PSY17

Real-World Cost Difference in Patients With Psoriasis Newly Initiating Apremilast vs. Biologic Treatment After Conventional Systemic Therapy: A Retrospective Analysis of German Sickness Fund Data

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INTRODUCTION

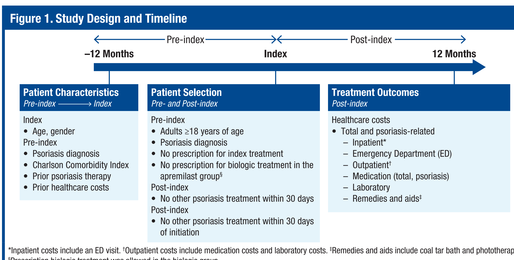
- Psoriasis is a chronic, systemic, inflammatory disease[1] that affects 1.2% to 11.4% of the European population across various countries.[2]
- Psoriasis causes great physical, emotional, and social burden to patients.[3]
- The economic burden of patients with moderate to severe psoriasis is particularly high, with reported annual total costs per patient of 6709 € in Germany,[4] 5226 € to 11,434 € in Italy,[5] and 3613 CHF to 20,076 CHF in Switzerland.[6]
- Available treatment options for moderate to severe psoriasis include systemic therapies, such as apremilast and biologics. In Europe, these may be used after treatment with conventional systemic drugs, such as methotrexate or cyclosporine.
  - Apremilast, a targeted oral phosphodiesterase 4 inhibitor with selective effects on innate immune responses,[7] was approved for use in Europe in 2015.[8]
  - Biologics, a class of injectable immunosuppressive medications, target or quiet the portion of the immune system that is overactive because of psoriasis.[9]
- Previous trial-based economic models have demonstrated the cost-effectiveness of using apremilast vs. biologics after treatment with conventional systemics (i.e., as second-line treatment) in Europe.[10] However, real-world differences in economic burden in patients newly initiating apremilast or a biologic after conventional systemics are currently unknown.
- The objective of this study was to estimate the cost differences in patients with psoriasis newly initiating apremilast vs. a biologic after using conventional systemics using real-world data obtained from a European healthcare claims database.

METHODS

Study Design

- This retrospective cohort study used administrative healthcare claims data from the large, longitudinal German sickness fund database known as Wissenschaftliches Institut für Gesundheitsökonomie und Gesundheitssystemforschung (WIG2).
- **Figure 1** provides an overview of the study design and timeline, including patient selection and study measures assessed.

Figure 1. Study Design and Timeline



*Inpatient costs include an ED visit. †Outpatient costs include medication costs and laboratory costs. ‡Remedies and aids include coal tar bath and phototherapy. §Prescription biologic treatment was allowed in the biologic group.

Data Description

- The WIG2 database contains anonymized longitudinal data on the inpatient and outpatient care provided to ~4.5 million individuals insured through the German Statutory Health Insurance (SHI) funds from 1 January 2010 through 31 December 2017.[11]
- Data on patients' diagnoses, procedures, laboratory tests, as well as medications, remedies and aids, and associated costs, are available.

Study Approval

- The study was approved by the individual WIG2 sickness funds.

Patient Selection

- Adults diagnosed with psoriasis were included if they initiated a treatment of interest (i.e., apremilast or a biologic) during the study period, 15 February 2015 to 30 June 2017.
- The index date and treatment groups were defined based on initiation of the treatment of interest.
  - If there was a record of apremilast, the index date was assigned to the date of the first receipt of apremilast and the treatment group was called "apremilast."
  - If there was no record of apremilast, the index date was assigned to the date of the first receipt of a biologic and the treatment group was called "biologics" (i.e., all approved biologics*).
- No prescription for the index treatment was allowed pre-index.
- No prescription for biologics* was allowed in the apremilast group pre-index.
- All inclusion/exclusion criteria are shown in **Figure 2**.

*All biologic treatments approved for psoriasis at the time of the study were included (i.e., adalimumab, etanercept, infliximab [including biosimilars]; certolizumab pegol, golimumab; secukinumab, ixekizumab, and ustekinumab.

Statistical Analysis

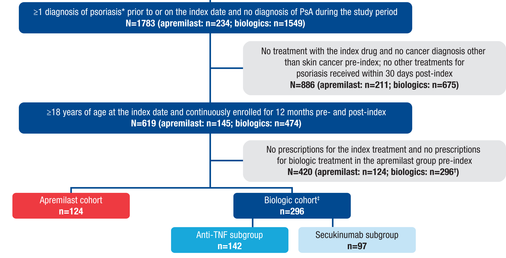
- Data were analyzed using descriptive statistics and presented as means (± standard deviations [SDs]) or proportions.
- The 12-month post-index healthcare costs were analyzed following treatment initiation using an intention-to-treat approach to account for between-group treatment changes and to assess the overall impact of treatment on cost.
- Using linear regression adjusted for demographics and Charlson Comorbidity Index (CCI) scores, adjusted mean total costs were calculated to determine the cost difference between treatment with apremilast vs. biologics.
- Sensitivity analyses of the following biologic subgroups were conducted to investigate differences between apremilast and:
  - Anti-tumor necrosis factor agents (anti-TNFs; i.e., adalimumab, etanercept or infliximab [including biosimilars†]).
  - Secukinumab (i.e., interleukin-17A).
- Costs were standardized to 2017 using a compounding rate of 5%, and a *P* value ≤0.05 was considered to be statistically significant.

†Sample size for biosimilars was also evaluated.

RESULTS

- A total of 9695 patients initiating either apremilast (n=420) or a biologic (n=9275) were identified during the study period (**Figure 2**).
- In all, 420 patients were identified, including 124 initiating apremilast and 296 initiating a biologic (anti-TNFs: n=142; secukinumab: n=97) (**Figure 2**).

Figure 2. Patient Selection Flow



*ICD-10-CM codes used to identify patients with psoriasis were L40.0, L40.1, L40.2, L40.3, L40.4, L40.8 and L409. †Included biosimilars (n=9); biosimilar same size precluded further subgroup analysis. ‡27 patients received prior biologic treatment.

Patient Characteristics

- Key differences in baseline characteristics are shown in **Table 1**.
  - Apremilast initiators were significantly older (mean age: 50.3 vs. 45.2 years) and had higher CCI scores (mean: 2.81 vs. 1.96) vs. biologic initiators (both *P*<0.005).
  - A significantly higher proportion of apremilast initiators previously used topical therapy compared with biologic initiators (78.2% vs. 67.6%), whereas a lower proportion of apremilast initiators previously used methotrexate compared with biologic initiators (22.6% vs. 53.4%) (both *P*<0.03).
  - The pre-index average total healthcare costs were numerically but not significantly lower in apremilast vs. biologic initiators (mean: 5234 € vs. 6170 €; *P*=0.314). Other significant cost differences were seen between treatment groups as follows:
    - The average pre-index psoriasis-related costs were almost half in apremilast vs. biologic initiators (2143 € vs. 4027 €; *P*=0.003).
    - The average pre-index psoriasis medication costs were less than half in apremilast vs. biologic initiators (932 € vs. 2745 €; *P*=0.003).
    - The average pre-index laboratory costs were decreased in apremilast vs. biologics (88 € vs. 141 €; *P*≤0.001).

Unadjusted Cost Outcomes

- **Table 2** shows the results of the unadjusted 12-month cost analysis.
- The unadjusted average total cost per patient was significantly and substantially lower among apremilast initiators (17,417 €) vs. biologic initiators (29,959 €), including anti-TNFs (30,372 €) and secukinumab (29,486 €) (all *P*<0.001).
- Differences were primarily driven by psoriasis healthcare resource use (apremilast: 14,358 €; biologics: 27,165 €), namely psoriasis medications (apremilast: 13,438 €; biologics: 26,224 €) and, more specifically, the index psoriasis medication (apremilast: 9916 €; biologics: 23,746 €) (all *P*<0.001).
- The unadjusted average outpatient cost per patient was significantly and modestly higher among apremilast initiators vs. biologic initiators (964 € vs. 803 €; *P*<0.05).

RESULTS (cont'd)

Table 1. Baseline Patient Characteristics

Characteristic	Apremilast n=124	Biologics n=296	*P* Value	Biologic Subgroups: Anti-TNF n=142	*P* Value	Secukinumab n=97	*P* Value
Male, n (%)	81 (65.3)	201 (67.9)	0.607	97 (68.3)	0.605	68 (70.1)	0.452
Age, mean ± SD, years	50.3 ± 13.3	45.2 ± 14.2	**0.001**	44.9 ± 13.6	**0.001**	45.7 ± 15.8	**0.020**
CCI score, mean ± SD	2.81 ± 2.04	1.96 ± 1.28	**<0.001**	2.22 ± 1.43	**0.006**	1.59 ± 0.90	**<0.001**
Prior psoriasis therapies, n (%)							
Phototherapy	24 (19.4)	69 (23.3)	0.373	27 (19.0)	0.944	32 (33.0)	**0.021**
Topical therapies	97 (78.2)	200 (67.6)	**0.029**	85 (59.9)	**0.001**	72 (74.2)	0.487
Methotrexate	28 (22.6)	158 (53.4)	**<0.001**	87 (61.3)	**<0.001**	39 (40.2)	**0.005**
Fumarates	35 (28.2)	83 (28.0)	0.969	31 (21.8)	0.228	40 (41.2)	**0.043**
Other systemic therapies*	18 (14.5)	46 (15.5)	0.790	23 (16.2)	0.705	13 (13.4)	0.813
Prior healthcare costs, mean ± SD, €							
Total	5234 ± 10,002	6170 ± 8077	0.314	7181 ± 9962	0.114	4799 ± 4610	0.692
Psoriasis-related	2143 ± 2392	4027 ± 6935	**0.003**	4332 ± 8494	**0.006**	3241 ± 3554	**0.007**
Inpatient	1815 ± 3494	1842 ± 3568	0.944	1926 ± 3186	0.786	2048 ± 4236	0.654
ED	352 ± 1120	509 ± 1732	0.354	515 ± 1750	0.374	565 ± 1924	0.304
Outpatient	914 ± 1020	860 ± 667	0.527	953 ± 708	0.711	818 ± 660	0.423
Medication	2194 ± 9021	3262 ± 6958	0.191	4015 ± 8902	0.099	1795 ± 1860	0.669
Psoriasis medication	932 ± 938	2745 ± 6675	**0.003**	3289 ± 8493	**0.002**	1488 ± 1769	**0.003**
Laboratory	88 ± 135	141 ± 148	**0.001**	158 ± 160	**<0.001**	122 ± 145	0.079
Remedies and aids	312 ± 1042	207 ± 609	0.198	286 ± 788	0.821	138 ± 388	0.119

P values in bold are significant. *Included acitretin and cyclosporine.

Table 2. Unadjusted 12-Month Average Costs by Treatment Group

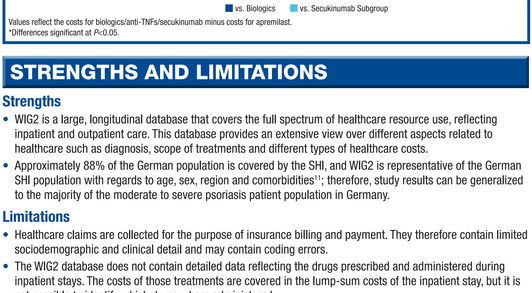
Types of Costs, Mean ± SD, €	Apremilast n=124	Biologics n=296	*P* Value	Biologic Subgroups: Anti-TNF n=142	*P* Value	Secukinumab n=97	*P* Value
Total	17,417 ± 8213	29,959 ± 8694	**<0.001**	30,372 ± 10,506	**<0.001**	29,486 ± 6943	**<0.001**
Psoriasis-related	14,358 ± 6810	27,165 ± 7860	**<0.001**	26,293 ± 9567	**<0.001**	28,130 ± 6159	**<0.001**
Inpatient	2031 ± 4567	2035 ± 5029	0.993	2867 ± 5944	0.204	1114 ± 3902	0.116
ED	649 ± 2503	674 ± 3235	0.941	738 ± 3046	0.798	492 ± 3475	0.695
Outpatient	964 ± 1000	803 ± 613	**0.045**	910 ± 690	0.604	724 ± 522	**0.033**
Medication	14,118 ± 6941	26,934 ± 7504	**<0.001**	26,282 ± 9038	**<0.001**	27,592 ± 5994	**<0.001**
Psoriasis medication	13,438 ± 6925	26,224 ± 7785	**<0.001**	25,164 ± 9417	**<0.001**	27,300 ± 6057	**<0.001**
Index psoriasis medication	9916 ± 5745	23,746 ± 8169	**<0.001**	20,971 ± 9104	**<0.001**	26,172 ± 6745	**<0.001**
Laboratory	110 ± 189	97 ± 137	0.430	116 ± 127	0.762	76 ± 152	0.150
Remedies and aids	304 ± 787	187 ± 638	0.111	313 ± 882	0.932	56 ± 163	**0.003**

P values in bold are significant.

Adjusted Cost Outcomes

- **Figure 3** shows the incremental adjusted 12-month average cost difference per patient for initiators of apremilast vs. biologics.
- The adjusted difference in average total cost per patient was significantly lower for initiators of apremilast vs. biologics (+12,934 €), anti-TNFs (+13,015 €) and secukinumab (+12,608 €).
- These differences were driven by significantly lower medication costs for apremilast (biologics: +12,628 €; anti-TNFs: +11,887 €; secukinumab: +13,265 €).
- The remaining differences were not significant, regardless of healthcare resource use type (i.e., inpatient, ED, outpatient, laboratory, remedies and aids).

Figure 3. Incremental Adjusted 12-Month Average Costs Per Patient (Apremilast vs. Biologic Treatment)



Values reflect the costs for biologics/anti-TNFs/secukinumab minus costs for apremilast.
*Differences significant at *P*<0.05.

STRENGTHS AND LIMITATIONS

Strengths

- WIG2 is a large, longitudinal database that covers the full spectrum of healthcare resource use, reflecting inpatient and outpatient care. This database provides an extensive view over different aspects related to healthcare such as diagnosis, scope of treatments and different types of healthcare costs.
- Approximately 88% of the German population is covered by the SHI, and WIG2 is representative of the German SHI population with regards to age, sex, region and comorbidities[11]; therefore, study results can be generalized to the majority of the moderate to severe psoriasis patient population in Germany.

Limitations

- Healthcare claims are collected for the purpose of insurance billing and payment. They therefore contain limited sociodemographic and clinical detail and may contain coding errors.
- The WIG2 database does not contain detailed data reflecting the drugs prescribed and administered during inpatient stays. The costs of those treatments are covered in the lump-sum costs of the inpatient stay, but it is not possible to identify which drugs where administered.
- Costs here do not reflect costs to the insurer nor costs to the patient.
  - The WIG2 database contains the pharmacy retail price, which is fixed for prescription drugs. Other discounts and possible co-payments may result in lower costs for the insurer; these are not contained in WIG2. Patient out-of-pocket costs are also not captured.
  - Study results from this SHI-covered population are not generalizable to the portion of the German population not covered by SHI (~12%).[11]
  - Study data and results reflect the time lag associated with the data source and the study period. Therefore, this study may not reflect the latest available psoriasis treatments, costs, etc.

DISCUSSION

- To our knowledge, this is the first study to investigate the economic burden of psoriasis in patients who have taken conventional systemic therapy using German sickness fund data.
- Prior therapy use and baseline costs reported here indicate apremilast is generally considered an earlier-use treatment in Germany, relative to biologics.
- In accordance with previous trial-based models, this 12-month intention-to-treat analysis showed substantial cost savings of 12,000 € to 13,000 € associated with initiation of apremilast vs. biologics (i.e., biologics, anti-TNFs and secukinumab) in patients who tried prior conventional systemic therapy.
- In treatment selection, cost considerations should be weighed carefully with other critical factors both clinical and patient-centric, including disease severity, patient preference, efficacy, safety and tolerability, ease of administration, and treatment initiation.[12,13]
- These data further encourage use of apremilast after use of conventional systemic therapies and prior to use of biologics in appropriate patients.
- Our findings are consistent with published studies that have documented use of apremilast and its associated benefits in moderate psoriasis,[14,15] and data from several European psoriasis registries indicate biologics are used more prevalently in severe psoriasis.[16]
- Further studies are warranted to inform real-world treatment patterns and the associated economic burden in patients diagnosed with moderate to severe psoriasis as new treatments become available (e.g., tildrakizumab, risankizumab, biosimilars).

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DISCLOSURES

NK & TS: WIG2 GmbH – employment. **MS & MP:** Kantar GmbH, Health Division – employment; Celgene Corporation – research contract. **SM & TN:** Celgene Corporation – employment. **SW:** MArS Market Access & Pricing GmbH – employment; Celgene Corporation – advisory board; Eli Lilly and UCB – honoraria.

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