

Supplementary material

Table S1 .Appendix for search terms and findings of electronic search.

Search terms	Database	Number of retrieved articles		Number of articles	Causes for exclusion
((tapinarof AND cream AND 1% AND 0.5%) AND ((atopic AND dermatitis) OR (atopic AND eczema)))	PubMed	19	included after removal of duplicates	164	Automatic duplicate removal
	Science direct	109			
	WOS	26	included after abstract screening	28	
	Scopus	26	included after full text screening i.e. to extraction	5	irrelevant (N=6), duplicate (N=7), conference abstract (N=10)
	CENTRAL	39			
	Manual	1			
	total		219		

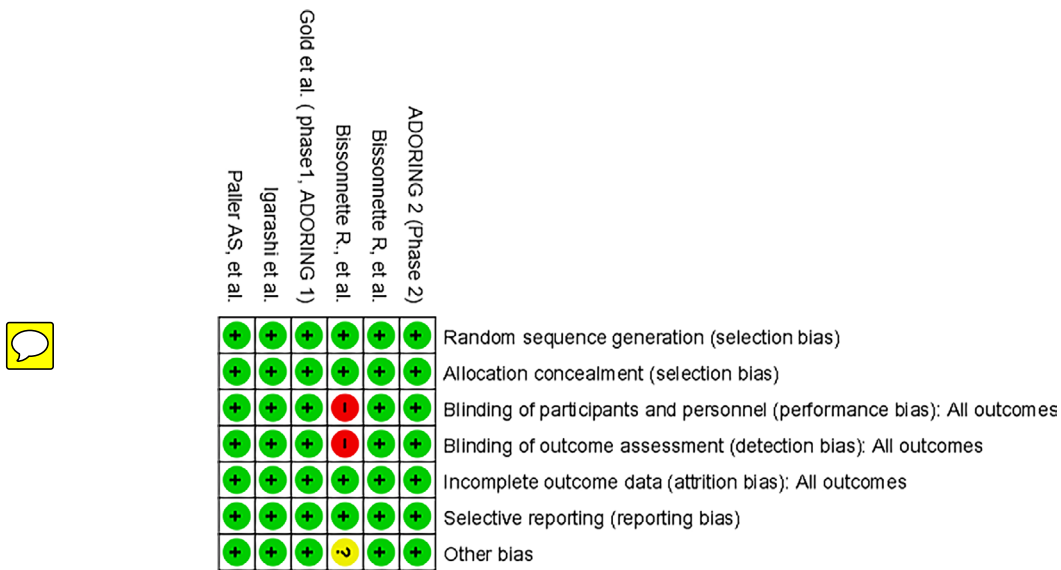


Figure 1S. Risk of bias graph.

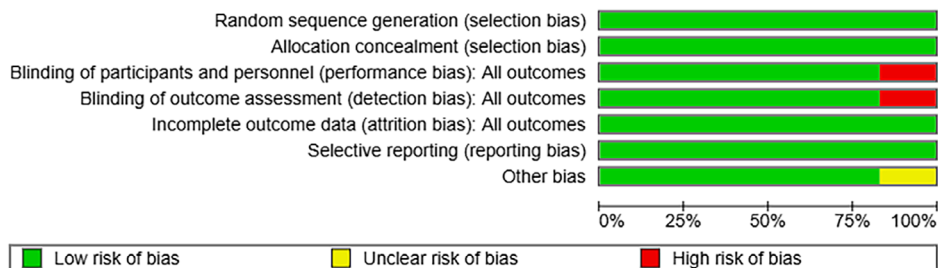


Figure 2S. Risk of bias summary.

Table S2. Summary of study characteristics.

Author, year	Country	Study design	Age (intervention vs control)	Sex (male Age (intervention vs control)	Sample size (intervention vs control)	Intervention	control	Side effects	Follow-up duration
Bissonnette R, et al., 2012 [5]	Canada	Phase 2b, randomized, double-blind, placebo-controlled clinical trial	18–65 years (Mean: 33.3 years)	47% (Placebo), 40% (WBI-1001 0.5%), 34% (WBI-1001 1.0%) males	47 (1%), 51 (0.5%)	148 randomized (51 placebo, 50 WBI-1001 0.5%, 47 WBI-1001 1.0%)	51	Folliculitis, contact dermatitis, headache (most mild or moderate)	12 weeks (6 weeks initial, 6 weeks additional for active groups)
Bissonnette R, et al., 2018 [6]	Canada	RCT	31.6 (10.55) vs 38.0 (15.66)	5 vs 3	5	2% cream (5)	Tapinarof 1% cream (6)	three subjects in the 2% tapinarof cohort discontinued due to systemic AEs	21 days
Gold et al., 2025 (phase 1, ADORING 1) [7]	USA (Multicenter)	Phase 3, randomized, double-blind, vehicle-controlled trials	15.6 (16.6) vs 15.6 (16.5)	133 vs 66	270	Tapinarof cream 1% once daily (270)	vehicle cream (137)	Minimal local irritation: no significant adverse events reported	8 weeks
Igarashi et al., 2024 [8]	Japan	Two Phase 3 Trials: ZBB4-1: 8-week double-blind, vehicle-controlled treatment period with a 16-week extension • ZBB4-2: 52-week open-label trial	31.7 (12.3) vs 35.4 (13.0)	105 vs 46	144	Tapinarof cream 1% once daily	vehicle cream	folliculitis, acne, and headache; most adverse events were mild or moderate in severity.	8 weeks with extent of 16 weeks

Paller AS, et al., 2021 [9]	USA, Canada, Japan	Phase 2b, randomized, double-blind, vehicle-controlled clinical trial	12-65 years	NM	NM tapinarof 1% twice daily, N=40; tapinarof 1% once daily, N=41; tapinarof 0.5% twice daily, N=43; tapinarof 0.5% once daily, N=41;	vehicle twice daily, n = 42; and vehicle once daily, n = 40).	Tapinarof cream 0.5% or 1% (once or twice daily)	vehicle control once or twice daily	Mostly mild or moderate adverse events (AEs), low application-site irritation reported	12 weeks of treatment + 4 weeks of follow-up
Phase 2, ADORING 2 [7]	USA (Multicenter)	Phase 3, randomized, double-blind, vehicle-controlled trials	16.4(16.2) vs 16.8(16.1)	117 vs 57	271	133	Tapinarof cream 1% once daily	vehicle cream	Minimal local irritation: no significant adverse events reported	8 weeks

NM, not mentioned.

Table S3. Summary of treatment rankings based on SUCRA scores, mean differences, and probability of best/worst ranking across 75% improvement over baseline in EASI.

Rank	Tapinarof 1% twice daily	Tapinarof 1% once daily	Tapinarof 0.5% twice daily	Tapinarof 0.5% once daily	Placebo twice daily	Placebo once daily
1st	70.3%	19.5%	10.1%	0.1%	0.0%	0.0%
2nd	19.5%	50.2%	28.9%	1.4%	0.0%	0.0%
3rd	10.1%	28.9%	40.5%	20.3%	0.2%	0.0%
4th	0.1%	1.4%	20.3%	50.0%	28.2%	0.0%
5th	0.0%	0.0%	0.2%	28.2%	50.4%	21.2%
6th	0.0%	0.0%	0.0%	0.0%	21.2%	78.8%

Table S4. Summary of treatment rankings based on SUCRA scores, mean differences, and probability of best/worst ranking across IGA of 0 or 1 and a minimum 2-point improvement over baseline in IGA.

Rank	Tapinarof 1% twice daily	Tapinarof 1% once daily	Tapinarof 2% twice daily	Tapinarof 0.5% twice daily	Tapinarof 0.5% once daily	Placebo twice daily	Placebo once daily
1st	57.4%	25.7%	15.5%	0.6%	0.8%	0.0%	0.0%
2nd	34.0%	45.3%	19.8%	12.2%	2.6%	0.0%	0.0%
3rd	7.9%	22.6%	35.4%	45.2%	16.5%	0.2%	0.0%
4th	0.7%	6.0%	20.3%	31.5%	43.1%	9.8%	0.0%
5th	0.0%	0.4%	6.5%	9.3%	29.7%	41.0%	21.2%
6th	0.0%	0.0%	2.5%	1.2%	6.5%	48.4%	78.8%