Appendix C. Design Details

Table C-1. Design details

| Author Year PMID (Country/Region) | Number of centers | Funding | Inclusion criteria\* | Exclusion criteria\* | Method of diagnosis | Preoperative tumor size assessment | N enrolled/ randomized/ analyzed |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **RCT** |  |  |  |  |  |  |  |
| Abbade 2015 (Conference abstract) (Brazil) | Unclear | Not reported | primary nodular BCC in the head and neck, <=2 in Ø | no histologic confirmation of nodular BCC, Gorlin syndrome or contraindication to surgical resection or PDT. | Biopsy/pathologic confirmed | Method of assessment not reported | 92 lesions/68 lesions/68 lesions |
| Al-Niaimi 2015 26157307 (UK) | Single center | Not reported | >18 y/o, BCC > 1 x 1 cm2 requiring treatment with MMS | morphoeic, infiltrative and subtypes, a photosensitive skin disorder, hypersensitivity to MAL, participation in another investigational drug or research study within 30 days, and females of child-bearing potential | Method of diagnosis not reported | Visual assessment | 19/19/19 |
| Allen 1979 298425 (UK) | Single center | Not reported | BCC anywhere in the body | <18 y/o; previous deep x-ray tx or cryotherapy; lesion near the eye when the other eye sees less than 6/18. | Method of diagnosis not reported | Method of assessment not reported | 31/31/31 |
| Alpsoy 1996 8708151 (Turkey) | Unclear | Not reported | adults with histologically confirmed BCC | recurrent lesions, genetic or nevoid conditions, or lesions with deep tissue involvement | Biopsy/pathologic confirmed: histologically confirmed BCC | Method of assessment not reported | 45/45/45 |
| Arits 2013 23683751 (Netherlands) | Multicenter | No industry support | 1 primary, histologically proven superficial BCC per patient | using immunosuppressive drugs, had genetic skin cancer disorders, tumour was located in the H zone or scalp, or were breastfeeding or pregnant | Biopsy/pathologic confirmed: 3 mm punch biopsy and was assessed by consensus | Method of assessment not reported | 601/601/583 |
| Avril 1997 9218740 (France) | Unclear | Not reported | previously untreated BCC of the face, Ø < 4 cm. | contraindication to surgery and radiotherapy, BCC on the scalp or the neck, pts with total removal of BCC at biopsy, pts w/ >=5 BCCs, LE <3 yrs | Biopsy/pathologic confirmed | Method of assessment not reported | 360/360/347 |
| Basset-Seguin 2008 18693158 (13 centers in 7 european countries) | Multicenter | No industry support | >=18 y/o w/ previously untreated primary superficial BCC lesions suitable for cryotherapy. confirmed by histology using 4 mm punch biopsy. <=10 eligible lesions. Ø 6-15 mm on the face or scalp, <20 mm on the extremities or neck and <30 mm on the trunk, which were not pigmented, morpheaform or infiltrating. | xeroderma pigmentosum, porphyria, Gorlin’s syndrome, history of arsenic exposure, allergy to MAL or other topical photosensitizers or excipients of the cream, participated in other investigational studies in last 30 days and pregnant or breast-feeding women. Concomitant treatment with immunosuppressive medication | Biopsy/pathologic confirmed | Method of assessment not reported | 120/118/115 |
| Bath-Hextall 2014 24332516 (UK) | Multicenter | Industry supplied materials | histologically confirmed, primary, previously untreated, nodular or superficial BCC not arising at sites at high risk for subclinical tumour spread | morphoeic or recurrent BCC and those with Gorlin syndrome | Biopsy/pathologic confirmed: Histologically proven BCC (usually a punch or shave biopsy specimen of no more than 25% of the total lesion, though sometimes at surgery) | Method of assessment not reported | 501/501/485 |
| Berroeta 2007 17573890 (United Kingdom) | Single center | No industry support | <= 2 cm, well-define, nodular BCC on anatomically noncritical sites | < 18 y/o; pregnancy; photosensitivity; morphoeic BCCs; high-risk site; recurrent BCCs; immunodeficiency; size > 2 cm. | Method of diagnosis not reported | Visual assessment: well defined <=2 cm | 31/31/31 |
| Beutner 1999 10570388 (USA) | Unclear | Industry funded | biopsy-confirmed BCC with clearly visible margins, nodular w/ area 0.5 -1.5 cm^2, or superficial w/ area of 0.5-2 cm^2, and that was suitable for tx by surgical excision. | central facial/periorificial sites | Biopsy/pathologic confirmed | Method of assessment not reported | 35/35/35 |
| Brinkhuizen 2016 27067393 (Netherlands) | Single center | Industry supplied materials | Patients with histologically proven primary sBCC or (micro) nBCC >=4 mm, not located on the face or on the hairy scalp |  | Biopsy/pathologic confirmed | Visual assessment | 128/128/119 |
| Butler 2009 19018814 (texas, usa) | Single center | Industry funded | Immunocompetent, non-pregnant, >=18 y/o, primary nodular nasal BCCs, <1 cm | superficial, morpheaform, or micronodular histologic BCC | Biopsy/pathologic confirmed: histological confirmation of BCC before study enrollment with a 2-mm punch biopsy by a pathol- ogist. | Method of assessment not reported | 31/31/31 (ITT) 28 actual |
| Cai 2015 25899562 (china) | Single center | No industry support | having skin BD upon biopsy | porphyria or photosensitivity | Biopsy/pathologic confirmed | Method of assessment not reported | 18/18/18 |
| Carija 2016 27516420 | Single center | No industry support | >18 years, >2 BCCs, biopsy proven | lactating and pregnant women, heavily pigmented BCC, diagnosed porphyria | Biopsy/pathologic confirmed | assessment: traced onto graph paper and count squares | 15/15/15 |
| Choi 2016 26551044 (korea) | Single center | No industry support | ≥18 y/o, untreated thin primary nBCC, maximum tumour depth of 2 mm in a biopsy specimen and clinical evaluation, surgical excision would be difficult because of bleeding abnormalities or cardiac problems. | >5 eligible lesions; lesions located in the midface region, nose, orbital areas or ears; Ø >15 mm; non-nodular; known allergies to MAL or lidocaine; pregnancy or lactation; active systemic infectious disease; immunosuppressive treatment; personal history of malignant melanoma; tendency toward melasma or keloid formation; any indication of poor compliance. | Biopsy/pathologic confirmed | Method of assessment not reported | 39 (42 lesions)/39 (42 lesions)/34 patients (37 lesions) |
| Choi 2017 28199463 | Single center | Not reported | > 18 years with previously untreated microinvasive SCC, tumor invasion into the papillary dermis (Clark level II) according to a biopsy specimen and difficulty in surgical excision because of health problems | pregnancy or lactation; active systemic infectious disease; other inflammatory, infectious, or neoplastic skin diseases in the treated area; allergy to MAL,other topical photosensitizers, or excipients of the cream; history of photosensitivity; use of immunosuppressive or photosensitizing drugs; participation in any other investigational study in the preceding 30 days; history or indicators of poor compliance. Histological findings of acantholysis, desmoplasia, perineural or lymphovascular invasion, and echographic features of regional lymph node metastasis | Biopsy/pathologic confirmed: 4 mm punch biopsy | Visual assessment: photographed for baseline measurement | 45/45/40 |
| Cornell 1990 2229497 (US) | Multicenter | No industry support | superficial or noduloulcerative BCC confirmed by biopsy, 32-70 y/o, not pregnant, and in good general health. | previous therapy to the test lesion, immunosuppressive or cytotoxic therapy (within the prior 4 wks), or exogenous interferon/interferon-inducer except interferonalfa-2b (Intron A), BCC located in the perioral or central area of the face or penetrating to deep tissue | Biopsy/pathologic confirmed: punch or shave biopsy | Visual assessment: photographed and its size and anatomic location were precisely defined. | 172/172/165 |
| Edwards 1990 2107219 (U.S.) | Unclear | Industry supplied materials | clinically typical, sharply defined BCC easily excisable at the end of the study | any serious or debilitating illness, history of thromboembolic phenomena or CVD, received rt to the test site area or who had a history of arsenic ingestion, pregnant or nursing women, immunosuppressed, pts taking nonsteroidal anti-inflammatory medications | Biopsy/pathologic confirmed | Visual assessment: at randomization, immediately before treatment and at the beginning of each treatment week | 29/29/29 |
| Edwards 1990 2383027 (U.S.) | Unclear | Industry supplied materials | otherwise healthy 35-65 y/o; 1 clinically typical, sharply defined basal cell carcinoma with clearly visible margins, Ø 0.5 to 1.5 cm for nodular tumors or 2 cm for superficial lesions, per pt. | Morpheic BCC, recurrent cancers, deeply invasive lesions, periorificial tumors, and central facial BCC; serious or debilitating illness, a history of thromboembolic or CVD, rt to the test site area, or a history of arsenic ingestion. Pregnancy, breast-feeding, and immunosuppression as a result of medication or illness, nonsteroidal anti-inflammatory medications | Biopsy/pathologic confirmed: confirmatory diagnostic shave or punch skin biopsy that removed less than 25% of the lesion | Visual assessment: The size and a clinical description of each basal cell carcinoma were recorded. The lesion was then photographed. | 65/65/63 |
| Eigentler 2007 17610993 (Germany) | Unclear | Not reported | adults w/ >=1 clinically typical and histologically confirmed primary nBCC Ø <=1.5 cm | micronodular, infiltrative, superficial, or morpheic BCC, BCCs w/ multicentric growth pattern, w/in 0.5 cm of the eyes | Biopsy/pathologic confirmed | Visual assessment: the lesion was documented by photography and the silhouette was traced on a plastic film. | 102/102/90 |
| Eimpunth 2014 (Conference abstract) (unclear) | Unclear | Not reported | biopsy proven, superficial or nodular BCCs located on trunk or extremities |  | Biopsy/pathologic confirmed | Method of assessment not reported | 24/24/24 |
| Foley 2009 20064185 (U.S. and australia) | Multicenter | Industry funded | 18 y/o, primary nodular BCC verified by local histologic exam of 2-3 mm punch biopsy and suitable for a simple excision surgery. | periorbital area, ears, nasaolabial fold; Ø < 6mm (any site) or >15 mm (face or scalp), > 20 mm (extremities or neck), or > 30 mm (trunk); pigmented, morpheaform or infiltrating pattern. porphyria, Gorlin's syndrome, xeroderma pigmentosum, history of arsenic exposure or allergy to MAL, ALA, or excipients, participated in any other investigational study in the previous 30 days or were likely to be poorly compliant, pregnant or breast-feeding. concomitant treatment with any immunosuppressive medication was prohibited. | Biopsy/pathologic confirmed | Method of assessment not reported | 131 (160 lesions)/131 (160 lesions)/128 |
| Garcia-Martin 2011 21242584 (Spain) | Unclear | Not reported | nodular BCC on the eyelid | previous tx, other dermatological diseases such as Gorlin syndrome or psoriasis, immunocompromised status, aggressive varieties of BCC such as morpheaform (sclerosing or infiltrative) BCC | Biopsy/pathologic confirmed: punch of diameter 4 mm | Visual assessment | 27/27/27 |
| Geisse 2002 12196749 (U.S.) | Multicenter | Industry funded | >=18 y/o, histologically confirmed superficial BCC 0.5-2.0 cm^2 | w/in 1 cm of the hairline, eyes, nose, mouth, or ears; the anogenital area; hands and feet, previously treated, recurrent, or w/in 5 cm of another BCC tumor | Biopsy/pathologic confirmed: A biopsy specimen of no more than 25% of the tumor area was taken for histologic confirmation of sBCC. | Visual assessment | 128/128/125 |
| Geisse 2004 15097956 (U.S.) | Multicenter | Industry funded | >=18 y/o, primary, histologically-confirmed superficial BCC >= 0.5 cm2, Ø <= 2.0 cm on the limbs, trunk (excluding the anogenital area), neck, or head (excluding the H-zone) | any dermatological disease in the target sBCC site or surrounding area that could be exacerbated by imiquimod or cause difficulty with examination (such as subjects with nevoid basal cell carcinoma syndrome) | Biopsy/pathologic confirmed: confirmatory punch or shave biopsy < 25% of the tumor area | Visual assessment: clinically evident tumor margins and local landmarks | 724/724/694 |
| Haak 2015 24903544 (Denmark) | Single center | No industry support | >=18 y/o, previously untreated facial tumours. histologically verified nBCC either: Ø > 15 mm, located in the H-zone, located on severely sun-damaged skin with one or more co-existing actinic lesions requiring treatment | lactating or pregnant women, porphyria, known allergy to MAL, Gorlin syndrome, immunosuppressive treatment, Fitzpatrick skin type IV–VI, history of keloid formation and conditions associated with risk of poor compliance | Biopsy/pathologic confirmed: histologically verified | Visual assessment: photographed and mapped on a template | 32/32/32 |
| Hall 1986 3514075 (UK) | Single center | Not reported | BCC proven by biopsy, considered suitable for tx w/ rt | Recurrent tumors, location on nose or pinna, electrons considered Tx of choice, lesion near eye and vision in contralateral eye <6/18 | Biopsy/pathologic confirmed: "Proven by biopsy" | Method of assessment not reported | 105/105/93 |
| Ko 2014 24102369 (Korea) | Single center | No industry support | Korean, ≥ 18 y/o, biopsy-confirmed Bowen's Disease lesions on lower extremities, >=2 comparable symmetrical lesions of similar severity and <=twofold difference in number of lesions between the right and left sides. | porphyria, known allergies to the MAL cream or lidocaine, pregnancy, lactation, any active systemic infectious disease, immunosuppressive treatment, personal history of malignant melanoma, tendency towards melasma or keloid formation, prior treatment of the lesions w/in 4 wks, and any indication of poor compliance. | Biopsy/pathologic confirmed | Visual assessment: photographed, mapped and numbered | 21/19/18 |
| Kuijpers 2006 16865869 (Netherlands) | Single center | No industry support | nodular, primary BCC located anywhere but periocular area and hairy scalp; clinical Ø <20 mm. | pigmented BCC; contra-indications to surgery; hypersensitivity to daylight or creams; porphyria; >5 BCCs. | Method of diagnosis not reported | Method of assessment not reported | 43/43/43 |
| Kuijpers 2007 17451581 (Netherlands) | Single center | No industry support | >=18 y/o, untreated, primary histologically proven BCC, nodular or superficial, on the head and neck, <20mm Ø | Recurrent, not superficial or nodular, >20 mm Ø, contraindications to either procedure, presence of 5+ BCCs | Biopsy/pathologic confirmed | Method of assessment not reported | 88/88/88 |
| Marks 2001 11312429 (Australia and New Zealand) | Multicenter | Industry funded | >=18 y/o, biopsy-proven superficial BCC on head, neck, trunk or limbs, SA 0.5-2 cm^2, primary tumor, biopsy <25% of the lesion | Infection, recurrent, w/in 1 cm of the hairline, eyes, nose, mouth, ears, anogenital region, hands, and feet | Biopsy/pathologic confirmed | Method of assessment not reported | 99/99/99 |
| Migden 2015 25981810 (worldwide) | Multicenter | Industry funded | >= 18 y/o; histologically confirmed, locally advanced BCC not amenable to rt or curative surgery; adequate bone marrow, liver function, and renal function | previous tx with sonidegib or another Hedgehog pathway inhibitor, major surgery, other antineoplastic therapy, taken an investigational agent w/in 4 wks before the start of the study, currently taking strong inhibitors or inducers of CYP3A4 or CYP3A5 expression or drugs metabolised by CYP2B6 or CYP2C9; gastrointestinal dysfunction or known malabsorption syndromes, neuromuscular disorders, or other uncontrolled medical disorders; treatment with drugs known to cause rhabdomyolysis (pravastatin allowed w/ extra caution); pregnancy or breastfeeding | Biopsy/pathologic confirmed | Visual assessment: standard annotated photography | 269/230/230 |
| Miller 1997 8996264 (USA) | Multicenter | No industry support | 6-15 mm Ø, well-defined margins, <=50 mm from any other malignancy that would otherwise be treated with surgery or curettage/electrodesiccation | lesions already received tx, high-risk sites, tumors considered to be more appropriately treated w/ Mohs, deep tissue involved lesions, morpheaform lesions, lesions associated with basal cell nevus syndrome, known hypersensitivities or allergies to 5-FU, sulfites, epinephrine, or bovine collagen; history of autoimmune disease or immunosuppression; women who were pregnant or lactating | Biopsy/pathologic confirmed: punch or shave biopsy of no more than 25% of total legion | Visual assessment: 6-15mm in largest diameter, well-defined margins | 122/122/116 |
| Morton 1996 8977678 (Scotland) | Unclear | Not reported | <=21 mm Ø |  | Biopsy/pathologic confirmed: 4-mm punch biopsy | Method of assessment not reported | 19/19/19 |
| Morton 2006 16785375 (Europe) | Multicenter | Industry funded | >= 18 y/o, histologically confirmed SCC in situ | treated w/in the previous 3 mo or strongly pigmented, <6mm or >40 mm Ø, located on the genitalia | Biopsy/pathologic confirmed: biopsy specimen taken within 5 months, and with no evidence of any change in appearance suggestive of lesion progression | Visual assessment | 229/229/209 |
| Mosterd 2008 18717680 (Netherlands) | Single center | Not reported | >18 y/o, untreated nBCC w/ Ø <=20 mm | Pregnancy, LE <5 years, known skin cancer syndromes, use of phototoxic ⁄photosensitive drugs, hypersensitivity to light or ALA cream, recurrent or pigmented BCC, not nodular BBC, and a localization on concave areas or hairy skin | Biopsy/pathologic confirmed: 3mm punch biopsy | Visual assessment | 151/149/149 |
| Mosterd 2008 19010733 (Netherlands) | Multicenter | No industry support | >= 1 untreated, histologically confirmed primary BCC >=1cm Ø located in the H-zone or a facial primary BCC of an aggressive histological subtype (ie, morpheaform, micronodular, trabecular, infiltrative, or BCC with squamous differentiation) | LE<3 yrs | Biopsy/pathologic confirmed | Visual assessment: overall and close-up photographs were taken before each treatment | 443/374/251 |
| Orenberg 1992 1430394 (USA) | Unclear | Not reported | Biopsy-proven nodular BCC, 06-1.5 cm Ø | Previous local tx or systemic cancer therapy w/in 6 mo; Gorlin's syndrome, morpheaform, pigmented or deeply invasive lesions; any serious or debilitating illness, chronic respiratory disease, depressed bone marrow, autoimmunedisease, or w/ hypersensitivity to 5-FU, epinephrine, or bovine couagen; Pregnant or lactating women and subjects requiring the use of nonsteroidal antiinflammatory drugs, nonselective beta-blocking drugs, aspirin, and topical or systemic steroids | Biopsy/pathologic confirmed | Method of assessment not reported | 20/20/20 |
| Patel 2006 16713457 (United Kingdom) | Single center | Industry funded | biopsy-proven cutaneous SCC in situ; full-thickness epidermal dysplasia; no active treatment 1 mo; post-biopsy legion 1-20 cm^2; >=1 cm away from eye; had to be able to attend clinical trials room. |  | Biopsy/pathologic confirmed: biopsy specimen, which by conventional histologic examination showed full-thickness epidermal dysplasia | Method of assessment not reported | 31/31/28 |
| Rhodes 2004 14732655 (Europe) | Multicenter | Industry funded | >=18 y/o w/ perviously untreated primary nodular BCC suitable for simple excision surgery | > 10 eligible lesions; lesions in midface region, orbital areas, or ears; 6mm-15mm Ø (face and scalp), > 20mm Ø (extremities or neck), >30mm Ø (trunk); pigmented or morpheaform BCCs; polyphyria; Gorlin syndrome; history of arsenic exposure; in another study in past 30 days; likely to be poor compliers; taking immunosuppresive medication; pregnant or breasfeeding | Biopsy/pathologic confirmed | Visual assessment | 103/103/101 |
| Salim 2003 12653747 (UK) | Multicenter | Not reported | Bowen's disease | Not reported | Biopsy/pathologic confirmed | Method of assessment not reported | 49/40/40 |
| Salmanpoor 2012 (Iran) | Single center | Not reported | Pathologically confirmed BCC | Tumors with indications for Mohs | Biopsy/pathologic confirmed | Method of assessment not reported | 55/55/55 |
| Schleier 2007 25047438 (Germany (Friedrich-Schiller University Jena)) | Single center | No industry support | histologically verified superficial BCC w/ no deep infiltration (<2 mm), no morpheic and pigmented BCC, and good compliance. | unclear histology, clinically nodular BCC, expected poor compliance, untreated diabetes mellitus, and pregnancy | Biopsy/pathologic confirmed | Method of assessment not reported | 24/24/24 |
| Schulze 2005 15888150 (Europe) | Multicenter | Industry funded | non-pregnant, >= 18 y/o; histologically confirmed primary sBCC on limbs, trunk, neck, or head; area >=0.5 cm^2 and Ø <=2.0 cm prior to biopsy. | clinically significant, unstable medical conditions; metastatic tumor or tumor with high probability of metastatic spread; tumor on anogenital area or w/in 1 cm of the hairline, nose, mouth, ears, and eyes; histological evidence morphoeic, severe squamous metaplasia, or any infliltrative or desmoplastic features; dermatological disease w/in 5 cm of target site margins that would be exacerbated by treatment and would affect assessment. | Biopsy/pathologic confirmed | Visual assessment: multiplying the two largest diameters perpendicular to each other | 166/166/166 |
| Shumack 2002 12224977 (12 weeks) (Australia and New Zealand; And United States) | Multicenter | Not reported | >=18 y/o, primary target tumor, histologically confirmed as nodular BCC. 0.5-1.5 cm^2 area and >1 cm from the eyes, nose, mouth, ear, and hairline. | BCC with morpheic infiltrating and micronodular patterns | Biopsy/pathologic confirmed: punch or shave biopsy of the target tumor. | Visual assessment: Target tumors were measured and photographed prior to the prestudy biopsy and rephotographed prior to treatment initiation and at each interval visit. | 92/92/77 |
| Shumack 2002 12224977 (6 weeks) (Australia and New Zealand; And United States) | Multicenter | Not reported | >=18 y/o, primary target tumor, histologically confirmed as nodular BCC. 0.5-1.5 cm^2 area and >1 cm from the eyes, nose, mouth, ear, and hairline. | BCC with morpheic infiltrating and micronodular patterns | Biopsy/pathologic confirmed: punch or shave biopsy of the target tumor. | Visual assessment: Target tumors were measured and photographed prior to the prestudy biopsy and re-photographed prior to treatment initiation and at each interval visit. | 92/92/77 |
| Siller 2010 20546215 (8 private dermatology clinics Australia) | Multicenter | Industry funded | >=18 y/o, with one sBCC lesion suitable for surgical excision on the arm, shoulder, chest, face, neck, abdomen, back, leg or scalp. Lesions with pre- and post-biopsy Ø 4–15 mm and thickness <=4 mm | women of childbearing potential; recurrent or atypical lesions, immunosuppression, and prior, concomitant or anticipated therapy with the potential to confound the study results. | Biopsy/pathologic confirmed | Visual assessment | 60/60/60 |
| Spencer 2006 16393600 (United States) | Single center | Industry funded | >= 18 y/o; previously untreated histologically confirmed nBCC. | comorbidities that would interfere with or be exacerbated by treatment. | Biopsy/pathologic confirmed: histologically confirmed | Visual assessment | 20/20/20 |
| Sterry 2002 12452875 (nodular) (Europe) | Multicenter | Industry funded | >=18 y/o, primary tumour, histologically confirmed superficial or nodular BCC, area 0.5 cm^2-2.0 cm^2 for superficial or 0.25 cm^2-1.5 cm^2 for nodular | previous therapy to the target tumour or any dermatological conditions that would interfere with local assessments. | Biopsy/pathologic confirmed: prestudy confirmatory punch, deep shave, or wedge biopsy that removed no more than approximately 25% of the tumour | Visual assessment: measuring and multiplying the two largest perpendicular dimensions of the tumour. The tumour site and appropriate anatomic landmarks were mapped using a clear plastic sheet as a template to guide the excision at the end of the study | 183/177 |
| Sterry 2002 12452875 (superficial) (Europe) | Multicenter | Industry funded | >=18 y/o, primary tumour, histologically confirmed superficial or nodular BCC, area 0.5 cm^2-2.0 cm^2 for superficial or 0.25 cm^2-1.5 cm^2 for nodular | previous therapy to the target tumour or any dermatological conditions that would interfere with local assessments. | Biopsy/pathologic confirmed: prestudy confirmatory punch, deep shave, or wedge biopsy that removed no more than approximately 25% of the tumour | Visual assessment: measuring and multiplying the two largest perpendicular dimensions of the tumour. The tumour site and appropriate anatomic landmarks were mapped using a clear plastic sheet as a template to guide the excision at the end of the study | 183/177 |
| Szeimies 2008 18624836 (United Kingdom/Germany/Switzerland/Australia) | Multicenter | Industry funded | >= 18 y/o; primary sBCC suitable for simple excision surgery; confirmed by histology; no histological evidence of aggressive growth patterns | > 5 eligible lesions; lesions located in nose, nasolabial, or orbial areas; lesions w/ Ø <8 mm or >20 mm; recurrent lesions; lesions located in severely sun-damaged skin where surgery was not suitable due to frequent recurrence/ occurrence of other BCCs in the same area; lesions located close to or involving a scar of SCC; pigmented, morpheaform or infiltrating lesions on the treated area; at risk in terms of precautions, warnings, and contraindications as indicated in MAL-PDT package insert; pregnant or breastfeeding women. | Biopsy/pathologic confirmed: biopsy at screening | Method of assessment not reported | 196/196/196 |
| Thissen 2000 10940063 (Netherlands) | Single center | No industry support | superficial or nodular BCCs, clinically <2 cm Ø, localized anywhere in the head and neck area | recurrent BCCs, histologic subtypes not nodular or superficial, >2 cm Ø, >=5 BCCs, and contraindications to surgery or cryosurgery (eg, cold intolerance). LE <1 yr. | Method of diagnosis not reported | Visual assessment: Before treatment, the tumors were documented with photographs | 96/96/96 |
| Torres 2004 15606733 (loma linda, CA; boston, MA) | Multicenter | Industry funded | biopsy proven BCC; <=25% of the lesion removed at time of biopsy. 18 y/o, histologically confirmed, primary, superficial, nodular, or mixed superficial and nodular BCC. Target tumor consistent w/ BCC w/ no histologic evidence of aggressive growth patterns, including severe squamous metaplasia, morpheaform or infiltrative/desmoplastic features, or basosquamous features, and suitable for treatment with Mohs. area >=0.5 cm2 and Ø <2.0 cm and could be located on an acceptable area of the body as determined by the investigator. | previous therapy to the target tumor or dermatologic conditions that could interfere with skin assessments. | Biopsy/pathologic confirmed | Visual assessment: use of tattoo in center of lesion | 72/72/69 |
| Tran 2012 22511036 (US) | Single center | Not reported | Caucasian, Fitzpatrick skin type I or II, 46-84 y/o. Superficial, nodular, multicentric BCCs, and SCCIS 0.4–3 cm | Morpheaform, infiltrating, and recurrent BCCs and invasive SCCs or lesions on the head and neck, hands, feet, and genital areas. | Biopsy/pathologic confirmed | Visual assessment | 20/20/20 |
| van der Geer 2012 22385074 (Netherlands) | Single center | No industry support | >18 y/0ears w/ nodular (or nodular and partially superficial) BCC 1–5 cm Ø in the face | pregnant women, women who were breastfeeding, recurrent BCC, aggressive growth pattern, pts w/ BCC w/in 1 cm from the eyes, lips or mucosa of the nose, another skin tumour w/in 5 cm of the target tumour, and allergy to imiquimod 5% cream or components of the cream | Biopsy/pathologic confirmed | Phtotgraphy and computer assesment | 70/70/70 |
| Wang 2001 11298545 (England) | Single center | Industry funded | histopathologically verified BCC suitable for PDT and cryosurgery, 20-90 y/o | pregnancy/lactation; severe malignancies; daily intake of vitamins E or C, b-carotene, iron preparations, non-steroidal anti-inflammatory agents or strong analgesics in higher than specified doses; BCC on the nose; morphoeic growth; porphyria; abdominal pain of unknown aetiology; photosensitivity;and treatment of the BCC with topical steroids type III or IV within the last month. | Biopsy/pathologic confirmed | Method of assessment not reported | 88/88/83 |
| Wettstein 2013 23566745 (Switzerland) | Single center | Industry supplied materials | diagnosed clinically or by biopsy w/ primary nodular BCC of the face presenting at the University Hospital Basel between June 2007 and February 2008 | patients under steroid medication or immunosuppressive therapy; patients with direct defect closure; pathological analysis revealed incomplete tumour resection or another BCC sub-type than solid/nodular | Biopsy/pathologic confirmed | Confocal assessment | 32/23/23 |
| NRCS |  |  |  |  |  |  |  |
| Ahmed 2000 11069453 (UK) | Multicenter | Not reported | clinical diagnosis of Bowen's Disease | Patients with recurrent lesions and those on immunosuppression | Biopsy/pathologic confirmed: biopsy-proven | Method of assessment not reported | 73/67 |
| Ballester-Sanchez 2016 26985197 (Spain) | Single center | Industry funded | adults, primary superficial or nodular BCC w/ T1 and T2 clinical stage | Ø >20 mm , depth >4 mm, or located on irregular surfaces | Biopsy/pathologic confirmed: histopathologic examination | Visual assessment: clinically aided by dermoscope | 40/40 |
| Chren 2013 23190903 (U.S.) | Multicenter | No industry support | consecutive patients with nonrecurrent NMSC diagnosed in 1999 and 2000 and treated in 2 sites, a university-affiliated private dermatology practice and the dermatology clinic at the nearby VA medical center affiliated with the university |  | Biopsy/pathologic confirmed: Biopsies were performed either by dermatology faculty members or by dermatology residents | Method of assessment not reported | 1253/1174 |
| Cosgarea 2012 22738399 (Romania) | Single center | No industry support | Men or women >18 y/o, clinically diagnosised primary BCC, superficial or nodular BCC, with a maximum 3 mm above the skin level | recurrent, pigmented or morpheaform lesions; use of phototoxic ⁄ photosensitive drugs, hypersensitivity to light or ALA cream, pregnant or breastfeeding women | Biopsy/pathologic confirmed: histologically confirmed | Method of assessment not reported | 72/72 |
| Graells 2014 24139468 (Spain) | Single center | Not reported | patients treated for their first BCC at the hospital between January 2003 and December 2011 | patients followed for less than 3 months | Biopsy/pathologic confirmed: histologically confirmed BCCs | Method of assessment not reported | 623/621 |
| Lippert 2013 23725586 (Czech Republic) | Single center | No industry support | one confirmed nBCC, and there was one tested nBCC per person, Ø 20-30 mm | tumors in the middle portion of the face and areas adjacent to the eyes and ears | Biopsy/pathologic confirmed: Verified by biopsy sample from the peripheral portion of the tumor, which was as small as possible so that the area intended for the experiment was not reduced, | Other: thickness measured using high-resolution ultrasound | 56/56 |
| Pampena 2016 26589877 (Italy) | Single center | No industry support | Histologically verified NMSC | lymphatic or visceral metastases | Biopsy/pathologic confirmed: histologically confirmed | Method of assessment not reported | 385/385 |
| Shah 2009 19588534 (U.S.) | Single center | No industry support | male patients w/ biopsy-proven BCCs on the trunk and extremities | Morpheaform, infiltrative, and recurrent BCCs | Biopsy/pathologic confirmed: biopsy-proven | Method of assessment not reported | 32/32 |
| Sofen 2015 25913533 (U.S.) | Multicenter | Industry funded | >=21 y/o, new, operable, biopsy-confirmed, nodular BCC and willing to delay excision |  | Biopsy/pathologic confirmed: biopsy-confirmed | Method of assessment not reported | 74/49 |
| Sullivan 2003 14725659 (US) | Single center | Not reported | biopsy confirmed superficial BCC, Ø 0.8-2.0 cm on the neck, trunk, or limbs. | recurrent or previously treated tumors or tumors located on the head | Biopsy/pathologic confirmed | Method of assessment not reported | 12/12 |
| Wilson 2012 22145798 (U.S.) | Multicenter | No industry support | NMSCs identified by daily review of pathology records and defined according to final histopathologic diagnosis of BCC or SCC. | No "recurrent" or "possibly recurrent" skin cancers | Biopsy/pathologic confirmed | Method of assessment not reported | 1777/1777 |

\*y/o = years old; w/ = with, Ø = diameter; LE = life expectancy; tx = treatment; mo = month; rt = radiation therapy