

## Epithelioid sarcoma

Anna M. Czarnecka

Department of Soft Tissue, Bone Sarcoma and Melanoma, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland

Epithelioid sarcoma (ES) is a very rare sarcoma characterized by loss of *INI1*. Enzinger first described ES in 1970, but the histopathologic differential diagnosis of ES remains challenging. There are two ES subtypes, the classical type with spindle epithelioid to the central pseudogranulomatous cells, and the proximal type, which is predominantly composed of epithelioid and rhabdoid cells. ES symptoms and signs are not specific and depend on tumor localization. The only treatment for ES is radical excision with a microscope-radical margin. In general, the best treatment for ES in extremities is radical resection with a wide margin or amputation with or without lymph node dissection. Surgery may be followed by adjuvant chemotherapy and/or radiation therapy. Referral of patients with ES to a sarcoma center that offers hypofractionation RT trials and multidisciplinary clinical trials should be considered upfront. Neoadjuvant chemotherapy with ifosfamide and doxorubicin with / or without radiation therapy must be used after a multidisciplinary team discussion. On 23 January 2020, the US Food and Drug Administration (FDA) first approved tazemetostat – an inhibitor of zeste homolog 2 enhancer – therapy for metastatic ES or locally advanced ES not eligible for radical resection.

**Key words:** sarcoma, epithelioid sarcoma, Enzinger, tazemetostat

### Introduction

Epithelioid sarcoma is a very rare (less than 1% of all soft tissue sarcomas) high-grade soft tissue sarcoma (STS) with a known propensity for locoregional recurrence and dissemination [1]. In general, ES tumors are built by spindled and epithelioid cells that circumscribe areas of central hyalinization and necrosis. Although ESs are of mesenchymal origin, their mixed differentiation makes their histopathological differential diagnosis challenging. The incidence in the EU and the United States is less than 0.2 and 0.5 new cases per million inhabitants per year, respectively. Enzinger first described epithelioid sarcoma (ES) in 1970 as a rare tumor of the distal extremities with epithelioid cytomorphology on pathological examination [2, 3]. The 5- and 10-year survival rates for ES are approximately 68% and 61%, respectively. No survival advantage was found for any gender, race, or ethnic group [4]. In the course of the natural history of ES, local failure occurs in approximately 25%, lymph

node involvement in 30% and distant metastases are found in more than 40% of patients [5]. However, ES is commonly initially diagnosed as a benign condition, thus delaying definitive treatment. ES can also be misdiagnosed as another subtype of sarcoma:

- clear cell sarcoma,
- fibrosarcoma,
- synovial sarcoma,
- peripheral nerve sheath tumor,
- spinal cell sarcoma,
- fibrous histiocytosarcoma or other fibrohistiocytic tumor,
- nodular tenosynovitis or fasciitis,
- squamous cell carcinoma,
- Dupuytren's disease,
- necrotising granuloma,
- rheumatoid nodule [6, 7].

#### Jak cytować / How to cite:

Czarnecka AM. *Epithelioid sarcoma*. NOWOTWORY J Oncol 2023; 73: 154–161.

There are two typical ES morphologies:

- the classical type, which is a spindle-epithelioid to central pseudogranulomatous cells, and
- the proximal type, which is predominantly composed of epithelioid and rhabdoid cells.

Proximal ES is also known as the large cell subtype. The classic ES type is epidemiologically more common than the proximal type. Furthermore, the classic subtype is most commonly diagnosed in adolescents and young adults (10 to 40 years of age), while the proximal one in adults between 20 and 65 years of age. Classic ES is usually diagnosed in locations of the distal upper extremities with more than 50% developing in the hand and fingers. Proximal ESs develop more often in the hip, trunk, pelvis, peritoneal cavity, or inguinal and genital area. Proximal ES type is built of large cells with prominent nucleoli that resemble a poorly differentiated carcinoma and a frequent rhabdoid phenotype. In ES, periosteal bone invasion may also occur, as well as central necrosis of the tumor, its hemorrhage or ulceration [8].

Epithelioid sarcoma symptoms and signs are not specific and depend on tumor location, therefore include a lump or swelling in the area, with masses greater than 20 cm, slightly mobile tumors, painful on palpation and without skin changes, or ulcerated and indurated lesions, but also rectum bleeding, vaginal bleeding, epistaxis, hemoptysis, nausea, vomiting, abdominal pain, abdominal fullness, ptosis, headaches, neck pain, eye pain and swelling, diarrhea or constipation, depression, anorexia, weight loss, or fever [2]. Regional spread of ES through lymphatic drainage and/or direct infiltration results in lymph node metastases, while distant metastases arise with hematogenous spread mainly in the lungs or liver [9]. Indolent tumor growth along with distal location may also lead to inappropriate primary diagnosis and subsequent surgical procedures prior to referral to the reference sarcoma clinic [10, 11]. Most often, at first, ES presents as a slowly growing, painless, and firm nodule, but the course of ES is unpredictable, including rapid progression with extensive lymph node or distant metastasis development. Furthermore, the natural history of ES is characterized by a high risk of multiple recurrences. ES tends to spread along the fascia and muscles, resulting in multifocality of the tumor [10, 12–14]. The 5-year risk of recurrence after radical treatment is high, up to 70% [5, 13, 15, 16]. The ES tends to have regional lymphatic spread by more than 20% [6, 17, 18]. Patients with proximal-type tumor, ES tumor diameter >5 cm, multifocal tumors, nodal involvement, ES tumor necrosis, vascular invasion, and high mitotic index have shorter 5-year disease-specific survival (DSS) [14].

Epithelioid sarcoma has a complex genome with a high mutational rate that is comparable to that of ovarian carcinoma. More than 90% of ES cases are characterized by the loss of function of integrase interactor 1 (*INI1*; *SMARCB1*/hSNF5 – chromatin regulator, subfamily B, member 1 or malignant rhabdoid tumor suppressor) [11, 19]. The INI1 protein is a core

component of the SWItch/ sucrose non-fermentable (SWI/SNF) chromatin remodeling complex that alters the structure of chromatin and facilitates transcription, replication, and DNA repair. *INI1* is located on chromosome 22q11.2 [20]. Other key SWI/SNF complex subunits are *BRG1* (SMARCA4), *BRM* (SNF2L2, SMARCA2), *PBRM1* (hPB1, BAF180), and *BAF155* (SMARCC1) that can all be lost in ES [21]. In ES, multiple mechanisms lead to inactivation of *SMARCB1*, including homozygous deletions, monoallelic deletion, nonsense point mutations, epigenetic mechanisms, and microRNA down-regulation of mRNA [22]. *INI1* signals regulate chromosomal stability by signaling through the p16INK4a-Rb-E2F pathway. At the same time, in tumors with the *INI1* gene, zeste homolog 2 (EZH2) signaling is up-regulated [23]. As a result, EZH2 is recruited to Polycomb targets and trimethylation of histone 3 lysine 27 in these regions leads to repression of target genes [24]. The loss of *INI1* expression is characteristic for both conventional ES and proximal ES [20].

Epithelioid sarcoma is characterized by the expression of carcinoma markers (e.g. cytokeratin and EMA) and sarcoma markers (e.g. vimentin), as well as CD34, while negative for: S-100, and CD31 [14]. Other alterations found in ES cells include activation of PI3K/AKT/mTOR, overexpression of EGFR, and activation of *MET* [11]. In an animal model, it was proven that *smarcb1* deficiency with concordant *TP53* mutation is sufficient to induce the development of ES [25]. In ES cells, it was shown that *SMARCB1* negatively controls the expression of cyclin D1, E2F, and AURKA. As a result of the loss of *SMARCB1* in these tumors, cyclin D1, E2F, and AURKA are upregulated and stimulate the cell cycle. In normal cells, *SMARCB1/INI1* suppresses tumor progression by p16INK4a signaling to pRb (retinoblastoma), a tumor suppressor that negatively regulates cell cycle progression from G0/G1 to the S phase. At the same time, enhanced MYC activity and increased DNA replication are found in cells with *SMARCB1* loss. Importantly, *SMARCB1* interacts with the BRCA1, BARD1 and XPC proteins responsible for nucleotide excision repair. It also regulates chromosomal stability [26]. As a result, *SMARCB1* loss results in the fast proliferation of cells and mutation accumulation. *SMARCB1* also inhibits the signaling of the sonic hedgehog (SHH) pathway, and this pathway is important in the development of radio and chemo-resistance [27, 28]. Next-generation sequencing (NGS) may enable further insights into the pathogenesis of ES, allowing genetic classification and biomarker discovery. NGS may also be used to verify diagnoses [29, 30].

## Radical treatment

The curative treatment of ES is radical excision with wide R0 margins. In general, the best treatment for ES in the extremities is *en bloc* excision. In cases with large tumors, amputation must often be performed in order to obtain radical resection with tumor-free margins. Primary tumor resection may be accompanied by lymph node dissection. After MDT

adjuvant chemotherapy and/or radiation therapy can also be used in high-risk patients [31–33]. MDT should consider neoadjuvant chemotherapy for ES patients based on prognostic stratification with Sarculator nomogram for STS (<https://www.sarcuator.com/>) [32, 34, 35].

The proximal subtype of ES is more aggressive, has higher rates of recurrence and metastases, and generally worse prognosis and higher mortality compared to classical ES [36]. In ES treatment, a sophisticated and well-planned surgical reconstruction can be performed with microsurgery, including free flap reconstruction or tendon transfers. In general practice, most ESs are extracompartmental and infiltrate surrounding tissues, including the neurovascular plexus. Consequently, due to anatomical constraints, conservative surgery is not always possible in the case of locally advanced tumors. Furthermore, due to a common location in the distal part of the extremities, in cases of extensive infiltration of the soft tissues that limits the possibility of reconstruction, amputation can also be required [10, 12, 13]. In centrally located ES tumors, the complex anatomy surrounding the spine further complicates the treatment and often makes complete resection R0 extremely difficult or impossible [37]. If lymph node metastases occur, therapeutic lymph node dissection (LND) should be performed [6, 10, 38]. The high rate of nodal involvement may justify performing a sentinel node biopsy (SLNB) in selected cases of ES, but a low percentage of occult metastases was reported in this subtype of sarcoma. However, SLNB should be considered as a minimally invasive N disease staging procedure [17, 39–41].

Neoadjuvant chemotherapy and radiotherapy (RT) can be considered in patients with ES after multidisciplinary team evaluation (MDT) [42]. In fact, radiation therapy has been reported to reduce the risk of local recurrence, but not overall survival (OS) [43]. At this point in time, radical surgery with conventionally fractionated perioperative RT is considered the standard of care in ES [44], while patients should be referred to trials with RT hypofractionation and combined therapy clinical trials when available in a sarcoma center. There are no phase III data on the role of RT in recurrent and metastatic ES. If RT was not used in radical treatment, perioperative RT may be considered in recurrent ES. In the event of a local recurrence in the field, re-irradiation should be considered only in selected cases. Patients with a limited volume of local ES recurrence can be treated with perioperative or definitive brachytherapy in sarcoma centers [45]. Select ES patients with oligometases may receive definitive radiation therapy [46, 47]. Patients with large recurrent ES tumors may receive multidisciplinary treatment with chemotherapy with RT with/without hyperthermia after MDT [48]. Palliative RT can be used for symptomatic ES metastases (palliative single fraction) [11].

In some cases, after MDT, perioperative chemotherapy can be considered [5, 13, 49, 50]. According to the current ESMO–EURACAN–GENTURIS Clinical Practice Guidelines, neo-

adjuvant treatment of operable localized STS of the extremities and the trunk wall is not yet standard treatment, although it can be proposed for fit patients with high-risk disease [51]. In patients with ES, MDT may advise perioperative chemotherapy for patients with large, high-grade tumors. After surgery with incomplete resection, as well as in cases of up-front metastases, chemotherapy is also considered [42, 52]. In studies by NIO-PIB, the Royal Marsden Hospital, Japan, and the French Sarcoma Group, doxorubicin with ifosfamide (AI) was the most commonly used [13, 49, 53, 54]. After neoadjuvant chemotherapy, objective and/or pathological responses are expected in 15% of cases [13, 49, 55]. Chemotherapy regimens used in radical and / or first-line treatment should be based on doxorubicin. In addition to the AI regimen and doxorubicin monotherapy, the use of CyVADIC (cyclofosfamide, vincristine, doxorubicin, and dacarbazine) and VAIA (vincristine, doxorubicin, ifosfamide, actinomycin-D) have also been reported [11, 50]. Most recently, ES patients were recruited into a trial of radiation therapy with or without combination chemotherapy or pazopanib prior to surgery to treat patients with newly diagnosed nonrhabdomyosarcoma soft tissue sarcomas that can be removed by surgery. There are no reports on the association between perioperative chemotherapy and OS, DMFS, or LRFS [5, 42, 50, 52].

### Systemic therapies in advanced epithelioid sarcoma

Epithelioid sarcoma metastasizes most frequently to the lungs or pleura [6, 12, 15, 56]. High-risk epithelioid sarcomas are patients with large tumors, high tumor grade, inadequate tumor resection, and metastatic disease, predicting a relatively poor clinical outcome [57]. There are no specific guidelines based on high-quality evidence on systemic therapy in advanced ES [58]. Patients treated at Royal Marsden Hospital benefit from significantly longer OS when treated with palliative chemotherapy versus BSC (mOS: 16.8 vs. 8.7 months,  $p = 0.044$ ) [50]. Most available data on systemic ES therapy are reported as retrospective studies, case series, and case reports. Only a small number of patients with ES were treated in clinical trials. 27 ES patients were treated in EORTC trials 62012, 62043, 62072 and 62091. Among these cases, objective responses were reported for those treated with doxorubicin with ifosfamide (12.5 – 1/8), pazopanib (objective response rate [ORR] 100% – 2/2), or trabectedin (33.3% – 1/3), but without OR when treated with doxorubicin monotherapy. The median progression-free survival (PFS) for patients treated first-line was 4.04 months. The median OS of these patients was only 10.93 months [59]. The analysis of 74 patients with ES has shown that patients receiving first-line systemic therapy have ORR of 15%, disease control rate (DCR) of 20%, and a median duration of response (DOR) of 3.3 months (95% CI: 2.1–5.2 months). In these patients, the mPFS was 2.5 months (95% confidence interval [CI]: 1.7–6.9 months), and the mOS was 15.2 months (95%

CI: 11.4–21.7 months). More than half of these patients were treated with regimens based on doxorubicin [60]. In general, the most extensive evidence on the use of chemotherapy in ES comes from a recently published series of 115 patients with advanced or metastatic ES. These patients were not treated with chemotherapy in a perioperative setting before treatment was reported. This analysis has shown that there is no difference in response rates between patients treated with monotherapy anthracycline or with anthracycline combined with ifosfamide [61]. In clinical practice, anthracyclines can be combined not only with ifosfamide, but also vincristine, dacarbazine, actinomycin D, cyclofosfamide, or carboplatin [38, 49, 50, 55, 62]. Anthracycline-based therapy results in favorable disease control. In reported studies, ORR for anthracycline-based regimens is 22% (1 complete response [CR], 18 partial response [PR]), while DCR = 75%. The response rate was numerically higher in proximal ES cases than in classical ES (26% vs. 19%,  $p = 0.44$ ). The median PFS was 6.76 months (95%CI: 23–35). The median OS from the beginning of palliative chemotherapy was only 12 months (95% CI: 29–73). The six-month OS was 79% and the 12-month OS rate was 46% [49].

Another common regimen used in ES treatment is gemcitabine with docetaxel (GD) [50, 61, 63]. In 12 patients treated with gemcitabine-based chemotherapy, the ORR and DCR rates were 58% and 83%, respectively. When gemcitabine was used, the median PFS was 9 months in patients treated first-line and 8 months in the mixed population [63]. In another report on the use of gemcitabine in ES, the ORR was reported to be 27%, while the DCR was reported to be 66% with the median PFS of 4 months. Interestingly, a trend toward higher response rates has been reported in the classical ES subtype (30% vs. 22%;  $p = 0.72$ ) and the location of the distal tumor (40% vs. 14%;  $p = 0.08$ ). No differences in ORR were reported between patients treated with gemcitabine monotherapy and GD chemoregimen [61]. Recently, albumin-bound paclitaxel (nab-paclitaxel) 300 mg/m<sup>2</sup> *via* intravenous bolus on day 1, and gemcitabine 1250 mg/m<sup>2</sup> gemcitabine *via* intravenous bolus on days 1 and 8 chemoregimen was used in ES therapy and has been shown to be safe and moderately effective [64].

Only case reports on other chemotherapy agents in ES have been published and include high-dose ifosfamide, trofosfamide, gemcitabine with cisplatin, dacarbazine, and trabectedin [63, 65]. An interesting case report was published showing complete remission (CR) of ES pulmonary metastases treated with vinorelbine (17–30 mg/m<sup>2</sup> every 2 to 4 weeks) therapy. In this case, the response CR was 4 years long [66]. Another ES case achieved a partial response (PR) with a duration of 27.4 months [67].

Targeted therapies for ES are still in development. **Pazopanib** is the first tyrosine kinase inhibitor (TKI) approved for ES therapy [50, 61]. In a case series of 18 pazopanib patients treated, no ORRs were reported, 50% of the patients benefited with stable diseases (SD), but PFS was only 3 months. How-

ever, PR case reports on pazopanib treatment in patients with metastatic ES have also been published [68, 69]. In the pulled analysis of the EORTC trial, pazopanib was used in patients with ES in the second line and resulted in ORR 11.1% (1/9) and a median PFS of 2.73 months [59]. A case report on **sunitinib** therapy in ES was published. This patient achieved long-term stabilization of the disease (>32 months) after progression in two lines of chemotherapy [70]. Sunitinib in combination with nivolumab was found to improve PFS in patients with advanced epithelioid sarcoma [71].

Another therapy that has shown some benefit in case series is another TKI, anlotinib, in combination with PD-1 inhibitors [72]. Some data on **dasatinib** activity in ES are also available. In an open-label single-arm SARC0009 study 2/7 patients achieved objective tumor responses according to Choi's criteria. The mPFS was 7.9 months and the PFS rate at 6 months was 57%. However, the OS was poor with a 2-year OS rate of 21% [73]. Another study investigates ipilimumab in combination with dasatinib in patients with refractory and/or unresectable GIST or other STS, including epithelioid sarcoma [74].

As ES sarcoma was reported to have a relatively high mutation rate, it is a candidate for **immune checkpoint inhibitor** therapies [75]. ES patient were recruited in a KEYNOTE-051 study of **pembrolizumab** in patients with PD-L1 positive, advanced, refractory, or refractory solid tumors, but no subgroup ORR was reported until now [76]. Case reports of the efficacy of pembrolizumab in advanced ES in adults have also been published. Pembrolizumab was used in the second line of palliative therapy, after chemotherapy with doxorubicin-ifosfamide [77]. In the study of **nivolumab**, a 24-year-old male ES metastatic lung patient had PR after 4 immunotherapy cycles, but the response was not durable as the patient progressed after the next 4 cycles [78]. An interesting case of long-term response to camrelizumab was recently published. This patient had high expression of PD-L1 and a high number of tumor-infiltrating lymphocytes in the tumor [79]. Currently, patients with ES are enrolled in a study of nivolumab and ipilimumab in children and young adults with *INI1* negative cancers and tigolumab and atezolizumab for the treatment of *SMARCB1* or *SMARCA4* deficient tumors.

On 23 January 2020, the US Food and Drug Administration (FDA) approved the first EZH2 methyltransferase inhibitor – **tazemetostat** – for the treatment of patients with locally advanced and metastatic epithelioid sarcoma not eligible for complete resection in patients older than 16 years. In a phase I trial (NCT02601937) for patients with tazemetostat ES, they achieved SD and continued treatment for >20 months [80]. Later, FDA approval was granted based on the results of a phase 2 trial (NCT02601950). In the analyzed ES cohort (cohort 5), 62 patients were treated, 24 in the first line and 38 in the second or further lines. In the trial, patients were treated with 800 mg of tazemetostat twice daily. In the phase 2 trial, ORR was 15% (95% CI: 6.9–25.8), while DCR was 26% (95%

CI: 15.5–38.5). In particular, ORR was 25% in patients treated in the first line, but only 8% in patients treated in other lines [81]. In this trial, 26% of the patients had disease control at 32 weeks and 21% remained progression-free at 1 year. The median response duration (DOR) was 16.1 months [82]. After FDA approval, the results of the treatment of patients from an additional cohort of ES (cohort 6) were reported. In cohort 6, ORR was 11.4% and DCR – 50% [82]. The final pooled analysis confirmed mPFS of 3.7 months and mOS – 18.0 months. The toxicity profile of tazemetostat is favorable. The most common AE are nausea and fatigue (in 40% of patients). Grade 3 treatment-related AEs were reported in 16% of the patients [81, 82]. Currently, in the next trial, tazemetostat is tested with doxorubicin in the Phase 1b/3 trial as the first-line therapy for patients with advanced epithelioid sarcoma [83]. Furthermore, potential synergism between prior radiotherapy and TAZ requires further investigation [84]. A phase II study of temozolomide and olaparib for the treatment of advanced uterine leiomyosarcoma is ongoing [85]. ES patients are enrolled in cohort D of the CAIRE: A multicenter open-label phase 2 basket study evaluating the EZH2 inhibitor tazemetostat in combination with durvalumab in patients with advanced solid tumors [86].

## Conclusions

Epithelioid sarcoma is built by pleomorphic epithelioid cells and the proximal subtype is more aggressive than the classical subtype, as it has higher recurrence and metastasis rates, and shorter overall survival. ES occurs more frequently in adolescents and young adults with a slight predominance of men. Loss of expression of SWI/SNF chromatin-remodeling complex proteins plays an important role in ES development. At initial diagnosis, the tumor stage should be evaluated not only with clinical and radiological examination, but also with imaging focused on regional lymph nodes and the chest (pulmonary metastases). Surgical resection of primary tumors may be curative. The patient should be treated with wide local excision or with surgery plus lymphadenectomy. Radiation therapy should be considered after MDT to decrease the local recurrence rate. Currently hypofractionated preoperative RT may be advised [87, 88]. Referral to a sarcoma center for hypofractionated radiotherapy with hyperthermia may be considered in patients with marginally resectable or unresectable ES and in patients who are not eligible for chemotherapy [89]. Adjuvant radiation therapy is recommended in cases with positive margins (R1/R2 resections). Local recurrences are common in ES and most often develop within six months after radical treatment. Up to 75% of cases with local recurrence also develop distant metastases [9]. However, most patients have an advanced stage at first diagnosis with lymph node and / or lung metastases. Chemotherapy may provide palliation in patients with metastatic and unresectable epithelioid sarcoma, but responses are short and there is still an unmet need for more effective novel targeted therapies.

Immunotherapy may be an alternative option for patients with metastatic ES. Most recently, tazemetostat showed activity in advanced ES with loss of *INI1/SMARCB1*. Tazemetostat therapy is a new treatment option for patients with ES approved by the FDA [90, 91].

## Acknowledgements

The authors thank Prof. Ewa Bartnik for her expertise and assistance in the language editing of the manuscript. This work was supported by a NCN 2019/35/O/NZ2/03761 grant.

**Conflict of interest:** none declared

**Anna M. Czarnecka**

*Maria Skłodowska-Curie National Research Institute of Oncology  
Department of Soft Tissue, Bone Sarcoma and Melanoma  
ul. Roentgena 5  
02-781 Warszawa, Poland  
e-mail: anna.czarnecka@pib-nio.pl*

*Received: 23 Mar 2023*

*Accepted: 28 Mar 2023*

## References

1. Gliński B, Dymek P, Ryś J, et al. Epithelioid sarcoma – a case report and literature review. *Contemporary Oncology/Współczesna Onkologia*. 2008; 12(2): 95–98.
2. Fisher C. Epithelioid sarcoma of Enzinger. *Adv Anat Pathol*. 2006; 13(3): 114–121, doi: 10.1097/00125480-200605000-00002, indexed in Pubmed: 16778474.
3. Enzinger FM. Epithelioid sarcoma. A sarcoma simulating a granuloma or a carcinoma. *Cancer*. 1970; 26(5): 1029–1041, doi: 10.1002/1097-0142(197011)26:5<1029::aid-cnrcr2820260510>3.0.co;2-r.
4. Jawad MU, Extejn J, Min ES, et al. Prognostic factors for survival in patients with epithelioid sarcoma: 441 cases from the SEER database. *Clin Orthop Relat Res*. 2009; 467(11): 2939–2948, doi: 10.1007/s11999-009-0749-2, indexed in Pubmed: 19224301.
5. Baratti D, Pennacchioli E, Casali PG, et al. Epithelioid sarcoma: prognostic factors and survival in a series of patients treated at a single institution. *Ann Surg Oncol*. 2007; 14(12): 3542–3551, doi: 10.1245/s10434-007-9628-9, indexed in Pubmed: 17909905.
6. Sobanko JF, Meijer L, Nigra TP. Epithelioid sarcoma: a review and update. *J Clin Aesthet Dermatol*. 2009; 2(5): 49–54, indexed in Pubmed: 20729965.
7. Alexander L. Epithelioid Sarcoma of Upper Extremity: Diagnostic Dilemma With Therapeutic Challenges. *Cureus*. 2021; 13(3): e14156, doi: 10.7759/cureus.14156, indexed in Pubmed: 33936870.
8. Hasegawa T, Matsuno Y, Shimoda T, et al. Proximal-type epithelioid sarcoma: a clinicopathologic study of 20 cases. *Mod Pathol*. 2001; 14(7): 655–663, doi: 10.1038/modpathol.3880368, indexed in Pubmed: 11454997.
9. Zegarra Buitron E, Vidal Panduro DA, Morales Luna D. Clinicopathological Characteristics, Treatment, and Survival in Patients Diagnosed With Proximal-Type Epithelioid Sarcoma: A Case Report and Systematic Review. *Cureus*. 2022; 14(12): e32962, doi: 10.7759/cureus.32962, indexed in Pubmed: 36712724.
10. Pradhan A, Grimer RJ, Abudu A, et al. Epithelioid sarcomas: How important is loco-regional control? *Eur J Surg Oncol*. 2017; 43(9): 1746–1752, doi: 10.1016/j.ejso.2017.07.002, indexed in Pubmed: 28756018.
11. Czarnecka AM, Sobczuk P, Kostrzanowski M, et al. Epithelioid Sarcoma-From Genetics to Clinical Practice. *Cancers (Basel)*. 2020; 12(8), doi: 10.3390/cancers12082112, indexed in Pubmed: 32751241.
12. Rutkowski P. *Soft Tissue Sarcomas*. Via Medica, Gdańsk 2016.
13. Levy A, Le Péchoux C, Terrier P, et al. Epithelioid sarcoma: need for a multimodal approach to maximize the chances of curative conservative treatment. *Ann Surg Oncol*. 2014; 21(1): 269–276, doi: 10.1245/s10434-013-3247-4, indexed in Pubmed: 24046109.



14. Regalbuto A, Tudosie A, Klenotic E. A metastatic distal-type epithelioid sarcoma: Case report and review. *Int J Surg Case Rep.* 2020; 71: 144–146, doi: 10.1016/j.ijscr.2020.04.096, indexed in Pubmed: 32450373.
15. Guzzetta AA, Montgomery EA, Lyu H, et al. Epithelioid sarcoma: one institution's experience with a rare sarcoma. *J Surg Res.* 2012; 177(1): 116–122, doi: 10.1016/j.jss.2012.04.030, indexed in Pubmed: 22575361.
16. Thway K, Jones RL, Noujaim J, et al. Epithelioid Sarcoma: Diagnostic Features and Genetics. *Adv Anat Pathol.* 2016; 23(1): 41–49, doi: 10.1097/PAP.000000000000102, indexed in Pubmed: 26645461.
17. Daigeler A, Kuhnen C, Moritz R, et al. Lymph node metastases in soft tissue sarcomas: a single center analysis of 1,597 patients. *Langenbecks Arch Surg.* 2009; 394(2): 321–329, doi: 10.1007/s00423-008-0371-x, indexed in Pubmed: 18594854.
18. Andreou D, Boldt H, Werner M, et al. Sentinel node biopsy in soft tissue sarcoma subtypes with a high propensity for regional lymphatic spread—results of a large prospective trial. *Ann Oncol.* 2013; 24(5): 1400–1405, doi: 10.1093/annonc/mds650, indexed in Pubmed: 23372051.
19. Jamshidi F, Bashashati A, Shumansky K, et al. The genomic landscape of epithelioid sarcoma cell lines and tumours. *J Pathol.* 2016; 238(1): 63–73, doi: 10.1002/path.4636, indexed in Pubmed: 2635879.
20. Hornick JL, Dal Cin P, Fletcher CDM. Loss of INI1 expression is characteristic of both conventional and proximal-type epithelioid sarcoma. *Am J Surg Pathol.* 2009; 33(4): 542–550, doi: 10.1097/PAS.0b013e3181882c54, indexed in Pubmed: 19033866.
21. Li Li, Fan XS, Xia QY, et al. Concurrent loss of INI1, PBRM1, and BRM expression in epithelioid sarcoma: implications for the cocontributions of multiple SWI/SNF complex members to pathogenesis. *Hum Pathol.* 2014; 45(11): 2247–2254, doi: 10.1016/j.humpath.2014.06.027, indexed in Pubmed: 25200863.
22. Ngo C, Postel-Vinay S. Immunotherapy for SMARCB1-Deficient Sarcomas: Current Evidence and Future Developments. *Biomedicines.* 2022; 10(3), doi: 10.3390/biomedicines10030650, indexed in Pubmed: 35327458.
23. Le Loarer F, Zhang L, Fletcher CD, et al. Consistent SMARCB1 homozygous deletions in epithelioid sarcoma and in a subset of myoepithelial carcinomas can be reliably detected by FISH in archival material. *Genes Chromosomes Cancer.* 2014; 53(6): 475–486, doi: 10.1002/gcc.22159, indexed in Pubmed: 24585572.
24. Kohashi K, Oda Y. Oncogenic roles of SMARCB1/INI1 and its deficient tumors. *Cancer Sci.* 2017; 108(4): 547–552, doi: 10.1111/cas.13173, indexed in Pubmed: 28109176.
25. Oppel F, Shao S, Gendrezig S, et al. p53 Pathway Inactivation Drives SMARCB1-deficient p53-wildtype Epithelioid Sarcoma Onset Indicating Therapeutic Vulnerability Through MDM2 Inhibition. *Mol Cancer Ther.* 2022; 21(11): 1689–1700, doi: 10.1158/1535-7163.MCT-21-0770, indexed in Pubmed: 36099437.
26. Kohashi K, Oda Y. Oncogenic roles of SMARCB1/INI1 and its deficient tumors. *Cancer Sci.* 2017; 108(4): 547–552, doi: 10.1111/cas.13173, indexed in Pubmed: 28109176.
27. Carballo GB, Honorato JR, de Lopes GP, et al. A highlight on Sonic hedgehog pathway. *Cell Commun Signal.* 2018; 16(1): 11, doi: 10.1186/s12964-018-0220-7, indexed in Pubmed: 29558958.
28. Del Savio E, Maestro R. Beyond SMARCB1 Loss: Recent Insights into the Pathobiology of Epithelioid Sarcoma. *Cells.* 2022; 11(17), doi: 10.3390/cells11172626, indexed in Pubmed: 36078034.
29. Szurian K, Kashofer K, Liegl-Atzwanger B. Role of Next-Generation Sequencing as a Diagnostic Tool for the Evaluation of Bone and Soft-Tissue Tumors. *Pathobiology.* 2017; 84(6): 323–338, doi: 10.1159/000478662, indexed in Pubmed: 28817827.
30. Rutkowski P, Prochorec-Sobieszek M, Wągródzki M, et al. Diagnostyka z wykorzystaniem sekwencjonowania następnej generacji (NGS) w mięsakach — rekomendacje. *Onkol Prakt Klin Edu.* 2020; 6(1): 1–8.
31. Spunt SL, Francotte N, De Salvo GL, et al. Clinical features and outcomes of young patients with epithelioid sarcoma: an analysis from the Children's Oncology Group and the European paediatric soft tissue Sarcoma Study Group prospective clinical trials. *Eur J Cancer.* 2019; 112: 98–106, doi: 10.1002/ejca.2019.02.001, indexed in Pubmed: 30954717.
32. Pasquali S, Palmerini E, Quagliuolo V, et al. Neoadjuvant chemotherapy in high-risk soft tissue sarcomas: A Sarculator-based risk stratification analysis of the ISG-ST5 1001 randomized trial. *Cancer.* 2022; 128(1): 85–93, doi: 10.1002/cncr.33895, indexed in Pubmed: 34643947.
33. Adjuvant chemotherapy for localised resectable soft-tissue sarcoma of adults: meta-analysis of individual data. *Sarcoma Meta-analysis Collaboration. Lancet.* 1997; 350(9092): 1647–1654, indexed in Pubmed: 9400508.
34. Bonvalot S, Wunder J, Gronchi A, et al. Complete pathological response to neoadjuvant treatment is associated with better survival outcomes in patients with soft tissue sarcoma: Results of a retrospective multicenter study. *Eur J Surg Oncol.* 2021; 47(8): 2166–2172, doi: 10.1016/j.ejso.2021.02.024, indexed in Pubmed: 33676792.
35. Pasquali S, Colombo C, Bottelli S, et al. The sarculator predicted risk of distant metastasis and overall survival in patients with high-risk soft tissue sarcoma treated with perioperative chemotherapy in a randomized controlled trial. *Eur J Surg Oncol.* 2018; 44(10): e2, doi: 10.1016/j.ejso.2018.07.012, indexed in Pubmed: 29475197.
36. Thway K, Jones RL, Noujaim J, et al. Epithelioid Sarcoma: Diagnostic Features and Genetics. *Adv Anat Pathol.* 2016; 23(1): 41–49, doi: 10.1097/PAP.000000000000102, indexed in Pubmed: 26645461.
37. Hu W, Wu X, Ma H, et al. Systematic Review of Published Cases of Primary Epithelioid Sarcoma of the Spine. *Med Sci Monit.* 2023; 29: e938416, doi: 10.12659/MSM.938416, indexed in Pubmed: 36604864.
38. de Visscher SA, van Ginkel RJ, Wobbes T, et al. Epithelioid sarcoma: Still an only surgically curable disease. *Cancer.* 2006; 107(3): 606–612, doi: 10.1002/cncr.22037, indexed in Pubmed: 16804932.
39. Maduekwe UN, Hornicek FJ, Springfield DS, et al. Role of sentinel lymph node biopsy in the staging of synovial, epithelioid, and clear cell sarcomas. *Ann Surg Oncol.* 2009; 16(5): 1356–1363, doi: 10.1245/s10434-009-0393-9, indexed in Pubmed: 19259743.
40. Seal A, Tse R, Wehrli B, et al. Sentinel node biopsy as an adjunct to limb salvage surgery for epithelioid sarcoma of the hand. *World J Surg Oncol.* 2005; 3: 41, doi: 10.1186/1477-7819-3-41, indexed in Pubmed: 15987509.
41. Blazer DG, Sabel MS, Sondak VK. Is there a role for sentinel lymph node biopsy in the management of sarcoma? *Surg Oncol.* 2003; 12(3): 201–206, doi: 10.1016/s0960-7404(03)00030-6, indexed in Pubmed: 12957624.
42. Callister MD, Ballo MT, Pisters PW, et al. Epithelioid sarcoma: results of conservative surgery and radiotherapy. *Int J Radiat Oncol Biol Phys.* 2001; 51(2): 384–391, doi: 10.1016/s0360-3016(01)01646-7, indexed in Pubmed: 11567812.
43. Regalbuto A, Tudosie A, Klenotic E. A metastatic distal-type epithelioid sarcoma: Case report and review. *Int J Surg Case Rep.* 2020; 71: 144–146, doi: 10.1016/j.ijscr.2020.04.096, indexed in Pubmed: 32450373.
44. Casali PG, Abecassis N, Bauer S, et al. Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2018; 29: iv51–iv67, doi: 10.1093/annonc/mdy096, indexed in Pubmed: 29846498.
45. Naghavi AO, Fernandez DC, Mesko N, et al. American Brachytherapy Society consensus statement for soft tissue sarcoma brachytherapy. *Brachytherapy.* 2017; 16(3): 466–489, doi: 10.1016/j.brachy.2017.02.004, indexed in Pubmed: 28342738.
46. Stragliotto CL, Karlsson K, Lax I, et al. A retrospective study of SBRT of metastases in patients with primary sarcoma. *Med Oncol.* 2012; 29(5): 3431–3439, doi: 10.1007/s12032-012-0256-2, indexed in Pubmed: 22815154.
47. Lindsay AD, Haupt EE, Chan CM, et al. Treatment of Sarcoma Lung Metastases with Stereotactic Body Radiotherapy. *Sarcoma.* 2018; 2018: 9132359, doi: 10.1155/2018/9132359, indexed in Pubmed: 29808081.
48. de Jong MAA, Oldenburg S, Bing Oei S, et al. Reirradiation and hyperthermia for radiation-associated sarcoma. *Cancer.* 2012; 118(1): 180–187, doi: 10.1002/cncr.26252, indexed in Pubmed: 21713762.
49. Jones RL, Constantinidou A, Olmos D, et al. Role of palliative chemotherapy in advanced epithelioid sarcoma. *Am J Clin Oncol.* 2012; 35(4): 351–357, doi: 10.1097/COC.0b013e3182118cf7, indexed in Pubmed: 21422990.
50. Kim C, Yoo KH, Kim MH, et al. Different subtypes of epithelioid sarcoma and their clinical implication: long-term multi-institutional experience with a rare sarcoma. *APMIS.* 2017; 125(3): 223–229, doi: 10.1111/apm.12656, indexed in Pubmed: 28233450.
51. Casali PG, Blay JY, Abecassis N, et al. ESMO Guidelines Committee, EURACAN and GENTURIS. Electronic address: clinicalguidelines@esmo.org, ESMO Guidelines Committee, EURACAN and GENTURIS. Electronic address: clinicalguidelines@esmo.org. Soft tissue and visceral sarcomas: ESMO–EURACAN–GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2021; 32(11): 1348–1365, doi: 10.1016/j.annonc.2021.07.006, indexed in Pubmed: 34303806.
52. Rekhi B, Gorad BD, Chinoy RF. Clinicopathological features with outcomes of a series of conventional and proximal-type epithelioid sarcomas, diagnosed over a period of 10 years at a tertiary cancer hospital in India. *Virchows Arch.* 2008; 453(2): 141–153, doi: 10.1007/s00428-008-0639-0, indexed in Pubmed: 18607629.

53. Outani H, Imura Y, Tanaka T, et al. Clinical outcomes of patients with epithelioid sarcomas: impact and management of nodal metastasis. *Int J Clin Oncol*. 2018; 23(1): 181–188, doi: 10.1007/s10147-017-1179-x, indexed in Pubmed: 28799063.
54. Spillane AJ, Thomas JM, Fisher C. Epithelioid sarcoma: the clinicopathological complexities of this rare soft tissue sarcoma. *Ann Surg Oncol*. 2000; 7(3): 218–225, doi: 10.1007/BF02523657, indexed in Pubmed: 10791853.
55. Casanova M, Ferrari A, Collini P, et al. Italian Soft Tissue Sarcoma Committee. Epithelioid sarcoma in children and adolescents: a report from the Italian Soft Tissue Sarcoma Committee. *Cancer*. 2006; 106(3): 708–717, doi: 10.1002/cncr.21630, indexed in Pubmed: 16353216.
56. Ross HM, Lewis JJ, Woodruff JM, et al. Epithelioid sarcoma: clinical behavior and prognostic factors of survival. *Ann Surg Oncol*. 1997; 4(6): 491–495, doi: 10.1007/BF02303673, indexed in Pubmed: 9309338.
57. Tang F, Tie Y, Wei YQ, et al. Targeted and immuno-based therapies in sarcoma: mechanisms and advances in clinical trials. *Biochim Biophys Acta Rev Cancer*. 2021; 1876(2): 188606, doi: 10.1016/j.bbcan.2021.188606, indexed in Pubmed: 34371128.
58. Rutkowski P, Kosela-Paterczyk H, Kozak K, et al. Postępowanie diagnostyczno-terapeutyczne u chorych na mięsaki tkanek miękkich u dorosłych — zalecenia ekspertów. *Onkol Prakt Klin Edu*. 2022.
59. Touati N, Schöffski P, Litière S, et al. European Organisation for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group Experience with Advanced/Metastatic Epithelioid Sarcoma Patients Treated in Prospective Trials: Clinical Profile and Response to Systemic Therapy. *Clin Oncol (R Coll Radiol)*. 2018; 30(7): 448–454, doi: 10.1016/j.clon.2018.02.065, indexed in Pubmed: 29550245.
60. Gounder MM, Merriam P, Ratan R, et al. Real-world outcomes of patients with locally advanced or metastatic epithelioid sarcoma. *Cancer*. 2021; 127(8): 1311–1317, doi: 10.1002/cncr.33365, indexed in Pubmed: 33296083.
61. Frezza AM, Jones RL, Lo Vullo S, et al. Anthracycline, Gemcitabine, and Pazopanib in Epithelioid Sarcoma: A Multi-institutional Case Series. *JAMA Oncol*. 2018; 4(9): e180219, doi: 10.1001/jamaoncol.2018.0219, indexed in Pubmed: 29800950.
62. Tsakonas GP, Kallistratos MS, Balamoti EK, et al. Rare and aggressive metastatic, axial multifocal local epithelioid sarcoma associated with paraneoplastic granulocytosis and hypoglycaemia. *Lancet Oncol*. 2007; 8(1): 82–84, doi: 10.1016/S1470-2045(06)71015-4, indexed in Pubmed: 17196515.
63. Pink D, Richter S, Gerdes S, et al. Gemcitabine and docetaxel for epithelioid sarcoma: results from a retrospective, multi-institutional analysis. *Oncology*. 2014; 87(2): 95–103, doi: 10.1159/000362602, indexed in Pubmed: 25011671.
64. Tian Z, Zhang F, Li Po, et al. Albumin-bound paclitaxel and gemcitabine combination therapy in soft tissue sarcoma. *BMC Cancer*. 2020; 20(1): 698, doi: 10.1186/s12885-020-07199-0, indexed in Pubmed: 32723378.
65. Palmerini E, Sanfilippo R, Grignani G, et al. Transcription regulators and ultra-rare and other rare translocation-related sarcomas treated with trabectedin: A proof of principle from a analysis. *Front Oncol*. 2022; 12: 1042479, doi: 10.3389/fonc.2022.1042479, indexed in Pubmed: 36568164.
66. Tariq Z, Ghose A, Bawany MZ, et al. A case report of complete remission of pulmonary metastases from epithelioid sarcoma to navelbine chemotherapy. *Am J Ther*. 2012; 19(2): e95–e97, doi: 10.1097/MJT.0b013e-3181e70a50, indexed in Pubmed: 20634676.
67. Anderson SE, Keohan ML, D'Adamo DR, et al. A retrospective analysis of vinorelbine chemotherapy for patients with previously treated soft-tissue sarcomas. *Sarcoma*. 2006; 2006: 15947, doi: 10.1155/SRCM/2006/15947, indexed in Pubmed: 17496991.
68. Nakamura T, Matsumine A, Kawai A, et al. The clinical outcome of pazopanib treatment in Japanese patients with relapsed soft tissue sarcoma: A Japanese Musculoskeletal Oncology Group (JMOG) study. *Cancer*. 2016; 122(9): 1408–1416, doi: 10.1002/cncr.29961, indexed in Pubmed: 26970174.
69. Irimura S, Nishimoto K, Kikuta K, et al. Successful Treatment with Pazopanib for Multiple Lung Metastases of Inguinal Epithelioid Sarcoma: A Case Report. *Case Rep Oncol*. 2015; 8(3): 378–384, doi: 10.1159/000439427, indexed in Pubmed: 26500539.
70. Penot P, Bouaziz JD, Battistella M, et al. Stabilization of multiple metastatic epithelioid sarcoma under treatment with sunitinib malate. *Br J Dermatol*. 2013; 168(4): 871–873, doi: 10.1111/bjd.12038, indexed in Pubmed: 22963050.
71. Broto J, Hindi N, Grignani GE, et al. IMMUNOSARC: A collaborative Spanish (GEIS) and Italian (ISG) sarcoma groups phase I/II trial of sunitinib plus nivolumab in advanced soft tissue and bone sarcomas: Results of the phase II- soft-tissue sarcoma cohort. *Ann Oncol*. 2019; 30: v684, doi: 10.1093/annonc/mdz283.002.
72. Yao W, Du X, Wang J, et al. Long-Term Efficacy and Safety of Anlotinib as a Monotherapy and Combined Therapy for Advanced Sarcoma. *Onco Targets Ther*. 2022; 15: 669–679, doi: 10.2147/OTT.S365506, indexed in Pubmed: 35726279.
73. Schuetze SM, Bolejack V, Choy E, et al. Phase 2 study of dasatinib in patients with alveolar soft part sarcoma, chondrosarcoma, chordoma, epithelioid sarcoma, or solitary fibrous tumor. *Cancer*. 2017; 123(1): 90–97, doi: 10.1002/cncr.30379, indexed in Pubmed: 27696380.
74. D'Angelo SP, Shoushtari AN, Keohan ML, et al. Combined KIT and CTLA-4 Blockade in Patients with Refractory GIST and Other Advanced Sarcomas: A Phase Ib Study of Dasatinib plus Ipilimumab. *Clin Cancer Res*. 2017; 23(12): 2972–2980, doi: 10.1158/1078-0432.CCR-16-2349, indexed in Pubmed: 28007774.
75. Clemente O, Ottaiano A, Di Lorenzo G, et al. Is immunotherapy in the future of therapeutic management of sarcomas? *J Transl Med*. 2021; 19(1): 173, doi: 10.1186/s12967-021-02829-y, indexed in Pubmed: 33902630.
76. Georger B, Kang HJ, Yalon-Oren M, et al. Pembrolizumab in paediatric patients with advanced melanoma or a PD-L1-positive, advanced, relapsed, or refractory solid tumour or lymphoma (KEYNOTE-051): interim analysis of an open-label, single-arm, phase 1-2 trial. *Lancet Oncol*. 2020; 21(1): 121–133, doi: 10.1016/S1470-2045(19)30671-0, indexed in Pubmed: 31812554.
77. Wang J, Lu C, Tang Xi. Response to immunotherapy in a patient with advanced epithelioid sarcoma of adrenal gland: A case report. *Exp Ther Med*. 2022; 24(5): 659, doi: 10.3892/etm.2022.11595, indexed in Pubmed: 36168426.
78. Paoluzzi L, Cacavio A, Ghesani M, et al. Response to anti-PD1 therapy with nivolumab in metastatic sarcomas. *Clin Sarcoma Res*. 2016; 6: 24, doi: 10.1186/s13569-016-0064-0, indexed in Pubmed: 28042471.
79. Gong TJ, Tang F, Zheng CX, et al. Case Report: Pulmonary Metastases From Epithelioid Sarcoma in Extremity Favourably Responding to Immunotherapy With Camrelizumab. *Front Oncol*. 2021; 11: 728437, doi: 10.3389/fonc.2021.728437, indexed in Pubmed: 34692503.
80. Italiano A, Soria JC, Toulmonde M, et al. Tazemetostat, an EZH2 inhibitor, in relapsed or refractory B-cell non-Hodgkin lymphoma and advanced solid tumours: a first-in-human, open-label, phase 1 study. *Lancet Oncol*. 2018; 19(5): 649–659, doi: 10.1016/S1470-2045(18)30145-1, indexed in Pubmed: 29650362.
81. Stacchiotti S, Schöffski P, Jones R, et al. Safety and efficacy of tazemetostat, a first-in-class EZH2 inhibitor, in patients (pts) with epithelioid sarcoma (ES) (NCT02601950). *J Clin Oncol*. 2019; 37(15\_suppl): 11003–11003, doi: 10.1200/jco.2019.37.15\_suppl.11003.
82. Gounder M, Stacchiotti S, Schöffski P, et al. Efficacy, safety, and immune priming effect of tazemetostat in patients with epithelioid sarcoma. *J Clin Oncol*. 2020; 38(15\_suppl): 11564–11564, doi: 10.1200/jco.2020.38.15\_suppl.11564.
83. Sen S, McKean M, Sierra L, et al. A phase Ib/III randomized, double-blind, placebo-controlled study of tazemetostat plus doxorubicin as frontline therapy for patients with advanced epithelioid sarcoma. *J Clin Oncol*. 2020; 38(15\_suppl): TPS11573–TPS11573, doi: 10.1200/jco.2020.38.15\_suppl.tps11573.
84. Chi S, Bourdeaut F, Casanova M, et al. Update on phase 1 study of tazemetostat, an enhancer of zeste homolog 2 inhibitor, in pediatric patients with relapsed or refractory integrase interactor 1–negative tumors. *J Clin Oncol*. 2022; 40(16\_suppl): 10040–10040, doi: 10.1200/jco.2022.40.16\_suppl.10040.
85. Bose S, Ingham M, Chen Li, et al. Correlative results from NCI protocol 10250: A phase II study of temozolomide and olaparib for the treatment of advanced uterine leiomyosarcoma. *J Clin Oncol*. 2022; 40(16\_suppl): 11509–11509, doi: 10.1200/jco.2022.40.16\_suppl.11509.
86. Italiano A, Isambert N, Metges JP, et al. CAIRE: A basket multicenter open-label phase 2 study evaluating the EZH2 inhibitor tazemetostat in combination with durvalumab in patients with advanced solid tumors. *J Clin Oncol*. 2022; 40(16\_suppl): TPS2703–TPS2703, doi: 10.1200/jco.2022.40.16\_suppl.tps2703.
87. Spalek MJ, Kosela-Paterczyk H, Borkowska A, et al. Combined Preoperative Hypofractionated Radiotherapy With Doxorubicin-Ifosfamide Chemotherapy in Marginally Resectable Soft Tissue Sarcomas: Results of a Phase 2 Clinical Trial. *Int J Radiat Oncol Biol Phys*. 2021; 110(4): 1053–1063, doi: 10.1016/j.ijrobp.2021.02.019, indexed in Pubmed: 33600887.
88. Spalek M, Borkowska A. Current advances in radiotherapy for soft tissue sarcomas. *Nowotwory. Journal of Oncology*. 2020; 70(6): 288–295, doi: 10.5603/njo.2020.0056.

89. Spalek MJ, Borkowska AM, Telejko M, et al. The Feasibility Study of Hypofractionated Radiotherapy with Regional Hyperthermia in Soft Tissue Sarcomas. *Cancers (Basel)*. 2021; 13(6), doi: 10.3390/cancers13061332, indexed in Pubmed: 33809547.
90. Simeone N, Frezza AM, Zaffaroni N, et al. Tazemetostat for advanced epithelioid sarcoma: current status and future perspectives. *Future Oncol*. 2021; 17(10): 1253–1263, doi: 10.2217/fon-2020-0781, indexed in Pubmed: 33289402.
91. Dudzisz-Śledź M, Rogala P. Advances in systemic treatment of advanced soft tissue sarcomas. *Oncol Clin Pract*. 2019; 14(6): 377–391, doi: 10.5603/ocp.2018.0051.