

Table SII. Trial characteristics, patient demographics and disease characteristics at baseline

Trial	Trial phase	Blinding status	Sample size, <i>n</i>	Interventions	Outcomes reported			Patient demographics		Disease characteristics
					Complete clearance rate	Partial clearance rate	Withdrawal rate due to AEs	Age, years, mean	Male, %	Lesions, <i>n</i> per patient, mean
Akar 2001 (S1)	NR	Double	16	Colchicine cream (0.5% or 1%)	No	No	No	64	62.5	< 15
Akarsu 2011 (19)	NR	Single	61	DFS 3% IMQ 5%	Yes	No	Yes	66.6	55.7	1
Alirezai 1994 (S2)	NR	Double	100	Isotretinoin Vehicle	No	No	No	NR	NR	≤ 5
Alomar 2007 (20)	Unknown	Double	259	IMQ 5% Vehicle	Yes	Yes	Yes	71.1	88.0	6.5 ^a
Augustin 2015 (21)	3	Double	547	Ing Meb 0.015% or 0.05%	Yes	Yes	Yes	65.1	74.7	4–8 ^b
Azimi 2012 (S3)	Unknown	Double	112	Cryotherapy ± acnalen 0.1%	No	No	Yes	67.2	88.0	7.4
Berman 2014 (S4)	Unknown	Unknown	24	ALA-PDT ± Ing Meb 0.015% or Ing Meb 0.015%	No	No	No	NR	NR	NR
Berman 2014 (S5)	3	Double	329	Cryotherapy ± Ing Meb 0.015%	Yes	Yes	Yes	67 ^d	82.4	6 ^a
Braathen 2009 (S6)	Unknown	Open-label	112	MAL-PDT	No	No	No	73	56.3	4 ^b
Chen 2003 (S7)	Unknown	Double	44	IMQ Vehicle	Yes	Yes	Yes	63.9	70	10.6
Choi 2015 (S8)	1	Double	33	ER:YAG AFL MAL-PDT MAL-PDT	No	No	Yes	68.1	60.6	NR
Choi 2015 (S9)	1	Single	93	AFL-PDT MAL-PDT	Yes	No	No	70.9	43.2	2–10
Cunningham 2017 (S10)	1	Double	132	Calcipotriol 0.005% + 5-FU 5%	Yes	Yes	No	69.5	81.0	≥ 12 ^a
Dirschka 2012 (24)	3	Single	571	PDT + BF-200 ALA; PDT + MAL; PDT + placebo	Yes	No	Yes	70.7	84.0	6.2
Foley 2011 (S11)	Unknown	Unknown	71	Cryotherapy; IMQ	Yes	Yes	Yes	71.5	78.9	≥ 10 ^b
Freeman 2003 (25)	Unknown	Double	204	PDT+MAL; PDT + placebo; cryotherapy	No	No	Yes	64	62.3	1–28 ^c
Garbe 2016 (S12)	3	Double	450	Ing Meb 0.015%	Yes	No	Yes	72 ^a	88.2	6.2
Haddad 2011 (S13)	NR	NR	24	Intense pulse light ± ALA	No	No	No	NR	NR	≥ 5 ^b
Hanke 2010 (S14)	3	Double	490	IMQ 2.5%, 3.75%; placebo	Yes	Yes	Yes	64.7	79	10.7
Hauschild 2009 (17)	3	Single	149	ALA + PDT	Yes	No	No	70.8	74.0	NR
Hauschild 2009 (18)	3	Open-label	449	ALA + PDT; placebo + PDT; cryosurgery	Yes	No	No	70.8	76.4	5.7
HDFUDR045 (22)	2	Single	121	5-FU 4%; 5-FU 5%; vehicle	Yes	Yes	Yes	66.2	90.0	10.4
HDFUP3B048 (48)	3	Single	841	5-FU 4%; 5-FU 5%; vehicle	Yes	Yes	Yes	68.1	81.3	15.0
HDFUP3S049 (23)	3	Double	100	5-FU 4%; vehicle	Yes	Yes	Yes	67.4	85.0	21.2
Hoover 2014 (S15)	NR	Single	60	Cryotherapy + 5-FU 0.5% or vehicle	Yes	Yes	Yes	67 ^a	91.7	12 ^a
Jorizzo 2002 (27)	Unknown	Double	207	5-FU 0.5%; vehicle	Yes	No	No	NR	80.0	14.6–15.8
Jorizzo 2006 (28)	NR	Double	144	Cryotherapy + 5-FU 0.5% or vehicle	Yes	No	Yes	62.6	83.8	21.1
Jorizzo 2007 (26)	NR	Double	246	IMQ 5%; vehicle	Yes	Yes	No	NR	NR	6.0 ^a
Jorizzo 2010 (S16)	3	Double	247	Cryosurgery ± IMQ 3.75% or placebo	Yes	No	Yes	66.7	86.6	16.0
Jury 2005 (S17)	NR	Single	20	5-FU 5%; vehicle	No	No	No	73	NR	17.5
Ko 2014 (S18)	NR	Open-label	45	Fractional laser-PDT; MAL-PDT	No	No	No	67.8	47.5	2–10 ^b
Korman 2005 (S19)	3	Double	492	IMQ 5%; vehicle	Yes	Yes	Yes	67 ^a	87.6	4–8 ^b
Kose 2008 (S20)	NR	Open-label	49	DFS 3%; IMQ 5%	No	No	Yes	56.4	57.1	≥ 3 ^b
Krawtchenko 2007 (29)	NR	NR	75	IMQ 5%; 5-FU 5%; cryosurgery	Yes	No	No	73	81.3	8.0
Kulp-Shorten 1993 (S21)	Unknown	Double	54	Masoprocol 10%; 5-FU 5%	No	No	No	69.7	90.7	14.0
Lebwohl 2004 (30)	3	Double	436	IMQ 5%; vehicle	Yes	Yes	Yes	66.1	87.2	6.0 ^a
Levy 2001 (31)	NR	Open-label	21	5-FU 0.5%, 5%	No	No	Yes	63.5	71.4	8–9
NCT00828568 (32)	1	Double	422	IMQ 5%, vehicle	Yes	No	No	67.2	82.2	4–8 ^b
NCT01203878 (S22)	4	Open-label	21	IMQ 3.75% ± PDT	Yes	No	No	62	66.7	19.0
NCT02239679 (S23)	2	Double	166	Cryotherapy + ALA + BLU-U; cryotherapy + ALA; cryotherapy + vehicle + BLU-U	Yes	No	No	66.8	81.3	4–15 ^b
Neittaanmäki-Perttu 2016 (S24)	NR	Double	70	Daylight-PDT; light-emitting diode-PDT	Yes	No	No	76	55.7	3
Ortonne 2010 (33)	Pilot	Double	12	IMQ 5% + FD or CPL	No	No	No	66	NR	≥ 5 ^b
Ostertag 2006 (S25)	NR	NR	55	5-FU 5%; laser resurfacing	No	No	No	71.6	90.9	15.1
Pariser 2003 (35)	NR	Double	80	MAL-PDT; placebo-PDT	Yes	No	Yes	65	87.5	6.3
Pariser 2008 (34)	NR	Double	96	MAL-PDT; vehicle-PDT	Yes	No	No	66.4	82.3	8 ^a
Pariser 2016 (S26)	NR	Double	234	ALA-PDT; vehicle-PDT	Yes	Yes	No	68	90.2	12.6 ^a
Pellacani 2015 (S27)	3	Open-label	199	Ing Meb 0.015%	Yes	No	Yes	74.5	84.4	5.5
Pflugfelder 2012 (S28)	4	Open-label	418	DIC 3% in HA 2.5%	Yes	No	No	69 ^a	79	NR
Piacquadio 2004 (S29)	3	Single	243	ALA-PDT; vehicle-PDT	Yes	Yes	Yes	65.8	83.5	4–15 ^b
Samorano 2015 (36)	NR	Open-label	100	Ing Meb 0.015%; 5-FU 5%	No	No	Yes	74	35	4–8 ^b
Sarbu 2012 (37)	NR	Double	81	DIC 1%, 3%, 5%; vehicle	No	Yes	No	NR	NR	NR
Serra-Guillén 2012 (38)	Pilot	Unknown	105	PDT; IMQ 5%; PDT-IMQ 5%	Yes	Yes	No	73.3	87.6	9.1

Table SII. Contd.

Trial	Trial phase	Blinding status	Sample size, n	Interventions	Outcomes reported			Patient demographics		Disease characteristics
					Complete clearance rate	Partial clearance rate	Withdrawal rate due to AEs	Age, years, mean	Male, %	Lesions, n per patient, mean
Smith 2003 (S30)	NR	NR	36	ALA + blue light; ALA + 595 nm pulsed dye laser; 5-FU 0.5%	Yes	Yes	Yes	61.4	80.6	6.4
Song 2015 (S31)	NR	NR	69 A	FXL-PDT; PDT	No	No	No	74.3	7.2	1-8
Spencer 2010 (39)	2	Double	265	Ing Meb 0.005%, 0.01%, 0.015%; vehicle	Yes	Yes	No	NR	NR	NR
Stockfleth 2011 (1)	3	Double	470	5-FU 0.5% + SA; DIC 3% HA; vehicle	Yes	No	No	71.8	84.7	5.7
Stockfleth 2017 (4)	3	Double	166	5-FU 0.5% + SA 10%; vehicle	Yes	Yes	Yes	72.2	87.7	5.6
Stockfleth 2017 (40)	4	Open-label	502	Ing Meb 0.015%; DIC 3%	Yes	Yes	Yes	75	85	6 ^a
Swanson 2010 (41)	3	Double	479	IMQ 2.5%, 3.75%; placebo	Yes	Yes	Yes	64	81.2	11.1
Szeimies 2002 (S32)	NR	Open-label	202	ALA-PDT; cryotherapy	No	No	Yes	71.5	61.4	≤10 ^b
Szeimies 2004 (S33)	3	Double	286	IMQ 5%; vehicle	Yes	Yes	No	71	86.7	5-9 ^b
Szeimies 2008 (S34)	2	Double	132	Resiquimod 0.01%, 0.03%, 0.06%, 0.1%	Yes	Yes	Yes	69.9	82.3	6 ^a
Szeimies 2009 (43)	NR	Double	115	MAL-PDT; placebo-PDT	Yes	No	No	68.3	79.1	7 ^a
Szeimies 2010 (44)	3	Double	122	BF-200 ALA-PDT; placebo-PDT	Yes	No	No	70.5	86.1	5.6
Szeimies 2016 (42)	3	Double	87	BF-200 ALA-PDT; placebo-PDT	Yes	Yes	Yes	71.6	91	5.4
Tan 2007 (S35)	NR	Double	65	IMQ 5%; vehicle	Yes	No	Yes	70.2	87.7	8.3
Tanghetti 2007 (45)	NR	Single	39	5-FU 5%; IMQ 5%	Yes	No	No	NR	NR	29.1
Tarstedt 2005 (S36)	3	Open-label	211	MAL-PDT	Yes	No	No	68.5	38.9	1.96
von Felbert 2010 (S37)	NR	Double	80	MAL-PDT VIS + wIRA; MAL-PDT LEDs	Yes	Yes	No	69.5 ^a	88.8	NR
Weiss 2002 (46)	3	Double	177	5-FU 0.5%; vehicle	Yes	No	Yes	63.1	85.9	14.7
Weiss 2017 (S38)	2	Double	163	Ingenol disoxate 0.037%, 0.05%; vehicle	Yes	Yes	No	72.0 ^a	100	13.0 ^a
Wiegell 2011 (S39)	NR	Single	120	MAL-PDT + daylight exposure	No	No	No	72	80	13.1
Zane 2014 (S40)	NR	Open-label	200	Laser ablation; cryotherapy	Yes	Yes	No	71	64.0	2.7
Zane 2014A (47)	NR	Open-label	200	MAL-PDT; DHA	Yes	Yes	No	73	71.0	8.4

^aMedian reported; ^bper inclusion criteria (mean number at baseline not reported); ^crange reported.

AE: adverse event; NR: not reported; DFS: diclofenac sodium plus hyaluronic acid; Er:YAG AFL MAL-PDT: erbium:yttrium-aluminium-garnet ablative fractional laser-assisted methyl aminolaevulinate-PDT; BLU-U: blue light; FD: fluorescence diagnosis; CPL: cross polarized light; HA: hyaluronic acid; AFXL: ablative CO2 fractional lasers; VIS: visible light; wIRA: water-filtered infrared A; LED: light-emitting diodes; DHA: diclofenac and hyaluronic acid.

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