

APPENDIX S1

S1. Additional methods

Cox proportional hazard regression analyses

We performed Cox proportional hazards regression analysis to assess the impact of predictors on the overall drug survival, defined as the time until treatment discontinuation. Prior to fitting the model, we ensured that key assumptions of the Cox model were met:

1. Proportional hazard assumption: Checked using Schoenfeld residuals with the `cox.zph()` function from the survival package. Variables with statistically significant violations ($p < 0.05$) were either excluded from the analysis or stratified to address the proportional hazards assumption.
2. Linearity with the Log-Hazard: evaluated for continuous predictors (age) using Martingale residuals to ensure linearity with the log-hazard function.
3. Multicollinearity: Assessed using Variance Inflation Factor (VIF) values from the car package, with VIF values below 5 confirming acceptable levels of multicollinearity.
4. Outliers: Identified using the Mahalanobis distance to detect outliers. Observations flagged as outliers were analyzed separately, and their influence on model performance was evaluated by comparing models with and without outliers.

The final Cox model was constructed using the `coxph()` function from the survival package. To avoid overfitting, we limited the maximum number of predictors in the model to four, based on the event-per-variable rule. Variables included were age at treatment initiation, gender, Fitzpatrick skin types and history of using three or more immunosuppressants. Fitzpatrick skin types was categorized into binary groups: types 1 and 2 were combined into one group, and type 3,4,5 and 6 formed another group to meet binary criteria for inclusion. Model fit was compared using Akaike Information Criterion (AIC) values, with the model having the lowest AIC selected as the best fit. Results are reported as hazard ratios with 95% confidence intervals. Statistical significance was set at a p-value of < 0.05 .

Statistical analyses, R packages

SPSS datasets were imported into R using the Haven package. The Sankey diagram visualization was conducted using R (version 4.3.2). The following R packages were utilized:

- ggplot2 (version 3.5.1) for data visualization.
- dplyr (version 1.1.4) and tidyr (version 1.3.1) for data manipulation and cleaning.
- ggalluvial (version 0.12.5) for visualizing alluvial diagrams.
- ggsankey (available from GitHub) for creating Sankey plots.

Packages not available on CRAN were installed from GitHub using the devtools package (version 2.4.5), specifically ggsankey (“davidsjoberg/ggsankey”).

For the cox proportional hazard regression analyses, the following R packages were utilized:

- survival (3.7.0) for fitting Cox proportional hazards models.
- survminer (0.5.0) for visualization.
- car (3.1.3) for assessing multicollinearity via variance Inflation Factor (VIF).

Data preprocessing and outlier detection were facilitated using base R functions and the Mahalanobis distance.

APPENDIX S2

S2. Additional results

Cox hazard regression analysis

Variables definitions:

- Age_med_start: Age at treatment initiation
- Pat_sex: Gender. 0 (female); 1 (male).
- Pat_fitzpatrick: Fitzpatrick skin types. 0 (type1, type 2); 1 (type 3, type 4, type 5, type 6)
- Immunosup_3: History of three or more immunosuppressive. 0 (no); 1 (yes)

Dupilumab

We excluded six multivariate outliers to improve model fit. Conclusion: no significant predictors for dupilumab discontinuation were identified in this study population.

Call:

```
coxph(formula = Surv(Treatment_duration, med_stopped) ~ Age_med_start +
      pat_sex + pat_fitzpatrick + Immunosup_3, data = data_no_outliers)
```

n= 484, number of events= 195
(2 observations deleted due to missingness)

	coef	exp(coef)	se(coef)	z	Pr(> z)
Age_med_start	-0.006748	0.993275	0.004986	-1.353	0.176
pat_sex	-0.165850	0.847173	0.144680	-1.146	0.252
pat_fitzpatrick	0.172257	1.187983	0.157154	1.096	0.273
Immunosup_3	-0.153453	0.857741	0.149644	-1.025	0.305

	exp(coef)	exp(-coef)	lower .95	upper .95
Age_med_start	0.9933	1.0068	0.9836	1.003
pat_sex	0.8472	1.1804	0.6380	1.125
pat_fitzpatrick	1.1880	0.8418	0.8731	1.617
Immunosup_3	0.8577	1.1659	0.6397	1.150

Concordance= 0.553 (se = 0.023)

Likelihood ratio test= 6.95 on 4 df, p=0.1

wald test = 6.87 on 4 df, p=0.1

Score (logrank) test = 6.9 on 4 df, p=0.1

Tralokinumab

We excluded one multivariate outlier to improve model fit. Conclusion: no significant predictors for tralokinumab discontinuation were identified in this study population.

Call:

```
coxph(formula = Surv(Treatment_duration, med_stopped) ~ Age_med_start +  
      pat_sex + pat_fitzpatrick + Immunosup_3, data = data_no_outliers)
```

n= 50, number of events= 22

	coef	exp(coef)	se(coef)	z	Pr(> z)
Age_med_start	-0.01848	0.98169	0.01884	-0.981	0.327
pat_sex	-0.58907	0.55484	0.54708	-1.077	0.282
pat_fitzpatrick	-0.35530	0.70097	0.56757	-0.626	0.531
Immunosup_3	0.36015	1.43354	0.52923	0.681	0.496

	exp(coef)	exp(-coef)	lower .95	upper .95
Age_med_start	0.9817	1.0187	0.9461	1.019
pat_sex	0.5548	1.8023	0.1899	1.621
pat_fitzpatrick	0.7010	1.4266	0.2304	2.132
Immunosup_3	1.4335	0.6976	0.5081	4.045

Concordance= 0.641 (se = 0.071)

Likelihood ratio test= 2.19 on 4 df, p=0.7

Wald test = 2.18 on 4 df, p=0.7

Score (logrank) test = 2.23 on 4 df, p=0.7

Baricitinib

No outliers were detected. The proportional hazards assumption was not met for the variable sex (pat_sex, $p=0.0211$). Consequently, this variable was excluded from the final Cox regression model. Stratification was not feasible due to the limited number of events in the male and female subsets, which would have led to overfitting. Conclusion: no significant predictors for baricitinib discontinuation were identified in this study population.

call:

```
coxph(formula = Surv(Treatment_duration, med_stopped) ~ Age_med_start +  
      Immunosup_3 + pat_fitzpatrick, data = baricitinib_data)
```

n= 62, number of events= 44

	coef	exp(coef)	se(coef)	z	Pr(> z)
Age_med_start	-0.015363	0.984754	0.009173	-1.675	0.094 .
Immunosup_3	0.384400	1.468733	0.309080	1.244	0.214
pat_fitzpatrick	-0.293335	0.745772	0.359175	-0.817	0.414

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

	exp(coef)	exp(-coef)	lower .95	upper .95
Age_med_start	0.9848	1.0155	0.9672	1.003
Immunosup_3	1.4687	0.6809	0.8014	2.692
pat_fitzpatrick	0.7458	1.3409	0.3689	1.508

Concordance= 0.581 (se = 0.049)

Likelihood ratio test= 4.69 on 3 df, $p=0.2$

Wald test = 4.54 on 3 df, $p=0.2$

Score (logrank) test = 4.63 on 3 df, $p=0.2$

Upadacitinib

We excluded one multivariate outlier to improve model fit. Conclusion: no significant predictors for upadacitinib discontinuation were identified in this study population.

Call:

```
coxph(formula = Surv(Treatment_duration, med_stopped) ~ Age_med_start +  
      pat_sex + pat_fitzpatrick + Immunosup_3, data = data_no_outliers)
```

n= 110, number of events= 39

	coef	exp(coef)	se(coef)	z	Pr(> z)
Age_med_start	-0.01569	0.98443	0.01203	-1.305	0.1921
pat_sex	0.61660	1.85262	0.34924	1.766	0.0775 .
pat_fitzpatrick	0.16440	1.17868	0.35057	0.469	0.6391
Immunosup_3	-0.25619	0.77399	0.34496	-0.743	0.4577

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

	exp(coef)	exp(-coef)	lower .95	upper .95
Age_med_start	0.9844	1.0158	0.9615	1.008
pat_sex	1.8526	0.5398	0.9344	3.673
pat_fitzpatrick	1.1787	0.8484	0.5929	2.343
Immunosup_3	0.7740	1.2920	0.3936	1.522

Concordance= 0.617 (se = 0.052)

Likelihood ratio test= 6.24 on 4 df, p=0.2

wald test = 5.83 on 4 df, p=0.2

Score (logrank) test = 5.89 on 4 df, p=0.2

Abrocitinib

We excluded one multivariate outlier to improve model fit. Conclusion: no significant predictors for abrocitinib discontinuation were identified in this study population.

call:

```
coxph(formula = surv(Treatment_duration, med_stopped) ~ Age_med_start +  
      pat_sex + pat_fitzpatrick + Immunosup_3, data = data_no_outliers)
```

n= 42, number of events= 18

	coef	exp(coef)	se(coef)	z	Pr(> z)
Age_med_start	-0.02356	0.97671	0.02104	-1.120	0.2627
pat_sex	-0.59072	0.55393	0.51138	-1.155	0.2480
pat_fitzpatrick	-1.79656	0.16587	1.03694	-1.733	0.0832 .
Immunosup_3	0.15411	1.16662	0.50431	0.306	0.7599

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

	exp(coef)	exp(-coef)	lower .95	upper .95
Age_med_start	0.9767	1.0238	0.93726	1.018
pat_sex	0.5539	1.8053	0.20331	1.509
pat_fitzpatrick	0.1659	6.0289	0.02173	1.266
Immunosup_3	1.1666	0.8572	0.43417	3.135

Concordance= 0.684 (se = 0.058)

Likelihood ratio test= 6.99 on 4 df, p=0.1

wald test = 5.32 on 4 df, p=0.3

Score (logrank) test = 6.01 on 4 df, p=0.2