

SUPPLEMENTAL MATERIAL

Adverse Effects of Treatments for Anogenital Warts in Non-Immunocompromised Adults: A Network Meta-Analysis of Randomized Controlled Trials

Réda Saib (MD)¹, Elisa Joly (MD)¹, Sébastien Fouere (MD)², Christian Derancourt³, Babacar Tounkara (MSc)⁴, Cyril Ferdynus (MD, PhD)⁴, Antoine Bertolotti (MD, PhD)^{1,4}

(1) Department de Maladies-Infectieuses, Dermatologie, Saint Pierre, CHU de La Réunion, France

(2) CeGIDD Saint-Louis, Fernand-Widal, Le Checkpoint, Hôpitaux Universitaires Saint-Louis, Lariboisière, Fernand-Widal, Assistance Publique des Hôpitaux de Paris, Paris, France

(3) Cabinet libéral, 623 Rue du Barry, 05130 Tallard.

(4) Inserm CICEC 1410, La Réunion, France

Corresponding Author: Prof. Antoine Bertolotti, MD, PhD

Dermatologist and Venereologist

Department of Infectious Diseases – Dermatology, Saint-Pierre Hospital, Reunion Island, France

Email: antoine_bertolotti@yahoo.fr

APPENDIX S1. List of keywords

		Inclusion	Exclusion
Treatment of anogenital condyloma	Pubmed, Medline et Embase	MJMESH.EXACT("Condylomata Acuminata -- surgery") OR MJMESH.EXACT("Condylomata Acuminata -- therapy") OR MJMESH.EXACT("Condylomata Acuminata -- drug therapy") OR MJEMB.EXACT("condyloma acuminatum -- surgery") OR MJEMB.EXACT("condyloma acuminatum -- drug therapy") OR MJEMB.EXACT("condyloma acuminatum -- therapy")	(MESH.EXACT("Buschke- Lowenstein Tumor") OR MJEMB.EXACT("giant condyloma acuminatum") OR TI(Buschke) OR TI(neoplasm*) OR TI(cancer) OR TI(carcinoma) OR TI(foot) OR TI(feet) OR TI(hand*) OR TI(throat) OR TI(larynx) OR TI(pharynx))
		MJMESH.EXACT("Condylomata Acuminata") OR MJEMB.EXACT("condyloma acuminatum") OR MJEMB.EXACT("condyloma") OR TI(condyloma*) OR TI(genital wart*) OR TI(veneral wart*) OR TI(anogenital wart*) OR TI(rectal wart*)) AND (MJMESH.EXACT.EXPLODE("Anti-Infective Agents") OR MJMESH.EXACT.EXPLODE("Antiviral Agents") OR MJMESH.EXACT.EXPLODE("Antiviral Agents") OR MJMESH.EXACT("Viral Vaccines -- therapeutic use") OR MJMESH.EXACT.EXPLODE("Drug Therapy") OR MJMESH.EXACT.EXPLODE("Therapeutics") OR MJMESH.EXACT.EXPLODE("Ablation Techniques") OR MJMESH.EXACT.EXPLODE("Surgical Procedures, Operative") OR MJMESH.EXACT.EXPLODE("Laser Therapy") OR MJEMB.EXACT.EXPLODE("antiinfective agent") OR MJEMB.EXACT.EXPLODE("antivirus agent") OR MJEMB.EXACT.EXPLODE("therapy") OR MJEMB.EXACT.EXPLODE("drug therapy") OR MJEMB.EXACT.EXPLODE("virus vaccine -- therapy") OR MJEMB.EXACT.EXPLODE("surgery") OR MJEMB.EXACT.EXPLODE("surgical technique") OR TI(*treatment) OR TI (*therap*))	

APPENDIX S2. Methods

Registration, Databases, and Search Strategy

A librarian from the French National Authority for Health (HAS), Aurélien Dancoisne, conducted a systematic search in two databases (PubMed and Embase) from their inception to 1st August, 2025. The search strategy utilized specific descriptors (in English) combined with Boolean operators (AND and OR), employing parentheses to delimit search terms and quotation marks to identify compound words. After adjustment for each database, the keywords used are available in the online appendix document (refer to Appendix 1). No language restrictions were imposed.

Study Selection

Based on an initial review of titles and abstracts, three independent reviewers (M.B, M.B, and R.S) selected the studies. Discrepancies were resolved through discussion with two additional reviewers (A.B and E.J). The inclusion criteria for study selection were as follows: (1) inclusion of immunocompetent adults and pregnant women with a diagnosis of anogenital warts, (2) administration of treatments via oral, topical, intravenous, or injectable, (3) randomized controlled trials (RCTs). Exclusion criteria included: immunosuppressed patients, human immunodeficiency virus positive individuals, pediatric populations. Non- RCTs were also excluded. The selected studies were analyzed and read in full.

Outcome Measures

The primary outcome measure was medication safety, assessed by the occurrence of AEs (local and systemic), classified into different grades (low, moderate, or high). LGL include erythema, mild localized pain, and a stinging sensation. MGL encompass erosion, edema, moderate localized pain, and minor bleeding. HGL are characterized by ulceration, significant bleeding, and intense localized pain. LGG include mild diffuse pain and a pseudo-flu-like syndrome. Other general adverse effects of medium and high grade were not considered in this analysis.

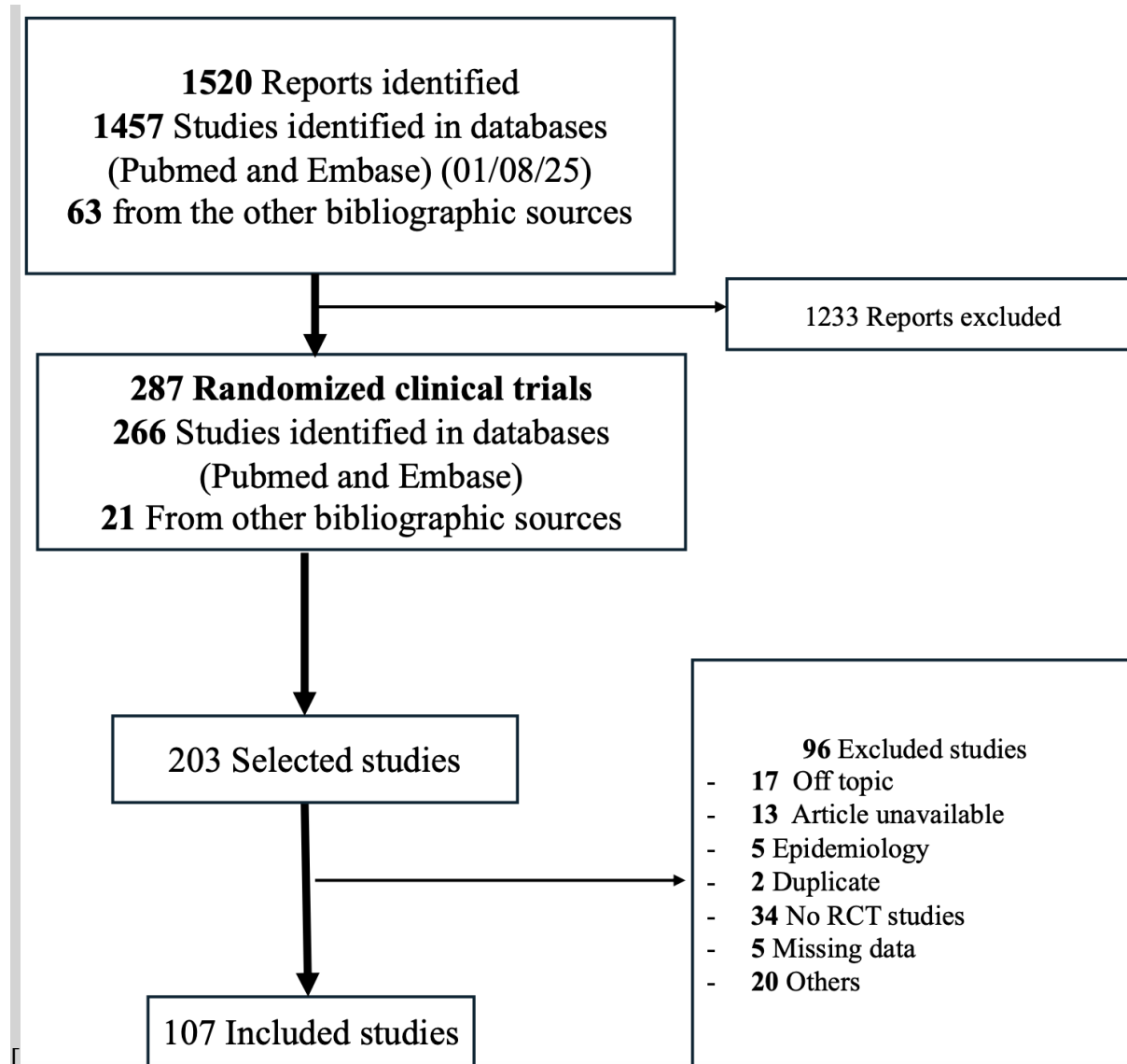
Data Extraction

Data extraction grids were developed following a discussion involving the entire working group. The primary outcome measures were initially determined by A.B, E.J, and R.S. For each study, R.S independently extracted and recorded relevant information. Discrepancies were resolved through discussion with two additional reviewers (A.B and E.J). This NMA was based on the aforementioned systematic review. The statistical data were processed using the R software.

Assessment of Risk of Bias in Included Studies

The risk of bias in RCTs was evaluated using the Cochrane Collaboration Risk of Bias tool, which includes seven specific domains: (1) generation of randomization sequence (selection bias), (2) allocation concealment (selection bias), (3) blinding of participants and caregivers (performance bias), (4) blinding of outcome assessors (detection bias), (5) incomplete outcome data (attrition bias), (6) selective reporting of outcomes (reporting bias), and (7) other biases. For each domain, the risk of bias was classified as low, high, or intermediate. The risk of bias assessment was conducted independently by M.B, M.B, and R.S. Discrepancies among the three evaluators were resolved through discussion with two additional reviewers (A.B and E.J).

APPENDIX S3. Flow chart



APPENDIX S4. List and exclusion criteria for randomized clinical trials

1st author	Year	Exclusion criteria
Abcarian ¹	1976	No RCT studie
Abcarian ²	1977	No RCT studie
Abcarian ³	1982	No RCT studie
Alfonso (a) ⁴	2009	No RCT studie
Alfonso (b) ⁵	2009	No RCT studie
Alfonso ⁶	2021	Missing data
Anggraini ⁷	2020	HIV population
Ardébol ⁸	2015	No RCT studie
Association of Genitourinary Medicine and the Medical Society for the Study of Venereal Diseases – National guideline for the managemet of anogenital warts. Clinical Effectiveness Group ⁹	1999	Old guideline > 25 years
Armstrong ¹⁰	1996	Missing data
Azab ¹¹	2023	Off-topic
Badawi ¹²	2006	No RCT studie
Beutner ¹³	2000	Article unavailable
Belli ¹⁴	1991	Article unavailable
Bonnez ¹⁵	1997	Off-topic
Cao ¹⁶	2010	Off-topic
Cardamakis ¹⁷	1996	No RCT studie
Chamseddin ¹⁸	2019	No RCT studie
Christophersen ¹⁹	1993	Article unavailable
Ciccarese ²⁰	2019	No RCT studie
Coremans ²¹	2003	No RCT studie
Douglas ²²	1990	HIV population
Du ²³	2015	Off-topic : cervical warts
El-fakkar ²⁴	2023	Article unavaible
Elmaadawy ²⁵	2019	No RCT studie

Farschchian ²⁶	2020	Off-topic : non-genital warts
Fayed ²⁷	2009	No RCT studie
Ferenczy ²⁸	1984	No RCT studie
Ferenczy ²⁹	1993	Article unavailable
Ferenczy ³⁰	1995	HIV population
Ferenczy ³¹	2000	No RCT studie
Fleshhner ³²	1994	HIV population
Fife ³³	2001	Comparison of the same treatment at different rates of application
Foldvari ³⁴	2011	Article unavailable
Frega ³⁵	2006	Off-topic
Fu ³⁶	2016	Off-topic
Gaspari ³⁷	2022	Article unavailable
Ghahatars ³⁸	2023	Off-topic
Ghazvini ³⁹	2024	Unavailable
Gilson ⁴⁰	1999	HIV population
Goldenberg ⁴¹	2014	Pediatric population
Goldmeier ⁴²	2005	Off-topic
Golusin ⁴³	2019	Article unavailable
Gori ⁴⁴	1992	Off-topic
Guenthner ⁴⁵	2021	Missing data
Guerra ⁴⁶	1998	Off-topic
Halim ⁴⁷	2023	Off-topic
Hasumi ⁴⁸	1987	No RCT studie
Isik ⁴⁹	2014	Missing data
Jardine ⁵⁰	2012	No treatment recommended
Khawaja ⁵¹	1986	Epidemiology
Klutke ⁵²	1995	No RCT studie
Komericki ⁵³	2006	No RCT studie
Krebs ⁵⁴	1988	No RCT studie
Krebs ⁵⁵	1990	No RCT studie
Lahoria ⁵⁶	2023	Article unavailable
Larsen ⁵⁷	2018	No RCT studie

Loureiro ⁵⁸	2008	No RCT studie
Matteelli ⁵⁹	2001	HIV population
Mehrabi Rad ⁶⁰	2023	Article unavailable
Metawea ⁶¹	2005	No RCT studie
Murray ⁶²	2018	HIV population
Nofal ⁶³	2022	Pediatric population
Orlando ⁶⁴	2002	HIV population
Puri ⁶⁵	2009	Out of scope
Reichel ⁶⁶	1992	No treatment recommended
Reichman ⁶⁷	1988	Pediatric population
Reid ⁶⁸	1992	Off-topic : oncology
Rizzo ⁶⁹	2018	No RCT studie
Rockley ⁷⁰	1995	Unsystematic review
Pezeshkian ⁷¹	2024	Article unavailable
Sauder ⁷²	2003	Duplicate
Schou et Helin ⁷³	1977	Off-topic (no genital warts)
Schwartz ⁷⁴	1988	No RCT studie
Shahidi Dadras ⁷⁵	2021	No RCT studie
Shahidi ⁷⁶	2020	No RCT studie
Simmons ⁷⁷	1981	Missing data
Tatti 2010 ⁷⁸	2010	Duplicate
Thompson ⁷⁹	1999	Epidemiology
Troffater Jr ⁸⁰	1998	Unsystematic review
Tsambaos ⁸¹	1997	No RCT studie
Tyring ⁸²	2001	Epidemiology
Tyring ⁸³	1998	Epidemiology
Usman ⁸⁴	1996	Off-topic
Wang ⁸⁵	2024	Article unavailable
Wang ⁸⁶	2007	5 doses of the same treatment
Ward ⁸⁷	1997	No RCT studie
Weck ⁸⁸	1988	Epidemiology
Wiltz ⁸⁹	1995	No RCT studie
Xu ⁹⁰	2013	HIV population

Xu ⁹¹	2020	Off-topic
Yaghoobi ⁹²	2021	Off-topic
Yang ⁹³	2008	No RCT studie
Yang ⁹⁴	2016	No RCT studie
Yang ⁹⁵	2019	No RCT studie
Yüksekdağ ⁹⁶	2019	No RCT studie

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APPENDIX S5. Characteristics of RCTs included

Reference	Country	Intervention	Patient analyzed (per protocol)	Follow-up (mo)	Comments
Abdullah 1993 ¹	UK	Cryo TCA	43 30	3	
Akhavan 2014 ²	Iran	Podophyllin Imiquimod Cryo	38 37 36	8	
Arıcan 2004 ³	Turkey	Imiquimod 5% Placebo	33 10	9	
Armstrong 1994 ⁴	UK	IFN alfa 2a + podophyllin Placebo + podophyllin	59 59	6.5	
Azizjalali 2012 ⁵	Iran	CO2 laser Cryo	80 80	3	
Baker 2011 ⁶	USA	Imiquimod 2.5% Imiquimod 3.75% Placebo	139 149 77	4	Only women

Benedetti Panici 1989 ⁷	Italy	Electro Placebo	51 48	12	Only women, some patients with AGWs on cervix ; IFN arm (data not shown)
Beutner 1989 ⁸	USA	Podophyllotoxin 0.5% gel Placebo	56 53	4	Only men
Beutner 1998 ⁹	USA	Imiquimod 5% Imiquimod 1% Placebo	69 71 67	7	
Bilensoy 2011 ¹⁰	Turkey	Placebo 5-FU cream 5% Placebo intra-lesional 5-FU intra-lesional	6 14 6 18	6	Only women ; both 5-FU arms used with cyclodextrin thermosensitive gel
Bonnez 1995 ¹¹	USA	Cryo + interféron alpha Cryo + INF beta Cryo + INF gamma	24 35 31	12	
Bornstein 1997 ¹²	Israel	IFN-1a intra-lesional Placebo intra-lesional	30 30	6	
Buzza 2021 ¹³	Brazil	MAL-PDT TCA	10 9	30	
Camargo 2014 ¹⁴	Brazil	KOH	20	3	1st treatment, only men

		Cryo	22		
Carpiniello 1988 ¹⁵	NR	CO2 laser	41	4	Only men
		CO2 laser + 5-FU	27		
Chen 2007 ¹⁶	China	CO2 laser	21	3	
		PDT	65		
Claesson 1996 ¹⁷	Sweden, Finland, France	Podophyllotoxin 0.15% cream	60	4	
		Podophyllotoxin 0.3% cream	60		
		Podophyllotoxin 0.5% sol	60		
Davidson-Parker 1988 ¹⁸	UK	Inosine	14	3	
		Placebo	13		
Dinsmore 1997 ¹⁹	NR	IFN B 1A	27	3	
		Placebo	13		
Dos Santos 2025 ²⁰	Brazil	Ultrasonic Scalpel Surgery + PDT	13	18	
		TCA	16		
Duus 1985 ²¹	Denmark	CO2 laser	21	6	
		Ablative treatment (surgery, electro)	23		
Edwards 1988 ²²	UK	Podophyllotoxin 0.5% sol	32	6	Only men
		Podophyllin 20%	19		

Edwards 1998 ²³	Multicentric : Hawaii, New York, Pennsylvania & Canada	Imiquimod 5% Imiquimod 1% Placebo	90 71 73	7	
Eron 1986 ²⁴	USA	IFN-2b intra-lesional Placebo intra-lesional	125 132	7	
Eron 1993 ²⁵	NR	IFN alfa 2a + Cryo Cryo + Placebo	36 37	6	
Firooz 2019 ²⁶	Iran	Cryochirurgie Azote liquid	13 13	1,5	Only men
Friedman klein 1995 ²⁷	USA	Alferon N Placebo	74 64	12	
Gabriel 1983 ²⁸	UK	Podophyllin 25% Podophyllin 25% + TCA 50%	29 31	3	Only men
Gilson 2009 ²⁹	UK	Cryo + placebo Cryo + podophyllotoxin 0.15% cream	51 55	9	
Godley 1987 ³⁰	UK	TCA Cryo	57 49	4,5	Only men
Greenberg 1991 ³¹	USA	Podophyllotoxin 0.5% sol & cream Placebo	48 21	3	Only women
Gross 1998 ³²	Germany and Poland	IFN B 1 MUI	34	6	

		IFN B 0.15 MUI	35		
		Placebo	36		
Gross 2007 ³³	Germany & Russia	Polyphenon 15%	73	6	
		Polyphenon 10%	72		
		Placebo	76		
Handley 1991 ³⁴	NR	IFN alfa 2a + Cryo	28	3	
		Cryo + Placebo	28		
Hellberg 1995 ³⁵	Sweden	Podophyllotoxin 0.5% cream	28	4	Only women
		Podophyllin 20%	27		
Holmes 1999 ³⁶	USA	5-FU 5% cream	14	18	Only women
		Placebo	16		
Jensen 1985 ³⁷	Denmark	Podophyllin 25%	30	12	
		Surgery	30		
Kaur 2022 ³⁸	India	Hydrogen peroxide 40%	20	3,5	
		TCA 80%	20		
Keay 1988 ³⁹	USA	IFN alpha cream	30	4	Only women
		Placebo	28		
Khawaja 1989 ⁴⁰	UK	Podophyllin 25%	19	10.5	1st treatment
		Surgery	18		
Khondker 2020 ⁴¹	Bangladesh	Imiquimod 5%	32	4	

		Cryo	32		
Kinghorn 1993 ⁴²	UK	Podophyllotoxin 0.5% sol	138	3	
		Podophyllin 25%	62		
Kirby 1990 ⁴³	USA	Podophyllotoxin 0.5% sol	19	4	
		Placebo	19		
Kokelj 1996 ⁴⁴	Italy	Electro	31	8	
		IFN B	21		
		Electro + IFN B	23		
Kumar 2014 ⁴⁵	India	Imiquimod 5%	41	8	
		Mycobacterium intra-lesional	39		
Lacey 2003 ⁴⁶	UK	Podophyllin 25%	96	4	
		Podophyllotoxin 0.15% cream	82		
		Podophyllotoxin 0.5% sol	98		
Lassus 1987 ⁴⁷	Finland	Podophyllotoxin 0.5% sol	48	3	Only men
		Podophyllin 20%	52		
Liu 2012 ⁴⁸	China	CO2 laser + ALA PDT	60	3	
		CO2 laser + Placebo	60		
Lotfabadi 2015 ⁴⁹	Iran	Cryo	34	6	
		TCA 70%	34		
Mahajan 2014 ⁵⁰	India	Cryo + podophyllin 20%	24	6	

		Bleomycin + placentrex intra-lesional	25		
Malison 1982 ⁵¹	USA	Autogenous vaccine	18	6	
		Placebo	16		
Mazurkiewicz 1990 ⁵²	Poland	Podophyllin	13	1,5	
		Podophyllotoxin 0.5% sol	14		
		Podophyllotoxin 0.5% cream	16		
Mendelson 1993 ⁵³	NR	CO2 laser + IFN alfa 2a	68	9	
		CO2 laser + Placebo	67		
Meng 2018 ⁵⁴	China	Imiquimod 5% et PDT	52	6	
		Interferon alfa 2b	52		
Mi 2011 ⁵⁵	China	ALA PDT + Cryo	40	3	
		Cryo + Placebo	40		
Mistrangelo 2010 ⁵⁶	Italy	Surgery	122	6	
		Surgery + post op immunostimulation	139		
Mohanty et scott 1986 ⁵⁷	UK	Inosine	36	6	
		Podophyllin 25%	91		
		Conventional treatment + inosine	38		
Monsonago 1996 ⁵⁸	NR	Interféron beta 33 MUI	23	2	
		Interféron beta 1 MUI	23		
		Placebo	23		

Mousavi 2018 ⁵⁹	Iran	Extract garlic Cryotherapy	33 33	2	Only men
Nath 1990 ⁶⁰	India	Podophyllin TCA	47 48	6	
Nieminen 1994 ⁶¹	Finland	CO2 laser + interféron alfa-2b CO2 laser + Placebo	47 47	6	
Olmos 1994 ⁶²	Spain	IFN béta Placebo	49 45	12	
Olsen 1989 ⁶³	NR	IFN alfa n1 Isorétinoïn	9 8	9	
Ormerod 2015 ⁶⁴	Germany, Uk, Holland, Switzerland, Poland	Placebo Sodium nitrite 3% + citric acid 4.5% Sodium nitrite 6% + citric acid 9% 1/day Sodium nitrite 6% + citric acid 9% 2/day	74 72 74 70	6	
On 2014 ⁶⁵	USA	Polyphenone 15% + cryo Cryo	NR NR	16	
Padhiar 2006 ⁶⁶	India	Imiquimod 5% Podophyllin 20%	30 30	10	
Petersen 1991 ⁶⁷	Denmark	Interferon alfa-2b Placebo	27 22	6	

Petersen 1995 ⁶⁸	Denmark	Podophyllotoxin 0.5% sol	18	3	Only men
		Podophyllotoxin 0.5% cream	18		
Recanati 2018 ⁶⁹	USA	Cantharidine	6	0.5	
		TCA	6		
Reichman 1990 ⁷⁰	USA	IFN alpha 2a	43	4	
		IFN alpha 2b	46		
		IFN alpha n1	44		
		Placebo	42		
Relakis 1996 ⁷¹	Brazil & Greece	CO2 laser	71	12	Only men
		5-FU	218		
		CO2 laser + 5-FU	47		
Reyna-Rodriguez 2021 ⁷²	Mexico	Cryo + isotretinoin	23	4	
		Cryo	23		
Rosen 2015 ⁷³	USA	Imiquimid 3.75%	183	2	Only men
		Imiquimod 2.5%	168		
		Placebo	96		
Schofer 2006 ⁷⁴	Germany	Ablative procedure (Electro, cryo, laser, surgery)	100	6	
		Imiquimod 5%	155		
			103		

		Ablative procedure (Electro, cryo, laser, surgery) + imiquimod			
Schonfeld 1984 ⁷⁵	Israel	IFN B Placebo	11 11	3	
Sherrard 2007 ⁷⁶	UK	Podophyllin 25% TCA Cryo TCA + Podophyllin Cryo + Podophyllin	56 58 66 65 59	2	
Simmons 1981 ⁷⁷	UK	Cryo Electro	16 11	3	
Snoeck 2001 ⁷⁸	Belgium	Cidofovir Placebo	19 11		
Stefanaki 2008 ⁷⁹	Greece	Imiquimod 5% Cryo	35 45	12	1st treatment
Stefanaki 2015 ⁸⁰	Greece	Beta-sitosterol + Cryo Cryo	62 54	6	Open label
Stockfelth 2008 ⁸¹	Multicentric (Europe, South Africa)	Polyphenon 15% Polyphenon 10% Placebo	161 170 80	7	

Stone 1990 ⁸²	USA	Podophyllin 25% Cryo Electro	63 86 88	5	
Strand 1995 ⁸³	Sweden	Podophyllotoxin 0.15% cream Podophyllotoxin 0.3% cream Podophyllotoxin 0.5% sol	30 31 29	4	Only men
Swinehart 1997 ⁸⁴	USA	5-FU injection intra-lesional 5-FU 5% Placebo	78 76 33	5	
Syed 1994 ⁸⁵	Pakistan	Podophyllotoxin 0.3% cream Podophyllotoxin 0.5% cream Placebo	30 30 20		Only women
Syed 1995 (a) ⁸⁶	Pakistan	IFN alpha cream Podophyllotoxin 0.5% cream Placebo	20 20 20	4	Only men
Syed 1995 (b) ⁸⁷	Pakistan	IFN alpha cream Podophyllotoxin 0.5% cream Placebo	20 20 20	4	Only women
Syed 1998 ⁸⁸	Pakistan	Imiquimod 2% Placebo	30 30	4	Only women

Syed 2000 ⁸⁹	Pakistan	Imiquimod 2% Placebo	30 30	18	Only men
Szeimies 2009 ⁹⁰	Germany	PDT + CO2 laser CO2 laser	84 91	12	
Tabari 2010 ⁹¹	Iran	Podophyllin 20% TCA 30%	60 60	6	
Tatti 2008 ⁹²	Multicentric : USA, Europe, South Africa	Polyphenon 15% Polyphenon 10% Placebo	159 162 83	7	
Tu 2021 ⁹³	China	PDT CO2 Laser	331 111	3	
Tyring 1998 a ⁹⁴	USA	Imiquimod 5% Placebo	16 3	4	
Tyring 1998 b ⁹⁵	USA	Podophyllotoxin 0.5% gel Placebo	197 95	4	
Tyring 2018 ⁹⁶	USA	SB206 topique (berdazimère sodique + hydrogel de carboxyméthylcellulose) Placebo	197 95	3	
Vance 1986 ⁹⁷	USA	IFN-2b intra-lesional IFN alpha-2b intra-lesional	30 32	3	

		Placebo intra-lesional	29		
Vandepapelière 2005 ⁹⁸	NR	Vaccination + CO2 laser OR Electro	97	6	
		Placebo + CO2 laser OR Electro	94		
		Vaccin + podophyllotoxin	64		
		Placebo + podophyllotoxin	65		
Vesterinen 1984 ⁹⁹	Finland	IFN cream	8	2	
		Placebo	5		
Von Krogh 1992 ¹⁰⁰	Sweden	Podophyllotoxin 0.5% cream	44	3	
		Placebo	11		
Von Krogh 1994 ¹⁰¹	Sweden	Podophyllotoxin 0.25% sol	18	6	1st treatment
		Podophyllotoxin 0.5% sol	16		
		Placebo	17		
Wallin 1977 ¹⁰²	Sweden	5-FU 5%	18	9	Only men
		Podophyllin 25% sol	19		
Weisman 1982 ¹⁰³	Denmark	5-FU	30	2	
		Placebo	29		
Welander 1990 ¹⁰⁴	USA	IFN alpha-2b intra-lesional	16	NR	
		Placebo intra-lesional	21		
White 1997 ¹⁰⁵	UK	Podophyllotoxin 0.5% sol	50	3	
		Podophyllin 0.5%	55		

		Podophyllin 2%	53		
Zervoudis 2010 ¹⁰⁶	Greece	CO2 laser	30	6	
		CO2 laser + podotimod + vit c	32		
Zhang 2020 ¹⁰⁷	China	M- PDT	20	3	
		C-PDT	20		

Abbreviations: AGWs, Ano-genital warts ; NR, not reported; 5-FU 5 fluorouracil ; Conventional treatment (podophyllin 25%, cryotherapy or electrocautery) ; Cryo cryotherapy ; Electro, electrosurgery ; KOH, potassium hydroxide ; PDT, photodynamic therapy ; TCA trichloroacetic acid

APPENDIX S6. Risk of bias in randomised clinical trials (RoB)

	Randomization	Distribution of treatment	Blind (participant)	Blind (assessors)	ITT/lost of view	Selective ratio	Other bias
Abdullah 1993							
Akhavan 2014							
Arican 2004							
Armstrong 1994							
Azizjalali 2012							
Baker 2011							
Benedetti Panici 1989							
Beutner 1989							
Beutner 1998							
Bilensoy 2011							
Bonnez 1995							
Bornstein 1997							
Buzza 2021							
Camargo 2014							
Carpiniello 1988							
Chen 2007							
Claesson 1996							
Davidson-Parker 1988							
Dinsmore 1997							
Dos santos 2025							
Duus 1985							
Edwards 1988							
Edwards 1998							
Eron 1986							
Eron 1993							
Firooz 2019							
Friedman Klein 1995							
Gabriel 1983							
Gilson 2009							
Godley 1987							
Greenberg 1991							
Gross 1998							
Gross 2007							
Handley 1991							
Hellberg 1995							
Holmes 1999							
Jensen 1985							
Kaur 2022							
Keay 1988							
Khawaja 1989							
Khondker 2020							
Kinghorn 1993							
Kirby 1990							
Kokelj 1996							
Kumar 2014							
Lacey 2003							
Lassus 1987							
Liu 2012							
Lotfabadi 2015							
Mahajan 2014							
Malison 1982							
Mazurkiewicz 1990							
Mendelson 1993							
Meng 2018							
Mi 2011							
Mistrangelo 2010							
Mohanty et scott 1986							
Monsonogo 1996							
Mousavi 2018							
Nath 1990							
Nieminen 1994							
Olmos 1994							
Olsen 1989							
Ormerod 2015							
On 2014							
Padhiar 2006							
Petersen 1991							



APPENDIX S7. Methodological evaluation by PRISMA grid of our systematic review



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Y (Method)
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Y (Method)
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Y (Introduction)
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Y (Introduction)
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Y (Appendix 2)
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Y (Method)
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Y (Appendix 1 and 2)
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Y (Appendix 1 and 2)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Y (Appendix 2)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Y (Appendix 2,3,4)
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Y (Appendix 2 and 6)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Y (Appendix 2 and 6)
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Y (Appendix 2)
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Y (Appendix 2 and 5)
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Y (Appendix 2)
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Y (Appendix 2)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Y (Appendix 2)
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Y (Method)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Y (Appendix 2)
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Y (Appendix 3)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Y (Appendix 4)
Study characteristics	17	Cite each included study and present its characteristics.	Y (Appendix 5)
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Y (Appendix 8)
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Y (Results)
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Y (Results)
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Y (Results)
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Y (Results)
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Y
	23b	Discuss any limitations of the evidence included in the review.	Y
	23c	Discuss any limitations of the review processes used.	Y
	23d	Discuss implications of the results for practice, policy, and future research.	Y
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Y (Prospero, Method)
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Y
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Y (Appendix 2)
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Y
Competing interests	26	Declare any competing interests of review authors.	Y
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Y

APPENDIX S8. Extraction grid

REVCAE Data Extraction Form template

Review Author:

Study ID:

DESCRIPTION OF INTERVENTIONS

	Intervention 1:	Intervention 2:	3
Presentation cream / ointment / gel/solution/ spray/ Concentration of active ingredient			
Dose /frequency/			
Others modalities for interventions (precise)			
Total dose			
Duration given for			
Supplier and trade name if relevant			
Were instructions given to patients adequate? give details			

PARTICIPANTS

Inclusion criteria				
a) clinical diagnostic of external ano-genital condylomas among immunocompetents adults				
b) number of condylomas				
c) duration of condition				
d) site evaluated (eg penis/vulva/ perianal area/perineum))				
e) others				
Exclusion criteria				
comorbidities				
addictions				
Prior treatments				
others				
Setting (eg primary or secondary care, country, number of centres)				
Baseline demographic data	Intervention 1	Intervention 2	T o t a l	Notes
Age (mean; SD; median)				

REVCAE Data Extraction Form template

Review Author:

Study ID:

Duration of condition				
Number of condylomas (n; DS)				
Total warts area (mm2) : mean (SD) median				
Male/female				
Circumcision (men)				
Number of participants randomised				
Losses to follow –up - reasons				
1.discontinued				
2. adverse event				
3.lost to follow up				
4. other				
5.				
Number lost to follow up				
% lost to follow up				
Final number of participants evaluable				
Intention to treat analysis				

Primary outcome measures 1. % of clearance (3 months, if not you do precise delay): Y/N 2. % of recurrence (3 months after end of treatment, if not you do precise delay):Y/ N 3: others (precise)
Methods of assessing primary outcome measures 1.
Secondary outcome measures <i>(these must be taken from the protocol)</i>
Methods of assessing secondary outcome measures

OUTCOME MEASURES

REVCAE Data Extraction Form template

Review Author:

Study ID:

	Intervention 1, N=	Intervention 2, N=	3 Placebo	Notes
Total clearance Time point: 16w				
Partial clearance (at least 50%) = >75% Time point: 16w+12w				
Recurrence Time point: 3 months				
Time for complete clearance (weeks)				
Recurrence 6 months				
Recurrence 12 months				
QOL during ttt				
Satisfaction during ttt				
Ratio cost-efficacy				
Compliance				
Side effects				
local				
1.local- low grade				
2.local- medium grade				
3.local severe				
4.general- mild				
5.general- moderate				
6.general severe				

METHODS

Design: parallel group

Duration of trial:

Interval of assessment:

Unit of randomisation (eg. whole person, condylomas):

Unit of analysis (eg. whole person, condylomas, group of condylomas):

REVCAE Data Extraction Form template

Review Author:

Study ID:

METHODOLOGICAL QUALITY OF STUDY

Major Criteria	Method
1. Generation of randomisation sequence Any information given? Y/N	
2. Allocation concealment Adequate - eg third party or opaque sealed envelopes A Unclear - insufficient details provided B Inadequate - eg open list or day of week C Not used D	
3. Blinding Participant Y/N Clinician Y/N Outcome assessor Y/N	
4. Loss to follow-up Were all randomised participants included in the analysis in the groups to which they were randomised? Y/N	
Other criteria (take from protocol)	Notes
5. Clear definition of disease Y/N <i>How defined</i>	
6. Were groups comparable at baseline?Y <i>Note any differences</i>	
7. Interventions adequately described? Y/N	
8. Previous treatment stopped	
8. Study duration adequate > 3 months Y/N	
9. Concomitant treatment permitted? Y/N	<i>Details:</i>
10 Adequate information re taking treatment Y/N	
12. Assessment of compliance undertaken? Y/N	<i>Method:</i>

Funding body

Declared: Y/N

Name:

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APPENDIX S9. Bibliography of included RCTs

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