



Universitätsklinikum
Hamburg-Eppendorf

IVDP - Institut für Versorgungsforschung
in der Dermatologie und bei Pflegeberufen

CVderm
Competenzzentrum Versorgungsforschung
in der Dermatologie

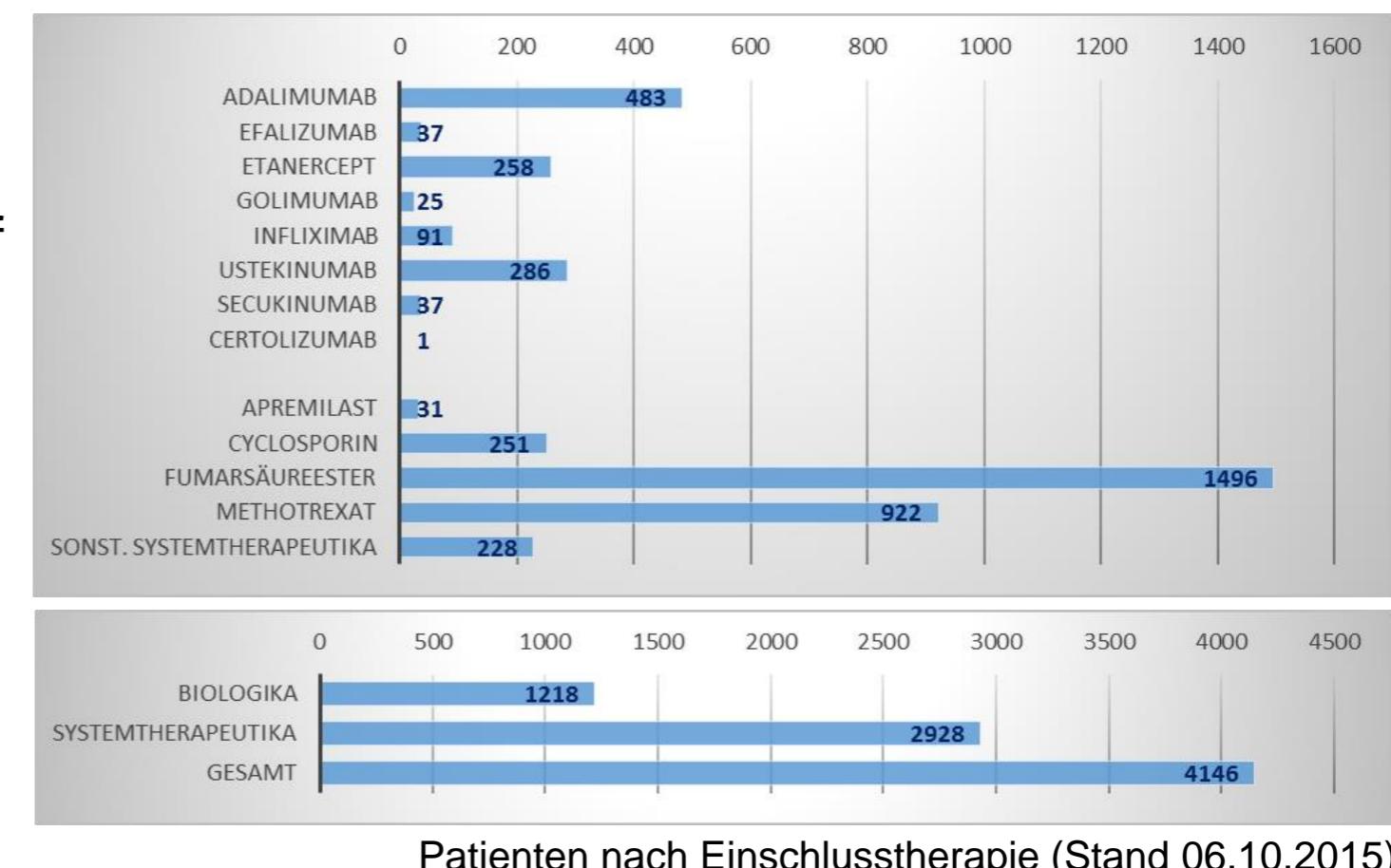
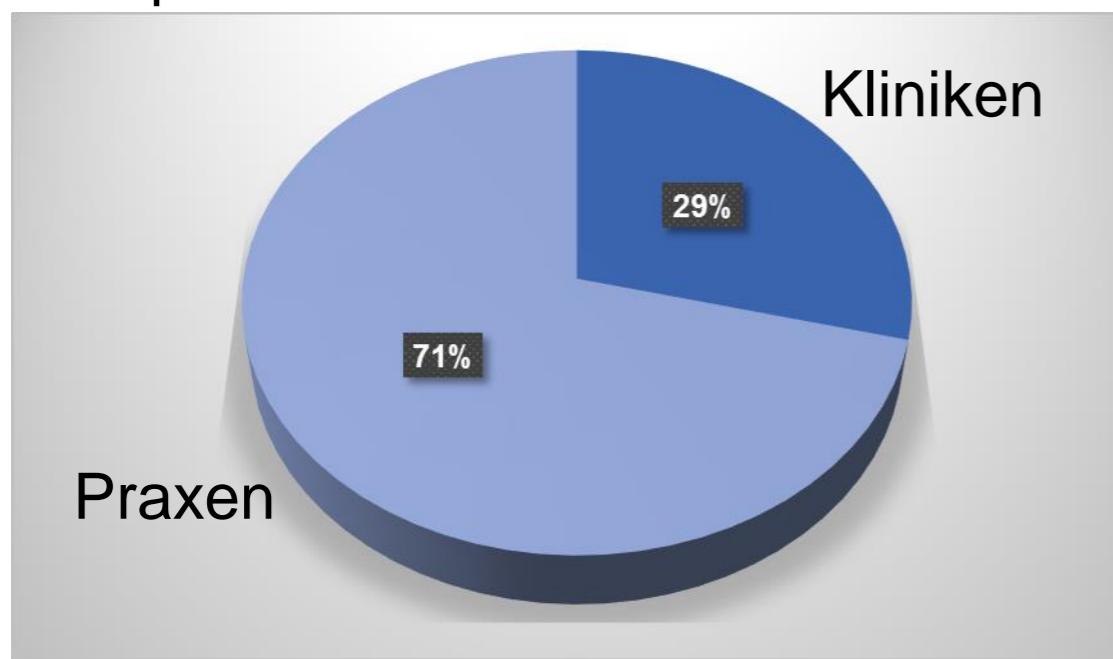
PsoBest: Pharmakovigilanz systemischer Psoriasistherapie in der Routineversorgung



Lüdcke HJ, Rustenbach SJ, von Kiedrowski R, Radtke M, Spehr C, Knopf S, Augustin M
für die aktiven Studienzentren und den wissenschaftlichen Beirat von PsoBest

Das Deutsche Psoriasis-Register PsoBest

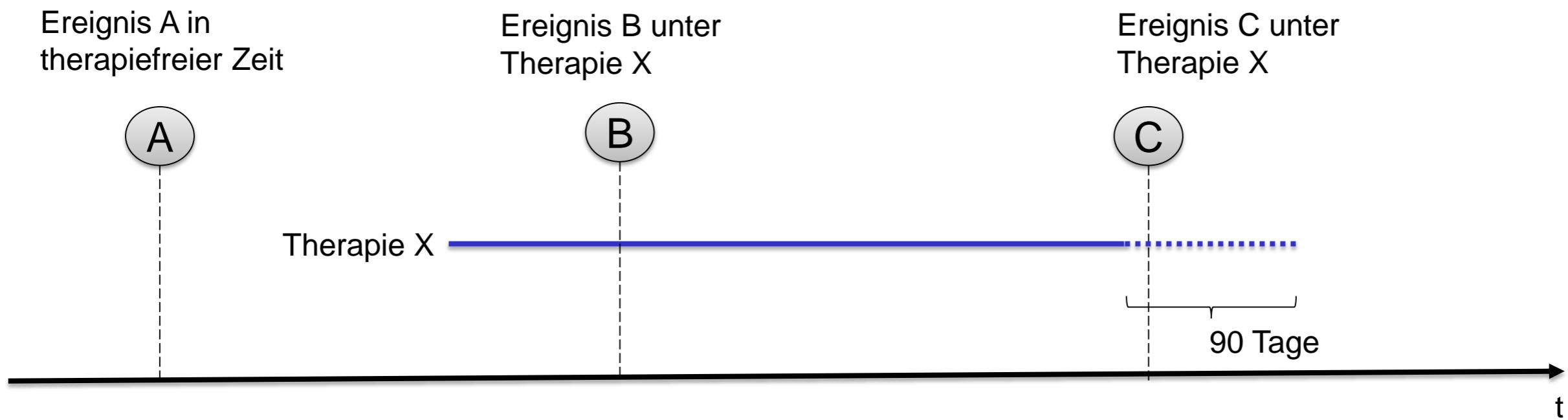
- Nationale Langzeitbeobachtung bei Erstverordnung einer systemischen Therapie
- Unabhängig vom weiteren Therapieverlauf
- Bis zu 10 Jahre Beobachtung
- Arzt- und Patientenbefragung (alle 6 Monate)
- Postalische Zwischenerhebungen
- First patient in: 07.12.2007



- Über 600 teilnehmende Dermatologen und Klinikambulanzen (ca. 250 aktiv)

Analyse (schwerwiegender) unerwünschter Ereignisse - Methoden

- Stand 30.06.2014, n=3322 Patienten
- Patienten mit validierten Therapieinformationen
- Biologika (ADA, ETA, EFA, INF, GOL, UST) vs. konventionelle Systemtherapie (CYA, FSE, MTX, RET, LEF, syst. PUVA)
- Baseline-Beschreibung
- Analyse aller gemeldeten Ereignisse nach Manchester-Template





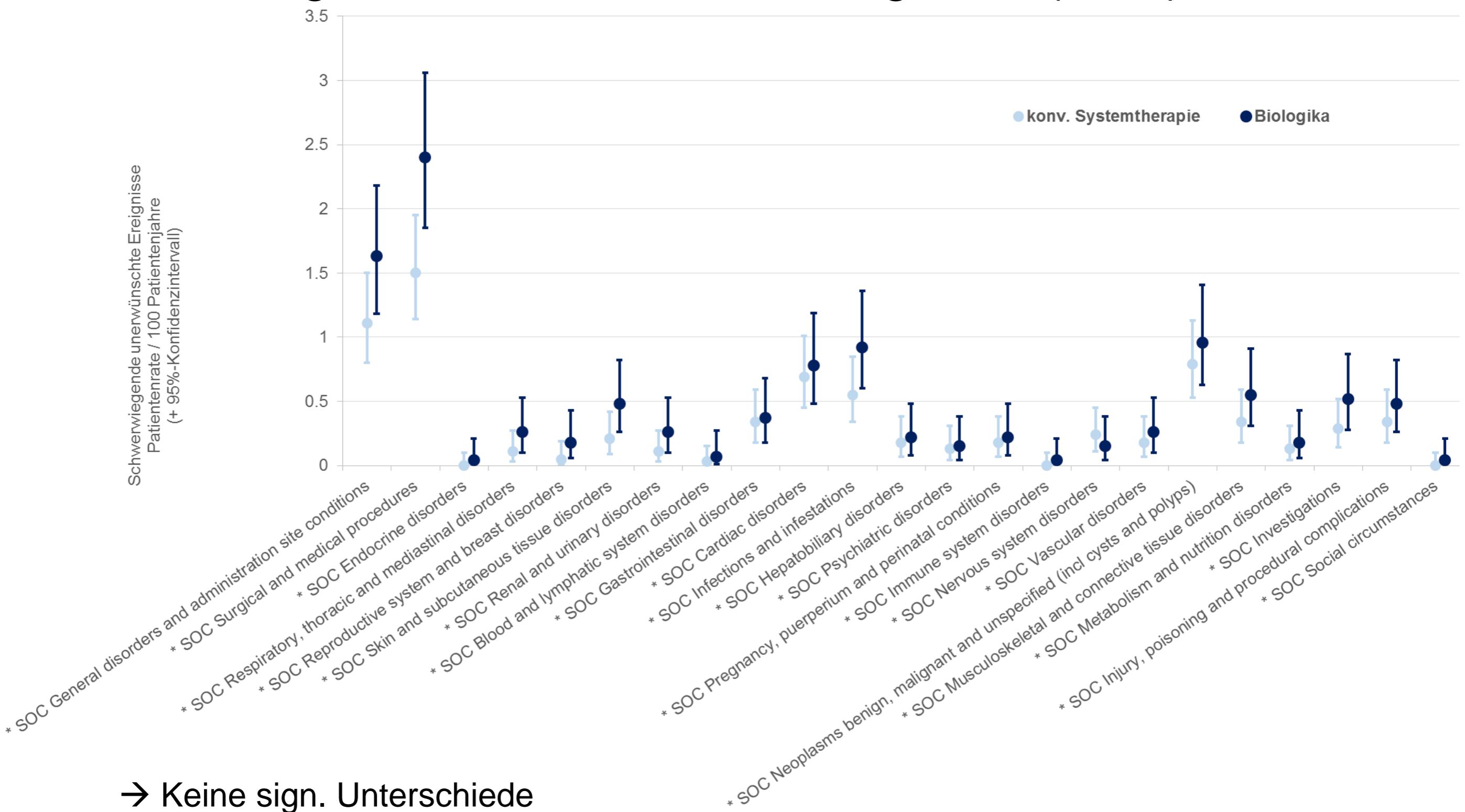
Baseline

	p≤	Biologika			konv. Systemtherapien		
		N	% / MW	SD	N	% / MW	SD
weiblich	0.002	439	37.1	.	1042	40.9	.
Nagelbeteiligung	0.001	729	61.6	.	1283	50.4	.
Psoriasis-Arthritis	0.001	566	47.8	.	672	26.4	.
Alter [Jahre]	0.578	1182	47.5	13.3	2543	47.4	14.5
Alter Body Mass Index [kg/m ²]	0.001	1177	28.8	6.0	2530	28.3	5.8
Erkrankungsdauer [Jahre]	0.001	1101	20.9	13.8	2329	16.9	14.1
Body surface area (BSA, befallene Körperoberfläche in %)	0.001	1160	25.9	22.1	2486	23.3	19.8
Psoriasis Area and Severity Index (PASI); Range 0 -72 (höchster Schweregrad)	0.001	1163	15.6	10.6	2484	14.2	9.3
Schweregrad der Psoriasis, Patientenurteil, VAS 0-10 (höchster Schweregrad)	0.132	1151	6.5	2.5	2480	6.4	2.3
Aktivität der Psoriasis-Arthritis, Arzturteil, VAS 0-10 (höchste Aktivität)	0.001	669	3.0	3.0	1091	2.2	2.7
Schmerzen bei Psoriasis-Arthritis, Patientenurteil, VAS 0-10 (stärkster Schmerz)	0.001	701	3.8	3.0	1238	2.9	3.0
EQ 5-D VAS-Gesundheitszustand, VAS 0-100 (bester Gesundheitszustand)	0.001	1134	50.7	23.9	2436	54.8	23.2
Dermatology Life Quality Index (DLQI); Range 0-30 (stärkste Einschränkung)	0.001	1159	11.9	7.4	2501	11.1	7.0

Expositionszeiten:

- 2704 Jahre Biologika (ever-exposed 2913 Jahre)
- 3787 Jahre konv. Systemtherapie (ever-exposed 4144 Jahre)

Schwerwiegende unerwünschte Ereignisse (SUE)





SUE – TOP10

	Systemics, cumulative (12/13/2007 to 06/30/2014)			Patients cumulative/100 Patient Years (95% confidence interval)		
	events	patients	% patients	male	female	total
Condition aggravated	27	23	0.90	0.41 (0.19-0.78)	0.81 (0.43-1.39)	0.58 (0.36-0.88)
Death	9	9	0.35	0.32 (0.13-0.66)	0.12 (0.02-0.45)	0.24 (0.11-0.45)
Myocardial infarction	9	9	0.35	0.27 (0.10-0.60)	0.19 (0.04-0.55)	0.24 (0.11-0.45)
Pregnancy	7	7	0.27	0.00 (0.00-0.17)	0.44 (0.18-0.90)	0.18 (0.07-0.38)
Basal cell carcinoma	6	6	0.24	0.18 (0.05-0.47)	0.12 (0.02-0.45)	0.16 (0.06-0.34)
Joint arthroplasty	4	4	0.16	0.05 (0.00-0.25)	0.19 (0.04-0.55)	0.11 (0.03-0.27)
Stent placement	4	4	0.16	0.18 (0.05-0.47)	0.00 (0.00-0.23)	0.11 (0.03-0.27)
Gastritis	4	4	0.16	0.05 (0.00-0.25)	0.19 (0.04-0.55)	0.11 (0.03-0.27)
Cholelithiasis	4	4	0.16	0.00 (0.00-0.17)	0.25 (0.07-0.64)	0.11 (0.03-0.27)
Cerebrovascular accident	4	4	0.16	0.14 (0.03-0.40)	0.06 (0.00-0.35)	0.11 (0.03-0.27)

	Biologics, cumulative (12/13/2007 to 06/30/2014)			Patients cumulative/100 Patient Years (95% confidence interval)		
	events	patients	% patients	male	female	total
Condition aggravated	36	28	2.37	0.52 (0.24-0.99)	1.93 (1.16-3.01)	1.04 (0.69-1.50)
Myocardial infarction	9	9	0.76	0.47 (0.20-0.92)	0.10 (0.00-0.57)	0.33 (0.15-0.63)
Death	6	6	0.51	0.23 (0.06-0.60)	0.20 (0.02-0.73)	0.22 (0.08-0.48)
Joint arthroplasty	5	5	0.42	0.06 (0.00-0.32)	0.41 (0.11-1.04)	0.18 (0.06-0.43)
Pneumonia	5	5	0.42	0.17 (0.04-0.51)	0.20 (0.02-0.73)	0.18 (0.06-0.43)
Erysipelas	5	5	0.42	0.23 (0.06-0.60)	0.10 (0.00-0.57)	0.18 (0.06-0.43)
Basal cell carcinoma	5	5	0.42	0.12 (0.01-0.42)	0.30 (0.06-0.89)	0.18 (0.06-0.43)
Cardiac failure	4	4	0.34	0.23 (0.06-0.60)	0.00 (0.00-0.37)	0.15 (0.04-0.38)
Pregnancy	5	4	0.34	0.00 (0.00-0.21)	0.41 (0.11-1.04)	0.15 (0.04-0.38)
Osteoarthritis	4	4	0.34	0.06 (0.00-0.32)	0.30 (0.06-0.89)	0.15 (0.04-0.38)



SUE – ever exposed

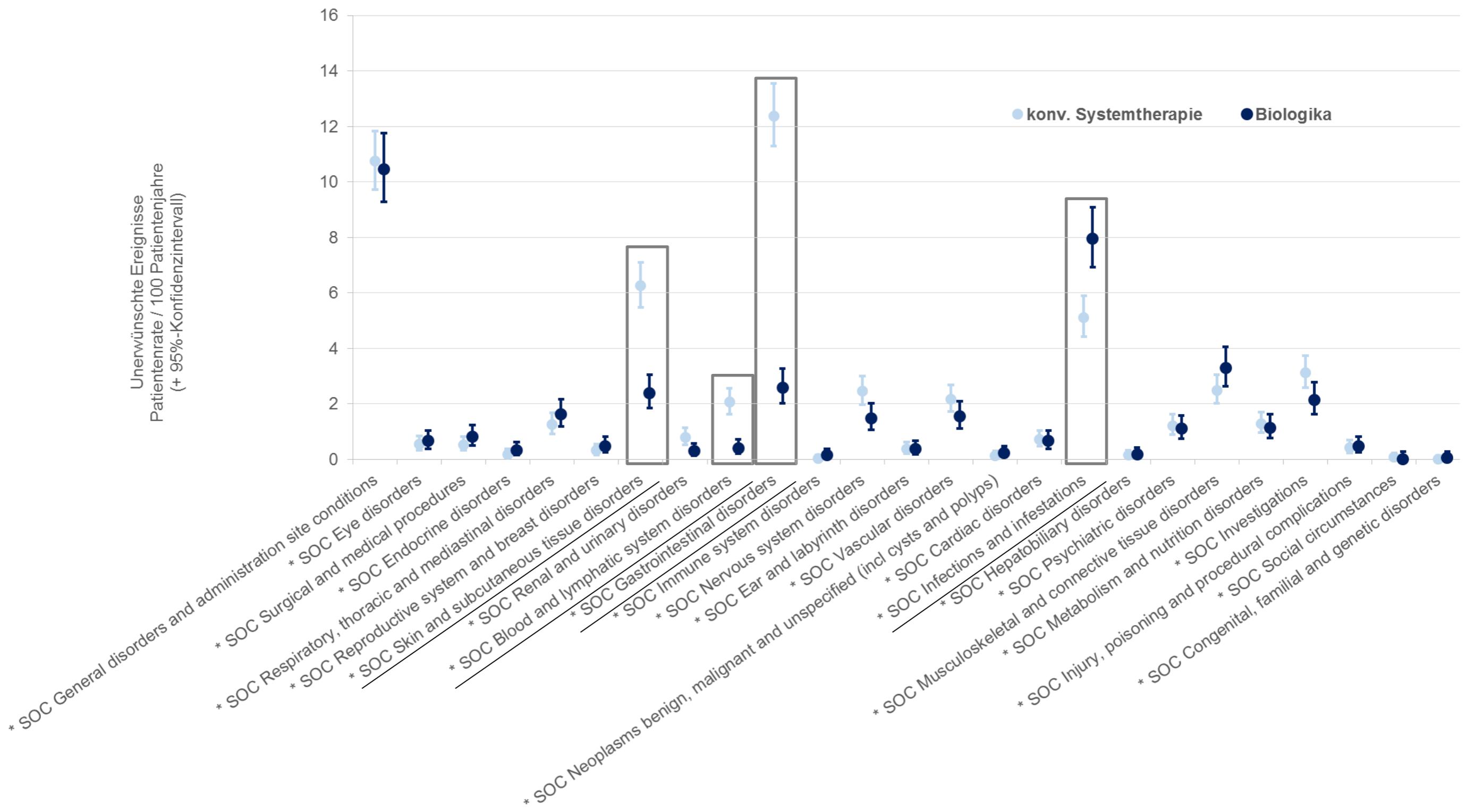
All cause death

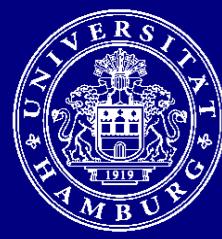
	male			female			Patients cumulative/100 Patient Years (95% confidence interval)		
	events	patients	% patients	events	patients	% patients	male	female	total
	Systemics	17	17	1.13	4	4	0.38	0.71 (0.41-1.13)	0.23 (0.06-0.59)
Biologics	11	11	1.48	3	3	0.68	0.61 (0.30-1.08)	0.27 (0.06-0.80)	0.48 (0.26-0.81)

Malignancies

	male			female			Patients cumulative/100 Patient Years (95% confidence interval)		
	events	patients	% patients	events	patients	% patients	male	female	total
	Systemics	26	19	1.26	11	10	0.96	0.79 (0.48-1.24)	0.57 (0.28-1.06)
Biologics	24	16	2.15	9	9	2.05	0.88 (0.50-1.43)	0.82 (0.38-1.56)	0.86 (0.56-1.27)

Unerwünschte Ereignisse (UE)





UE TOP10 für differente SOCs: SYS vs. BIOL

	Systemics, cumulative (12/13/2007 to 06/30/2014)			Systemics, Patients cumulative/100 Patient Years (95% confidence interval)			Biologics, Patients cumulative/100 Patient Years (95% confidence interval)		
	events	patients	% patients	male	female	total	male	female	total
* SOC Skin and subcutaneous tissue disorders	319	237	9.31	6.04 (5.05-7.16)	6.56 (5.36-7.94)	6.26 (5.49-7.11)	1.80 (1.22-2.56)	3.45 (2.39-4.82)	2.40 (1.85-3.06)
Erythema	160	131	5.15	3.93 (3.15-4.86)	2.81 (2.05-3.76)	3.46 (2.89-4.10)	0.12 (0.01-0.42)	0.51 (0.16-1.18)	0.26 (0.10-0.53)
Pruritus	26	24	0.94	0.41 (0.19-0.78)	0.94 (0.52-1.55)	0.63 (0.41-0.94)	0.23 (0.06-0.60)	0.51 (0.16-1.18)	0.33 (0.15-0.63)
Hyperhidrosis	16	15	0.59	0.46 (0.22-0.84)	0.31 (0.10-0.73)	0.40 (0.22-0.65)	0.17 (0.04-0.51)	0.30 (0.06-0.89)	0.22 (0.08-0.48)
Alopecia	16	15	0.59	0.18 (0.05-0.47)	0.69 (0.34-1.23)	0.40 (0.22-0.65)	0.06 (0.00-0.32)	0.20 (0.02-0.73)	0.11 (0.02-0.32)
Alopecia effluvium	10	10	0.39	0.09 (0.01-0.33)	0.50 (0.22-0.98)	0.26 (0.13-0.49)	0.06 (0.00-0.32)	0.20 (0.02-0.73)	0.11 (0.02-0.32)
Skin burning sensation	9	9	0.35	0.23 (0.07-0.53)	0.25 (0.07-0.64)	0.24 (0.11-0.45)	0.06 (0.00-0.32)	0.00 (0.00-0.37)	0.04 (0.00-0.21)
Urticaria	7	7	0.27	0.18 (0.05-0.47)	0.19 (0.04-0.55)	0.18 (0.07-0.38)	0.12 (0.01-0.42)	0.20 (0.02-0.73)	0.15 (0.04-0.38)
Rash	7	7	0.27	0.14 (0.03-0.40)	0.25 (0.07-0.64)	0.18 (0.07-0.38)	0.06 (0.00-0.32)	0.20 (0.02-0.73)	0.11 (0.02-0.32)
Dermatitis	4	4	0.16	0.00 (0.00-0.17)	0.25 (0.07-0.64)	0.11 (0.03-0.27)	0.00 (0.00-0.21)	0.10 (0.00-0.57)	0.04 (0.00-0.21)
Cheilitis	4	3	0.12	0.09 (0.01-0.33)	0.06 (0.00-0.35)	0.08 (0.02-0.23)	0.12 (0.01-0.42)	0.00 (0.00-0.37)	0.07 (0.01-0.27)
* SOC Blood and lymphatic system disorders	118	78	3.06	2.33 (1.74-3.07)	1.69 (1.11-2.45)	2.06 (1.63-2.57)	0.23 (0.06-0.60)	0.71 (0.29-1.46)	0.41 (0.20-0.73)
Lymphopenia	62	46	1.81	1.51 (1.04-2.12)	0.81 (0.43-1.39)	1.21 (0.89-1.62)	0.00 (0.00-0.21)	0.00 (0.00-0.37)	0.00 (0.00-0.14)
Eosinophilia	17	15	0.59	0.32 (0.13-0.66)	0.50 (0.22-0.98)	0.40 (0.22-0.65)	0.00 (0.00-0.21)	0.00 (0.00-0.37)	0.00 (0.00-0.14)
Leukopenia	15	15	0.59	0.59 (0.32-1.02)	0.12 (0.02-0.45)	0.40 (0.22-0.65)	0.00 (0.00-0.21)	0.00 (0.00-0.37)	0.00 (0.00-0.14)
Lymphadenopathy	7	2	0.08	0.05 (0.00-0.25)	0.06 (0.00-0.35)	0.05 (0.01-0.19)	0.06 (0.00-0.32)	0.30 (0.06-0.89)	0.15 (0.04-0.38)
Thrombocytopenia	6	6	0.24	0.18 (0.05-0.47)	0.12 (0.02-0.45)	0.16 (0.06-0.34)	0.06 (0.00-0.32)	0.00 (0.00-0.37)	0.04 (0.00-0.21)
Anaemia	5	4	0.16	0.09 (0.01-0.33)	0.12 (0.02-0.45)	0.11 (0.03-0.27)	0.06 (0.00-0.32)	0.10 (0.00-0.57)	0.07 (0.01-0.27)
Iron deficiency anaemia	2	2	0.08	0.00 (0.00-0.17)	0.12 (0.02-0.45)	0.05 (0.01-0.19)	0.00 (0.00-0.21)	0.00 (0.00-0.37)	0.00 (0.00-0.14)
Leukocytosis	1	1	0.04	0.00 (0.00-0.17)	0.06 (0.00-0.35)	0.03 (0.00-0.15)	0.00 (0.00-0.21)	0.10 (0.00-0.57)	0.04 (0.00-0.21)
Monocytosis	1	1	0.04	0.00 (0.00-0.17)	0.06 (0.00-0.35)	0.03 (0.00-0.15)	0.00 (0.00-0.21)	0.00 (0.00-0.37)	0.00 (0.00-0.14)
Pancytopenia	1	1	0.04	0.00 (0.00-0.17)	0.06 (0.00-0.35)	0.03 (0.00-0.15)	0.00 (0.00-0.21)	0.10 (0.00-0.57)	0.04 (0.00-0.21)
* SOC Gastrointestinal disorders	835	469	18.42	11.52 (10.14-13.04)	13.55 (11.81-15.48)	12.38 (11.29-13.56)	2.27 (1.61-3.10)	3.15 (2.14-4.47)	2.59 (2.02-3.27)
Diarrhoea	256	221	8.68	5.49 (4.55-6.56)	6.31 (5.14-7.67)	5.83 (5.09-6.66)	0.35 (0.13-0.76)	0.51 (0.16-1.18)	0.41 (0.20-0.73)
Nausea	144	121	4.75	2.52 (1.89-3.27)	4.12 (3.19-5.24)	3.19 (2.65-3.82)	0.52 (0.24-0.99)	0.61 (0.22-1.33)	0.55 (0.31-0.91)
Abdominal pain upper	91	85	3.34	2.06 (1.50-2.75)	2.50 (1.78-3.40)	2.24 (1.79-2.77)	0.00 (0.00-0.21)	0.41 (0.11-1.04)	0.15 (0.04-0.38)
Abdominal pain	73	67	2.63	1.46 (1.00-2.07)	2.19 (1.52-3.04)	1.77 (1.37-2.25)	0.06 (0.00-0.32)	0.10 (0.00-0.57)	0.07 (0.01-0.27)
Abdominal discomfort	67	62	2.44	1.46 (1.00-2.07)	1.87 (1.26-2.68)	1.64 (1.25-2.10)	0.23 (0.06-0.60)	0.30 (0.06-0.89)	0.26 (0.10-0.53)
Gastrointestinal pain	36	34	1.34	0.55 (0.28-0.96)	1.37 (0.86-2.08)	0.90 (0.62-1.25)	0.06 (0.00-0.32)	0.10 (0.00-0.57)	0.07 (0.01-0.27)
Abdominal distension	23	21	0.82	0.50 (0.25-0.90)	0.62 (0.30-1.15)	0.55 (0.34-0.85)	0.06 (0.00-0.32)	0.10 (0.00-0.57)	0.07 (0.01-0.27)
Vomiting	20	18	0.71	0.14 (0.03-0.40)	0.94 (0.52-1.55)	0.48 (0.28-0.75)	0.06 (0.00-0.32)	0.10 (0.00-0.57)	0.07 (0.01-0.27)
Gastrointestinal disorder	16	15	0.59	0.27 (0.10-0.60)	0.56 (0.26-1.07)	0.40 (0.22-0.65)	0.00 (0.00-0.21)	0.00 (0.00-0.37)	0.00 (0.00-0.14)
Dyspepsia	14	13	0.51	0.41 (0.19-0.78)	0.25 (0.07-0.64)	0.34 (0.18-0.59)	0.12 (0.01-0.42)	0.20 (0.02-0.73)	0.15 (0.04-0.38)



UE TOP10 für differente SOCs: BIOL vs. SYS

	Biologics, cumulative (12/13/2007 to 06/30/2014)			Biologics, Patients cumulative/100 Patient Years (95% confidence interval)			Systemics, Patients cumulative/100 Patient Years (95% confidence interval)		
	events	patients	% patients	male	female	total	male	female	total
* SOC Infections and infestations	323	215	18.17	6.98 (5.79-8.34)	9.64 (7.80-11.79)	7.95 (6.92-9.09)	4.66 (3.80-5.66)	5.75 (4.63-7.05)	5.12 (4.43-5.90)
Nasopharyngitis	144	115	9.72	3.78 (2.92-4.82)	5.08 (3.77-6.69)	4.25 (3.51-5.10)	1.83 (1.31-2.49)	2.87 (2.10-3.83)	2.27 (1.82-2.80)
Bronchitis	20	18	1.52	0.29 (0.09-0.68)	1.32 (0.70-2.26)	0.67 (0.39-1.05)	0.18 (0.05-0.47)	0.37 (0.14-0.82)	0.26 (0.13-0.49)
Sinusitis	12	12	1.01	0.29 (0.09-0.68)	0.71 (0.29-1.46)	0.44 (0.23-0.78)	0.27 (0.10-0.60)	0.12 (0.02-0.45)	0.21 (0.09-0.42)
Influenza	11	6	0.51	0.23 (0.06-0.60)	0.20 (0.02-0.73)	0.22 (0.08-0.48)	0.14 (0.03-0.40)	0.25 (0.07-0.64)	0.18 (0.07-0.38)
Erysipelas	10	8	0.68	0.23 (0.06-0.60)	0.41 (0.11-1.04)	0.30 (0.13-0.58)	0.09 (0.01-0.33)	0.06 (0.00-0.35)	0.08 (0.02-0.23)
Pneumonia	9	9	0.76	0.35 (0.13-0.76)	0.30 (0.06-0.89)	0.33 (0.15-0.63)	0.18 (0.05-0.47)	0.06 (0.00-0.35)	0.13 (0.04-0.31)
Upper respiratory tract infection	9	9	0.76	0.17 (0.04-0.51)	0.61 (0.22-1.33)	0.33 (0.15-0.63)	0.14 (0.03-0.40)	0.31 (0.10-0.73)	0.21 (0.09-0.42)
Gastrointestinal infection	8	8	0.68	0.23 (0.06-0.60)	0.41 (0.11-1.04)	0.30 (0.13-0.58)	0.14 (0.03-0.40)	0.19 (0.04-0.55)	0.16 (0.06-0.34)
Herpes simplex	7	6	0.51	0.12 (0.01-0.42)	0.41 (0.11-1.04)	0.22 (0.08-0.48)	0.00 (0.00-0.17)	0.12 (0.02-0.45)	0.05 (0.01-0.19)
Herpes zoster	7	7	0.59	0.23 (0.06-0.60)	0.30 (0.06-0.89)	0.26 (0.10-0.53)	0.23 (0.07-0.53)	0.12 (0.02-0.45)	0.18 (0.07-0.38)



Fazit

- ❖ klinische Unterschiede bei Behandlung in entsprechenden Therapiearmen
- ❖ therapie- und indikationsspezifische Unterschiede
- ❖ Keine erhöhten Risiken im allg. Sicherheitsprofil

- ❖ Weitere Beobachtungszeit zur klinischen Einordnung bei UE-Unterschieden und Langzeiteffekten



**Drug Safety of systemic treatments for psoriasis:
results from The German Psoriasis Registry PsoBest**
Reich et al. Arch Dermatol Res