

1

Online-Only Supplements**Table of Content**

Supplemental Table 1: Data sources	2
Supplemental Table 2: Cohort Characteristics	4
Supplemental Table 3: Outcome	5
Supplemental Figure 1: Exclusion/Inclusion Criteria	6
Supplemental Figure 2: Case numbers and deaths reported to FAERS.	7
Supplemental Figure 3: Multivariable regression analysis for the event month	8
Supplemental Figure 4: Univariable regression analysis	9

Supplemental Table 1: Data sources

	Unit	Source
Age	years	FAERS
Sex		FAERS
Mortality		FAERS, based on "Outcomes"
Diagnosis		FAERS, based on «Reason for use»
Region		FAERS, based on "Country"
Medication		FAERS, based on "Product Active Ingredient"
Ratio of total reports to FAERS to the number of reported deaths to FAERS for each drug in 2018-2020 excluding COVID-19 cases		FAERS (Computed)
Hospital beds per 1000 persons per country		The World Bank
Health expenditure per Capita (USD) per country	USD	The World Bank
Case fatality rate per month and country		Our World in Data (Computed)
New cases per population, month and country		Our World in Data (Computed)
New deaths per population/ month and country		Our World in Data (Computed)

3

Variables and data sources. The following search terms were used in FAERS[1]: "COVID-19", "Coronavirus-Infection", "Exposure to SARS-CoV2", "SARS-CoV2-Test", "Exposure/ occupational exposure to SARS-CoV2". Healthcare system variables (derived from "Our World In Data"[2] and World Bank[3,4]) were matched with the FAERS data set on case level by country code and FDA or event reported month. For categorical variables with more than two groups, we choose the category with the highest number of cases as reference being "anti-TNF α " (medication), USA/Canada (region) and December (month "initial FDA received date" or "event"). Sex is coded by FAERS as male, female or not specified. Only male and female cases were included in analyses. Region based on the FAERS country code, diagnoses on FAERS "Reason for use". Outcome was generated from the FAERS variable "Outcomes" with the following categories: non-serious, hospitalized, life threatening, congenital anomaly (not present in our cohort), disabled, other outcomes, died. Following the FAERS information[5], all categories except "died" were grouped as "survived" (0) and the category "died" was labelled as "died" (1). The case fatality rate per month and country, the new cases and –deaths per population, month and country were computed based on "World in Data". The ratio of total reports to FAERS to the number of reported deaths to FEARS for each drug in 2018-2020 (without the COVID-cases) was computed based on the FAERS public dashboard. Abbreviations: FAERS; FDA Adverse Event Reporting System; USD: U.S. Dollar; COVID-19: Coronavirus Disease 2019

References

- 1 U.S. Food and Drug Administration (FAERS) - FDA Adverse Event Reporting System. 2021.<https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard> (accessed 22 Feb 2021).
- 2 Roser M, Ortiz-Ospina E. Coronavirus Pandemic (COVID-19). Our World in Data. Accessed March 13, 2021. <https://ourworldindata.org/coronavirus> (accessed 13 Mar 2021).
- 3 Worldbank. Hospital beds (per 1,000 people). 2021.<https://data.worldbank.org/indicator/SH.MED.BEDS.ZS> (accessed 13 Mar 2021).
- 4 Worldbank. Current health expenditure per capita (current US\$). <https://data.worldbank.org/indicator/SH.XPD.CHEX.PC.CD> (accessed 13 Mar 2021).
- 5 FDA. CFR - Code of Federal Regulations Title 21, Volume 5. 2020.<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/cfrsearch.cfm?fr=312.32> (accessed 23 Mar 2021).

Supplemental Table 2: Cohort Characteristics

		Overall n = 2103 No. (%)	Dead n = 107 No. (%)	Survived n = 1996 No. (%)
Age in years (mean (SD))		51.3 (SD 14.9)	62.7 (SD 14.2)	50.6 (SD 14.7)
Sex	Male	731 (34.8)	51 (47.7)	680 (34.1)
	Female	1372 (65.2)	56 (52.3)	1316 (65.9)
Region	USA/Canada	1285 (61.1)	51 (47.7)	1234 (61.8)
	Europe	497 (23.6)	42 (39.3)	455 (22.8)
	South- and Central America	321 (15.3)	14 (13.1)	307 (15.4)
	Inflammatory joint disease	846 (40.2)	39 (36.5)	807 (40.4)
	Vasculitis	12 (0.6)	3 (2.8)	9 (0.5)
	Connective tissue disease	4 (0.2)	1 (0.9)	3 (0.2)
	Sarcoidosis	1 (0.04)	0 (0)	1 (0.1)
	Inflammatory bowel disease	168 (8.0)	5 (4.7)	163 (8.2)
	Inflammatory eye disease	5 (0.2)	0 (0)	5 (0.3)
	Inflammatory skin disease	435 (20.7)	12 (11.2)	423 (21.2)
	Spondyloarthritis	135 (6.4)	5 (4.7)	130 (6.5)
	Neuroimmunological disease without MS	6 (0.3)	2 (1.9)	4 (0.2)
	Multiple Sclerosis	474 (22.5)	38 (35.5)	436 (21.8)
	Immunotherapy - NOS	4 (0.2)	0 (0)	4 (0.2)
	Multiple autoimmune diseases	13 (0.6)	2 (1.9)	11 (0.6)
	Anti-TNF α	714 (34.0)	34 (31.8)	680 (34.1)
	Adalimumab	336 (47.1)	20 (58.8)	316 (46.5)
	Etanercept	145 (20.3)	3 (8.8)	142 (20.9)
	Certolizumab	76 (10.6)	3 (8.8)	73 (10.7)
	Golimumab	97 (13.6)	3 (8.8)	94 (13.8)
	Infliximab	60 (8.4)	5 (14.7)	55 (8.1)
	Anti-CD20	388 (18.4)	43 (40.2)	345 (17.3)
	Rituximab	58 (15.0)	16 (37.2)	42 (12.2)
	Ocrelizumab	320 (82.5)	27 (62.8)	293 (84.9)
	Ofatumumab	10 (2.6)	0 (0)	10 (2.9)
	JAKinib	312 (14.8)	14 (13.1)	298 (14.9)
	Tofacitinib	248 (79.5)	10 (71.4)	238 (79.9)
	Upadacitinib	58 (18.6)	4 (28.6)	54 (18.1)
	Baricitinib	6 (1.9)	0 (0)	6 (2.0)
	Anti-IL12/23	199 (9.5)	9 (8.4)	190 (9.5)
	Ustekinumab	152 (76.4)	7 (77.8)	145 (76.3)
	Risankizumab	32 (16.1)	2 (22.2)	30 (15.8)

		Overall n = 2103 No. (%)	Dead n = 107 No. (%)	Survived n = 1996 No. (%)
	Guselkumab	15 (7.5)	0 (0)	15 (7.9)
	PDE4-Inhibitor	104 (4.9)	2 (1.9)	102 (5.1)
	Apremilast	104 (100)	2 (100)	102 (100)
	Anti-IL17	278 (13.2)	2 (1.9)	276 (13.8)
	Secukinumab	233 (83.8)	2 (100)	231 (83.7)
	Ixekizumab	43 (15.5)	0 (0)	43 (15.6)
	Brodalumab	2 (0.7)	0 (0)	2 (0.7)
	S1P-Receptor Modulator	108 (5.1)	3 (2.8)	105 (5.3)
	Fingolimod	92 (4.4)	2 (66.7)	90 (85.7)
	Siponimod	15 (0.7)	1 (33.3)	14 (13.3)
	Ozanimod	1 (0.1)	0 (0)	1 (1.0)

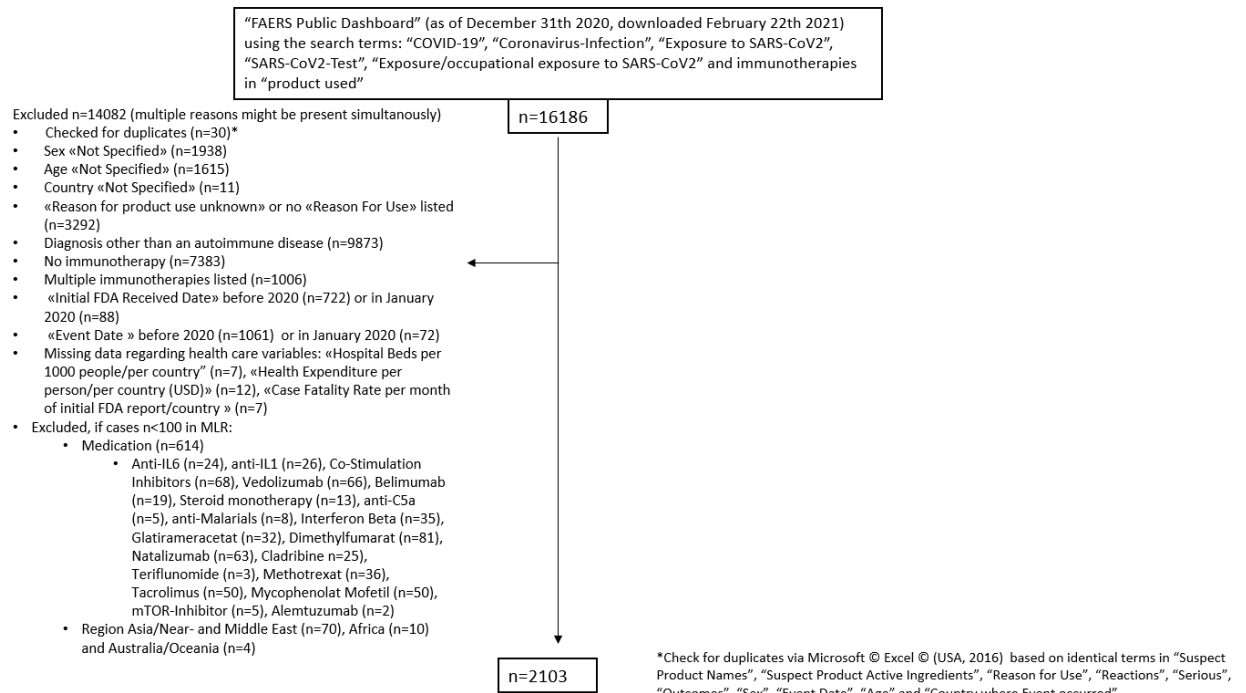
Absolute numbers of reported deaths and survived cases are displayed. The percentages here relate to the dead or survived population. Percentage of the drugs listed below the medication groups (e.g. Adalimumab) in respect to their proportion within their medication group (e.g. anti-TNF α). Abbreviations: CD-20: Cluster of Differentiation-20, IL-12/23: Interleukin 12/23, IL-17: Interleukin 17, JAKinib: Janus Kinase inhibitor, MS: Multiple Sclerosis, n: sample size, nos: not otherwise specified, PDE4-Inhibitor: Phosphodiesterase-4 inhibitor, S1P-Receptor Modulator: Sphingosine-1 phosphate modulator, TNF α : Tumor necrosis factor α , USA: United States of America

Supplemental Table 3: Numerically reported outcomes.

		n	%
Outcomes	Non Serious	569	27.1
	Hospitalized	553	26.3
	Life Threatening	36	1.7
	Died	107	5.1
	Other Outcomes	834	39.7
	Disabled	4	0.2
Died	Survived	1996	94.9
	Died	107	5.1

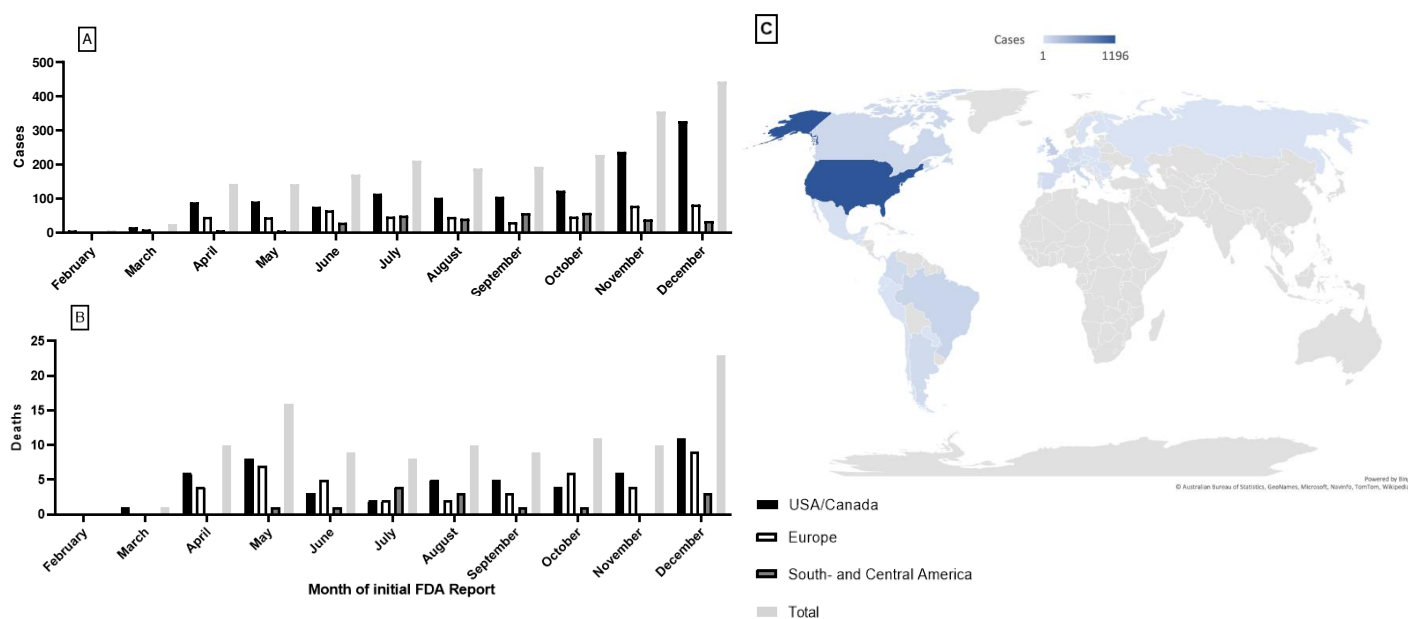
6

Supplemental Figure 1: Exclusion/Inclusion Criteria



Cohort constitution and exclusion criteria. 16186 cases were initially identified using the search terms in FAERS (up to 5 possible) listed above. Cases with missing values, implausible cases (e.g. coronavirus cases before 2020), duplicates, and cases without immunotherapies or "Reason for Use" that does not constitute an autoimmune disorder were excluded. Medications and regions with <100 cases in final MLR were excluded. The final cohort size is 2103 with regards to the independent variable "month of initial FDA received date". Abbreviations: C5a: Complement Factor 5A, COVID-19: Coronavirus Disease 2019, FDA: U.S. Food and Drug Administration, FAERS: FDA Adverse Event Reporting System, IL-6/IL-1 Interleukin 6 or 1, SARS-CoV2: Severe Acute Respiratory Syndrome Coronavirus Type

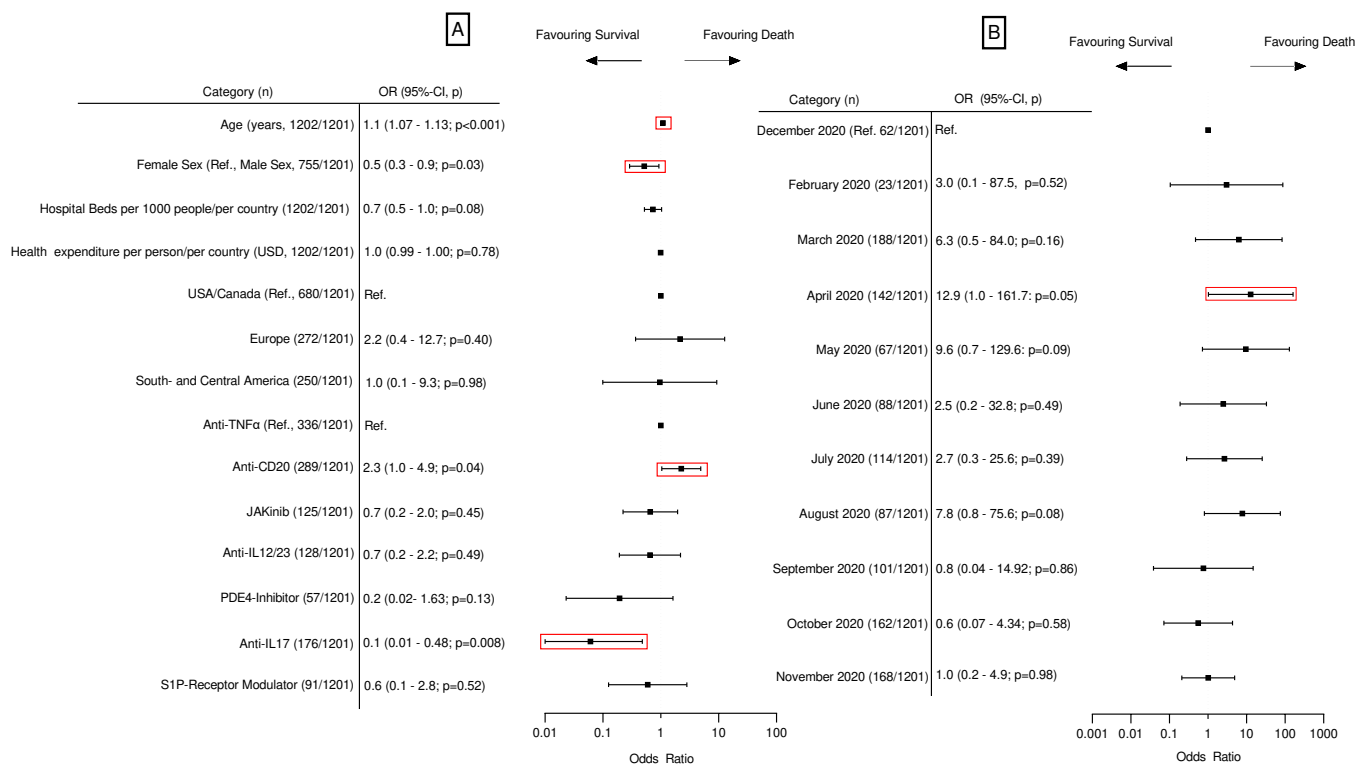
7



Supplemental Figure 2: Case numbers and deaths reported to FAERS.

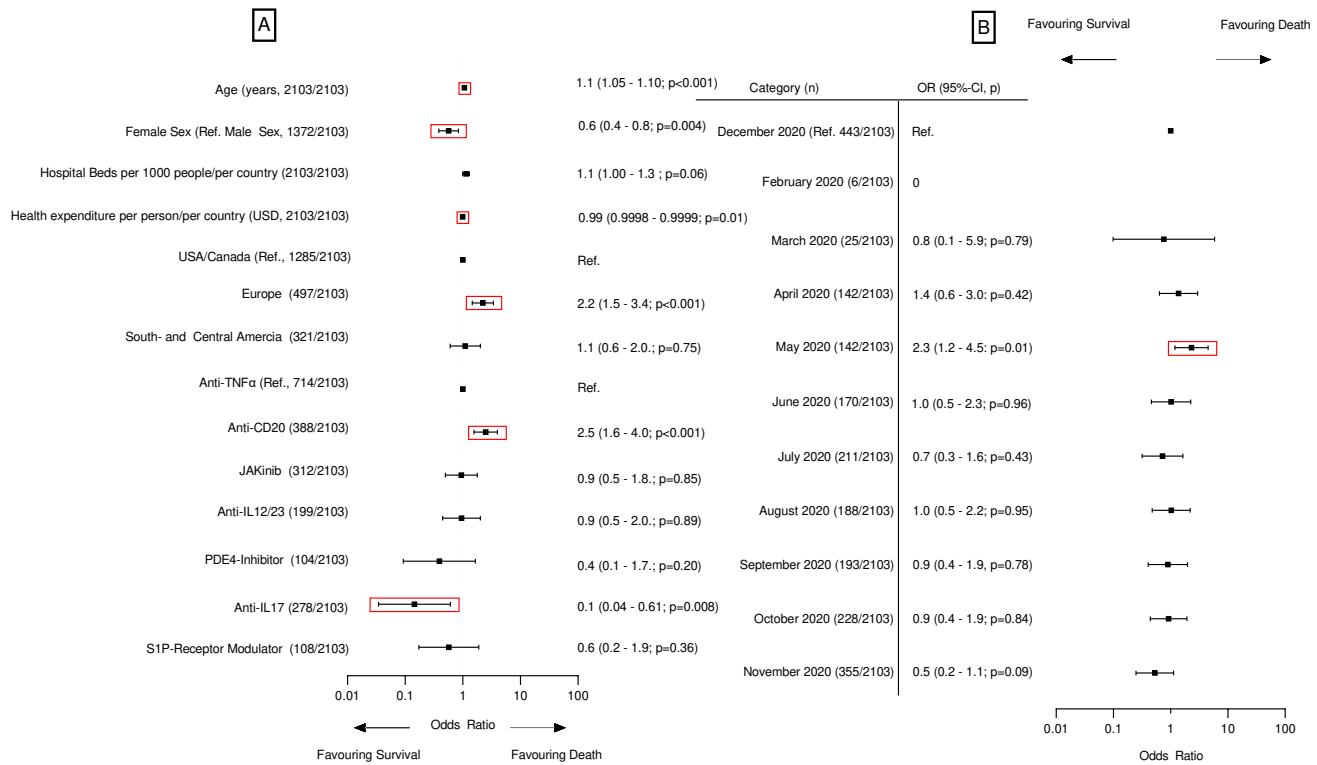
Supplemental Figure 2: A: Distribution of cases and B: deaths reported to FAERS for each month of initial FDA received date (February 2020 – December 2020) for each region (USA/Canada, Europe, South- and Central America) and in total. C) Geographical distribution of reported cases (Feb 2020 – Dec 2020). Depth of blue represents higher number. Created with Microsoft® Powerpoint®, Bing®, Australian Bureau of Statistics®, GeoNames®, Navinfo®, TomTom® and Wikipedia. Abbreviations: FDA: U.S. Food and Drug Administration

Supplemental Figure 3: Multivariable regression analysis for the event month.



Multivariable-adjusted OR for “death” using the reported “month of event” instead of the month of the initial FDA report: 95% - CIs and p-values of the independent variables on a 10-log scale. A: ORs for age, sex, hospital beds per 1000 persons/per country, health expenditure per person/per country (in USD), region and medication. B: ORs of the reported “month of event”. The following controls are not displayed: case fatality rate per month of event/country” (3.4; 0.0 - 250982244.8, p=0.89), the “ratio of total reports to FAERS to the number of reported deaths to FAERS for each drug in 2018-2020 excluding COVID-19 cases” (0.93; 0.02 - 49.02; p=0.97), “new cases per population per month and country” (1.4746E70; 1401551.6- 1.5514E134, p=0.03) and “new deaths per population per month and country” (0; p=0.155). Nagelkerkes R^2 is 0.268. For February 2020, no deaths have been reported to FAERS, therefore the OR for February is 0. Abbreviations: CD-20: Cluster of Differentiation 20, CI: confidence interval, FDA: U.S. Food and Drug Administration, IL-12/23: Interleukin 12/23, IL-17: Interleukin 17, JAKinib: Janus kinase inhibitor, MLR: multivariable logistical regression, OR: Odds Ratio, n: sample size, Ref./ref.: Reference; p: p-value, PDE4-Inhibitor: Phosphodiesterase-4 inhibitor, S1P-Receptor Modulator: Sphingosine-1 phosphate modulator, TNF α : Tumor necrosis factor α , USA: United States of Americas

Supplemental Figure 4: Univariable regression analysis



Univariate OR for "death" for the month of the Report to FDA: 95% - CIs and p-values of each independent variable on a 10-log scale. A: ORs for age, sex, hospital beds per 1000 persons/per country, health expenditure per person/per country (in USD), region and medication B: ORs for each individual "month of the initial FDA report". The following controls are not displayed: case fatality rate per month of event/country" (1833.1; 26.0 - 129348.8, p=0.001), the "ratio of total reports to FAERS to the number of reported deaths to FAERS for each drug in 2018-2020 excluding COVID-19 cases" (1.8, 0.2 - 13.0; p=0.56), "new cases per population per month and country" (6.4815E20; 8.158E-35 - 0.000052, p=0.01) and "new deaths per population per month and country" (1.0054E-165; 0.0E0; p=0.73). Abbreviations: CD-20: Cluster of Differentiation 20, CI: confidence interval, FDA: U.S. Food and Drug Administration, IL-12/23: Interleukin 12/23, IL-17: Interleukin 17, JAKinib: Janus kinase inhibitor, OR: Odds Ratio, n: sample size, Ref./ref.: Reference; p: p-value, PDE4-Inhibitor: Phosphodiesterase-4 inhibitor, S1P-Receptor Modulator: Sphingosine-1 phosphate modulator, TNF α : Tumor necrosis factor α , USA: United States of America