Long-term costs and outcomes in psoriatic arthritis patients not responding to conventional therapy treated with tumour necrosis factor inhibitors: an extension of the Psoriatic Arthritis Cost Evaluation (PACE) study

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Abstract

Objective

Poor information on long-term outcomes and costs on tumour necrosis factor (TNF) inhibitors in psoriatic arthritis (PsA) are available. Our aim was to evaluate long-term costs and benefits of TNF- inhibitors in PsA patients with inadequate response to conventional treatment with traditional disease-modifying anti-rheumatic drugs (tDMARDs).

Methods

Fifty-five out of 107 enrolled patients included in the study at one year, completed the 5-year follow-up period. These patients were enrolled in 8 of 9 centres included in the study at one year. Patients aged older than 18 years, with different forms of PsA and failure or intolerance to tDMARDs therapy were treated with anti-TNF agents. Information on resource use, health-related quality of life (HRQoL), disease activity, function and laboratory values were collected at baseline and through the 5 years of therapy. Costs (expressed in Euro 2011) and utility (measured by EQ-5D instrument) before TNF inhibitor therapy and after 1 and 5 years were compared.

Results

The majority of patients (46 out of 55; 83.6%) had a predominant or exclusive peripheral arthritis and 16.4% had predominant or exclusive axial involvement. There was a statistically significant improvement of the most important clinical variables after 1 year of follow-up. These improvements were maintained also after 5 years. The direct costs increased by approximately €800 per patient-month after 1 year, the indirect costs decreased by €100 and the overall costs increased by more than €700 per patient-month due to the cost of TNF inhibitor therapy. Costs at 5 year were similar to the costs at 1 year. The HRQoL parameters showed the same trends of the clinical variables. EQ-5D VAS, EQ-5D utility and SF-36 PCS score showed a significant improvement after 1 year, maintained at 5 years. SF-36 MCS showed an improvement only at 5 years.

Conclusion

The results of our study suggest that TNF blockers have long-term efficacy. The higher cost of TNF inhibitor therapy was balanced by a significant improvement of HRQoL, stable at 5 years of follow-up. Our results need to be confirmed in larger samples of patients.

Key words

psoriatic arthritis, anti-tumour necrosis factor agents, costs, quality of life.

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Received on May 18, 2015; accepted in revised form on July 24, 2015.

Funding: this study was sponsored by Pfizer Italy through an unrestricted research grant.

Competing interests: P.A. Cortesi has declared no competing interests; all the other authors received funding from Abbvie, Pfizer and MSD to attend scientific meetings.

Introduction

As with other chronic rheumatic disease, psoriatic arthritis (PsA) generates impairment in quality of life (QoL) to patients and significant cost to society. As a consequence, the rationale for economic assessment of available therapeutic strategies, particularly with costly treatments, has been established (1-5). However, empirical evidence of long-term cost and outcomes of biologic drug treatments is still scarce and sparse.

The costs and benefits of PsA in patients with inadequate response to traditional disease-modifying anti-rheumatic drugs (DMARDs) to be treated with tumour necrosis factor (TNF) inhibitors in clinical practice was assessed in a observational, longitudinal, ambispective (*i.e.* both retrospective and prospective) multicentre and cost evaluation study (6). The objective of the study, named Psoriatic Arthritis Cost Evaluation (PACE) Study, was to evaluate costs and benefits and cost effectiveness of the class of TNF blockers over one year of follow-up (6). Patients were eligible for the insertion in the study if they satisfied the following inclusion criteria: age older than 18 years, established diagnosis of PsA and failure or intolerance of conventional therapy.

Our aim was to evaluate long-term costs and benefits of the TNF inhibitors class in PsA patients with inadequate response to conventional treatment with DMARDs, by following patients in the PACE study at five years from enrolment.

Methods

Study design and patients

The study design is described extensively in the paper by Olivieri *et al.* (6) and can be accessed also from clinicaltrials.gov (ClinicalTrials.gov number, NCT00303186).

Briefly, patients with predominant or solely peripheral arthritis had not to have responded to adequate therapeutic trials of at least 2 non-steroidal anti-inflammatory drugs (NSAIDs) given for at least 3 months (unless contraindicated or not tolerated), to at least two steroid injections (in cases of mono- or oligoarthritis) as well as to adequate therapeutic trials of at least one of the DMARDs most commonly used in PsA (cyclosporine, leflunomide, methotrexate, sulfasalazine). Patients also had to have at least one swollen joint along with at least 2 of the following 3: patient global assessment ≥40 mm on a 100 mm visual analogue scale (VAS), ≥3 tender joints and erythrocyte sedimentation rate (ESR) ≥28 mm/1st h or C-reactive protein (CRP) ≥15 mg/L. Patients with prevalent or exclusively axial disease had to have met the modified New York criteria (7) for the diagnosis of ankylosing spondylitis (AS), had to have active disease for ≥4 weeks with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (8) ≥4 and had to have failed adequate trials of at least 2 NSAIDs given for at least 3 months, unless contraindicated or not tolerated, in accordance with the 2003 ASAS (Assessment in SpondyloArthritis international Society) recommendations for the use of anti-TNF agents in patients with AS (9).

A total of 107 patients with PsA were enrolled in nine Italian tertiary referral centres (6) and followed to evaluate costs and benefits of the class of TNF-α inhibitor over five years.

The study protocol was approved by the institutional review board of each participating centre and the written informed consent was obtained for each subject according to the declaration of Helsinki. The study was monitored by a contract research organisation and was sponsored by Pfizer Italy through an unrestricted research grant.

Observation period

Patients enrolled were studied globally for 66 months, by extending the original one year prospective follow-up period up to five years (+6 months retrospective assessment). They were asked to provide information on resource use and health-related QoL (HRQoL) in the 6 months preceding the baseline visit and at the 1-year follow-up visit and in the three years preceding the end of the study, *i.e.* the third, fourth and fifth year of follow-up.

Data collection

To assess the cost of care and the HRQoL, patients were questioned by

means of a specifically designed structured electronic case report form (CRF; available on request from author), which was administered to them by a physician at each participating centre and filled in by the physician to make certain that data were of high quality.

As previously reported, at the time of the enrolment visit information was obtained on demographic and clinical characteristics, HRQoL and economic aspects (6). This information was also collected prospectively during the follow-up period at 12 and 60 months. At the 60-month follow-up visit, the information on resource absorption of health care and non-health care resources referred to the last three years of follow-up. To minimise the potential for recall bias on cost estimates, most of the information were collected from medical records.

As described in the previous article (6), information on clinical and outcomes data recorded at enrolment and during the follow-up visits included laboratory parameters (blood cell count, transaminases, creatininemia, ESR mm/h, CRP mg/liter and rheumatoid factor), 68/66 tender/swollen joint count (10), number of digits with dactylitis, Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) (11), BASDAI (8), Bath Ankylosing Spondylitis Functional Index (BASFI) (12), occiput-to-wall distance, chest expansion, modified Schober's test (13), physician's and patient's global assessments of pain and overall disease activity (0–10-cm VAS), duration of morning stiffness, Psoriasis Area and Severity Index (PASI) (14), Health Assessment Questionnaire (HAQ) (15), EuroQol (EQ-5D) (16, 17) and Medical Outcome Survey Short Form-36 (SF-36) (18, 19). At inclusion, data on previous and current treatment with DMARDs, analgesic, NSAIDs and corticosteroids were recorded. During follow-up, any modifications of these drugs and of TNF-α inhibitor treatment were registered.

Cost-of-care analysis

As in the one year follow-up (6), costs were quantified considering the societal perspective, using updated unit cost estimates. Health care resources absorbed were computed into monetary terms in the perspective of the third-party payer, the National Health Service (NHS), which in Italy, is in charge of funding and providing health care services to patients with PsA. Direct medical costs paid by the NHS were computed by multiplying resources absorbed by their unit cost. They included the cost of therapies, laboratory and other diagnostic examinations, hospitalisations, surgery, rehabilitation procedures, physicians' visits, and any other possible cost (20, 21). Diagnosis-related group (DRG) charges were applied to estimate the cost of hospitalisations (22).

Costs of transport were quantified in the patients' perspective. Indirect costs absorbed for patients' assistance, and caregivers' and patients' absenteeism were quantified in the perspective of patients and their family, using the human capital approach. As salaries we used the average reported by the Italian Institute of Statistics for each work category (23). Indirect cost attributable to reduction in or cessation of working ability were not quantified because of the relatively short-term observation period before the enrolment visit and of the nature itself of PsA.

We report costs as overall social cost, which include direct costs and indirect costs as defined above. All costs are expressed in Euro from the year 2011 and are computed as Euro per patient-month.

Health-related Quality of Life

Health-related quality of life was assessed with a battery of two well established and standardised instruments suitable for patients with Psoriatic Arthritis: the generic EQ-5D (16, 17) and the SF-36 (18, 19).

EQ-5D consists of two main parts: the first part generates a health profile (EQ-5D profile) made of 5 domains, namely "mobility", "self care", "anxiety or depression", "usual activities" and "pain or discomforts", each one with three levels of severity ("no problem", "some/moderate problems", "extreme problems/impossible to do"). The second part of the questionnaire consists of a visual analogue scale (EQ-5D VAS), measuring overall health-related quality of life ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). Results from the EQ-5D descriptive system can be converted to utility index, useful to conduct economic evaluations, by means of an algorithm that uses population-based (social) values (24). Specific conversion values for the Italian population were used to convert our EQ-5D descriptive system results in EQ-5D utility index (24).

SF-36 assesses HRQoL in eight dimensions related to the physical and mental components of health. It is possible to synthesise the information obtained with the eight domains into two summary scores, one specific for physical health (Physical Summary Score - PCS) and the other for mental health (Mental Summary Score - MCS): the higher the score, the better the component of HRQoL measured.

Statistical analysis

For cost-of-care analysis, we used means as central tendency parameters, generally expressed as mean cost per patient per month and per patient per year, because this parameter can be easily used to make projections on different populations and is of easy use for policy makers. Costs were stratified according to their category, *i.e.* direct healthcare and indirect costs. Descriptive statistics were applied also to define HRQOL and health status measurement variables.

To evaluate the comparability between individuals participating only in one year study (6) and patients included in a 5-year follow-up analysis, between-group testing was performed with an independent sample *t*-test for continuous variables and a Chi-square test or Fisher's exact test for nominal variables.

One-way repeated measures ANOVA (with time set as repeated factor) was used to assess the trend of patient clinical characteristics and HRQoL during the observational period. A Greenhouse-Geisser correction was applied if the assumption of sphericity was not respected. If the trend was statistically significant ($p<0.05$), multiple comparisons using the Bonferroni correction

Table I. Baseline patient characteristics.

Variable description		All sample‡	Patients with only one year of follow-up	Patients with five year of follow-up	*p*-value
Total number of patients		107	52	55	
Patients with predominant peripheral arthritis, no (%)		87 (81.3%)	41 (78.9%)	46 (83.6%)	0.525*
Patients with predominant axial involvement, no (%)		19 (18.8%)	10 (19.3%)	9 (16.4%)	0.698*
Patients with exclusive peripheral enthesitis, no (%)		1 (0.9%)	1 (1.9%)	0 (0.0%)	0.486**
Male patients, no (%)		51 (47.7%)	22 (42.3%)	34 (61.8%)	0.043*
Age (years)	Mean (SD)	49.68 (11.70)	50.43 (12.08)	48.94 (11.09)	0518†
	95% CI Lower, Upper	47.47; 51.90	47.07; 53.80	45.94; 51.94	
Years since diagnosis of PsA	Mean (SD)	7.32 (7.40)	7.00 (6.68)	7.64 (7.41)	0.654†
	95% CI Lower, Upper	2.89; 8.28	5.08; 8.92	5.57; 9.70	
Patient's assessment of pain (0-100)	Mean (SD)	62.83 (21.10)	64.96 (19.92)	60.85 (22.15)	0.319†
	95% CI Lower, Upper	58.77; 66.90	59.36; 70.56	54.87; 66.84	
Patient's assessment of disease activity (0-100)	Mean (SD)	63.51 (17.25)	65.94 (14.96)	61.24 (19.03)	0.164†
	95% CI Lower, Upper	60.18; 66.86	61.73; 70.15	56.03; 66.44	
Physician's assessment of disease activity (0-100)	Mean (SD)	60.15 (13.33)	59.84 (12.15)	60.44 (14.47)	0.818†
	95% CI Lower, Upper	57.57; 62.37	56.43; 63.26	56.50; 64.39	
Swollen joint count (0-66)	Mean (SD)	7.60 (6.39)	8.06 (6.43)	7.16 (6.39)	0.473†
	95% CI Lower, Upper	6.37; 8.82	6.27; 9.85	5.44; 8.89	
Tender joint count (0-68)	Mean (SD)	16.97 (11.80)	20.02 (11.70)	14.09 (11.27)	0.009†
	95% CI Lower, Upper	14.71; 19.24	16.76; 23.28	11.04; 17.14	
MESES index (0-13)	Mean (SD)	3.65 (3.76)	3.96 (3.29)	3.36 (4.17)	0.411†
	95% CI Lower, Upper	2.93; 4.37	3.05; 4.88	2.24; 4.49	
BASDAI (0-10)					
All patients	Mean (SD)	5.95 (1.82)	6.35 (1.48)	5.57 (2.04)	0.025†
	95% CI Lower, Upper	5.60; 6.30	5.94; 6.77	5.02; 6.12	
Patients with axial involvement	Mean (SD)	6.40 (1.72)	6.56 (1.45)	6.23 (2.07)	
	95% CI Lower, Upper	5.57; 7.24	5.52; 7.60	4.64; 7.82	
Patients with peripheral involvement	Mean (SD)	5.86 (1.84)	6.35 (1.49)	5.45 (2.03)	
	95% CI Lower, Upper	5.48; 6.26	5.87; 6.82	4.84; 6.05	
BASFI (0-100)					
All patients	Mean (SD)	43.37 (24.49)	51.83 (22.35)	5.38 (23.92)	<0.001†
	95% CI Lower, Upper	38.68; 48.07	45.61; 58.05	28.91; 41.85	
Patients with axial involvement	Mean (SD)	49.94 (22.29)	58.45 (20.30)	40.49 (21.54)	
	95% CI Lower, Upper	39.19; 60.69	43.92; 72.97	23.93; 57.04	
Patients with peripheral involvement	Mean (SD)	41.87 (24.96)	50.28 (23.03)	34.38 (24.46)	
	95% CI Lower, Upper	36.55; 47.19	43.01; 57.55	27.12; 41.64	
PASI (0-72)	Mean (SD)	5.04 (7.29)	4.42 (7.63)	5.63 (6.99)	0.393†
	95% CI Lower, Upper	3.64; 6.44	2.30; 6.54	3.74; 7.52	
HAQ (0-3)	Mean (SD)	1.14 (0.57)	1.23 (0.57)	1.06 (0.58)	0.119†
	95% CI Lower, Upper	1.03; 1.25	1.07; 1.39	0.90; 1.21	
Therapies in the 6 months before enrolment					
Leflunomide		12 (11.2%)	6 (11.5%)	6 (10.9%)	
Methotrexate		53 (49.5%)	33 (63.5%)	20 (36.4%)	
Sulfasalazine		15 (14.0%)	10 (19.2%)	5 (9.1%)	
Glucorticoids		46 (43.0%)	31 (59.6%)	15 (27.3%)	
NSAIDs		42 (39.3%)	21 (40.4%)	21 (38.2%)	
COXIBx		27 (25.2%)	10 (19.2%)	17 (30.9%)	
no DMARDs		37 (34.6%)	20 (38.5%)	17 (30.9%)	

‡Baseline characteristics of all patients included in the 2008 study (5).
**p*-value is produced using Chi Square test; ***p*-value is produced using Fisher's exact test; †*p*-value is produced using the Independent Sample *t*-test.

were performed to assess the differences between each pair of examinations. Bootstrap *t*-test with 500 replications was used to compare direct and indirect healthcare costs. *P*-values <0.05 were considered statistically significant. All analyses were performed using STATA version 12.0 software.

Results

A total of 55 out of 107 enrolled patients included in the study at one year (6), completed the 5 years follow-up period (January 2005-December 2010) (Table I). These patients were enrolled in 8 of 9 centre included in the study at one year (5). Fifty-two out of 107 patients evaluated at one year were lost to follow-up. Twenty patients enrolled in one centre were lost since one of the authors (EL) moved to another centre. The remaining 32 patients were lost to follow-up because they denied their consent to long-term study, mainly for logistic reasons (20 pts) or because

Table II. Number of patients (%) according to the use of TNF-α inhibitor drugs during the study period.

Variable description	1st year of follow-up	5 years of follow-up
Patients using only one TNF inhibitor, of which:	54 (98.2%)	44 (80.0%)
Etanercept	45 (81.8%)	35 (63.6%)
Adalimumab	3 (5.5%)	3 (5.5%)
Infliximamb	6 (10.9%)	6 (10.9%)
Patients using 2 drugs in mono therapy, of which:	1 (1.8%)	7 (12.7%)
Adalimumab switched to Etanercept	1 (1.8%)	1 (1.8%)
Etanercept switched to Adalimumab	-	5 (9.1%)
Etanercept switched to Infliximamb	-	1 (1.8%)
Patients using 3 drugs in mono therapy, of which:	0	1 (1.8%)
Etanercept switched to Adalimumab switched to Infliximamb	-	1 (1.8%)
Patients interrupted TNF inhibitor without switching to another, of which:	0	3 (5.5%)
Etanercept	-	3 (5.5%)

they had side effects (7 pts) or their disease entered in a state of persistent remission (5 pts).

Fifty-five patients involved in the analysis at 5 years were comparable to 52 lost after the first year of treatment (Table I). Thirty patients were males (61.8%) and mean age 48.94±11.09 years. The majority of patients (83.6%) had a predominant or exclusive peripheral arthritis and 16.4% had predominant or exclusive axial involvement. During the 5 years of follow-up, 44 out of the 55 patients (80.0%) received only one TNF inhibitor (Table II). One patient switched from one to another TNF blocker one time during the first year of follow-up, while at the 5-year follow-up, seven patients switched one time and 1 patient switched two times. Three patients stopped the treatment with TNF blocker after the first year of follow-up without switching to another one.

Table III shows the trends of the most important clinical variables during the 5 years of follow-up. There was a statistically significant improvement of levels of pain and disease activity, numbers of swollen and tender joints, MASES, BASDAI, BASFI, HAQ and PASI after 1 year of follow-up. These improvements were maintained at 5 years. Statistical significant differences ($p<0.05$) were observed in all clinical variables between the baseline and 1 year of follow, while no significant differencse ($p>0.05$) were observed between 1 and 5 years of follow-up.

There was a statistically significant increase of the overall costs from the baseline to 1 year of follow-up (Table IV). The overall cost remained similar between 1 and 5 years of follow-up (Table IV). Cost items varied during the observational period. The main cost item before the enrolment was the indirect costs while at one and five years was the pharmaceutical treatment. Indirect cost were 50.2% of total costs before enrolment, but decreased to 3.5% and 1.2% after one and five years of follow-up. Pharmacological treatment increased from 35.6% before enrolment to 91.7% and 96.0% after 1 and 5 years. The overall cost significantly increased by approximately € 700 per patient-month at one and five years and direct cost by more than € 800, caused by an increase of drug cost due to TNF-α inhibitors. The increase of direct cost was partially offset by the decrease in indirect cost.

As regards HRQoL, after 1 year of follow-up there was a statistically significant improvement in the EQ-5D VAS, EQ-5D utility and SF-36 PCS scores (Table V). After 1 year, an improvement of 18.4 was observed in the EQ-5D VAS and an improvement of 0.12 in the EQ-5D utility. The SF-36 PCS showed an improvement of 7.3. These improvements were maintained at 5 years (Table V). No difference was observed in the SF-36 MCS score after 1 year, while a statistically significant improvement was observed in this parameter after 5 years of follow-up (Table V).

Figure 1 shows the EQ-5D profile results. At baseline, 70% or more of patients reported "some/moderate" problems in all five domains. Seventy-six percent of the patients declared moderate pain or discomfort and 22.2% re-

Table III. Trends of clinical characteristics during the study period.

Variable description		Baseline	1 year of follow-up	5 year of follow-up	*p*-value*
Patient's assessment of pain	Mean (SD)	60.9 (22.2)	29.4 (24.9)	32.8 (26.7)	<0.01
Physician's assessment of disease activity	Mean (SD)	60.4 (14.3)	26.7 (19.7)	24.3 (17.9)	<0.01
Patient's assessment of disease activity	Mean (SD)	61.2 (18.9)	31.1 (23.8)	33.2 (24.5)	<0.01
Swollen joint count	Mean (SD)	7.2 (6.4)	1.2 (2.0)	1.0 (1.9)	<0.01
Tender joint count	Mean (SD)	14.1 (11.3)	6.2 (8.6)	5.5 (9.3)	<0.01
MASES	Mean (SD)	3.4 (4.2)	2.0 (3.6)	1.4 (2.5)	<0.01
BASDAI	Mean (SD)	5.6 (2.0)	3.1 (2.3)	3.3 (2.5)	<0.01
BASFI	Mean (SD)	35.4 (23.9)	22.4 (20.8)	23.0 (23.1)	<0.01
HAQ	Mean (SD)	1.1 (0.6)	0.6 (0.5)	0.7 (0.6)	<0.01
PASI	Mean (SD)	5.6 (7.0)	1.7 (2.2)	2.0 (3.7)	<0.01

*p-value is produced using one-way repeated measures ANOVA.

Table IV. Trends of Direct and Indirect costs during the study period.

Variable description	Baseline		1 year of follow-up		*p*-value*	5 years of follow-up		*p*-value**
	Mean €/pat-month	%	Mean €/pat-month	%		Mean €/pat-month	%	
Pharmacological treatment	94.6	35.6	892.3	91.7	<0.01	946.7	96.0	0.507
Hospitalisations	18.8	7.1	20.8	2.1	0.914	17.0	1.7	0.817
Diagnostic examinations, laboratory analysis and specialist visits	11.3	4.2	15.8	1.6	0.060	8.6	0.9	<0.01
Transport	7.8	2.9	10.6	1.1	0.212	2.6	0.3	<0.05
Indirect costs	133.4	50.2	33.7	3.5	<0.05	11.6	1.2	<0.05
Total costs	265.9		973.3		<0.01	986.5		0.872

*p-value is produced using the bootstrap T-test comparing baseline with 1 year of follow-up data.
**p-value is produced using the bootstrap T-test comparing 1 year of follow-up with 5 years of follow-up data.

ported severe pain or discomfort. Thirteen percent of the patients declared severe anxiety or depression. After one year and at the end of follow-up the number of patients with "no problems" increased significantly in all five domains.

The results of the SF-36 8 domains are shown in Figure 2. Low levels were detected at baseline in all domains with the lowest values in the role-physical and bodily-pain and the highest in social functioning, energy/vitality and mental health. HRQoL improved as demonstrated by the significantly higher values also in SF-36 after 1 and 5 years of follow-up. Only energy/vitality and mental health domains showed a similar score after one year of follow-up, however, also these domains reported an improvement after 5 years.

Discussion

Anti-TNF agents are very costly new treatments, which provide an important option for the management of PsA (26-31). These drugs reduce inflammation, slow radiographic joint damage progression and increase function and QoL (27-30). However, poor information on long-term outcomes and costs on anti TNF-α in PsA are available. To the best of our knowledge, ours is the first pharmacoeconomic study on anti-TFN drugs in PsA in clinical practice with a long-term follow-up. The previous 1 year published results of this study were the only ones based on data directly collected (6), while the other studies dealt with data from published international trials (32-34).

The monthly cost for the society of PsA treatment before the beginning of the study was €266, the same of the results in the 1 year follow-up study (€253) (6). These results were different from what found in two other European countries (Germany and Hungary), where the total cost per year was higher: €11,075 and €4,281, respectively. (35, 36). The differences were due to the type of costs considered in the studies but also to the economic status, health care and insurance systems. Indeed, when comparable costs (*i.e.* direct healthcare cost) are considered, our estimate of pre-treatment cost of approximately €133 per patient-month is in line with the estimate of about €3,100 and €1,681 per patient-year, taking into account that our patients have shorter disease duration and higher functional status (6).

Table V. Trends of HRQoL during the study period.

Variable description		Baseline	1 year of follow-up	5 years of follow-up	*p*-value*
EQ-5D VAS	Mean (SD)	50.6 (20.5)	69.0 (21.2)	64.2 (20.9)	<0.01
EQ-5D Utility	Mean (SD)	0.67 (0.18)	0.79 (0.15)	0.80 (0.14)	<0.01
SF-36 PCS	Mean (SD)	34.6 (7.9)	41.9 (11.8)	40.8 (9.5)	<0.01
SF-36 MCS	Mean (SD)	39.8 (6.2)	39.7 (9.1)	45.0 (12.4)	<0.01

*p-value is produced using one-way repeated measures ANOVA.

The patients of the present study had low EQ-5D and SF-36 scores at baseline. As explained in the 1-year follow-up study (6), utility values appeared to be lower than the ones that could have been expected from disease activity and function values. This probably reflects the negative effect of psoriasis on HRQoL (37) even if the baseline PASI score was only 5.6.

After 1 and 5 years of observation there was a significant increase in the vast majority of SF-36 and EQ-5D domain scores resulting in a gain in EQ-5D utility of 0.12 and 0.13 after 1 and 5 years of follow-up. This was due to the significant improvement of PsA disease activity, function status and psoriasis that persisted after 5 years from the beginning of the treatment. These improvements were lower to 0.25 obtained at 1 year with the full sample (6) only because in this study we used the Italian algorithm, to estimate the EQ-5D utility values, that was not available at the time of the publication of the 1-year follow-up study (6). In that study we used the UK algorithm (38) that showed a large differences, however using the Italian algorithm also in the 1-year follow-up study the EQ-5D utility improvements was 0.14 similar of what obtained in this study.

The overall cost for the society increased by €707.4 and €720.6 per patient-month after 1 and 5 years of follow-up, as a consequence of the high costs of TNF-α inhibitors. This increase due to the pharmacological treatment was only partially offset by the reduction of €99.7 (after 1 year) and €121.8 (after 5 year) of the indi-

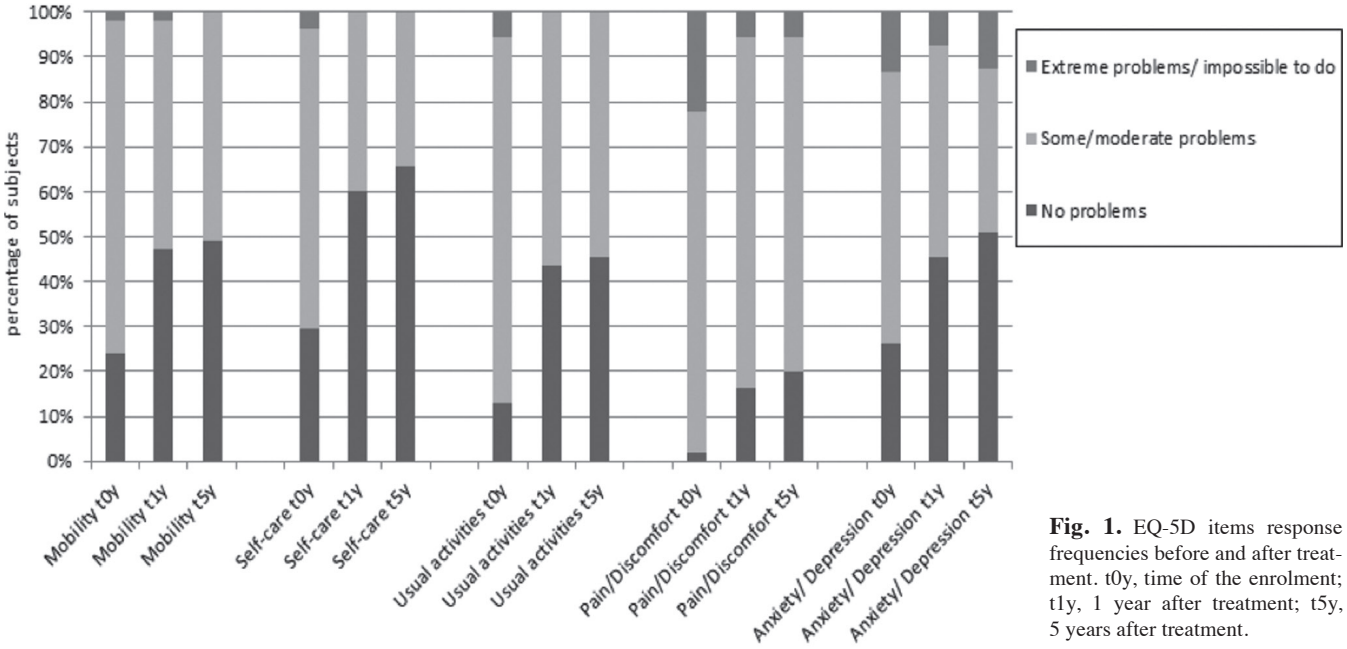

Fig. 1. EQ-5D items response frequencies before and after treatment. t0y, time of the enrolment; t1y, 1 year after treatment; t5y, 5 years after treatment.

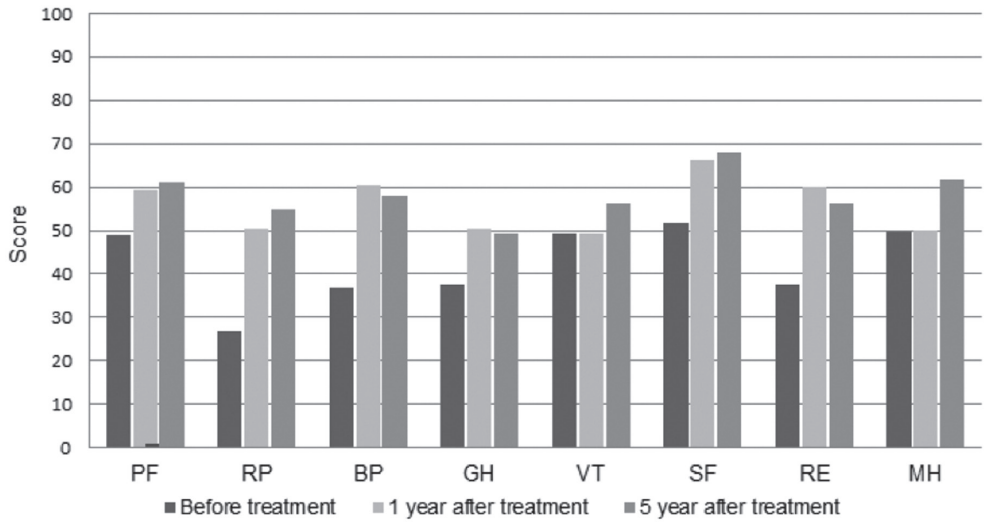

Fig. 2. SF-36 8 domains results before and after treatment with TNF inhibitors. PF: physical functioning; RP: role-physical; BP: bodily pain; GH: general health; VT: energy/vitality; SF: social functioning; RE: role-emotional; MH: mental health.

rect costs. The increasing of the overall cost and the decreasing of the indirect cost at 1 and 5 years of follow-up were similar to what found in the 1-year follow-up study (6).

Few limitations could be ascribed to our study. Firstly, our results could be less reliable since 55 out of the 107 enrolled patients included in the study at one year (6) completed the 5-year follow-up period. Indeed, 52 out of the 107 patients evaluated at one year were lost to follow-up. However, almost 40% of the 52 patients were lost to follow-up because enrolled in a centre that was not involved in the 5 years follow-up study since the Principal Investigator (EL) moved to another centre. The remaining 32 patients were lost for different reasons *i.e.* they denied their consent to long-term study, mainly for logistic reasons (long distance from home and the study site, etc.), their disease entered in a state of persistent remission or they had side effects. Despite some patients (12 of 107, 11.2%) denied their consent to long-term study due to anti-TNF side effects or because the diseases entered in a state of persistent remission, the majority were lost for non-drug related specific reasons, so our results can be considered reliable for assessing the impact of patients with PsA constantly treated with anti-TNF over a 5-year period. Other limitations are related to the comparison between the baseline and 5 year of follow-up since it is possible that in the period between 2005 and 2010, costs and QoL of these patients changed for causes independent from the use of TNF inhibitors *i.e.* increasing age, change in the health care system, new comorbidities, etc. However, some of these causes (*e.g.* increasing age and new comorbidities) should lead to an increasing in costs and an impairment of the QoL and this issue could make our results conservative.

In conclusion, this study provides empirical evidence of long-term efficacy of TNF inhibitors in the treatment of PsA in clinical practice. The total cost of a patient treated with TNF inhibitors

is high, but this cost is balanced by a significant and lasting improvement of HRQoL and patients' productivity with a reduction of indirect costs. Ideally, our results should be confirmed by prospective studies in larger numbers of patients with different disease duration, severity and functional disability.

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