

In Vitro Anti-tumor Effects of Photodynamic Therapy on Oral Squamous Cell Carcinoma: A Review

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Supplementary file 1

Table S1. Characteristics and Outcome of the Included Studies Based on the Inclusion/Exclusion Criteria

No	Author, year	Type of PS ^a and concentration	Light source/ Wavelength(nm), Energy density(J/cm ²)	Power (W), Power density(mW/cm ²)	Cell line	Cell line origin [@]	Type(s) of Evaluation	Method(s)	Main Outcome(s)
1	Ahn MY,2013 ²⁹	Pha ^b 0.1,0.5,2 μM	Diode laser/664 , 4.24	NR ^c NR	YD-10B	Tongue	-cell viability -exclusion assay -intercellular ROS formation -Detection of change in mitochondrial membrane potential -apoptosis -autophagy - Lactate dehydrogenase (LDH) release assay - Propidium iodide (PI) staining assay	-MTT Trypan blue -H2DCFDA -fluorescence microscopy - Western blot Flow cytometry Annexin V staining -Detection of acidic vesicular organelles_flow cytometry and Monodansylcadaverine (MDC) staining (fluorescence microscopy) -Cytotoxicity Detection Kit	-Pa-PDT induced cell growth inhibition in a dose- and time-dependent manner. -Pa-PDT treatment significantly induced intracellular ROS generation. -Pa-PDT Induced apoptotic cell death and reduced mitochondrial membrane potential.

								- fluorescence microscopy)	
2	Beyer K, 2017 ³⁰	Curcumin 0.01µg/ml to 1µg/ml	UVA, Visible/NR 1, NR	NR NR	HN#	Oral cavity (metastatic site)	-Morphological properties -Cell proliferation -Membrane integrity -Reactive oxygen species generation -Apoptosis -Immunohistochemical analysis of cleaved caspase-3	- Monitoring with microscope - immunosorbent assay - cytotoxicity detection kit - Oxidation of dihydrorhodamine 123, an oxidation-sensitive indicator - DNA fragmentation with Cell Death Detection ELISA - photograph	Curcumin + UVA or visible light irradiation reduced cell proliferation as well as the development of reactive oxygen Species, whereas DNA fragmentation was increased.
3	<u>Bhuvaneshwari R, 2015</u> ³¹	Chlorine e6 50,100 µM	NR/665 1	NR NR	CAL-27, HSC-3, SCC-25#	Tongue	-Immunofluorescence -Apoptosis -Chemotaxis cell migration assay -Extracellular matrix cell invasion assay -Endothelial tube formation assay -Cell viability assay	- fluorescence microscope -Western blot -QCM chemotaxis cell migration assay with a fluorescence plate reader - QCM ECMatrix cell invasion assay with a fluorescence plate reader -(BD BioCoat™ Angiogenesis With a fluorescence microscope -CellTiter-Glo® luminescent	Both Chlorin e6-PDT and the combination of PDT and nimotuzumab and cetuximab increased tumor cell death in different oral cancer and endothelial cells.
4	<u>Cangussu LMB, 2022</u> ³²	AlPc-NE ^d 0.7, 0.35, & 0.17 nM	LED ^a /660 28.35	NR 47.2	SCC9#	Tongue	Cell proliferation cell viability, migration, and cell death assays, immunoassays	- Counting - MTT assay, - orange/ethidium bromide (AO/EB) staining assay - wound healing assay - immunocytochemical assay	-PDT mediated by all AlPc-NE concentrations significantly reduced the viability of SCC9 cells. -PDT with AlPc-NE significantly reduced the rate of migration and increased cell death compared to the control groups. -PDT with AlPc-NE reduced Ki-67 and mutated TP53 immunoexpression.
5	Chen HM, 2011 ³³	5-ALA ^f 1mM	NR/635 4	NR NR	Ca9–22	Gingiva	- Analysis of cellular DNA content, - TUNEL assay - Apoptosis - Immunofluorescence - Western blot - Small interfering RNA	- propidium iodine staining -(TdT)-mediated dUTP Nick End Labeling (TUNEL) assay -ELISA -microscope -western blot -western blot	-5-ALA-PDT induces apoptosis in Ca9–22 cells. -5-ALAPDT activates both the caspase-8 and caspase-9 pathways. -Bay (NF-KB inhibitor) and SP600125 (JNK inhibitor) almost completely abolished ALA-PDT-induced apoptosis
6	Date M, 2003 ³⁴	PAD-S31 ^g 1–100 µg/ml	Diode laser/ 670 1–30	NR NR	SAS, HSC-4	Tongue	-Cell viability -Apoptosis	-MTT	-PDT showed cytotoxicity that was a function of laser energy, drug concentration, and time to the SAS and HSC-4 cell lines.

								-TUNEL assay and detection of fragmented mono- and oligo-nucleosomes by ELISA	
7	Fang CY,2018 ³⁵	5-ALA NR	NR/635±5 NR	NR NR	SAS#	Tongue	-Self-renewal capacity -CD44 -Invasion capacity -miR-145 expression	-RT-PCR -Self-renewal assay -Flow cytometry -Transwell invasion assay	-ALA-PDT upregulated the expression of microRNA-145 (miR-145) in two oral cancer cell lines. -Overexpression of miR-145 in oral CSCs further enhanced the treatment effect of ALA-PDT with lower self-renewal, invasion capacities and reduced CD44 expression.
8	Garg AD,2012 ³⁶	Erythrosine 0.5, 0.25, 0.125 & 0.0625 mg/ml	Tungsten filament lamp /500–550 40.86, 81.72, 122.58	400 22.7	H357#	Tongue	-Cell viability -Sub-cellular Localization -Mitochondrial Trans-Membrane Potential -Cell Death Morphology -Caspase Activity	-CellTiter 96HAQueous One Solution Cell Proliferation Assay -CLSM -Flow cytometry -SEM -Caspase-Glo3/7 assay	-PDT caused higher cell killing rate in the DOK cell line than in H357. - extensive necrosis with high dose PDT occurred in DOK cells, whereas apoptosis was observed at lower doses of PDT for both cell lines. For H357 cells, high dose PDT produced both apoptotic and necrotic responses.
9	Li Q,2020 ³⁷	S-CD ^h 5-ALA 5 nmol/L, 10 nmol/L, 50 nmol/L, 100 nmol/L & 500 nmol/L	Laser/420 NR	2.8125 NR	UM1	Tongue	-Reactive oxygen species (ROS) -Calcium concentration (Ca ²⁺) detection -Cell viability -Bax, Bcl-2 and caspase-3	-Cell counting Kit-8 Assay -AO/PI test -Western blot -Immunofluorescence	-The study showed that under the condition of light irradiation, the S-CDs may act as a more effective nano-weapon for anticancer therapy compared with traditional PS 5-ALA.
10	Ma Y,2020 ⁹	5-ALA 5, 10, 25, 50, 100 mg/L	Laser/635 10.4	NR 87	SCC25	Tongue	-Activity of cells -Apoptosis -Cell cycle	- MTT - annexin V-fluorescein isothiocyanate/propidium iodide double staining flowcytometry - flow cytometry	-5-ALA-PDT inhibited the growth of SCC-25 cells in a concentration-dependent manner. -5-ALA-PDT had a significant effect on apoptosis (also concentration-dependent).
11	Moon S,2013 ³⁸	Pha 0.3 μM	Diode laser / 664 0.5	NR NR	YD10B, YD38#	Tongue, gingiva	-Cell viability -ROS generation	- MTT - fluorescent probe 2',7'-dichlorofluorescein diacetate dye	- YD38 cell viability decreased 60% and YD10B decreased 70% (compared to the control group) -IHOK(S) had more sensitivity to Pa-PDT than IHOK(P)

							-Proteins (caspase-3, caspase-9 and cleaved forms of both) -Apoptosis	- western blot - annexin V-fluorescein isothiocyanate/propidium iodide double staining flowcytometry -Real time-PCR, reverse transcriptase PCR - RUNX3 small interfering RNA transfection	- cytotoxicity of Pa-PDT was proportional to RUNX-3 expression. - RUNX3 knockdown cells showed increased viability in all cell lines.
12	Moon S,2017 ³⁹	Pha 0.3 μ M	NR/NR 0.5	NR NR	YD9, YD10B, YD32, YD38, YD15, YD15M#	Buccal mucosa, tongue, oral cavity, gingiva, tongue, tongue (metastatic site)	- Cell viability -ROS generation -Proteins (caspase-3, caspase-9 and cleaved forms of both) -Apoptosis	- MTT - fluorescent probe 2',7'-dichlorofluorescein diacetate dye - western blot - annexin V-fluorescein isothiocyanate/propidium iodide double staining flowcytometry -miRNA micro-array - Real time-PCR, reverse transcriptase PCR - miRNA transfection	-miRNA-145-5p was consistently down-regulated by Pa-PDT in all cell lines -The higher expression of miR-145-5p led to a better PDT effect. -Cleaved forms of caspase-9 and caspase-3 increased after treatment with the miR-145-5p mimic.
13	Moon Y,2010 ⁴⁰	ALA, ALA-hx ester 0.3mM	LED/613-645 (peak=635) 5	NR 35	YD-10B	Tongue	-Cytotoxicity -Intracellular Reactive Oxygen Species - Caspase-3 Activity -Proteins (caspase-3/-7, cleaved PARP, actin, and Bcl-2)	- MTT - ApoAlert Caspase Colorimetric Assay kit - western blot - Real-Time Reverse Transcriptase-Polymerase Chain Reaction Analysis for Coproporphyrinogen Oxidase	- cell viability decreased 24 hours after treatment with ALA-hx PDT. - the decrease of cell viability by PDT was dependent on the dose of ALA-hx. - ALA-hx PDT induced the apoptosis of YD-10B cells through the mitochondrial-dependent pathway.

								- Alexa Fluor 488 Annexin V and propidium iodide flow cytometry	
14	Nakagawa H,2007 ⁴¹	NPe6 ⁱ 0-10 µg/ml	Diode laser /664 0.1-100	NR 150	HSC-3	Tongue	-VEGF expression	-Enzyme linked immunosorbent assay test -Reverse transcription polymerase chain reaction	-Npe6-PDT induced VEGF expression. -Pre-treatment with CHX and SB203580 inhibited VEGF expression. - Npe6-PDT induced c-jun and c-fos expression.
15	Pan W,2022 ⁴²	HMnO2-IR780 ⁱ 0.125, 0.25, 0.5, 1, 2 mg/ml	Diode laser /808 NR	NR 1000	HN-6	Tongue	-Generation of oxygen - Singlet oxygen generation -Cellular uptake	-Collaborative identification test of calcein acetoxymethyl ester (calcein-AM) and propidium iodide (PI) with CLSM observation -recovered SOSG fluorescence - PA imaging -In vitro fluorescence imaging	-The ROS level of HMnO2-IR780 was lower than that of free IR780 in the absence of H2O2. - The fluorescence signal of the HMnO2-IR780 NPs became stronger as the NP concentration raised from 0.25 to 2 mg/mL, demonstrating that HMnO2-IR780 NP was an effective fluorescent imaging contrast agent. - The HMnO2-IR780+Laser group demonstrated potent photodynamic lethality of HMnO2-IR780 NPs under the 808nm laser. - HMnO2-IR780 killed more cells than free IR780.
16	Parihar A,2011 ⁴³	Chlorin p6 5 µM	LC-122A (Specially Designed Quartz Halogen (mixed) Lamp /635-685 0-3.8	NR 7.9	PECA-4451#	Oral cavity	-Cell viability(phototoxicity) -Detection of histamine H2 receptor -Apoptosis and necrosis	- MTT -Detection of histamine H2 receptor=western blot -Hoechst and propidium iodide5 stain - thin layer chromatography	-The light dose required to achieve 50–60% cell killing was 12 and 32 kJ/m2 for Cp6-his and Cp6 respectively. -At 28 kJ/m2 light dose, Cp6-his and Cp6 cytotoxicities were 95 and 50% respectively.
17	Piskorz J,2014 ⁴⁴	Diazepinoporphyrazines(liposome nanodelivery) Pz1: 0.05, 0.25, 1 µM Pz2,3: 0.1, 1, 10 µM	High power light-emitting diode multichip emitter /690 3.6	NR 3	HSC-3, H413	Tongue, buccal mucosa	-Singlet oxygen generation -Cell viability	-ZnPc as a reference and 1,3-diphenylisobenzofuran (DPBF) as a chemical quencher for singlet oxygen -alar blue assay	-pz1 showed better singlet oxygen generation and lower cell viability than pz2 and pz3. -Encapsulation of Pz1 into liposomes increased its photocytotoxicity three-fold.

18	Qi F,2019 ⁴⁵	PaH ^k 10μM (different in separate assays)	Semicond uctor laser /405nm 1.2, 1.8, 2.4	NR 10-15-20	SCC-9	Tongue	-Cell viability -Cell migration -Apoptosis and cell cycle -Intracellular ROS -Proteins	-Cellular uptake assay - MTT - scratch wound-healing assay - annexin V-fluorescein isothiocyanate/propidium iodide double staining flowcytometry - flowcytometry -oxygen species assay kit - western blot -Immunofluorescence	- cell viability was drug and laser-dose dependent. - PaH-PDT inhibited the migration ability of the cells and induced a G0/G1 cell cycle arrest. - PaH-PDT greatly increased the early and late apoptosis rate of SCC-9 cells. - PaH-PDT significantly increased p53 expression
19	Qin J,2020 ⁴⁶	5-ALA+iron chelation 5-ALA: 0, 10, 25, 50, 100, & 150 μg/ mL 5-ALA/DFX mixtures: 5-ALA concentrat ion of 25μg/mL & DFX concentrat ions of 0.5, 1.0, 1.5, 2.0, 3.0, 5.0 μg/mL	Laser/635 NR	NR 200	SCC-25	Tongue	-Intracellular ROS generation -Cell viability -Apoptosis -Permeability of mitochondrial membrane -Release of Cyt c from mitochondria to cytoplasm	- stain with DAPI -MTT - LIVE/DEAD cell staining kit - Annexin V-FITC/PI apoptosis kit flow cytometry - Rh123+ DAPI stain - immunofluorescence	-DFX enhanced intracellular accumulation of PpIX, ROS generation, and cell apoptosis. - 5-ALA/DFX mixture showed evidently stronger cytotoxic activity after laser irradiation than 5-ALA alone.
20	Senadi GC,2016 ⁴⁷	1- benzothiaz olylphenyl benzotriaz oles 5 μM 2 μM (sublethal)	UV-A lamp/pea k wavelengt h=365 -1 -0.5 (sublethal)	NR 4.762	Ca9-22	Gingival	-cell viability -cell migration (in sub-lethal dose) - Cell invasion assay. (in sub-lethal dose) -Metastasis-associated gene expression: syndecan-1, MMP-2, 9, TIMP-3	- MTT assay -wound healing assay - Boyden chamber invasion assay -RT-PCR -western blotting	-Significant suppression of migration and invasion - Induction of anti-metastatic effect by up-regulation of syndecan-1 and TIMP-3 and down-regulation of heparanase, MMP-2, and MMP-9 mRNA Expressions -Decreased levels of p-EGFR and p-ERK, MMP-2 and MMP-9, increased level of TIMP-3

							-Anticellular migration protein expression of EGFR, ERK and MMPs		
21	Sharma S,2007 ⁴⁸	5-ALA 200µg/ml	Red light/ 630 0.84	NR 0.007	PECA- 4451#	Oral cavity	- Phototoxicity	- - MTT assay	-No significant increase in phototoxicity of cancer cells
22	Sharwani A,2006 ⁴⁹	m-THPC ^l -VB6 (0.5 µg/ml) -H376 (0.25 µg/ml)	Diode laser/652 0.25, 4	NR 25	H376, VB6#	Floor of the mouth, tongue	-Cell viability - Protein expression of MMP-2, MMP-9, MMP-13, uPA and VEGF	MTT assay -zymography and ELISA	Suppression of the activity of the tumor promoting factors MMP-2, -9 and -13, uPA and VEGF
23	Skupin- Mrugalska P,2018 ⁵⁰	liposome- incorporat ed 2- (morpholin -4-yl) ethoxy phthalocya nines 0.1, 1.0 & 10.0µM	LED/690 or 735 3.6	NR NR	HSC-3, H413	Tongue	-Cell viability	-Modified Alamar Blue assay	- Significant loss of HSC-3 cell viability, by >90% at 1.0 and 10.0 µM and >80% at 0.1 µM
24	Song L,2015 ⁵¹	Rose Bengal 10µM	LED/530 1.6	1 20	Cal-27	Tongue	--Activation of apoptosis- related molecules - Intracellular ROS generation -Cell viability -Apoptosis assay	-Western blot - dichloro-dihydro- fluorescein diacetate (DCFHDA) method - MTT -simultaneous staining of cells with propidium iodide (PI) and annexin V (annexinV-FITC)	-Stimulation of the apoptosis signaling pathway and induction of apoptosis -Inhibition of the growth and viability of the Cells -The ROS level was threefold higher in the PDT- treated cells than in the control and RB alone- treated cells.
25	Wang X,2020 ⁵²	5-ALA 0.25 to 2mM	He-Ne laser/ 635 10	NR 18	CAL-27#	Tongue	-Cell viability -Apoptosis - ROS generation -mRNA and protein expression levels of MMP-2 and MMP-9	-MTT assay -flow cytometry, Annexin- V apoptosis detection kit - ROS generation -RT-PCR and western blotting	- Inhibition of the proliferation of cells in a dose- and time-dependent manner - Apoptosis induction - Significant increase in the ROS level -both the mRNA and protein expression levels of MMP-2 and MMP-9 were found to be regulated
26	Zhang XL,2020 ⁵³	GQD-PEG ^m 25, 50, & 100µg/mL	NR/560 NR	NR 1000	SCC 25, SCC 9	Tongue	-cell proliferation -cellular apoptosis	-CCK-8 assay - flow cytometry, and live/dead cell fluorescence staining assay	- SCC 9 and SCC 25 cells showed variability decreases of 70% and 30% respectively - More effective in killing SCC 9
27	Ahn JC,2013 ⁵⁴	9-HpbD-a ⁿ 0-10µg/ml	Laser/670 3.2	0.5 NR	HN3	Tongue	-Cytotoxicity -Apoptosis and necrosis -cytochrome c, caspase 9, caspase 3 and PARP	- MTT -Hoechst 33342 and PI stain -Western blot	-increase in incubation time and 9-HpbD-a concentration led to decreased cell viability. -increase of necrosis with concentration of 9- HpbD-a.

								- Transmission electron microscopy (TEM)	- Cytochrome c, caspase 9 and caspase 3 expression increased at 3hr intervals.
28	Allman R,2000 ⁵⁵	5-ALA 1mM/L	Tungsten-halogen lamp/400-750 NR	NR 50	SCC61	Tongue	-Cell survival -Cell cycle kinetics	-Pooled experiments	-Survival fraction for SCC61 after combined PDT and 8GY was 0.35 and 0.496 depending on which treatment was prior.
29	Boonkitticharoen V,1997 ⁵⁶	HpD ^o 5mg/ml	Black light lamp (UV light lamp)/340-380 0.23	6 NR	SCC4#	Tongue	-Cell survival	-MTT	- The PDT sensitivity of the SCC-4 tumor cell line was not significantly different from those of LS174T, FaDu and A204.
30	Chen WH,2015 ⁵⁷	PpIX ^p 0, 0.5, 1, 2µg/ml	LED/640 100	NR 320	SCC4	Tongue	-Cell viability	-MTT	- A significant difference (p < 0.001; **) in the survival rate was seen between HIF1α siRNA/PDT versus PDT alone. - A significant difference (p < 0.005; *) in the survival rate was seen between HIF1α siRNA/PDT and scrambled siRNA/PDT, while no significant difference was seen with scrambled siRNA when compared to PDT alone.
31	Cohen EM,2010 ⁵⁸	mTHPP ^a 0.18mg/ml	Laser/532, 420 12	NR 20	HSC-3, HN5	Tongue	-Cytotoxicity -Phototoxicity and dark toxicity	-MTT	- Even for mTHPP concentrations less than 25 g/mL, significant cytotoxicity was observed for both cell lines.
32	Ding HY,2011 ⁵⁹	mTHPP 100µg/ml	Laser/532 12	NR 20	HN5	Tongue	-Singlet Oxygen Yield -Cytotoxicity and dark toxicity	-Singlet Oxygen Yield=per dye	- Overall, the O2 generation efficiency increased with increased loading, peaking at the 2% loaded micelles. - 100% HN5 cell death for 0.2%, 2% loaded micelles. - The 10% loaded micelles demonstrated significant dark toxicity in both cell lines.
33	Hung HI,2013 ⁶⁰	Pc4 ⁱ 75–300, 100 –372, 125–451nM	Intense HPD 7404 diode laser/670 0.39	NR NR	UMSCC1, UMSCC 14#	Floor of the mouth	-Cell death -Mfrn2 mRNA and protein levels -Mitochondrial iron uptake and membrane potential	-Propidium iodide (PI) fluorometry -RNAi Knockdown -qPCR -Western blot	-Lysosomal iron release and Mfrn2-dependent mitochondrial iron uptake act synergistically to induce PDT-mediated and iron-dependent mitochondrial dysfunction and subsequent cell killing.

									- Mfrn2 represents a possible biomarker of sensitivity of head and neck cancers to cell killing after PDT.
34	Kofler B,2018 ²³	MB ³ 0, 40, 80, 120, 160µM	GaAlAs diode area laser sources/6 60 95	0.35 NR	SCC25	Tongue	-Cell viability -Clonogenic survival	-MTT -Clone counting assay	-The combination of MB and diode laser evidenced high-efficient loss of cell viability by 5% of the control. -MB combined with the laser allowed significant abrogation of clonogenic growth (p < 0.01).
35	Lim SH,2011 ⁶¹	15(1)-hydroxypurpurin-7-lactone ethyl methyl ester, Pha 0.1-3µM	a 300 W tungsten halogen lamp 2.9, 4.8, 9.6, 14.4	NR 16	HSC3#	Tongue	-Singlet oxygen generation -Phototoxicity -Apoptosis -Cell cycle -PS uptake	-MTT -Annexin V-FITC flow cytometry	- compound 1 was slightly more potent as a PS than Pha by consistently having marginally lower IC50 values across different cell lines. - compound 1 was observed to induce more pronounced apoptosis compared with Pha.
36	Lippert BM,2004 ⁶²	photofrin-II, photosan-3, 0.1–10µg/ml	Laser/ 500, 630 5	NR NR	UMSCC-14A, UMSCC-1, HCFMK-1, UMSCC-27#	Floor of the mouth, floor of the mouth, floor of the mouth, tongue	-Cell Viability -Protein synthesis	-Trypan blue test - ³ H-methionin	- A statistically significant difference for photodynamic effects of both cytostatic agents and the hematoporphyrin derivates could not be shown.
37	Master A,2013 ⁶³	Pc 4-loaded nanoparticles 200, 400 & 800nM	Light-emitting diode array/ 675 NR	NR 6	SCC-15	Tongue	-Cell viability -Clonogenic Cell Survival -Uptake of pc4 nanoparticles	-MTT -Clonogenic Cell Survival assay	-EGFR-targeted Pc 4-nanoformulation underwent faster and higher uptake in EGFR-overexpressing HN SCC-15 cells. - Enhanced Pc 4 uptake resulted in significant cell-killing and drastically reduced post-PDT clonogenicity.
38	Saberi S,2022 ⁶⁴	Spirulina platensis 0.3mg/ml & 0.6mg/ml	Diode laser / 635 2, 4, 12, 24	0.1 200	CAL-27#	Tongue	-Cell viability	-MTT	-The survival rate in CAL-27 and FaDu cell lines were significantly different following irradiation with various laser energy densities. - Different concentrations of S. platensis had no significant effect on the viability of CAL-27 cells and FaDu cells and showed no significant cytotoxicity against HGF cells, with or without the laser.
39	van Driel P,2016 ⁶⁵	IRDye700D X 20-100nM	LED/ 670 ± 10 10	NR 4	OSC19-luc2-cGFP (high EGFR expression) #	Tongue	-Cell viability -Singlet oxygen quantum yield	-Alamar blue fluorescent -Cell binding assay Co-culture assay	-The PS solely bound to cells and induced phototoxicity on cells overexpressing the epidermal growth factor receptor (EGFR), when conjugated to the EGFR targeted nanobodies.

40	Yang TH,2007 ⁶⁶	5-ALA 1mM	Diode laser/633 Up to 6	NR NR	Ca9-22#	Gingiva	-Cytotoxicity -Phosphorylation of the FAK, Src kinase, and ERK -Migration and invasion	-MTT -Wound healing assay -Cell migration assay -Matrigel invasion assay -Immunoblotting	-Sublethal PDT significantly suppressed the migration and invasion of both KJ-1 and Ca9-22 cells.
41	Yu CH,2014 ⁶⁷	5-ALA 1mM	NR/635±5 NR	NR 4	SAS, Ca9-22, primary HNSCC1, primary HNSCC2	Tongue, gingiva, both primaries from head & neck	-ALDH1 activity -Self-renewal capacity -CD44 positivity -stemness	-Aldefluor assay -SYBR RT-PCR -Western blot -Transwell migration assay -Soft agar colony forming assay	-Inhibition of ALDH1 activity in HNC cells under ALA-PDT treatment. -ALA-PDT effectively eliminated self-renewal capacity, CD44 positivity, and stemness signatures in HNC-CSCs. -

*Calculated by Author

Other cell lines were also evaluated but have not been included in this review based on the exclusion criteria

@ Cell line origins have been stated in the same order as the cell lines specified in the Table cells to their left

Abbreviations: ^aPS= photosensitizer, ^bPha= pheophorbide-a, ^cNR= Not Reported, ^dAlPc-NE= aluminum-phthalocyanine chloride nano emulsion, ^eLED=light emitting diode, ^f5-ALA=5-Aminolevulinic acid, ^gPAD-S31=13,17-bis [1-carboxypropion] carbamoyl ethyl 3-ethenyl-8-ethoxyiminoethylidene-7-hydroxy-2,7,12,18- tetramethyl porphyrin sodium, ^hS-CD- = Sulfur-doped carbon dots, ⁱNPe6= Mono-L-aspartyl chlorin e6, ^jHMnO2-IR780= IR780 loaded hollow MnO2 nanoparticles, ^kPaH= Palmatine hydrochloride, ^lDFX= iron chelator deferasirox, ^mm-THPC= meso-tetra(3-hydroxyphenyl)chlorin, ⁿGQD-PEG= Graphene quantum dots conjugated to polyethylene glycol, ^o9-HpbD-a= 9-Hydroxypheophorbide-a, ^pHpD= hematoporphyrin derivative, ^qPpIX=Protoporphyrin IX, ^rmTHPP=meso-tetra(3-hydroxyphenyl)porphyrin, ^sPc4= silicon phthalocyanine, ^tMB= methylene blue