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## Adverse drug events observed with 150 mg versus 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis

A systematic review and meta-analysis

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#### Abstract

**Background:** Secukinumab has been approved for the treatment of moderate to severe plaque psoriasis. However, safety measures concerning drug administration is vital during treatment. Understanding the right way to administer drugs is important to reduce any serious adverse drug event. In this analysis we aimed to systematically show the risk of adverse drug events which were observed with 150 mg versus (vs) 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis.

**Methods:** The major online databases: Cochrane Central, MEDLINE, www.ClinicalTrials.com and EMBASE were searched for relevant publications based on the comparison of secukinumab 150 mg vs 300 mg for the treatment of moderate to severe plaque psoriasis. Adverse drug events were considered as the clinical endpoints. Statistical analysis was carried out by the RevMan 5.3 software. Risk ratios (RR) and 95% confidence intervals (CIs) were generated to represent the data following statistical analysis.

**Results:** Seven studies with a total number of 2361 participants were included. Results of this analysis showed that the risk of any adverse event (RR: 1.00, 95% CI: 0.96–1.05; P = .94), the risk of serious adverse events (RR: 1.04, 95% CI: 0.75–1.43; P = .82) and the risk of adverse events leading to drug discontinuation (RR: 0.98, 95% CI: 0.61–1.57; P = .92) were not significantly different between 150 mg vs 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis. When the detailed adverse drug events were studied, the risks of infection or infestation (RR: 1.11, 95% CI: 0.98–1.25; P = .09), naso-pharyngitis (RR: 1.05, 95% CI: 0.90–1.23; P = .55), headache (RR: 0.92, 95% CI: 0.68–1.25; P = .60), diarrhea (RR: 1.14, 95% CI: 0.75–1.73; P = .55), pruritus (RR: 0.82, 95% CI: 0.56–1.22; P = .33), arthralgia (RR: 0.96, 95% CI: 0.67–1.38; P = .83), upper respiratory tract infection (RR: 0.98, 95% CI: 0.70–1.36; P = .89), hypertension (RR: 1.22, 95% CI: 0.83–1.81; P = .31), nausea (RR: 1.39, 95% CI: 0.63–3.04; P = .42), and cough (RR: 1.46, 95% CI: 0.67–3.19; P = .34) were still not significantly different between these 2 dosage regimens.

**Conclusion:** Secukinumab 150 mg and 300 mg were both equally tolerable and might safely be used for the treatment of moderate to severe plaque psoriasis. No significant adverse drug events were observed with any of the dosage.

**Abbreviations:** ADEs = adverse drug events, CI = confidence intervals, RR = risk ratios.

Keywords: adverse drug events, drug discontinuation, Psoriasis, secukinumab

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Drs LZ and HY contributed equally to this work and they are the co-first authors.

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#### 1. Introduction

Psoriasis which is an autoimmune disorder of the skin, has reached more than seven million cases in the United States.<sup>[1]</sup> This chronic disease is often characterized by red, itchy, dry, and scaly skin patches. There are several types of psoriasis, however, plaque psoriasis is the most common comprising of up to 90% of cases.<sup>[2]</sup>

Plaque psoriasis is characterized by raised red patches covered with a whitish build-up of dead skin and it mainly appears on the elbow, knees, scalp, and lower back, but it might also be present in the other surfaces of the body.

To understand the treatment of psoriasis, it is necessary to have a knowledge of the pathogenesis involved in the development of this chronic disease. In brief, the mechanism of this autoimmune disease is based on the expression of the cytokine interleukin 17A.<sup>[3]</sup>

Secukinumab (Cosentyx), a human IgG1k monoclonal antibody, binds and inhibits/neutralizes interleukin 17A and this is how it is involved in the treatment of psoriasis.<sup>[4]</sup> This novel drug was approved by the Food and Drug Administration in January 2015 for the treatment of adults with moderate to severe plaque psoriasis and was prescribed as secukinumab 150 mg and 300 mgrespectively.<sup>[5]</sup>

Several recent research showed secukinumab to be effective in the treatment of moderate to severe plaque psoriasis.<sup>[6]</sup> However, the dosage to be used was often a question to both the physicians and the patients.

Safety measures concerning drug administration is vital during the treatment of patients with specific drugs.<sup>[7]</sup> Drugs might be harmful even if they are meant to improve the health of a patient and taking them correctly and understanding the right way to administer them is important to reduce any serious adverse drug event.

In this analysis we aimed to systematically show the risk of adverse drug events which were observed with 150 mg versus (vs) 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis.

#### 2. Methods

#### 2.1. Search databases and search strategies

The major online databases: Cochrane Central, MEDLINE, www.ClinicalTrials.com and EMBASE were searched for relevant publications based on the comparison of secukinumab 150 mg vs 300 mg for the treatment of moderate to severe plaque psoriasis. The time frame for retrieval of articles was from the beginning of August to the end of September 2018.

Only English publications were considered for this research article and the search process was carried out using the following search terms:

- Secukinumab and psoriasis;
- Secukinumab and plaque psoriasis;
- Secukinumab and moderate to severe psoriasis;
- Secukinumab, psoriasis and adverse drug events.

#### 2.2. Inclusion and exclusion criteria

Inclusion criteria was based on studies which:

- Were randomized trials or observational studies;
- Compared secukinumab 150 mg vs 300 mg for the treatment of moderate to severe plaque psoriasis;
- Reported adverse drug events as their clinical endpoints;
- Reported data which could be used in this meta-analysis.

Exclusion criteria was based on studies which:

- There were not randomized trials and observational cohorts;
- Did not compare secukinumab 150 vs 300 mg for the treatment of psoriasis;
- Did not report the relevant adverse drug events;
- Reported data which were not compatible with this analysis;
- Were duplicated studies.

## 2.3. Endpoints (adverse drug events), types of participants and follow-up time periods

Most of the participants were patients who were treated for moderate to severe plaque psoriasis as shown in Table 1.

The adverse drug events which were assessed included:

- 1. Any adverse event;
- 2. Serious adverse events;
- 3. Adverse events leading to drug discontinuation;
- 4. Infection or infestation;
- 5. Naso-pharyngitis;
- 6. Headache;
- 7. Pruritus;
- 8. Arthralgia;
- 9. Upper respiratory tract infection
- 10. Hypertension;
- 11. Nausea;
- 12. Cough.

#### Table 1

Types of p	participants,	adverse dru	g events	reported	and	follow-up	time	period
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Studies	Types of participants	Adverse drug events reported	Follow-up time period	
ERASURE <sup>[10]</sup>	Moderate to severe plaque psoriasis	Any adverse event, serious adverse events, discontinuation of drug due to adverse event. Naso-pharvnoitis, pruritus	52 weeks	
FIXTURE <sup>[11]</sup>	Moderate to severe plaque psoriasis	Any adverse event, death, non-fatal serious adverse events, discontinuation of drug due to adverse event, infection or infestation, naso-pharyngitis, headache, diarrhea, pruritus, arthralgia, upper respiratory tract infection, back pain, cough, hypertension, nausea	52 weeks	
FEATURE <sup>[12]</sup>	Moderate to severe plaque psoriasis	Any adverse event, death, serious adverse events, discontinuation of drug due to adverse event, diarrhea, naso-pharyngitis, headache, pyrexia, back pain, cough, depression, nausea, rhinitis	12 weeks	
GESTURE <sup>[13]</sup>	Difficult to treat palmo-plantar psoriasis	Any adverse event, death, non-fatal serious adverse event, discontinuation of drug due to adverse event, headache, naso- pharyngitis, upper respiratory tract infection	16 weeks	
JUNCTURE <sup>[14]</sup>	Moderate to severe plaque psoriasis	Any adverse event, death, serious adverse event, discontinuation of drug due to adverse event, naso-pharyngitis, headache, cough, pruritus, upper respiratory tract infection, hypertension, influenza, arthraloia, severe infection, sinusitis	52 weeks	
Schwensen2017 <sup>[15]</sup>	Moderate to severe plaque psoriasis	Any adverse event, infection, pruritus, headache, arthralgia, discontinuation of drug due to adverse event	12 weeks	
SCULPTURE <sup>[16]</sup>	Moderate to severe plaque psoriasis	Any adverse event, serious adverse events, infections and infestations, discontinuation of drug due to adverse events, naso-pharyngitis, headache, upper respiratory tract infection, pruritus, hypertension, couch, arthralgia	52 weeks	



Figure 1. Flow diagram representing the selection of studies for this analysis.

Four studies reported a follow-up time period of 52 weeks, 2 studies reported a follow-up time period of 12 weeks and one study reported a follow-up time period of 16 weeks as shown in Table 1.

## 2.4. Data extraction, quality assessment, and statistical analysis

The original studies were reviewed and the following data were extracted by the respective four authors (LZ, HY, QC, JZ):

Table 2			
Main featu	res of t	the stu	dies.

Studies	Enrollment of participants	Total no of participants assigned to 150 mg secukinumab (n)	Total no of participants assigned to 300 mg secukinumab (n)	Type of study
ERASURE	2011-2013	43	40	RT
FIXTURE	2011-2013	469	467	RT
FEATURE	2012-2013	59	59	RT
GESTURE	2014	68	69	RT
JUNCTURE	2012-2014	89	88	RT
Schwensen2017	2015	33	36	OS
SCULPTURE	2011-2013	408	433	RT
Total no of participants (n)		1169	1192	

OS = observational study, RT = randomized trials.

#### Table 3

#### Baseline features of the participants.

	Age,y	Male (%)	BMI (kg/m²)	Psoriatic arthritis (%)	Duration of psoriasis (years)
Studies	150/300 mg	150/300 mg	150/300 mg	150/300 mg	150/300 mg
ERASURE	44.9/44.9	68.6/69.0	29.8/30.3	18.8/23.3	17.5/17.4
FIXTURE	45.4/44.5	72.2/68.5	28.4/28.4	15.0/15.3	17.3/15.8
FEATURE	46.0/45.1	67.8/64.4	-	_	20.4/18.0
GESTURE	52.4/48.8	58.8/51.1	28.8/29.2	_	7.50/7.90
JUNCTURE	43.9/46.6	67.2/76.7	30.6/30.0	26.2/23.3	20.6/21.0
Schwensen2017	47.0/49.0	-	-	33.3/52.8	_
SCULPTURE	44.8/46.3	62.8/69.8	28.6/28.7	-	17.0/17.2

BMI = body mass index.

- 1. Total number of participants assigned to 150 vs 300 mg secukinumab respectively;
- 2. The endpoints reported, with respective follow-up time periods;
- 3. The baseline characteristics of the participants;
- 4. The main features of the original articles;
- 5. The total number of adverse events in each category of subgroup.

The methodological quality of the trials was assessed with reference to the recommendations from the Cochrane collaboration<sup>[8]</sup> whereby bias risk was labelled as 'low risk', 'moderate risk' and 'high risk'. Any disagreement which followed was completely resolved by consensus.

Statistical analysis was carried out by the RevMan 5.3 software. Risk ratios (RR) and 95% confidence intervals (CIs) were generated to represent the data following statistical analysis.

Heterogeneity was assessed by the Q statistic test whereby a result with a *P* value less or equal to .05 was considered as statistically significant, and a result reporting a *P* value above .05 was considered statistically insignificant.

Heterogeneity was also assessed by the  $I^2$  statistic test. The  $I^2$  value was represented by percentage. A higher percentage of

	300 ma secuki	numab	150 ma secuki	numab		Risk Ratio	Risk Ratio
Study or Subaroup	Events	Total	Events	Total	Weiaht	M-H. Fixed, 95% C	M-H. Fixed, 95% Cl
1.1.1 Any adverse dru	ua event						
FRASURE	31	40	37	43	3.6%	0 90 [0 73 1 11]	-
FEATURE	30	59	34	59	3.5%	0.88 [0.63, 1.23]	
FIXTURE	376	467	364	469	37.0%		<u> </u>
GESTURE	40	69	44	68	4.5%	0.90 [0.69, 1.17]	
JUNCTURE	78	88	70	89	7.1%	1 13 [0 99 1 29]	+
Schwensen2017	,0	36	12	33	1.3%	0.46 [0.19, 1.08]	
SCUL PTURE	329	433	312	408	32.7%	0.99 [0.92 1.07]	
Subtotal (95% CI)	020	1192	012	1169	89.6%	1.00 [0.96, 1.05]	
Total events	890		873				
Heterogeneity: Chi <sup>2</sup> = 9	9.65 df = 6 (P = 0)	$(14) \cdot 1^2 = 3$	8%				
Test for overall effect:	Z = 0.07 (P = 0.94)	4)	.0.10				
	L 0.07 (1 0.0	''					
1.1.2 Serious adverse	events						
ERASURE	1	40	3	43	0.3%	0.36 [0.04, 3.31]	
FEATURE	3	59	0	59	0.1%	7.00 [0.37, 132.61]	<b></b>
FIXTURE	27	467	24	469	2.4%	1.13 [0.66, 1.93]	_ <del></del>
GESTURE	2	69	4	68	0.4%	0.49 [0.09, 2.60]	
JUNCTURE	7	88	12	89	1.2%	0.59 [0.24, 1.43]	
SCULPTURE	32	433	25	408	2.6%	1.21 [0.73, 2.00]	
Subtotal (95% CI)		1156		1136	7.0%	1.04 [0.75, 1.43]	◆
Total events	72		68				
Heterogeneity: Chi <sup>2</sup> = 5	5.27, df = 5 (P = 0	).38); l <sup>2</sup> = 5	5%				
Test for overall effect:	Z = 0.23 (P = 0.82	2)					
1.1.3 Adverse events	leading to drug	discontin	uation				
ERASURE	0	40	4	43	0.4%	0.12 [0.01, 2.15]	· · · · · · · · · · · · · · · · · · ·
FEATURE	1	59	0	59	0.1%	3.00 [0.12, 72.18]	
FIXTURE	14	467	10	469	1.0%	1.41 [0.63, 3.13]	
GESTURE	2	69	1	68	0.1%	1.97 [0.18, 21.23]	
JUNCTURE	0	88	1	89	0.2%	0.34 [0.01, 8.16]	
Schwensen2017	4	36	8	33	0.8%	0.46 [0.15, 1.38]	<del></del>
SCULPTURE	10	433	7	408	0.7%	1.35 [0.52, 3.50]	
Subtotal (95% CI)		1192		1169	3.3%	0.98 [0.61, 1.57]	<b>•</b>
Total events	31		31				
Heterogeneity: Chi <sup>2</sup> = 6	6.31, df = 6 (P = 0	).39); l² = 5	5%				
Test for overall effect:	Z = 0.10 (P = 0.92	2)					
Total (95% CI)		3540		3474	100.0%	1.00 [0.95, 1.05]	
Total events	993		972				
Heterogeneity: Chi <sup>2</sup> = C	21 13 df = 10 (P	= 0 33). 12 :	= 10%				
Test for overall effect:	Z = 0.13 (P = 0.0)	- 0.00 <i>j</i> , 1 - 1)	1070				0.01 0.1 1 10 100
Test for subgroup diffe	rences: $Chi^2 = 0.90$	-) )6 df= 2 (	$P = 0.97$ ) $I^2 = 0$	%			Favours [300 mg dose] Favours [150 mg dose]
		, ui – 2 (	. 0.07,1 = 0		~		
Figure 2. Advers	e arug events	observe	a with 150m	ıg vs 30	umg se	cukinumab for the	e treatment of moderate to severe plaque psoriasis.

1 7 7 10 10 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Events	Total	Events	numab Total	Weight	Risk Ratio M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
. I. I Intection of Inte	ISIGIION	407	040	400	20 50/	4 49 14 00 4 07	L
	269	407	240	469	20.5%	1.13 [1.00, 1.27]	
UNCTURE	6	88	5	89	0.6%	1.21 [0.38, 3.83]	· · · · · · · · · · · · · · · · · · ·
chwensen2017	0	36	5	33	0.7%	0.08 [0.00, 1.45]	•
CULPTURE	8	433	6	408	0.7%	1.26 [0.44, 3.59]	
uuutotai (95% CI)		1024		999	30.5%	1.11 [0.98, 1.25]	▼
otal events leterogeneity: Chi <sup>2</sup> = est for overall effect:	283 3.30, df = 3 (P = 0 Z = 1.69 (P = 0.09	1.35); I² = 9% 9)	256				
.1.2 Naso-pharyngit	is	10			0.00/		
RASURE	8	40	20	43	2.3%	0.43 [0.21, 0.86]	
EATURE	3	59	3	59	0.4%	1.00 [0.21, 4.75]	
IXTURE	122	467	108	469	12.8%	1.13 [0.91, 1.42]	
BESTURE	2	69	5	68	0.6%	0.39 [0.08, 1.96]	
UNCTURE	35	88	28	89	3.3%	1.26 [0.85, 1.89]	
CULPTURE	77	433	69	408	8.5%	1.05 [0.78, 1.41]	+
ubtotal (95% CI)		1156		1136	27.8%	1.05 [0.90, 1.23]	•
otal events eterogeneity: Chi <sup>2</sup> = ! est for overall effect:	247 9.01, df = 5 (P = 0 7 = 0.60 (P = 0.56	0.11); l² = 44	233 %				
.1.3 Headache	2 0.00 (1 0.00	~,					
EATURE	0	59	4	59	0.5%	0.11 [0.01. 2.02]	· · · · · · · · · · · · · · · · · · ·
IXTURE	38	467	36	469	4.3%	1.06 [0.68. 1.64]	<u> </u>
ESTURE	7	69	4	68	0.5%	1.72 [0.53. 5.62]	
UNCTURE	10	88	8	89	0.9%	1.26 [0.52 3.05]	<del></del>
chwensen2017	'n	36	1	33	0.2%	0.31 [0.01 7.27]	
CULPTURE	21	433	28	409	3 /0/	0.71 [0.41 1.22]	
ubtotal (95% CI)	21	1152	20	1126	9.9%	0.92 [0.68 1 25]	▲
otal events	76		Q.1	. 120	0.070	0.02 [0.00, 1.20]	Ť
leterogeneity: Chi <sup>2</sup> = : est for overall effect:	5.37, df = 5 (P = 0 Z = 0.52 (P = 0.60	1.37); l² = 7% 0)	01				
.1.4 Diarrhea							
EATURE	5	59	2	59	0.2%	2.50 [0.50, 12.38]	
IXTURE	38	467	36	469	4.3%	1.06 [0.68, 1.64]	±
Subtotal (95% CI)		526		528	4.5%	1.14 [0.75, 1.73]	<b>+</b>
otal events	43		38				
leterogeneity: Chi <sup>2</sup> =	1.03, df = 1 (P = 0	.31); l² = 3%	5				
est for overall effect:	Z = 0.60 (P = 0.5	5)					
.1.5 Pruritus	1	40	1	43	0.1%	1 07 0 07 16 621	
	16	467	21	460	2.5%	0.77 [0.07, 10.02]	
INICTURE	10	407	21	409	2.370	0.77 [0.40, 1.45]	
UNCTORE	0	00		69	0.1%	8.09 [1.03, 63.35]	
Schwensen2017	2	36	1	33	0.1%	1.83 [0.17, 19.29]	
on won bon 20 m							
CULPTURE	17	433	28	408	3.4%	0.57 [0.32, 1.03]	
SCULPTURE Subtotal (95% CI)	17	433 1064	28	408 1042	3.4% 6.3%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22]	<b>•</b>
SCULPTURE Subtotal (95% CI) Total events Heterogeneity: Chi <sup>2</sup> = 1 Fest for overall effect:	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.33	433 1064 1.15); I <sup>2</sup> = 41 3)	28 52 %	408 1042	3.4% 6.3%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22]	•
ColleTURE Subtotal (95% CI) Total events Heterogeneity: Chi <sup>2</sup> = + Test for overall effect:	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.33	433 1064 1.15); I <sup>2</sup> = 41 <sup>-</sup> 3)	28 52 %	408 1042	3.4% 6.3%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22]	•
CULPTURE Subtotal (95% CI) Total events leterogeneity: Chi <sup>2</sup> = Test for overall effect: .1.6 Arthralgia	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.33 24	433 1064 1.15); I <sup>2</sup> = 41 <sup>;</sup> 3) 467	28 52 % 33	408 <b>1042</b> 469	3.4% 6.3% 3.9%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22]	▲
SCULPTURE Subtotal (95% CI) otal events leterogeneity: Chi <sup>2</sup> = 1 est for overall effect: .1.6 Arthralgia IXTURE UNCTURE	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.33 24 5	433 1064 (.15); I <sup>2</sup> = 41 <sup>-</sup> 3) 467 88	28 52 % 33 3	408 1042 469 89	3.4% 6.3% 3.9% 0.4%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84]	
SCULPTURE Subtotal (95% CI) otal events leterogeneity: Chi <sup>2</sup> = 1 cest for overall effect: .1.6 Arthralgia IXTURE UNCTURE Schwensen2017	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.3) 24 5 1	433 1064 (.15);   <sup>2</sup> = 41 3) 467 88 36	28 52 % 33 3 0	408 1042 469 89 32	3.4% 6.3% 3.9% 0.4% 0.1%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2 76 [0.12, 65, 64]	
CULPTURE Jubtotal (95% CI) Total events leterogeneity: Chi <sup>2</sup> = est for overall effect: 1.6 Arthralgia IXTURE UNCTURE UNCTURE CHURENEN2017 SCHURE	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.33 24 5 1 25	433 <b>1064</b> (.15);   <sup>2</sup> = 41 <sup>1</sup> 3) 467 88 36 433	28 52 % 33 3 0 20	408 1042 469 89 33 408	3.4% 6.3% 3.9% 0.4% 0.1% 2.4%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65.41] 1.18 [0.65, 2.02]	
SCULPTURE subtotal (95% CI) Total events feterogeneity: Ch <sup>2</sup> = I rest for overall effect: I.1.6 Arthralgia IXTURE IUNCTURE Schwensen2017 SCULPTURE Subtotal (95% CI)	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.33 24 5 1 25	433 1064 (.15);   <sup>2</sup> = 41 <sup>-</sup> 3) 467 88 36 433 1024	28 52 % 33 3 0 20	408 1042 469 89 33 408 999	3.4% 6.3% 3.9% 0.4% 0.1% 2.4% 6.8%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65.41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38]	
SCULPTURE Subtotal (95% CI) Total events teterogeneity: Chi <sup>2</sup> = - Test for overall effect: I.1.6 Arthralgia TXTURE UNCTURE Schwensen2017 SCULPTURE Subtotal (95% CI) Total events	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.3) 24 5 1 25	433 1064 (.15);  ² = 41 3) 467 88 36 433 1024	28 52 % 33 3 0 20 56	408 1042 469 89 33 408 999	3.4% 6.3% 3.9% 0.4% 0.1% 2.4% 6.8%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65,41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38]	• 
SCULPTURE subtotal (95% CI) otal events teterogeneity: Ch <sup>2</sup> = : est for overall effect: .1.6 Arthralgia :XTURE UNCTURE UNCTURE SCULPTURE Subtotal (95% CI) otal events leterogeneity: Ch <sup>2</sup> = : 'est for overall effect:	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.3: 24 5 1 25 2.64, df = 3 (P = 0 Z = 0.22 (P = 0.8:	433 1064 (.15); l <sup>2</sup> = 41 3) 467 88 36 433 1024 (.45); l <sup>2</sup> = 0% 3)	28 52 % 33 3 0 20 56	408 1042 469 89 33 408 999	3.4% 6.3% 3.9% 0.4% 0.1% 2.4% 6.8%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65, 41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38]	• 
SULPTURE Subtotal (95% CI) otal events tetorogeneity: Chi <sup>2</sup> = : est for overall effect: 1.6 Arthralgia IXTURE UNCTURE UNCTURE Subtotal (95% CI) otal events tetorogeneity: Chi <sup>2</sup> = est for overall effect: 1.7 Upper respirato	17 44 6.75, df = 4 (P = 0 Z = 0.97 (P = 0.3: 24 5 1 25 2.64, df = 3 (P = 0 Z = 0.22 (P = 0.8: vry tract infection	433 1064 (1.15);   <sup>2</sup> = 41 3) 467 88 36 433 1024 (1.45);   <sup>2</sup> = 0% 3)	28 52 % 33 3 0 20 56	408 1042 469 89 33 408 999	3.4% 6.3% 0.4% 0.1% 2.4% 6.8%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65,41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38]	• 
SCULPTURE Subtotal (95% CI) Total events Heterogeneity: Ch <sup>2</sup> = - Test for overall effect: 1.1.6 Arthralgia StatURE UNCTURE Schwensen2017 SCULPTURE Subtotal (95% CI) Total events Heterogeneity: Ch <sup>2</sup> = : Test for overall effect: 1.1.7 Upper respirato FIXTURE	17 44 6.75, df = 4 (P = 0 2 = 0.97 (P = 0.3) 24 5 1 25 55 2.64, df = 3 (P = 0 Z = 0.22 (P = 0.8) ry tract infection 26	433 1064 (1.15);   <sup>2</sup> = 41 3) 467 88 86 433 1024 (1.45);   <sup>2</sup> = 0% 3)	28 52 % 33 3 0 20 56 , 26	408 1042 469 89 33 408 999	3.4% 6.3% 0.4% 0.1% 2.4% 6.8% 3.1%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65.41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38]	
CULPTURE Collevents Valevents Valevents Valevents vest for overall effect: .1.6 Arthralgia IXTURE UNCTURE UNCTURE UNCTURE CULPTURE Solution CULPTURE Valevents Valevents Vestorgeneity: Chi <sup>2</sup> = : est for overall effect: .1.7 Upper respirato IXTURE SESTURE	17 44 6.75, df = 4 (P = 0.3) 2 = 0.97 (P = 0.3) 5 1 25 2.64, df = 3 (P = 0 Z = 0.22 (P = 0.8) ry tract infection 26 3	$\begin{array}{c} 433\\ 1064\\ 1.15); \ l^2=41\\ 3)\\ \begin{array}{c} 467\\ 88\\ 36\\ 433\\ 1024\\ 1.45); \ l^2=0\%\\ 3)\\ 1\\ 467\\ 69\end{array}$	28 52 % 33 3 0 20 56 56 26 4	408 1042 469 89 33 408 999 469 68	3.4% 6.3% 3.9% 0.4% 0.1% 2.4% 6.8% 3.1% 0.5%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.82 [0.56, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65.41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38]	• 
CULPTURE initial (95% CI) ofal events iderogeneity: Ch <sup>2</sup> = - est for overall effect: .1.6 Arthralgia iXTURE UNCTURE UNCTURE UNCTURE iderogeneity: Ch <sup>2</sup> = - est for overall effect: .1.7 Upper respirato iXTURE BESTURE UNCTURE	17 44 6.75, df = 4 (P = 0, 3) 24 5 1 25 55 2.84, df = 3 (P = 0, 8) Z = 0.22 (P = 0.8) vy tract infection 26 3 5	433 1064 1.15); l <sup>2</sup> = 41 3) 467 88 36 433 1024 1024 1024 1024 1024 1024 1024 1024 1024 1066 1066 1066 1066 1066 1066	28 52 % 33 3 0 20 56 56 26 4 8	408 1042 469 89 33 408 999 469 68 89	3.4% 6.3% 3.9% 0.4% 0.1% 2.4% 6.8% 3.1% 0.5% 0.9%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65.41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38] 1.00 [0.59, 1.70] 0.74 [0.17, 3.18] 0.63 [0.22, 1.86]	
SCULPTURE Subtotal (95% CI) Total events Heterogeneity: Ch <sup>2</sup> = Fest for overall effect: 1.1.6 Arthralgia Schwensen2017 ScuLPTURE Subtotal (95% CI) Total events Heterogeneity: Ch <sup>2</sup> = Fest for overall effect: 1.1.7 Upper respirato "IXTURE SESTURE UNCTURE SCULPTURE	17 44 6.75, df = 4 (P = 0, 3) 24 5 1 25 2.64, df = 3 (P = 0, 3) Z = 0.22 (P = 0.8) vy tract infection 26 3 5 31	433 1064 1.15);   <sup>2</sup> = 41 3) 467 88 36 433 1024 1.45);   <sup>2</sup> = 0% 3) 467 69 88 433	28 52 33 3 0 20 56 56 26 4 8 27	408 1042 469 89 33 408 999 469 68 89 999	3.4% 6.3% 0.4% 0.1% 2.4% 6.8% 3.1% 0.5% 0.9% 3.3%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.82 [0.56, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65, 41] 1.18 [0.62, 2.09] 0.96 [0.67, 1.38] 1.00 [0.59, 1.70] 0.74 [0.17, 3.18] 0.63 [0.22, 1.86] 1.08 [0.66, 1.78]	
SCULPTURE Subtotal (95% CI) Total events Heterogeneity: Ch <sup>2</sup> = - rest for overall effect: 1.6 Arthralgia FIXTURE Schwensen2017 SCULPTURE Subtotal (95% CI) Total events Heterogeneity: Ch <sup>2</sup> = : rest for overall effect: .1.7 Upper respirato TXTURE SESTURE UNCTURE SULPTURE Subtotal (95% CI)	$\begin{array}{c} 17\\ 44\\ C.75, df = 4 \ (P = 0.3)\\ 24\\ 5\\ 1\\ 25\\ 2.64, df = 3 \ (P = 0.3)\\ 7\\ 25\\ 2.64, df = 3 \ (P = 0.3)\\ 7\\ 2 = 0.22 \ (P = 0.8)\\ 7\\ 7\\ 7\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\ 1\\$	433 1064 1.15);  ² = 41 3) 467 88 36 433 1024 1.45);  ² = 0% 3) 467 69 88 433 1057	28 52 % 33 3 0 20 56 56 56 56 56 56 56 56 56 56 56 56 56	408 1042 469 89 33 408 999 408 89 408 1034	3.4% 6.3% 0.4% 0.1% 6.8% 3.1% 0.5% 0.9% 3.3% 7.8%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65.41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38] 0.96 [0.67, 1.38] 0.74 [0.17, 3.18] 0.63 [0.22, 1.86] 1.08 [0.66, 1.78] 0.98 [0.67, 1.38]	
SCULPTURE Subtotal (95% CI) Total events leterogeneity: Ch <sup>2</sup> = "est for overall effect: .1.6 Arthralgia 'XTURE UNCTURE Subvensen2017 ;CULPTURE Subtotal (95% CI) Total events leterogeneity: Ch <sup>2</sup> = 'est for overall effect: .1.7 Upper respirato 'XTURE SESTURE UNCTURE :CULPTURE iubtotal (95% CI) Total events leterogeneity: Ch <sup>2</sup> = est for overall effect:	17 44 6.75, df = 4 (P = 0, 3; 2 = 0.97 (P = 0.3; 5 2.64, df = 3 (P = 0 2 = 0.22 (P = 0.8; 1 = 0.22 (P = 0.8; 5 3 = 0.22 (P = 0.8; 5 3 = 0.22 (P = 0.8; 6 5 0.94, df = 3 (P = 0 0 = 0.22 (P = 0.8; 5 3 = 0.22 (P = 0.8; 5 5 3 = 0.22 (P = 0.8; 5 5 5 5 5 5 5 5 5 5 5 5 5	433 1064 1.15);  ² = 41 3) 467 88 36 433 1024 1024 1024 1024 1024 1024 1024 1024	28 52 33 3 0 20 56 5 5 5 5 5 5	408 1042 469 89 33 408 999 408 899 408 1034	3.4% 6.3% 0.4% 0.1% 2.4% 6.8% 3.1% 0.5% 0.9% 3.3% 7.8%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65, 41] 1.18 [0.42, 6.84] 2.76 [0.12, 65, 41] 0.96 [0.67, 1.38] 0.96 [0.67, 1.38] 0.96 [0.67, 1.38] 0.63 [0.22, 1.86] 1.08 [0.66, 1.78] 0.98 [0.70, 1.36]	
CULPTURE Collevents dotal events deterogeneity: Ch <sup>2</sup> = - est for overall effect: .1.6 Arthralgia IXTURE UNCTURE Schwensen2017 SCULPTURE subtotal (95% Cl) otal events deterogeneity: Ch <sup>2</sup> = - est for overall effect: .1.7 Upper respirato IXTURE SESTURE UNCTURE SESTURE UNCTURE SESTURE UNCTURE SESTURE UNCTURE SESTURE UNCTURE SESTURE UNCTURE SEST	17 44 6.75, df = 4 (P = 0.3) 24 5 1 25 55 2.64, df = 3 (P = 0.3) 7 2 = 0.22 (P = 0.8) ry tract infection 26 3 5 31 65 0.94, df = 3 (P = 0.2) 2 = 0.24 (P = 0.8) 5 5 0.94, df = 3 (P = 0.2) 5 3 1 5 5 5 5 5 5 5 5 5 5 5 5 5	433 1064 1.15); l <sup>2</sup> = 41 3) 467 836 433 1024 1.45); l <sup>2</sup> = 0% 3) 467 88 433 1057 1.82); l <sup>2</sup> = 0% 9)	28 52 % 33 0 20 56 56 56 26 4 8 27 65	408 1042 469 89 33 408 999 469 68 89 408 1034	3.4% 6.3% 0.4% 0.1% 2.4% 6.8% 3.1% 0.5% 0.9% 3.9% 3.9% 7.8%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65.41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38] 0.96 [0.67, 1.38] 0.63 [0.22, 1.86] 1.08 [0.66, 1.78] 0.98 [0.70, 1.36]	
CULPTURE isolational (95% CI) otal events est for overall effect: 1.6 Arthralgia iXTURE UNCTURE UNCTURE UNCTURE UNCTURE Elerogeneity: Chi <sup>2</sup> = : est for overall effect: 1.7 Upper respirato iXTURE SESTURE UNCTURE SULPTURE UNCTURE SULPTURE isolat events est for overall effect: 1.8 Hypertension iXTURE	17 44 6.75, df = 4 (P = 0.3; 5 24 5 2.64, df = 3 (P = 0.3; 25 2.64, df = 3 (P = 0.3; 31 0.94, df = 3 (P = 0.8; 20	433 1064 (15);   <sup>2</sup> = 41 (15);   <sup>2</sup> = 41 (16);   <sup>2</sup> = 41 (16);   <sup>2</sup> = 0% (16);	28 52 % 33 3 0 20 56 56 56 56 56 56 56 56 56 56 56 56 56	408 1042 469 89 33 408 999 469 68 89 408 1034	3.4% 6.3% 3.9% 0.4% 0.1% 2.4% 6.8% 3.1% 0.5% 0.9% 3.3% 7.8%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.82 [0.56, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65, 41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38] 0.96 [0.67, 1.38] 0.74 [0.17, 3.18] 0.63 [0.22, 1.86] 1.00 [0.65, 1.70] 0.98 [0.70, 1.36]	
CULPTURE CULPTURE vibitotal (95% CI) otal events vest for overall effect: 1.6 Arthralgia IXTURE UNCTURE Schwensen2017 SCULPTURE vibitotal (95% CI) otal events telerogeneity: Ch <sup>2</sup> = - est for overall effect: 1.7 Upper respirato IXTURE UNCTURE SESTURE UNCTURE Set for overall effect: 1.8 Hypertension IXTURE UNCTURE	17 44 Z = 0.97 (P = 0.3) 24 5 1 25 55 2.64, df = 3 (P = 0.8) 7 7 7 8 9 9 9 9 1 1 25 55 2.64, df = 3 (P = 0.8) 7 8 9 9 1 1 25 55 2.64, df = 3 (P = 0.8) 5 5 2.25 1 2.25 1 2.25 1 2.25 5 5 2.264, df = 3 (P = 0.8) 5 5 2.264, df = 3 (P = 0.8) 5 5 5 2.264, df = 3 (P = 0.8) 5 5 5 2.264, df = 3 (P = 0.8) 5 5 5 5 5 5 5 5 5 5 5 5 5	433 1064 1.15);   <sup>2</sup> = 41 3) 467 86 433 1024 1.45);   <sup>2</sup> = 0% 3) 467 69 88 433 1057 69 88 433 1057 69 88 467 69 88 467 88	28 52 % 33 3 0 20 56 56 56 56 56 56 56 56 56 56 56 56 56	408 1042 469 89 33 408 999 408 89 408 1034	3.4% 6.3% 0.4% 0.4% 2.4% 6.8% 3.1% 0.5% 0.9% 3.3% 7.8% 2.6% 0.2%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.73 [0.44, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65.41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38] 0.96 [0.67, 1.38] 0.74 [0.17, 3.18] 0.63 [0.22, 1.86] 1.08 [0.66, 1.78] 0.98 [0.70, 1.36]	
CULPTURE COLPTURE Viabtotal (95% CI) Viale vents Viale vents vents for overall effect: 1.6 Arthralgia IXTURE UNCTURE Viabtotal (95% CI) Viale vents Viale vents Viale vents VistURE Viale vents VistURE Viale vents VistURE	17 44 6.75, df = 4 (P = 0, 3) 24 5 1 25 2.64, df = 3 (P = 0, 8) 27 2 (P = 0.8) 1 2 (P = 0.8) 1 3 5 31 0.94, df = 3 (P = 0, 8) 2 2 (P = 0.8) 1 3 5 31 0.94, df = 3 (P = 0, 8) 2 2 0.94, df = 3 (P = 0, 8) 3 1 0.94, df = 3 (P = 0, 8) 2 2 0.94, df = 3 (P = 0, 8) 3 1 0.94, df = 3 (P = 0, 8) 2 2 0.94, df = 3 (P = 0, 8) 3 1 0.94, df = 3 (P = 0, 8) 2 2 2 2 2 2 2 2 2 2 2 2 2	$\begin{array}{c} 433\\ 1064\\ 1.15); \  ^2 = 41\\ 3)\\ 467\\ 88\\ 36\\ 433\\ 1024\\ 1.45); \  ^2 = 0\\ 3)\\ 467\\ 69\\ 88\\ 433\\ 1057\\ 1.82); \  ^2 = 0\\ 3)\\ 467\\ 88\\ 433\\ 1057\\ 1.82; \  ^2 = 0\\ 3\end{array}$	28 52 % 33 3 0 20 56 56 5 56 5 56 5 56 5 56 5 56 5 5	408 1042 469 89 33 408 999 408 1034 469 89 408 1034	3.4% 6.3% 9.4% 0.1% 6.8% 3.1% 6.8% 3.3% 7.8% 2.6% 0.2%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.82 [0.56, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65, 41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38] 0.96 [0.67, 1.38] 1.00 [0.59, 1.70] 0.74 [0.17, 3.18] 0.63 [0.22, 1.86] 1.08 [0.66, 1.78] 0.98 [0.70, 1.36] 0.98 [0.70, 1.36]	
CULPTURE CULPTURE Coll Points detorgeneity: Ch <sup>2</sup> = : est for overall effect: 1.6 Arthralgia iXTURE UNCTURE tokwensen2017 CCULPTURE UNCTURE detorgeneity: Ch <sup>2</sup> = : est for overall effect: 1.7 Upper respirato iXTURE UNCTURE UNCTURE UNCTURE UNCTURE detorgeneity: Ch <sup>2</sup> = : est for overall effect: 1.8 Hypertension iXTURE UNC	17 44 6.75, df = 4 (P = 0.3) 24 5 1 25 2.64, df = 3 (P = 0.3) ry tract infection 26 3 5 0.94, df = 3 (P = 0.8) 65 0.94, df = 3 (P = 0.8) 20 6 28 20 6 28	$\begin{array}{c} 433\\ 1064\\ 1.15); \  ^2 = 41\\ 3)\\ \begin{array}{c} 467\\ 88\\ 36\\ 433\\ 1024\\ 1.45); \  ^2 = 0\%\\ 3)\\ \begin{array}{c} 467\\ 69\\ 88\\ 433\\ 1057\\ 0.82); \  ^2 = 0\%\\ 3)\\ \begin{array}{c} 467\\ 88\\ 433\\ 988\\ 433\\ 988\\ \end{array}$	28 52 33 3 0 20 56 56 56 56 56 56 56 56 56 56 56 56 56	408 1042 469 89 33 408 999 68 89 999 68 89 909 1034	3.4% 6.3% 3.9% 0.4% 0.4% 0.5% 0.9% 7.8% 2.6% 0.2% 2.5%	0.57 [0.32, 1.03] 0.82 [0.56, 1.22] 0.82 [0.56, 1.22] 1.69 [0.42, 6.84] 2.76 [0.12, 65,41] 1.18 [0.66, 2.09] 0.96 [0.67, 1.38] 0.96 [0.67, 1.38] 0.74 [0.17, 3.18] 0.63 [0.22, 1.86] 1.08 [0.66, 1.78] 0.98 [0.70, 1.36] 0.98 [0.70, 1.36] 3.03 [0.63, 14.63] 1.39 [0.79, 2.45] 1.22 [0.83, 1.81]	
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Figure 3. Detailed adverse drug events observed with 150 mg vs 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis.

 $I^2$  denoted a higher heterogeneity whereas a lower percentage denoted a lower heterogeneity.

In addition, a fixed statistical model was used if the  $I^2$  value was less than 50%, whereas a random statistical model was used if the  $I^2$  value was more than 50%.

Sensitivity analysis was carried out by a method of exclusion. Each study was excluded at a time and a new analysis was generated to observe for any significant difference from the main results.

Publication bias was visually observed by assessing funnel plots.



Figure 4. Cough as an adverse drug event observed with 150 mg vs 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis.

#### 2.5. Ethical approval

Ethical approval or board review approval was not required for this study.

#### 3. Results

#### 3.1. Search outcomes

Following the PRISMA guideline,<sup>[9]</sup> a total number of 675 publications were retrieved from online databases. Following a careful assessment of the titles and abstracts, 596 articles were eliminated due to irrelevance.

Seventy-nine (79) full text articles were assessed for eligibility. Following further assessments, other full text publications were eliminated due to the following reasons:

- Literature review (2);
- Meta-analysis and pooled studies (7);
- Did not report relevant endpoints (6);
- Control group was absent (7);
- Did not report the relevant dosage of drug (2);
- Included data which could not be used (3);
- Duplicated studies (45).

Table 4

Finally, only 7 studies<sup>[10-16]</sup> were included in this metaanalysis. The flow diagram for the study selection has been demonstrated in Figure 1.

## 3.2. Main and baseline features of the studies and participants respectively

The main features of the original studies were listed in Table 2.

A total number of 2361 participants were included in this metaanalysis comparing 150 mg vs 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis. The 1169 participants were assigned to 150 mg secukinumab whereas 1192 participants were assigned to 300 mg secukinumab as shown in Table 2.

Six studies were randomized trials and 1 study was an observational cohort.

The enrollment time period of the participants varied from year 2011 to 2015.

The baseline characteristics of the participants were listed in Table 3. Mean age of the participants ranged from 43.9 to 52.4 years. Male participants (51.1–72.2) % were pre dominant in comparison to female participants. The body mass index (BMI) varied from 28.4 to 30.6 kg/m<sup>2</sup>. A minor population of the participants also suffered from psoriatic arthritis. Duration of psoriasis varied from 7.5 to 20.4 years as shown in Table 3.

# 3.3. Comparing the adverse drug events observed with 150 mg vs 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis

Results of this analysis showed that the risk of any adverse event (RR: 1.00, 95% CI: 0.96–1.05; P=.94), the risk of serious

Results of this analysis.									
Adverse drug events	RR with 95% Cl	5% Cl P value							
Any adverse drug event	1.00 [0.96–1.05]	.94	38						
Serious adverse event	1.04 [0.75–1.43]	.82	5						
Adverse events leading to drug discontinuation	0.98 [0.61–1.57]	.92	5						
Infection or infestation	1.11 [0.98–1.25]	.09	9						
Naso-pharyngitis	1.05 [0.90-1.23]	.55	44						
Headache	0.92 [0.68–1.25]	.60	7						
Diarrhea	1.14 [0.75–1.73]	.55	3						
Pruritus	0.82 [0.56-1.22]	.33	41						
Arthralgia	0.96 [0.67-1.38]	.83	0						
Upper respiratory tract infection	0.98 [0.70-1.36]	.89	0						
Hypertension	1.22 [0.83–1.81]	.31	17						
Nausea	1.39 [0.63-3.04]	.42	31						
Cough	1.46 [0.67-3.19]	.34	61						

CI = confidence intervals, RR = risk ratios.



adverse events (RR: 1.04, 95% CI: 0.75–143; P=.82) and the risk of adverse events leading to drug discontinuation (RR: 0.98, 95% CI: 0.61–1.57; P=.92) were not significantly different between 150 mg vs 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis as shown in Figure 2.

When the adverse drug events were studied in details, the risks of infection or infestation (RR: 1.11, 95% CI: 0.98–1.25; P=.09), naso-pharyngitis (RR: 1.05, 95% CI: 0.90–1.23; P=.55), headache (RR: 0.92, 95% CI: 0.68–1.25; P=.60), diarrhea (RR: 1.14, 95% CI: 0.75–1.73; P=.55), pruritus (RR: 0.82, 95% CI: 0.56–1.22; P=.33), arthralgia (RR: 0.96, 95% CI: 0.67–1.38; P=.83), upper respiratory tract infection (RR: 0.98, 95% CI: 0.70–1.36; P=.89), hypertension (RR: 1.22, 95% CI: 0.83–1.81; P=.31), nausea (RR: 1.39, 95% CI: 0.63–3.04; P=.42), and cough (RR: 1.46, 95% CI: 0.67–3.19; P=.34) were still not significantly different between 150 mg vs 300 mg secukinumab for the treatment of moderate to severe plaque psoriasis as shown in Figures 3 and 4.

A summarized version of the results has been listed in Table 4.

Sensitivity analysis resulted in consistent results throughout. Additionally, a low evidence of publication bias was observed across all the studies that assessed the adverse drug events observed between the two different dosages of secukinumab for the treatment of patients with moderate to severe plaque psoriasis as shown in Figure 5.

#### 4. Discussion

Our results showed that both dosages of secukinumab were equally safe to be used for the treatment of moderate to severe plaque psoriasis. There was no significant difference in adverse drug events observed with any of the dosage.

Similar to the results of this analysis, in order to assess the longterm safety of secukinumab, a pooled analysis of 10 phase II and III clinical studies in patients with moderate to severe plaque psoriasis showed comparable adverse drug events during this 52 week follow-up time period.<sup>[17]</sup> However, in this current analysis, we only compared secukinumab 150 mg vs 300 mg, and we did not include phase II trials.

Results from 2 randomized phase 3 trials showed secukinumab to significantly improve physical function in participants with plaque psoriasis and psoriatic arthritis.<sup>[18]</sup> In addition, it was observed that physical functioning as well as the condition of this chronic disease were more significantly improved with secukinumab 300 mg.

Even in the JUNCTURE trial, the authors concluded that secukinumab was effective, well-tolerated and was associated with high usability for the treatment of moderate to severe psoriasis.<sup>[19]</sup> The fact that responses were much better with secukinumab 300 mg should not be ignored. Better response with tolerable safety drug events might further guide therapies in patients with moderate to severe plaque psoriasis. The drug was also well accepted in North Americans.<sup>[20]</sup>

Our research aimed to compare the adverse drug events observed with secukinumab 150 mg vs 300 mg for the treatment of moderate to severe plaque psoriasis and the results showed both dosages to be well-tolerated without any significantly higher adverse event. Other research have shown secukinumab to be very effective, especially the 300 mg dosage, for the treatment of moderate to severe plaque psoriasis. Therefore, secukinumab 300 mg might be considered by physicians for the treatment of this chronic autoimmune condition. However, future phase IV trials should further assess this interesting drug.

#### 4.1. Limitations

The limitations were as followed: The total number of participants was limited in comparison to other studies. Secondly, we also included one study with participants who were being treated for palmo-plantar psoriasis in comparison to all the other original studies which included patients with moderate to severe plaque psoriasis. In addition, most of the follow-up time periods reported were 52 weeks, however, one study had a follow-up time period of 16 weeks and 2 other studies had a follow-up time period of 12 weeks. Also, whether other drugs were being alternatively used were not reported or taken into consideration in this analysis and this might have influenced the endpoints.

#### 5. Conclusion

Secukinumab 150 mg and 300 mg were both equally tolerable and might safely be used for the treatment of moderate to severe plaque psoriasis. No significant adverse drug events were observed with any of the dosage.

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All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

#### **Author contributions**

LZ, HY, QC and JZ were responsible for the conception and design, acquisition of data, analysis and interpretation of data, drafting the initial manuscript and revising it critically for important intellectual content.

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