To Supporting Information: Local management of anogenital warts in non-immunocompromised adults: a network meta-analysis of randomized controlled trials

A. Bertolotti,[1,2,3] C. Ferdynus,[3] B. Milpied,[4] N. Dupin,[5] L. Huiart,[3,6] C. Derancourt[2,7]

[1]*Department of Infectious Disease, Saint-Pierre Hospital, Reunion Island, France*

[2]*EA 4537, Antilles-Guyane University, Martinique, France*

[3]*INSERM CICEC 1410, Reunion Island, France*

[4]*Department of Dermatology and Pediatric Dermatology, National Center for Rare Skin Disorders, Saint-André and Pellegrin Hospitals, Bordeaux, France*

[5]*Department of Dermatology, Cochin Hospital, Paris Descartes University, Paris, France*

[6]*Luxembourg Institute of Health, Department of Population Health, Luxembourg*

[7]*Department of dermatology, Hôpital de Briançon, Briançon, France.*

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Treatments are reported in order of relative ranking for efficacy. Comparisons between treatments should be read from left to right. The relative risk of each comparison is in the cell in common between the column-defining treatment and the row-defining treatment. A relative risk (RR) above 1 favors the column-defining treatment for the network estimates and the row-defining treatment for the direct estimates. IFN = interferon. Data presented as RR (95% CI). Cryo: cryotherapy; ablative: ablative treatment (surgery or electrosurgery or CO2 laser or cryotherapy); imi: imiquimod 5%; 5-FU: 5 fluorouracil; 5-FU intra: intralesional 5 fluorouracil; TCA: trichloroacetic acid; podo: podophyllin 20-25%; citric ac: citric acid 9%; polyph: polyphenon 15%; podotox cr: podophyllotoxin 0.5% cream; podotox cr/gel: podophyllotoxin 0.5% gel + cream: podotox gel: podophyllotoxin 0.5% gel; PDT: photodynamic therapy; mycobac intra: intralesional mycobacterium; KOH: potassium

hydroxide; electro: electrosurgery; INF-1a intra: intralesional interferon-1α; INF-2b intra: intralesional interferon-2β.

Appendix S6. Forest plot of the estimates of relative risk between each treatment and the reference placebo for complete lesion response. Sensitivity analyses: (A) Worst-case scenario, (B) Best-case scenario.

Data presented as RR (95% CI). Cryo: cryotherapy; ablative: ablative treatment (surgery or electrosurgery or CO2 laser or cryotherapy); imi: imiquimod 5%; 5-FU: 5 fluorouracil; 5-FU intra: intralesional 5 fluorouracil; TCA: trichloroacetic acid; podo: podophyllin 20-25%; citric ac: citric acid 9%; polyph: polyphenon 15%; podotox cr: podophyllotoxin 0.5% cream; podotox cr/gel: podophyllotoxin 0.5% gel + cream: podotox gel: podophyllotoxin 0.5% gel; PDT: photodynamic therapy; mycobac intra: intralesional mycobacterium; KOH: potassium hydroxide; electro: electrosurgery; INF-1a intra: intralesional interferon-1α; INF-2b intra: intralesional interferon-2β.

Appendix S7. Network meta-analysis estimates (lower triangle) and direct estimates (upper triangle) of complete lesion response for all therapies. Sensitivity analyses: Intention to treat.

Treatments are reported in order of relative ranking for efficacy. Comparisons between treatments should be read from left to right. The relative risk of each comparison is in the cell in common between the column-defining treatment and the row-defining treatment. A relative risk (RR) above 1 favors the column-defining

treatment for the network estimates and the row-defining treatment for the direct estimates. IFN = interferon. Data presented as RR (95% CI). Cryo: cryotherapy; ablative: ablative treatment (surgery or electrosurgery or CO2 laser or cryotherapy); imi: imiquimod 5%; 5-FU: 5 fluorouracil; 5-FU intra: intralesional 5 fluorouracil; TCA: trichloroacetic acid; podo: podophyllin 20-25%; citric ac: citric acid 9%; polyph: polyphenon 15%; podotox cr: podophyllotoxin 0.5% cream; podotox cr/gel: podophyllotoxin 0.5% gel + cream: podotox gel: podophyllotoxin 0.5% gel; PDT: photodynamic therapy; mycobac intra: intralesional mycobacterium; KOH: potassium hydroxide; electro: electrosurgery; INF-1a intra: intralesional interferon-1α; INF-2b intra: intralesional interferon-2β.

Appendix S8. Probabilities of treatment ranking. Sensitivity analyses: (A) Worst-case scenario, (B) Best-case scenario.

SUCRA: surface under the cumulative ranking curve**.** Cryo: cryotherapy; ablative: ablative treatment (surgery or electrosurgery or CO2 laser or cryotherapy); imi: imiquimod 5%; 5-FU: 5 fluorouracil; 5-FU intra: intralesional 5 fluorouracil; TCA: trichloroacetic acid; podo: podophyllin 20-25%; citric ac: citric acid 9%; polyph: polyphenon 15%; podotox cr: podophyllotoxin 0.5% cream; podotox cr/gel: podophyllotoxin 0.5% gel + cream: podotox gel: podophyllotoxin 0.5% gel; PDT: photodynamic therapy; mycobac intra: intralesional mycobacterium; KOH: potassium hydroxide; electro: electrosurgery; INF-1a intra: intralesional interferon-1α; INF-2b intra: intralesional interferon-2β.

Appendix S1: Search terms used to screen all databases

MEDLINE and Web of Science

1 hpv.all
2 papillomavirus.all.
3 acuminat*.all.
4 condyloma*.all.
5 wart*.all.
6 genital wart*.all.
7 or/1-6
8 randomized controlled trial.all.
9 controlled clinical trial.all.
10 random*.all.
11 placebo.all.
12 clinical trial*.all.
13 trial.all.
14 or/8-13
15 7 AND 14
16 hand.all.
17 foot.all.
18 feet.all.
19 animal*.all.
20 nonhuman*.all.
21 child*.all.
22 cancer*.all.
23 neoplasi*.all.
24 cervical.all.
25 laryn*.all.
26 vacci*.all.
27 tumor.all.
28 verruc*.all.
29 or/ 16-28
30 15 NOT 29

SCOPUS.com

#1.1 wart*:ab,ti
#1.2 condylom*:ab,ti
#1.3 acuminat*:ab,ti
#1.4 verruc*:ab,ti
#1.5 hpv:ab,ti
#1.6 papillomavirus*:ab,ti
#1.7 genital wart* :ab.ti
#1.8 condylomata acuminata : ab.ti
#1.9 wart virus:ab.ti
#1.10 #1.1 OR #1.2 OR #1.3 OR #1.4 OR #1.5 OR #1.6 OR #1.7 OR #1.8 OR #1.9
#1.11 clinical trial:ab,ti
#1.12 random*:ab,ti
#1.13 randomized controlled trial;ab,ti
#1.14 controlled clinical:ab,ti
#1.15 placebo*:ab,ti

#1.16 trial:ab,ti
#1.17 #1.11 OR #1.12 OR #1.13 OR #1.14 OR #1.15 OR #1.16
#1.18 #1.10 AND #1.17
#1.19 hand:ab,ti
#1.20 foot:ab,ti
#1.21 feet:ab,ti
#1.22 animal*:ab,ti
#1.23 nonhuman*:ab,ti
#1.24 child*:ab,ti
#1.25 cancer*:ab,ti
#1.26 neoplasi*:ab,ti
#1.27 cervical:ab,ti
#1.28 laryn*:ab,ti
#1.29 vacci*:ab,ti
#1.30 tumor:ab,ti
#1.31 verruc*:ab,ti
#1.32 #1.19 OR #1.20 OR #1.21 OR #1.22 OR #1.23 OR #1.24 OR #1.25 OR #1.26 OR #1.27 OR #1.28 OR #1.29 OR #1.30 OR #1.31
#1.33 #1.18 AND NOT #1.32

LILACS
(tw:(condylom*)) AND (tw:(Randomi*))

Ovid Platform
(condyloma OR acuminat OR wart) AND (clinical trial OR trial OR randomized trial OR randomized controlled trial OR controlled clinical OR placebo OR Randomized OR randomly)

Cochrane Library
(condyloma OR acuminata OR wart) and (randomized controlled trial OR controlled clinical trial OR random OR placebo OR clinical trial) not (hand OR foot OR feet OR animal OR nonhuman OR child OR cancer OR neoplasia OR cervical OR laryn OR vacci OR tumor OR verruc) in Trials

Cochrane Register and International Clinical Trials Registry Platform (ICTRP):
Using the terms: warts, condylomas, condyloma, genital warts in title, abstract and keywords.

Clinical Trials
Wart OR condylomas OR condyloma OR genital warts OR acuminata

EM-PREMIUM bibliography from 2010 in title and abstract:
English and french request: condylo*
English request: anogenital wart*
French request: verrue anogénitale*

Open Grey, SUDOC (title) and BABORD + bibliography (in French):
Condylome
Verrue

Appendix S2: Characteristics of RCTs included

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Abdullah 1993[1]	UK	Cryo	53 (43)	1×/wk, maximum 6 wk	Applied with a cotton Q-tip until wart is frozen with 1-mm margin, 2×	3	Clearance after 6 wk, side effects	1st treatment
		TCA	33 (30)	Same	A pointed plastic probe			
Akhavan 2014[2]	Iran	Podophyllin 20%	42 (38)	1×/wk, maximum 8 wk	NR	8	Clearance after 8 wk, recurrence after 3 mo, recurrence after 6 mo	1st treatment, only women
		Imiquimod	42 (37)	3×/wk, maximum 8 wk	Same			
		Cryo	42 (36)	1×; no other information given	Same			
Arican 2004[3]	Turkey	Imiquimod 5%	34 (33)	3×/wk, maximum 12 wk	Applied with the tip of the stick and then cleaned with abundant amounts of water	9	Clearance after 3 mo, recurrence after 6 mo, side effects	ITT modified
		Placebo	11 (10)	Same	Same			
Azizjalali 2012[4]	Iran	CO_2 laser	80 (80)	1× every 2 wk, maximum 6 wk	Local anesthesia, 30 W, 10,600 nm, 4.5 J/cm^2	3	Clearance after 6 wk, recurrence after 3 mo, side effects	ITT
		Cryo	80 (80)	Same	2 freezing cycles			
Baker 2011[5]	USA	Imiquimod 2.5%	202 (139)	1×/d for 8 wk	Wash after 8 hr	4	Clearance after 4 mo, side effects	ITT, only women
		Imiquimod 3.75%	204 (149)	Same	Same			
		Placebo	105 (77)	Same	Same			
Benedetti Panici 1989[6]	Italy	Electro	51 (51)	Until apparent elimination of the genital wart, interval: 3 wk	Local anesthesia, diathermocoagulation with bipolar electrodes	12	Clearance after 1 mo, recurrence after 2.6 mo, side effects	ITT, only women, some patients with AGWs on cervix; IFN arm (data not shown)
		Placebo	48 (48)	NR	NR			
Beutner 1989[7]	USA	Podophyllotoxin 0.5% gel	56 (56)	2×/d, 3 consecutive d, maximum 4 wk	NR	4	Clearance after 6 wk, recurrence after 10 wk, side effects, new warts	ITT, only men
		Placebo	53 (53)	Same	Same			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Beutner 1998[8]	USA	Imiquimod 5%	94 (69)	1×/d, maximum 16 wk	Wash after 8 hr with soap and water	7	Clearance after 8, 12, 16 wk, recurrence after 3 mo, side effects, partial clearance, time for complete clearance, new warts	ITT
		Imiquimod 1%	90 (71)	Same	Same			
		Placebo	95 (67)	Same	Same			
Bilensoy 2011[9]	Turkey	Placebo	6 (6)	3×/wk, 1 wk/2, maximum 12 wk	Applied with a cotton-tipped swab	6	Clearance after 12 wk, recurrence after 3 mo, partial clearance	ITT, only women; both 5-FU arms used with cyclodextrin thermosensitive gel
		5-FU cream	14 (14)	Same	Same			
		Placebo intra-lesional	6 (6)	Same	NR			
		5-FU intra-lesional	18 (18)	Same	Same			
Bornstein 1997[10]	Israel	IFNβ-1a intra-lesional 1 MIU	30 (30)	3×/wk, maximum 3 wk	NR	6	Clearance after 12 wk, recurrence after 3 mo, partial clearance, time to complete clearance	ITT
		Placebo intra-lesional	30 (30)	Same	Same			
Camargo 2014[11]	Brazil	KOH	24 (20)	1×/d, maximum 12 wk	Applied with a cotton wrapped toothpick	3	Clearance after 12 wk, recurrence after 1 mo, side effects, time to complete clearance	1st treatment, only men
		Cryo	24 (22)	Every 2 wk, maximum 12 wk	Freezing 1× 5-20 s			
Carpiniello 1988[12]	NR	CO_2 laser	41 (NR)	NR		4	Clearance after treatment, recurrence after 4 mo	Only men
		CO_2 laser + 5-FU	27 (NR)	5-FU every night maximum 30 d	5-FU initiated 1 wk after CO_2 laser			
Chen 2007[13]	China	CO_2 laser	21 (21)	1×/wk for 3 wk if not removed	topical anesthesia with 2% lidocaine	3	Clearance after 3 wk, recurrence after 2 mo, side effects	ITT, no quantification for side effects
		PDT	65 (65)	Same	ALA dissolved in sterile 0.9% NaCl just before application, 3 hr before light illumination (632 nm)			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Claesson 1996[14]	Sweden, Finland, France	Podophyllotoxin 0.15% cream	60 (60)	2×/d for 3 consecutive d, maximum 4 wk		4	Clearance after 4 wk, recurrence after 3 mo, side effects	ITT
		Podophyllotoxin 0.3% cream	60 (60)	Same				
		Podophyllotoxin 0.5% sol	60 (60)	Same				
Duus 1985[15]	Denmark	CO_2 laser	25 (21)	1×, maximum 2×	Continuous wave (5-20 W), spot diameter of 0-7 mm	6	Clearance after treatment, recurrence after 3 mo, side effects	
		Ablative treatment (surgery, Electro)	25 (23)	1×, maximum 2×	NR			
Edwards 1998[16]	Multicentric: Hawaii, New York, Pennsylvania & Canada	Imiquimod 5%	109 (90)	3×/wk for 16 wk	Wash after 6-10 hr with soap and water	7	Clearance after 4 mo, recurrence after 3 mo, side effects, partial clearance	ITT
		Imiquimod 1%	102 (71)	Same	Same			
		Placebo	100 (73)	Same	Same			
Edwards 1988[17]	UK	Podophyllotoxin 0.5% sol	32 (32)	2×/d for 3 consecutive d, maximum 6 wk	Self-applied	6	Clearance after 6 wk, side effects	ITT, only men
		Podophyllin 20%	19 (19)	1×/wk, maximum 6 wk	Provider-applied			
Eron 1986[18]	USA	IFNα-2b (1 MIU) intra-lesional	147 (125)	NR	NR	7	Clearance after 4,16 wk; recurrence after 3 mo, side effects	
		Placebo intra-lesional	149 (132)	Same	Same			
Gabriel 1983[19]	UK	Podophyllin 25%	38 (29)	1×/wk, maximum 6 wk	Applied with the tip of the stick	3	Clearance after 6 wk, recurrence after 6 wk, side effect, time to complete clearance	Only men
		Podophyllin 25% + TCA 50%	35 (31)	Same	Same			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Gilson 2009[20]	UK	Cryo + placebo	75 (40)	Cream 2×/d for 3 consecutive d, maximum 4 wk, Cryo: 45-s freezing/wk, maximum 12 wk	NR	9	Clearance after 3 mo, recurrence after 3 mo, side effects	ITT modified
		Cryo + podophyllotoxin 0.15% cream	74 (31)	Same	Same			
Godley 1987[21]	UK	TCA	69 (57)	1×/wk maximum 10 wk	Applied with an orange stick	4,5	Clearance after 10 wk; recurrence after 2 mo, side effects, time to complete clearance	Only men
		Cryo	61 (49)	Same	Freeze for 15 sec twice			
Greenberg 1991[22]	USA	Podophyllotoxin 0.5% sol & cream	48 (48)	2×/d for 3 consecutive d, maximum 4 wk	Applied with a cotton tip		Clearance after 4 wk; recurrence after 2 mo, distinctive side effects for gel & cream, new warts	ITT modified, only women
		Placebo	24 (21)	Same	Same			
Gross 2007[23]	Germany & Russia	Polyphenon 15%	80 (46)	3×/d, maximum 16 wk	NR	6	Clearance after 12 wk, recurrence after 3 mo, side effects	
		Polyphenon 10%	79 (36)	Same	Same			
		Placebo	83 (31)	Same	Same			
Hellberg 1995[24]	Sweden	Podophyllotoxin 0.5% cream	30 (28)	2×/d for 3 consecutive d, maximum 4 wk	NR	4	Clearance after 4 wk; recurrence after 3 mo, side effects	Only women
		Podophyllin 20%	30 (27)	1×/wk, maximum 4 wk	Wash 4 hr after application			
Isik 2014[25]	Turkey	KOH	30 (30)	1×/d for 12 wk	Perilesional application of Vaseline	6	Clearance after 3 mo, recurrence after 3 mo, partial clearance	ITT
		5-FU + salicylic acid	30 (30)	Same	Same			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Jensen 1985[26]	Denmark	Podophyllin 25%	30 (30)	1×/wk, maximum 6 wk	Wash after 6 hr	12	Clearance after 4 wk; recurrence after 1.5, 4.5, 10.5 mo; side effects, time to complete clearance	ITT
		Surgery	30 (30)	Same	Local anesthesia with lignocaine			
Keay 1988[27]	USA	IFNα cream	32 (31)	3×/d, maximum 4 wk	Applied topically by gentle 30-s rubbing	4	Clearance after 4, 16 wk, side effects	ITT modified, only women
		Placebo	33 (30)	Same	Same			
Khawaja 1989[28]	UK	Podophyllin 25%	19 (19)	1×/wk, maximum 6 wk	Wash after 6 hr	10.5	Clearance after 6 wk, recurrence after 3, 9 mo; side effect, time to complete clearance	ITT, 1st treatment
		Surgery	18 (18)	1×	Local anesthesia with lignocaine			
Kinghorn 1993[29]	UK	Podophyllotoxin 0.5% sol	168 (138)	2×/d for 3 consecutive d, maximum 5 wk		3	Clearance after 54 wk; recurrence after 2 mo, side effects	
		Podophyllin 25%	84 (62)	2×/wk, maximum 5 wk	Wash off after 4 hr			
Kirby 1990[30]	USA	Podophyllotoxin 0.5% sol	19 (19)	2×/d for 3 consecutive d, maximum 4 wk	NR	4	Clearance after 4 wk; recurrence after 3 mo, side effects	ITT
		Placebo	19 (19)	Same	Same			
Komericki 2011[31]	Austria	Podophyllotoxin 0.5% sol	26 (25)	2×/d for 3 consecutive d, maximum 4 wk	NR	4	Clearance after 4 wk for podophyllotoxin and 16 wk for imiquimod, side effects	1st treatment
		Imiquimod 5%	25 (20)	3×/wk maximum 16 wk	Same			
Kumar 2014[32]	India	Imiquimod 5%	44 (41)	3×/wk, maximum 16 wk	Intradermal injections of the Mw vaccine and vehicle on both shoulders at baseline to sensitize and improve local immune response to intralesional therapy	8	Clearance after 20 wk; recurrence after 3 mo, side effects, time to complete clearance, partial clearance	ITT
		Mycobacterium intra-lesional	45 (39)	Every 2 wk, maximum 16 wk	–			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Lacey 2003[33]	UK	Podophyllin 25%	116 (96)	2×/wk, maximum 4 wk	In the clinic	4	Clearance after 4 wk; recurrence after 3 mo, side effects, cost/efficacy ratio	
		Podophyllotoxin 0.15% cream	118 (82)	2×/d for 3 consecutive d, maximum 4 wk	NR			
		Podophyllotoxin 0.5% sol	120 (98)	Same	Same			
Lassus 1987[34]	Finland	Podophyllotoxin 0.5% sol	48 (48)	2×/d for 3 consecutive d, maximum 4 wk	At home	3	Clearance after 4 wk; recurrence after 2 mo	ITT, only men
		Podophyllin 20%	52 (52)	1×/wk, maximum 4 wk	In the clinic			
Lotfabadi 2015[35]	Iran	Cryo	34 (34)	Every 2 wk, maximum 12 wk	Freeze with 1-mm margin, 10-15 s	6	Clearance 1 mo after 12 wk of treatment; recurrence after 2 mo; side effects	
		TCA	34 (34)	Same	Applied by an applicator then washed			
Mahajan 2014[36]	India	Cryo + podophyllin 20%	30 (24)	Cryo once & podo every 2 wk	Cryo: freezing with a 5-mm margin from a distance of 2-mm Podo: Wash 3 hr after therapy	6	Clearance after 8,12, 24 wk; recurrence after 1 mo; side effects; time to complete clearance	
		Bleomycin + placentrex intra-lesional	30 (25)	Bleomycin every 2 wk, maximum 10 wk; placentrex every night	After bleomycin, ice water soaks twice daily for 4 d			
Mazurkiewicz 1990[37]	Poland	Podophyllin 20%	16 (13)	Once/wk, maximum 6 wk	Doctor-applied	1,5	Clearance after 6 wk, side effects	
		Podophyllotoxin 0.5% sol	16 (14)	2×/d for 3 consecutive d, maximum 6 wk	Patient-applied			
		Podophyllotoxin 0.5% cream	22 (16)	Same	Same			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Nath 1990[38]	India	Podophyllin 25%	50 (47)	1×/wk, maximum 12 wk	Wash after 2 hr	6	Clearance after 3 mo, recurrence after 3 mo, time to complete clearance	Incompletely randomization (pregnant women got TCA)
		TCA 50%	50 (48)	Same	Applied with a swab stick			
On 2014[39]	USA	Polyphenon 15% + cryo	21 (NR)	Polyphenon: 2×/d, maximum 16 wk; Cryo: 1×	Cryo: 2 5-s cycles/5-s interval rest	16	Clearance after 9 & 17 wk, side effects, partial clearance	ITT
		Cryo	21 (NR)	1×	Same			
Ormerod 2015[40]	Germany, UK, Holland, Switzerland, Poland: 40 centers	Placebo	75 (74)	2×/d for 12 wk	Sodium nitrite was applied first, then citric acid, & the 2 creams were mixed.	6	Clearance after 3 mo, recurrence after 3 mo, side effects, time to complete clearance	
		Sodium nitrite 3% + citric acid 4.5%	74 (72)	2×/d for 12 wk	Same			
		Sodium nitrite 6% + citric acid 9%	77 74)	1×/d for 12 wk	Same			
		Sodium nitrite 6% + citric acid 9%	73 (70)	2×/d for 12 wk	Same			
Padhiar 2006[41]	India	Imiquimod 5%	30 (30)	3×/wk, maximum 16 wk	Wash after 6-10 hr	10	Clearance after 4 mo, recurrence after 3 & 6 mo, side effects, partial clearance, time to complete clearance	ITT
		Podophyllin 20%	30 (30)	1×/wk, maximum 6 wk	Applied with a swab stick, wash after 4-6 hr			
Petersen 1995[42]	Denmark	Podophyllotoxin 0.5% sol	18 (18)	2×/d for 3 consecutive d, maximum 4 wk	Fingertip application	3	Clearance after 6 wk, recurrence after 6 wk, side effects	ITT, only men, individual lesion analysis
		Podophyllotoxin 0.5% cream	18 (18)	Same	Same			
Reichman 1988[43]	USA	IFNα-n1 intra-lesional	17 (15)	3×/wk, maximum 4 wk	NR	12	Clearance after 5, 10 & 15 wk, side effects; time to complete clearance	
		IFNβ (1 MIU) intra-lesional	20 (20)	Same	Same			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Reichman 1988[43](continued)		IFNα-2b intra-lesional	23 (23)	Same	Same		Clearance after 5, 10 & 15 wk, side effects; time to complete clearance	
		Placebo intra-lesional	19 (18)	Same	Same			
Relakis 1996[44]	Brazil & Greece	CO_2 laser	71 (71)	1×	Applied Vaseline & ZnO_2 10% cream	12	Clearance after 3 mo, recurrence after 3, 6 & 9 mo, side effects	ITT, only men
		5-FU	218 (218)	5×/wk, maximum 4 wk	Applied Vaseline 5% ZnO_2, before 5-FU			
		CO_2 laser + 5-FU	47 (47)	Both	Both			
Schofer 2006[45]	Germany	Ablative procedure (Electro, Cryo, laser, surgery)	100 (100)	1×/wk, maximum 4 wk	NR	6	Clearance after 4 wk, recurrence after 3 & 6 mo, side effects	ITT
		Imiquimod 5%	155 (155)	3×/d, maximum 16 wk	Same	6	Clearance after 4 wk, recurrence after 3 & 6 mo, side effects	
		Ablative procedure + imiquimod	103 (103)	Both	Same			
Sherrard 2007[46]	UK	Podophyllin 25%	79 (56)	Times/wk NR, but maximum 8 wk	NR	2	Clearance after 8 wk, side effects	
		TCA	88 (58)	Same	Same			
		Cryo	81 (66)	Same	Same			
		TCA + Podophyllin	85 (65)	Same	Same			
		Cryo + Podophyllin	76 (59)	Same	Same			
Simmons 1981[47]	UK	Cryo	24 (16)	1× every 2 wk, maximum 12 wk	Produced 2-mm ice-balls larger than wart	3	Clearance after 12 wk	
		Electro	18 (11)	1× every 2 wk, maximum 12 wk	2% lignocaine anesthesia			
Snoeck 2001[48]	Belgium	Cidofovir	19 (19)	1×/d, 5 d/wk, 1 wk/2 for 12 wk	Applied with a cotton tipped swab or a rubber glove		Clearance after 3 mo, recurrence after 3 mo, side effects, partial clearance	ITT
		Placebo	11 (11)	Same	Same			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Stefanaki 2008[49]	Greece	Imiquimod	60 (35)	3×/wk, maximum 12 wk	NR	12	Clearance after 4, 8,12 & 24 wk, recurrence after 9 mo, side effects	1st treatment
		Cryo	60 (45)	1× every 3 wk, maximum 12 wk	Frozen 1× for 10-20 s			
Stockfelth 2008[50]	Multicentric (Europe, South Africa)	Polyphenon 15%	201 (161)	3×/d, maximum 16 wk	NR	7	Clearance after 3 mo, recurrence after 3 mo, side effects, partial clearance, time to complete clearance	ITT modified
		Polyphenon 10%	199 (170)	Same	Same			
		Placebo	103 (80)	Same	Same			
Stone 1990[51]	USA	Podophyllin (dose NR)	144 (53)	Times/week NR, but maximum 6 wk	NR	5	Clearance after 6 wk, recurrence after 3 mo, side effects	
		Cryo	154 (60)	1×/wk, maximum 6 wk	Each AGW was frozen 1×			
		Electro	152 (51)	Same	1% lidocaine anesthesia			
Strand 1995[52]	Sweden	Podophyllotoxin 0.15% cream	30 (30)	2×/d for 3 consecutive d, maximum 4 wk	Applied with an applicator	4	Clearance after 4 wk; recurrence after 3 mo, side effects	ITT, only men
		Podophyllotoxin 0.3% cream	31 (31)	Same	Same			
		Podophyllotoxin 0.5% sol	29 (29)	Same	NR			
Swinehart 1997[53]	USA	5-FU injection intra-lesional	80 (78)	1×/wk, maximum 6× over 8 wk	NR	5	Clearance after 8 wk, recurrence after 3 mo, side effects, partial clearance, time to complete clearance	Individual lesion analysis
		5-FU	80 (76)	NR	Same			
		Placebo	40 (33)	Same	Same			
Syed 1998[54]	Pakistan	Imiquimod 2%	30 (30)	2×/d for 5 consecutive d, maximum 6 wk	Wash & dry warts before each application and apply	4	Clearance after 6 wk, recurrence after 2.5 mo, side effects	ITT, only women, individual lesion analysis
		Placebo	30 (30)	Same	Same			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Syed 1995 (a)[55]	Pakistan	IFNα cream	20 (20)	3×/d for 3 consecutive d, maximum 4 wk	Applied with a finger cot	4	Clearance after 4 wk, recurrence after 9 mo, side effects	ITT, only men, individual lesion analysis
		Podophyllotoxin 0.5% cream	20 (20)	Same	Same			
		Placebo	20 (20)	Same	Same			
Syed 1995 (b)[56]	Pakistan	IFNα cream	20 (20)	3×/d for 3 consecutive d, maximum 4 wk	Applied with a finger cot	4	Clearance after 4 wk, side effects	ITT, only women, individual lesion analysis
		Podophyllotoxin 0.5% cream	20 (20)	Same	Same			
		Placebo	20 (20)	Same	Same			
Syed 1994[57]	Pakistan	Podophyllotoxin 0.3% cream	30 (30)	2×/d for 3 consecutive d, maximum 4 wk	Let dry for at least 1 min without washing	4	Clearance after 4 wk, recurrence after 3 mo, side effects	ITT, only women, individual lesion analysis
		Podophyllotoxin 0.5% cream	30 (30)	Same	Same			
		Placebo	20 (20)	Same	Same			
Syed 2000[58]	Pakistan	Imiquimod 2%	30 (30)	3 consecutive d, maximum 4 wk	Applied with a finger cot	18	Clearance after 16 wk, recurrence after 18 mo, side effects	ITT, only men, individual lesion analysis
		Placebo	30 (30)	Same	Same			
Szeimies 2009[59]	Germany	PDT + CO_2 laser	84 (84)	1×	PDT: 100 J/cm^2, 100 mW/cm^2 (640-740 nm) occlusion for 4-6 hr	12	Clearance after treatment, recurrence after 1, 2, 3, 6 & 12 mo, side effects, satisfaction	ITT
		CO_2 laser	91 (91)	Same	Continuous wave, defocused beam (2-mm diameter), 10-20 W, general or local anesthesia			
Tabari 2010[60]	Iran	Podophyllin 20%	60 (60)	2×/wk	Wash after 20 min	6	Clearance after 4 or 8 wk, recurrence after 3 mo, side effects	ITT
		TCA 30%	60 (60)	NR	With a topical cotton soap and washed after 1 min			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Tatti 2008[61]	USA, Europe, S Africa multicenter	Polyphenon 15%	196 (159)	3×/d, maximum 16 wk	NR	7	Clearance after 16 wk, recurrence after 3 mo, side effects, partial clearance	ITT modified
		Polyphenon 10%	202 (162)	Same	Same			
		Placebo	104 (83)	Same	Same			
Tyring 1998 (a)[62]	USA	Imiquimod 5%	18 (16)	3×/wk, maximum 16 wk	Applied with cotton swab tip	4	Clearance after 16 wk, side effects, partial clearance	
		Placebo	4 (3)	Same	Same			
Tyring 1998 (b)[63]	USA	Placebo	107 (95)	2×/d for 3 consecutive d, maximum 8 wk	NR	4	Clearance after 4 & 8 wk, recurrence after 3 mo, side effects	
		Podophyllotoxin 0.5% gel	219 (197)	Same	Same			
Vance 1986[64]	USA	IFNα-2b (1 MIU) intra-lesional	37 (30)	3×/wk, maximum 3 wk	NR	3	Clearance after 4, 5, 7 & 12 wk, side effects, partial clearance	ITT
		IFNα-2b (0.1 MIU) intra-lesional	38 (32)	Same	Same			
		Placebo intra-lesional	39 (29)	Same	Same			
von Krogh 1992[65]	Sweden	Placebo	12 (11)	2×/d, 3 d/wk for 2 wk	NR	3	Clearance after 3 wk, recurrence after 2 mo, side effects	
		Podophyllotoxin 0.5% cream	48 (44)	Same	Same			
von Krogh 1994[66]	Sweden	Podophyllotoxin 0.25% sol	19 (18)	2×/d, 3 d/wk for 2 wk	Applied with wool swabs	6	Clearance after 3 wk, recurrence after 2 & 6 mo, side effects	1st treatment
		Podophyllotoxin 0.5% sol	19 (16)	Same	Same			
		Placebo	19 (17)	Same	Same			
Wallin 1977[67]	Sweden	5-FU	21 (18)	1×/d for 2 wk	Applied with cotton swab tip	9	Clearance after 4 wk, recurrence after 6 mo, side effects	Only men
		Podophyllin 25% sol	21 (19)	1×/wk for 4 wk	Provider-applied, wash 4-6 hr later			

Appendix S2: Characteristics of RCTs included (continued)

Reference	Country	Intervention	No. of Patients randomized (analyzed)	Frequency	Modalities	Follow-Up (mo)	Outcomes	Comments
Weismann 1982[68]	Denmark	5-FU	30 (30)	2×/wk for women, once/d for men	NR	2	Clearance after 8 wk, side effects, partial clearance, time to complete clearance	ITT
		Placebo	29 (29)	Same	Same			
Welander 1990[69]	USA	IFNα-2b (1 MIU) intra-lesional	20 (16)	3×/wk, maximum 3 wk	NR	NR	Clearance after 4 or 15 wk, side effects	
		Placebo intra-lesional	22 (21)	Same	Same			
White 1997[70]	UK	Podophyllotoxin 0.5% sol	106 (77)	2×/d for 3 consecutive d, maximum 12 wk	NR	3	Clearance after 5 wk, side effects	ITT, only men, 1st treatment
		Podophyllin 0.5%	103 (86)	Same	Same			
		Podophyllin 2%	106 (81)	Same	Same			

Abbreviations: ITT, intention-to-treat; NR, not reported; KOH, potassium hydroxide; ALA, 5-aminolaevulinic acid; Mw, *Mycobacterium* w; Sol, solution; PDT, photodynamic therapy; Electro, electrosurgery; Cryo, cryotherapy; IFN, interferon.

Appendix S3: Reason for exclusion

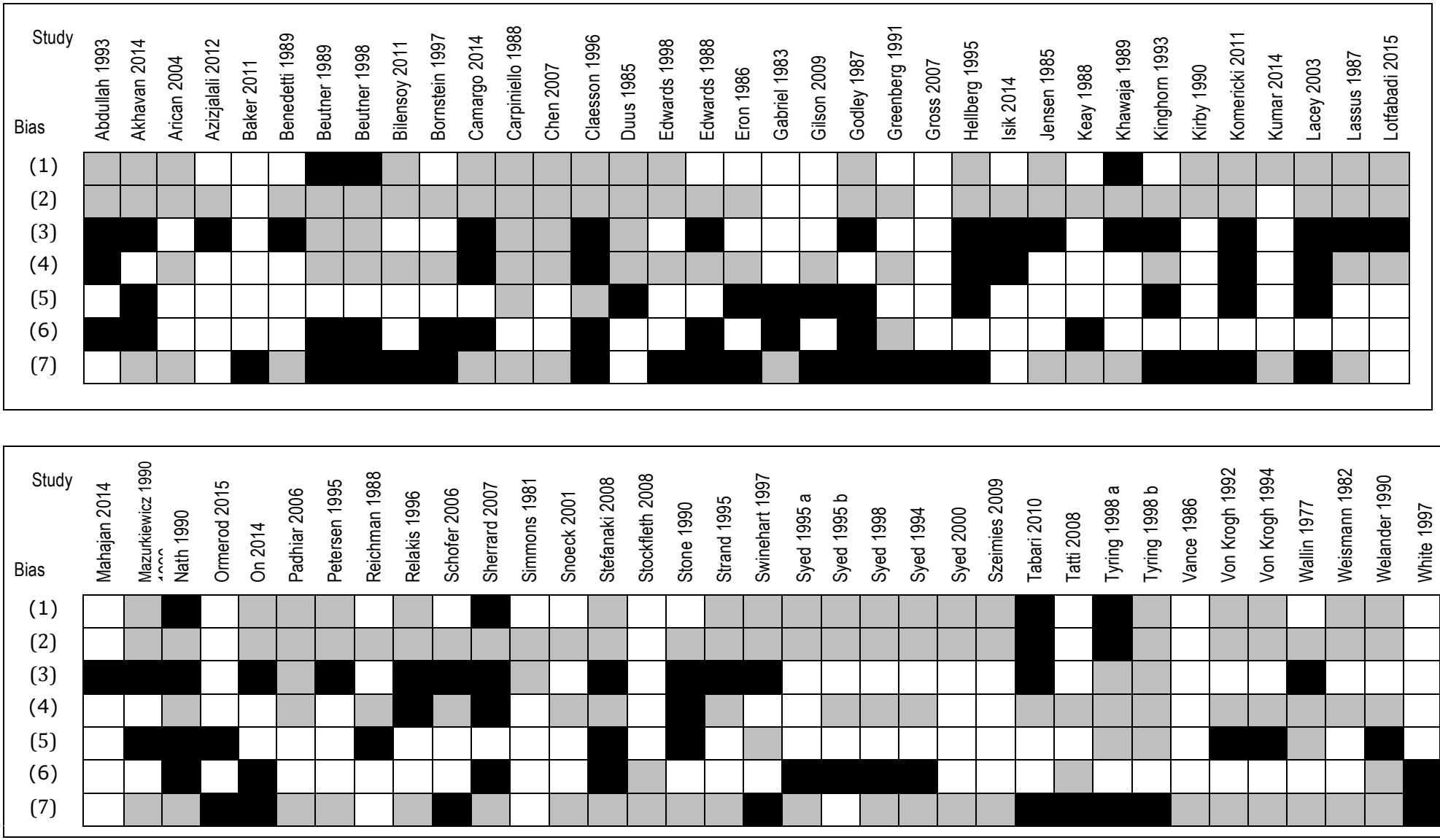
1st Author	Year	Exclusion Criteria
Alfonso-Trujillo[71]	2008	not RCT
Alfonso-Trujillo[72]	2008	not RCT
Alfonso-Trujillo[73]	2009	not RCT
Alfonso-Trujillo[74]	2009	not RCT
Arany[75]	1999	duplicate of Tyring[62]
Armstrong[76]	1996	another treatment not considered herein
Bar-Am[77]	1993	dose escalation
Bashi[78]	1985	not RCT
Beutner[79]	1998	duplicate of Beutner[8]
Beutner[80]	1995	duplicate of Beutner[8]
Botacini[81]	1993	other localization
Buck[82]	2002	not RCT
Chen[83]	2009	missing data (no English translation of Chinese)
Chopra[84]	1997	duplicate of Tyring[62]
Collaborative Study Group[85]	1991	another treatment not considered herein
Collaborative Study Group[86]	1993	another treatment not considered herein
Damstra[87]	1991	missing data
Davidson-Parker[88]	1988	another treatment not considered herein
Dinsmore[89]	1997	not RCT
Douglas[90]	1990	HIV
Edwards[91]	1998	duplicate of Edwards[17]
Edwards[92]	1995	duplicate of Edwards[17]
Eron[93]	1993	another treatment not considered herein
Ferenczy[94]	1998	duplicate of Edwards[17]
Ferenczy[95]	1995	HIV
Fife[96]	2001	dose escalation
Fleshner[97]	1994	another treatment not considered herein
Fouere[98]	2014	missing data
Garland[99]	2006	dose escalation
Garland[100]	2001	not RCT
Goh[101]	1998	dose escalation
Gollnick[102]	2001	dose escalation
Gross[103]	1996	another treatment not considered herein
Gross[104]	1998	another treatment not considered herein
Handley[105]	1991	another treatment not considered herein
Handley[106]	1992	missing data (randomization unclear)
Hohenleutner[107]	1990	another treatment not considered herein
Hoy[108]	2012	not RCT
IRCT2017011531949N1[109]	2017	missing data (recruiting)
IRCT2015090514386N1[110]	2015	missing data (not recruiting)
IRCT2013111015364N1[111]	2014	missing data (not recruiting)
IRC 201202138992N1[112]	2012	not RCT
IRCT201412207848N1[113]	2014	not RCT
Jardine[114]	2012	another treatment not considered herein
Klutke[115]	1995	another treatment not considered herein
Lafuma[116]	2003	duplicate of Tyring[62] and Edwards[17]
Landthaler[117]	1987	HIV
Langley[118]	2010	not RCT
Lassus[119]	1984	duplicate of Lassus[34]
Li[120]	2011	dose escalation
Liang[121]	2009	missing data (condyloma analysis)

Appendix S3: Continued

Liu[122]	2012	missing data (condyloma analysis)
Maiti[123]	1985	dose escalation
Maw[124]	2002	not RCT
Mazurkiewicz[125]	1990	missing data (not accessible)
Meltzer[126]	2009	not RCT and duplicate of Stockfleth[49]
Metawea[127]	2005	not RCT
Mi[128]	2011	missing data (condyloma analysis)
Mistrangelo[129]	2010	another treatment not considered herein
Monsonego[130]	1996	missing data (condyloma analysis)
NCT00674739[131]	2011	duplicate of Baker[5]
NCT00735462[132]	2011	duplicate of Baker[5]
NCT02520986[133]	2016	missing data (not recruiting)
NCT02724254[134]	2016	missing data (recruiting)
NCT01796821[135]	2017	missing data (recruiting)
NCT03153566[136]	2017	missing data (recruiting)
NCT01943630[137]	2017	missing data (recruiting)
NCT02849262[138]	2016	missing data (recruiting)
NCT02462187[139]	2015	missing data (not recruiting)
NCT02482428[140]	2015	missing data (not recruiting)
NCT02147353[141]	2014	missing data (not recruiting)
NCT02015260[142]	2013	missing data (not recruiting)
Nieminen[143]	1994	another treatment not considered herein
Owens[144]	1999	duplicate of Edwards[17]
Potocnik[145]	1997	missing data (not accessible)
Rosen[146]	2015	missing data (no placebo data)
Sauder[147]	2003	duplicate from of Edwards[17]
Sharma[148]	2017	missing data (condyloma analysis)
Shi[149]	2013	not RCT
Stefanaki[150]	2014	missing data
Stellato[151]	1997	another treatment not considered herein
Swinehart[152]	1997	duplicate from Swinehart[53]
Syed[153]	2002	missing data (not accessible)
Syed[154]	1994	other localization
Syed[155]	1993	dose escalation
Trofatter[156]	2002	dose escalation
Tuncel[157]	2005	missing data
Urban[158]	2006	missing data (not accessible)
Vesterinen[159]	1984	other localization
Viazis[160]	2007	HIV and other localization
von Krogh[161]	1981	not RCT
Xu[162]	2009	missing data (no English translation of Chinese)
Yaghoobi[163]	2014	not RCT
Yin[164]	1998	another treatment not considered herein
Yu[165]	2004	another treatment not considered herein
Zarcone[166]	1996	not RCT
Zervoudis[167]	2010	another treatment not considered herein

Abbreviations: RCT: randomized-controlled trial; HIV: human immunodeficiency virus

Appendix S4. Risk of bias assessment (Bertolotti et al. *J Am Acad Dermatol* 2019.pii:S0190-9622(19)30525-0)



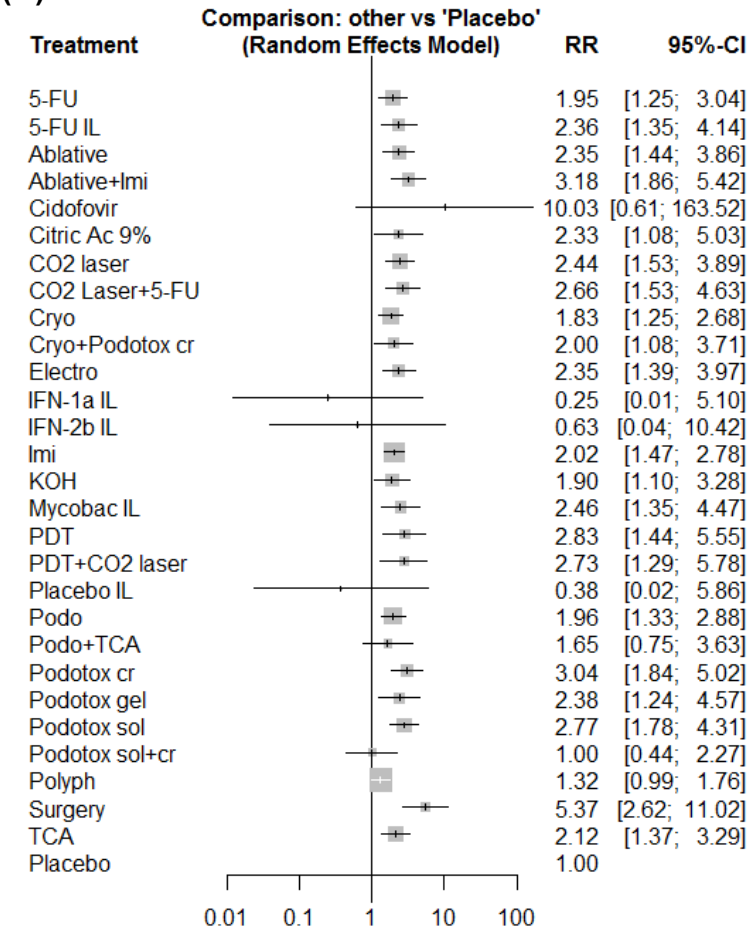
White square: low; grey square: uncertain; black square: high; (1) Random sequence generation (selection bias); (2) Allocation concealment (selection bias); (3) Blinding of participants and personnel (performance bias); (4) Blinding of outcome assessment (detection bias); (5) Incomplete outcome data (attrition bias); (6) Selective reporting (reporting bias); (7) Other bias.

Appendix S5. Network meta-analysis estimates (lower triangle) and direct estimates (upper triangle) of complete lesion response for all therapies.

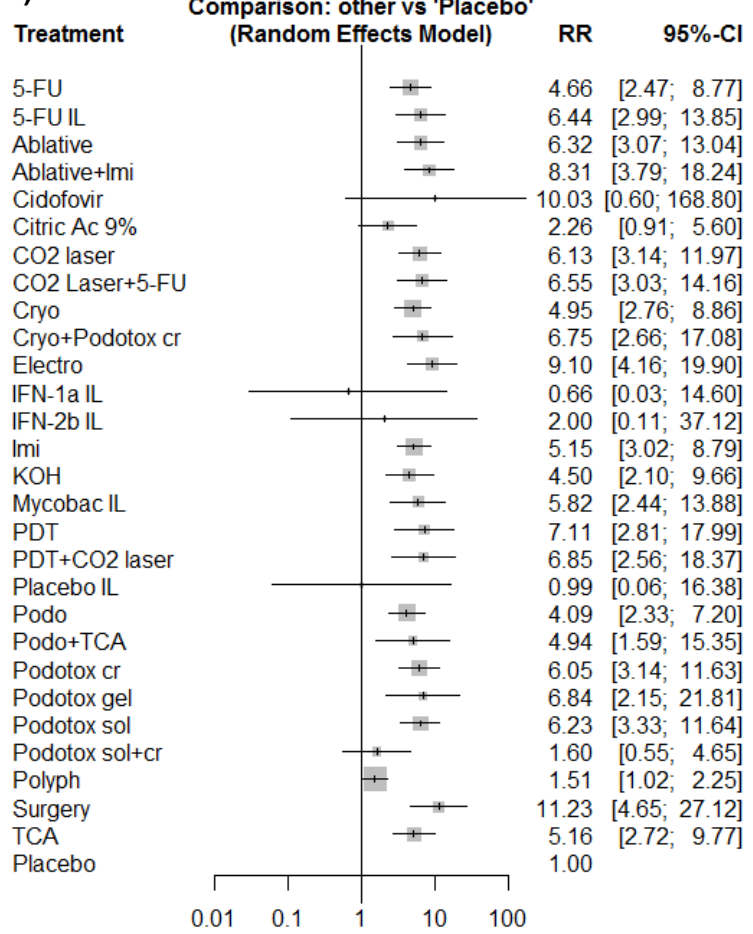
	Surgery	Ablative+Imi	Electro	Cidofovir	PDT	Podotox gel	PDT+CO2 laser	CO2 Laser+5-F	Podotox sol	Mycobac IL	CO2 laser	Podotox cr	Ablative	Cryo+Podotox cr	Imi	TCA	KOH	5-FU	Cryo	Polyph
Surgery																				
Ablative+Imi	1.40 [0.56; 3.52]												1.36 [0.78; 2.40]		1.55 [0.88; 2.73]					
Electro	1.48 [0.63; 3.47]	1.06 [0.48; 2.35]																	1.21 [0.68; 2.14]	
Cidofovir	1.05 [0.06; 19.79]	0.75 [0.04; 13.68]	0.71 [0.04; 12.88]																	
PDT	1.62 [0.59; 4.46]	1.15 [0.47; 2.83]	1.09 [0.45; 2.67]	1.54 [0.08; 29.12]							1.16 [0.64; 2.09]									
Podotox gel	1.56 [0.38; 6.38]	1.11 [0.29; 4.25]	1.05 [0.28; 3.99]	1.49 [0.07; 30.68]	0.96 [0.23; 3.98]															
PDT+CO2 laser	1.68 [0.58; 4.87]	1.20 [0.46; 3.11]	1.13 [0.44; 2.93]	1.60 [0.08; 30.75]	1.04 [0.42; 2.54]	1.07 [0.25; 4.61]					1.12 [0.57; 2.19]									
CO2 Laser+5-FU	1.74 [0.71; 4.32]	1.24 [0.57; 2.74]	1.18 [0.54; 2.55]	1.66 [0.09; 30.23]	1.08 [0.51; 2.30]	1.12 [0.29; 4.26]	1.04 [0.46; 2.38]				1.31 [0.80; 2.16]							1.14 [0.65; 2.00]		
Podotox sol	1.86 [0.90; 3.87]	1.33 [0.65; 2.73]	1.26 [0.67; 2.37]	1.77 [0.10; 31.38]	1.15 [0.50; 2.66]	1.19 [0.33; 4.27]	1.11 [0.45; 2.73]	1.07 [0.53; 2.16]				1.00 [0.47; 2.13]								
Mycobac IL	1.83 [0.69; 4.88]	1.31 [0.57; 2.97]	1.23 [0.52; 2.95]	1.74 [0.09; 32.37]	1.13 [0.42; 3.06]	1.17 [0.29; 4.67]	1.09 [0.38; 3.11]	1.05 [0.43; 2.56]	0.98 [0.44; 2.18]						1.21 [0.65; 2.25]					
CO2 laser	1.88 [0.82; 4.28]	1.34 [0.68; 2.63]	1.26 [0.64; 2.48]	1.78 [0.10; 31.81]	1.16 [0.64; 2.09]	1.20 [0.33; 4.36]	1.12 [0.57; 2.19]	1.08 [0.67; 1.73]	1.01 [0.55; 1.83]	1.02 [0.46; 2.28]			0.94 [0.45; 1.96]					0.75 [0.42; 1.35]	**2.40 [1.29; 4.46]**	
Podotox cr	1.88 [0.83; 4.25]	1.34 [0.61; 2.95]	1.27 [0.61; 2.61]	1.79 [0.10; 31.88]	1.16 [0.47; 2.86]	1.21 [0.33; 4.37]	1.12 [0.43; 2.93]	1.08 [0.50; 2.34]	1.01 [0.60; 1.68]	1.03 [0.44; 2.42]	1.00 [0.51; 1.98]									
Ablative	1.88 [0.78; 4.50]	1.34 [0.78; 2.31]	1.26 [0.60; 2.66]	1.79 [0.10; 32.16]	1.16 [0.52; 2.60]	1.20 [0.32; 4.47]	1.12 [0.47; 2.68]	1.08 [0.54; 2.16]	1.01 [0.52; 1.95]	1.03 [0.46; 2.26]	1.00 [0.58; 1.74]	1.00 [0.48; 2.08]			1.14 [0.64; 2.02]					
Cryo+Podotox cr	1.95 [0.74; 5.14]	1.39 [0.56; 3.42]	1.31 [0.57; 3.00]	1.85 [0.10; 34.86]	1.20 [0.45; 3.21]	1.25 [0.30; 5.10]	1.16 [0.41; 3.26]	1.12 [0.46; 2.68]	1.04 [0.47; 2.30]	1.06 [0.40; 2.80]	1.04 [0.47; 2.27]	1.03 [0.44; 2.44]	1.04 [0.44; 2.43]						1.25 [0.66; 2.37]	
Imi	**2.22 [1.04; 4.76]**	1.58 [0.92; 2.73]	1.50 [0.81; 2.76]	2.11 [0.12; 36.76]	1.37 [0.63; 2.99]	1.42 [0.41; 4.89]	1.32 [0.57; 3.08]	1.27 [0.67; 2.42]	1.19 [0.72; 1.97]	1.21 [0.65; 2.25]	1.18 [0.71; 1.97]	1.18 [0.65; 2.14]	1.18 [0.72; 1.94]	1.14 [0.54; 2.41]					0.95 [0.59; 1.53]	
TCA	**2.28 [1.09; 4.75]**	1.62 [0.81; 3.25]	1.53 [0.85; 2.78]	2.17 [0.12; 38.41]	1.41 [0.63; 3.14]	1.46 [0.41; 5.23]	1.36 [0.57; 3.24]	1.31 [0.67; 2.54]	1.22 [0.76; 1.96]	1.24 [0.57; 2.70]	1.21 [0.70; 2.10]	1.21 [0.67; 2.19]	1.21 [0.65; 2.27]	1.17 [0.56; 2.43]	1.03 [0.64; 1.64]				1.10 [0.71; 1.71]	
KOH	**2.48 [1.02; 6.01]**	1.77 [0.79; 3.93]	1.67 [0.79; 3.51]	2.35 [0.13; 42.81]	1.53 [0.65; 3.59]	1.59 [0.42; 6.01]	1.48 [0.59; 3.68]	1.42 [0.71; 2.84]	1.33 [0.67; 2.62]	1.35 [0.56; 3.27]	1.32 [0.71; 2.45]	1.32 [0.62; 2.80]	1.32 [0.63; 2.74]	1.27 [0.55; 2.96]	1.11 [0.59; 2.09]	1.09 [0.58; 2.05]		0.95 [0.49; 1.84]	1.02 [0.50; 2.07]	
5-FU	**2.44 [1.07; 5.56]**	1.74 [0.85; 3.57]	1.64 [0.83; 3.26]	2.32 [0.13; 41.05]	1.50 [0.71; 3.17]	1.56 [0.44; 5.59]	1.45 [0.64; 3.28]	1.40 [0.84; 2.32]	1.31 [0.72; 2.37]	1.33 [0.59; 3.02]	1.30 [0.82; 2.05]	1.29 [0.66; 2.54]	1.30 [0.69; 2.45]	1.25 [0.56; 2.80]	1.10 [0.64; 1.88]	1.07 [0.61; 1.87]	0.98 [0.58; 1.68]			
Cryo	**2.43 [1.17; 5.03]**	1.73 [0.92; 3.27]	1.64 [0.97; 2.76]	2.31 [0.13; 40.54]	1.50 [0.71; 3.15]	1.56 [0.44; 5.45]	1.45 [0.64; 3.26]	1.39 [0.77; 2.53]	1.30 [0.82; 2.06]	1.33 [0.64; 2.74]	1.29 [0.82; 2.04]	1.29 [0.73; 2.29]	1.29 [0.74; 2.26]	1.25 [0.66; 2.37]	1.09 [0.75; 1.60]	1.07 [0.75; 1.51]	0.98 [0.57; 1.70]	1.00 [0.61; 1.62]		
Polyph	**7.07 [2.82; 17.72]**	**5.04 [2.24; 11.37]**	**4.76 [2.13; 10.63]**	6.73 [0.40; 114.51]	**4.37 [1.72; 11.12]**	**4.53 [1.39; 14.78]**	**4.22 [1.57; 11.35]**	**4.05 [1.81; 9.09]**	**3.79 [1.89; 7.61]**	**3.86 [1.61; 9.30]**	**3.77 [1.82; 7.79]**	**3.76 [1.82; 7.75]**	**3.77 [1.75; 8.10]**	**3.63 [1.45; 9.12]**	**3.19 [1.71; 5.94]**	**3.11 [1.54; 6.27]**	**2.86 [1.28; 6.36]**	**2.90 [1.44; 5.86]**	**2.91 [1.51; 5.63]**	

Appendix S6. Forest plot of the estimates of relative risk between each treatment and the reference placebo for complete lesion response. Sensitivity analyses: (A) Worst case scenario, (B) Best case scenario.

(A)



(B)



Appendix S7. Network meta-analysis estimates (lower triangle) and direct estimates (upper triangle) of complete lesion response for all therapies. Sensitivity analyses, worst-case scenari

	Surgery	Cidofovir	Ablative+Imi	Podotox cr	Podotox sol	PDT	CO2 Laser+5-FI	PDT+CO2 laser	CO2 laser	Mycobac IL	Electro	Podotox gel	Ablative	TCA	Cryo+Podotox c	Imi	5-FU	KOH	Cryo	Polyph
Surgery																				
Cidofovir	0.54 [0.03; 9.57]																			
Ablative+Imi	1.69 [0.76; 3.77]	3.15 [0.18; 54.11]											1.36 [0.86; 2.16]			1.55 [0.98; 2.45]				
Podotox cr	1.77 [0.85; 3.69]	3.30 [0.19; 56.24]	1.05 [0.55; 1.99]		1.00 [0.51; 1.97]															
Podotox sol	**1.94 [1.00; 3.76]**	3.62 [0.21; 61.05]	1.15 [0.64; 2.04]	1.10 [0.71; 1.70]																
PDT	1.90 [0.78; 4.60]	3.54 [0.20; 62.60]	1.12 [0.54; 2.33]	1.07 [0.51; 2.27]	0.98 [0.49; 1.95]				1.16 [0.71; 1.89]											
CO2 Laser+5-F	2.02 [0.90; 4.50]	3.76 [0.22; 64.81]	1.19 [0.63; 2.27]	1.14 [0.60; 2.18]	1.04 [0.58; 1.86]	1.06 [0.56; 2.00]			1.34 [0.88; 2.05]								1.14 [0.72; 1.80]			
PDT+CO2 lase	1.97 [0.77; 5.06]	3.67 [0.20; 66.14]	1.16 [0.52; 2.60]	1.11 [0.49; 2.53]	1.02 [0.47; 2.18]	1.04 [0.48; 2.22]	0.98 [0.48; 2.00]		1.12 [0.62; 2.01]											
CO2 laser	**2.20 [1.05; 4.60]**	4.11 [0.24; 69.62]	1.30 [0.75; 2.25]	1.25 [0.71; 2.20]	1.14 [0.70; 1.85]	1.16 [0.71; 1.89]	1.09 [0.73; 1.64]	1.12 [0.62; 2.01]					1.00 [0.55; 1.83]				0.75 [0.46; 1.22]		**2.40 [1.42; 4.06]**	
Mycobac IL	2.19 [0.93; 5.11]	4.08 [0.23; 70.90]	1.29 [0.66; 2.53]	1.24 [0.61; 2.50]	1.13 [0.59; 2.15]	1.15 [0.51; 2.60]	1.08 [0.52; 2.24]	1.11 [0.46; 2.67]	0.99 [0.52; 1.91]							1.21 [0.73; 2.01]				
Electro	**2.28 [1.10; 4.74]**	4.26 [0.25; 72.98]	1.35 [0.72; 2.53]	1.29 [0.73; 2.29]	1.18 [0.73; 1.91]	1.20 [0.58; 2.48]	1.13 [0.61; 2.12]	1.16 [0.52; 2.57]	1.04 [0.61; 1.78]	1.04 [0.52; 2.08]									1.09 [0.70; 1.71]	
Podotox gel	2.25 [0.85; 5.96]	4.21 [0.24; 74.02]	1.33 [0.57; 3.10]	1.28 [0.56; 2.91]	1.16 [0.53; 2.56]	1.19 [0.47; 3.03]	1.12 [0.48; 2.63]	1.15 [0.42; 3.10]	1.02 [0.46; 2.28]	1.03 [0.43; 2.50]	0.99 [0.43; 2.28]									
Ablative	**2.28 [1.05; 4.93]**	4.26 [0.25; 72.51]	1.35 [0.87; 2.10]	1.29 [0.70; 2.37]	1.18 [0.69; 2.01]	1.20 [0.62; 2.33]	1.13 [0.64; 2.01]	1.16 [0.55; 2.43]	1.04 [0.66; 1.63]	1.04 [0.55; 1.99]	1.00 [0.56; 1.80]	1.01 [0.45; 2.29]				1.14 [0.71; 1.83]				
TCA	**2.53 [1.30; 4.94]**	4.73 [0.28; 79.81]	1.50 [0.86; 2.62]	1.43 [0.88; 2.35]	1.31 [0.89; 1.92]	1.33 [0.69; 2.60]	1.26 [0.72; 2.19]	1.29 [0.61; 2.71]	1.15 [0.73; 1.81]	1.16 [0.62; 2.17]	1.11 [0.70; 1.75]	1.12 [0.51; 2.47]	1.11 [0.67; 1.85]						1.08 [0.76; 1.56]	
Cryo+Podotox c	**2.68 [1.18; 6.07]**	5.01 [0.29; 87.35]	1.59 [0.79; 3.20]	1.52 [0.77; 2.98]	1.38 [0.76; 2.53]	1.41 [0.65; 3.09]	1.33 [0.66; 2.67]	1.36 [0.58; 3.19]	1.22 [0.66; 2.25]	1.23 [0.57; 2.62]	1.17 [0.63; 2.21]	1.19 [0.48; 2.92]	1.18 [0.61; 2.28]	1.06 [0.60; 1.86]					1.09 [0.67; 1.78]	
Imi	**2.65 [1.34; 5.25]**	4.95 [0.30; 82.24]	**1.57 [1.01; 2.44]**	1.50 [0.92; 2.44]	1.37 [0.92; 2.04]	1.40 [0.74; 2.64]	1.32 [0.78; 2.22]	1.35 [0.66; 2.76]	1.21 [0.80; 1.82]	1.21 [0.73; 2.01]	1.16 [0.73; 1.86]	1.18 [0.57; 2.43]	1.16 [0.78; 1.74]	1.05 [0.72; 1.52]	0.99 [0.56; 1.74]				1.04 [0.73; 1.49]	
5-FU	**2.75 [1.32; 5.76]**	5.14 [0.30; 86.80]	1.63 [0.91; 2.90]	1.56 [0.89; 2.74]	1.42 [0.87; 2.31]	1.45 [0.78; 2.69]	1.37 [0.90; 2.07]	1.40 [0.70; 2.81]	1.25 [0.86; 1.82]	1.26 [0.65; 2.44]	1.21 [0.70; 2.08]	1.22 [0.55; 2.69]	1.21 [0.72; 2.02]	1.09 [0.68; 1.73]	1.03 [0.55; 1.92]	1.04 [0.68; 1.58]		1.05 [0.59; 1.87]		
KOH	**2.83 [1.29; 6.20]**	5.28 [0.31; 90.85]	1.67 [0.87; 3.21]	1.60 [0.85; 3.01]	1.46 [0.84; 2.55]	1.49 [0.73; 3.04]	1.40 [0.79; 2.51]	1.44 [0.66; 3.15]	1.29 [0.77; 2.16]	1.29 [0.63; 2.65]	1.24 [0.68; 2.25]	1.26 [0.54; 2.94]	1.24 [0.68; 2.26]	1.12 [0.66; 1.89]	1.06 [0.54; 2.05]	1.07 [0.64; 1.77]	1.03 [0.65; 1.62]		1.06 [0.60; 1.90]	
Cryo	**2.94 [1.52; 5.67]**	5.48 [0.33; 91.73]	**1.74 [1.05; 2.89]**	**1.66 [1.04; 2.66]**	**1.52 [1.06; 2.18]**	1.55 [0.84; 2.86]	1.46 [0.88; 2.40]	1.49 [0.74; 3.00]	1.33 [0.92; 1.94]	1.34 [0.75; 2.41]	1.29 [0.86; 1.92]	1.30 [0.61; 2.77]	1.29 [0.82; 2.02]	1.16 [0.87; 1.54]	1.09 [0.67; 1.78]	1.11 [0.83; 1.48]	1.07 [0.72; 1.59]	1.04 [0.66; 1.63]		
Polyph	**4.07 [1.88; 8.83]**	7.60 [0.46; 125.86]	**2.41 [1.32; 4.42]**	**2.31 [1.30; 4.11]**	**2.10 [1.24; 3.56]**	**2.15 [1.03; 4.46]**	**2.02 [1.08; 3.77]**	2.07 [0.93; 4.62]	**1.85 [1.07; 3.20]**	1.86 [0.96; 3.62]	1.78 [0.98; 3.24]	1.81 [0.89; 3.68]	**1.79 [1.01; 3.16]**	1.61 [0.95; 2.72]	1.52 [0.77; 3.00]	**1.54 [1.00; 2.36]**	1.48 [0.87; 2.51]	1.44 [0.78; 2.67]	1.39 [0.86; 2.24]	

Appendix S8. Probabilities of treatment ranking. Sensitivity analyses: (A) Worst case scenario, (B) Best case scenario.

(A)

	SUCRA
Surgery	0.949
Cidofovir	0.856
Ablative+Imi	0.802
Podotox cr	0.777
Podotox sol	0.727
PDT	0.712
CO2 Laser+5-FU	0.685
PDT+CO2 laser	0.677
CO2 laser	0.617
Mycobac IL	0.612
Electro	0.585
5-FU IL	0.583
Podotox gel	0.582
Ablative	0.581
Citric Ac 9%	0.566
TCA	0.492
Cryo+Podotox cr	0.450
Imi	0.440
5-FU	0.408
Podo	0.407
KOH	0.399
Cryo	0.339
Podo+TCA	0.338
IFN-2b IL	0.250
Polyph	0.190
Podotox sol+cr	0.150
Placebo IL	0.131
Placebo	0.105
IFN-1a IL	0.091

(B)

	SUCRA
Surgery	0.890
Electro	0.829
Ablative+Imi	0.787
PDT	0.693
Cidofovir	0.689
PDT+CO2 laser	0.668
Cryo+Podotox cr	0.663
CO2 Laser+5-FU	0.658
Podotox gel	0.647
5-FU IL	0.643
Ablative	0.633
Podotox sol	0.631
CO2 laser	0.616
Podotox cr	0.606
Mycobac IL	0.578
TCA	0.495
Podo+TCA	0.495
Imi	0.489
Cryo	0.457
5-FU	0.421
KOH	0.415
IFN-2b IL	0.330
Podo	0.329
Citric Ac 9%	0.211
Placebo IL	0.167
Podotox sol+cr	0.148
Polyph	0.127
IFN-1a IL	0.122
Placebo	0.062

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