Table SI. Study population characteristics compared with target population

	Study population[a] (n=230)	van Winden et al, 2020 (n=413)	Phan et al, 2020 (n=135)	Piaserico et al, 2014 (n=187)
Age, years, mean±SD	71.1±4.9	72.4±5.9	73.5±6.3	71.3±5
Sex, n (%)				
Male	127 (55.2)	246 (59.6)	79 (58.5)	109 (58.3)
Female	103 (44.8)	167 (40.4)	56 (41.5)	78 (41.7)

[a]Comparisons were done using the complete study population (n=230), without selection for systemic antipsoriatic treatment only.

Table SII. Overview of causality assessment of reported adverse events in systemic antipsoriatic therapy in older adults using the WHO-causality assessment tool

WHO-scale[a]	**Methotrexate (TE=42)**					**Dimethyl fumarate (TE=43)**					**Acitretin (TE=26)**					**Adalimumab (TE=20)**					**Ustekinumab (TE=18)**					**Etanercept (TE=13)**				
	1	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
Total AEs[b]	6	18	36	31	–	–	11	11	32	–	4	14	4	17	–	2	2	3	29	–	3	12	4	27	–	–	11	6	27	–
Total SAEs[b]	–	4	2	–	–	–	–	–	–	–	–	2	1	1	–	–	1	1	2	–	1	3	1	2	–	–	4	1	1	–
Infections	–	–	26	1	–	–	–	6	–	–	–	2	–	–	–	–	–	1	19	–	–	1	–	23	–	–	–	–	27	–
Laboratory test deviations	–	2	2	13	–	–	2	1	15	–	–	3	2	4	–	–	–	–	5	–	–	1	3	–	–	–	–	2	–	–
Neoplasms	–	7	2	–	–	–	–	–	–	–	1	5	–	–	–	–	–	1	–	–	–	2	1	–	–	–	2	2	–	–
General disorder	–	–	1	7	–	–	1	2	–	–	–	–	–	5	–	–	–	–	2	–	–	–	–	–	–	–	–	1	–	–
Gastro-intestinal disorder	–	1	1	8	–	–	–	–	14	–	–	1	–	3	–	–	–	–	1	–	–	–	–	1	–	–	2	–	–	–
Cardiovascular disorder	1	2	1	–	–	–	–	–	3	–	1	2	1	–	–	1	1	1	–	–	–	1	–	–	–	–	2	–	–	–
Hepatobiliary disorder	–	–	1	–	–	–	1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1	–	–	–	–	1	–	–	–
Neurological disorder	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1	–	–	–	–	–	–	1	–	–
Musculoskeletal disorders	1	2	–	–	–	–	4	–	–	–	1	–	1	–	–	1	–	–	1	–	–	3	–	3	–	–	1	–	–	–
Skin disorder	1	–	–	–	–	–	1	2	–	–	–	1	–	4	–	–	–	–	1	–	–	1	–	–	–	–	–	–	–	–
Eye disorders	–	1	1	–	–	–	1	–	–	–	–	–	–	1	–	–	1	–	–	–	–	2	–	–	–	–	1	–	–	–
Psychological disorder	–	–	1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Other or unknown AE's	3	3	–	2	–	–	–	–	–	–	1	–	–	–	–	–	–	–	–	–	2	–	–	–	–	–	2	–	–	–

[a] With the WHO-UMC causality assessment system, the best possible estimate of the probability of a causal relationship with the antipsoriatic treatment was assessed in a standardized way. The following categories are displayed; unassessable (1), unlikely (2), possible (3), probable (4), certain (5). The following categories were defined as causal in this study; possible, probable and certain. The categories conditional (0) and certain (5) were not scored in this study. [b]Adverse events were only recorded occurring at the age of 65 or over and if they were of significant nature (e.g. required medical attention, dose alterations, treatment discontinuation, other medical interventions). A specified overview of all reported (S)AEs is shown in Table SIII, before and after causality assessment.

TE: treatment episode; (S)AEs, (severe) adverse events.

Table SIII. Overview of adverse events (AEs) in older adults with psoriasis using systemic antipsoriatic treatment before and after causality assessment

AEs[a] (number)	Methotrexate (TE=42)	Dimethyl fumarate (TE=43)	Acitretin (TE=26)	Adalimumab (TE=20)	Ustekinumab (TE=18)	Etanercept (TE=13)
Infections	Dermatomycosis (2) Flu-like symptoms (6) Pneumonia (6) Urinary tract infection (4) Middle ear infection (2) Oral infection (1) Abscess (1) Erysipelas (2) Other skin infection[b] (2) Post-operative infection (1)	Dermatomycosis (1) Pneumonia (1) Urinary tract infection (1) Herpes zoster (1) Unknown bacterial infection (1) Other skin infection[b] (1)	*Urinary tract infection (1)* *Other skin infection[b] (1)*	Dermatomycosis (2) Flu-like symptoms (3) **Pneumonia (1)** Urinary tract infection (4) Oral infection (1) Abscess (3) **Epididymitis (1)** **Erysipelas (1)** Lung disease with antibodies (1) Other skin infection[b] (2)	Flu-like symptoms (8) **Pneumonia (2)** Urinary tract infection (6) Oral infection (1) *Paronychia (1)* Middle ear infection (1) Epididymitis (1) Herpes zoster (1) Other skin infection[b] (2)	Flu-like symptoms (11) Pneumonia (2) Urinary tract infection (6) Oral infection (1) **Abdominal infection (1)** Abdominal infection (1) Other skin infection[b] (5)
Symptoms	Abdominal pain (4) Nausea (5) Weight loss (1) Fatigue (5) Headache (1) Sleep problems (1) *Skin bruising (1)* *Musculoskeletal[c] (2)*	Abdominal pain (2) Nausea (2) Vomiting (1) Diarrhoea (9) *Hemorroïd (1)* *Hemoptoë (1)* Fatigue (2) Hot flashes (1) Flushing (2) *Skin bruising (1)* *Musculoskeletal[c] (2)*	Dry eyes (1) Dry lips (2) **Severe dry mouth (1)** Exfoliation of hand/feet palms and lips (1) *Reflux laryngitis (1)* Obstipation (1) *Musculoskeletal[c] (1)* Musculoskeletal[c] (1) Pruritus (1) Nausea (2) Hair loss (1) *Cold feet and hands (1)* Headache (1)	Pruritus (1) Abdominal pain (1) Musculoskeletal[c] (1) *Musculoskeletal[c] (1)* Dizziness (2)	*Dry eyes (1)* Gastric reflux (1) *Restless limbs (1)* Dry cough (1) *Palpitations (1)*	Paraesthesia (1) Dizziness (1)

Laboratory test deviations	Anaemia (4) Neutropenia (1) Leukopenia (1) ↑ Transaminase levels (5) ↑ P3NP (4) ↑*infection parameters (2)*	Lymphocytopenia (11) Leukopenia (2) *Monocytosis (1)* Proteinuria (3) Abnormal urine sediment (1) ↑ *y-GT (1)*	*Anaemia (2)* *Leucocytosis (1)* Renal function deterioration (2) ↑ Cholesterol, TG (1) ↑ Transaminase levels (1) ↑ Transaminase levels and y-GT (1) ↑ CK (1)	Leukopenia (1) ↑ Cholesterol, TG (1) ↑ Transaminase levels (2) ↑ TG (1)	Anaemia (1) *Anaemia (1)* Haematuria (1) ↑ Transaminase levels and y-GT (1)	Anaemia (1) ↑ AP and y-GT (1)
Neoplasms	*Basal cell carcinoma (2)* **Non Hodgkin lymphoma (1)** **Lung cancer (1)** ***Angiosarcoma breas t(1)*** *Gallbladder polyp (1)*	None	***Squamous cell carcinoma (1)*** *Lentigo maligna (1)* *MELTUMP (1)* *Myelodysplastic syndrome (1)* *Gallbladder polyp (1)*	None	*Colon polyp (1)* **Kidney cancer (1)** ***Kidney cancer (1)***	*Colon polyp (1)* **Tubulair adenoma (1)** *Adrenal gland incidentaloma (1)*
Other AEs	Pneumonitis (2) *Fracture (2)* *Wound/injury (2)* *Actinic keratosis (2)* *Lipoma (1)* Depression (1) *Epistaxis (2)* *Thrombotic event (1)* Thrombotic event (1) *Cataract (1)* Liver cirrhosis (1) ***MI (1)***	*NASH (1)* *Arthrosis (1)* *Polymyalgia rheumatica (1)* Rash (2) *Ablatio retinae (1)*	***CVA (1)*** **Syncope (1)** *Hypertension (1)* *Actinic keratosis (1)* *Epidermoid cyst (1)* Other skin conditions[d] (2) *Unknown (1)*	Actinic keratosis (1) Claudicatio intermittens (1) *Cataract (1)* *Aorta valve sclerosis (1)* ***Angina pectoris (1)***	*Polymyalgia rheumatica (1)* *Tendinitis (1)* *Osteoporosis (1)* ***Choledocholithiasis (1)*** ***Fracture (1)*** *Wound/injury (1)* *Cataract (1)* ***Dermatitis medicamentosa (1)***	*Tendinitis (1)* Actinic keratosis (1) *TIA (1)* ***Ileus (1)*** *Cataract (1)* ***Cholecystolithiasis (1)*** *Gastric parese (1)* *Increased risk of falling (1)* ***Fracture (1)***

	PVC (1) Ablatio retinae (1) ***Ileus (1)*** *Arthrosis(1)*					***Dilatation Crossover femorofemoral surgery (1)***
Total AEs	91	54	39	36	46	44
caAEs	67	43	21	32	31	33
Total SAEs	6	0	4	4	7	6
caSAEs	2	0	2	3	3	2

[a]Adverse events were only recorded occurring at the age of 65 or over and if they were of significant nature (e.g. required medical attention, dose alterations, treatment discontinuation, other medical interventions). The (S)AEs in italics were unassessable or unlikely related to the antipsoriatic treatment. All SAEs are reflected in bold. [b]Other skin infection, including impetigo, infection of epidermoidcyste, infection of ulcus cruris, balanoposthitis and other undiagnosed skin infections. [c]Musculoskeletal conditions, including;joint pain, musclepain, shoulder surgery, muscle cramps, bursitis. [d]Other skin conditions, including; pustels on the chest and retinoïd dermatitis.

Data not shown: 3 AEs occurred when using ciclosporin; hypertension (n=2) and renal function deterioration (n=1). 1 AE occurred when using ixekizumab; pneumonia (n=1), 1 AE occurred on guselkumab, proteinuria (n=1) and 4 AE's occurred on apremilast; flu-like symptoms (n=1), arthrosis (n=1), morbus bowen (n=1) and struma (SAE, n=1, unlikely related to antipsoriatic treatment). No adverse events were reported for infliximab, certolizumab pegol, and secukinumab.

TE: treatment episode; SAEs: severe adverse events; caAEs: causality assessed adverse events; caSAEs: causality assessed serious adverse events; MI: myocardial infarction; PVC: premature ventricular contraction; MELTUMP: melanocytic tumours of uncertain malignant potential; CK: creatine kinase; NASH: non-alcoholic fatty liver disease; y-GT: gamma-glutamyl transferase; TG: triglycerides; P3NP: amino terminal type III procollagen peptide; AP: alkaline phosphatase; ↑: elevated.

Table SIV. Negative binomial model on the incidence rate ratios (IRR) of causality assessed adverse events (caAEs) per year of selected treatment episode (TEs) of patients aged 65 years and over, with added treatment duration.

Antipsoriatic treatment[a]	*IRR*[b]	*95% CI*	*P-value*
Methotrexate	Reference		
Dimethyl fumarate	1.363	0.767–2.469	0.297
Acitretin	0.657	0.330–1.275	0.221
Adalimumab	1.390	0.704–2.766	0.343
Ustekinumab	1.317	0.653–2.713	0.445
Etanercept	1.639	0.735–3.844	0.238

[a]The above shown antipsoriatic treatments were selected, based on a minimum of ten treatment episodes. [b]When treatment duration was unknown (n=17), TEs were not excluded from this analysis. Instead the mean of the specific antipsoriatic treatment duration was used, consequently all cases could be included in the analysis.

CI: confidence interval.

Table SV. Negative binomial model on the incidence rate ratios (IRR) of all adverse events (AEs) per year of selected treatment episodes (TEs) of patients aged 65 years and over, without selecting for causal AEs only

Antipsoriatic treatment[a]	*IRR*[b]	*95% CI*	*P-value*
Methotrexate	Reference		
Dimethyl fumarate	1.183	0.675–2.072	0.557
Acitretin	1.052	0.545–2.029	0.880
Adalimumab	0.949	0.485–1.855	0.878
Ustekinumab	1.305	0.679–2.505	0.424
Etanercept	1.407	0.665–2.974	0.372

[a]The above shown antipsoriatic treatments were selected, based on a minimum of ten treatment episodes. [b]The IRRs are only calculated with the treatment episodes of which the treatment duration was known, 17 TEs were excluded from this analysis including corresponding AEs (n=8).

CI: confidence interval.

Table SVI. Multiple logistic regression model on the relation of different factors with the occurrence of all adverse events (AEs) in older adults with psoriasis, without selecting for causal AEs only

Variables[a]	*Odds ratio*	*95% CI*	*P-value*
Age, years	1.239	1.040–1.477	**0.017**
CCI score[b] (<1 vs. ≥1)	1.929	0.573–6.489	0.289
Polypharmacy[c]	0.748	0.221–2.537	0.642
Type of systemic treatment[d]			0.342
Methotrexate	Reference		
Dimethyl fumarate	1.338	0.324–5.523	0.687
Acitretin	0.491	0.098–2.472	0.389
Biological[e]	2.451	0.576–10.441	0.225

[a]The following variables are also assessed in this model but did not show a significant relation: sex, age at onset of psoriasis, overweight, kidney disease, history of cancer, liver disease, cardiovascular disease. [b]The CCI score was divided into two groups, CCI<1 and CCI≥1 based on the data distribution. [c]Polypharmacy was defined as the simultaneous use of ≥5 medications. [d]Six patients were excluded due to the simultaneous use of two types of antipsoriatic treatment.

Including etanercept, adalimumab, ustekinumab, ixekizumab.

CCI: Charlson Comorbidity Index; CI, confidence interval.

Table SVII. Causes of treatment discontinuation in older adults with psoriasis using systemic antipsoriatic treatment

Causes of treatment discontinuation, n (%)	Methotrexate (TE=42)	Dimethyl fumarate (TE=43)	Acitretin (TE=26)	Adalimumab (TE=20)	Ustekinumab (TE=18)	Etanercept (TE=13)
AE	8 (19.0)	15 (34.9)	6 (23.1)	1 (5.0)	4 (22.2)	1 (7.7)
AE and ineffectiveness	3 (7.1)	2 (4.7)	3 (11.5)	0 (0.0)	0 (0.0)	0 (0.0)
Ineffectiveness	4 (9.5)	4 (9.3)	6 (23.1)	9 (45.0)	5 (27.8)	5 (38.5)
Remission	1 (2.4)	3 (7.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other[a]	1 (2.4)	1 (2.3)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	0 (0.0)	1 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Still active[b]	25 (59.5)	17 (39.5)	10 (38.5)	10 (50.0)	9 (50.0)	7 (53.8)

The above shown antipsoriatic therapies were selected, based on a minimum of 10 treatment episodes.

[a]Other includes, methotrexate; fear of cancer recurrence malignancy (n=1), acitretin; dissatisfied with treatment (n=1), dimethyl fumarate; discontinuation on patient initiative during summer holiday (n=1).

[b]Including, patients that still used antipsoriatic treatment at the moment of inclusion and chart review.

TE: treatment episode; AE: adverse event.