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Title: Impact of Psychiatric Disease and Treatment on Biologic Drug Survival in Patients with Hidradenitis Suppurativa

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Nikolaj Holgersen and Valdemar Wendelboe Nielsen have no potential conflicts of interests regarding this paper.
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Dear Editor,

Biologic therapies have improved hidradenitis suppurativa (HS) treatment options[1], yet their limited drug survival remains a concern, with few studies exploring discontinuation reasons[2]. Psychiatric disease (PD) impairs the adherence to treatment for chronic diseases[3]. Hence, we assessed biologic drug survival and discontinuation risk in HS patients with and without PD, stratified by active psychopharmacotherapy treatment.

We conducted a nationwide cohort study between 2005-2022, using the Danish national registries, including all patients with an HS diagnosis initiated on a biologic treatment. PD was defined as a hospital diagnosis of depression, anxiety, or schizophrenia, or ≥3 relevant psychopharmacotherapy prescriptions. Patients were considered under active treatment if they filled a psychopharmacotherapy prescription 12 months prior to biologic initiation. Discontinuation risk was assessed using age- and sex-adjusted hazard ratios (HR) from Cox regression models. Additional methodological details are provided in the supplementary material.

Among 584 patients (1,040 treatment series), 255 (43.7%) had a history of PD. Patients with PD were slightly older (mean age 42.0 (SD 12.3)) vs. 41.3 (SD 13.8)) and more often female (68.2% vs. 53.3%) compared to those without PD (Supplementary table 1). History of smoking (42.0% vs. 28.4%), alcohol abuse (20.0% vs. 13.5%), and recreational drug use (20.4% vs. 13.5%) was more common in the PD group. Median drug survival for patients with- and without PD was 33.0 vs. 36.9 weeks, respectively (Supplementary Figure 1). Patients receiving psychopharmacotherapy had similar drug survival to patients with no PD (34.9 weeks, p=0.34), and no increased discontinuation risk (HR=1.01 (0.85-1.18)) (Table 1). Patients not receiving psychopharmacotherapy had shorter drug survival (28.9 weeks, p=0.030) and higher discontinuation risk (HR=1.22 (1.02-1.45)) than those without PD (Supplementary Figure 2). Patients with prior psychiatric hospitalizations showed significantly shorter drug survival (28.9 weeks, p=0.030) and higher discontinuation risk (HR=1.24 (1.02–1.50)) compared to patients without PD (Supplementary table 2+3). This effect was more pronounced in those hospitalized not receiving active psychopharmacotherapy, with a median survival of 24.9 weeks (p=0.030) and an increased discontinuation risk (HR=1.41 (1.03–1.93)) (Figure 1).

We found an overall PD history in 43.7% of patients, which is higher than prior estimates[4,5], likely due to more severe disease and higher comorbidity burden in patients starting biologics. Additionally, PD may impair adherence to prior HS treatments, potentially contributing to the initiation of biologics due to more severe disease trajectories.

Patients with PD on psychopharmacotherapy had drug survival similar to those without PD, while untreated PD was linked to significantly shorter drug survival. Psychiatric hospitalization predicted the poorest outcomes, likely reflecting more severe PD and warranting greater clinical attention for this group of patients.

A strength of this study is the large number of biologic treatment series as well as the long follow-up. Limitations include missing data on discontinuation reasons and potential underestimation of PD due to reliance on hospital diagnoses and prescriptions.

Overall, untreated PD decreases biologic drug survival in HS, an effect which is mitigated by psychopharmacotherapy. An integrated dermatologic-psychiatric approach may enhance biologic drug survival and improve patient outcomes.

Tables

	Years of follow-up	Number of discontinuations	IR per PY (95% CI)	Adjusted HR*	95 % CI	P-value
Overall	990.9	831	0.84 (0.78-0.90)			
No PD	563.6	445	0.79 (0.72-0.87)	[Reference]		
Any PD	427.3	386	0.90 (0.82-1.00)	1.08	0.94-1.24	0.27
Depression	319.3	295	0.92 (0.82-1.04)	1.11	0.95-1.29	0.17
Schizophrenia	98.0	76	0.77 (0.61-0.97)	0.99	0.77-1.26	0.91
Anxiety	325.1	298	0.92 (0.82-1.03)	1.08	0.93-1.26	0.28
> 1 PD	236.5	219	0.92 (0.81-1.06)	1.11	0.95-1.31	0.20
Untreated PD						
Any PD	169.6	174	1.03 (0.88-1.19)	**1.22**	**1.02-1.45**	**0.032**
Depression	107.7	117	1.09 (0.90-1.30)	**1.25**	**1.02-1.54**	**0.031**
Schizophrenia	10.1	11	1.09 (0.54-1.95)	1.23	0.67-2.23	0.51
Anxiety	119.0	124	1.04 (0.87-1.24)	**1.24**	**1.01-1.52**	**0.036**
> 1 PD	62.0	73	1.18 (0.92-1.48)	**1.34**	**1.04-1.72**	**0.022**
Current psychopharmacotherapy						
Any PD	257.7	212				
Depression	211.6	178	0.82 (0.72-0.94)	1.01	0.85-1.18	0.98
Schizophrenia	87.9	65	0.84 (0.72-0.97)	1.03	0.87-1.24	0.69
Anxiety	206.0	174	0.74 (0.57-0.94)	1.05	0.74-1.24	0.74
> 1 PD	174.4	146	0.84 (0.72-0.98)	1.00	0.84-1.20	0.93

Table 1: Drug survival and risk of discontinuation of a biologic drug, both overall, and by depression, anxiety, schizophrenia and whether the patient had more than 1 psychiatric disease. Data shown for overall groups and stratified for whether the patients where currently receiving pharmacotherapy for their PD.
*Adjusted for age and sex.
CI, confidence interval; HR, hazard ratio; IR, incidence rate; PD, psychiatric disease, PY; person years.

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Figure Legends:

Figure 1: Kaplan-Meier curve (smoothened) for drug survival of biologic drugs in the intra group analysis of patients with HS and psychiatric disease (PD), for the first two years after initiation. Data stratified by history of hospital admission for PD and whether the patients are currently receiving psychopharmacotherapy.
Orange: patients with a history of hospital admission for PD and currently receiving pharmacotherapy. Blue: patients not previously hospitalized for PD in current psychopharmacotherapy. Green: patients not previously hospitalized for PD not in current psychopharmacotherapy. Pink: patients previously hospitalized for PD not in current psychopharmacotherapy.