

## Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

## eText 1. Search strategy

### MEDLINE

("areata"[title] OR "totalis"[title] OR "universalis"[title]) AND  
("sensitizer"[title] OR "sensitization"[title] OR "immunotherapy"[title] OR  
"Diphenylcyclopropenone"[title] OR "diphenylcyclopropenone"[title] OR "diphencyprone"[title] OR  
"Squaric acid dibutyl ester"[title] OR "squaric"[title])

### Embase

('areata':ti OR 'totalis':ti OR 'universalis':ti) AND  
( 'sensitizer':ti OR 'sensitization':ti OR 'immunotherapy':ti OR  
'Diphenylcyclopropenone':ti OR 'diphenylcyclopropenone':ti OR 'diphencyprone':ti OR  
'Squaric acid dibutyl ester':ti OR 'squaric':ti)

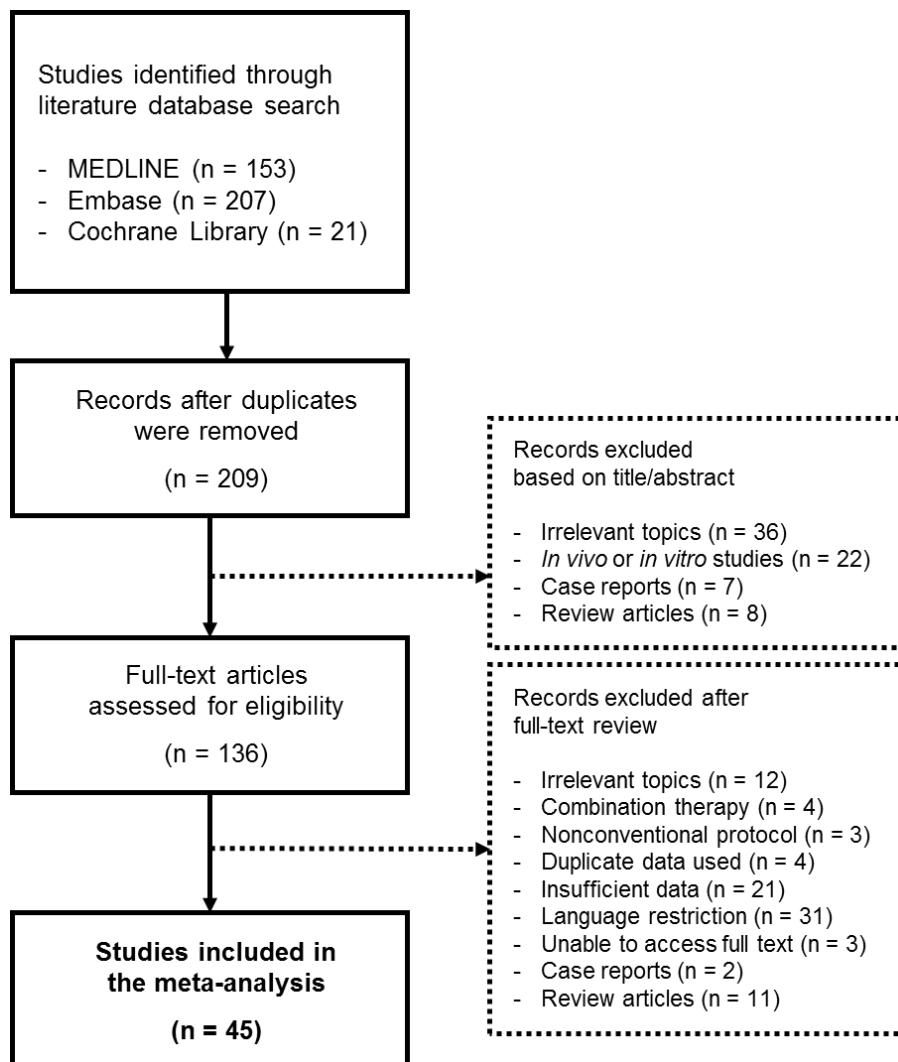
### Cochrane Library

#1: 'areata':ti OR 'totalis':ti OR 'universalis':ti

#2: 'sensitizer':ti OR 'sensitization':ti OR 'immunotherapy':ti OR  
'Diphenylcyclopropenone':ti OR 'diphenylcyclopropenone':ti OR 'diphencyprone':ti OR  
'Squaric acid dibutyl ester':ti OR 'squaric':ti

Final query: #1 AND #2

**eFigure 1. Literature search**



PRISMA flow diagram of literature search and study selection for the systematic review of studies on contact immunotherapy for patients with alopecia areata.

**eTable 1. Definition of therapeutic regrowth**

<b>Grade</b>	<b>Quantitative criteria<sup>a</sup></b>	<b>Qualitative criteria</b>
<b>Any regrowth</b>	<10% regrowth	Any or little regrowth Hull and Norris <sup>29</sup> grade I (vellus hair) Any improvement in Hull and Norris grade No clear definition of therapeutic regrowth
<b>Minor regrowth</b>	10–59% regrowth	Partial, some, good, or moderate regrowth Cosmetically unacceptable regrowth Hull and Norris grade II (sparse terminal hair)
<b>Major regrowth</b>	60–89% regrowth	Diffuse or persistent regrowth Cosmetically acceptable regrowth Hull and Norris grade III (terminal hair with patchy alopecia)
<b>Complete regrowth</b>	90–100% regrowth	Complete or excellent regrowth Hull and Norris grade IV (terminal hair all over the head)

<sup>a</sup>Only studies using quantitative criteria for therapeutic regrowth were included in the sensitivity analysis (see eTable 3).

**eTable 2. Study characteristics and quality assessment**

Study name	Study setting	Sensitizer	Study population	Total, n	Female, n	Age, y	AT/AU, n	Follow-up, m	Any regrowth	Minor regrowth	Major regrowth	Complete regrowth	SA LT ≥ 50	Duration ≥ 1 y	Atopic disease	Nail involvement	Adverse effects	Recurrence rate
Thuangtong et al <sup>30</sup>	Thailand, 2017	Diphenylcyclopropanone	Recalcitrant AT/AU	20	12	35	20	2.7	-	-	0	-	0	-	-	-	0	-
Tiwary et al <sup>31</sup>	India, 2016	Diphenylcyclopropanone, squaric acid dibutyl ester	AA (>20%)	24	10	NA	0	6	-	0	0	-	0	-	-	-	0	-
Lamb et al <sup>32</sup>	UK, 2016	Diphenylcyclopropanone	AA	133	99	35	53	NA	0	-	-	0	0	0	0	0	0	-
Durdu et al <sup>33</sup>	Turkey, 2015	Diphenylcyclopropanone	Chronic, extensive, recalcitrant AA	22	9	17	9	12	-	0	0	-	0	-			0	0
Chiang et al <sup>34</sup>	US, 2015	Diphenylcyclopropanone	AA	50	36	37.5	39	36	-	0	-	-	0	-			0	0
Luk et al <sup>35</sup>	China, 2013	Diphenylcyclopropanone	AA	29	15	28.9	15	NA	0	-	0	0	0	0	0	0	0	0
Khoury et al <sup>36</sup>	Lebanon, 2013	Diphenylcyclopropanone	AA	34	15	24.72	14	16	-	-	-	-	0	-	-	-	0	0
Dhurat et al <sup>37</sup>	India, 2013	Diphenylcyclopropanone	AA with at least two patches	29	NA	NA	0	6	0	-	-	-	0	-	-	-	-	-

Study name	Study setting	Sensitizer	Study population	Total, n	Female, n	Age, y	AT/AU, n	Follow-up, m	Any regrowth	Minor regrowth	Major regrowth	Complete regrowth	SA LT ≥ 50	Duration ≥ 1 y	Atopic disease	Nail involvement	Adverse effects	Recurrence rate
Ohlmeier et al <sup>38</sup>	Germany, 2012	Diphenylcyclopropanone	AA	135	95	36	24	20	0	-	-	-	0	-	-	-	-	0
Khan et al <sup>39</sup>	UK, 2011	Diphenylcyclopropanone	AA	60	43	NA	22	10.5	0	0	-	-	0	-	-	-	0	0
Bhat et al <sup>40</sup>	UK, 2011	Diphenylcyclopropanone	Recalcitrant AA	29	23	NA	14	12	-	0	-	-	0	-	-	-	-	0
Avgerinou et al <sup>41</sup>	Greece, 2007	Diphenylcyclopropanone	Extensive or chronic (>25% or >1 year)	54	15	27.2	6	6.1	-	-	-	-	0	-	-	-	0	0
Sotiriadis et al <sup>42</sup>	Greece, 2006	Diphenylcyclopropanone	Severe AA (>50%)	38	19	24.5	16	12	-	0	0	0	0	0	0	-	0	0
Ajith et al <sup>43</sup>	India, 2006	Squaric acid dibutyl ester	Recalcitrant AA	60	32	25	20	3.2	-	0	-	-	0	-	0	0	0	0
Kwon et al <sup>44</sup>	Korea, 2005	Squaric acid dibutyl ester	AA (>25%)	22	12	27.8	7	6	0	-	-	-	0	-	-	-	0	0
Dall'oglio et al <sup>45</sup>	Italy, 2005	Squaric acid dibutyl ester	Recalcitrant AA (>40%)	54	26	25	23	8	-	-	0	0	0	-	-	-	-	0
Mun et al <sup>46</sup>	Korea, 2004	Diphenylcyclopropanone	Recalcitrant AA	36	23	NA	10	NA	0	-	0	0	0	-	0	0	0	-

Study name	Study setting	Sensitizer	Study population	Total, n	Female, n	Age, y	AT/AU, n	Follow-up, m	Any regrowth	Minor regrowth	Major regrowth	Complete regrowth	SA LT ≥ 50	Duration ≥ 1 y	Atopic disease	Nail involvement	Adverse effects	Recurrence rate
			(>25%)															
Lee et al <sup>47</sup>	Korea, 2004	Diphenylcyclopropanone	Extensive AA (>50%)	39	17	25	16	5.8	-	-	0	0	0	0	-	-	0	0
Wiseman et al <sup>48</sup>	Canada, 2001	Diphenylcyclopropanone	AA (>25%)	148	91	36.3	35	7.2	-	0	-	-	0	-	-	-	0	0
Pardasani et al <sup>49</sup>	US, 2001	Squaric acid dibutyl ester	AA	36	22	27.2	8	7	0	-	-	-	0	-	-	0	-	-
Pericin et al <sup>50</sup>	Switzerland, 1998	Diphenylcyclopropanone	Severe AA (>40%)	68	36	NA	52	15.8	0	-	0	0	0	-	-	-	0	0
Iijima et al <sup>13</sup>	Japan, 1997	Squaric acid dibutyl ester	AA (>25%)	48	32	NA	14	6	0	-	-	-	0	0	0	-	-	-
Amer et al <sup>51</sup>	Egypt, 1997	Diphenylcyclopropanone	AA	49	21	NA	27	NA	0	0	0	0	0	-	-	-	0	-
Weise et al <sup>52</sup>	Germany, 1996	Diphenylcyclopropanone	Severe AA	105	78	32	62	NA	-	0	-	-	0	-	0	0	-	-
Tosti et al <sup>53</sup>	Italy, 1996	Squaric acid dibutyl ester	Pediatric severe AA	33	13	9.5	33	NA	0	-	0	0	0	-	0	0	0	0
Schuttelaar et al <sup>24</sup>	Netherlands, 1996	Diphenylcyclopropanone	Pediatric AA	25	14	10.7	15	10.8	0	-	0	0	0	0	0	-	-	-
Micali	Italy,	Squaric acid	Recal	14	77	23	15	12	-	-	-	-	0	-	-	-	-	-



Study name	Study setting	Sensitizer	Study population	Total, n	Female, n	Age, y	AT/AU, n	Follow-up, m	Any regrowth	Minor regrowth	Major regrowth	Complete regrowth	SA LT ≥ 50	Duration ≥ 1 y	Atopic disease	Nail involvement	Adverse effects	Recurrence rate
et al <sup>54</sup>	1996	dibutyl ester	citrant AA	4														
van Baar et al <sup>55</sup>	Netherlands, 1995	Diphenylcyclopropanone	Severe AA	139	73	NA	85	43	-	-	0	0	0	-	-	-	0	-
Orechia et al <sup>56</sup>	Italy, 1994	Squaric acid dibutyl ester	Pediatric recalcitrant AA (>75%)	28	16	10	11	NA	0	0	-	-	0	0	0	-	0	0
Shapiro et al <sup>57</sup>	Canada, 1993	Diphenylcyclopropanone	AA (>50%)	7	4	32.7	4	NA	-	0	-	-	0	0	0	0	-	0
van der Steen et al <sup>58</sup>	Netherlands, 1992	Diphenylcyclopropanone	AA (>40%)	139	NA	NA	85	NA	-	0	-	-	0	0	-	0	-	-
Hull et al <sup>21</sup>	UK, 1991	Diphenylcyclopropanone	Pediatric severe AA	12	4	11.2	8	7.3	0	-	0	0	0	0	0	-	0	0
Hull et al <sup>59</sup>	UK, 1991	Diphenylcyclopropanone	AA (>6 months)	78	61	NA	45	8	-	-	0	0	0	-	-	-	-	-
Chun et al <sup>60</sup>	Korea, 1991	Diphenylcyclopropanone	Recalcitrant AA	20	6	20.1	10	5	0	-	0	0	0	0	-	-	0	-
Berth-Jones	UK, 1990	Diphenylcyclopropanone	AT (>1 year)	11	6	39	11	6	0	-	-	-	0	0	-	-	-	-

Study name	Study setting	Sensitizer	Study population	Total, n	Female, n	Age, y	AT/AU, n	Follow-up, m	Any regrowth	Minor regrowth	Major regrowth	Complete regrowth	SA LT ≥ 50	Duration ≥ 1 y	Atopic disease	Nail involvement	Adverse effects	Recurrence rate
et al <sup>61</sup>																		
Monk et al <sup>62</sup>	UK, 1989	Diphenylcyclopropanone	Extensive AA (>50%, >5 years)	18	10	26.9	14	NA	-	0	-	-	0	0	-	-	0	-
Hull et al <sup>63</sup>	UK, 1988	Diphenylcyclopropanone	Extensive AA (>1 year)	28	25	NA	13	8	-	-	-	-	0	0	-	-	-	-
Hatzis K et al <sup>16</sup>	Greece, 1988	Diphenylcyclopropanone	Extensive AA	45	19	25.4	22	NA	0	0	-	-	0	-	-	-	0	-
Casero et al <sup>64</sup>	US, 1987	Squaric acid dibutyl ester	Recalcitrant AA	14	11	16.5	12	7.6	-	0	-	-	0	-	-	-	0	-
Valsecchi et al <sup>65</sup>	Italy, 1986	Squaric acid dibutyl ester	Recalcitrant AA	45	NA	NA	23	NA	-	-	-	-	0	-	-	-	-	0
Valsecchi et al <sup>66</sup>	Italy, 1985	Squaric acid dibutyl ester	AA (>30%)	38	17	NA	20	NA	-	0	-	-	0	-	-	-	0	-
Orechia et al <sup>12</sup>	Italy, 1985	Diphenylcyclopropanone	AA (>50%)	26	11	NA	17	5.1	0	-	0	0	0	0	0	0	0	0
Case et al <sup>67</sup>	US, 1984	Squaric acid dibutyl ester	AA (>30%)	21	11	34	10	3	-	0	0	0	0	-	-	-	0	0
Giannetti et al <sup>68</sup>	Italy, 1983	Squaric acid dibutyl ester	AA	26	11	20	6	3.6	-	0	0	0	0	0	0	-	0	0

Study name	Study setting	Sensitizer	Study population	Total, n	Female, n	Age, y	AT/AU, n	Follow-up, m	Any regrowth	Minor regrowth	Major regrowth	Complete regrowth	SALT $\geq$ 50	Duration $\geq$ 1 y	Atopic disease	Nail involvement	Adverse effects	Recurrence rate
Flowers et al <sup>69</sup>	US, 1982	Squaric acid dibutyl ester	AA (>30%)	8	5	33.9	5	2.3	0	-	0	0	0	0	-	-	0	-

AT, alopecia totalis; AU, alopecia universalis; AA, alopecia areata; SALT, The Severity of Alopecia Tool; NA, not available

**eTable 3. Sensitivity analysis**

Original analysis (both quantitative and qualitative studies)								
AA subtype	Any regrowth		Minor regrowth		Major regrowth		Complete regrowth	
	Response rate (%) (95% CI [%])	No. of studies, (No. of patients)	Response rate (%) (95% CI [%])	No. of studies, (No. of patients)	Response rate (%) (95% CI [%])	No. of studies, (No. of patients)	Response rate (%) (95% CI [%])	No. of studies, (No. of patients)
PA	74.6 (67.9–80.3)	15 (459)	64.9 (57.7–71.6)	20 (409)	56.1 (45.9–65.8)	18 (430)	42.6 (29.9–56.3)	17 (371)
AT/AU	54.5 (46.2–62.6)	16 (285)	45.0 (35.9–54.4)	20 (357)	28.7 (24.1–33.8)	18 (405)	24.9 (18.2–33.0)	18 (443)
Overall	65.5 (59.1–71.3)	16 (744)	55.5 (49.0–61.9)	22 (766)	39.4 (31.8–47.6)	19 (835)	32.3 (25.3–40.2)	18 (814)
Sensitivity analysis (quantitative studies only)								
AA subtype	-		10–59% regrowth		60–89% regrowth		90–100% regrowth	
	Response rate (%) (95% CI [%])	No. of studies, (No. of patients)	Response rate (%) (95% CI [%])	No. of studies, (No. of patients)	Response rate (%) (95% CI [%])	No. of studies, (No. of patients)	Response rate (%) (95% CI [%])	No. of studies, (No. of patients)
PA	-	-	65.1 (56.5–72.7)	11 (275)	52.2 (23.2–79.8)	4 (41)	43.5 (26.4–62.4)	7 (112)
AT/AU	-	-	52.0 (37.5–66.1)	9 (184)	23.3 (15.4–33.8)	5 (83)	27.7 (20.4–36.4)	7 (126)
Overall	-	-	59.8 (52.0–67.2)	11 (459)	39.1 (27.5–52.2)	5 (124)	34.4 (21.8–49.7)	7 (238)

AA, alopecia areata; 95% CI, 95% confidential interval; PA, patchy alopecia; AT, alopecia totalis; AU, alopecia universalis

**eTable 4. Treatment-related adverse effects**

<b>Adverse effects</b>	<b>Incidence rate (%) (95% confidence interval [%])</b>	<b>No. of studies</b>	<b>No. of patients</b>
Severe eczema	30.8 (22.7–40.3)	13	1220
Lymphadenopathy	25.7 (18.2–35.0)	24	1213
Generalized eczema	15.8 (10.1–23.8)	17	814
Hyperpigmentation	12.7 (4.7–30.2)	5	304
Influenza-like symptoms	11.1 (5.2–21.9)	7	239
Contact urticaria	9.0 (5.2–15.2)	7	295
Folliculitis	7.1 (3.6–13.6)	4	116
Hypopigmentation	5.5 (3.0–9.7)	11	549
Erythema multiforme-like eruption	1.7 (0.6–4.4)	3	246

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