	0.8 (\pm 0.9)	$p=0.432$
Drugs for hypertension, no. (%)	28 (33.7%)	33 (33.7%)	61 (33.7%)	$p=1.000$
Drugs for diabetes, no. (%)	5 (6.0%)	13 (13.3%)	18 (9.9%)	$p=0.104$
Drugs for high cholesterol, no. (%)	12 (14.5%)	20 (20.4%)	32 (17.7%)	$p=0.301$
Drugs for joint pain, no. (%)	14 (16.9%)	14 (14.3%)	28 (15.5%)	$p=0.631$

Table 1: Characteristics of the patients receiving a biologic or a conventional systemic therapy upon enrollment.

During the follow-up, 2 patients (2.4%) in treatment with a biologic discontinued (partial failure) and changed (other biological) the treatment ongoing on the index date, while the number of patients who discontinued (1 partial failure, 5 failures and 5 toxicities) the conventional systemic therapy ongoing on the index date rose to 11

(11.2%; $p=0.0233$). Among these 11 patients, in only one case the discontinuation of the treatment did not result in the change of the ongoing therapy, but only in its interruption. In 2 cases, patients under conventional systemic therapy were switched to a topical therapy; in 7 cases it was decided to change the conventional systemic therapy with

another conventional systemic therapy and in 1 case only the conventional systemic therapy was switched to a biologic.

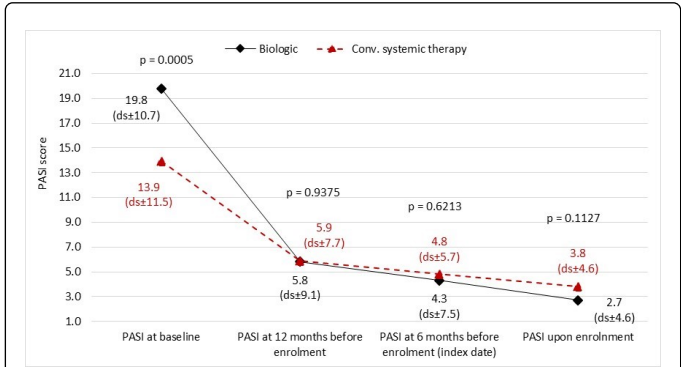


Figure 5: Evolution of the average PASI score over time.

Outcomes

Figures 4 and 5, differentiating as for the treatment administered on the index date, showed the evolution over time of the severity of psoriasis by means of the distribution of patients per PASI classes or average PASI score, respectively. In view of with a greater concentration of patients in the moderate-to-severe classes (95% vs. 57%), at the beginning of treatment (baseline) a picture emerged of a more compromised disease activity in patients with the biologic versus those with the conventional systemic therapy (Figure 4); the mean PASI score, in fact, showed a significant difference of 5.9 points (19.8 vs. 13.9; $p=0.0005$) (Figure 5). Twelve months before enrolment, a significant improvement in the clinical picture for both treatment groups was to be noted. The concentration of patients in the moderate-to-severe classes dropped to 20% for the subjects receiving a biologic and to 16% for those under conventional systemic therapy, while the average PASI score showed a substantial overlap of the degree of disease between the two groups (5.9 vs. 5.8; $p=0.9375$). Both 6 months before enrolment (index date) and upon enrollment, the improvement of the clinical picture for both groups continued; patients treated with the biologic reported the lowest concentrations for the moderate-to-severe PASI classes and the lowest mean PASI scores (in this case the differences are not significant) (Figures 4 and 5).

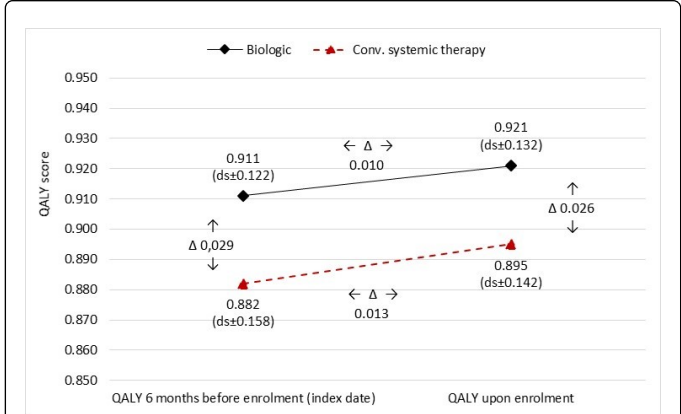


Figure 6: Evolution of QALYs (follow-up at six months).

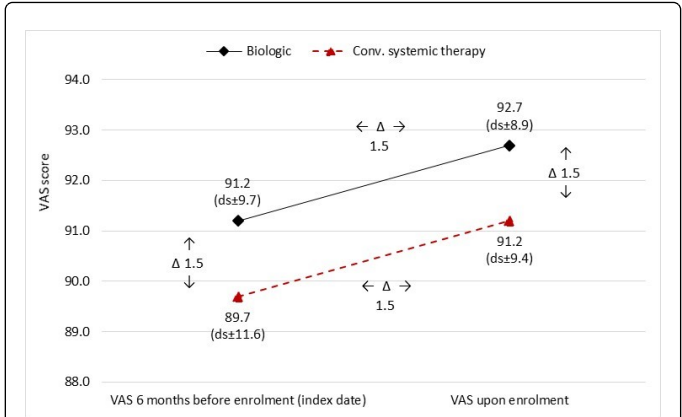


Figure 7: Evolution of the VAS score (follow-up at six months).

Figures 6 and 7, QALYs and VAS respectively showed the variation, during the follow-up, of the quality of life perceived by the subjects being treated with a biologic or a conventional systemic therapy. For both treatments it was to be noted an improvement in the 6-month follow-up, both in terms of QALYs and VAS score. The differences between the index date and the enrolment date were not significant.

Treatment cost

The difference between the two half-yearly average cost of treatment was significant ($p<0.0001$), both in terms of total costs (€ 5,657 vs. € 321) and direct costs (€ 5,611 vs. € 270) (Table 2).

During the 6-month follow-up, the patient treated with the biologic generated a cost of € 5,657 (± 1.667), of which 99.2% were direct medical costs for the NHS. Among these, the highest incidence was determined by the cost for the biologic (98.2%), while very small was that associated with visits (Psocare, specialist and general medicine) and examinations (blood and instrumental) (Table 2).

Parameters	Biological treatment	Conventional systemic treatment	p value
	Cost per patient (€)	Cost per patient (€)	
	Average (\pm std. dev.)	Average (\pm std. dev.)	
Drugs for psoriasis	5,511 (± 1.671)	159 (± 157)	$p<0.001$
Psocare visits	35 (± 10)	36 (± 13)	$p=0.562$
MMG visits	27 (± 21)	42 (± 30)	$p=0.002$
Specialist visits	5 (± 11)	5 (± 10)	$p=1.000$
Blood tests	20 (± 10)	23 (± 11)	$p=0.058$
Instrumental exam.	13 (± 30)	5 (± 23)	$p=0.050$
Direct costs	5,611 (± 1.675)	270 (± 169)	$p<0.001$
-lost days (patient)	44 (± 78)	34 (± 71)	$p=0.375$
-lost (caregiver) days	2 (± 14)	17 (± 51)	$p=0.006$
Indirect costs	46 (± 78)	51 (± 84)	$p=0.680$

Total cost	5,657 (± 1.667)	321 (± 201)	p<0.001
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Table 2: Six-month average cost per patient treated.

The semiannual average cost for a patient in treatment with a conventional systemic therapy was instead equal to € 321 (± 201); in this case direct medical costs covered 84.1% of the total amount. Among direct medical costs, the pharmacological component accounted for 58.9%, visits for 30.7% and examinations for 10.4% (Table 2).

No patient treated with a biologic or a conventional systemic therapy was hospitalized or required an outpatient access because of psoriasis (Table 2).

Unlike what happened for direct medical costs, the expenditure associated with lost workdays (indirect costs) was similar for the two treatment groups (biologic: € 46 vs. conventional systemic therapy: € 51; p=0.680) (Table 2).

Finally, it can be seen how-both for the conventional systemic therapy and for the biologic-the cost for the management of psoriasis was significantly higher in patients with moderate-to-severe PASI (Figure 8).

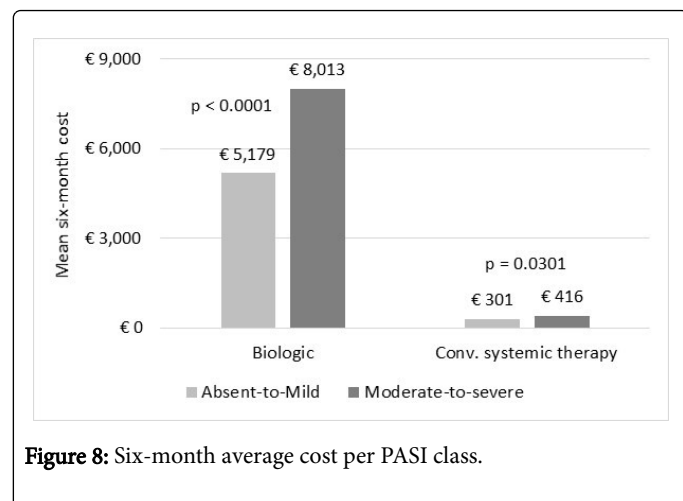


Figure 8: Six-month average cost per PASI class.

Discussion

This retrospective, observational study was conducted with the aim to estimate the cost of psoriasis in patients under conventional systemic therapy or biologic in the Piedmont Region. The cohort, consisting of 181 patients (mean age 58.4 years (± 14.9); males: 65.2%), was created including all subjects who-with a diagnosis of psoriasis and under treatment for at least 6 months with a conventional systemic therapy or with a biologic-were referred to the Center during the enrollment period (July 1, 2017-January 31, 2018).

During the follow-up, the evolution of the psoriasis status showed a good clinical picture, constantly improving both in patients receiving a conventional systemic therapy and a biologic. In the first case, the PASI index was reduced by 1 point, going from 4.8 (index date) to 3.8 (enrollment date), while for the biologic the reduction was 1.6 points, from 4.3 (index date) to 2.7 (enrollment date). The good state of health and its continuous improvement was also confirmed by the evolution of the health-related quality of life indicators. Both QALYs and the

VAS score showed an increase in the quality of life perceived by patients with psoriasis during the follow-up (Figures 6 and 7).

With regard to the observation period, methotrexate was the conventional systemic therapy most prescribed (52 cases out of 98 total; 53.1%), while adalimumab (29 cases out of 83 total; 34.9%) and ustekinumab (27 cases out of 83 total; 32.5%) were the most frequently administered biologics. In the six-month follow-up, the discontinuation rate was significantly higher for patients receiving conventional systemic therapy than those with a biologic (11.2% vs. 2.4%; p=0.0233).

The patients' good health status was reflected in the healthcare consumption profile; no outpatient accesses or hospitalizations caused by psoriasis were reported by the Center during the six-month follow-up. Consumption of visits and blood tests/instrumental examinations was also minimal: an average of 2.0 visits (with the exclusion of those provided for in the Psocare program) and 1.9 blood tests/instrumental examinations per patient during the follow-up.

Since patients were characterized by a good state of health, the semiannual average cost was found to mainly consist of the expenditure on medicinal products, higher for the biologics than the conventional systemic therapy (€ 5,511 vs. 159, p<0.001). Actually, it would be incorrect to compare these costs, since they represented two different moments of psoriasis care; the conventional systemic therapy was used in the forms of psoriasis refractory to topical treatments, or characterized by large lesions, while the biologic was used against an inadequate response, or contraindications/intolerance to a conventional systemic therapy. It would therefore be admissible, in accordance with the main guidelines, to expect a greater severity in the patients who started a biologic than in those who started a conventional systemic therapy. This was in fact confirmed by the evolution of the PASI index, shown in Figure 5. The severity at baseline, which corresponded to the first administration of the ongoing treatment, highlighted a significantly greater severity for the biologic than for the conventional systemic therapy (19.8 vs. 13.9; p=0.0005).

Overall (direct and indirect costs), during the six-month follow-up, the average cost per patient treated with a biologic was € 5.657 (± 1.667), while that of the conventional systemic therapy was € 321 (± 201). In both groups, direct medical costs (conventional systemic therapy: 84.1%; biologic: 99.2%) were greater than the indirect ones caused by the loss of working days.

Regardless of the ongoing pharmacological therapy, a greater severity of psoriasis corresponded to a higher cost of treatment. In the patient treated with a conventional systemic therapy costs ranged from a six-month average of 301 € with absent-mild psoriasis to a six-month average of € 416 with moderate-to-severe psoriasis (+38%; p=0.0301). In the patient treated with the biologic the increase was instead of 55% (p<0.0001), from € 5,179 (absent-mild psoriasis) to € 8,013 (moderate-to-severe psoriasis).

It was not possible to make a direct comparison of the results found here versus those estimated by other national experiences, due to differences in the duration of the observation, in the case histories of patients enrolled and in the costs of treatment considered. However, in order to allow a rough comparison, it was necessary to "adjust" the data collected here to those of other experiences. For example, the retrospective observational study conducted by Guerriero et al. estimated, using data from an administrative database of a South Italian Local Healthcare Unit (ASL, Azienda Sanitaria Locale), an average annual cost per patient treated with a biologic of € 10,536. If-

with regard to the data collected by us-we considered only the direct healthcare costs for patients receiving a biologic, under the hypothesis of being able to extrapolate them to one year, we would get an average cost per patient treated equal to € 11,222, in line with what estimated by Guerriero et al. [18].

Colombo et al. reported an average social annual cost per patient with moderate-to-severe psoriasis of € 8,372: also in this case, the equivalent figure extrapolated from our analysis, equal to € 7,584, was consistent with Colombo's results [14].

Among the limitations attributable to this analysis, some are to be highlighted. First, the sample refers to a single Center, although as a reference for an entire Region. Unfortunately, there are no elements to define the extent to which it can be considered representative of the entire Italian reality, that is how the costs of the disease reported here may be over- or underestimated, with respect to such reality. However, we have seen that-compared with other analyses made in relation to the national context-the degree of information inequality appears to be minimal.

It may be hypothesized that these results may underestimate the total costs of the disease. For example, the analysis did not consider the costs borne directly by patients (out-of-pocket). The adoption of the human capital method to estimate indirect costs (lost workdays) took account only of patients or caregivers who have a paid job, excluding the unemployed, pensioners, students and housewives. Probably, the inclusion of these subjects would have increased the average amount determined by indirect costs. The study, also, did not consider the costs associated with the presence of comorbidities.

Maybe, even the choice of the time horizon may to some extent have caused an underestimation of the cost of treatment. A time horizon of one year or more would have perhaps allowed to also collecting data on the consumption of healthcare resources associated with hospitalizations or outpatient accesses for psoriasis. As a justification, it can however be observed (Figures 6 and 7) that, for the patients analyzed here, the clinical picture was good and in constant improvement; in fact, this trend is likely to exclude, over one year, the need for hospitalizations or outpatient accesses due to the worsening of the disease state.

This analysis did not have as its objective the estimation of the cost of treatment of a patient with psoriasis who started a conventional systemic therapy or a biologic, but showed a cross-section of the clinical practice being implemented in a Center of Northwest Italy. In the 6-month follow-up, in fact, most patients had already been treated for some time; only 13.3% of patients with the biologic and 3.1% of those with the conventional systemic therapy were in induction and therefore had just started therapy. It would probably have been interesting to be able to estimate a cost of treatment differentiating between prevailing patient (our case) and incidental patient. This aspect could be examined in depth in the course of future analyses.

Conclusions

The data collected and presented here-albeit limited to a single experience related to a Center of Northwest Italy-seem to be sufficient to state that psoriasis is a disease with a quite high overall cost for the

NHS and/or society, and that, due to its chronicity, such cost is likely to increase with the progression of severity.

Providing information based on real-world data is critical to explore and investigate the dynamics that characterize the use of a conventional systemic therapy and a biologic in a specific context, with the aim of optimizing the use of resources during the treatment period.

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