SUPPLEMENTARY MATERIAL

Post-Marketing Safety Surveillance of Tofacitinib over 9 Years in Patients with Psoriatic Arthritis and Rheumatoid Arthritis

Gerd R. Burmester • Laura C. Coates • Stanley B. Cohen • Yoshiya Tanaka • Ivana Vranic • Edward Nagy • Irina Lazariciu • All-shine Chen • Kenneth Kwok • Lara Fallon • Cassandra Kinch

G. R. Burmester
Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin Berlin, Berlin, Germany

L. C. Coates
Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Botnar Research Centre, Oxford, UK

S. B. Cohen
Metroplex Clinical Research Center and Department of Internal Medicine,
The University of Texas Southwestern Medical Center, Dallas, TX, USA

Y. Tanaka
First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

I. Vranic • E. Nagy
Pfizer Ltd, Tadworth, UK

I. Lazariciu • K. Kwok
Pfizer Inc, New York, NY, USA

A.-s. Chen
Pfizer Inc, Groton, CT, USA

L. Fallon • C. Kinch (corresponding author)
Inflammation & Immunology, Pfizer Canada ULC, 17300 Trans-Canada Hwy, Kirkland, QC H9J 2M5, Canada
e-mail: cassandra.kinch@pfizer.com

Supplementary Methods

Search Criteria for AESIs

AESI	**MedDRA/SMQ level | MedDRA term(s)/SMQ (MedDRA version 24.1)**
Venous thromboembolism (deep vein thrombosis/pulmonary embolism)	SMQ Narrow | Embolic and thrombotic events, venous
Serious and other important infections	(Adverse events that met serious criteria only) SOC | Infections and infestations [Primary path] PT | Febrile neutropenia
Herpes zoster reactivation	PT | Disseminated varicella zoster virus infection PT | Genital herpes zoster PT | Herpes zoster PT | Herpes zoster cutaneous disseminated PT | Herpes zoster disseminated PT | Herpes zoster infection neurological PT | Herpes zoster meningitis PT | Herpes zoster meningoencephalitis PT | Herpes zoster meningomyelitis PT | Herpes zoster meningoradiculitis PT | Herpes zoster necrotising retinopathy PT | Herpes zoster oticus PT | Herpes zoster pharyngitis PT | Herpes zoster reactivation PT | Ophthalmic herpes zoster
Non-melanoma skin cancer	HLT | Skin neoplasms malignant and unspecified (excluding melanoma) (primary path) PT | Squamous cell carcinoma

Malignancy (terms covered under non-melanoma skin cancer are not included here)	SMQ Narrow | Malignancy related conditions SMQ Narrow | Malignancy related therapeutic and diagnostic procedures SMQ Narrow | Malignant or unspecified tumours SMQ Narrow | Tumour markers
Cardiovascular events	SMQ Narrow | Central nervous system vascular disorders SMQ Narrow | Myocardial infarction SMQ Narrow | Other ischaemic heart disease PT | Cardiac death PT | Cardiac failure congestive PT | Sudden cardiac death PT | Pulmonary embolism
All-cause mortality	Clinical outcome = Fatal

AESI adverse event of special interest, *HLT* High Level Term, *MedDRA* Medical Dictionary for Regulatory Activities, *PT* Preferred Term, *SMQ* Standardised MedDRA Query, *SOC* System Organ Class

Fig. S1 Most frequent AEs occurring in ≥ 2% of patients with PsA and RA (tofacitinib formulation not reported). Percentages were calculated from the total case reports with no tofacitinib formulation reported. *AE* adverse event, *COVID-19* Coronavirus disease 2019, *HZ* herpes zoster, *PsA* psoriatic arthritis, *RA* rheumatoid arthritis

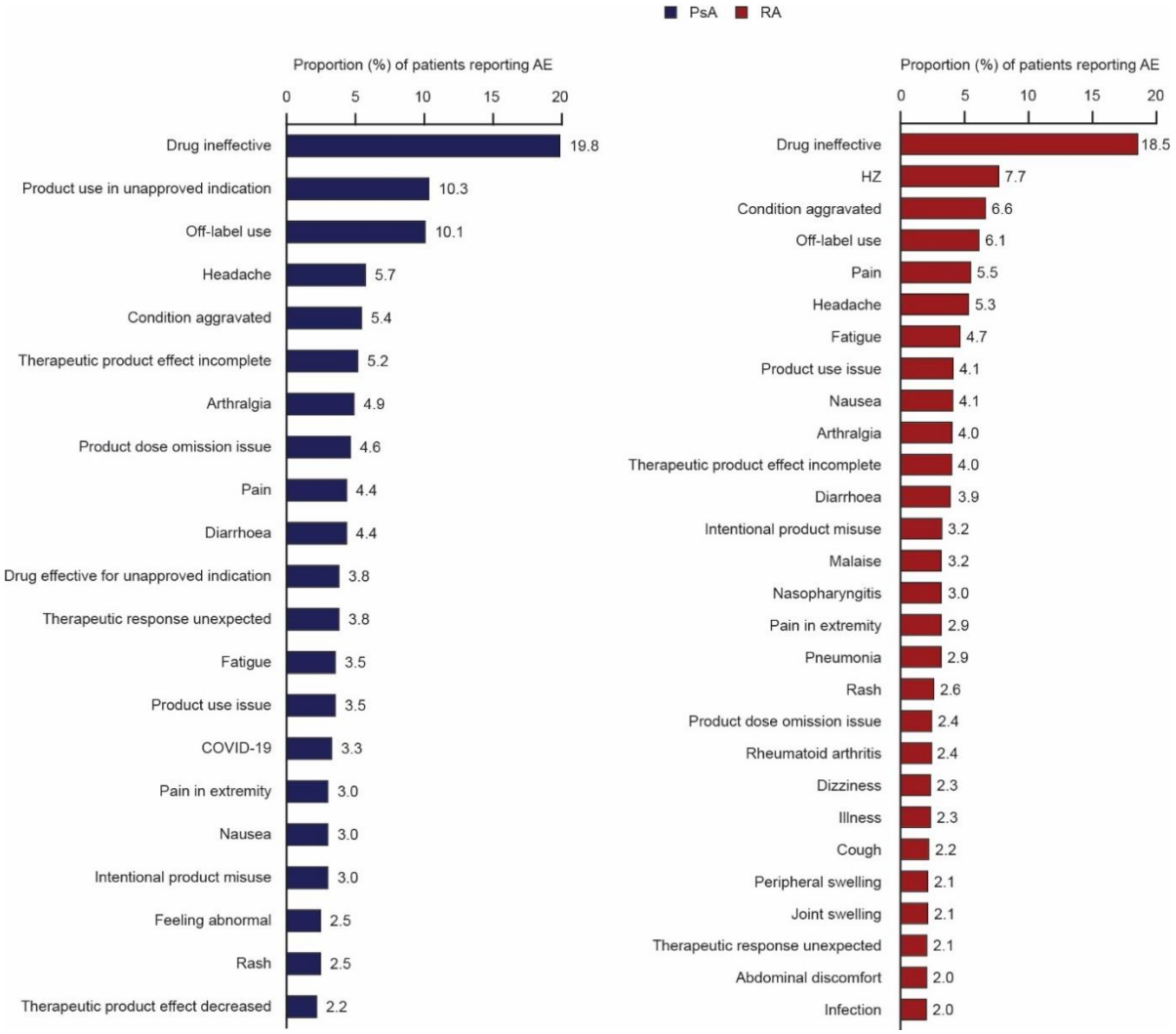

Table S1 Patient characteristics among patients with PsA and RA (tofacitinib formulation not reported)

	Tofacitinib formulation not reported			
	PsA		**RA**	
	N	**% of case reports**	***N***	**% of case reports**
Case reports	368		4239	
Sex				
Male	94	25.5	638	15.1
Female	197	53.5	2778	65.5
Not reported	77	20.9	823	19.4
Age				
Median (SD) [range], years	57.0 (12.83) [12.0–86.0]		61.0 (13.3) [2.58–96.0]	
< 65 years	158	42.9	1700	40.1
≥ 65 years	67	18.2	1176	27.7
Not reported	143	38.9	1363	32.2
Geographical region				
North America[a]	222	60.3	2129	50.2
Europe[b]	84	22.8	532	12.6
Rest of the world[c]	62	16.8	1579	37.2

PsA psoriatic arthritis, *RA* rheumatoid arthritis, *SD* standard deviation

[a]Includes case reports from Canada, Puerto Rico and the US

[b]Includes case reports from Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the UK

[c]Includes case reports from Argentina, Australia, Brazil, Chile, China, Colombia, Ecuador, Egypt, Hong Kong, India, Japan, Korea, Kuwait, Lebanon, Malaysia, Mexico, Morocco, New Zealand, Peru, Philippines, Saudi Arabia, Singapore, South Africa, Thailand, Tunisia and the United Arab Emirates

Table S2 Safety outcomes among patients with PsA and RA (tofacitinib formulation not reported)

	Tofacitinib formulation not reported			
	PsA		**RA**	
	N	**%[a]**	***N***	**%[a]**
Case reports	368		4239	
AEs	905		12,216	
SAEs	134	14.81	3163	25.89
AESI[b]				
Serious infections	29	3.20	582	4.76
HZ (serious and nonserious)	7	0.77	340	2.78
Cardiovascular events[c]	9	0.99	130	1.06
Malignancies (excluding NMSC)	2	0.22	195	1.60
NMSC	2	0.22	23	0.19
VTE[d]	8	0.88	81	0.66
Fatal cases	1	0.27[e]	78	1.84[e]

AE adverse event, *AESI* adverse event of special interest, *BID* twice daily, *HZ* herpes zoster, *MedDRA* Medical Dictionary for Regulatory Activities, *NMSC* nonmelanoma skin cancer, *PsA* psoriatic arthritis, *PT* Preferred Term, *RA* rheumatoid arthritis, *SAE* serious adverse event, *VTE* venous thromboembolism

[a]Percentages are based on total AEs by indication except where otherwise indicated

[b]Search criteria for AESI categories are described in the Supplementary Methods

[c]Includes the following Standardised MedDRA Queries: central nervous system vascular disorders, myocardial infarction and associated terms, ischaemic heart disease and associated terms; and the following PTs: cardiac death, cardiac failure congestive, sudden cardiac death and pulmonary embolism

[d]Pulmonary embolism events are captured in the cardiovascular events and VTE categories

[e]Percentages are based on the total case reports by indication

Table S3 Safety outcomes by tofacitinib formulation in the first 4 years post-approval among patients with RA

	November 2012 to November 2016								
	Tofacitinib IR 49,439 PY			**Tofacitinib MR 2000 PY**			**All tofacitinib 51,439 PY**		
	N	**%[a]**	**RR[b]**	***N***	**%[a]**	**RR[b]**	***N***	**%[a]**	**RR[b]**
Case reports	12,298			757			13,055		
AEs	47,389		95.85	2940		147.00	50,329		97.84
SAEs	9449	19.94	19.11	489	16.63	24.45	9938	19.75	19.32
AESI[c]									
Serious infections	1745	3.68	3.53	82	2.79	4.10	1827	3.63	3.55
HZ (serious and nonserious)	324	0.68	0.66	24	0.82	1.20	348	0.69	0.68
Cardiovascular events[d]	212	0.45	0.43	20	0.68	1.00	232	0.46	0.45
Malignancies (excluding NMSC)	252	0.53	0.51	10	0.34	0.50	262	0.52	0.51
NMSC	69	0.15	0.14	2	0.07	0.10	71	0.14	0.14
VTE[e]	44	0.09	0.09	5	0.17	0.25	49	0.10	0.10
Fatal cases	196	1.59[f]	0.40	7	0.92[f]	0.35	203	1.55[f]	0.39

AE adverse event, *AESI* adverse event of special interest, *HZ* herpes zoster, *IR* immediate release, *MedDRA* Medical Dictionary for Regulatory Activities, *MR* modified release, *NMSC* nonmelanoma skin cancer, *PT* Preferred Term, *PY* patient-years, *RA* rheumatoid arthritis, *RR* reporting rate, *SAE* serious adverse event, *VTE* venous thromboembolism

[a]Percentages are based on total AEs by formulation except where otherwise indicated

[b]Events/100 PY (exposure estimated from IQVIA's Multinational Integrated Data Analysis System and Prescriber Insights databases)

[c]Search criteria for AESI categories are described in the Supplementary Methods

[d]Includes the following Standardised MedDRA Queries: central nervous system vascular disorders, myocardial infarction and associated terms, ischaemic heart disease and associated terms; and the following PTs: cardiac death, cardiac failure congestive, sudden cardiac death and pulmonary embolism

[e]Pulmonary embolism events are captured in the cardiovascular events and VTE categories

[f]Percentages based on total case reports by formulation