

Table SII. Hazard ratio (HR) for flares when having Psoriasis Area and Severity Index (PASI)=0 as reference, PASI=0 as reference since introduction of ustekinumab to the Danish market (1 March 2009), PASI=0 as reference since introduction of secukinumab to the Danish market (1 April 2015), and sensitivity analyses of different definitions of flares

	Unadjusted HR (95% CI)	p-value	Adjusted for drug, sex, and age HR (95% CI)	p-value	Fully adjusted* HR (95% CI)	p-value	Fully adjusted* with adjustment for pretreatment PASI HR (95% CI)	p-value
Flare (PASI ≥3)								
PASI=0	Ref.	-	Ref.	-	Ref.	-	Ref.	-
PASI >0-≤2	1.46 (1.16-1.83)	0.0013	1.37 (1.09-1.73)	0.0069	1.35 (1.07-1.70)	0.011	1.36 (1.11-1.72)	0.0086
PASI >2-≤4	2.70 (2.12-3.45)	<0.0001	2.39 (1.86-3.07)	<0.0001	2.32 (1.80-2.99)	<0.0001	2.23 (1.65-2.89)	<0.0001
PASI >4	2.92 (2.24-3.80)	<0.0001	2.51 (1.92-3.30)	<0.0001	2.38 (1.80-3.15)	<0.0001	2.24 (1.65-2.97)	<0.0001
Flare (PASI ≥5)								
PASI=0	Ref.	-	Ref.	-	Ref.	-	Ref.	-
PASI >0-≤2	1.47 (1.03-2.10)	0.033	1.40 (0.98-1.99)	0.07	1.39 (0.97-1.99)	0.07	1.39 (0.99-1.99)	0.07
PASI >2-≤4	3.00 (2.09-4.31)	<0.0001	2.83 (1.95-4.10)	<0.0001	2.85 (1.96-4.14)	<0.0001	2.70 (1.82-3.94)	<0.0001
PASI >4	3.38 (2.30-4.96)	<0.0001	3.16 (2.13-4.69)	<0.0001	3.28 (2.19-4.92)	<0.0001	3.00 (2.01-4.53)	<0.0001
Introduction of ustekinumab								
Flare (PASI ≥3)								
PASI =0 (n=698)	Ref.	-	Ref.	-	Ref.	-	Ref.	-
PASI >0-≤2 (n=441)	1.35 (1.06-1.73)	0.015	1.28 (1.00-1.63)	0.05	1.26 (0.98-1.61)	0.07	1.28 (1.00-1.63)	0.05
PASI >2-≤4 (n=208)	2.57 (1.96-3.35)	<0.0001	2.33 (1.77-3.07)	<0.0001	2.29 (1.73-3.02)	<0.0001	2.22 (1.65-2.94)	<0.0001
PASI >4 (n=151)	2.82 (2.09-3.81)	<0.0001	2.58 (1.90-3.51)	<0.0001	2.53 (1.85-3.45)	<0.0001	2.36 (1.65-3.22)	<0.0001
Flare (PASI ≥5)								
PASI =0 (n=698)	Ref.	-	Ref.	-	Ref.	-	Ref.	-
PASI >0-≤2 (n=441)	1.32 (0.90-1.94)	0.15	1.26 (0.86-1.85)	0.24	1.26 (0.86-1.85)	0.24	1.26 (0.82-1.84)	0.25
PASI >2-≤4 (n=208)	3.02 (2.05-4.45)	<0.0001	2.93 (1.97-4.36)	<0.0001	2.95 (1.98-4.40)	<0.0001	2.83 (1.82-4.22)	<0.0001
PASI >4 (n=151)	2.95 (1.88-4.61)	<0.0001	2.84 (1.80-4.47)	<0.0001	2.94 (1.85-4.68)	<0.0001	2.67 (1.65-4.26)	<0.0001
Introduction of secukinumab								
Flare (PASI ≥3)								
PASIO, n=325	Ref.	-	Ref.	-	Ref.	-	Ref.	-
PASIO-2, n=187	1.54 (0.88-2.71)	0.13	1.43 (0.79-2.57)	0.23	1.42 (0.79-2.57)	0.24	1.49 (0.90-2.72)	0.19
PASIO-4, n=67	4.89 (2.77-8.64)	<0.0001	4.61 (2.49-8.54)	<0.0001	4.68 (2.52-8.71)	<0.0001	5.09 (2.72-9.97)	<0.0001
PASI>4, n=42	4.41 (2.22-8.76)	<0.0001	4.17 (2.03-8.55)	<0.0001	4.23 (2.02-8.85)	<0.0001	3.61 (2.72-7.39)	0.0007
Flare (PASI ≥5)								
PASIO, n=325	Ref.	-	Ref.	-	Ref.	-	Ref.	-
PASIO-2, n=187	0.62 (0.20-1.95)	0.42	0.51 (0.16-1.64)	0.26	0.49 (0.15-1.59)	0.23	0.51 (0.16-1.64)	0.26
PASIO-4, n=67	5.40 (2.36-12.5)	<0.0001	4.59 (1.89-11.1)	0.0008	4.31 (1.75-10.7)	0.0015	4.96 (1.99-12.4)	0.0006
PASI>4, n=42	6.7 (2.71-16.8)	<0.0001	6.17 (2.36-16.1)	0.0002	7.26 (2.62-20.1)	0.0001	5.98 (2.16-16.6)	0.0006
Sensitivity analyses of different definitions of flares								
Flare (absolute PASI ≥5)								
PASI =0	Ref.	-	Ref.	-	Ref.	-	Ref.	-
PASI >0-≤2	5.38 (2.75-10.5)	<0.0001	4.95 (2.52-9.73)	<0.0001	4.75 (2.40-9.38)	<0.0001	4.91 (2.49-9.71)	<0.0001
PASI >2-≤4	14.9 (7.74-28.8)	<0.0001	12.8 (6.53-25.1)	<0.0001	12.6 (6.38-25.0)	<0.0001	11.2 (5.64-22.2)	<0.0001
Flare (relative increase in area subcategory of PASI ≥2)								
PASI=0 (n=346)	Ref.	-	Ref.	-	Ref.	-	Ref.	-
PASI >0-≤2 (n=338)	1.93 (0.83-4.51)	0.13	1.73 (0.74-4.06)	0.21	1.78 (0.75-4.21)	0.19	1.76 (0.74-4.16)	0.20
PASI >2-≤4 (n=177)	5.86 (2.59-13.0)	<0.0001	5.11 (2.27-11.5)	<0.0001	5.97 (2.63-13.5)	<0.0001	5.61 (2.47-12.7)	<0.0001
PASI >4 (n=151)	15.2 (7.09-32.5)	<0.0001	13.4 (6.18-29.1)	<0.0001	15.1 (6.82-33.6)	<0.0001	13.7 (6.16-30.5)	<0.0001

*Adjusted for drug, sex, age, methotrexate, psoriatic arthritis, body weight, and hospital.
Ref.: reference group; 95% CI: 95% confidence interval.