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Data synthesis

Extracted information was tabulated by cancer type to facilitate a qualitative analysis of trends or patterns across studies. Where possible, pooled effect estimates were calculated (e.g., weighted mean differences).

Results

Over 3,000 studies were identified through the literature search, of which 266 met the selection criteria and were included in the review. The 266 studies, which spanned 33 different cancers, comprised 44 comparative (Table 1) and 222 non-comparative studies (Table 2), and involved a total of 11,427 patients.

Comparative studies

Cancer indications with the greatest number of comparative studies were lung (9 studies) and basal cell carcinoma (BCC) (9 studies). All of the BCC studies were randomized controlled trials (RCTs). In contrast, the vast majority of lung cancer studies were cohort studies. Of the BCC RCTs, most were: 1) single-blinded (patients were unaware of the treatment received), 2) compared PDT with aminolevulinic acid (ALA) to surgery, and 3) followed patients for approximately one year. Although all 7 cohort studies of lung cancer employed the same photosensitizing agent (porfimer sodium), they were retrospective in design and typically included patients with different types of lung cancer. Further, findings were presented for the sample in its entirety, rather than by lung cancer sub-type.

Among the remaining cancers with comparative studies available, all were associated with 3 or fewer RCTs. Moreover, the RCTs were often non-blinded, involved small sample sizes, and had follow-up periods of less than 1 year. Also, in several cases, the comparator was not 'active' conventional treatment (e.g., in the case of breast cancer and mesothelioma). Therefore, despite the availability of RCTs, the quality of the evidence was limited.

Non-comparative studies

Of the non-comparative studies, the majority were small retrospective case series, a study design near the bottom of the strength/level of evidence scale. Despite the large number of studies found for esophageal cancer and non-melanoma skin cancers, patient inclusion criteria (e.g., cell line involved, stage of cancer, previous treatments, etc.) frequently varied across studies, as did the PDT protocol (e.g., photosensitizing agents and light sources). Finally, for 20% of the cancer indications, the evidence base comprised a single study.

Against this backdrop, the following section provides a brief summary of the findings of studies conducted to date for each cancer.

Anal or perianal cutaneous

The 4 non-comparative studies collectively included 19 patients with different types of cancer in the perianal or anal region, and used 3 different photosensitizing agents: oral ALA, topical ALA, and porfimer sodium [2-5]. While'pain at the treatment site' comprised the only adverse event reported across the 4 studies, it was experienced by almost all of the patients. The percentage of patients who achieved and maintained a complete response (i.e., initial eradication of the lesion) ranged from 40% to 100%, based on follow-up periods from less than 6 months to 8 years.

Bile duct

Twelve of the 17 studies were non-comparative [6-17]. Of the 5 comparative studies, 2 were small RCTs involving patients with advanced or unresectable disease [18-22]. Typically, the studies compared stenting alone to stenting plus PDT. Among comparative studies, the most commonly reported serious adverse event was bacterial infection, which affected patients in both the PDT and non-PDT treatment groups. Almost all of the studies reported skin photosensitivity in some patients receiving PDT. In general, the main outcome measured was survival. Findings were consistent

Type of cancer	Comparative studies (N)	Type of comparative study					Total number of patients in comparative studies
		Randomized Controlled Trial	Non-randomized controlled trial	Cohort study	Case-control study	Other	
Bile duct [18-22]	5	2	0	2	1	0	327
Breast [35]	1	1	0	0	0	0	68
Cervical [41-43]	3	1	2	0	0	0	99
Esophageal - early [50]	1	0	0	1	0	0	88
Esophageal – advanced/ inoperable [51,74,75]	3	1	0	1	0	1	251
Gastrointestinal [95]	1	0	1	0	0	0	11
Head and neck – nasopharyngeal [101]	1	1	0	0	0	0	30
Lung [133-141]	9	2	0	7	0	0	597*
Mesothelioma [160,161]	2	1	1	0	0	0	62
Skin – basal cell [175-183]	9	9	0	0	0	0	942
Skin – squamous [184-186]	3	1	2	0	0	0	288
Skin – Bowen [187-189]	3	3	0	0	0	0	96
Skin – multiple (non-melanoma) [190]	1	1	0	0	0	0	23
Vulval [257,258]	2	0	1	1	0	0	226
Total	**44**	**23**	**7**	**11**	**1**	**1**	**3108**

*Number of patients not reported for one study (reported number of lesions instead)

Table 1: Number of comparative studies according to cancer type.

Type of cancer	Non-comparative studies	Type of non-comparative study				Total number of patients in non-comparative studies
		Single arm trial	Prospective case series	Retrospective case series	Case report	
Anal [2-5]	4	0	2	1	1	19
Bile duct [6-17]	12	4	1	7	0	181
Bladder [23-29]	7	5	0	2	0	190
Brain [30-34]	5	3	0	2	0	292
Breast [36-40]	5	3	0	2	0	48
Cervical [44-49]	6	5	0	1	0	327
Esophageal - early [51-73]	23	0	14	9	0	413
Esophageal – advanced/inoperable [62,76-83]	9	0	3	6	0	566
Eye [84-94]	11	1	1	6	3	97
Gastrointestinal [96-100]	5	3	1	1	0	96
Head and neck – nasopharyngeal [102]	1	0	0	0	1	1
Head and neck – oral and laryngeal [103,104,261]	3	1	0	3	0	326
Head and neck – oral [108-116,262]	10	3	1	6	0	393
Head and neck – laryngeal [263,264]	2	2	0	0	0	34
Head and neck – oral and pharyngeal [118-120]	3	0	0	3	0	27
Head and neck [121-128,265,266]	10	7	1	2	0	343
Intraperitonealcarcinomatosis and sarcomatosis [130,131]	2	2	0	0	0	122
Colorectal – metastatic (liver) [132,267]	2	2	0	0	0	31
Lung [142-159]	18	4	2	10	2	1154
Mesothelioma [162,163,268]	3	3	0	0	0	104
Ovarian [165]	1	1	0	0	0	8
Pancreatic [269]	1	0	0	1	0	16
Pituitary [167]	1	1	0	0	0	12
Prostate [168-173]	6	5	0	1	0	111
Sarcoma [174]	1	1	0	0	0	10
Skin – basal cell [191-213]	23	1	14	7	1	1302
Skin – Bowen's [237,238]	2	0	1	0	1	15
Skin – multiple (non-melanoma) [214-236]	23	3	9	11	0	1887*
Skin – cutaneous T-cell lymphoma [243-249]	7	1	0	3	3	22
Skin – Kaposi's sarcoma [241,242]	2			1	1	26
Skin – melanoma [239,240]	2	0	0	2	0	63
Skin – Paget's disease, extra-mammary [4,220,222,250-256]	10	1	2	4	3	52
Vulval [259,260]	2	1	1	0	0	31
Total	**222**	**61**	**52**	**89**	**16**	**8319**

*Number of patients not reported for one study (reported number of lesions instead)

Table 2: Number of non-comparative studies according to cancer type.

across comparative studies, with median survival in patients treated with stenting and PDT statistically significantly greater (2 to 3 times longer) than in those receiving stenting alone. In contrast, some studies reported complete elimination of bile duct stenosis in patients who underwent PDT and stenting, while others reported only partial clearance in such patients. Across studies that assessed quality of life, scores either remained stable or improved following PDT treatment. Therefore, despite the lack of 'level 1' evidence, given the severity of the disease and magnitude of the effect observed, PDT appears to be a promising treatment for this indication.

Bladder

All 7 studies were either case series (2) or single arm phase I/II clinical trials (5), and the majority used 5-ALA as the photosensitizing agent [23-29]. While they involved similar patients, sample sizes were small. Further, patients in over half of the studies had received additional therapies immediately prior to treatment or during the follow-up period, making it difficult to assess the effect of PDT. Across studies, commonly reported adverse events included hematuria (13% to 100%) and dysuria (13% to 100%), both of which resolved within 3 weeks. More serious adverse events, such as vesicoureteral reflux (14% of patients), bladder contracture (39% of patients), and bladder spasm (29% of patients) were associated with higher doses of photosensitizing agents. Although the main outcomes assessed in studies were typically 'complete response' (total eradication of the lesion(s)) and 'recurrence', the time points at which they were measured varied. Based on findings for the most frequently used points, the percentage of patients who had achieved a complete response at 3 months follow-up ranged from 44% to 100% across studies. The percentage of those patients who

subsequently experienced a recurrence within 2 years ranged from 46% to 79%.

Brain

The 5 studies found represented 3 single arm clinical trials and 2 retrospective case series, which collectively involved 292 patients [30-34]. Studies typically involved patients with different types of brain tumours who were also receiving concurrent surgical resection and/or chemotherapy. Therefore, it was not possible to isolate the effect of PDT on disease progression or survival in patients with specific tumour types. Similarly, although 3 treatment-related deaths and a series of other non-fatal adverse eventswere reported across the 5 studies, any cause-effect relationship to PDT could not be determined. The most commonly experienced adverse events were cerebral edema and temporary neurological deficits (including facial weakness and partial paralysis), both occurring in less than 6% of patients. Median survival following PDT varied by tumour type, and ranged from 6 months to 77 months.

Breast

Six small studies, all published between 1998 and 2005, were identified - 5 non-comparative and 1 comparative (RCT) [35-40]. Combined, they represented 116 patients who were followed for a maximum of 6 months post treatment with PDT. The single RCT, which compared PDT to no treatment in patients who had failed salvage external beam radiation, was non-blinded and multi-centered. Five of the 6 studies reported on adverse events. Approximately 40% of patients experienced chest wall pain within the first few weeks of treatment. In addition, 14% to 40% (depending on the study) developed redness and inflammation in light exposed areas. Across studies, 'complete response' measured at 6 months comprised the main outcome. The percentage of patients in whom lesions were totally eradicated ranged from 43% to 100%. None of the studies presented information on recurrence within the 6 month follow-up period. In those that reported healing time, the period was 2 to 3 months.

Cervical

One double-blind, placebo controlled RCT, 2 non-RCTs, 5 single arm clinical trials, and 1 retrospective case series, all published between 1999 and 2004, were found [41-49]. While the 3 comparative trials recruited similar patient populations, comparators, PDT protocol (including photosensitizing agent, route of administration, and light source), and follow-up time differed. This was also the case with the non-comparative studies. Nonetheless, with one exception, similar adverse events were reported. They included vaginal discomfort, vaginal discharge, pelvic pain, vaginal bleeding, and mild cramping. The exception was skin photosensitivity and cervical stenosis, which was only experienced by patients who had received porfimer sodium or hematoporphyrin derivative. Across all studies, complete response ranged from 0% to 97%. Importantly, among comparative studies, no statistically significant difference in the proportion of patients achieving a complete response between treatment and control groups was observed. Further, there was no difference in recurrence or the likelihood of eradicating signs of HPV between groups.

Esophageal – early

Of the 24 studies found, all but one was non-comparative [50-73]. In general, patients had TI tumours or stage I disease. Published in 2003, the single comparative study was a small, retrospective cohort study (88 patients) that compared endomucosal resection and PDT to esophagectomy in 2 groups of patients who were followed for approximately 12 months [50]. Regardless of study type, the most commonly reported adverse events associated with PDT included esophageal stricture, redness, and skin photosensitivity, occurring in up to about half of patients. From the results of the single comparative study, strictures were more common following esophagectomy than after PDT (16% of patients vs. 8% of patients). Also, anastomotic leaks and infections were reported in 8% of patients, and 3% developed severe bleeding requiring a transfusion or atrial fibrillation. Moreover, treatment-related deaths were reported in 2% of patients who underwent surgery, but in none of the patients who received PDT. Combining findings from all of the studies, the percentage of patients achieving a complete response appeared to vary with cell type. For esophageal adenocarcinoma (ACC) and squamous cell esophageal carcinoma (SCC), the pooled mean complete response was 54% and 71%, respectively. Across studies of SCC, recurrence was reported in 19% of patients after an average follow-up of 18 months. In contrast, only 3% of the ACC patients relapsed after an average follow-up of 24 months. In the ACC studies, recurrence did not appear to vary with photosensitizing agent. Although 6 of the studies reported 5 year survival (cause-specific or overall), it was not possible to accurately estimate the survival benefit attributable to PDT because patients who relapsed typically received other treatments, the details of which were not presented.

Esophageal – advanced or inoperable

Between 1999 and 2009, twelve studies were published – 3 comparative and 9 non-comparative [51,62,74-83]. The 3 comparative studies comprised 1 RCT, 1 prospective cohort study, and 1 comparative case series. Of the non-comparative studies, there were 8 retrospective case series and 1 case report. Neither the RCT nor the cohort study compared PDT to non-PDT interventions. Rather, the RCT used PDT plus chemotherapy with 5-flurouracil as the comparator, and the cohort compared two different photosensitizing agents. In the comparative case series, only patients who failed PDT received the comparator treatment (radiotherapy). Therefore, from the comparative studies, it was not possible to assess the *incremental* benefits and risks of PDT to existing treatments. Regarding adverse events, among the most commonly reported were chest pain (10% to 17%), fistulae (2% to 17%), stricture (2% to 11%), stenosis (7% to 25%), pain on swallowing (33% to 64%), and skin photosensitivity (4% to 100%). Across studies, dysphagia improved after PDT in almost all patients (87% to 100%). This improvement was maintained for approximately 2 months. No survival information was presented for the RCT. However, based on findings from the cohort study, survival did not statistically significantly vary with type of photosensitizing agent (ALA: 8 months vs. Polyhematoporphyrin: 9 months).

Eye

All 11 studies found, published between 2004 and 2009, were non-comparative [84-94]. Collectively, they involved 97 patients with different types of cancer (in many cases, metastases from other organs), almost all of whom were treated with the same photosensitizing agent. Adverse events, presented in less than half of the studies, included retinal haemorrhage and edema, retinal detachment, cystoid macular edema, and epiretinal membrane formation. In all studies, complete eradication of or significant reduction in tumour mass following PDT was demonstrated. In addition, most reported slight improvements in visual acuity.

Gastrointestinal

The 6 studies (1 non-RCT, 3 single arm clinical trials, and 2 case series) were all published between 1998 and 2002 [95-100]. Of the collective 107 patients treated, the majority had early gastric carcinoma. The remaining patients were those with intraperitoneal tumours which had spread from gastrointestinal malignancies. The single non-RCT examined PDT with and without the use of a device for marking the area to be irradiated prior to treatment. Therefore, no information regarding the relative effectiveness of PDT (i.e., PDT compared to existing treatment(s)) appears to be available. In patients with early gastric carcinoma, adverse events included skin photosensitivity (8% to 86%) and temporary epigastric pain (55%). In patients with intraperitoneal tumours, more serious adverse events, such as capillary leak syndrome (100%) and intra-abdominal abscesses (7%) were reported. The percentage of patients with early gastric cancer who achieved a complete response ranged from 67% to 100%. Tumour eradication was not reported for patients with intraperitoneal tumours. In patients with early gastric cancer, survival following PDT ranged from 3 years to over 13 years. In patients with intraperitoneal tumours, survival was significantly shorter, averaging 21 months.

Head and neck

A total of 30 studies involving 1,323 patients were found [101-129]. Published between 1998 and 2010, all but 1 was non-comparative. Also, for many of the studies, information on patient demographics and the PDT protocol applied was not presented. Across studies in which such information was presented, cancer type and location, photosensitizing agents,and methods for determining treatment response differed. Further, in many of the studies, patients received therapies in addition to PDT during follow-up, precluding an assessment of the effect associated with PDT, alone. Commonly reported adverse events included 'pain at the treatment site' (11% to 82%), edema (10% to 100%), and skin photosensitivity (2% to 25%). One death attributed to carotid blow out after erosion of the treated tumour in a patient with metastatic disease was reported. The percentage of patients in whom an initial complete response with PDT was reported ranged from 8% to 100%. However, disease recurrence was observed in 8% to 75% of patients across studies. In studies that assessed functional status, no significant detrimental changes in oral cavity functional status after PDT were found. In the single RCT, which compared PDT to chemotherapy, greater improvements in quality of life were demonstrated for PDT.

Intraperitoneal carcinomatosis or sarcomatosis

Two studies were found, one published in 2003 and the other in 2006 [130,131]. Both comprised small, single arm clinical trials that employed PDT as an adjunct to surgical debulking in 122 patients. The most common adverse event was capillary leak syndrome. There were 2 deaths, 1 from a myocardial infarction and 1 due to intra-abdominal bleeding. Minor adverse events, which occurred in 29% of patients, were primarily related to skin photosensitivity. In both studies, less than 25% of patients achieved a complete response with PDT. Median overall survival following treatment ranged from 13 months to 22 months.

Colorectal with liver metastases

Two single arm clinical trials involving a total of 31 patients were identified [14,132]. Published between 2005 and 2007, they employed different PDT protocols and followed patients for a maximum of 60 days. Serious adverse events included severe abdominal pain, bleeding from the treated tumour, and pancreatic injury. The main outcome measure in both trials was tumour response. None of the patients in either of the studies experienced complete tumour regression.

Lung

Twenty-seven studies published between 1997 and 2009 were found [133-159]. Collectively, they involved 1,751 patients, each of whom participated in 1 of 9 comparative and 18 non-comparative studies. The majority, including the 2 RCTs, involved patients with non-small cell lung cancer (NSCLC). Both RCTs and 2 of the 7 retrospective cohort studies compared PDT to laser therapy (ND:YAG). Of the remaining 5 retrospective cohort studies, 2 compared PDT alone to PDT combined with other non-surgical therapies, 1 compared PDT or laser therapy to surgery, 1 compared PDT to bronchoscopic electrocautery or laser therapy, and 1 compared PDT to stenting, laser therapy, or high dose brachytherapy, either alone or in combination with laser therapy. In general, the 18 non-comparative studies involved small patient populations with various types and stages of cancer who were followed over short periods. In addition, PDT was often applied in combination with other therapies. The most commonly reported adverse events were skin photosensitivity (3% to 91%) and pneumonia (2% to 9%). While several deaths were noted, they occurred in patients who had received PDT as an adjunct to brachytherapy or surgery. Based on findings from the multiple comparative studies of PDT versus laser therapy, no statistically significant differences in response rates at 1 month post treatment were found. Also, no differences in symptom improvement between treatment groups were demonstrated. However, the overall survival rate at 1 year following treatment was greater in patients treated with PDT compared to those who had received laser therapy. Equivalent information was not available for patients with other types of lung cancer.

Mesothelioma

Five studies published between 1994 and 2004 and involving a total of 166 patients were identified [160-164]. They comprised 1 RCT, 1 non-RCT, and 3 single arm (phase I/II) clinical trials. In both the RCT and non-RCT, PDT plus conventional therapy (surgery without or without chemotherapy) was compared to conventional therapy. Similarly, across all 3 non-comparative studies, PDT was performed as an adjunct to surgery. Therefore, it was not possible to determine the effects of PDT, alone. Neither comparative trial reported statistically significant differences in the type and frequency of adverse events between patients who received PDT plus conventional therapy and those who received just conventional therapy. Also, there were no statistically significant differences in time to disease recurrence between those treated with PDT plus conventional therapy and those treated with conventional therapy, alone. Across all studies, median survival ranged from 8 months to 15 months. However, based on findings from the single RCT, survival did not improve with the addition of PDT. Also, no statistically significant differences in relief from clinical symptoms or improvement in pulmonary function were found between patients who received PDT in addition to conventional therapy and those who just received conventional therapy.

Ovarian

Existing studies appear limited to 1 retrospective case series published in 1997 [165]. It included 131 patients in whom PDT was performed as an adjunct to surgical debulking by laparotomy or laparoscopy. Adverse events included skin photosensitivity and intestinal ileus (incidence not reported). Decreasing concentrations

of serum cancer markers reaching tumour free levels at 8 weeks were observed in 50% of patients. In addition, an improvement of 10% or greater in Karnofsky index scores were reported in 38% of patients.

Pancreatic

One single arm clinical trial of 16 patients who underwent PDT plus stenting was found [166]. Adverse events included hematoma (6 patients), duodenal bleeding requiring transfusion (2 patients), and duodenal stenosis (3 patients). Median survival post-PDT was 9.5 months. After 2 years of follow-up, overall survival was 13%.

Pituitary

The search identified 1 small single arm trial of PDT for pituitary gland cancer [167]. Twelve patients who had failed surgical treatment, radiotherapy, and chemotherapy underwent intra-operative PDT with porfimer sodium. Follow-up ranged from 10 days to 24 months. Adverse events were reported in one patient, who experienced temporary partial paralysis and skin photosensitivity. In the majority of patients, tumour volume decreased (mean reduction of 46%). All 12 patients demonstrated an improvement in visual acuity and field.

Prostate

All 6 studies identified, which involved a total of 111 patients, were non-comparative [168-173]. Five comprised single arm clinical trials published between 2002 and 2011. The remaining study was a retrospective case series published in 1998. Across studies, disease stage varied, as did the photosensitizing agent. Commonly reported adverse events included irritative urinary symptoms, reported in up to 46% of patients. The percentage of patients achieving a complete response with PDT ranged from 0% to 40%. Although PSA levels also decreased, they were not maintained over time. None of the studies reported on quality of life or survival.

Sarcoma

One small single arm trial of 10 patients followed for up to 51 months was found [174]. No adverse events were reported, and recovery of limb function to pre-operative levels was observed in 90% of patients. At the time of follow-up, overall survival among patients was 100%.

Skin – non-melanoma

Sixteen comparative studies [175-190] and 48 non-comparative studies [191-238] involving 1,349 patients and 3,189 patients, respectively, were identified. Nine of the 16 comparative studies were RCTs of patients with BCC. Of those 9 RCTs, 4 compared PDT to either surgical excision (2 trials) or cryotherapy (2 trials) and 5 compared different PDT protocols. The 7 remaining comparative studies included 3 trials in patients with squamous cell carcinoma - 1 single-blinded RCT comparing PDT to no treatment and 2 non-RCTs comparing PDT to placebo, cryotherapy, or topical 5-flurouracil and PDT with 2 different photosensitizing agents. It also included 3 RCTs of patients with Bowen's disease. However, none compared PDT to other treatment modalities. Instead, different PDT protocols were examined. Commonly reported adverse events related to PDT were similar for comparative and non-comparative studies of different cell types, and included intra- and post-procedural pain that resolved within a few days, redness and swelling lasting less than 2 weeks, and hyper- or hypo-pigmentation lasting several months. Across the comparative studies, no statistically significant difference in pain following treatment with PDT compared to cryosurgery was found. However, where surgical resection was compared to PDT, PDT was associated with statistically significantly more pain. In contrast, among patients treated with 5-fluorouracil, post-procedural pain was statistically significantly greater than that reported in patients who underwent PDT. In almost all of the studies, the main outcomes measured were the proportions of patients achieving a 'complete response' and experiencing recurrence. Across all studies of basal cell carcinoma, a complete response was reported for 42% to 97% of lesions, and recurrence ranged from 0% to 45%. Among the comparative studies, 1 RCT reported a statistically significantly higher complete response rate in patients who underwent surgery compared to those who received PDT. In trials of PDT compared to cryotherapy, no statistically significant differences were observed. Among the RCTs of various PDT protocols, 2 sessions of treatment (versus 1 session) were associated with higher complete response rates and less recurrence. Across comparative and non-comparative studies of squamous cell carcinoma, a complete response was reported for 25% to 100% of lesions treated with PDT. Recurrence ranged from 0% to 69%. With 1 exception, none of the comparative studies of PDT for squamous cell carcinoma presented information on the statistical significance of differences between treatment groups. The single study that did, an RCT of PDT versus no treatment in organ transplant recipients, found no difference in complete response rates between groups. For Bowen's disease, the proportion of patients achieving a complete response in studies ranged from 25% to 100%. While 1 of the comparative trials assessed PDT relative to a different treatment modality, the statistical significance of the difference in complete response rates was not reported.

Skin – melanoma

Only 2 small retrospective case series, 1 published in 2002 and the other in 2004, were identified [239,240]. Collectively, they included 63 patients. Across studies, PDT protocols and follow-up times differed. One study reported no adverse events. In the other, pain lasting less than 5 days was observed in just over half of patients, and 15% developed a fever. While 93% of patients achieved a complete response in one of the studies, none responded completely in the other study. However, 84% experiences at least a 50% decrease in lesion size.

Skin – Kaposi's sarcoma

Two small retrospective studies, 1 case report (published in 2006) and 1 retrospective case series of 26 patients (published in 1999), were found [241,242]. Only the case series presented information on adverse events, which consisted of skin photosensitivity in 28% of patients. The pooled proportion of patients achieving a complete response was 32%. No information on recurrence was presented.

Skin – cutaneous T-cell lymphoma

All 7 studies identified were non-comparative and published between 1997 and 2008 [243-249]. Involving a total of 22 patients, they comprised 3 retrospective case series, 3 case reports, and 1 single arm trial. All but 1 of the studies reported on adverse events, which frequently included pain, redness, and swelling. Across studies, the percentage of patients who experienced a complete response ranged from 78% to 100%. During follow-up periods of 4 to 34 months (depending on the study), no recurrence was observed.

Skin – extra-mammary Paget's disease

Ten non-comparative studies published between 2000 and 2011 were found [4,220,222,250-256]. They included 52 patients, and represented 1 single arm clinical trial, 2 prospective case series,

2 retrospective case series, and 3 case reports. In almost half of the studies, no information related to adverse events was presented. Among those reporting on adverse events, the most common were pain and burning during and several hours following PDT. All studies assessed complete response, which was achieved in approximately half of the lesions treated.

Vulval

Of the 4 studies identified, 2 were comparative and 2 were non-comparative [257-260]. The 2 comparative studies, published in 2002 and 2006, included 1 non-RCT and 1 prospective cohort study, and collectively involved 226 patients. The 2 non-comparative studies, published in 2000 and 2004, comprised 1 single arm trial of 25 patients and 1 prospective case series of 6 patients. Both the non-RCT and cohort study compared PDT to laser therapy or surgical excision. Reporting of adverse events appeared to be limited to patients who underwent PDT. The most common was pain lasting up to 1 week. Across all studies, the proportion of patients experiencing a complete response with PDT ranged from 50% to 67%. Based on findings from the comparative studies, recurrence and disease free survival was similar among patients receiving PDT, laser, or surgery.

Conclusion

This review considered 44 comparative studies and 222 non-comparative studies of PDT for 33 different types of cancer. Despite the availability of double blind RCTs, few involved treatment and control groups that facilitated an assessment of the increment benefit of PDT alone.

References

1. Phillips B, Ball C, Sackett D, Badenoch D, Straus S, et al. (2001) Oxford Centre for Evidence-based Medicine levels of evidence and grades of recommendation. Oxford (UK) Oxford Centre for Evidence-based Medicine.
2. Webber J, Fromm D (2004) Photodynamic therapy for carcinoma in situ of the anus. Arch Surg 139: 259-261.
3. Hamdan KA, Tait IS, Nadeau V, Padgett M, Carey F, et al (2003) Treatment of Grade III anal intraepithelial neoplasia with photodynamic therapy - Report of a case. Diseases of the Colon & Rectum 46: 1555-1559.
4. Runfola MA, Weber TK, Rodriguez-Bigas MA, Dougherty TJ, Petrelli NJ (2000) Photodynamic therapy for residual neoplasms of the perianal skin. Dis Colon Rectum 43: 499-502.
5. Allison RR, Sheng C, Cuenca R, Bagnato VS, Austerlitz C, et al. (2010) Photodynamic therapy for anal cancer. Photodiagnosis Photodyn Ther 7: 115-119.
6. Pereira SP, Ayaru L, Rogowska A, Mosse A, Hatfield ARW, et al. Photodynamic therapy of malignant biliary strictures using meso-tetrahydroxyphenylchlorin. European Journal of Gastroenterology and Hepatology 19: 479-485.
7. Pereira SP, Ragunath K, Devlin J, Meadows HM (2005) Preliminary results of a phase II trial to examine the safety and efficacy of porfimer sodium photodynamic therapy (PDT) in locally advanced biliary tract carcinoma (BTC). Journal of Clinical Oncology 23: 4180.
8. Harewood GC, Baron TH, Rumalla A, Wang KK, Gores GJ, et al. Pilot study to assess patient outcomes following endoscopic application of photodynamic therapy for advanced cholangiocarcinoma. J Gastroenterol Hepatol 20: 415-420.
9. Berr F, Wiedmann M, Tannapfel A, Halm U, Kohlhaw KR, et al. (2000) Photodynamic therapy for advanced bile duct cancer: evidence for improved palliation and extended survival. Hepatology 31: 291-298.
10. Prasad GA, Wang KK, Baron TH, Buttar NS, Wongkeesong L, et al. (2007) Factors associated with increased survival after photodynamic therapy for cholangiocarcinoma. *Clinical* Gastroenterology and Hepatology 5: 743-748.
11. Nanashima A, Yamaguchi H, Shibasaki S, Ide N, Sawai T, et al. (2004) Adjuvant photodynamic therapy for bile duct carcinoma after surgery: A preliminary study. Journal of Gastroenterology 39: 1095-1101.
12. Shim CS, Cheon YK, Cha SW, Bhandari S, Moon JH, et al. (2005) Prospective study of the effectiveness of percutaneous transhepatic photodynamic therapy for advanced bile duct cancer and the role of intraductal ultrasonography in response assessment. Endoscopy 37: 425-433.
13. Suzuki S, Inaba K, Yokoi Y, Ohata K, Ota S, et al. (2004) Photodynamic therapy for malignant biliary obstruction: A case series. Endoscopy 361: 83-87.
14. Rumalla A, Baron TH, Wang KK, Gores GJ, Stadheim LM, et al (2001) Endoscopic application of photodynamic therapy for cholangiocarcinoma. Gastrointest Endosc 53: 500-504.
15. Zoepf T, Jakobs R, Arnold JC, Apel D, Rosenbaum A, et al. (2001) Photodynamic therapy for palliation of nonresectable bile duct cancer--preliminary results with a new diode laser system. Am J Gastroenterol 96: 2093-2097.
16. Zoepf T, Jakobs R, Rosenbaum A, Apel D, Arnold JC, et al. (2001) Photodynamic therapy with 5-aminolevulinic acid is not effective in bile duct cancer. Gastrointest Endosc 54:763-766.
17. Ortner M (2001) Photodynamic therapy for cholangiocarcinoma. J Hepatobiliary Pancreat Surg 20018: 137-139.
18. Zoepf T, Jakobs R, Arnold JC, Apel D, Riemann JF (2005) Palliation of nonresectable bile duct cancer: improved survival after photodynamic therapy. Am J Gastroenterol 100: 2426-2430.
19. Ortner ME, Caca K, Berr F, Liebetruth J, Mansmann U, et al. (2003) Successful photodynamic therapy for nonresectable cholangiocarcinoma: a randomized prospective study. Gastroenterology 125: 1355-1363.
20. Kahaleh M, Mishra R, Shami VM, Northup PG, Berg CL, et al. (2008) Unresectable cholangiocarcinoma: comparison of survival in biliary stenting alone versus stenting with photodynamic therapy. Clin Gastroenterol Hepatol 6: 290-297.
21. Witzigmann H, Berr F, Ringel U, Caca K, Uhlmann D, et al. (2005) Surgical and palliative management and outcome in 184 patients with hilar cholangiocarcinoma: Palliative photodynamic therapy plus stenting is comparable to R1/R2 resection. Annals of Surgery 244: 230-239.
22. Dumoulin FL, Gerhardt T, Fuchs S, Scheurlen C, Neubrand M, et al. (2003) Phase II study of photodynamic therapy and metal stent as palliative treatment for nonresectable hilar cholangiocarcinoma. Gastrointest Endosc 57: 860-867.
23. Skyrme RJ, French AJ, Datta SN, Allman R, Mason MD, et al. (2005) A phase-1 study of sequential mitomycin C and 5-aminolaevulinic acid-mediated photodynamic therapy in recurrent superficial bladder carcinoma. BJU Int 95:1206-1210.
24. Szygula M, Pietrusa A, Adamek M, Wojciechowski B, Kawczyk-Krupka A, et al. (2004) Combined treatment of urinary bladder cancer with the use of photodynamic therapy (PDT) and subsequent BCG-therapy: A pilot study. Photodiagnosis and photodynamic therapy1: 241-246.
25. Berger AP, Steiner H, Stenzl A, Akkad T, Bartsch G, et al. (2003) Photodynamic therapy with intravesical instillation of 5-aminolevulinic acid for patients with recurrent superficial bladder cancer: A single-center study. Urology 61: 338-341.
26. Manyak MJ, Ogan K (2003) Photodynamic therapy for refractory superficial bladder cancer: long-term clinical outcomes of single treatment using intravesical diffusion medium. Journal of Endourology 17: 633-639.
27. Waidelich R, Beyer W, Knuchel R, Stepp H, Baumgartner R, et al. (2003) Whole bladder photodynamic therapy with 5-aminolevulinic acid using a white light source. Urology 61: 332-337.
28. Shackley DC, Briggs C, Gilhooley A, Whitehurst C, O'Flynn KJ, et al. (2002) Photodynamic therapy for superficial bladder cancer under local anaesthetic. BJU Int 89: 665-670.
29. Nseyo UO, DeHaven J, Dougherty TJ, Potter WR, Merrill DL, et al. (1998) Photodynamic therapy (PDT) in the treatment of patients with resistant superficial bladder cancer: A long term experience. *Journal of Clinical Laser Medicine and Surgery* 16: 61-68.
30. Beck TJ, Kreth FW, Beyer W, Mehrkens JH, Obermeier A, et al. (2007) Interstitial photodynamic therapy of nonresectable malignant glioma recurrences using 5-aminolevulinic acid induced protoporphyrin IX. Lasers in surgery and medicine 39: 386-393.

31. Muller PJ, Wilson BC (2006) Photodynamic therapy of brain tumors - A work in progress. Lasers in Surgery and Medicine 38: 384-389.

32. Stylli SS, Kaye AH, MacGregor L, Howes M, Rajendra P (2005) Photodynamic therapy of high grade glioma - long term survival. J Clin Neurosci 12: 389-398.

33. Schmidt MH, Meyer GA, Reichert KW, Cheng J, Krouwer HG, et al. (2004) Evaluation of photodynamic therapy near functional brain tissue in patients with recurrent brain tumors. Journal of Neuro-Oncology 67: 201-207.

34. Aziz F, Telara S, Moseley H, Goodman C, Manthri P, et al. (2009) Photodynamic therapy adjuvant to surgery in metastatic carcinoma in brain. Photodiagnosis Photodyn Ther 6: 227-230.

35. Keefe K, Hashad R, Tromberg B, Monk B, DiSaia P, et al. (2000) Photodynamic therapy (PDT) of high-grade cervical intraepithelial neoplasia (CIN) with 5-aminolevulinic acid (ALA) . Gynecologic Oncology 79:141.

36. Wyss P, Schwarz V, Dobler-Girdziunaite D, Hornung R, Walt H, et al. (2001) Photodynamic therapy of locoregional breast cancer recurrences using a chlorin-type photosensitizer. Int J Cancer 9: 720-724.

37. Allison R, Mang T, Hewson G, Snider W, Dougherty D (2003) Photodynamic therapy for chest wall progression from breast carcinoma is an underutilized treatment modality. Cancer 91: 1-8.

38. Taber SW, Fingar VH, Coots CT, Wieman TJ (1998) Photodynamic therapy using mono-L-aspartyl chlorin e6 (Npe6) for the treatment of cutaneous disease: a Phase I clinical study. Clin Cancer Res 4: 2741-2746.

39. Sibata C, Allison R, Downie G, Childs C, Cuenca R (2005) Photodynamic therapy for salvage of radiation failure in breast cancer. International Journal of Radiation Oncology Biology Physics 63: 53-54.

40. Mang TS, Allison R, Hewson G, Snider W, Moskowitz R (1998) A phase II/III clinical study of tin ethyl etiopurpurin (Purlytin)-induced photodynamic therapy for the treatment of recurrent cutaneous metastatic breast cancer. Cancer J Sci Am 4: 378-384.

41. Barnett AA, Haller JC, Cairnduff F, Lane G, Brown SB, et al. (2003) A randomised, double-blind, placebo-controlled trial of photodynamic therapy using 5-aminolaevulinic acid for the treatment of cervical intraepithelial neoplasia. Int J Cancer 103: 829-832.

42. Kim SJ, Kim IH, Na YJ, Jeong CH, Kim JY, et al. (2004) Photodynamic therapy in the management of cervical intraeipthelial neoplasia. International Journal of Gynecological Cancer 14: 84.

43. Bodner K, Bodner-Adler B, Wierrani F, Kubin A, Szolts-Szolts J, et al. (2003) Cold-knife conization versus photodynamic therapy with topical 5-aminolevulinic acid (5-ALA) in cervical intraepithelial neoplasia (CIN) II with associated human papillomavirus infection: A comparison of preliminary results. Anticancer Research 23: 1785-1788.

44. Yamaguchi S, Tsuda H, Takemori M, Nakata S, Nishimura S, et al. (2005) Photodynamic therapy for cervical intraepithelial neoplasia. Oncology 69: 110-116.

45. Keefe KA, Tadir Y, Tromberg B, Berns M, Osann K, et al. (2002) Photodynamic therapy of high-grade cervical intraepithelial neoplasia with 5-aminolevulinic acid. Lasers Surg Med 31: 289-293.

46. Hillemanns P, Korell M, Schmitt-Sody M, Baumgartner R, Beyer W, et al. (1999) Photodynamic therapy in women with cervical intraepithelial neoplasia using topically applied 5-aminolevulinic acid. Int J Cancer 81: 34-38.

47. Muroya T, Kawasaki K, Suehiro Y, Kunugi T, Umayahara K, et al. (1999) Application of PDT for uterine cervical cancer. Diagnostic and Therapeutic Endoscopy 5: 183-190.

48. Wierrani F, Kubin A, Jindra R, Henry M, Gharehbaghi K, et al. (1999) 5-aminolevulinic acid-mediated photodynamic therapy of intraepithelial neoplasia and human papillomavirus of the uterine cervix--a new experimental approach. Cancer Detect Prev 23: 351-355.

49. Monk BJ, Brewer C, VanNostrand K, Berns MW, McCullough JL, et al. (1997) Photodynamic therapy using topically applied dihematoporphyrin ether in the treatment of cervical intraepithelial neoplasia. Gynecologic Oncology 64: 70-75.

50. Pacifico RJ, Wang KK, Wongkeesong LM, Buttar NS, Lutzke LS (2003) Combined endoscopic mucosal resection and photodynamic therapy versus esophagectomy for management of early adenocarcinoma in Barrett's esophagus. Clin Gastroenterol Hepatol 1: 252-257.

51. Corti L, Skarlatos J, Boso C, Cardin F, Kosma L, et al. (2000) Outcome of patients receiving photodynamic therapy for early esophageal cancer. Int J Radiat Oncol Biol Phys 47: 419-424.

52. Craig C, Gray J, Macpherson M, Hodgson H, Zammit M, et al. (2007) Porfimer sodium photodynamic therapy in the treatment of early oesophageal carcinoma. Photodiagn Photodyn Ther 4: 244-248.

53. Duvall GA, Scheider D, Cirocco M, Siemens M, Marcon N (1996) Photodynamic therapy (PDT) for early esophageal cancer in high risk surgical patients and patients refusing esophagectomy. Gastrointest Endosc 43:334.

54. Etienne J, Dorme N, Bourg-Heckly G, Raimbert P, Flejou JF (2004) Photodynamic therapy with green light and m-tetrahydroxyphenyl chlorin for intramucosal adenocarcinoma and high-grade dysplasia in Barrett's esophagus. Gastrointest Endosc 59: 880-889.

55. Foroulis CN, Thorpe JA (2006) Photodynamic therapy (PDT) in Barrett's esophagus with dysplasia or early cancer. Eur J Cardiothorac Surg 29: 30-34.

56. Gossner L, May A, Pech O (1999) Photodynamic therapy of Barrett's esophagus with dysplasia or early cancer. Gastroenterology 116: 1811.

57. Gossner L, May A, Sroka R, Stolte M, Hahn EG, et al. (1999) Photodynamic destruction of high grade dysplasia and early carcinoma of the esophagus after the oral administration of 5-aminolevulinic acid. Cancer 86: 1921-1928.

58. Jamieson NF, Mosse A, Bown SG, Lovat LB (2002) Photodynamic therapy to eradicate dysplasia and early carcinoma in Barrett's oesophagus. Gut 50: 6-7.

59. Keeley SB, Pennathur A, Gooding W, Landreneau RJ, Christie NA, et al. (2007) Photodynamic therapy with curative intent for Barrett's esophagus with high grade dysplasia and superficial esophageal cancer. Ann Surg Oncol 14: 2406-2410.

60. Lovat LB, Jamieson NF, Novelli MR, Mosse CA, Selvasekar C, et al. (2005) Photodynamic therapy with m-tetrahydroxyphenyl chlorin for high-grade dysplasia and early cancer in Barrett's columnar lined esophagus. Gastrointest Endosc 62: 617-623.

61. Messmann H, Szeimies RM, Baumler W, Knuchel R, Zirngibl H, et al. (1997) Enhanced effectiveness of photodynamic therapy with laser light fractionation in patients with esophageal cancer. Endoscopy 29: 275-280.

62. Moghissi K, Dixon K (2003) Photodynamic therapy (PDT) in esophageal cancer: a surgical view of its indications based on 14 years experience. Technol Cancer Res Treat 2: 319-326.

63. Nakamura T, Fukui H, Shirakawa K, Fujii Y, Fujimori T, et al. (2004) Photodynamic therapy of superficial esophageal cancer with a transparent hood. Gastrointest Endosc 60: 120-124.

64. Okunaka T, Kato H, Conaka C, Yamamoto H, Bonaminio A, et al. (1990) Photodynamic therapy of esophageal carcinoma. Surg Endosc 4:150-153.

65. Overholt BF, Panjehpour M (1995) Photodynamic therapy in Barrett's esophagus: reduction of specialized mucosa, ablation of dysplasia, and treatment of superficial esophageal cancer. Semin Surg Oncol 11: 372-376.

66. Overholt BF, Panjehpour M, Ayres M (1997) Photodynamic therapy for Barrett's esophagus: cardiac effects. Lasers Surg Med 21: 317-320.

67. Overholt BF, Panjehpour M, Halberg DL (2003) Photodynamic therapy for Barrett's esophagus with dysplasia and/or early stage carcinoma: long-term results. Gastrointest Endosc 58: 183-188.

68. Savoy AD, Wolfsen HC, Raimondo M, Woodward TA, Noh K, et al. (2008) The role of surveillance endoscopy and endosonography after endoscopic ablation of high-grade dysplasia and carcinoma of the esophagus. Dis Esophagus 21:108-113.

69. Shim CS, Cheon YK, Jung IS, Ko BM, Cho JY, et al. (2007) Photodynamic therapy for early esophageal cancer. Gastrointest Endosc 65: 149.

70. Yachimski P, Puricelli WP, Nishioka NS (2008) Patient predictors of esophageal stricture development after photodynamic therapy. Clin Gastroenterol Hepatol 6: 302-308.

71. Yano T, Muto M, Minashi K, Ohtsu A, Yoshida S (2006) Salvage photodynamic therapy (PDT) for local failure after definitive chemoradiotherapy (CRT) for esophageal cancer (EC). 2006 Gastrointestinal Cancers Symposium Abstract #34.

72. Yoshida K, Suzuki S, Mimura S, Narahara H, Tanimura H, et al. (1998) A clinical study of photodynamic therapy for superficial esophageal carcinoma by YAG-OPO Laser. Diagn Ther Endosc;4: 173-176.

73. Tan WC, Fulljames C, Stone N, Dix AJ, Shepherd N, et al. (1999) Photodynamic therapy using 5-aminolaevulinic acid for oesophageal adenocarcinoma associated with Barrett's metaplasia. J Photochem Photobiol B 53: 75-80.

74. Zhang NZ, Zhu Y, Pan W, Ma WQ, Shao AL (2007) Photodynamic therapy combined with local chemotherapy for the treatment of advanced esophagocardiac carcinoma. Photodiagn Photodyn Ther 4: 60-64.

75. Maier A, Tomaselli F, Matzi V, Rehak P, Pinter H (2001) Does new photosensitizer improve photodynamic therapy in advanced esophageal carcinoma? Lasers Surg Med 29: 323-327.

76. Goodell T (2006) Measuring subjective side effects and symptoms in palliative photodynamic therapy. Oncol Nurs Forum 33: 647-650.

77. Xu K, Niu L, Guo Z, Zuo J (2006) Endoscopic photodynamic therapy for symptomatic palliation in advanced esophageal cancer. Ann Oncol 17:91.

78. Maunoury V, Mordon S, Bulois P, Mirabel X, Hecquet B, et al. (2005) Photodynamic therapy for early oesophageal cancer. Dig Liver Dis 37: 491-495.

79. Litle VR, Luketich JD, Christie NA, Buenaventura PO, velo-Rivera M, et al. (2003) Photodynamic therapy as palliation for esophageal cancer: experience in 215 patients. Ann Thorac Surg 76: 1687-1692.

80. Maier A, Tomaselli F, Gebhard F, Rehak P, Smolle J, et al. (2000) Palliation of advanced esophageal carcinoma by photodynamic therapy and irradiation. Ann Thorac Surg 69:1006-1009.

81. Kashtan H, Umansky M, Birkenfeld S, Scherubl H, Haddad R, et al. (2002) Photodynamic therapy of Barrett's esophagus with dysplasia using systemic aminolevulinic acid and a non-laser light source: A phase I/II study. Gastrointestinal Oncology 4: 153-157.

82. McCaughan JS (1999) Photodynamic therapy for obstructive esophageal malignancies. Diagn Ther Endosc 5: 167-174.

83. Scheider DM, Siemens M, Cirocco M, Haber GB, Kandel G, et al. Photodynamic therapy for the treatment of tumor ingrowth in expandable esophageal stents. Endoscopy 29: 271-274.

84. Mauget-Faysse M, Gambrelle J, Quaranta-El MM, Moullet I (2006) Photodynamic therapy for choroidal metastasis from lung adenocarcinoma. Acta Ophthalmol Scand 84: 552-554.

85. Soucek P, Cihelkova I (2006) Photodynamic therapy with verteporfin in subfoveal amelanotic choroidal melanoma (a controlled case). Neuro Endocrinol Lett 27: 145-148.

86. Soucek P, Cihelkova I (2006) Photodynamic therapy with verteporfin in subfoveal choroidal metastasis of breast carcinoma (a controlled case). Neuro Endocrinol Lett 27: 725-728.

87. Liggett PE, Lavaque AJ, Chaudhry NA, Jablon EP, Quiroz-Mercado H (2005) Preliminary results of combined simultaneous transpupillary thermotherapy and ICG-based photodynamic therapy for choroidal melanoma. Ophthalmic Surg Lasers Imaging 36: 463-470.

88. Wachtlin J, Bechrakis NE, Foerster MH (2005) [Photodynamic therapy with verteporfin for uveal melanoma]. Ophthalmologe 102: 241-246.

89. Donaldson MJ, Lim L, Harper CA, Mackenzie J, Campbell G (2005) Clin Experiment Ophthalmol 33: 548-549.

90. Barbazetto IA, Lee TC, Abramson DH (2004) Treatment of conjunctival squamous cell carcinoma with photodynamic therapy. Am J Ophthalmol 138:183-189.

91. Harbour JW (2004) Photodynamic therapy for choroidal metastasis from carcinoid tumor. Am J Ophthalmol 137: 1143-1145.

92. Blasi MA, Tiberti AC, Scupola A, Balestrazzi A, Colangelo E, et al. (2010) Photodynamic therapy with verteporfin for symptomatic circumscribed choroidal hemangioma: five-year outcomes. Ophthalmology 117: 1630-1637.

93. Boixadera A, Garcia-Arumi J, Martinez-Castillo V, Encinas JL, Elizalde J, et al. (2009) Prospective clinical trial evaluating the efficacy of photodynamic therapy for symptomatic circumscribed choroidal hemangioma. Ophthalmology 116: 100-105.

94. Puccioni M, Santoro N, Giansanti F, Ucci F, Rossi R, et al. (2009) Photodynamic therapy using methyl aminolevulinate acid in eyelid basal cell carcinoma: A 5-year follow-up study. Ophthalmic Plastic and Reconstructive Surgery 25: 115-118.

95. Nakamura T, Fukui H, Ishii Y, Fujita M, Hori K, et al. (2000) Shape-memory alloy loop snare for endoscopic photodynamic therapy of early gastric cancer. Endoscopy 32: 609-613.

96. Karanov SI (2002) Long-term results after photodynamic therapy (PDT) of T1N0M0 gastrointestinal (GI) tumors. Hepatogastroenterology 49: 1579-15781.

97. Hendren SK, Hahn SM, Spitz FR, Bauer TW, Rubin SC, et al. (2001) Phase II trial of debulking surgery and photodynamic therapy for disseminated intraperitoneal tumors. Ann Surg Oncol 8: 65-71.

98. Nakamura H, Yanai H, Nishikawa J, Okamoto T, Hirano A, et al. (2001) Experience with photodynamic therapy (endoscopic laser therapy) for the treatment of early gastric cancer. Hepato-Gastroenterology 48: 1599-1603.

99. Ell C, Gossner L, May A, Schneider HT, Hahn EG, et al. Photodynamic ablation of early cancers of the stomach by means of mTHPC and laser irradiation: preliminary clinical experience. Gut 1998;43: 345-349.

100. Mimura S, Narahara H, Hirashima T, Fukutomi H, Nakahara A, et al. (1998) Cooperative clinical trial of photodynamic therapy for early gastric cancer with Photofrin injection and YAG-OPO laser. Diagnostic and Therapeutic Endoscopy 4: 165-171.

101. Li L, Luo R, Liao W, Zhang M, Luo Y, et al. (2006) Clinical study of Photofrin photodynamic therapy for the treatment of relapse nasopharyngeal carcinoma. Photodiagnosis and photodynamic therapy 3: 266-271.

102. Wang CP, Chang YL, Chen CT, Yang TH, Lou PJ (2006) Photodynamic therapy with topical 5-aminolevulinic acid as a post-operative adjuvant therapy for an incompletely resected primary nasopharyngeal papillary adenocarcinoma: A case report. Lasers in surgery and medicine 38: 435-438.

103. Rigual NR, Thankappan K, Cooper M, Sullivan MA, Dougherty T, et al. (2009) Photodynamic therapy for head and neck dysplasia and cancer. Arch Otolaryngol Head Neck Surg 135: 784-788.

104. Biel MA (2007) Photodynamic therapy treatment of early oral and laryngeal cancers. Photochem Photobiol 83: 1063-1068.

105. Schweitzer VG (2001) PHOTOFRIN-mediated photodynamic therapy for treatment of early stage oral cavity and laryngeal malignancies. Lasers in surgery and medicine 29: 305-313.

106. National Institute for Health and Clinical Excellence. Audit criteria: photodynamic therapy for early-stage oesophageal cancer [Interventional Procedure Guidance]. London: National Institute for Health and Clinical Excellence (NICE) 2006.

107. Jerjes W, Upile T, Hamdoon Z, Abbas S, Akram S, et al. (2011) Photodynamic therapy: The minimally invasive surgical intervention for advanced and/or recurrent tongue base carcinoma. Lasers Surg Med 43: 283-292.

108. Chen HM, Yu CH, Tsai T, Hsu YC, Kuo RC, et al (2007) Topical 5-aminolevulinic acid-mediated photodynamic therapy for oral verrucous hyperplasia, oral leukoplakia and oral erythroleukoplakia. Photodiagnosis and photodynamic therapy 4: 44-52.

109. Vakulovskaya E, Lubaev V (2007) Photodynamic therapy in oral cancer patients with second-generation photosensitizers. Oral Oncology Suppl 2: 215-216.

110. Hopper C, Kubler A, Lewis H, Tan IB, Putnam G (2004) mTHPC-mediated photodynamic therapy for early oral squamous cell carcinoma. Int J Cancer 111: 138-146.

111. Tanaka H, Hashimoto K, Yamada I, Masumoto K, Ohsawa T, et al. (2001) Interstitial photodynamic therapy with rotating and reciprocating optical fibers. Cancer 91: 1791-1796.

112. Kubler AC, de CJ, Hopper C, Leonard AG, Putnam G (2001) Treatment of squamous cell carcinoma of the lip using Foscan-mediated photodynamic therapy. Int J Oral Maxillofac Surg 30: 504-509.

113. Kubler A, Haase T, Rheinwald M, Barth T, Muhling J (1999) Treatment of oral leukoplakia by topical application of 5-aminolevulinic acid. Int J Oral Maxillofac Surg 27: 466-469.

114. Fan KFM, Hopper C, Speight PM, Buonaccorsi GA, Bown SG (1997) Photodynamic therapy using mTHPC for malignant disease in the oral cavity. International Journal of Cancer 73: 25-32.

115. Grant WE, Speight PM, Hopper C, Bown SG (1997) Photodynamic therapy: an effective, but non-selective treatment for superficial cancers of the oral cavity. International Journal of Cancer 71: 937-942.

116. Hauschild A, Lischner S, Lange-Asschenfeldt B, Egberts F (2005) Treatment of actinic cheilitis using photodynamic therapy with methylaminolevulinate: Report of three cases. Dermatologic Surgery 31: 1344-1347.

117. Schweitzer VG, Somers ML (2010) PHOTOFRIN-mediated photodynamic therapy for treatment of early stage laryngeal malignancies. Oncology Reviews 4: 203-209.

118. Karakullukcu B, Van OK, Copper MP, Klop WMC, Van VR, et al. (2011) Photodynamic therapy of early stage oral cavity and oropharynx neoplasms: An outcome analysis of 170 patients. European Archives of Oto-Rhino-Laryngology 268: 281-288.

119. Schweitzer VG, Somers ML (2010) PHOTOFRIN-mediated photodynamic therapy for treatment of early stage (Tis-T2N0M0) SqCCa of oral cavity and oropharynx. Lasers Surg Med 42: 1-8.

120. Titova VA, Kharchenko V, Dykhno Y, Petrovsky Y, Stranadko F, et al. Photodynamic therapy and lazer intensed thermotherapy in locally advanced and recurrent oro-pharyngeal cancer multimodal treatment. Radiotherapy and Oncology 82: 70.

121. Tan IB, Dolivet G, Ceruse P, Vander P V, Roest G, et al. (2010) Temoporfin-mediated photodynamic therapy in patients with advanced, incurable head and neck cancer: A multicenter study. Head Neck 32: 1597-1604.

122. Smucler R, Vlk P (2006) Combination of laser induced interstitial thermotherapy and photodynamic therapy in the treatment of neck cancer. Lasers in surgery and medicine 38: 28.

123. Jager HR, Taylor MN, Theodossy T, Hopper C (2005) MR imaging-guided interstitial photodynamic laser therapy for advanced head and neck tumors. AJNR Am J Neuroradiol 26:1193-1200.

124. D'Cruz AK, Robinson MH, Biel MA (2004) mTHPC-mediated photodynamic therapy in patients with advanced, incurable head and neck cancer: a multicenter study of 128 patients. Head Neck 26: 232-240.

125. Lou PJ, Jager HR, Jones L, Theodossy T, Bown SG, et al. (2004) Interstitial photodynamic therapy as salvage treatment for recurrent head and neck cancer. Br J Cancer 91: 441-446.

126. Rauschning W, Tan IB, Dolivet G (2004) Photodynamic therapy (PDT) with mTHPC in the palliation of advanced head and neck cancer in patients who have failed prior therapies and are unsuitable for radiotherapy, surgery or systemic chemotherapy. Journal of Clinical Oncology 22: 512.

127. Dilkes MG, Benjamin E, Ovaisi S, Banerjee AS (2003) Treatment of primary mucosal head and neck squamous cell carcinoma using photodynamic therapy: results after 25 treated cases. J Laryngol Otol 117: 713-717.

128. Hopper C, Suhr M, Jones L, Nakanishi H, Jaeger R, (2000) et al. Interstitial photodynamic therapy in head and neck cancer. British Journal of Cancer 83: 48.

129. Kulapaditharom B, Boonkitticharoen V (2000) Photodynamic therapy in management of head and neck cancers and precancerous lesions. J Med Assoc Thai 83: 249-258.

130. Hahn SM, Fraker DL, Mick R, Metz J, Busch TM, et al. (2006) A phase II trial of intraperitoneal photodynamic therapy for patients with peritoneal carcinomatosis and sarcomatosis. Clin Cancer Res 12: 2517-2525.

131. Wilson JJ, Jones H, Burock M, Smith D, Fraker DL, et al. (2004) Patterns of recurrence in patients treated with photodynamic therapy for intraperitoneal carcinomatosis and sarcomatosis. Int J Oncol 24: 711-717.

132. van Duijnhoven FH, Rovers JP, Engelmann K, Krajina Z, Purkiss SF, (2005) et al. Photodynamic therapy with 5,10,15,20-tetrakis(m-hydroxyphenyl) bacteriochlorin for colorectal liver metastases is safe and feasible: results from a phase I study. Ann Surg Oncol 12: 808-816.

133. Diaz-Jimenez JP, Martinez-Ballarin JE, Llunell A, Farrero E, Rodriguez A Efficacy and safety of photodynamic therapy versus Nd-YAG laser resection in NSCLC with airway obstruction. Eur Respir J 14: 800-805.

134. Leroy M, Diaz-Jimenez JP, Moghissi K, Diaz-Agero P, Spinelli P, et al. A phase III randomized, comparative trial of photodynamic therapy (PDT) utilizing Photofrin r versus thermal ablation therapy using the Nd: YAG laser for obstructing endobronchial lung cancer. Ann Oncol 9: 83.

135. Hill HC, Nwogu CE, Loewen G, Pelow J, Dougherty TJ, et al. (2004) Off-label management of primary and metastatic endobronchial tumors with photodynamic therapy. Clinical Pulmonary Medicine 11: 107-111.

136. Santos RS, Raftopoulos Y, Keenan RJ, Halal A, Maley RH, et al. (20004) Bronchoscopic palliation of primary lung cancer: single or multimodality therapy? Surg Endosc 18: 931-936.

137. Morris CD, Budde JM, Godette KD, Kerwin TL, Miller JI 2002) Palliative management of malignant airway obstruction. Ann Thorac Surg 74: 1928-1932.

138. Nakamura H, Kawasaki N, Hagiwara M, Ogata A, Saito M, et al. (2007) Early hilar lung cancer - Risk for multiple lung cancers and clinical outcome. Lung Cancer 33: 51-77.

139. Van Boxem AJM, Westerga J, Venmans BJW, Postmus PE, Sutedja G (2001) Photodynamic therapy, Nd-YAG laser and electrocautery for treating early-stage intraluminal cancer: Which to choose? Lung Cancer 31: 31-36.

140. Furukawa K, Okunaka T, Yamamoto H, Tsuchida T, Usuda J, et al. (1999) Effectiveness of photodynamic therapy and Nd-YAG laser treatment for obstructed tracheobronchial malignancies. Diagnostic and Therapeutic Endoscopy 5: 161-166.

141. Taber SW, Buschemeyer WC, III, Fingar VH, Wieman TJ (1999) The treatment of malignant endobronchial obstruction with laser ablation. Surgery 126: 730-733.

142. Friedberg JS, Mick R, Stevenson JP, Zhu T, Busch TM, et al. (2004) Phase II trial of pleural photodynamic therapy and surgery for patients with non-small-cell lung cancer with pleural spread. J Clin Oncol 22: 2192-2201.

143. Tomaselli F, Maier A, Pinter H, Stranzl H, Smolle-Juttner FM (2001) Photodynamic therapy enhanced by hyperbaric oxygen in acute endoluminal palliation of malignant bronchial stenosis. Eur J Cardiothorac Surg 19: 549-554.

144. Cortese DA, Edell ES, Kinsey JH (1997) Photodynamic therapy for early stage squamous cell carcinoma of the lung. Mayo Clinic Proceedings 72: 595-602.

145. McCaughan JS, Williams TE (1997) Photodynamic therapy for endobronchial malignant disease: A prospective fourteen-year study. Journal of Thoracic and Cardiovascular Surgery 114: 940-947.

146. Corti L, Toniolo L, Boso C, Colaut F, Fiore D (2007) et al. Long-term survival of patients treated with photodynamic therapy for carcinoma in situ and early non-small-cell lung carcinoma. Lasers in surgery and medicine 39: 394-402.

147. Ragulin Y, Kaplan M, Medvedev V (2007) Photodynamic therapy with chlorine photosensitizers on the central lung cancer. Lung Cancer 55: S3-S4.

148. Kato H, Usuda J, Okunaka T, Furukawa K, Honda H, et al (2006) Basic and clinical research on photodynamic therapy at Tokyo Medical University Hospital. Lasers in Surgery and Medicine 38: 371-375.

149. Mortman KD, Frankel KM (2006) Pulmonary resection after successful downstaging with photodynamic therapy. Annals of Thoracic Surgery 82: 722-724.

150. Magro CM, Abbas AE, Ross J (2006) The application of photodynamic therapy in the treatment of metastatic endobronchial disease. Lasers in Surgery and Medicine 38: 376-383.

151. Ross P, Grecula J, Bekaii-Saab T, Villalona-Calero M, Otterson G, et al. (2006) Incorporation of photodynamic therapy as an induction modality in non-small cell lung cancer. Lasers in surgery and medicine 38: 881-889.

152. Downie C, Ya HY, Xin-Hua H, Claudio S, Ron A, et al. (2005) Tumor ablation through self-expandable metal stent (SEMS) for airway neoplasm: The dosimetry and efficacy of photodynamic therapy. Lung Cancer 49: S11-S12.

153. Moghissi K, Dixon K (2005) Photodynamic therapy (PDT) of central type lung cancer: Current indications based on 15 years experience and literature review. Lasers in surgery and medicine 36: 61.

154. Ernst A, Freitag L, Feller-Kopman D, LoCicero IJ, Ost D (2003) Photodynamic therapy for endobronchial obstruction is safely performed with flexible bronchoscopy. Journal of Bronchology 10: 260-263.

155. Litle VR, Christie NA, Fernando HC, Buenaventura PO, Ferson PF, et al. (2003) Photodynamic therapy for endobronchial metastases from nonbronchogenic primaries. Ann Thorac Surg 76: 370-375.

156. Jones BU, Helmy M, Brenner M, Serna DL, Williams J, et al. (2001) Photodynamic therapy for patients with advanced non-small-cell carcinoma of the lung. Clinical Lung Cancer 3: 37-41.

157. Sanfilippo NJ, Hsi A, DeNittis AS, Ginsberg GG, Kochman ML, et al. (2001)

Toxicity of photodynamic therapy after combined external beam radiotherapy and intraluminal brachytherapy for carcinoma of the upper aerodigestive tract. Lasers Surg Med 28: 278-281.

158. Radu A, Grosjean P, Fontolliet C, Wagnieres G, Woodtli A, et al. (1999) Photodynamic therapy for 101 early cancers of the upper aerodigestive tract, the esophagus, and the bronchi: a single-institution experience. Diagn Ther Endosc 5: 145-154.

159. Endo C, Miyamoto A, Sakurada A, Aikawa H, Sagawa M, et al. (2009) Results of long-term follow-up of photodynamic therapy for roentgenographically occult bronchogenic squamous cell carcinoma. Chest 136: 369-375.

160. Matzi V, Maier A, Sankin O, Lindenmann J, Woltsche M, et al. (2004) Photodynamic therapy enhanced by hyperbaric oxygenation in palliation of malignant pleural mesothelioma: clinical experience. Photodiagnosis and Photodynamic Therapy 1: 57-65.

161. Pass HI, Temeck BK, Kranda K, Thomas G, Russo A, et al. (1997) Phase III randomized trial of surgery with or without intraoperative photodynamic therapy and postoperative immunochemotherapy for malignant pleural mesothelioma. Annals of surgical oncology 4: 628-633.

162. Friedberg JS, Mick R, Stevenson J, Metz J, Zhu T, et al. (2003) A phase I study of Foscan-mediated photodynamic therapy and surgery in patients with mesothelioma. Ann Thorac Surg 75: 952-959.

163. Schouwink H, Rutgers ET, Van der SJ, Oppelaar H, Van ZN, et al. (2001) Intraoperative photodynamic therapy after pleuropneumonectomy in patients with malignant pleural mesothelioma: Dose finding and toxicity results. Chest 120: 1167-1174.

164. Overholt BF, Lightdale CJ, Wang KK, Canto MI, Burdick S, et al. (2005) Photodynamic therapy with porfimer sodium for ablation of high-grade dysplasia in Barrett's esophagus: international, partially blinded, randomized phase III trial. Gastrointest Endosc 62: 488-498.

165. Wierrani F, Fiedler D, Grin W, Henry M, Krammer B, et al. (1997) Intraoperative meso-tetrahydroxyphenylchlorin-based photodynamic therapy in metastatic gynecologic cancer tissue: Initial results. Journal of Gynecologic Surgery 113: 23-29.

166. Bown SG (2003) Photodynamic therapy for cancer of the pancreas. Acta Endoscopica 33: 531-538.

167. Marks PV, Belchetz PE, Saxena A, Igbaseimokumo U, Thomson S, et al. (2000) Effect of photodynamic therapy on recurrent pituitary adenomas: clinical phase I/II trial--an early report. Br J Neurosurg 14: 317-325.

168. Trachtenberg J, Bogaards A, Weersink RA, Haider MA, Evans A, et al. (2007) Vascular targeted photodynamic therapy with palladium-bacteriopheophorbide photosensitizer for recurrent prostate cancer following definitive radiation therapy: assessment of safety and treatment response. J Urol 178: 1974-1979.

169. Du KL, Mick R, Busch TM, Zhu TC, Finlay JC, et al. (2006) Preliminary results of interstitial motexafin lutetium-mediated PDT for prostate cancer. Lasers Surg Med 38: 427-434.

170. Moore CM, Nathan TR, Lees WR, Mosse CA, Freeman A, et al. (2006) Photodynamic therapy using meso tetra hydroxy phenyl chlorin (mTHPC) in early prostate cancer. Lasers Surg Med 38: 356-363.

171. Nathan TR, Whitelaw DE, Chang SC, Lees WR, Ripley PM, et al. (2002) Photodynamic therapy for prostate cancer recurrence after radiotherapy: a phase I study. J Urol 168: 1427-1432.

172. Arokianathan TR, Whitelaw DE, Lees WR, Chang SSC, Gillams A, et al. (1998) Photodynamic therapy for recurrent prostate cancer after radiotherapy: a pilot study. British Journal of Cancer 78: 8.

173. Arumainayagam N, Moore CM, Mosse CA, Bown SG, Allen C, et al. (2011) Tookad soluble (WST-11) second generation vascular targeted photodynamic therapy (VTP) for prostate cancer: safety and feasibility [abstract]. British Journal of Surgery 98: E10.

174. Kusuzaki K, Murata H, Matsubara T, Miyazaki S, Okamura A, et al. (2005) Clinical trial of photodynamic therapy using acridine orange with/without low dose radiation as new limb salvage modality in musculoskeletal sarcomas. Anticancer Res 25: 1225-1235.

175. Berroeta L, Clark C, Dawe RS, Ibbotson SH, Fleming CJ (2007) A randomized study of minimal curettage followed by topical photodynamic therapy compared with surgical excision for low-risk nodular basal cell carcinoma. Br J Dermatol 157: 401-403.

176. Rhodes LE, De Rie MA, Leifsdottir R, Yu RC, Bachmann I, et al. (2007) Five-year follow-up of a randomized, prospective trial of topical methyl aminolevulinate photodynamic therapy vs surgery for nodular basal cell carcinoma. Arch Dermatol 143: 1131-1316.

177. Kuijpers DI, Thissen MR, Thissen CA, Neumann MH (2006) Similar effectiveness of methyl aminolevulinate and 5-aminolevulinate in topical photodynamic therapy for nodular basal cell carcinoma. J Drugs Dermatol 5: 642-645.

178. De Haas ER, Kruijt B, Sterenborg HJ, Martino Neumann HA, Robinson DJ (2006) Fractionated illumination significantly improves the response of superficial basal cell carcinoma to aminolevulinic acid photodynamic therapy. J Invest Dermatol 126: 2679-2686.

179. Basset-Seguin N (2006) Photodynamic therapy using topical methyl aminolaevulinate versus cryotherapy for treatment of primary superficial basal cell carcinoma: results of a five-year prospective randomized trial. British Journal of Dermatology 155: 57.

180. Wang I, Bendsoe N, Klinteberg CA, Enejder AM, ndersson-Engels S, et al. (2001) Photodynamic therapy vs. cryosurgery of basal cell carcinomas: results of a phase III clinical trial. Br J Dermatol 144: 832-840.

181. Soler AM, Angell-Petersen E, Warloe T, Tausjo J, Steen HB, et al. (2000) Photodynamic therapy of superficial basal cell carcinoma with 5-aminolevulinic acid with dimethylsulfoxide and ethylendiaminetetraacetic acid: a comparison of two light sources. Photochem Photobiol 71: 724-729.

182. Szeimies RM, Ibbotson S, Murrell DF, Rubel D, Frambach Y, et al. (2008) A clinical study comparing methyl aminolevulinate photodynamic therapy and surgery in small superficial basal cell carcinoma (8-20 mm), with a 12-month follow-up. J Eur Acad Dermatol Venereol 22: 1302-1311.

183. Foley P, Freeman M, Menter A, Siller G, El-Azhary RA, et al. (2009) Photodynamic therapy with methyl aminolevulinate for primary nodular basal cell carcinoma: results of two randomized studies. Int J Dermatol 48: 1236-1245.

184. de Graaf YG, Kennedy C, Wolterbeek R, Collen AF, Willemze R, et al. (2006) Photodynamic therapy does not prevent cutaneous squamous-cell carcinoma in organ-transplant recipients: results of a randomized-controlled trial. J Invest Dermatol 126: 569-574.

185. Morton C, Horn M, Leman J, Tack B, Bedane C, et al. (2006) Comparison of topical methyl aminolevulinate photodynamic therapy with cryotherapy or Fluorouracil for treatment of squamous cell carcinoma in situ: results of a multicenter randomized trial. Arch Dermatol 142: 729-735.

186. Ziolkowski P, Osiecka BJ, Oremek G, Siewinski M, Symonowicz K, et al. (2004) Enhancement of photodynamic therapy by use of aminolevulinic acid/glycolic acid drug mixture. J Exp Ther Oncol 4: 121-129.

187. De Haas ER, Sterenborg HJ, Neumann HA, Robinson DJ (2007) Response of Bowen disease to ALA-PDT using a single and a 2-fold illumination scheme. Arch Dermatol 143: 264-265.

188. Salim A, Leman JA, McColl JH, Chapman R, Morton CA (2003) Randomized comparison of photodynamic therapy with topical 5-fluorouracil in Bowen's disease. Br J Dermatol 148: 539-543.

189. Morton CA, Whitehurst C, Moore JV, MacKie RM (2000) Comparison of red and green light in the treatment of Bowen's disease by photodynamic therapy. Br J Dermatol 143: 767-772.

190. Lui H, Hobbs L, Tope WD, Lee PK, Elmets C, et al. (2004) Photodynamic therapy of multiple nonmelanoma skin cancers with verteporfin and red light-emitting diodes: two-year results evaluating tumor response and cosmetic outcomes. Arch Dermatol 140: 26-32.

191. Smucler R, Vlk M (2008) Combination of Er:YAG laser and photodynamic therapy in the treatment of nodular basal cell carcinoma. Lasers Surg Med 40: 153-158.

192. Surrenti T, De AL, Di CA, Fargnoli MC, Peris K (2007) Efficacy of photodynamic therapy with methyl aminolevulinate in the treatment of superficial and nodular basal cell carcinoma: an open-label trial. Eur J Dermatol 17: 412-415.

193. Whitaker IS, Shokrollahi K, James W, Mishra A, Lohana P, et al. (2007) Combined CO(2) laser with photodynamic therapy for the treatment of nodular basal cell carcinomas. Ann Plast Surg 59: 484-488.

194. Star WM, van't Veen AJ, Robinson DJ, Munte K, De Haas ER, et al. (2006) Topical 5-aminolevulinic acid mediated photodynamic therapy of superficial

basal cell carcinoma using two light fractions with a two-hour interval: long-term follow-up. Acta Derm Venereol 86: 412-417.

195. Triesscheijn M, Ruevekamp M, Antonini N, Neering H, Stewart FA, et al. (2005) Optimizing meso-tetra-hydroxyphenyl-chlorin-mediated photodynamic therapy for basal cell carcinoma. Photochem Photobiol 82: 1686-1690.

196. Morton CA, Fraser C, Leman JA, Smith B (2005) Effects of protocol variation on response rate of superficial basal cell carcinoma to topical photodynamic therapy. Br J Dermatol 153: 25.

197. Nikkels AF, Pierard-Franchimont C, Nikkels-Tassoudji N, Bourguignon R, Pierard GE (2005) Photodynamic therapy and imiquimod immunotherapy for basal cell carcinomas. Acta Clin Belg 60: 227-234.

198. Vinciullo C, Elliott T, Francis D, Gebauer K, Spelman L, et al. (2005) Photodynamic therapy with topical methyl aminolaevulinate for 'difficult-to-treat' basal cell carcinoma. Br J Dermatol 152: 765-772.

199. Degiovanni CV, Oliver P, Woollons A (2005) Recurrence rates of superficial basal cell carcinoma treated with photodynamic therapy: an audit of current practice in a district general hospital [abstract]. Br J Dermatol 153: 28.

200. Kaviani A, taie-Fashtami L, Fateh M, Sheikhbahaee N, Ghodsi M, et al. (2005) Photodynamic therapy of head and neck basal cell carcinoma according to different clinicopathologic features. Lasers Surg Med 36: 377-382.

201. Cappugi P, Mavilia L, Campolmi P, Reali EF, Mori M, et al. (2004) New proposal for the treatment of nodular basal cell carcinoma with intralesional 5-aminolevulinic acid. J Chemother 16: 491-493.

202. Naidenov N, Dencheva R, Tsankov N (2004) Recurrence rate of basal cell carcinoma after topical aminolevulinic acid-based photodynamic therapy. Acta Dermatovenerol Croat 12: 157-161.

203. Itkin A, Gilchrest BA (2004) Delta-Aminolevulinic acid and blue light photodynamic therapy for treatment of multiple basal cell carcinomas in two patients with nevoid basal cell carcinoma syndrome. Dermatol Surg 30: 1054-1061.

204. Horn M, Wolf P, Wulf HC, Warloe T, Fritsch C, et al. (2003) Topical methyl aminolaevulinate photodynamic therapy in patients with basal cell carcinoma prone to complications and poor cosmetic outcome with conventional treatment. Br J Dermatol 149: 1242-1249.

205. Zimmermann A, Walt H, Haller U, Baas P, Klein SD (2003) Effects of chlorin-mediated photodynamic therapy combined with fluoropyrimidines in vitro and in a patient. Cancer Chemother Pharmacol 51: 147-154.

206. Soler AM, Warloe T, Berner A, Giercksky KE (2001) A follow-up study of recurrence and cosmesis in completely responding superficial and nodular basal cell carcinomas treated with methyl 5-aminolaevulinate-based photodynamic therapy alone and with prior curettage. Br J Dermatol 145: 467-471.

207. Haller JC, Cairnduff F, Slack G, Schofield J, Whitehurst C, et al. (2000) Routine double treatments of superficial basal cell carcinomas using aminolaevulinic acid-based photodynamic therapy. Br J Dermatol 143: 1270-1275.

208. Thissen MR, Schroeter CA, Neumann HA (2000) Photodynamic therapy with delta-aminolaevulinic acid for nodular basal cell carcinomas using a prior debulking technique. Br J Dermatol 142: 338-339.

209. Soler AM, Warloe T, Tausjo J, Berner A (1999) Photodynamic therapy by topical aminolevulinic acid, dimethylsulphoxide and curettage in nodular basal cell carcinoma: a one-year follow-up study. Acta Derm Venereol 79: 204-206.

210. Wang I, Bauer B, ndersson-Engels S, Svanberg S, Svanberg K (1999) Photodynamic therapy utilising topical delta-aminolevulinic acid in non-melanoma skin malignancies of the eyelid and the periocular skin. Acta Ophthalmol Scand 77: 182-188.

211. Christensen E, Skogvoll E, Viset T, Warloe T, Sundstrom S (2009) Photodynamic therapy with 5-aminolaevulinic acid, dimethylsulfoxide and curettage in basal cell carcinoma: A 6-year clinical and histological follow-up. J Eur Acad Dermatol Venereol 23: 58-66.

212. Betz CS, Rauschning W, Stranadko EP, Riabov MV, Albrecht V, et al. (2008) Optimization of treatment parameters for Foscan-PDT of basal cell carcinomas. Lasers Surg Med 40: 300-311.

213. Fantini F, Greco A, Del GC, Cesinaro A, Venturini M, et al. (2011) Photodynamic therapy for basal cell carcinoma: clinical and pathological determinants of response. J Eur Acad Dermatol Venereol 25: 896-901.

214. Souza CS, Neves AB, Felicio LA, Ferreira J, Kurachi C, et al. (2007) Optimized photodynamic therapy with systemic photosensitizer following debulking technique for nonmelanoma skin cancers. Dermatol Surg 33: 194-198.

215. Baptista J, Martinez C, Leite L, Cochito M (2006) Our PDT experience in the treatment of non-melanoma skin cancer over the last 7 years. J Eur Acad Dermatol Venereol 20: 693-697.

216. Moseley H, Ibbotson S, Woods J, Brancaleon L, Lesar A, et al. (2006) Clinical and research applications of photodynamic therapy in dermatology: experience of the Scottish PDT Centre. Lasers Surg Med 38: 403-416.

217. Chan AL, Juarez M, Allen R, Volz W, Albertson T (2005) Pharmacokinetics and clinical effects of mono-L-aspartyl chlorin e6 (NPe6) photodynamic therapy in adult patients with primary or secondary cancer of the skin and mucosal surfaces. Photodermatol Photoimmunol Photomed 21: 72-78.

218. Schleier P, Hyckel P, Berndt A, Bode HP, Albrecht V, et al. (2004) Photodynamic therapy of virus-associated epithelial tumours of the face in organ transplant recipients. J Cancer Res Clin Oncol 130: 279-284.

219. Sieron A, Kawczyk-Krupka A, Wojciech Cebula MA, Szygula M, Zieleznik W, et al. (2004) Photodynamic therapy (PDT) using topically applied delta-aminolevulinic acid (ALA) for the treatment of malignant skin tumors. Photodiagnosis and Photodynamic Therapy 1: 311-317.

220. Clark C, Bryden A, Dawe R, Moseley H, Ferguson J, et al. (2003) Topical 5-aminolaevulinic acid photodynamic therapy for cutaneous lesions: outcome and comparison of light sources. Photodermatol Photoimmunol Photomed 19: 134-141.

221. Vaicova M (2003) A comparison of photodynamic therapy with TPPS4 and ALA [abstract]. Journal of the European Academy of Dermatology & Venereology 17: 301.

222. Xu S, Wang X, Xu W, Xia Y, Zhang C (2001) Evaluation of photodynamic therapy of skin cancers with delta-aminolevulinic acid. Chinese Medical Journal 115: 1141-1145.

223. Xu S, Wang X, Xu W, Xia Y, Zhang C (2002) Evaluation of photodynamic therapy of skin cancers with partial differential alpha-aminolevulinic acid. Chin Med J (Engl) 115: 1141-1145.

224. Schweitzer VG (2001) Photofrin-mediated photodynamic therapy for treatment of aggressive head and neck nonmelanomatous skin tumors in elderly patients. Laryngoscope 111: 1091-1098.

225. Varma S, Wilson H, Kurwa HA, Gambles B, Charman C, et al. (2001) Bowen's disease, solar keratoses and superficial basal cell carcinomas treated by photodynamic therapy using a large-field incoherent light source. Br J Dermatol 144: 567-574.

226. Morton CA, Whitehurst C, McColl JH, Moore JV, MacKie RM (2001) Photodynamic therapy for large or multiple patches of Bowen disease and basal cell carcinoma. Arch Dermatol 137: 319-324.

227. Dijkstra AT, Majoie IM, van Dongen JW, van WH, van Vloten WA (2001) Photodynamic therapy with violet light and topical 6-aminolaevulinic acid in the treatment of actinic keratosis, Bowen's disease and basal cell carcinoma. J Eur Acad Dermatol Venereol 15: 550-4.

228. Wennberg AM (2000) Basal cell carcinoma--new aspects of diagnosis and treatment. Acta Derm Venereol Suppl (Stockh) 209: 5-25.

229. Chapas A, Zeltser R, Geronemus R, Gilchrest B (2006) Intralesional photodynamic therapy of nonmelanoma skin cancer [abstract]. Lasers in Surgery & Medicine (Suppl 18): 27(Abstract no. 83).

230. Fink-Puches R, Soyer HP, Hofer A, Kerl H, Wolf P (1998) Long-term follow-up and histological changes of superficial nonmelanoma skin cancers treated with topical delta-aminolevulinic acid photodynamic therapy. Arch Dermatol 134: 821-6.

231. Alecu M, Ursaciuc C, Halalau F, Coman G, Merlevede W, et al. (1998) Photodynamic treatment of basal cell carcinoma and squamous cell carcinoma with hypericin. Anticancer Res 18: 4651-464.

232. Kubler AC, Haase T, Staff C, Kahle B, Rheinwald M, et al. (1999) Photodynamic therapy of primary nonmelanomatous skin tumours of the head and neck. Lasers Surg Med 25: 60-68.

233. Harth Y, Hirshowitz B, Kaplan B (1998) Modified topical photodynamic therapy of superficial skin tumors, utilizing aminolevulinic acid, penetration enhancers, red light, and hyperthermia. Dermatol Surg 24: 723-726.

234. Wang Y, Shi T, Liu B, Li M (2009) Comparison of photodynamic therapy for skin cancers and pre-cancers with -aminolevulinic acid. Chinese-German Journal of Clinical Oncology 8: 726-728.

235. De Haas ERM, De Vijlder HC, Sterenborg HJCM, Neumann HAM, Robinson DJ (2008) Fractionated aminolevulinic acid-photodynamic therapy provides additional evidence for the use of PDT for non-melanoma skin cancer. J Eur Acad Dermatol Venereol 22: 426-430.

236. Souza CS, Felicio LB, Ferreira J, Kurachi C, Bentley MV, et al. (2009) Long-term follow-up of topical 5-aminolaevulinic acid photodynamic therapy diode laser single session for non-melanoma skin cancer. Photodiagnosis Photodyn Ther 6: 207-213.

237. Britton JE, Goulden V, Stables G, Stringer M, Sheehan-Dare R (2005) Investigation of the use of the pulsed dye laser in the treatment of Bowen's disease using 5-aminolaevulinic acid phototherapy. Br J Dermatol 153: 780-784.

238. Souza CS, Felicio LB, Bentley MV, Tedesco AC, Ferreira J, et al. (2005) Topical photodynamic therapy for Bowen's disease of the digit in epidermolysis bullosa. Br J Dermatol 153: 672-674.

239. Sheleg SV, Zhavrid EA, Khodina TV, Kochubeev GA, Istomin YP, et al. (2004) Photodynamic therapy with chlorin e(6) for skin metastases of melanoma. Photodermatol Photoimmunol Photomed 20: 21-26.

240. Vakulovskaya EG, Shental VV (2002) Combination of photodynamic therapy and cryosurgery in treatment of advanced skin cancer [abstract]. International Journal of Cancer Suppl 13: 404.

241. Tardivo JP, Giglio AD, Paschoal LH, Baptista MS (2006) New photodynamic therapy protocol to treat aids-related Kaposi's sarcoma. Photomedicine and Laser Surgery 24: 528-531.

242. Bernstein ZP, Wilson BD, Oseroff AR, Jones CM, Dozier SE, et al. (1999) Photofrin photodynamic therapy for treatment of AIDS-related cutaneous Kaposi's sarcoma. AIDS 13: 1697-1704.

243. Recio ED, Zambrano B, Alonso ML, de EE, Martin M, et al. (2008) Topical 5-aminolevulinic acid photodynamic therapy for the treatment of unilesional mycosis fungoides: a report of two cases and review of the literature. Int J Dermatol 47: 410-413.

244. Zane C, Venturini M, Sala R, Calzavara-Pinton P (2006) Photodynamic therapy with methylaminolevulinate as a valuable treatment option for unilesional cutaneous T-cell lymphoma. Photodermatol Photoimmunol Photomed 22: 254-258.

245. Leman JA, Dick DC, Morton CA. (2002) Topical 5-ALA photodynamic therapy for the treatment of cutaneous T-cell lymphoma. Clin Exp Dermatol 27: 516-518.

246. Markham T, Sheahan K, Collins P (2001) Topical 5-aminolaevulinic acid photodynamic therapy for tumour-stage mycosis fungoides. Br J Dermatol 144:1262-1263.

247. Edstrom DW, Porwit A, Ros AM (2001) Photodynamic therapy with topical 5-aminolevulinic acid for mycosis fungoides: clinical and histological response. Acta Derm Venereol 81: 184-188.

248. Orenstein A, Haik J, Tamir J, Winkler E, Trau H, et al. (2000) Photodynamic therapy of cutaneous lymphoma using 5-aminolevulinic acid topical application. Dermatol Surg 26: 765-769.

249. Stables GI, Stringer MR, Robinson DJ (1997) The treatment of cutaneous t-cell lymphoma by topical aminolaevulinic acid photodynamic therapy [abstract]. Br J Dermatol 1137(Suppl):50.

250. Zawislak AA, McCarron PA, McCluggage WG, Price JH, Donnelly RF, et al. (2004) Successful photodynamic therapy of vulval Paget's disease using a novel patch-based delivery system containing 5-aminolevulinic acid. BJOG 111: 1143-1145.

251. Tulchinsky H, Zmora O, Brazowski E, Goldman G, Rabau M (2004) Extramammary Paget's disease of the perianal region. Colorectal Dis 6: 206-209.

252. Shieh S, Dee AS, Cheney RT, Frawley NP, Zeitouni NC, et al. (2002) Photodynamic therapy for the treatment of extramammary Paget's disease. Br J Dermatol 146: 1000-1005.

253. Zollo JD, Zeitouni NC (2000) The Roswell Park Cancer Institute experience with extramammary Paget's disease. Br J Dermatol 142: 59-65.

254. Raspagliesi F, Fontanelli R, Rossi G, Ditto A, Solima E, et al. (2006) Photodynamic therapy using a methyl ester of 5-aminolevulinic acid in recurrent Paget's disease of the vulva: a pilot study. Gynecol Oncol 103: 581-586.

255. Housel JP, Izikson L, Zeitouni NC (2010) Noninvasive extramammary Paget's disease treated with photodynamic therapy: case series from the Roswell Park Cancer Institute. Dermatologic Surgery 36: 1718-1724.

256. Li Q, Gao T, Jiao B, Qi X, Long HA, et al. (2010) Long-term follow-up of in situ extramammary Paget's disease in Asian skin types IV/V treated with photodynamic therapy. Acta Dermato-Venereologica 90: 159-164.

257. Fehr MK, Hornung R, Degen A, Schwarz VA, Fink D, et al. (2002) Photodynamic therapy of vulvar and vaginal condyloma and intraepithelial neoplasia using topically applied 5-aminolevulinic acid. Lasers in Surgery and Medicine 30: 273-279.

258. Hillemanns P, Wang X, Staehle S, Michels W, Dannecker C (2006) Evaluation of different treatment modalities for vulvar intraepithelial neoplasia (VIN): CO(2) laser vaporization, photodynamic therapy, excision and vulvectomy. Gynecologic Oncology 100: 271-275.

259. Campbell SM, Gould DJ, Salter L, Clifford T, Curnow A (2004) Photodynamic therapy using meta-tetrahydroxyphenylchlorin (Foscan) for the treatment of vulval intraepithelial neoplasia. Br J Dermatol 151: 1076-1080.

260. Hillemanns P, Untch M, Dannecker C, Baumgartner R, Stepp H, et al. (2000) Photodynamic therapy of vulvar intraepithelial neoplasia using 5-aminolevulinic acid. Int J Cancer 85: 649-653.

261. Schweitzer VG (2001) PHOTOFRIN-mediated photodynamic therapy for treatment of early stage oral cavity and laryngeal malignancies. Lasers in surgery and medicine 29: 305-313.

262. Jerjes W, Upile T, Hamdoon Z, Abbas S, Akram S, et al. (2011) Photodynamic therapy: The minimally invasive surgical intervention for advanced and/or recurrent tongue base carcinoma. Lasers Surg Med 43: 283-292.

263. Schweitzer VG, Somers ML (2010) PHOTOFRIN-mediated photodynamic therapy for treatment of early stage laryngeal malignancies. Oncology Reviews 4: 203-209.

264. Franco RA Jr (2007) Aminolevulinic acid 585 nm pulsed dye laser photodynamic treatment of laryngeal keratosis with atypia. Otolaryngol Head Neck Surg 136: 882-887.

265. Tan IB, Dolivet G, Ceruse P, Vander P, V, Roest G, et al. (2010) Temoporfin-mediated photodynamic therapy in patients with advanced, incurable head and neck cancer: A multicenter study. Head Neck 32: 1597-604.

266. Kulapaditharom B, Boonkitticharoen V (2000) Photodynamic therapy in management of head and neck cancers and precancerous lesions. J Med Assoc Thai 83: 249-258.

267. Kujundzic M, Vogl TJ, Stimac D, Rustemovic N, Hsi RA, et al. (2007) A Phase II safety and effect on time to tumor progression study of intratumoral light infusion technology using talaporfin sodium in patients with metastatic colorectal cancer. J Surg Oncol 96: 518-524.

268. Moskal TL, Dougherty TJ, Urschel JD, Antkowiak JG, Regal AM, et al. (1998) Operation and photodynamic therapy for pleural mesothelioma: 6-year follow-up. Ann Thorac Surg 66: 1128-1133.

269. Bown SG (2003) Photodynamic therapy for cancer of the pancreas. [French, English]. Acta Endoscopica 33: 531-538.