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'Happy' drug survival of adalimumab, etanercept and ustekinumab in psoriasis in daily practice care: results from the BioCAPTURE network

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Summary

Background Drug survival is a marker for treatment success. To date, no analyses relating dermatological quality-of-life measures to drug survival have been published.

Objectives (i) To describe 1-year drug survival for adalimumab, etanercept and ustekinumab in a daily practice psoriasis cohort, and (ii) to introduce the concept of 'happy' drug survival, defined as Dermatology Life Quality Index (DLQI) ≤ 5 combined with being 'on drug' at a specific time point.

Methods Data were extracted from a prospective registry. Drug survival was analysed using Kaplan–Meier estimates. 'Happy' drug survival was calculated, with data split into 'happy' (DLQI ≤ 5) vs. 'unhappy' (DLQI > 5) at baseline and months 3, 6, 9 and 12.

Results 249 treatment episodes were included (101 adalimumab, 82 etanercept, 66 ustekinumab). The 1-year drug survival rates for ustekinumab, adalimumab and etanercept were 85%, 74% and 68%, respectively. Ustekinumab showed a better confounder-corrected drug survival vs. etanercept [hazard ratio (HR) 3·8, $P = 0{\cdot}02$] and a trend towards better survival vs. adalimumab (HR 2·3, $P = 0{\cdot}1$). At baseline, the majority ($n = 115$, 73%) was considered 'unhappy' and a minority 'happy' ($n = 42$, 27%) (ratio 'happy':'unhappy' was 1 : 2.7). The percentage of treatment episodes with 'happy' on-drug patients increased to 79% after 1 year.

Conclusions Ustekinumab showed a better overall drug survival than etanercept, and a trend towards a better overall drug survival than adalimumab. After 1 year, patients reported to be 'happy' in 79% of episodes and 'unhappy' in 21%. We introduced the new concept of 'happy' drug survival because the proportion of on-drug patients with good quality of life is an important indicator for treatment success.

What's already known about this topic?

- The Dermatology Life Quality Index is a validated score for dermatology-specific quality-of-life measurements.
- Drug survival studies of biologics for psoriasis show varying results and differ in study design and population.
- To date, studies including drug survival rates for ustekinumab are scarce.

What does this study add?

- The introduction of a concept named 'happy' drug survival, which combines drug survival rates with dermatology-specific quality-of-life measures to evaluate treatments for psoriasis.
- Analysis of 'happy' drug survival showed that the proportion of 'on-drug' biologic users with a good quality of life increased from 27% to 79% after 1 year of treatment.
- Ustekinumab showed a better overall drug survival vs. etanercept and a trend towards a better survival vs. adalimumab.

In daily practice, adalimumab, etanercept and ustekinumab are frequently used biologics for the treatment of moderate-to-severe psoriasis when patients do not respond, or have a contraindication to, classic antipsoriatic treatments. In January 2009 ustekinumab was registered; from that time point on, all three agents were equally available.

Etanercept and adalimumab share their target, as both agents inhibit tumour necrosis factor (TNF)-α.[1] In contrast, ustekinumab inhibits interleukins 12 and 23 by binding to the shared p40 unit.[2] All three agents have shown their efficacy and safety in multiple (randomized) controlled trials.[3–18] Real-world drug survival studies comprising survival rates and associated predictors of adalimumab and etanercept have been published and vary in study design and outcome.[19–23] Studies regarding drug survival of ustekinumab are scarce.[24,25] Clemmensen *et al.*[24] found that only 4·5% of patients discontinued ustekinumab after 321 days. Patients with lack of response to previous anti-TNF-α treatment showed no impaired response to ustekinumab, compared with patients without lack of response to anti-TNF-α agents. In a retrospective Japanese psoriasis cohort, the 1-year drug survival of ustekinumab was 97%.[25]

In addition to the above-mentioned drug survival studies, quality-of-life (QoL) measures are also important in the process of evaluating psoriasis treatments. For this purpose, we introduced a new concept named 'happy' drug survival, combining drug survival rates with QoL. We used the Dermatology Life Quality Index (DLQI), a frequently used QoL measure in dermatological research.[26,27] A DLQI < 5 is considered to reflect no or mild influence on QoL.[28] In this study, we explored the proportion of 'on-drug' patients who also achieved a good dermatological QoL, as defined by DLQI ≤ 5.

The objectives of this study were (i) to describe the 1-year drug survival for adalimumab, etanercept and ustekinumab in a daily practice psoriasis cohort during a period when all agents were equally available; and (ii) to analyse the proportion of treatment episodes in which patients showed a 'happy' drug survival in the first year of treatment (DLQI ≤ 5 and 'on drug').

Materials and methods

Bio-CAPTURE registry

Dermatology Life Quality Index measures and data on drug survival were extracted from a prospective registry containing daily practice data from all patients with psoriasis treated with biologics (Bio-CAPTURE, Continuous Assessment of Psoriasis Treatment Use REgistry with biologics). This registry was founded at the department of dermatology of the Radboud University Medical Center, Nijmegen in 2005 and is based there. Eight regional nonacademic centres have participated in the registry since 2011. The Bio-CAPTURE registry was approved by the medical ethics committee of the Radboud University Medical Center. According to Dutch law, informed consent from patients was not mandatory in this noninterventional study, but it is currently obtained from every newly included patient.

Protocol and data collection

Preferably, patients were treated according to the regimens recommended by the European Medicines Agency label and the European and Dutch national guidelines for treatment with biologics.[29,30] Patients started one of the following treatments: (i) etanercept 50 mg twice weekly for the first 12 weeks, then reduced to 50 mg weekly; (ii) adalimumab induction dose of 80 mg once in the first week, followed by a maintenance dose of 40 mg every other week; or (iii) ustekinumab 45 mg (body weight < 100 kg) or 90 mg (body weight ≥ 100 kg) at baseline, then after 4 weeks and every 12 weeks thereafter. Dosage adjustments, interval changes and/or combination therapy with topical or conventional antipsoriatic systemic therapies were allowed as this study reflects daily practice. When the biologic was considered ineffective by the treating physician and/or was considered to be related to severe or disturbing side-effects, it was withdrawn.

Patients were seen approximately once every 3 months at our outpatient department and data were collected at every visit. Collected data included effectiveness [including Psoriasis Area and Severity Index (PASI)], side-effects and medication adjustments. Every 3 months, patients received questionnaires (including DLQI) by mail. All data were entered into a Microsoft Access database and checked for completeness by the data manager. For further statistical analyses, data were analysed with SPSS Statistics v20.0 (IBM, Armonk, NY, U.S.A.).

Drug survival analysis

Adalimumab, etanercept and ustekinumab treatment episodes starting from January 2010 were analysed in this study. Inflix-

imab was left out of the analysis due to an insufficient number of patients. If patients received more than one treatment episode of the same agent (e.g. two episodes of etanercept) in our registry, only the first treatment episode was analysed. If patients received different agents in our registry, all treatment episodes were analysed. The follow-up period was ≥ 6 months. When a treatment episode was interrupted for < 90 days, it was considered as one continuous episode. Patients often discontinue their treatment for short intervals due to holidays, infections or (elective) surgery. In recently published drug survival studies, 90 days was an accepted maximum interruption period.[20,31]

We analysed drug survival rates using Kaplan–Meier estimates. Every discontinuation was considered as an event in the survival analysis. Patients were censored when lost to follow-up, or if still using the biologic at the moment of data lock. Drug survival rates were read from the Kaplan–Meier survival curves. Differences in drug survival between groups were analysed using a log-rank (Mantel–Cox) test, or described when survival curves crossed.

A sensitivity analysis for ustekinumab drug survival was carried out to take account of the different discontinuation dates that can be chosen when analyzing this agent. In this manuscript, we present the last date of injection plus 8, 10 or 12 weeks (depending on the original scheme of the patient) in our primary analyses (most positive approach). In contrast with this approach, the last date of injection can be chosen as the ustekinumab discontinuation date (most conservative approach). This sensitivity analysis is presented separately.

For all biologics taken together, the difference between overall drug survival curves was compared for biologic-naive vs. non-naive episodes.

Confounder-correction drug survival analysis

Patient and treatment characteristics were compared for adalimumab, etanercept and ustekinumab treatment episodes, and for biologic-naive and non-naive episodes. Pearson's chi square test was used for characteristics with categorical outcomes. For the comparison of characteristics between the three different agents, a one-way ANOVA for continuous outcomes with a parametric distribution, and a Kruskal–Wallis test for continuous outcomes with a nonparametric distribution was used. For the comparison based on biologic-naive vs. non-naive episodes, characteristics with continuous outcomes with a parametric distribution were analysed using an independent t-test, or, in case of a nonparametric distribution, using a Mann–Whitney U-test. When characteristics were significantly different between groups they were corrected for using multivariate Cox regression analysis. If closely related variables were both candidates for confounder correction (e.g. weight and body mass index), a selection based on biological mechanisms was made to choose one confounder. Sex and age were included as fixed variables in all models independent of their significance value. Subsequently, possible confounders were added as covariates to this model. Hazard ratios with P-values resulting from this multivariate Cox regression analysis are described.

'Happy' drug survival

'Happy' drug survival was defined as DLQI ≤ 5 and being 'on drug' at a specific time point. A DLQI > 5 while being 'on drug' was considered as an 'unhappy' treatment episode. All patients who returned at least one DLQI questionnaire in the first year of treatment were included in this analysis. Ratios and percentages for 'happy' vs. 'unhappy' episodes were calculated at 0, 3, 6, 9 and 12 months using a per protocol approach. Missing data were found to be at random time points and were handled as such. To synchronize the drug survival curve with the DLQI measurement points, an actuarial drug survival analysis was carried out. The actuarial survival curve and the frequencies of DLQI ≤ 5 ('happy') and DLQI > 5 ('unhappy') were visualized in one graph. Not all patients returned questionnaires; therefore this subanalysis consisted of a smaller group than the original cohort in this study. A head-to-head comparison of 'happy' drug survival curves between the different treatments was considered inappropriate due to lack of power.

Results

Patient and treatment characteristics

In total 249 treatment episodes in 213 unique patients were included in this drug survival analysis, comprising 101 adalimumab episodes, 82 etanercept episodes and 66 ustekinumab episodes. Patient and treatment characteristics for each drug are presented in Tables 1 and 2. For all agents taken together, 59 episodes (24%) were discontinued in the first year. The most frequent reason for discontinuation was ineffectiveness of therapy (n = 33, 13%), followed by side-effects (n = 16, 6%) and a combination of ineffectiveness and side-effects (n = 7, 3%). Three treatments were stopped due to other reasons (wish for pregnancy, ineffectiveness of biologic on arthritis symptoms, and work-related issues). The median dosage of adalimumab was 40 mg every 2 weeks, and the median dosage of etanercept was 75 mg per week. For ustekinumab, the median dosage was 45 mg per 12 weeks in patients weighing < 100 kg and 68 mg per 12 weeks in patients weighing ≥ 100 kg. Thus the median etanercept dose was higher, and the median ustekinumab dose in patients weighing ≥ 100 kg was lower than the recommended dose. Other median dosages corresponded with the recommended dose. All characteristics were compared for differences between drugs. Characteristics that were statistically different between drugs were incorporated into the confounder-corrected subanalysis as described later.

Drug survival rates

In the uncorrected survival curves, the highest absolute 1-year survival rates were seen for ustekinumab, followed by ada-

Table 1 Patient characteristics

	ADA, n = 101	ETA, n = 82	UST, n = 66	P-value
Sex male, n (%)	59 (58)	47 (57)	40 (61)	0·91[g]
Age (years), mean ± SD[a]	46·4 ± 12·2	46·1 ± 14·2	48·9 ± 12·5	0·35[h]
Age at onset of psoriasis (years), median (range)	22·2 (0–57·8)	19·8 (0–58·1)	25·8 (2·3–66·5)	0·07[f]
Disease duration (years), median (range)	20·8 (0·9–53·6)	19·3 (0·5–63·9)	17·1 (2·9–57·2)	0·55[f]
Psoriatic arthritis (yes), n (%)	29 (35)[c]	18 (27)[d]	16 (31)[e]	0·48[g]
Weight (kg), mean ± SD	89·8 ± 18·8	82·5 ± 17·8	93·0 ± 17·3	0·01[h]
Body mass index (kg m^{-2}), mean ± SD or median (range)	28·8 ± 5·6	26·8 (17·7–55·1)	29·4 (21·9–59·0)	0·02[f]
Baseline PASI, mean ± SD or median (range)[b]	11·3 (2·6–38·4)	11·8 (0·6–42·1)	15·4 ± 7·8	0·03[f]
Treated at an academic centre, n (%)	73 (72)	59 (72)	39 (59)	0·15[g]
Treated at a nonacademic centre, n (%)	28 (28)	23 (28)	27 (41)	

ADA, adalimumab; ETA, etanercept; UST, ustekinumab; PASI, Psoriasis Area and Severity Index. [a]Age at time of inclusion in this study. [b]90 days before, or 7 days after starting the study biologic. Psoriatic arthritis status for [c]82, [d]66 and [e]51 patients available. [f]Kruskal–Wallis test, [g]Pearson chi square test, [h]one-way ANOVA.

Table 2 Treatment characteristics

Characteristic	ADA, n = 101	ETA, n = 82	UST, n = 66	P-value
Naive for biologics, n (%)	49 (49)	53 (65)	21 (32)	< 0·001[f]
Naive for TNF-α antagonists, n (%)	51 (51)	54 (66)	25 (38)	< 0·001[f]
Median dose (range)	40·0 (26·7–93·3)[a]	75·3 (50·0–100·0)[b]	45·0 (35·8–135·0)[c]	NA
Median dose (range) (patients < 100 kg)	NA	NA	45·0 (35·8–113·5)[d]	
Median dose (range) (patients ≥ 100 kg)	NA	NA	68·3 (45·0–108·0)[e]	
Concomitant methotrexate, n (%)	27 (27)	16 (20)	10 (15)	0·18[f]
Concomitant acitretin, n (%)	1 (1)	4 (5)	2 (3)	NA[g]
Reason for discontinuation, n (%)				
Ineffectiveness	15 (15)	14 (17)	4 (6)	NA
Side-effects	5 (5)	8 (10)	3 (5)	
Ineffectiveness and side-effects	5 (5)	2 (2)	0 (0)	
Other reasons	1 (1)	0 (0)	2 (3)	
Lost to follow-up	1 (1)	2 (2)	2 (3)	

ADA, adalimumab; ETA, etanercept; UST, ustekinumab; TNF, tumour necrosis factor; NA, not applicable. Data from [a]101, [b]75, [c]63, [d]34 and [e]16 patients available. [f]Pearson chi square test. [g]Pearson chi square test not possible due to insufficient cases with acitretin.

limumab and etanercept, with percentages of 85%, 74% and 68%, respectively (Fig. 1). The drug survival of ustekinumab was significantly higher than that of etanercept (log-rank test, P = 0·032), and ustekinumab showed a trend towards a better survival than adalimumab (log-rank test, P = 0·066). The curves for adalimumab and etanercept drug survival crossed over frequently, therefore no statistical analysis was carried out. Sensitivity analysis of overall drug survival, with conservative handling of ustekinumab discontinuation dates (date of discontinuation was date of last injection), revealed a better drug survival for ustekinumab vs. etanercept, and a trend towards a better survival vs. adalimumab (log-rank test, P = 0·039 and P = 0·085, respectively).

Drug survival rates with confounder correction

The baseline variables of weight, PASI and prior biologics were significantly different when compared between the three agents (Tables 1 and 2). These variables were therefore included for confounder correction, together with the fixed variables age and sex. For confounder-corrected overall drug survival, ustekinumab drug survival was higher than that of etanercept [hazard ratio (HR) 3·822, 95% confidence interval (CI) 1·203–12·139; P = 0·023], and showed a trend towards a better survival than that of adalimumab (HR 2·330, 95% CI 0·837–6·489; P = 0·1). Etanercept and adalimumab showed similar drug survival curves (HR 1·132, 95% CI 0·565–2·269; P = 0·727).

As for the confounder-corrected sensitivity analysis with conservative handling of ustekinumab discontinuation dates, ustekinumab drug survival was still significantly higher than that of etanercept (HR 3·604, 95% CI 1·135–11·443; P = 0·03), and showed a trend towards a better survival than that of adalimumab (HR 2·147, 95% CI 0·769–5·991; P = 0·14).

Drug survival rates for biologic-naive vs. non-naive episodes

For adalimumab, etanercept and ustekinumab taken together, the Kaplan–Meier curves did not show different trends for

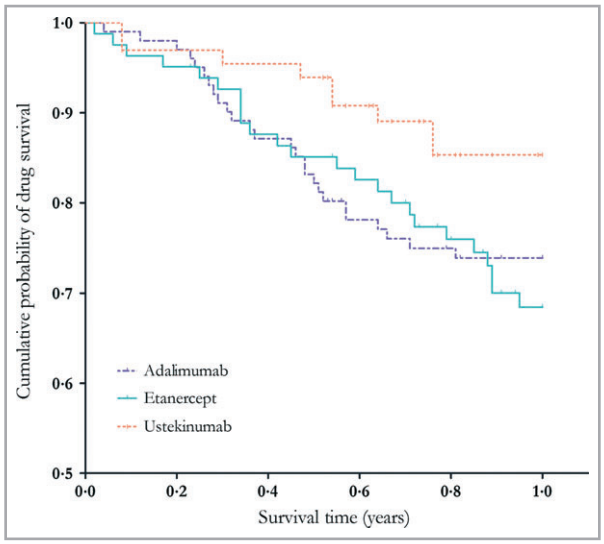

Fig 1. Overall 1-year drug survival of adalimumab, etanercept and ustekinumab for patients with psoriasis; n = 249, event = discontinuation in general. In all groups, no median drug survival time could be calculated as > 50% of patients were still on-drug at the end of study. In the first 3 months of treatment, survival curves for the different agents cross; after 3 months a trend towards better drug survival for ustekinumab is seen.

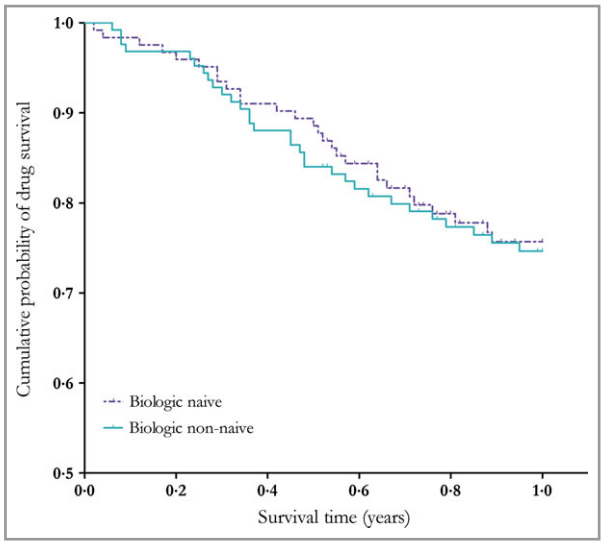

Fig 2. Overall 1-year drug survival of biologic-naive vs. non-naive patients with psoriasis. n = 249, event = discontinuation in general. In both groups, no median drug survival time could be calculated as > 50% of patients were still on-drug at the end of study. After 1 year, no trends towards a difference between the overall drug survival for naive vs. non-naive patients is seen.

biologic-naive vs. non-naive treatment episodes (log-rank test, P = 0·803) (Fig. 2). About half (49%, n = 123) of the treatment episodes considered biologic naive episodes and 51% (n = 126) biologic non-naive. The absolute 1-year drug survival percentages were 76% in biologic-naive and 75% in non-naive treatments. Survival curves were corrected for the following possible confounders: treatment setting, drug, disease duration and baseline PASI, together with age and sex as fixed variables. No statistically significant difference between biologic-naive and non-naive treatment episodes was seen after confounder correction (HR 0·99, 95% CI 0·536–1·814; P = 0·965).

'Happy' drug survival

Figure 3 shows the 'happy' drug survival curve. This subcohort consisted of 74 adalimumab (40%), 62 etanercept (33%) and 50 ustekinumab (27%) episodes where at least one DLQI questionnaire was returned in the first year of treatment. The subcohort accounted for 75% of the original cohort. At baseline, the majority of patients who returned the questionnaire at the start of the study (157 of 186) were considered 'unhappy' (n = 115, 73%), with a DLQI score > 5. A minority were considered 'happy' (n = 42, 27%). The ratio of 'happy' to 'unhappy' was 1 : 2·7 at that time. Of all returned questionnaires, the relative percentage considered 'happy' increased over time. In 64%, 69%, 72%, 79% of the episodes a DQLI ≤ 5 was scored after 3, 6, 9 and 12 months, respectively. This led to reversed ratios vs. the baseline ratio. Ratios of 1·8 : 1, 2·2 : 1, 2·6 : 1 and 3·7 : 1 were seen after 3, 6, 9 and 12 months, respectively.

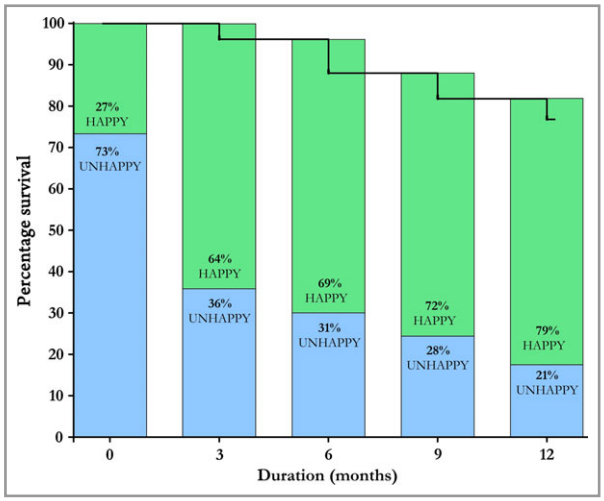

Fig 3. 'Happy' drug survival of patients with psoriasis on adalimumab, etanercept or ustekinumab. 'Happy' drug survival combines the actuarial drug survival of biologics (black line) with the percentage of patients with a Dermatology Life Quality Index (DLQI) ≤ 5 ('happy') vs. DLQI > 5 ('unhappy'). This cohort consisted of 186 treatment episodes: 74 with adalimumab, 62 with etanercept and 50 with ustekinumab. Data were available for only 157 patients at baseline.

Analysis comparing the group that returned DLQI questionnaires revealed no differences compared with the group in which no questionnaires were returned, except for the fact that the responder group was larger in nonacademic hospitals (Pearson's chi square test, P = 0·02). At baseline and months

3, 6, 9 and 12, questionnaires were not returned in 16%, 34%, 40%, 42% and 40% of cases, respectively.

Discussion

The 1-year drug survival rates of ustekinumab, adalimumab and etanercept were 85%, 74% and 68%, respectively. Multivariate Cox regression analysis of drug survival corrected for confounders showed that ustekinumab had a significantly better 1-year drug survival rate than etanercept, and had a trend towards better drug survival than adalimumab. Biologic-naive and non-naive treatment episodes showed comparable 1-year drug survival rates. The proportion of on-drug patients with a good QoL is an important indication of treatment success. For this purpose, we introduced the 'happy' drug survival analysis. At the moment of initiating a biologic in the majority of episodes patients reported to be 'unhappy' (DLQI > 5), with a ratio of 1 : 2·7 for 'happy' vs. 'unhappy'. In time, this ratio reversed, leading to a majority of 'happy' (DLQI ≤ 5) on-drug patients, with a ratio of 3·7 : 1 after 12 months.

Clemmensen *et al.*[24] have shown a better drug survival than adalimumab and etanercept together. We found a 1-year drug survival rate of 85% for ustekinumab, which was slightly lower than survival rates in the Danish cohort[24] and in a retrospective Japanese cohort.[25] In these studies, ustekinumab 1-year survival rates of > 90% were found. We found no differences in drug survival rates for biologic-naive vs. non-naive patients. These results correspond with many previous studies on drug survival and efficacy,[23,32–39] but contradict Danish studies on drug survival.[21,24] Dosages of biologics could influence drug survival curves. In the present cohort, the median doses of adalimumab, and ustekinumab in patients < 100 kg, corresponded with the dose recommended by the label. However, patients on ustekinumab weighing ≥ 100 kg used a slightly lower dose than the recommended dose, and patients on etanercept used a higher dose. From this study design we cannot evaluate whether lower etanercept dosages would lead to different survival curves. The influence of underdosing in ustekinumab is thought to be of limited influence, as doctors were free to increase the dose in case of nonresponse. Another hypothesis is that the lower frequency of ustekinumab dosing could lead to better compliance and therefore better drug survival. We were not able to test this in the present study.

The new concept of 'happy' drug survival was used to investigate whether drug survival corresponds with a good dermatological QoL. This concept provides a broader measurement of treatment success, combining drug survival with patient-reported outcomes. As DLQI is a frequently used QoL tool in daily practice and in clinical studies, the present concept is thought to be easily adaptable to various settings. Eventually, this broad measurement could be used in large groups to compare outcomes for different biologics. In the present cohort, we found a pronounced increase in the proportion of treatment episodes with 'happy' patients using biologics after 3 months, followed by a gradual rise until 12 months. After 1 year, most episodes with 'on-drug' patients showed a good disease-related QoL. Still, one-fifth of this treated group reported a DLQI > 5. It is important to identify the needs that are not fulfilled for this subgroup.

It must be taken into account that this drug survival study is based on daily practice, whereby different factors could be of influence. Important factors are the behaviour of physicians and patients and the availability of other treatment options. To minimize the influence of these factors, both academic and peripheral patients and doctors were represented, and data were collected in a time frame in which adalimumab, etanercept and ustekinumab were equally available. As the groups (adalimumab, etanercept and ustekinumab) were heterogeneous for specific characteristics, we corrected for possible confounders using a multivariate Cox regression model. For instance, we corrected for biologic naivety because more biologic-non-naive patients were present in the ustekinumab group. This could hypothetically lead to a longer persistence due a limited number of alternatives. The corrected survival curves still show the same results as the uncorrected versions, and we therefore think that the influence of non-naivety is limited. Moreover, in the vast majority of cases infliximab was available, and in many cases one of the other anti-TNF agents was as well.

Patients were not randomized to treatments, and this could have led to selection bias. However, this bias is inherent in a noninterventional daily practice study. As this study is based on daily practice research, dose adjustments and use of antipsoriatic comedication was allowed. Methotrexate use was substantial, but we found no difference in the amount of users between drugs. Therefore, it was not considered to be a confounder. To evaluate whether drug survival of a specific biologic could be improved by addition of methotrexate, a randomized study would be preferred.

The 'happy' drug survival analysis is based partly on questionnaires, wherein responder bias could have played a role. Missing questionnaires were from random time points, therefore no selection bias for questionnaires at specific time points was expected in this study. The DLQI is designed to measure disease-related Qol and the term 'happy' in the 'happy' drug survival concept refers to *cutaneous* disease-related Qol. However, it is plausible that major life events or nondisease-related issues could have influenced 'happy' drug survival.

This study shows that adalimumab, etanercept and ustekinumab have high real-world drug survival rates in the first year of therapy. Ustekinumab showed a better overall drug survival than etanercept and a trend towards a better drug survival than adalimumab. Treatment episodes with and without prior biologics showed no differences in drug survival rates, which is reassuring within the context of switching to other therapies.

We introduced the 'happy' drug survival analysis as a new concept combining QoL measures with drug survival. The proportion of episodes with 'happy' on-drug patients increased from 27% at baseline to 79% after 12 months. It is important to identify the needs that are not fulfilled for the subgroup of

'unhappy' patients. Measuring whether actively treated patients have a good disease-related QoL is an indicator for treatment success. The concept of 'happy' drug survival could be a meaningful tool to bring patient care to the next level.

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Appendix

Conflicts of interest: J.M.P.A.vdR. carries out clinical trials for AbbVie and Janssen, and has received speaking fees from AbbVie and reimbursement for attending a symposium from Janssen, Pfizer and AbbVie. Fees were paid directly to the institution. J.Z. carries out trials for AbbVie, Janssen and Sciderm and has received reimbursement for attending a symposium from AbbVie. Fees were paid directly to the institution. M.M.B.S. received grants from/was involved in clinical trials from AbbVie, Astellas, LEO Pharma and Pfizer, and served as a consultant for AbbVie, Astellas and Pfizer, gave lectures for Pfizer and travelled with Abbott, Pfizer and LEO Pharma to meetings; fees were paid directly to the institution. P.P.M.vL. carried out clinical trials for AbbVie and Janssen; has received speaking and consulting fees from Wyeth and Schering-Plough; and has received reimbursement for attending a symposium from Janssen, Schering-Plough and Pfizer. R.J.B.D. has received funding from Wyeth/Pfizer, Abbott/AbbVie, Janssen and Merck Serono and has carried out clinical trials for Wyeth, Schering-Plough, Centocor, Abbott, Merck Serono and Barrier Therapeutics; in addition, R.J.B.D. has received speaking and consulting fees from Wyeth Schering-Plough and Merck Sharp Dohme, as well as reimbursement for attending a symposium from Merck Serono, Wyeth and Janssen-Cilag. P.C.M.vdK. serves as a consultant for Merck Sharp Dohme, Celgene, Centocor, Almirall, UCB, Pfizer, SandozSofinnova, AbbVie, Actelion, Galderma, Novartis, Janssen, Ely Lilly, Amgen, Mitsubishi and LEO Pharma, and receives research grants from or carries out clinical trials for Centocor, Pfizer, Merck Sharp Dohme, Merck Serono, AbbVie and Philips Lighting. E.M.G.J.dJ. has received research grants for the independent research fund of the department of dermatology of the University Medical Center St Radboud, Nijmegen, the Netherlands, from AbbVie, Pfizer and Janssen, and has acted as a consultant and/or paid speaker for and/or participated in research sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie, Janssen, Merck Sharp Dohme and Pfizer. M.D.N. serves as a consultant for Janssen. W.P.A. served as a consultant for AbbVie and Janssen and travelled with Pfizer, AbbVie and Janssen to medical congresses for 50% of the fees. The other authors declare no conflicts of interest.

