Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

Data sources

In Denmark, all residents are assigned a unique personal identification number at birth or migration through the Danish Civil Registration System [1], that enables cross-linkage of data from nationwide registries on individual-level. Tax-supported healthcare ensures that all residents have equal and unfettered access to general practitioners and specialists (including dermatologists) without charge, and the Danish National Patient Registry [2] contains prospectively collected data from all inpatient and outpatient contacts at all Danish hospitals, as well as from a number of private clinics. Data includes not only diagnosis, but also information about smoking, treatment procedures and surgeries (including HS-related surgical procedures). The registry contains data on biologic therapies prescribed for HS, which is solely prescribed from academic hospital centers in Denmark. Medication is given free of charge to patients directly from five academic hospital outpatient dermatology clinics (Bispebjerg University Hospital, Herlev-Gentofte University Hospital, and Aarhus University Hospital, respectively). Data on all pharmacy-dispensed medications are recorded in the Danish National Prescription Registry [3]. All laboratory measurements (e.g. C-reactive protein [CRP]) are recorded in the Register of Laboratory Results for Research.

Study design

We all identified biologic treatment series with adalimumab, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, secukinumab, and ustekinumab prescribed specifically for HS during the study period. Treatment series were discontinued at the end of drug supply of the last prescription in the treatment series, or when a new biologic therapy was initiated, whichever

came first. Treatment sequences were merged if the same drug was used in two consecutive series and the discontinuation was less than 90 days.

Statistical analysis

Patient characteristics were presented as frequencies with percentages for categorical variables and continuous variables were presented as means with standard deviations (SDs) or medians with interquartile ranges (IQRs) depending on their distributions. Survival analyses were performed using Cox regression to create adjusted hazard ratios (aHRs) in which age, sex, and number of previous therapies were chosen a priori and included as covariates in the adjusted models. We furthermore explored predictors for drug survival of adalimumab and infliximab (i.e., the two most frequently used biologics for HS) using univariate Cox regression analysis. We generated descriptive (unadjusted) survival curves using Kaplan-Meier plots, and visualized switching patterns using Sankey diagrams. Kaplan-Meier plots were presented as overall, as well as stratified into bio-naïve and non-naïve treatment series. Due to data security requirements, groups containing data on only one or two patients are presented as "less than 3". All analyses were performed using SAS version 9.4 (SAS Institute Inc. Cary, NC, USA) and STATA version 15.0 (StataCorp, College Station, TX, USA). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [4] recommendations were used for conduct and reporting of this study.

eTable 1: Characteristics of HS patients, prescribing hospitals and treatment series

	All patients (n=241)
Age at first biologic, mean (SD)	41.8 (12.6)
Sex, n (%)	
Women	149 (61.8)
Men	92 (38.2)
Body mass index (kg/m2), mean (SD)	31.9 (8.0)
Body weight in kg, mean (SD)	101.5 (27.1)
Smoking, n [%] (%)*	
Current	29 [42.7] (12.0)
Former	27 [39.7] (11.2)
Never	12 [17.7] (5.0)
Unknown/missing	173 (71.8)
Year of first biologic, n (%)	
Pre-2010	42 (17.4)
2010-2014	78 (32.4)
2015-2018	121 (50.2)
Prescribing hospital, n (%)	
Bispebjerg	66 (27.4)
Gentofte	10 (4.2)
Roskilde	97 (40.2)
Odense	21 (8.7)
Aarhus	47 (19.5)
Number of treatment series, n (%)	386 (100.0)
Adalimumab	256 (66.3)
Anakinra	7 (1.8)
Certolizumab pegol	3 (0.8)
Etanercept	23 (6.0)
Golimumab	3 (0.8)
Infliximab	66 (17.1)
Secukinumab	6 (1.6)
Ustekinumab	22 (5.7)

* [%] are percentages among patients with available data, whereas (%) are among the entire cohort SD, Standard deviation

eTable 2 - Follow-up time, failure rates and median time to discontinuation in HS patients treated with biologics

|	Follow-up time (years)	Failures	Failure rate per 100 person-years	95% CI	Survival time (weeks), Median (IQR)
All					
Adalimumab	229.3	200	87.2	75.9-100.2	36.0 (21.9-63.0)
Infliximab	79.3	58	73.1	56.5-94.6	28.7 (15.1-62.9)
Etanercept	13.6	22	161.5	106.4-245.3	17.9 (12.9-41.0)
Ustekinumab	22.2	12	54.0	30.6-95.0	26 (16.9-155.9)
Bio-naïve					
Adalimumab	170.9	146	85.4	72.6-100.5	39.6 (22.9-63.4)
Infliximab	44.6	28	62.7	43.3-90.9	33.7 (12.9-65.3)
Etanercept	4.7	9	192.0	99.9-369.0	17.9 (12.9-23.0)
Ustekinumab	12.8	6	47.0	21.1-104.7	40.6 (NA)
Non-naïve					
Adalimumab	58.4	54	92.5	70.9-120.8	28.9 (13.3-60.1)
Infliximab	34.7	30	86.5	60.5-123.7	27.1 (18.6-56.9)
Etanercept	8.9	13	145.5	84.5-250.6	17.9 (12.9-41.0)
Ustekinumab	9.5	6	63.3	28.4-140.9	26.0 (20.3-155.9)

CI, confidence interval; NA, not applicable

eTable 3 – Univariate Cox regression analysis for adalimumab and infliximab

		Adalimumab			Infliximab	
	n	HR (95% CI)	p-value	n	HR (95% CI)	p-value
Age	256	1.01 (0.99-1.01)	0.7310	66	0.99 (0.97-1.00)	0.1329
Sex	256	**0.69 (0.51-0.91)**	**0.0101**	66	0.94 (0.56-1.58)	0.8165
BMI	140	0.99 (0.97-1.01)	0.3708	49	1.00 (0.96-1.03)	0.7905
CRP	141	1.00 (0.99-1.01)	0.5995	35	**1.01 (1.00-1.03)**	**0.0319**
Smoking	82			35		
Never		(reference)			(reference)	
Former		1.68 (0.76-3.72)	0.2020		1.31 (0.36-4.77)	0.6799
Current		2.05 (0.94-4.48)	0.0721		1.39 (0.37-5.16)	0.6220
Disease duration	256	1.00 (0.97-1.02)	0.7138	66	0.99 (0.95-1.04)	0.7365
Previous biologic treatment	256	1.09 (0.80-1.49)	0.5832	66	1.07 (0.64-1.80)	0.7855
Concomitant antibiotic treatment	256	1.15 (0.77-1.72)	0.4982	66	**2.82 (1.36-5.86)**	**0.0055**
HS surgery during treatment series	256	0.59 (0.29-1.21)	0.1516	66	0.62 (0.26-1.46)	0.2773

BMI, body-mass index; CI, confidence interval; CRP, C-reactive protein; HR, hazard ratio; HS, hidradenitis suppurativa

eFigure. Drug-specific persistence in bio-naïve and non-naïve patients
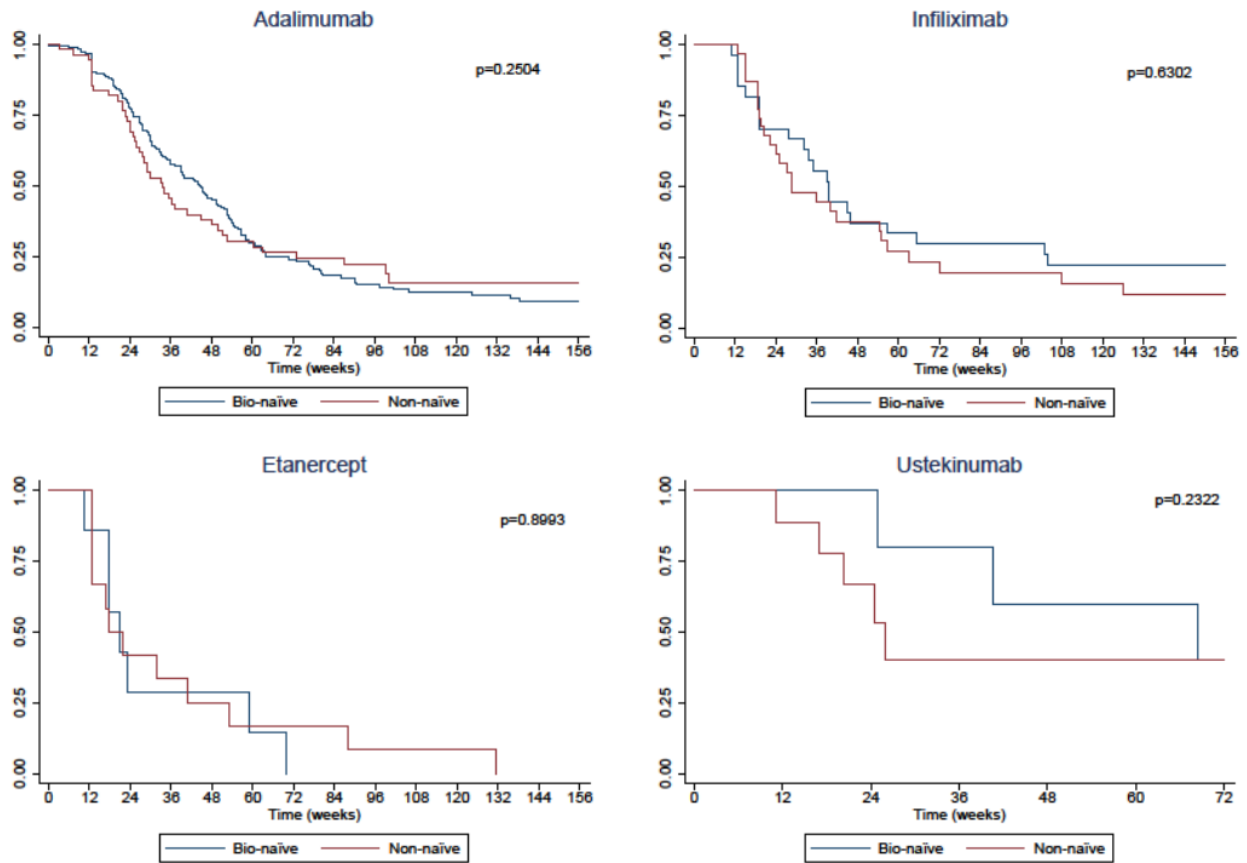
eFigure illustrates the drug-specific persistence of each biologics (Adalimumab, Infliximab, Etanercept and Ustekinumab, respectively) in bio-naïve and non-naïve HS patients

eReferences

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     tool in epidemiology. *European Journal of Epidemiology* vol. 29 541–549 (2014).

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