ORIGINAL ARTICLE

Secukinumab significantly reduces psoriasis-related work impairment and indirect costs compared with ustekinumab and etanercept in the United Kingdom

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Abstract

Background Psoriasis causes work productivity impairment that increases with disease severity. Whether differential treatment efficacy translates into differential indirect cost savings is unknown.

Objective To assess work hours lost and indirect costs associated with secukinumab versus ustekinumab and etanercept in the United Kingdom (UK).

Methods This was a post hoc analysis of work impairment data collected in the CLEAR study (secukinumab vs. ustekinumab) and applied to the FIXTURE study (secukinumab vs. etanercept). Weighted weekly and annual average indirect costs per patient per treatment were calculated from (i) overall work impairment derived from Work Productivity and Activity Impairment data collected in CLEAR at 16 and 52 weeks by Psoriasis Area and Severity Index (PASI) response level; (ii) weekly/annual work productivity loss by PASI response level; (iii) weekly and annual indirect costs by PASI response level, based on hours of work productivity loss; and (iv) weighted average indirect costs for each treatment. In the primary analysis, work impairment data for employed patients in CLEAR at Week 16 were used to compare secukinumab and ustekinumab. Secondary analyses were conducted at different time points and with patient cohorts, including FIXTURE.

Results In CLEAR, 452 patients (67%) were employed at baseline. At Week 16, percentages of weekly work impairment/mean hours lost decreased with higher PASI: PASI $<$ 50: 22.8%/7.60 h; PASI 50–74: 13.3%/4.45 h; PASI 75–89: 6.4%/2.14 h; PASI $\geq$ 90: 4.9%/1.65 h. Weighted mean weekly/annual work hours lost were significantly lower for secukinumab than ustekinumab (1.96/102.51 vs. 2.40/125.12; $P = 0.0006$). Results were consistent for secukinumab versus etanercept (2.29/119.67 vs. 3.59/187.17; $P<0.0001$). Average annual indirect cost savings with secukinumab were £355 vs. ustekinumab and £1061 versus etanercept. Results at 52 weeks were similar.

Conclusions Secukinumab significantly reduced work impairment and associated indirect costs of psoriasis compared with ustekinumab and etanercept at Week 16 through 52 in the United Kingdom.

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Conflict of interest

RB Warren has received research grants from AbbVie, Almirall, Amgen, Celgene, Janssen, Lilly, Leo, Novartis, Pfizer and UCB and has received consulting fees from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, Leo, Lilly, Novartis, Pfizer, Sanofi, Xenoport and UCB. A Halliday is an employee of Novartis Pharmaceuticals UK Limited, Frimley/Camberley, UK. CN Graham is an employee of RTI Health Solutions, Research Triangle Park, NC, USA. I Gilloteau is a full-time employee of Novartis Pharma AG, Basel, Switzerland. L Miles is an employee of RTI Health Solutions, Research Triangle Park, NC, USA. D McBride is an employee of RTI Health Solutions, Manchester, UK.

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Introduction

Psoriasis is a chronic, immune-mediated skin disease characterized by well-delineated, red, scaly patches of skin (plaques) that may vary in extent, from a few lesions, typically on the elbows, knees or scalp, to more generalized involvement impacting the entire body.[1] An estimated 1.3% to 2.6% of the population in the United Kingdom (UK) is affected by psoriasis.[1,2]

The economic burden of psoriasis in Europe is considerable.[3,4] Individuals of working age are generally affected by the disease,[5] and individuals with psoriasis are significantly more likely than those without to miss work for health-related reasons and to experience impaired productivity while at work.[6] Although limited data are available on indirect costs associated with psoriasis in the United Kingdom, a study in the United States found that indirect costs comprise an estimated one-third of the total economic burden of psoriasis.[7]

The Psoriasis Activity and Severity Index (PASI), the gold standard for measuring disease severity, is a clinician-reported weighted measure of the average redness, thickness and scaliness of psoriasis lesions.[8] PASI 75 response (i.e. ≥75% improvement in PASI score from baseline) is recognized as a clinically meaningful response in clinical trials of psoriasis treatments, particularly in patients with moderate-to-severe psoriasis.[9,10] However, PASI 90 response has been suggested as the best evidence of efficacy,[9] especially as an endpoint in clinical trials in moderate-to-severe psoriasis. Owing to its importance to people with psoriasis, PASI 90 is currently considered a critical outcome and the criterion of treatment success.[11,12]

Previous studies have shown that increasing disease severity, as assessed by body surface area involvement, baseline PASI score, or other measures, results in a higher negative impact on patients' professional lives.[13–15] Accordingly, improving disease outcomes results in an increase in workplace productivity and a reduction in annual indirect costs.[16,17] However, the indirect cost savings associated with the use of alternative biologic therapies have not previously been quantified.

The objective of these analyses was to estimate and compare psoriasis-related indirect costs associated with three biologics: secukinumab, a monoclonal antibody targeting interleukin (IL)-17A; ustekinumab, a monoclonal antibody targeting IL-12/23; and etanercept, a tumour necrosis factor-α (TNF-α) inhibitor. The analyses used a UK societal perspective to help characterize cost implications of psoriasis and its treatment, also providing context for treatment, policy and reimbursement decision-making.

Methods

This was a post hoc analysis of data from a phase 3b study comparing the efficacy and safety of secukinumab versus ustekinumab (CLEAR)[18] and a phase 3 study comparing the efficacy and safety of secukinumab versus etanercept (FIXTURE).[19] Trial data at Weeks 16 and 52 were analysed.

Psoriasis activity and severity index score

PASI response was stratified into four categories for the analyses: less than 50%; 50% to 74%; 75% to 89%; and at least 90% improvement from baseline (i.e. PASI < 50, PASI 50–74, PASI 75–89 and PASI ≥ 90).

Work productivity activity impairment questionnaire

The Work Productivity and Activity Impairment Questionnaire (WPAI) is a quantitative measure of health-related work productivity loss due to a specific health condition (in this case, psoriasis). The measure assesses work time missed (absenteeism), reduced on-the-job effectiveness (presenteeism), overall work impairment (absenteeism and presenteeism) and daily activity impairment during the past week.[20] Only employed patients answered the work productivity impairment questions of the WPAI.

The WPAI was administered at Weeks 16 and 52 of the CLEAR study. WPAI data enabled calculation of overall work impairment due to psoriasis, stratified by the four levels of PASI response (i.e. PASI < 50, PASI 50–74, PASI 75–89, PASI ≥ 90). Overall, work impairment was calculated as absenteeism + (1 – absenteeism) * presenteeism, in accordance with published WPAI methodology.[20]

WPAI data and employment status were not collected in FIXTURE.

Employment parameters and costs

A human capital approach was used to value the cost of work lost.[21] Average work productivity loss was calculated as the weighted average hours of work per week for full- and part-time workers multiplied by the percentage of work impairment, derived from the WPAI measure in CLEAR. Employment parameters – including the national average proportion of full-time versus part-time employment, hours worked per week and hourly wages – were obtained from the UK's Office for National Statistics (Table 1). Weekly and annual indirect costs for each PASI response level were calculated by multiplying the work productivity loss by the average hourly wage data for full- and part-time workers, assuming the same employment parameters across all PASI response categories.

Statistical analyses

Weighted weekly and annual average indirect costs per patient per treatment were calculated in four steps: (i) overall work impairment (in per cent) by PASI response level was estimated; (ii) weekly and annual work productivity loss (in hours) by PASI response level was estimated; (iii) weekly and annual indirect costs by PASI response level were calculated, based on hours of work productivity loss; and (iv) weighted average indirect costs were calculated for each treatment, based on the percentage of patients in each PASI response category.

Because only employed patients (n = 452; 67%) answered the work productivity impairment questions of the WPAI

Table 1 UK employment and cost parameters

Parameter	Value	Source
Percentage of part-time employment	27.9%	Office for National Statistics[22]
Average work hours per week		Office for National Statistics[22]
Full time	39.2	
Part time	18.3	
Average hourly wage		Calculated as the mean weekly full-time salary (gross pay, excluding bonuses) from the Annual Survey of Hours and Earnings (Office for National Statistics divided by the mean number of full-time hours worked in a week from the UK labour market[23]
Full time	£16.43	
Part time	£11.80	

UK, United Kingdom.

questionnaire, a primary analysis consisted of the calculation of the weighted weekly and annual average indirect costs per patient per treatment using the work impairment data and the PASI response level distribution of the employed patient cohort in the CLEAR study at Week 16 (i.e. excluding the non-employed patient cohort). Baseline characteristics of employed patients receiving secukinumab and ustekinumab in CLEAR were relatively similar, except for a younger population among those who were employed and a difference in the proportion of males and females who were employed (Table 2).

Table 2 Summary of baseline characteristics in CLEAR by employment status at baseline

	Not employed (n = 201)†	Employed (n = 452)†	P Value*
Age (years), mean (SD)	48.99 (17.086)	42.98 (11.800)	<0.001
Sex, female, n (%)	72 (35.8%)	118 (26.1%)	0.012
Weight (kg), mean (SD)	87.01 (23.466)	87.36 (20.072)	0.849
Body mass index (kg/m^2), mean (SD)	29.71 (7.372)	28.74 (5.812)	0.074
Time since first PsO diagnosis (years), mean (SD)	18.27 (13.997)	17.73 (11.423)	0.606
PASI total score, mean (SD)	13.61 (8.137)	13.18 (7.437)	0.512
DLQI, mean (SD)	22.05 (8.680)	21.46 (8.165)	0.399
Presence of PsA, n (%) yes	42 (20.9%)	76 (16.8%)	0.211

*P values are based on t-test for continuous data or chi-squared test for categorical data.
†Employment data were available for 653 of 676 patients in CLEAR.
DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; SD, standard derivation.

Secondary analyses were conducted to explore the sensitivity of the results at different time points, with different PASI response level distributions, and among different treatment subgroups:

- Secondary analysis 1: To assess the longer-term effect of secukinumab versus ustekinumab in CLEAR, weighted weekly and annual average indirect costs per patient per treatment were calculated using the work impairment estimates and PASI response level distribution for the employed patient cohort in CLEAR at Week 52.
- Secondary analysis 2: To test the sensitivity of the results to PASI response level distributions from CLEAR, weighted weekly and annual average indirect costs per patient per treatment were calculated among employed patients using the work impairment estimates for the employed patient cohort but using the PASI response level distribution for *all* CLEAR patients (employed and non-employed) at Weeks 16 and 52.
- Secondary analysis 3: Because employment patterns in CLEAR were similar to other psoriasis trials,[24] employment patterns in FIXTURE were assumed to be similar to those in CLEAR. To assess the indirect costs of secukinumab versus etanercept in FIXTURE in the absence of work impairment data collected in FIXTURE, weighted weekly and annual average indirect costs per patient per treatment were calculated using PASI response level distribution for all FIXTURE patients (employed and non-employed) at Weeks 16 and 52, with work impairment estimates for the employed patient cohort in CLEAR (applied to FIXTURE).

Analysis of variance was used to compare work productivity loss and annual indirect costs between secukinumab and ustekinumab and etanercept, separately.

Results

Baseline population characteristics and PASI response

CLEAR included a total of 676 patients with moderate-to-severe psoriasis (secukinumab = 337, ustekinumab = 339); 452 (67%) patients reported current employment at baseline and were included in the primary analysis. The analysis included 653 patients with moderate-to-severe psoriasis from FIXTURE (secukinumab 300 mg = 327, etanercept = 326).[19] Table 3 presents key baseline population characteristics for the CLEAR and FIXTURE studies. Table 4 presents PASI response distribution in the CLEAR and FIXTURE studies at Weeks 16 and 52.

Primary analysis of CLEAR employed patients at Week 16 using employed patient PASI response level distribution

In the primary analysis, results showed that weekly work impairment percentages and mean hours lost decreased with greater skin clearance based on PASI response. Patients with PASI < 50 response had 22.8% weekly work impairment and a weekly

Table 3 FIXTURE and CLEAR baseline population characteristics

Mean (SD)	CLEAR* Mean (SD)		FIXTURE† Mean (SD)	
Characteristics	**SEC 300 mg (*n* = 337)**	**UST (*n* = 339)**	**SEC 300 mg (*n* = 327)**	**ETN (*n* = 326)**
Age (years)	45.2 (13.96)	44.6 (13.67)	44.5 (13.2)	43.8 (13.0)
Weight (kg)	87.4 (19.95)	87.2 (22.11)	83.0 (21.6)	84.6 (20.5)
Body mass index (kg/m^2)	29.1 (5.87)	29.0 (6.69)	28.4 (6.4)	28.7 (5.9)
Time since first PsO diagnosis (years)	19.6 (12.90)	16.1 (11.24)	15.8 (12.3)	16.4 (12.0)
PASI total score	21.7 (8.50)	21.5 (8.07)	23.9 (9.9)	23.2 (9.8)
Male sex: *n* (%)	229 (68.0%)	252 (74.3%)	224 (68.5%)	232 (71.2%)
Presence of PsA (yes): *n* (%)	69 (20.5%)	54 (15.9%)	50 (15.3%)	44 (13.5)

*Source: Thaçi *et al.*[18]
†Source: Langley *et al.*[19]
ETN, etanercept; PASI, Psoriasis Activity and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; SD, standard deviation; SEC, secukinumab; UST, ustekinumab.

Table 4 PASI response distribution in CLEAR and FIXTURE studies

Clinical study	CLEAR				FIXTURE*	
	Employed patients		Employed and non-employed patients		Employed and non-employed patients	
PASI score	**SEC (*n* = 223)**	**UST (*n* = 214)**	**SEC (*n* = 328)**	**UST (*n* = 318)**	**SEC (*n* = 323)**	**ETN (*n* = 323)**
Week 16						
PASI < 50	2.2%	6.1%	1.8%	5.0%	6.5%	20.4%
PASI 50–74	4.0%	9.3%	3.7%	9.4%	6.8%	21.1%
PASI 75–89	14.8%	26.2%	14.0%	25.5%	14.2%	27.2%
PASI ≥ 90	78.9%	58.4%	80.5%	60.1%	72.4%	31.3%
Week 52						
PASI < 50	1.6%	4.1%	3.6%	9.6%	15.2%	27.6%
PASI 50–74	3.5%	8.6%	4.8%	12.2%	6.2%	17.0%
PASI 75–89	13.6%	23.3%	16.8%	17.6%	13.6%	22.0%
PASI ≥ 90	81.3%	64.1%	74.9%	60.6%	65.0%	33.4%

*Employment information is not available for FIXTURE.
Note: Non-responder imputation was used for missing data.
ETN, etanercept; PASI, Psoriasis Activity and Severity Index; SEC, secukinumab; UST, ustekinumab.

mean of 7.60 lost hours; those with PASI 50–74 had 13.3% impairment and 4.45 lost hours; those with PASI 75–89 had 6.4% impairment and 2.14 lost hours; and those with PASI ≥ 90 had 4.9% impairment and 1.65 lost hours (Table 5). Work productivity loss due to presenteeism was higher than work productivity loss due to absenteeism and decreased with greater skin clearance based on PASI response (Fig. 1). For instance, those with PASI < 50 had a mean productivity loss due to presenteeism of 20% and a mean productivity loss due to absenteeism of 1.4%. In contrast, those with PASI ≥ 90 had a 3.5% productivity loss due to presenteeism and a 2.1% productivity loss due to absenteeism. Mean weekly/annual work hours lost per patient were significantly lower for patients receiving secukinumab than for patients receiving ustekinumab (1.96/102.51 vs. 2.40/125.12, respectively; $P = 0.0006$) (Fig. 2). Average annual indirect costs, calculated as the product of work productivity loss and the hourly wage data, were £1967 with ustekinumab versus £1611 with secukinumab ($P = 0.0006$), resulting in an annual indirect cost savings at Week 16 of £356 with secukinumab vs. ustekinumab (Fig. 3).

Secondary analyses

All secondary analysis scenarios showed that mean weekly and annual work hours lost per patient were significantly lower for patients receiving secukinumab than for patients receiving ustekinumab or etanercept.

Secondary analysis 1: CLEAR employed patients at Week 52 using employed patient PASI response level distribution
Secondary analysis 1, using Week 52 data for employed patients in CLEAR, revealed similar results to those from the primary analysis, including an annual indirect cost savings of £357 with secukinumab versus ustekinumab (Figs 4-6).

Secondary analysis 2: CLEAR employed patients at weeks 16 and 52 using PASI response level distributions for all patients

Table 5 Overall percentage work impairment and weekly hours lost in CLEAR, by PASI response

	Work impairment (SE)	Weekly hours lost
Week 16		
PASI < 50	22.8% (0.15)	7.60
PASI 50–74	13.3% (0.08)	4.45
PASI 75–89	6.4% (0.06)	2.14
PASI ≥ 90	4.9% (0.07)	1.65
Week 52		
PASI < 50	26.3% (0.16)	8.77
PASI 50–74	16.4% (0.06)	5.46
PASI 75–89	10.4% (0.04)	3.46
PASI ≥ 90	6.9% (0.04)	2.30

PASI, Psoriasis Activity and Severity Index; SE, standard error.

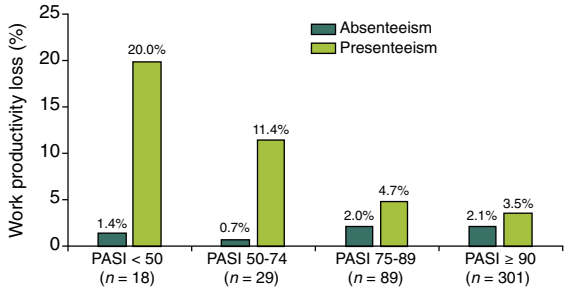

Figure 1 Primary analysis: work productivity loss (absenteeism and presenteeism), by PASI response level among employed patients in CLEAR at Week 16. Note: Overall work impairment is calculated as absenteeism + (1 – absenteeism) * presenteeism, in accordance with published WPAI methodology.[20] PASI, Psoriasis Activity and Severity Index.

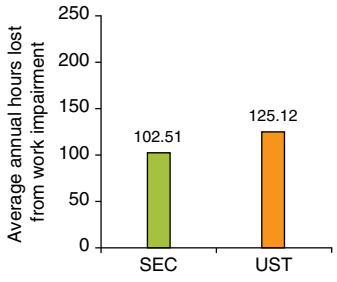

Figure 2 Primary analysis: average annual hours lost from work impairment among CLEAR employed patients at Week 16*. *P = 0.0006. PASI, Psoriasis Area and Severity Index; SEC, secukinumab; UST, ustekinumab.

Results from secondary analysis 2, conducted among employed patients in CLEAR using PASI response level distributions for all patients (employed and non-employed), were similar to those observed in the primary analysis and

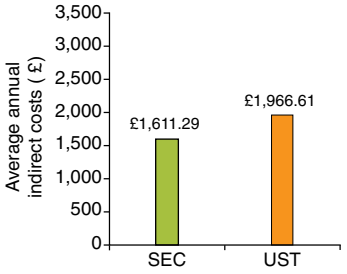

Figure 3 Primary analysis: average annual indirect costs among CLEAR employed patients at Week 16*. *P = 0.0006. SEC, secukinumab; UST, ustekinumab.

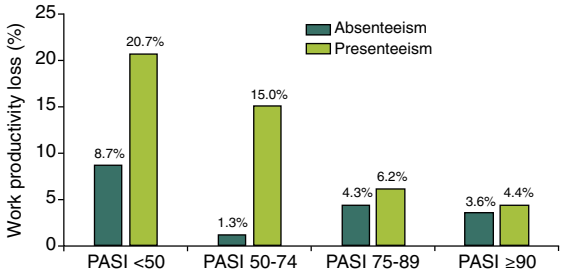

Figure 4 Secondary analysis 1: work productivity loss (absenteeism and presenteeism) by PASI response level among employed patients in CLEAR at Week 52. PASI, Psoriasis Activity and Severity Index. Note: Overall work impairment is calculated as absenteeism + (1 – absenteeism) * presenteeism, in accordance with published WPAI methodology.[20]

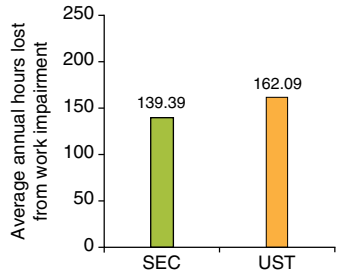

Figure 5 Secondary analysis 1: Average annual hours lost from work impairment among CLEAR employed patients at Week 52*. *P = 0.0002. PASI, Psoriasis Area and Severity Index; SEC, secukinumab; UST, ustekinumab.

secondary analysis 1, with annual indirect cost savings of £336 at Week 16 and £517 at Week 52 with secukinumab versus ustekinumab (Table 6).

Secondary analysis 3: FIXTURE employed patients at Weeks 16 and 52 using PASI response level distributions for all

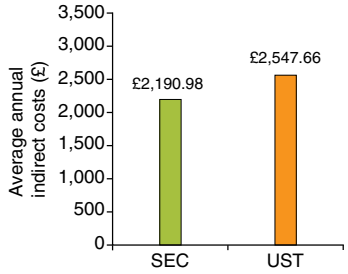

Figure 6 Secondary analysis 1: average annual indirect costs among CLEAR employed patients at Week 52*. *$P = 0.0002$. PASI, Psoriasis Area and Severity Index; SEC, secukinumab; UST, ustekinumab.

patients When work impairment data from CLEAR were applied to FIXTURE, results revealed annual indirect cost savings of £1061 at Week 16 and £1017 at Week 52 with secukinumab vs. etanercept (Table 6).

Discussion

In the CLEAR and FIXTURE studies, secukinumab demonstrated superior skin clearance based on PASI response compared with ustekinumab and etanercept in patients with moderate-to-severe psoriasis. This analysis showed that greater skin clearance based on PASI response with secukinumab translated into significantly reduced work impairment and associated indirect costs of psoriasis, leading to cost savings compared with ustekinumab and etanercept. This was shown at different time points and confirmed in multiple scenarios. To our knowledge, this is the first analysis showing comparative data on work-related indirect costs between different biologic treatments of moderate-to-severe psoriasis.

These results are important in regard to the substantial indirect cost burden imposed by moderate-to-severe psoriasis on society, particularly to employers and healthcare systems. From the CLEAR data source, we demonstrate that much of these costs is primarily caused by work impairment while at work (i.e. presenteeism) and that work productivity costs are negatively correlated with clinical responses.

These results must be interpreted in view of several limitations. First, this is a post hoc analysis. Employment statistics are based on the patients employed in a clinical trial and may not be representative of all patients with psoriasis. We assumed that the average wage for patients with psoriasis was similar to that of the general population. Employment patterns for FIXTURE were assumed to be similar to those for CLEAR; moreover, WPAI data by PASI severity were not available for patients in FIXTURE and may be different to those in CLEAR. In addition, work impairment reflects only impairment due to psoriasis and may be underestimated, as other conditions are not considered. Moreover, the results are driven by PASI response, but other measures not taken into account (e.g. psoriasis symptom burden,

Table 6 Secondary analyses 2 and 3: employed patients in CLEAR and FIXTURE, all-patient PASI distribution

Population	Secondary analysis 2: CLEAR, employed patients*		Secondary analysis 3: FIXTURE, employed patients†,*	
PASI response level distribution	PASI responses in all patients		PASI responses in all patients	
Effect on work impairment	SEC	UST	SEC	ETN
Week 16				
Weekly hours lost	1.93	2.33	2.29	3.59
Annual hours lost	100.48	121.83	119.67	187.17
Difference in annual hours lost (SEC vs. comparator)	21.35		67.49	
Weekly indirect costs in £ (mean)	30.27	36.70	36.05	56.38
Annual indirect costs in £ (mean)	1579.31	1914.86	1881.00	2941.86
Difference in annual indirect costs in £ (SEC vs. comparator)	335.55		1060.86	
Week 52				
Weekly hours lost	2.88	3.51	3.64	4.88
Annual hours lost	150.29	183.17	189.77	254.45
Difference in annual hours lost (SEC vs. comparator)	32.88		64.68	
Weekly indirect costs in £ (mean)	45.27	55.18	57.17	76.65
Annual indirect costs in £ (mean)	2362.23	2879.04	2982.83	3999.44
Difference in annual indirect costs in £ (SEC vs. comparator)	516.81		1016.61	

*$P < 0.0001$ for all comparisons of secukinumab versus comparator.
†Assumed to be 0.67 of the overall cohort (i.e. employment patterns as in CLEAR).
ETN, etanercept; PASI, Psoriasis Activity and Severity Index; SEC, secukinumab; UST, ustekinumab.

sustained response beyond 1 year or health-related quality of life impact as captured by the Dermatology Life Quality Index [DLQI]) could have an impact on the results. In particular, previous research has found that measures of psoriasis-related work productivity impairment and activity impairment are more closely associated with measures of health-related quality of life than with measures of clinical severity.[25–27] Finally, the analyses apply to comparisons of secukinumab versus ustekinumab and etanercept because head-to-head trial data were available for these treatments; similar analyses with different psoriasis comparators could yield different findings.

In conclusion, this postanalysis of two head-to-head trials showed that greater skin clearance with secukinumab treatment significantly contributes to reducing work impairment and indirect costs associated with psoriasis compared with ustekinumab or etanercept.

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