

Supplementary Table 1: Study and sample characteristics of the included studies

Study characteristics			Sample characteristics						
First author, year	Interventions	Pts. randomized (evaluated for CC)	Localization of warts	Age (y) [mean (SD)]	Female [n/N (%)]	Total wart area (mm ²) [mean (SD)]	No. of warts [mean (SD)]	Duration of disease (mo) [mean (SD)]	Previous treatment [n/N (%)]
Imiquimod 5% cream vs. placebo									
Arican et al. 2004 ³⁴	imiquimod 5% cream, unclear frequency of application (2 or 3x/w), up to 12w until clearance	34 (33)	external anogenital warts of different localizations	30.3 (6.1)	11/34	n.s.	n.s.	11.9 (22.5)	n.s.
	pure vaseline cream, unclear frequency of application (2 or 3x/w), up to 12w until clearance	11 (10)		32.3 (6.8)	2/11	n.s.	n.s.	12.1 (24.2)	
Beutner et al. 1998a ³⁵	imiquimod 5% cream, 3x/w, up to 8 weeks	51 (51)	external anogenital warts of different localizations	29 (8)	5/51	median 47 (range 6-1785)	median 6 (range 1-29)	median 28 (range 2-181)	35/51 (69%)
	placebo cream (vehicle), 3x/w, up to 8 weeks	57 (57)		30 (9)	5/57	median 63 (range 4-8784)	median 7 (range 1-105)	median 14 (range 1-277)	39/57 (68%)
Tyring et al. 1998a ³⁶	imiquimod 5% cream, 3x/w, up to 16w	16 (16)	condylomata acuminata, no further information	n.s.	8/16 (50%)	n.s.	n.s.	median: 60 (range: 3.5-204)	14/22 (63.6%)
	placebo cream (vehicle), 3x/w, up to 16w	4 (3)			2/4 (50%)			median: 19.7 (range: 6.6-100.3)	
Beutner et al. 1998b ³⁷	imiquimod 5% cream, 1x/d, up to 16w until clearance; rest periods for up to 7 days allowed	94 (94)	external genital warts (pts. with genital, perineal, and perianal warts were included, a minority had anal warts)	30 (10)	42/94 (45%)	median 137 (range 2-9588)	median 7 (range 1-47)	median 21.7 (range 1.0-485.3)	31/94 (33%)
	imiquimod 1% cream, 1x/d, up to 16w until clearance; rest periods for up to 7 days allowed	90 (90)		33 (11)	41/90 (46%)	median 148 (range 10-13461)	median 8 (range 1-50)	median 24.1 (range 0.3-491.4)	24/90 (27%)
	placebo cream (vehicle), 1x/d, up to 16w until clearance; rest periods for up to 7 days allowed	95 (95)		30 (9)	42/95 (44%)	median 121 (range 4-2603)	median 8 (range 1-45)	median 19.9 (range 0.6-318.3)	23/95 (24%)
Edwards et al. 1998 ³⁸	imiquimod 5% cream, 3x/w, up to 16w until clearance	109 (109)	external anogenital warts of different localizations	32 (12)	46/109 (42%)	median 69 (range 8-5525)	n.s.	median 4.2 (range 0.4-375))	n.s.
	imiquimod 1% cream, 3x/w, up to 16w until clearance	102 (102)		30 (10)	45/102 (44%)	median 74 (range 10-4271)		median 6.6 (range 0-182)	
	placebo cream (vehicle), 3x/w, up to 16w until clearance	100 (100)		31 (10)	40/100 (40%)	median 77 (range 7-5000)		median 5.8 (range 0-270)	

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Imiquimod 3.75% cream vs. placebo									
Baker et al. 2011 ³⁹	imiquimod 3.75% cream, 7x/w, up to 8w; rest periods to manage local reactions allowed as needed	216 (216)	vulvar (including mons), inguinal, perineal, perianal; genitoanal warts of other localization were not included in the assessments	34.2 (13.1)	534 (100%)	170.6 (463.0)	7.8 (6.1)	66.0 (97.2)	n.s.
	imiquimod 2.5% cream, 7x/w, up to 8w; rest periods to manage local reactions allowed as needed	212 (212)		32.8 (11.6)		161.9 (362.1)	7.9 (6.3)	68.4 (93.6)	
	placebo cream, 7x/w, up to 8w; rest periods to manage local reactions allowed as needed	106 (106)		32.9 (12.2)		166.5 (303.0)	8.3 (7.7)	66.0 (99.6)	
Rosen et al. 2015 ⁴⁰	imiquimod 3.75% cream, 7x/w, up to 8w; rest periods to manage local reactions allowed as needed	183 (183)	glans penis (10.1%), penile shaft (84.1%), scrotum (25.3%), foreskin (2.7%), inguinal (27.3%), perineal (7.6%), perianal (7.8%)	70.2% were 35 or younger	0 (0%)	more than 20% of pts. had a wart area greater than 150mm ²	50.6% had a wart count of 7 or less	duration was more than 1y in 60% of pts.	n.s.
	imiquimod 2.5% cream, 7x/w, up to 8w; rest periods to manage local reactions allowed as needed	168 (n.s.)							
	placebo cream, 7x/w, up to 8w; rest periods to manage local reactions allowed as needed	96 (96)							
Imiquimod 5% cream vs. podophyllotoxin 0.5% solution									
Komericki et al. 2011 ⁴¹	Imiquimod 5% cream, 3x/w, up to 16w	25 (20)	genital (60.0%), perianal (20.0%) and anogenital (20.0%) warts	30.8 (n.s.)	4/20	0-100mm ² : 8/20; 100-200mm ² : 7/20; >200mm ² : 5/20	n.s.	n.s.	None
	podophyllotoxin 0.5% solution, 2x/d for 3 consecutive days, then 4 days rest period; ≤4 treatment cycles	26 (25)		30.0 (n.s.)	3/25	0-100mm ² : 9/25; 100-200mm ² : 9/25; >200mm ² : 7/25			

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Podophyllotoxin 0.5 % solution vs. placebo									
Beutner et al. 1989 ⁴²	podophyllotoxin 0.5% solution, 2x/d for 3 consecutive days, then 4 days rest period; 2-4 treatment cycles	56 (56)	external genital warts, mainly penile shaft	30.0 (SEM 0.9)	0 (0%)	87.4 (SEM 18.3)	7.1 (SEM 0.7)	current episode: ≤ 12 mo: 29/56; >12 mo: 27/56	n.s.
	placebo solution (vehicle), 2x/d for 3 consecutive days, then 4 days rest period; 2-4 treatment cycles	53 (53)		31.7 (SEM 0.9)		101.9 (SEM 21.0)	7.8 (SEM 0.7)	current episode: ≤ 12 mo: 26/53; >12 mo: 27/53	
Kirby et al. 1990 ⁴³	podophyllotoxin 0.5% solution, 2x/d for 3 consecutive days, then 4 days rest period; 2-4 treatment cycles	19 (19)	external genital warts of different localizations	28.8 (1.66)	0	86.2 (19.43)	8.1 (1.09)	≤12mo: 9/19; >12mo: 10/19	15/19
	placebo solution (vehicle), 2x/d for 3 consecutive days, then 4 days rest period; 2-4 treatment cycles	19 (19)		29.8 (1.71)	0	118.2 (47.97)	9.5 (1.34)	≤12mo: 10/19; >12mo: 9/19	10/19
Krogh et al. 1994 ⁴⁴	podophyllotoxin 0.5% solution, 2x/d for 3 consecutive days, then 4 days rest period; 1-2 treatment cycles	19 (16)	penile warts only	25.4 (range: 17-48)	0%	n.s.	8.4	4.1 (range: 1-24)	none (exclusion criterion)
	podophyllotoxin 0.25% solution, 2x/d for 3 consecutive days, then 4 days rest period; 1-2 treatment cycles	19 (18)					12.1		
	placebo solution (vehicle), 2x/d for 3 consecutive days, then 4 days rest period; 1-2 treatment cycles	19 (17)					7.8		
Podophyllotoxin 0.5 % gel vs. placebo									
Tyring et al. 1998b ⁴⁵	podophyllotoxin 0.5 % gel, 2x/d for 3 consecutive days, then 4 days rest period; 2-8 treatment cycles	219 (181)	external genital (89.6%) and perianal (17.5%) warts	31.5	86/213 (40.4%)	159.2	5.5	27.3 (duration of present infection)	approx. 20% of pts. had received previous treatment
	placebo gel (vehicle), 2x/d for 3 consecutive days, then 4 days rest period; 2-8 treatment cycles	107 (93)		30.6	41/103 (39.8%)	141.8	5.4	24.0 (duration of present infection)	

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Podophyllotoxin 0.5% solution and 0.15% cream vs. placebo									
Claesson et al. 1996 ⁴⁶	podophyllotoxin 0.5% solution, 2x/d for 3 consecutive days, then 4 days rest period; 1-4 treatment cycles	60 (60)	penile, vulval, perianal	26.15	30/60 (50%)	n.s.	1-5: 22 pts. 6-10: 12 pts. >10: 26 pts.	2.2	n.s.
	podophyllotoxin 0.15% cream, 2x/d for 3 consecutive days, then 4 days rest period; 1-4 treatment cycles	60 (60)		25.35	30/60 (50%)		1-5: 22 pts. 6-10: 5 pts. >10: 33 pts.	1.8	
	podophyllotoxin 0.3% cream, 2x/d for 3 consecutive days, then 4 days rest period; 1-4 treatment cycles	60 (60)		26.3	30/60 (50%)		1-5: 22 pts. 6-10: 12 pts. >10: 26 pts.	1.6	
Lacey et al. 2003 ⁴⁷	podophyllotoxin 0.5% solution, 2x/d for 3 consecutive days, then 4 days rest period; 1-4 treatment cycles	120 (n.s.)	external genital warts	n.s.	58/120 (48%)	n.s.	n.s.	<3mo (per inclusion criterion)	none (inclusion criterion)
	podophyllotoxin 0.15% cream, 2x/d for 3 consecutive days, then 4 days rest period; 1-4 treatment cycles	118 (n.s.)			58/118 (49%)				
	podophyllin 25% in tincture of compound benzoin, 2x/w; up to 4w	116 (n.s.)			56/116 (48%)				
Strand et al. 1995 ⁴⁸	podophyllotoxin 0.5% solution, 2x/d for 3 consecutive days, then 4 days rest period; 1-4 treatment cycles	29 (29)	external genital warts	27.5 (range: 20-43)	0/90 (0%)	n.s.	7.9 (range: 1-27)	2.6 (range: 0.6-4.9)	6/29 (20.7%)
	podophyllotoxin 0.15% cream, 2x/d for 3 consecutive days, then 4 days rest period; 1-4 treatment cycles	30 (30)		25.7 (range 18-44)			6.9 (range: 1-23)	2.5 (range: 0.4-5.5)	5/30 (16.6%)
	podophyllotoxin 0.3% cream, 2x/d for 3 consecutive days, then 4 days rest period; 1-4 treatment cycles	31 (31)		27.2 (range: 20-48)			7.0 (range: 1-32)	2.5 (range: 0.7-5.6)	5/31 (16.1%)

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Polyphenon E (sinecatechins) 10% and 15% ointment vs. placebo ointment / cream									
Gross et al. 2007 ⁴⁹	polyphenon E 10% cream, 3x/d for up to 12w	79 (77)	Male pts.: penile shaft (57.4%), glans penis (24.6%), perianal (23.8%), foreskin (18.9%); Female pts.: vulva (64.7%), perianal (31.9%), perineal (19.0%)	33.2 (range 18-69)	38/79	n.s.	n.s.	52/238 (21.8%) had one previous episode; 24/238 (10.1%) had two previous episodes; 11/238 (4.6%) had three or more episodes	92/238 (38.7%)
	polyphenon E 15% ointment, 3x/d for up to 12w	80 (78)			38/80				
	placebo cream or ointment (vehicle), 3x/d for up to 12w	83 (83)			41/83				
Stockfleth et al. 2008 ⁵⁰	polyphenon E 15% ointment, 3x/d for up to 16w	201 (201)	Male pts.: penile shaft (65.0%), glans penis (24.2%), scrotum and foreskin Female pts.: vulva (84.1%), the perianal (21.7%), perineal and inguinal area	30.8 (11.1)	96/201 (47.8%)	94.2 (116.5)	8.2 (6.3)	462/503 (91.8%) had one previous episode; 19/503 (3.8%) had two previous episodes; 22/503 (4.4%) had three or more episodes	180/503 (35.8%)
	polyphenon E 10% ointment, 3x/d for up to 16w	199 (199)		30.6 (10.8)	89/199 (44.7%)	99.5 (117.1)	8.3 (5.8)		
	placebo ointment (vehicle), 3x/d for up to 16w	103 (103)		30.4 (10.9)	41/103 (39.8%)	75.6 (79.2)	7.2 (4.6)		
Tatti et al. 2008 ⁵¹	polyphenon E 15% ointment, 3x/d for up to 16w	196 (194)	vulva (41.2%), penis shaft (36.9%), perianal area (18.1%), perineal area (15.3%), glans penis (11.8%).	31.2 (12.26)	96/196 (49.0%)	n.s.	n.s.	44w (current episode)	n.s.
	polyphenon E 10% ointment, 3x/d for up to 16w	202 (197)		31.1 (11.53)	100/202 (49.5%)			55w (current episode)	
	placebo ointment (vehicle), 3x/d for up to 16w	104 (104)		32.5 (12.95)	48/104 (46.2%)			48w (current episode)	

Abbreviations: CC, complete clearance; d, days; f, female; m, male; mo, months; n, number; n.s., not stated; pts., participants; SD, standard deviation; SEM, standard error of the means; w, weeks; y, years.