PHOTODYNAMIC THERAPY WITH 5-AMINOLEVULINIC ACID FOR CUTANEOUS BASAL CELL CARCINOMA

Filonenko E.V.[1], **Ivanova-Radkevich V.I.**[2]
[1]P.A. Herzen Moscow Oncology Research Center – branch of FSBI NMRRC of the Ministry of Health of the Russian Federation, Moscow, Russia
[2]Peoples' Friendship University of Russia (RUDN University), Moscow, Russia

Abstract

The aim of the study was to collect and analyze published data from clinical trials on the efficacy of photodynamic therapy (PDT) using 5-ALA-based drugs and its esters in patients with basal cell carcinoma (BCC). The review was conducted using the PubMed and ClinicalTrials.gov databases for the period from 1995 to 2025. Large prospective and retrospective studies with more than 20 patients were included in the analysis. The efficacy of PDT was examined and compared with traditional treatment methods. The analysis demonstrated significant efficacy of PDT in the treatment of BCC. The complete regression rate ranged from 84% to 99% after 3 months of therapy, from 62% to 96% after 12 months, and from 70% to 91% after 5 years. A significantly better cosmetic outcome was recorded compared with surgical methods. Studies have confirmed that PDT has a high safety profile, with severe side effects rare. The most common adverse effects include mild skin irritation, redness, and mild discomfort, which resolve on their own.

Key words: photodynamic therapy, cutaneous basal cell carcinoma, 5-aminolevulinic acid, 5-aminolevulinic acid methyl ester.

Contacts: Filonenko E.V., e-mail: elena.filonenko@list.ru

For citations: Filonenko E.V., Ivanova-Radkevich V.I. Photodynamic therapy with 5-aminolevulinic acid for basal squamous cell carcinoma, *Biomedical Photonics*, 2025, vol. 14, no. 3, pp. 43–51. doi: 10.24931/2413–9432–2025–14–3 –43–51

ФОТОДИНАМИЧЕСКАЯ ТЕРАПИЯ С 5-АЛК БОЛЬНЫХ БАЗАЛЬНОКЛЕТОЧНЫМ РАКОМ КОЖИ

Е.В. Филоненко[1], **В.И. Иванова-Радкевич**[2]
[1]Московский научно-исследовательский онкологический институт им. П.А. Герцена – филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации, Москва, Россия
[2]Российский Университет дружбы народов, Москва, Россия

Резюме

Целью нашей работы были сбор и анализ опубликованных данных клинических исследований эффективности фотодинамической терапии (ФДТ) с препаратами на основе 5-АЛК и ее эфиров у пациентов с базальноклеточным раком кожи (БКРК). Анализ литературы проводился на основе базы данных PubMed и ClinicalTrials.gov за период с 1995 по 2025 гг. В анализ были включены крупные проспективные и ретроспективные исследования с количеством пациентов свыше 20 человек. Рассматривалась эффективность ФДТ, было выполнено сравнение с традиционными методами лечения. Проведенный анализ показал значительную эффективность ФДТ при лечении БКРК. Частота полных регрессий достигала от 84% до 99% через 3 мес после начала терапии, от 62% до 96% через 12 мес и от 70% до 91% через 5 лет. Зарегистрирован значительно лучший косметический результат по сравнению с хирургическими методами. Исследования подтвердили, что ФДТ обладает высоким профилем безопасности с редким развитием тяжелых побочных эффектов. Наиболее частые негативные последствия включают легкое раздражение кожи, покраснения и небольшой дискомфорт, проходящие самостоятельно.

Ключевые слова: фотодинамическая терапия, базальноклеточный рак кожи, 5-аминолевулиновая кислота, метиловый эфир 5-аминолевулиновой кислоты.

Контакты: Филоненко Е.В., e-mail: elena.filonenko@list.ru

Для цитирования: Филоненко Е.В., Иванова-Радкевич В.И. Фотодинамическая терапия с 5-АЛК больных базальноклеточным раком кожи // Biomedical Photonics. – 2025. – Т. 14, № 3. – С. 43–51. doi: 10.24931/2413–9432–2025–14–3–43–51

Introduction

Basal cell carcinoma (BCC) is the most common non-melanocytic skin tumor. It is a slow-growing skin tumor. While it rarely metastasizes, it often occurs in multiple forms and recurs on exposed skin areas, leading to significant treatment challenges. BCC is a heterogeneous group of tumors with histopathological and clinical characteristics ranging from superficial lesions to very extensive and destructive tumors [1].

Epidemiology

In the Russian Federation, when analyzing cancer incidence statistics, BCC is not separately considered from other non-melanocytic skin tumors. However, according to some data, BCC accounts for 75-97% of malignant epithelial skin neoplasms [2,3]. In 2024, the incidence of non-melanoma skin cancer in Russia was 313.9 cases per 100,000 population [3]. Thus, according to indirect estimates, the incidence of non-melanoma skin cancer is approximately 235-305 cases per 100,000 population.

In 2024, the number of newly diagnosed malignant neoplasms in the Russian Federation was 698,693. Of these, approximately 72,000 (10.3% of the overall cancer incidence) were cases of malignant skin cancer (excluding melanoma) [2]. Thus, according to indirect estimates, the number of newly diagnosed cases of non-melanoma skin cancer annually ranges from 54,000 to 70,000.

The incidence of BCC varies greatly depending on the geographic region. The highest incidence is recorded in Australia (up to 1,000 per 100,000 inhabitants per year), followed by the United States (approximately 210-410 per 100,000 inhabitants per year) and Europe (approximately 75-160 per 100,000 inhabitants per year) [1].

The risk of developing BCC is higher in older people and in women (approximately 2 times more often than in men) [1].

Risk factors

The most significant risk factor for developing BCC is sun exposure, both in childhood and in adulthood. The development of BCC is provoked by ultraviolet rays of the UVA and UVB spectrum (the latter to a greater extent). This explains why most BCC lesions occur on sun-exposed areas of skin and are more common in people with fair skin [1]. The cause of it may be mutations caused by UV radiation. BCC is generally characterized by a high mutational tumor load (tumor mutational burden (TMB)), which is 65 mutations/megabases (compared to 14 mutations/megabases for melanoma) and contains a high percentage of mutations induced by UV radiation [4]. Indirect confirmation of the risk associated with UV radiation may also be the results of studies demonstrating an increased risk of developing BCC in patients using solariums, with a confirmed dose-response relationship. Other risk factors include fair skin color, red hair, blue eyes, and older age. A number of authors also associate increased risks of developing BCC with existing hematological neoplasms in the patient [4]. Immunodeficiency, including iatrogenic immunosuppression, can provoke the development of BCC [4]. According to some authors, the risk of developing BCC increases more than 10-fold with tissue and organ transplantation [5].

Classification, Staging, and Clinical Manifestations

The 8th version of the American Joint Committee on Cancer (AJCC) TNM staging system is currently used for BCC staging [6]. Morphological confirmation is mandatory; lymph node status is assessed for staging using clinical examination and instrumental studies [6].

BCC originates from follicular and interfollicular keratinocyte stem cells [1].

BCC is characterized by a variety of clinical forms. The main ones are superficial, nodular, and scleroderma-like.

Superficial BCC is characterized by an erythematous, irregularly shaped lesion with clearly defined borders, often with serous and hemorrhagic crusts on the surface. This form is most often localized on the skin of the trunk [6].

Nodular form of BCC is characterized by a hemispherical nodule with a smooth surface, typically gray-pink in color with a pearly hue. This form is most often found on the face and scalp. One variant of this form is the *pigmented* form, which appears as a pigmented spot or nodule of gray-black color [6].

Scleroderma-like form of BCC is characterized by a whitish, scar-like area with no clear boundaries and peripheral "pearlescent" papules. The central portion of this area may contain punctate areas of hyperpigmentation, erosions of varying sizes, atrophic changes, and dyschromia [6].

Diagnosis

The primary method for the initial diagnosis of BCC is dermatoscopy. Compared to eye examination, dermatoscopy increases the sensitivity and specificity of diagnosis from 66.9% to 85.0% and from 97.2% to 98.2%, respectively [7]. Dermatoscopy can also determine the histopathological subtype of BCC [1].

According to most clinical guidelines, a biopsy is required for the diagnosis of BCC; however, in some cases, cytological diagnosis is acceptable for medical facilities with the appropriate technology [1,8].

Medical imaging, such as magnetic resonance imaging and ultrasound, is often required to determine the extent of locally advanced tumor spread [1].

BCC Prognosis

As noted above, BCC rarely metastasizes. Some researchers estimate the metastasis rate to be 0.0028–0.55% [9]. The development of metastases (especially distant ones) significantly worsens the prognosis of BCC. For example, in a study by McCusker M. *et al.,* the median survival was 87 months for regional metastases and 24 months for distant metastases, with every third patient receiving systemic chemotherapy [10].

The main problems with BCC are local tissue destruction, sometimes quite extensive, and a high recurrence rate. The risk of recurrence depends on the tumor location (e.g., zone H on the face, characterized by a high recurrence rate), histological subtype, perineural invasion, immunosuppression, and previous recurrences [1].

Severe forms of BCC are rare and heterogeneous. Data on the proportion of severe forms in the overall BCC structure vary significantly between studies and average between 0.01% and 0.8% [11-12].

Therapy

Surgical Treatment

Surgical treatment is the standard treatment for patients with BCC. Depending on the tumor characteristics (size, location, presence of recurrence, histology) and the surgeon's qualifications, standard excision or Mohs micrographic surgery may be used. The latter surgical treatment option is used for high-risk tumors, recurrent BCC lesions, and BCC located in critical anatomical zones [1]. Van Loo E. *et al.* showed that the 10-year cumulative risk of BCC recurrence after Mohs surgery is three times lower than after standard surgical treatment (4.4% and 12.2%, respectively), and for recurrent BCC, this difference is even higher (3.9% versus 13.5%) [13]. The main adverse effect of surgical treatment is the possibility of scarring [14].

Radiation Therapy

In elderly patients, with severe comorbidities, or those who refuse surgical treatment, radiation therapy may be an alternative to surgery. For BCC, external beam therapy, brachytherapy, or localized radiation therapy are used. The choice of radiation therapy depends on the tumor size, location, team experience, and resources. Radiation therapy can also be used as adjuvant therapy when re-excision of incompletely resected BCC lesions is not possible. Radiation therapy is comparable to surgical treatment in terms of recurrence-free survival [1]. However, radiation therapy may be associated with a risk of tissue fibrosis and secondary malignancies [14].

Local Drug Therapy

Local drug therapy is also an alternative to surgery [14]. This treatment is non-invasive but may cause local skin reactions including erythema, swelling, itching, hypopigmentation, crusting/scabbing/desquamation, erosions and pain. Topical drug therapy is also associated with lower complete cure rates compared with other treatments [14].

Imiquimod is an immune response modifier used to treat superficial and small nodular BCC in immunocompetent adults. Imiquimod's action is associated with the activation of antitumor immunity. Imiquimod promotes the production of proinflammatory cytokines, chemokines, and other mediators that activate antigen-presenting cells and other components of the innate immune system [1].

According to some authors, the efficacy of imiquimod in BCC is comparable to that of surgical intervention. For example, in a study by Williams H.C. *et al.,* in the treatment of BCC lesions, a positive outcome 5 years after treatment was achieved in 82.5% of cases using imiquimod, compared to 97.7% with surgery [15].

Applications with 5% 5-fluorouracil are also used for BCC. Studies show that 5-fluorouracil is inferior to imiquimod in efficacy in most cases [1].

Cryotherapy

Cryotherapy is indicated only for superficial, low-risk BCC lesions and is not recommended for tumors deeper than 3 mm [1,14]. Disadvantages of cryodestruction include lower efficacy compared to the methods described above, pain, and questionable cosmetic results (the procedure often leaves hypopigmented spots that can persist for years) [1].

Photodynamic Therapy

Photodynamic therapy (PDT) is another alternative treatment option for basal cell carcinoma [1,14,16]. Its high efficacy against a range of skin cancers and precancerous conditions has been demonstrated in numerous clinical and observational studies [17-20]. In particular, our recent reviews demonstrated that PDT can be considered as a first-line treatment option for non-invasive basal cell carcinoma [19,20].

We searched for published results of large randomized and observational clinical trials from 1995 to 2025 on the websites https://clinicaltrials.gov and https://pubmed.ncbi.nlm.nih.gov using the keywords "basal cell carcinoma" and "photodynamic therapy"/"5-aminolevulinic acid"/"MAL – 5-aminolevulinic acid methyl ester." The analysis included randomized controlled and observational studies with more than 20 patients. The table provides summary data on the effectiveness of PDT in patients with BCC.

Discussion

The studies reviewed demonstrated significant heterogeneity in the photosensitizer concentrations,

Таблица
Сводные данные результативности применения фотодинамической терапии у пациентов с базальноклеточным раком кожи

Table
Summary of the effectiveness of photodynamic therapy of basal cell carcinoma

Авторы Authors	Число пациентов / количество очагов / No. of patients/ No. of lesions	Форма БКРК BCC	Фотосенсибилизатор Photosensitizer	Режим облучения Light wavelength	Количество курсов ФДТ Number of PDT courses	Эффективность ФДТ PDT efficiency
Kessels et al., 2017 [21] Van Delft et al., 2022 [22]	80 пациентов 80 patients	Первичный БКРК Primary BCC	МЭ-АЛК за 4 ч до облучения MAL 4 hours before irradiation	75 Дж/см^2 75 J/cm^2	2 курса с интервалом 8 дней. 2 courses with an interval of 8 days	Полная регрессия: 95% через 3 мес 89% через 12 мес 91% через 60 мес Complete regression 95% after 3 months 89% after 12 months 91% after 60 months
Kessels et al., 2017 [21] Van Delft et al., 2022 [22]	82 пациента 82 patients	Первичный БКРК Primary BCC	5-АЛК за 4 ч до облучения 5-ALA 4 hours before irradiation	75 Дж/см^2 75 J/cm^2	Дважды в 1 день с интервалом 2 часа Twice on day 1, interval 1 hours	Полная регрессия: 96% через 3 мес 96% через 12 мес 76% через 60 мес Complete regression 96% after 3 months 96% after 12 months 76% after 60 months
Salmivuori et al., 2020 [23]	26 пациентов 33 очага 26 patients 33 lesions	Поверхностный БКРК на теле, но не на лице и волосистой части головы Superficial BCC on the body area, not face and scalp	5-АЛК (нано-эмульсия) за 3 ч до облучения 5-ALA (nano emulsion) 3 hours before irradiation	37 Дж/см^2 37 J/cm^2	2 курса с интервалом 8-14 дней 2 courses with an interval of 8-14 days	Полная регрессия: 91% через 3 мес Complete regression 91% after 3 months
Salmivuori et al., 2020 [23]	27 пациентов 31 очаг 27 patients 31 lesions	Поверхностный БКРК на теле, но не на лице и волосистой части головы Superficial BCC on the body area, not face and scalp	МЭ-АЛК за 3 ч до облучения MAL 3 hours before irradiation	37 Дж/см^2 37 J/cm^2	2 курса с интервалом 8-14 дней 2 courses with an interval of 8-14 days	Полная регрессия: 97% через 3 мес Complete regression 97% after 3 months
Salmivuori et al., 2020 [23]	24 пациента 31 очаг 24 patients 31 lesions	Поверхностный БКРК на теле, но не на лице и волосистой части головы Superficial BCC on the body area, not face and scalp	ГЭ-АЛК за 3 ч до облучения HAL 3 hours before irradiation	37 Дж/см^2 37 J/cm^2	2 курса с интервалом 8-14 дней 2 courses with an interval of 8-14 days	Полная регрессия: 94% через 3 мес Complete regression 94% after 3 months
Arits et al., 2013 [24], Roozeboom et al., 2016 [25], Jansen et al., 2018 [26]	202 пациента 202 patients	Поверхностный БКРК Superficial BCC	МЭ-АЛК за 3 ч до облучения MAL 3 hours before irradiation	37 Дж/см^2 37 J/cm^2	2 курса с интервалом 1 нед 2 courses with an interval of 1 week	Полная регрессия: 84% через 3 мес 87% через 12 мес 92% через 36 мес 70% через 60 мес Complete regression 84% after 3 months 87% after 12 months 92% after 36 months 70% after 60 months
Morton C. A. et al., 2018 [27]	121 пациент 148 очагов 121 patients 148 lesions	Поверхностный и узелковый БКРК Superficial and nodular BCC	5-АЛК за 3 ч до облучения 5-ALA 3 hours before irradiation	37 Дж/см^2 37 J/cm^2	2 курса с интервалом 1 нед 2 courses with an interval of 1 week	Полная регрессия: 93% через 3 мес 92% через 12 мес Complete regression 93% after 3 months 92% after 12 months

Morton C. A. et al., 2018 [27]	110 пациентов 127 очагов 110 patients 127 lesions	Поверхностный и узелковый БКРК Superficial and nodular BCC	МЭ-АЛК за 3 ч до облучения MAL 3 hours before irradiation	37 Дж/см^2 37 J/cm^2	2 курса с интервалом 1 нед 2 courses with an interval of 1 week	Полная регрессия: 92% через 3 мес 91% через 12 мес Complete regression 92% after 3 months 91% after 12 months
Церковский Д.А. и соавт., 2017 [28] Tserkovsky D.A. et al., 2017 [28]	130 пациентов 156 очагов 130 patients 156 lesions	Первичный и рецидивный БКРК Primary and recurrent BCC	Хлорин е6 за 2,5-3 ч до облучения Chlorin e6 2.5-3 hours before irradiation	50-300 Дж/см^2 50-300 J/cm^2	1 курс 1 course	Полная регрессия при первичном БКРК: 91% через 1-3 мес Полная регрессия при рецидивном БКРК: 90% через 1-3 мес Complete regression in primary BCRC: 91% in 1-3 months Complete regression in recurrent BCRC: 90% in 1-3 months
Mosterd et al., 2008 [29] Roozeboom et al., 2013 [30]	83 очага 83 lesions	Узелковый БКРК Nodular BCC	5-АЛК 5-ALA	–	2 сеанса облучения (интервал 1 ч) 2 irradiation sessions (interval 1 hour)	Полная регрессия: 73% через 60 мес Complete regression 73% after 60 months
Капинус В.Н. и соавт. [31] Kapinus V.N. et al., 2013 [31]	127 пациентов 127 patients	Рецидивный БКРК Recurrent BCC	Хлорин е6 за 3 ч до облучения Chlorin e6 3 hours before irradiation	100-600 Дж/см^2 100-600 J/cm^2	1-4 курса 1-4 courses	Полная регрессия: 68,5% (срок наблюдения 6-60 мес) У пациентов с рецидивами после лучевой терапии – 20,5% У пациентов с рецидивами после лучевой терапии – 20,5% У пациентов с рецидивами после крио-, электро-, лазеркоагуляции и хирургического лечения– 28,6-30,8% У пациентов с рецидивами после предшествующего комбинированного лечения – 47,2% Complete regression: 68.5% (observation period 6-60 months) In patients with relapses after radiation therapy - 20.5% In patients with relapses after radiation therapy - 20.5% In patients with relapses after cryo-, electro-, laser coagulation and surgical treatment - 28.6-30.8% In patients with relapses after previous combined treatment - 47.2%
De Haaset al., 2006 [32] de Vijlderet al., 2012 [33]	100 пациентов 243 очагов 100 patients 243 lesions	Поверхностный БКРК Superficial BCC	МЭ-АЛК за 4 ч до облучения MAL 4 hours before irradiation	75 Дж/см^2 75 J/cm^2	1 сеанс облучения 1 irradiation session	Полная регрессия: 75% через 60 мес Complete regression 75% after 60 months
De Haaset al., 2006 [32] de Vijlderet al., 2012 [33]	55 пациентов 262 очагов 55 patients 262 lesions	Поверхностный БКРК Superficial BCC	МЭ-АЛК за 4 ч до облучения MAL 4 hours before irradiation	20 и 80 Дж/см^2 20 and 80 J/cm^2	2 сеанса облучения (через 4 и 6 ч) 2 irradiation sessions (after 4 and 6 hours)	Полная регрессия: 88% через 60 мес Complete regression 88% after 60 months

Foley et al., 2009 [34]	66 пациентов 75 очагов 66 patients 75 lesions	Узелковый БКРК Nodular BCC	МЭ-АЛК за 3 ч до облучения MAL 3 hours before irradiation	75 Дж/см^2 75 J/cm^2	2 курса с интервалом 1 нед 2 courses with an interval of 1 week	Полная регрессия: 75% через 6 мес Complete regression 75% after 6 months
Basset-Seguin N. et al., 2008 [35]	60 пациентов 114 очагов 60 patients 114 lesions	Поверхностный БКРК Superficial BCC	МЭ-АЛК за 3 ч до облучения MAL 3 hours before irradiation	75 Дж/см^2 75 J/cm^2	1-3 курса в течение 3 мес 1-3 courses for 3 months	Полная регрессия: 88% через 3 мес 78% через 60 мес Complete regression 88% after 3 months 78% after 60 months
Smucler et al., 2008 [36]	286 пациентов 286 очагов 286 patients 286 lesions	Узелковый БКРК Nodular BCC	МЭ-АЛК за 3 ч до облучения MAL 3 hours before irradiation	75 Дж/см^2 75 J/cm^2	2 курса с интервалом 1 нед 2 courses with an interval of 1 week	Полная регрессия: 99% через 3 мес 95% через 12 мес Complete regression 99% after 3 months 95% after 12 months
Rhodes et al., 2004 [37] 2007 [38]	53 пациента 60 очагов 53 patients 60 lesions	Узелковый БКРК Nodular BCC	МЭ-АЛК за 3 ч до облучения MAL 3 hours before irradiation	75 Дж/см^2 75 J/cm^2	2 курса с интервалом 1 нед 2 courses with an interval of 1 week	Полная регрессия: 91% через 3 мес 83% через 12 мес 76% через 24 мес Complete regression 91% after 3 months 83% after 12 months 76% after 24 months
Berroeta et al., 2007 [39]	21 очаг 21 lesions	Узелковый БКРК Nodular BCC	5-АЛК 5-ALA	–	–	Полная регрессия: 62% через 12 мес Complete regression 62% after 12 months

*БКРК – базальноклеточный рак кожи, 5-АЛК – 5-аминолевулиновая кислота, МЭ-АЛК – метиловый эфир 5-аминолевулиновой кислоты, ГЭ-АЛК – гексиловый эфир 5-аминолевулиновой кислоты
*BCC – basal cell carcinoma, 5-ALA – 5-aminolevulinic acid, MAL – 5-aminolevulinic acid methyl ester, HAL – 5-aminolevulinic acid hexyl ester.

light sources, incubation times, and pretreatment strategies used. This precludes a comparative analysis of the efficacy of different PDT regimens and the generalization of results to develop standardized approaches. However, based on the analyzed results, it can be confidently stated that PDT with 5-ALA and MAL-based photosensitizers demonstrates high efficacy against superficial BCC lesions with excellent cosmetic results [14].

The rate of complete regression of BCC lesions at 3 months after PDT averaged 84-99%, 62-96% at 12 months, and 70-91% at 5 years. No difference in efficacy was observed between 5-ALA and MAL [19,20,25-39]. Our search also identified one study involving more than 20 patients using HAL [23]. It should be noted that in most studies, patients with an incomplete response could undergo an additional course of PDT. However, the authors did not demonstrate a relationship between the treatment effect and the number of PDT courses [22,25,26,27,29,30,34-38].

It should be noted that in global clinical practice, photosensitizers based on 5-ALA and its esters are most often used for the treatment of BCC [22,23,24-27,29-30,32-39]. Russian studies also use photosensitizers based on chlorin e6 for the treatment of BCC [28,31]. The treatment efficacy in both cases is quite high.

In most studies, the light dose per irradiation session was approximately 37-75 J/cm^2. However, some authors have demonstrated greater efficacy with fractionated irradiation (two irradiation sessions separated by 1-2 hours) [32,33].

A number of studies have assessed the efficacy of alternative treatments compared to PDT. PDT demonstrated similar complete response rates as most other treatments, with the exception of surgery and imiquimod, which demonstrated better results. The main disadvantage of surgery, especially compared with PDT, was unsatisfactory cosmetic results [22,23,24,37].

The most common adverse events associated with PDT are pain and discomfort. These may occur immediately or after completion of irradiation. Most patients tolerate the treatment well for BCC without the need for additional analgesics. Local adverse events such as mild to moderate erythema, local edema, pruritus, superficial crusting, and vesicular eruptions were also recorded during the observational studies. According to the data from the reviewed studies, all of these reactions were transient and self-limited. Based on these results, PDT has a favorable safety profile [22-39].

The main limitations of some of the reviewed studies included an observation period of less than 12 months, heterogeneity in the assessment of clinical outcomes, and the fact that not all studies reported treatment-related adverse events. The duration of the observation period was important for assessing the effectiveness of various treatments, as BCC can recur years after treatment [14].

Conclusion

Photodynamic therapy demonstrates high efficacy and good cosmetic results in patients with BCC. In some cases (eg, advanced age, severe comorbidities, patient refusal of surgery, contraindications to surgery), PDT can be considered as an alternative to surgery. Numerous clinical studies and observational studies convincingly demonstrate that PDT with 5-ALA and its derivatives is effective, safe, and cosmetically favorable for patients with BCC. However, the variability of treatment protocols highlights the need for further randomized controlled trials to determine optimal treatment parameters.

REFERENCES

1. Basset-Seguin N., Herms F. Update on the management of basal cell carcinoma. *Acta dermato-venereologica*, 2020, Vol. 100 (11), pp. 5750.
2. Samulenko A., Mordovsky A., Polyakov A. Modern Treatment Strategy for Basal Cell Carcinoma of the Head and Neck. *Vrach*, 2017, No. 12, pp. 5-8.
3. Edited by A.D. Kaprin, V.V. Starinsky, A.O. Shakhzadova. The State of Cancer Care in Russia in 2024. – *Moscow: P.A. Herzen Moscow Research Institute of Oncology, a branch of the National Medical Research Radiological Center of the Ministry of Health of the Russian Federation*, 2025, p. 275.
4. Peris K. et al. European consensus-based interdisciplinary guideline for diagnosis and treatment of basal cell carcinoma – update 2023. *European Journal of Cancer*, 2023, Vol. 192, pp. 113254.
5. Krynitz B. et al. Risk of basal cell carcinoma in Swedish organ transplant recipients: a population-based study. *British Journal of Dermatology*, 2016, Vol. 174(1), pp. 95-103.
6. Clinical Guidelines – Basal Cell Skin Cancer – 2020-2021-2022 (20.01.2023) – Approved by the Ministry of Health of the Russian Federation.
7. Reiter O. et al. The diagnostic accuracy of dermoscopy for basal cell carcinoma: A systematic review and meta-analysis. *Journal of the American Academy of Dermatology*, 2019, Vol. 80(5), pp. 1380-1388.
8. Filonenko E.V., Grigoriev N.I. Photodynamic Therapy for a Patient with Basal Cell Carcinoma of the Lower Eyelid Skin (Clinical Case). *Biomedical Photonics*, 2023, Vol. 12(4), pp. 30-32. doi: 10.24931/2413–9432–2023–12-4-30–32.
9. Peris K. et al. Diagnosis and treatment of basal cell carcinoma: European consensus–based interdisciplinary guidelines. *European Journal of cancer*, 2019, Vol. 118, pp. 10-34.
10. McCusker M. et al. Metastatic basal cell carcinoma: prognosis dependent on anatomic site and spread of disease. *European journal of cancer*, 2014, Vol. 50(4), pp. 774-783.
11. Morton C. et al. European Dermatology Forum Guidelines on topical photodynamic therap. *European Journal of Dermatology*, 2015, Vol. 25(4), pp. 296-311.
12. Schulten R. et al. Comparison of the uptake of 5-aminolevulinic acid and its methyl ester in keratinocytes and skin. *Naunyn-Schmiedeberg's archives of pharmacology*, 2012, Vol. 385(10), pp. 969-979.
13. Van Loo E. et al. Surgical excision versus Mohs' micrographic surgery for basal cell carcinoma of the face: a randomised clinical trial with 10 year follow-up. *European Journal of Cancer*, 2014, Vol. 50(17), pp. 3011-3020.
14. Zeitouni N. C. et al. 5-aminolevulinic acid photodynamic therapy for the treatment of basal and squamous cell carcinoma: A systematic review. *Photodiagnosis and Photodynamic Therapy*, 2025, pp. 104649.
15. Williams H. C. et al. Surgery versus 5% imiquimod for nodular and superficial basal cell carcinoma: 5-year results of the SINS randomized controlled trial. *Journal of Investigative Dermatology*, 2017, Vol. 137(3), pp. 614-619.
16. Wang J. Y. et al. Photodynamic Therapy: Clinical Applications in Dermatology. *Journal of the American Academy of Dermatology*, 2025.
17. Calzavara-Pinton P.G. et al. Methylaminolaevulinate-based photodynamic therapy of Bowen's disease and squamous cell carcinoma. *British Journal of Dermatology*, 2008, Vol. 159(1), pp. 137-144.
18. Keyal U. et al. Present and future perspectives of photodynamic therapy for cutaneous squamous cell carcinoma.

ЛИТЕРАТУРА

1. Basset-Seguin N., Herms F. Update on the management of basal cell carcinoma //Acta dermato-venereologica. – 2020. – Vol. 100 (11). – P. 5750.
2. Самуленко А., Мордовский А., Поляков А. Современная стратегия лечения базальноклеточного рака кожи головы и шеи // Врач. – 2017. – №. 12. – С. 5-8.
3. Под ред. А.Д. Каприна, В.В. Старинского, А.О. Шахзадовой. Состояние онкологической помощи населению России в 2024 году. – Москва: МНИОИ им. П.А. Герцена – филиал ФГБУ «НМИЦ радиологии» Минздрава России. – 2025. – С. 275.
4. Peris K. et al. European consensus-based interdisciplinary guideline for diagnosis and treatment of basal cell carcinoma – update 2023 // European Journal of Cancer. – 2023. – Vol. 192. – P. 113254.
5. Krynitz B. et al. Risk of basal cell carcinoma in Swedish organ transplant recipients: a population-based study // British Journal of Dermatology. – 2016. – Vol. 174(1). – P. 95-103.
6. Клинические рекомендации – Базальноклеточный рак кожи – 2020-2021-2022 (20.01.2023) – Утверждены Минздравом РФ.
7. Reiter O. et al. The diagnostic accuracy of dermoscopy for basal cell carcinoma: A systematic review and meta-analysis // Journal of the American Academy of Dermatology. – 2019. – Vol. 80(5). – P. 1380-1388.
8. Филоненко Е.В., Григорьевых Н.И. Фотодинамическая терапия больной базальноклеточным раком кожи нижнего века (клиническое наблюдение) // Biomedical Photonics. – 2023. – Т. 12, № 4. – С. 30-32. doi: 10.24931/2413–9432–2023–12-4-30–32.
9. Peris K. et al. Diagnosis and treatment of basal cell carcinoma: European consensus–based interdisciplinary guidelines // European Journal of cancer. – 2019. – Vol. 118. – P. 10-34.
10. McCusker M. et al. Metastatic basal cell carcinoma: prognosis dependent on anatomic site and spread of disease // European journal of cancer. – 2014. – Vol. 50(4). – P. 774-783.
11. Morton C. et al. European Dermatology Forum Guidelines on topical photodynamic therapy // European Journal of Dermatology. – 2015. – Vol. 25(4). – P. 296-311.
12. Schulten R. et al. Comparison of the uptake of 5-aminolevulinic acid and its methyl ester in keratinocytes and skin // Naunyn-Schmiedeberg's archives of pharmacology. – 2012. – Vol. 385(10). – P. 969-979.
13. Van Loo E. et al. Surgical excision versus Mohs' micrographic surgery for basal cell carcinoma of the face: a randomised clinical trial with 10 year follow-up // European Journal of Cancer. – 2014. – Vol. 50(17). – P. 3011-3020.
14. Zeitouni N. C. et al. 5-aminolevulinic acid photodynamic therapy for the treatment of basal and squamous cell carcinoma: A systematic review // Photodiagnosis and Photodynamic Therapy. – 2025. – P. 104649.
15. Williams H. C. et al. Surgery versus 5% imiquimod for nodular and superficial basal cell carcinoma: 5-year results of the SINS randomized controlled trial //Journal of Investigative Dermatology. – 2017. – Vol. 137(3). – P. 614-619.
16. Wang J. Y. et al. Photodynamic Therapy: Clinical Applications in Dermatology //Journal of the American Academy of Dermatology. – 2025.
17. Calzavara-Pinton P.G. et al. Methylaminolaevulinate-based photodynamic therapy of Bowen's disease and squamous cell carcinoma // British Journal of Dermatology. – 2008. – Vol. 159(1). – P. 137-144.
18. Keyal U. et al. Present and future perspectives of photodynamic therapy for cutaneous squamous cell carcinoma // Journal of the

Journal of the American Academy of Dermatology, 2019, Vol. 80(3), pp. 765-773.
19. Filonenko E.V., Ivanova-Radkevich V.I. Photodynamic therapy of cutaneous squamous cell carcinoma. *Biomedical Photonics*, 2024, Vol. 13(4), pp. 33-39. doi: 10.24931/2413-9432-2024-13-4-33-39
20. Filonenko E.V., Ivanova-Radkevich V.I. Photodynamic therapy of Bowen's disease. *Biomedical Photonics*, 2023, Vol. 12(4), pp. 22-29. doi: 10.24931/2413-9432-2023-12-4-22-29
21. Kessels J.P.H.M. et al. Treatment of superficial basal cell carcinoma by topical photodynamic therapy with fractionated 5-aminolaevulinic acid 20% vs. two-stage topical methyl aminolaevulinate: results of a randomized controlled trial. *British Journal of Dermatology*, 2018, Vol. 178(5), pp. 1056-1063.
22. Van Delft L.C.J. et al. Long-term efficacy of photodynamic therapy with fractionated 5-aminolevulinic acid 20% versus conventional two-stage topical methyl aminolevulinate for superficial basal-cell carcinoma. *Dermatology*, 2022, Vol. 238(6), pp. 1044-1049.
23. Salmivuori M. et al. Hexyl aminolevulinate, 5-aminolevulinic acid nanoemulsion and methyl aminolevulinate in photodynamic therapy of non-aggressive basal cell carcinomas: A non-sponsored, randomized, prospective and double-blinded trial. *Journal of the European Academy of Dermatology and Venereology*, 2020, Vol. 34(12), pp. 2781-2788
24. Arits A.H.M.M. et al. Photodynamic therapy versus topical imiquimod versus topical fluorouracil for treatment of superficial basal-cell carcinoma: a single blind, non-inferiority, randomised controlled trial. *The lancet oncology*, 2013, Vol. 14(7), pp. 647-654.
25. Roozeboom M. H. et al. Three-year follow-up results of photodynamic therapy vs. imiquimod vs. fluorouracil for treatment of superficial basal cell carcinoma: a single-blind, noninferiority, randomized controlled trial. *Journal of Investigative Dermatology*, 2016, Vol. 136(8), pp. 1568-1574.
26. Jansen M.H.E. et al. Five-year results of a randomized controlled trial comparing effectiveness of photodynamic therapy, topical imiquimod, and topical 5-fluorouracil in patients with superficial basal cell carcinoma. *Journal of Investigative Dermatology*, 2018, – Vol. 138(3), pp.527-533.
27. Morton C.A. et al. A randomized, multinational, noninferiority, phase III trial to evaluate the safety and efficacy of BF-200 aminolaevulinic acid gel vs. methyl aminolaevulinate cream in the treatment of nonaggressive basal cell carcinoma with photodynamic therapy. *British Journal of Dermatology*, 2018, Vol. 179(2), pp. 309-319.
28. Tserkovsky D.A., et al. Photodynamic therapy of basal cell skin cancer with the photosensitizer Photolon. *Biomedical Photonics*, 2017, Vol. 6(1), pp. 12-19.
29. Mosterd K. et al. Fractionated 5-aminolaevulinic acid–photodynamic therapy vs. surgical excision in the treatment of nodular basal cell carcinoma: results of a randomized controlled trial. *British Journal of Dermatology*, 2008, Vol. 159(4), pp. 864-870.
30. Roozeboom M.H. et al. Fractionated 5-aminolevulinic acid photodynamic therapy after partial debulking versus surgical excision for nodular basal cell carcinoma: a randomized controlled trial with at least 5-year follow-up. *Journal of the American Academy of Dermatology*, 2013, Vol. 69(2). – P. 280-287
31. Kapinus V.N. et al. Possibilities of photodynamic therapy in the treatment of basal cell skin cancer relapses. *Oncology. Journal named after PA Herzen*, 2013, Vol. 1(4), pp. 40-44.
32. de Haas E.R.M. et al. Fractionated illumination significantly improves the response of superficial basal cell carcinoma to aminolevulinic acid photodynamic therapy. *Journal of investigative dermatology*, 2006, Vol. 126(12), pp. 2679-2686
33. De Vijlder H.C. et al. Light fractionation significantly improves the response of superficial basal cell carcinoma to aminolaevulinic acid photodynamic therapy: five-year follow-up of a randomized, prospective trial. *Acta dermato-venereologica*, 2012, Vol. 92(6), pp. 641-647.
34. Foley P. et al. Photodynamic therapy with methyl aminolevulinate for primary nodular basal cell carcinoma: results of two randomized studies. *International journal of dermatology,* 2009, Vol. 48(11), pp. 1236-1245.

American Academy of Dermatology. – 2019. – Vol. 80(3). – P. 765-773.
19. Filonenko E.V., Ivanova-Radkevich V.I. Photodynamic therapy of cutaneous squamous cell carcinoma // Biomedical Photonics. – 2024. – Vol. 13(4). – P. 33-39.
20. Filonenko E.V., Ivanova-Radkevich V.I. Photodynamic therapy of Bowen's disease // Biomedical Photonics. – 2023. – Vol. 12(4). – P. 22-29.
21. Kessels J.P.H.M. et al. Treatment of superficial basal cell carcinoma by topical photodynamic therapy with fractionated 5-aminolaevulinic acid 20% vs. two-stage topical methyl aminolaevulinate: results of a randomized controlled trial //British Journal of Dermatology. – 2018. – Vol. 178(5). – P. 1056-1063.
22. Van Delft L.C.J. et al. Long-term efficacy of photodynamic therapy with fractionated 5-aminolevulinic acid 20% versus conventional two-stage topical methyl aminolevulinate for superficial basal-cell carcinoma // Dermatology. – 2022. – Vol. 238(6). – P. 1044-1049.
23. Salmivuori M. et al. Hexyl aminolevulinate, 5-aminolevulinic acid nanoemulsion and methyl aminolevulinate in photodynamic therapy of non-aggressive basal cell carcinomas: A non-sponsored, randomized, prospective and double-blinded trial // Journal of the European Academy of Dermatology and Venereology. – 2020. – Vol. 34(12). – P. 2781-2788
24. Arits A.H.M.M. et al. Photodynamic therapy versus topical imiquimod versus topical fluorouracil for treatment of superficial basal-cell carcinoma: a single blind, non-inferiority, randomised controlled trial // The lancet oncology. – 2013. – Vol. 14(7). – P. 647-654.
25. Roozeboom M. H. et al. Three-year follow-up results of photodynamic therapy vs. imiquimod vs. fluorouracil for treatment of superficial basal cell carcinoma: a single-blind, noninferiority, randomized controlled trial // Journal of Investigative Dermatology. – 2016. – Vol. 136(8). – P. 1568-1574.
26. Jansen M.H.E. et al. Five-year results of a randomized controlled trial comparing effectiveness of photodynamic therapy, topical imiquimod, and topical 5-fluorouracil in patients with superficial basal cell carcinoma // Journal of Investigative Dermatology. – 2018. – Vol. 138(3). – P. 527-533.
27. Morton C.A. et al. A randomized, multinational, noninferiority, phase III trial to evaluate the safety and efficacy of BF-200 aminolaevulinic acid gel vs. methyl aminolaevulinate cream in the treatment of nonaggressive basal cell carcinoma with photodynamic therapy // British Journal of Dermatology. – 2018. – Vol. 179(2). – P. 309-319.
28. Церковский Д. А. и др. Фотодинамическая терапия базально-клеточного рака кожи с фотосенсибилизатором фотолон // Biomedical Photonics. – 2017. – Т. 6, №. 1. – С. 12-19.
29. Mosterd K. et al. Fractionated 5-aminolaevulinic acid–photodynamic therapy vs. surgical excision in the treatment of nodular basal cell carcinoma: results of a randomized controlled trial // British Journal of Dermatology. – 2008. – Vol. 159(4). – P. 864-870.
30. Roozeboom M.H. et al. Fractionated 5-aminolevulinic acid photodynamic therapy after partial debulking versus surgical excision for nodular basal cell carcinoma: a randomized controlled trial with at least 5-year follow-up // Journal of the American Academy of Dermatology. – 2013. – Vol. 69(2). – P. 280-287
31. Капинус В.Н. и др. Возможности фотодинамической терапии при лечении рецидивов базально-клеточного рака кожи // Онкология. Журнал им. ПА Герцена. – 2013. – Т. 1, №. 4. – С. 40-44.
32. de Haas E.R.M. et al. Fractionated illumination significantly improves the response of superficial basal cell carcinoma to aminolevulinic acid photodynamic therapy //Journal of investigative dermatology. – 2006. – Vol. 126(12). – P. 2679-2686
33. De Vijlder H.C. et al. Light fractionation significantly improves the response of superficial basal cell carcinoma to aminolaevulinic acid photodynamic therapy: five-year follow-up of a randomized, prospective trial // Acta dermato-venereologica. – 2012. – Vol. 92(6). – P. 641-647.
34. Foley P. et al. Photodynamic therapy with methyl aminolevulinate for primary nodular basal cell carcinoma: results of two randomized studies // International journal of dermatology. – 2009. – Vol. 48(11). – P. 1236-1245.

35. Basset-Seguin N. et al. Topical methyl aminolaevulinate photodynamic therapy versus cryotherapy for superficial basal cell carcinoma: a 5 year randomized trial. *European Journal of dermatology*, 2008, Vol. 18(5), pp. 547-553.
36. Šmucler R., Vlk M. Combination of Er: YAG laser and photodynamic therapy in the treatment of nodular basal cell carcinoma. *Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery*, 2008, Vol. 40(2), pp. 153-158.
37. Rhodes L. E. et al. Photodynamic therapy using topical methyl aminolevulinate vs surgeryfor nodular basal cell carcinoma: results of a multicenter randomized prospective trial. *Archives of dermatology*, 2004, Vol. 140(1), pp. 17-23.
38. Rhodes L. E. et al. Five-year follow-up of a randomized, prospective trial of topical methyl aminolevulinate photodynamic therapy vs surgery for nodular basal cell carcinoma. *Archives of dermatology*, 2007, Vol. 143(9), pp. 1131-1136
39. Berroeta L. et al. A randomized study of minimal curettage followed by topical photodynamic therapy compared with surgical excision for low-risk nodular basal cell carcinoma. *British Journal of Dermatology*, 2007, Vol. 157(2), pp. 401-403.

35. Basset-Seguin N. et al. Topical methyl aminolaevulinate photodynamic therapy versus cryotherapy for superficial basal cell carcinoma: a 5 year randomized trial //European Journal of dermatology. – 2008. – Vol. 18(5). – P. 547-553.
36. Šmucler R., Vlk M. Combination of Er: YAG laser and photodynamic therapy in the treatment of nodular basal cell carcinoma // Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery. – 2008. – Vol. 40(2). – P. 153-158.
37. Rhodes L. E. et al. Photodynamic therapy using topical methyl aminolevulinate vs surgeryfor nodular basal cell carcinoma: results of a multicenter randomized prospective trial //Archives of dermatology. – 2004. – Vol. 140(1). – P. 17-23.
38. Rhodes L. E. et al. Five-year follow-up of a randomized, prospective trial of topical methyl aminolevulinate photodynamic therapy vs surgery for nodular basal cell carcinoma //Archives of dermatology. – 2007. – Vol. 143(9). – P. 1131-1136
39. Berroeta L. et al. A randomized study of minimal curettage followed by topical photodynamic therapy compared with surgical excision for low-risk nodular basal cell carcinoma // British Journal of Dermatology. – 2007. – Vol. 157(2). – P. 401-403.