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Conflict of interest

H Bachelez has paid activities as consultant, advisor, or speaker for Abbvie, Amgen, Baxalta, Biogen, Boehringer-Ingelheim, Cegene, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, UCB and Sun Pharmaceuticals; grant support from Pfizer; **C Paul** has been an investigator and consultant for AbbVie, Amgen, Boehringer Ingelheim, Celgene, GSK, Janssen, LEO Pharma, Lilly, Novartis, and Pfizer ; **M Beylot-Barry** has consultancies and is investigator for Abbvie, Amgen, Celgene, Janssen, Leo Pharma, Lilly, MSD, Novartis, Pfizer; **M Viguier** has been reimbursed for international conference attendance by Janssen and Abbvie and has been paid as consultant by MSD, Pfizer, Abbvie and Jansen; **JP Lacour** has received grants for investigation from AbbVie and Janssen ; has received honoraria as speaker from AbbVie and has been reimbursed for congress attendance by Abbvie; **P Bravard** has been an investigator for Abbvie; and has received speaker honoraria from Abbvie, Janssen, and Pfizer ; **E Mahé** is a consultant for Novartis, Abbvie, Pfizer, Janssen, has been an investigator for Leo Pharma, Amgen, AstraZeneca, Abbvie, Novartis, and Pfizer, and has received speakerhonoraria from Abbvie, Janssen, Novartis, and Pfizer; **N Beneton** has been an investigator for Pfizer, and Novartis; is a consultant for Janssen; and has received speaker honoraria from Janssen**; L Misery** was consultant for Abbvie, Almirall, Astellas, BASF, Beiersdorf, Bioderma, Clarins, Expanscience, Galderma, GSK, Janssen, Maruho, Novartis, Pierre Fabre, Sanofi and Uriage **; S Barbarot** has received research grants from Pierre Fabre Laboratory and Fondation pour la dermatite atopique **; S Regnier** has been reimbursed for international conference attendance by Pfizer and Abbvie**, D Jullien** is consultant for Abbvie, Celgen, Novartis, Lilly, Janssen, Pfizer, and Merck Sharpe & Dohme, **MA Richard** has consulting activities for Pfizer, Leo Pharma, Janssen, Galderma, AbbVie, Novartis, Pierre Fabre, Merck and BMS**; P Joly** is consultant for Roche, GSK, Lilly, Principabio, Sanofi Aventis; **O Chosidow** has received

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Abbreviations used

anti-TNFα: anti-tumor necrosis factor α

ADA: adalimumab

IFX: infliximab

ETA: etanercept

USK :Ustekinumab

OR: Odds ratio

95%CI: 95% confidence interval

IQR: interquartile range

Abstract

Background.

Decision making is a complex process. The aim of our study was to assess factors associated with the choice of the first biological treatment in patients with moderate-to-severe psoriasis.

Methods

Data on all patients included in the French prospective, observational, cohort, Psobioteq and initiating a first biologic prescription between July 2012 and July 2016 were analysed. Demographic information and clinical features were collected during routine clinical

assessments by the dermatology team at the recruiting centres using a standardized case report form. The primary outcome was the nature of the first biologic treatment. Four groups were identified: adalimumab, etanercept, ustekinumab and infliximab groups. Factors associated with the choice of the first biological agent were determined by a multinomial logistic regression model adjusted on year of inclusion.

Results

The study population included the 830 biological-naïve patients who initiated a first biological agent. The mean age was 46.6 years (+/-SD 13.9), and 318 patients (38.3%) were female. The most commonly prescribed biologic was adalimumab: 355 (42.8%) patients, then etanercept (n=247, 29.8%), ustekinumab (n=194, 23.4%) and infliximab (n=34, 4.0%). In the multinomial logistic regression analysis, patients were significantly more likely to receive adalimumab if they had a severe psoriasis as defined by baseline PASI or if they had psoriatic arthritis compared to etanercept (aOR, 0.42; 95%CI, 0.16 to 1.07) and ustekinumab (aOR, 0.15; 95%CI, 0.04 to 0.52). Patients were significantly more likely to receive ustekinumab (aOR, 2.39; 95%CI, 1.04 to 5.50) if they had a positive screening for latent tuberculosis compared to adalimumab. Younger patients were also more likely to receive ustekinumab. Patients with chronic obstructive pulmonary disease were more likely to be prescribed ustekinumab or etanercept compared to adalimumab. There was a trend in favor of etanercept prescription in patients with cardiovascular co-morbidities, metabolic syndrome and in patients with a history of cancer.

Conclusion

We identified patient and disease related factors that have important influence on the choice of the first biological agent in clinical practice. Clinicians appear to have a holistic approach to patient characteristics when choosing a biological agent in psoriasis.

Introduction

Psoriasis is a chronic inflammatory disease of the skin with a prevalence ranging from 0.9% (United States) to 8.5% (Norway) (1). Although there is currently no cure for psoriasis, various treatments strategies allow reaching sustained control of disease signs and symptoms. It is estimated that about 10-20% of patients with moderate-to-severe psoriasis require a systemic therapy, including phototherapy and conventional systemic treatments such as ciclosporine, methotrexate, fumaric acid and acitretin (2). Systemic biologic treatments, such as tumor necrosis factor antagonists (infliximab, etanercept, adalimumab), ustekinumab which targets interleukin-12 and 23 (IL12/23), and more recently the monoclonal antibodies secukinumab and ixekizumab that targets interleukin-17 have been developed in psoriasis since 2004, and have been positioned as third-line therapies by French and/or European regulatory bodies, with mandatory reimbursement criteria that patients must meet before being considered for these treatments : moderate to severe disease after failure, intolerance or contraindication to conventional systemic agents (2, 3).

National or European guidelines do not currently include decision rules for the choice of the treatment in moderate to severe psoriasis excepting the NICE clinical guidelines in the UK which propose methotrexate as first line conventional systemic treatment (4). Likewise, no recommendation address the choice of the first biological treatment leaving an area of uncertainty regarding factors that may influence treatment choices such as patients profile including age, sex and comorbidities. Additional extrinsic factors such as perceived benefice/risk balance of treatment, prescriptions habits, marketing, healthcare organization may have a role.

The aim of our study was to assess patient-related factors associated with the choice of the first biological treatment.

Materials and Methods

Study design

Psobioteq is the French prospective, observational, multicenter register that enrolls and follow prospectively adult patients with moderate to severe psoriasis. Patients treated with biologic therapies including, adalimumab, etanercept, infliximab and ustekinumab, i.e. all marketed biologics in the psoriasis indication in France. constitute the "exposed" group whereas patients treated with conventional systemic treatments form the "non-exposed" group. The objectives of Psobioteq are to describe the use, benefit and risks of conventional and biological systemic treatments in a real-life setting. Psobioteq is currently recruiting patients from 41 dermatology departments across France. Briefly, adult patients (≥18 years) with a diagnosis of psoriasis according to a dermatologist who started, a biological treatment or who switched to a different biological are eligible for inclusion into the "biological treatment" exposed group. To be eligible for inclusion into the non-exposed group (conventional systemic therapies), patients should have started therapy with methotrexate or ciclosporin within the previous 3 months, be aged ≥18 years. The choice of treatment was made in the context of usual care, at the physician's discretion and was not induced by the participation to the Psobioteq cohort.

The present cross-sectional ancillary study was nested in the exposed group of the Psobioteq cohort and included the subgroup of patients who were biologic naïve and received a first biological agent.

The study protocol was approved by the « Comité d'Evaluation de l'Ethique des projets de RechercheBiomédicale (CEERB) du GHU Nord » (Institutional Review Board (IRB) of Paris North Hospitals, Paris 7 University, AP-HP) (authorization n° JMD/MDM/177-11)**.** Clinical Trials.gov Identifier is NCT01617018**.** Written informed consent was obtained from all patients before study inclusion.

Population& data collection

All patients initiating a first biological agent included in the exposed group of the Psobioteq cohort from the inception (July 2012) to July 2016 were included.
Demographic information including age, sex, body mass index, tobacco use, alcohol intake) and clinical characteristics were collected during clinical assessments by the dermatology team at the recruiting centres using a standardized case report form. Details regarding type and severity of psoriasis (disease duration, baseline PASI, baseline DLQI, associated inflammatory disorders, previous systemic treatment), current and previous treatments for psoriasis, patients' co-morbidities (cardio-vascular diseases, hypertension, dyslipidaemia, diabetes, viral hepatitis, immunosuppressive disorders, previous tuberculosis, tuberculosis screening, chronic renal failure, chronic obstructive pulmonary disease (COPD), Previous cancer) were recorded.
The primary outcome was the nature of the first biological agent prescribed. Four groups were identified: etanercept group, adalimumab group, infliximab group and ustekinumab group.

Statistical analysis

First, we described the choice of the first biologic treatment with mean and standard deviation (SD) for quantitative variables and with number and percentage for qualitative variables. The cumulative enrolment of patients for each type of biologic therapy prescribed was described. We divided the study period into two parts (breakpoint), the first-one from July 2012 to July 2014 and the second one from July 2014 to July 2016 and used a linear regression model with an interaction term with accrual period to determine whether the choice of the first biologic treatment varied over time.

Assessment of significant differences between the different first biological treatments and baseline characteristics (socio-demographic, psoriasis characteristics and co-morbidities)

was based on the ANOVA test for quantitative variables and on the Chi² or Fisher's exact test for categorical variables as appropriate.

Factors associated with the choice of the first biological treatment were determined by a multinomial logistic regression model adjusted for year of inclusion with a center random effect. Variables with *p* values lower than 0.20 in the univariate analyses and with less than 10% of missing data entered the selection process for the final multinomial logistic regression model by upward stepwise method based on Akaike Information Criterion (AIC). All tests were two-tailed and *p* values <0.05 were considered statistically significant. Statistical analysis was performed with R software.

Results

Study population

From July 2012 to July 2016, 2 176 patients were included in the Psobioteq cohort study. The study population included 830 biological-naïve patients who initiated a biologic treatment (Fig. 1). Table 1 reports the main characteristics of the study patients. The mean age of the enrolled population was 46.6 years (+/-SD 13.9), and 318 (38.3%) were females. The mean disease duration was 18.9 years (+/- SD 12.9). At the time of enrolment, a majority of patients had plaque-type psoriasis (n= 591, 72.3%), the mean PASI and DLQI were 13.6 (+/- SD 8.4) and 11.8 (+/- SD 7.3), respectively. The most commonly prescribed biological agent was adalimumab in 355 (42.8%) patients, then etanercept (n=247, 29.8%), ustekinumab (n=194, 23.4%) and infliximab (n=34, 4.0%). Fig. 2 reports the cumulative enrollment of patients into the Psobioteq cohort for each type of biologic therapy prescribed. Significant changes occurred regarding the choice of the biological agent between the two periods (July 2012-2014 and July 2014-2016). The trend of the slopes significantly shifted after the breakpoint in July 2014) ($p < 0.001$). The coefficient between these 2 periods almost doubled

for adalimumab compared to etanercept. Ustekinumab prescription showed an increase of 20% (Fig. 2). The increase of adalimumab first choice prescription, during the follow up period, was higher as compared to etanercept and ustekinumab.

Patients related factors associated with the choice of the first biological treatment (Figure 3).

As the number of patients receiving infliximab as a first choice biologic treatment was very low (n=34, 4.0%), the analysis was restricted to patients initiating adalimumab, etanercept or ustekinumab (n=796).

The results of the univariate analyses are presented in Table 2, fifteen variables were associated (with $p<0.2$) with the choice of a biological agent: age, previous major adverse cardiac events, cardiac arrhythmia, dyslipidaemia, diabetes, hepatitis B infection, history of tuberculosis disease, screening test for latent tuberculosis, COPD, history of cancer excluding skin cancers, plaque psoriasis type, PASI at baseline, disease duration, psoriatic arthritis, previous systemic treatment with ciclosporin. Younger patients, patients with a high risk of infection (hepatitis B infection, previous tuberculosis or positive tuberculosis screening) or patients previously treated with ciclosporin were more likely to be prescribed ustekinumab whereas patients with a more severe psoriasis as defined by baseline PASI or with psoriatic arthritis were more likely to receive adalimumab. Finally, patients with co-morbidities nicluding cardio-vascular disorders, cardiac arrhythmia, diabetes, dyslipidaemia, co-morbidities, COPD, or history of cancer were more likely to receive etanercept.
Disease duration was missing for 40% of patients and was thus excluded from the multivariable analyses as previous treatment with ciclosporin due to a center effect. In the multivariable analysis, five variables were significantly associated with the choice of a biological agent (Table 3). In the multinomial logistic regression analysis, patients were significantly more likely to receive adalimumab if they had a psoriatic arthritis compared to

etanercept (aOR, 0.42; 95%CI, 0.16 to 1.07) and ustekinumab (aOR, 0.15; 95%CI, 0.04 to 0.52). Patients were significantly more likely to receive ustekinumab (aOR, 2.39; 95%CI, 1.04 to 5.50) if they had a positive tuberculosis screening test compared to adalimumab. Three other variables including the age, the presence of a chronic pulmonary disease and the PASI score had a significant global test in the multinomial logistic regression. The choice of adalimumab for the reference category did not allow definite conclusion about the direction of the association between the choice of the first biological treatment and these three variables. However, patients with COPD were more likely to be prescribed ustekinumab or etanercept compared to adalimumab. Younger patients were also more likely to receive ustekinumab whereas patients with a higher baseline PASI tended to receive adalimumab.

Discussion

In this study investigating the factors associated with the choice of a first biological agent with psoriasis we identified patient and disease related factors that have important influence on the choice of the first biological agent in clinical practice (Figure 3). The presence of psoriatic arthritis and severe psoriasis are key parameters determining prescription of adalimumab. A history of tuberculosis is associated with use of ustekinumab. The presence of COPD, predisposing to pulmonary infection appears to drive the use of etanercept or ustekinumab over adalimumab. Young patients receive ustekinumab rather than etanercept. Finally, both the results of the univariate and multivariate analyses allow to delineate specific profiles for patients initiating a first biological agent. Young patients and patients with infectious co-morbidities were more likely to receive ustekinumab. On the opposite, severe psoriasis patients or patients with psoriatic arthritis received more frequently adalimumab. Patients with cardiac comorbidities, metabolic syndrome, or history of previous cancer tend to receive etanercept.

The fact that patients with PsA receive predominantly adalimumab may be explained by the earlier date of adalimumab commercialization for psoriatic arthritis in France as compared to ustekinumab (2008 versus 2015). However the difference in prescription between adalimumab and etanercept is more difficult to decipher as there are no differences in efficacy in psoriatic arthritis between etanercept and adalimumab(5). The better efficacy of adalimumab for skin lesions might account for this difference (6, 7). Patients with a positive TB screening were more likely to receive ustekinumab than adalimumab or etanercept. Analysis of registries of patients treated with anti TNF-α for severe inflammatory conditions demonstrated a higher risk for tuberculosis (8, 9) leading to a systematic TB screen before the first prescription of anti TNF-α (2). The risk of tuberculosis in patients treated with ustekinumab is likely to be very low as only one case was reported in an Asia trial (10). Post marketing surveillance studies reported tuberculosis exclusively in patients treated with anti TNF-α agents including patients with initial negative TB screening (12, 13).

Other factors influencing decision on the choice of the first biological agents have been identified in this study. These factors provide important information on the different patient profiles associated with the different biological agents. Overall, adalimumab appears to be associated with efficacy attributes motivating prescription in patients with more severe diseases and patients with psoriasis arthritis. Conversely, etanercept is associated with safety attributes with a trend for prescription in patients with cardiovascular comorbidities and history of cancer. Ustekinumab appears to be favored in young patients and in patients with a higher risk of infection. These differences are important to consider, especially when comparing the safety profile of biological agents in registries. It is essential to take into account the individual baseline profile of patients which is not similar across agents.

In this study, the most commonly prescribed biologic for biologic-naïve patient was adalimumab. These results are consistent with previous reports from other European psoriasis

cohorts such as BADBIR in the UK (14), DERMBIO in Danmark(15). All the biological agents were already commercialized in France during the study period e.g. etanercept then infliximab, adalimumab and ustekinumab, were respectively commercialized in 2005, 2006, 2008 and 2010 in France. However, dissemination periods were different from a biological agent to another and could partly explain the differential choice of first biological agents in our study. Other factors may have influenced the prescriber, such as mode of administration, extrapolation of real life data in other indications, mainly rheumatological diseases, emphasizing different benefit-to-risk ratio across available TNF inhibitors. A recent study focusing on rheumatoid arthritis, spondyloarthritis and psoriatic arthritis, provided evidence-based decisional statement for the first-line tailored biologic therapy in patient with inflammatory arthritis(16). They clearly defined some algorithms for the choice of biologic therapy after performing a systematic review including variables that may influence the choice of biological treatment. For example, for psoriatic arthritis, ustekinumab may represent the best choice in patients at high risk of tuberculosis; moreover the choice between anti-TNF-α and ustekinumab for psoriatic patient should be driven by the severity of the skin as ustekinumab is more efficient in skin psoriasis than in arthritis.

Strengths of the present study include the real-life design, the sample size from a national database, the detailed assessments of patient factors and the fully independent data analysis. As the first prescription of a biological treatment, in France is hospital-based and as the number of participating centres is high, this national database should to be representative of the country specific pattern. The wide inclusion criteria ensure high external validity. Nevertheless, we cannot rule out reporting bias related to patient reported characteristics. The infliximab cohort was too small to be included in the analysis. Finally, the cross sectional design does not allow conclusion about causality of the observed associations.

In conclusion the present study identifies patient and disease related factors that have important influence on the choice of the first biological agent in clinical practice. Decision making is a complex multicomponent process relying on benefit-to-risk profiles of different agents but also on other parameters such as patient and disease characteristics, patients' preferences, prescriptions' habits, organization of care, costs of therapy and promotion activities of pharmaceutical companies. The construction of algorithms should optimally include all identified factors to better characterize the decision making process in a stratified and personalized manner.

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Table 1. Major baseline demographic and disease characteristics of the study cohort (n=830)

Characteristic n=Data missing (%)	Total (n=830)	Etanercept (n=247, 29.8%)	Adalimumab (n=355, 42.8%)	Infliximab (n=34, 4.0%)	Ustekinumab (n=194, 23.4%)
Socio-demographic characteristics					
Age (years)	46.6 (13.9)	49.0 (14.4)	46.0 (13.7)	49.2 (13.1)	44.4 (13.2)
Female	318 (38.3)	103 (41.7)	135 (38.0)	10 (29.4)	70 (36.1)
BMI n=75 (9.0)	27.6 (6.0)	27.3 (5.6)	27.5 (6.2)	30 (6.0)	27.8 (6)
Current smoker n= 217 (26.1)	215 (35.1)	65 (32.5)	98 (37.7)	9 (40.9)	43 (32.8)
Disease characteristics					
Disease duration n=330 (39.8)	18.9 (12.9)	20.9 (14.4)	18.5 (12.1)	14.1 (11.6)	18.1 (12.0)
Plaque-psoriasis N=13 (1.6)	591 (72.3)	189 (77.8)	251 (71.7)	21 (61.8)	130 (68.4)
baseline PASI n=76 (9.2)	13.6 (8.4)	13.1 (8.2)	14.3 (8.4)	14.0 (10.1)	12.8 (8.2)
baseline DLQI n=237 (28.6)	11.8 (7.3)	11.3 (7.0)	12.1 (7.4)	13.9 (8.3)	11.4 (7.5)
Baseline concomitant treatment With Methotrexate	39 (4.7)	16 (6.5)	16 (4.5)	3 (8.8)	4 (2.1)

Mean (SD) for continuous variables and n (%) for categorical variables, Body Mass Index, PASI: Psoriasis Area Severity Index , DLQI : Dermatology Quality of Life Index

Table 2. Univariate analysis of factors associated with the choice of the first biological agent (n=796).

Characteristics **Data missing, n= (%)**	**Etanercept** **(n=247, 31.0%)**	**Adalimumab** **(n=355, 44.6%)**	**Ustekinumab** **(n=194, 24.4%)**	**p†**
Socio-demographic characteristics				
Age (years, SD)*	49.0 (14.4)	46.0 (13.7)	44.4 (13.2)	0.001
Female	103 (41.7)	135 (38.0)	70 (36.1)	0.46
BMI (Kg/m^2, SD) **n=73 (9.2)**	27.3 (5.6)	27.5 (6.2)	27.8 (6.0)	0.67
Current smoker **n=205 (25.8)**	65 (32.5)	98 (37.7)	43 (32.8)	0.44
Alcohol **n= 239 (30.0)**	124 (64.6)	170 (70.3)	81 (65.9)	0.42
Co-morbidities				
Cardio-vascular diseases				
Coronary artery disorders and Stroke n=8 (1.0)	15 (6.2)	9 (2.6)	6 (3.1)	0.07
Cardiac arrhythmias* n=10 (1.3)	9 (3.7)	3 (0.9)	4 (2.1)	0.05
Hypertension **n=9 (1.1)**	56 (23.0)	79 (22.6)	35(18.1)	0.40
Dyslipidaemia* **n=9 (1.1)**	64 (26.1)	73 (20.9)	25 (13.0)	0.003
Diabetes* **n=8 (1.0)**	27 (11.0)	26 (7.4)	11 (5.7)	0.11
Viral hepatitis history				
Hepatitis B infection*	6 (2.5)	2 (0.6)	4 (2.1)	0.12

n=9 (1.1)				
Hepatitis C infection n=9 (1.1)	4 (1.6)	3 (0.9)	1 (0.5)	0.60
Immunosuppressive disorders (including HIV) n=9 (1.1)	2 (0.8)	2 (0.6)	1 (0.5)	1
Tuberculosis				
Previous tuberculosis disease* n=14 (1.8)	4 (1.7)	2 (0.6)	5 (2.6)	0.12
Positive tuberculosis screening* n=77 (9.7)	23 (10.4)	36 (11.1)	34 (19.7)	0.01
Chronic renal failure n=10 (1.3)	4 (1.6)	2 (0.6)	4 (2.1)	0.23
COPD* n=8 (1.0)	14 (5.7)	3 (0.9)	3 (1.6)	0.001
Previous Cancers				
Skin cancers n=7 (0.9)	7 (2.9)	4 (1.1)	2 (1.0)	0.25
Other types of cancers* n=8 (1.0)	9 (3.7)	6 (1.7)	2 (1.0)	0.15
Disease characteristics				
Disease duration* n=318 (40)	20.9 (14.4)	18.5 (12.1)	18.1 (12.0)	0.13
Plaque psoriasis* n=13 (1.6)	189 (77.8)	251 (71.7)	130 (68.4)	0.08
Baseline PASI* n=71 (8.9)	13.1 (8.2)	14.3 (8.4)	12.8 (8.2)	0.10
Baseline DLQI	11.3 (7.0)	12.1 (7.4)	11.4 (7.5)	0.40

n=224 (28.1)				
Associated inflammatory disorders				
Inflammatory bowel disorders n=8 (1.0)	0	2 (0.6)	2 (1.0)	0.28
Psoriatic arthritis* N=8 (1.0)	30 (12.3)	63 (18.0)	8 (4.2)	$<10^{-4}$
Uveitis n=7 (0.9)	1 (0.4)	0	1 (0.5)	0.31
Previous systemic treatment				
Phototherapy n=21 (2.6)	177 (75.6)	249 (71.4)	141 (73.4)	0.52
Ciclosporin*	28 (11.3)	55 (15.5)	37 (19.1)	0.08
Methotrexate	184 (74.5)	283 (79.7)	147 (75.8)	0.28
Acitretin	1 (0.4)	1 (0.3)	1 (0.5)	1

COPD, chronic obstructive pulmonary disease.

Mean, SD (standard deviation) for continuous variables, n, % cohort for categorical variables

† *P* value by the chi-square test or the Fisher's exact test, as appropriate and the ANOVA test for quantitative data

*variables selected for the multivariate analyses

Table 3. Patients' related factors independently associated with the choice of the first biological agent in the multivariable analysis (multivariable analysis; n=796).

Variables	Odds-Ratio** 95%CI	P***
Presence of psoriatic arthritis		
Adalimumab*	1	<0.001
Etanercept	0.42 (0.16 ; 1.07)	
Ustekinumab	0.15 (0.04 ; 0.52)	
Age		
Adalimumab *	1	<0.001
Etanercept	1.16[x] (0.98 ; 1.38)	
Ustekinumab	0.85[x] (0.59 ; 1.20)	
Positive tuberculosis screening		
Adalimumab *	1	0.001
Etanercept	0.74 (0.26 ; 2.06)	
Ustekinumab	2.39 (1.04 ; 5.50)	
COPD		
Adalimumab *	1	0.02
Etanercept	8.10 (0.46 ; 143.31)	
Ustekinumab	4.19 (0.09 ; 194.67)	
PASI score		
Adalimumab *	1	0.04
Etanercept	0.97[^] (0.93 ; 1.02)	
Ustekinumab	0.97[^] (0.94 ; 1.01)	

COPD, chronic obstructive pulmonary disease.

*Reference category

**Odds ratio with 95% confidence interval (95%CI) by multinomial logistic regression adjusted for year of inclusion and entering a random effect at the centre level, using the group of patients who received adalimumab (n=355) as the reference category.

*** p value of multinomial regression

[x]OR with 95% CI giving the risk increase for a 10-year increase in age

[^]OR with 95% CI giving the risk increase for a 1-point increase in PASI

Fig 1. Flow-chart

Fig 2. Cumulative enrollment of patients into the Psobioteq cohort for each type of biologic therapy prescribed

Fig 3. Individuals factors associated with the choice of the first biological