

## DAFTAR PUSTAKA

- Abou Ali B, Salman M, Ghanem KM, Boulos F, Haidar R, Saghieh S, Akel S, Muwakkit SA, El-Solh H, Saab R, Tamim H, Abboud MR. 2019. Clinical Prognostic Factors and Outcome in Pediatric Osteosarcoma: Effect of Delay in Local Control and Degree of Necrosis in a Multidisciplinary Setting in Lebanon. *J Glob Oncol*,5:1-8. doi: 10.1200/JGO.17.00241. PMID: 30946633; PMCID: PMC6528739.
- Ackland SP, Schilsky RL. 1987. High-dose methotrexate: a critical reappraisal. *J Clin Oncol*,5(12):2017-31. doi: 10.1200/JCO.1987.5.12.2017. PMID: 3316519.
- Adamopoulos C, Gargalionis AN, Basdra EK, Papavassiliou AG. 2016. Deciphering signaling networks in osteosarcoma pathobiology. *Exp Biol Med (Maywood)*,241:1296–305. Available at: <https://doi.org/10.1177/1535370216648806>.
- Alfranica A, Martinez-Cruzado L, Tornin J, Abarrategi A, Amaral T, de Alava E, Menendez P, Garcia-Castro J, Rodriguez R. 2015. Bone microenvironment signals in osteosarcoma development. *Cell Mol Life Sci*,72(16):3097-113. doi: 10.1007/s00018-015-1918-y.
- Aljubran AH, Griffin A, Pintilie M, Blackstein M. 2009. Osteosarcoma in adolescents and adults: Survival analysis with and without lung metastases. *Annals of Oncology*,20:1136–41. <https://doi.org/10.1093/annonc/mdn731>.
- Allegra CJ, Chabner BA, Drake JC, Lutz R, Rodbard D, Jolivet J. 1985. Enhanced inhibition of thymidylate synthase by methotrexate polyglutamates. *Journal of Biological Chemistry*,260:9720–6. [https://doi.org/10.1016/s0021-9258\(17\)39298-0](https://doi.org/10.1016/s0021-9258(17)39298-0).
- Alsdorf WH, Karagiannis P, Langebrake C, Bokemeyer C, Frenzel C. 2021. Standardized Supportive Care Documentation Improves Safety of High-Dose Methotrexate Treatment. *Oncologist*,26(2):e327-e332. doi: 10.1002/onco.13603. Epub 2020 Nov 28. PMID: 33215763; PMCID: PMC7873314.
- Álvaro Sanz E, Abilés J, Garrido Siles M, Rivas Ruíz F, Tortajada Goitia B, Domínguez AR. 2020. Evaluation of a protocol to detect malnutrition and provide nutritional care for cancer patients undergoing chemotherapy. *Sci Rep*,10(1):21186. doi: 10.1038/s41598-020-78246-w. PMID: 33273641; PMCID: PMC7713220.
- Angulo P, Kaushik G, Subramaniam D, Dandawate P, Neville K, Chastain K, Anant S. 2017. Natural compounds targeting major cell signaling pathways: a novel paradigm for osteosarcoma therapy. *J Hematol Oncol*,10(1):10. doi: 10.1186/s13045-016-0373-z. PMID: 28061797; PMCID: PMC5219787.
- Anthony M, Berg MJ. 2002. Biologic and molecular mechanisms for sex differences in pharmacokinetics, pharmacodynamics, and pharmacogenetics: Part II. *J Womens Health Gen Based Med*,11(7):617-29. doi: 10.1089/152460902760360568. PMID: 12396894.
- Anninga JK, Gelderblom H, Fiocco M, Kroep JR, Taminiou AH, Hogendoorn PC, Egeler RM. 2011. Chemotherapeutic adjuvant treatment for osteosarcoma: where do we stand?

*Eur J Cancer*,47(16):2431-45. doi: 10.1016/j.ejca.2011.05.030. Epub 2011 Jun 22. PMID: 21703851.

Armenian SH, Hudson MM, Mulder RL, Chen MH, Constone LS, Dwyer M, Nathan PC, Tissing WJ, Shankar S, Sieswerda E, Skinner R, Steinberger J, van Dalen EC, van der Pal H, Wallace WH, Levitt G, Kremer LC; International Late Effects of Childhood Cancer Guideline Harmonization Group. 2015. Recommendations for cardiomyopathy surveillance for survivors of childhood cancer: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group. *Lancet Oncol*,16(3):e123-36. doi: 10.1016/S1470-2045(14)70409-7.

Asada N, Tsuchiya H, Tomita K. 1999. De novo deletions of p53 gene and wild-type p53 correlate with acquired cisplatin-resistance in human osteosarcoma OST cell line. *Anticancer Res*, 19(6B):5131-7. PMID: 10697522.

Audinot B, Drubay D, Gaspar N, Mohr A, Cordero C, Marec-Bérard P, Lervat C, Piperno-Neumann S, Jimenez M, Mansuy L, Castex MP, Revon-Riviere G, Marie-Cardine A, Berger C, Piguet C, Massau K, Job B, Moquin-Beaudry G, Le Deley MC, Tabone MD, Berlanga P, Brugières L, Crompton BD, Marchais A, Abbou S. 2024. ctDNA quantification improves estimation of outcomes in patients with high-grade osteosarcoma: a translational study from the OS2006 trial. *Ann Oncol*,35(6):559-568. doi: 10.1016/j.annonc.2023.12.006. Epub 2023 Dec 22. PMID: 38142939.

Bacci G, Ferrari S, Delepine N, Bertoni F, Picci P, Mercuri M, Bacchini P, Brach del Prever A, Tienghi A, Comandone A, Campanacci M. 1998. Predictive factors of histologic response to primary chemotherapy in osteosarcoma of the extremity: study of 272 patients preoperatively treated with high-dose methotrexate, doxorubicin, and cisplatin. *J Clin Oncol*,16(2):658-63. doi: 10.1200/JCO.1998.16.2.658. PMID: 9469355.

Bacci G, Longhi A, Versari M, Mercuri M, Briccoli A, Picci P. 2006. Prognostic factors for osteosarcoma of the extremity treated with neoadjuvant chemotherapy: 15-year experience in 789 patients treated at a single institution. *Cancer*,106(5):1154-61. doi: 10.1002/cncr.21724. PMID: 16421923.

Bacci G, Forni C, Longhi A, Ferrari S, Mercuri M, Bertoni F, Serra M, Briccoli A, Balladelli A, Picci P. 2007. Local recurrence and local control of non-metastatic osteosarcoma of the extremities: a 27-year experience in a single institution. *J Surg Oncol*, 96(2):118-23. doi: 10.1002/jso.20628. PMID: 17577221.

Bajpai J, Chandrasekharan A, Talreja V, Simha V, Chandrakanth MV, Rekhi B, Khurana S, Khan A, Vora T, Ghosh J, Banavali SD, Gupta S. 2017. Outcomes in non-metastatic treatment naive extremity osteosarcoma patients treated with a novel non-high dose methotrexate-based, dose-dense combination chemotherapy regimen 'OGS-12'. *Eur J Cancer*,85:49-58. doi: 10.1016/j.ejca.2017.08.013. Epub 2017 Sep 8. PMID: 28888849.

Bajpai J, Chandrasekharan A, Simha V, Talreja V, Karpe A, Pandey N, Singh A, Rekhi B, Vora T, Ghosh J, Banavali S, Gupta S. 2018. Outcomes in Treatment-Naïve Patients With Metastatic Extremity Osteosarcoma Treated With OGS-12, a Novel Non-High-Dose Methotrexate-Based, Dose-Dense Combination Chemotherapy, in a Tertiary Care Cancer

Center. *J Glob Oncol*,4:1-10. doi: 10.1200/JGO.17.00137. PMID: 30241240; PMCID: PMC6223433.

Bajpai J, Chandrasekharan A, Simha V, Mandal T, Shah K, Hingmare S, Rangarajan B, Shetty N, Vora T, Ghosh J, Rekhi B, Banavali S, Gupta S. 2019. Osteosarcoma journey over two decades in India: Small steps, big changes. *Pediatr Blood Cancer*,66(9):e27877. doi: 10.1002/pbc.27877. Epub 2019 Jun 17. PMID: 31207015.

Bajpai J, Chandrashekharan A, Banavali S, Gupta S. 2020. Osteosarcoma journey in India: Each step reveals a new horizon! *Indian Journal of Medical and Paediatric Oncology*, 41:4–6. Available at: [https://doi.org/10.4103/ijmpo.ijmpo\\_15\\_20](https://doi.org/10.4103/ijmpo.ijmpo_15_20).

Behjati S, Tarpey PS, Haase K, Ye H, Young MD, Alexandrov LB, Farndon SJ, et al. 2017. Recurrent mutation of IGF signalling genes and distinct patterns of genomic rearrangement in osteosarcoma. *Nat Commun*, 8:15936. Epub 2017 Jun 23.

Belkov VM, Krynetski EY, Schuetz JD, Yanishevski Y, Masson E, Mathew S, Raimondi S, Pui CH, Relling MV, Evans WE. 1999. Reduced folate carrier expression in acute lymphoblastic leukemia: a mechanism for ploidy but not lineage differences in methotrexate accumulation. *Blood*,93(5):1643-50. PMID: 10029593.

Bielack SS, Kempf-Bielack B, Branscheid D, Carrle D, Friedel G, Helmke K, Kevric M, Jundt G, Kühne T, Maas R, Schwarz R, Zoubek A, Jürgens H. 2009. Second and subsequent recurrences of osteosarcoma: presentation, treatment, and outcomes of 249 consecutive cooperative osteosarcoma study group patients. *J Clin Oncol*,27(4):557-65. doi: 10.1200/JCO.2008.16.2305. Epub 2008 Dec 15. PMID: 19075282.

Bielack SS, Wulff B, Delling G, Göbel U, Kotz R, Ritter J, Winkler K. 1995. Osteosarcoma of the trunk treated by multimodal therapy: experience of the Cooperative Osteosarcoma study group (COSS). *Med Pediatr Oncol*,24(1):6-12. doi: 10.1002/mpo.2950240103. PMID: 7968796.

Bielack SS, Kempf-Bielack B, Delling G, Exner GU, Flege S, Helmke K, Kotz R, Salzer-Kuntschik M, Werner M, Winkelmann W, Zoubek A, Jürgens H, Winkler K. 2002. Prognostic factors in high-grade osteosarcoma of the extremities or trunk: an analysis of 1,702 patients treated on neoadjuvant cooperative osteosarcoma study group protocols. *J Clin Oncol*,20(3):776-90. doi: 10.1200/JCO.2002.20.3.776. PMID: 11821461.

Bielack SS, Smeland S, Whelan JS, Marina N, Jovic G, Hook JM, et al. 2015. Methotrexate, Doksorubisin, and Cisplatin (MAP) Plus Maintenance Pegylated Interferon Alfa-2b Versus MAP Alone in Patients With Resectable High-Grade Osteosarcoma and Good Histologic Response to Preoperative MAP: First Results of the EURAMOS-1 Good Response Randomized Controlled Trial. *J Clin Oncol*, 33(20):2279-87. doi: 10.1200/JCO.2014.60.0734.

Bini I, Asaftei SD, Riggi C, Tirtei E, Manicone R, Biasin E, et al. 2017. Anthracycline-induced cardiotoxicity in patients with paediatric bone sarcoma and soft tissue sarcoma. *Cardiol Young*. 2017,27(9):1815-1822. doi: 10.1017/S1047951117001536.

Bleyer WA. 1977. Methotrexate: clinical pharmacology, current status and therapeutic guidelines. *Cancer Treat Rev*,4(2):87-101. doi: 10.1016/s0305-7372(77)80007-8. PMID: 329989.

Bourdel-Marchasson I, Blanc-Bisson C, Doussau A, Germain C, Blanc JF, Dauba J, Lahmar C, Terrebonne E, Lecaille C, Ceccaldi J, Cany L, Lavau-Denes S, Houede N, Chomy F, Durrieu J, Soubeyran P, Senesse P, Chene G, Fonck M. 2014. Nutritional advice in older patients at risk of malnutrition during treatment for chemotherapy: a two-year randomized controlled trial. *PLoS One*, 9(9):e108687. doi: 10.1371/journal.pone.0108687. PMID: 25265392; PMCID: PMC4181649.

Buitenkamp TD, Mathôt RA, de Haas V, Pieters R, Zwaan CM. 2010. Methotrexate-induced side effects are not due to differences in pharmacokinetics in children with Down syndrome and acute lymphoblastic leukemia. *Haematologica*,95(7):1106-13. doi: 10.3324/haematol.2009.019778. Epub 2010 Apr 23. PMID: 20418240; PMCID: PMC2895034.

Campanacci M, Bacci G, Bertoni F, Picci P, Minuttillo A, Franceschi C. 1981. The treatment of osteosarcoma of the extremities: twenty year's experience at the Istituto Ortopedico Rizzoli. *Cancer*, 48(7):1569-81. doi: 10.1002/1097-0142(19811001)48:7<1569::aid-cnrcr2820480717>3.0.co;2-x. PMID: 6945143.

Casper ES, Gaynor JJ, Hajdu SI, Magill GB, Tan C, Friedrich C, et al. 1991. A prospective randomized trial of adjuvant chemotherapy with bolus versus continuous infusion of doksorubisin in patients with high-grade extremity soft tissue sarcoma and an analysis of prognostic factors. *Cancer*, 68(6):1221e9.

Cesari M, Alberghini M, Vanel D, Palmerini E, Staals EL, Longhi A, Abate M, Ferrari C, Balladelli A, Ferrari S. 2010. Periosteal osteosarcoma: a single-institution experience. *Cancer*,117(8):1731-5. doi: 10.1002/cncr.25718. Epub 2010 Nov 8. PMID: 21472720.

Chen G, Deng C, Li Y-P. 2012. TGF- $\beta$  and BMP Signaling in Osteoblas Differentiation and Bone Formation. *Int J Biol Sci*,8:272–88. <https://doi.org/10.7150/ijbs.2929>.

Cheng Q, Cheng C, Crews KR, Ribeiro RC, Pui CH, Relling MV, Evans WE. 2006. Epigenetic regulation of human gamma-glutamyl hydrolase activity in acute lymphoblastic leukemia cells. *Am J Hum Genet*,79(2):264-74. doi: 10.1086/505645. Epub 2006 Jun 6. Erratum in: *Am J Hum Genet*. 2010 Jul 9;87(1):161. PMID: 16826517; PMCID: PMC1559484.

Chitnis MM, Yuen JS, Protheroe AS, Pollak M, Macaulay VM. 2008. The type 1 insulin-like growth factor receptor pathway. *Clin Cancer Res*, 14(20):6364-70. doi: 10.1158/1078-0432.CCR-07-4879. PMID: 18927274.

Choeyprasert W, Natesirinilkul R, Charoenkwan P, Sittipreechacharn S. 2013. Carboplatin and doksorubisin in treatment of pediatric osteosarcoma: A 9-year single institute experience in the northern region of Thailand. *Asian Pacific Journal of Cancer Prevention*,14:1101–6. <https://doi.org/10.7314/APJCP.2013.14.2.1101>.

Choeypasert W, Pakakasama S, Sirachainan N, Songdej D, Chuansumrit A, Anurathapan U, Hongeng S, Nartthanarung A. 2014. Comparative outcome of Thai pediatric osteosarcoma treated with two protocols: the role of high-dose methotrexate (HDMTX) in a single institute experience. *Asian Pac J Cancer Prev*,15(22):9823-9. doi: 10.7314/apjcp.2014.15.22.9823. PMID: 25520112.

Chou AJ, Geller DS, Gorlick R. 2008. Therapy for osteosarcoma: where do we go from here? *Paediatr Drugs*,10(5):315-27. doi: 10.2165/00148581-200810050-00005. PMID: 18754698.

Ciernik IF, Niemierko A, Harmon DC, Kobayashi W, Chen YL, Yock TI, Ebb DH, Choy E, Raskin KA, Liebsch N, Hornicek FJ, Delaney TF. 2011. Proton-based radiotherapy for unresectable or incompletely resected osteosarcoma. *Cancer*,117(19):4522-30. doi: 10.1002/cncr.26037. Epub 2011 Mar 29. PMID: 21448934; PMCID: PMC3716000.

Clarke L, Waxman DJ. 1987. Human liver folylpolyglutamate synthetase: biochemical characterization and interactions with folates and folate antagonists. *Arch Biochem Biophys*,256(2):585-96. doi: 10.1016/0003-9861(87)90616-3. PMID: 3619447.

Clarke RT, Jenyon T, van Hamel Parsons V, King AJ. 2013. Neutropenic sepsis: management and complications. *Clin Med (Lond)*,13(2):185-7. doi: 10.7861/clinmedicine.13-2-185. PMID: 23681870; PMCID: PMC4952638.

Cole S, Gianferante DM, Zhu B, Mirabello L. 2022. Osteosarcoma: A Surveillance, Epidemiology, and End Results program-based analysis from 1975 to 2017. *Cancer*,128(11):2107-2118. doi: 10.1002/cncr.34163. Epub 2022 Feb 28. PMID: 35226758; PMCID: PMC11647566.

Comandone A, Passera R, Boglione A, Tagini V, Ferrari S, Cattel L. 2005. High dose methotrexate in adult patients with osteosarcoma: clinical and pharmacokinetic results. *Acta Oncol*,44(4):406-11. doi: 10.1080/02841860510029770. PMID: 16120550.

Corradi, D.; Wenger, D.E.; Bertoni, F.; Bacchini, P.; Bosio, S.; Goldoni, M.; Unni, K.K.; Sim, F.H.; Inwards, C.Y. 2011. Multicentric Osteosarcoma: Clinicopathologic and Radiographic Study of 56 Cases. *Am. J. Clin. Pathol*, 136, 799–807.

Crews KR, Liu T, Rodriguez-Galindo C, Tan M, Meyer WH, Panetta JC, Link MP, Daw NC. 2004. High-dose methotrexate pharmacokinetics and outcome of children and young adults with osteosarcoma. *Cancer*, 100(8):1724-33. doi: 10.1002/cncr.20152.

Czarnecka AM, Synoradzki K, Firlej W, Bartnik E, Sobczuk P, Fiedorowicz M, Grieb P, Rutkowski P. 2020. Molecular Biology of Osteosarcoma. *Cancers (Basel)*,12(8):2130. doi: 10.3390/cancers12082130. PMID: 32751922; PMCID: PMC7463657.

van Dalen EC, van As JW, de Camargo B. 2011. Methotrexate for high-grade osteosarcoma in children and young adults. *Cochrane Database Syst Rev*,2011(5):CD006325. doi: 10.1002/14651858.CD006325.pub3. PMID: 21563152; PMCID: PMC6466691.

Deng Z, Huang Z, Ding Y, Su Y, Chan CM, Niu X. 2020. High-Grade Surface Osteosarcoma: Clinical Features and Oncologic Outcome. *J Bone Oncol*,23:100288. doi: 10.1016/j.jbo.2020.100288. PMID: 32953434; PMCID: PMC7486478.

Ding WZ, Liu K, Li Z, Chen SR. 2020. A meta-analysis of prognostic factors of osteosarcoma. *Eur Rev Med Pharmacol Sci*, 24(8):4103-4112. doi: 10.26355/eurrev\_202004\_20989. PMID: 32373946.

Di Fiore R, Santulli A, Ferrante RD, Giuliano M, De Blasio A, Messina C, Pirozzi G, Tirino V, Tesoriere G, Vento R. 2009. Identification and expansion of human osteosarcoma-cancer-stem cells by long-term 3-aminobenzamide treatment. *J Cell Physiol*, 219(2):301-13. doi: 10.1002/jcp.21667. PMID: 19160414.

Duchman KR, Gao Y, Miller BJ. 2015. Prognostic factors for survival in patients with high-grade osteosarcoma using the Surveillance, Epidemiology, and End Results (SEER) Program database. *Cancer Epidemiol*,39(4):593-9. doi: 10.1016/j.canep.2015.05.001. Epub 2015 May 20. PMID: 26002013.

Duong LM, Richardson LC. 2013. Descriptive epidemiology of malignant primary osteosarcoma using population-based registries, United States, 1999-2008. *J Registry Managr*,40(2):59-64. PMID: 24002129; PMCID: PMC4476493.

Durfee, Ryan A., Mohammed, M., Luu, Hue H. 2016. Review of Osteosarcoma and Current Management. *Rheumatol Ther*,3: 221-243. doi: 10.1007/s40744-016-0046-y.

Ehrlich BS, McNeil MJ, Pham LTD, Chen Y, Rivera J, Acuna C, et al. 2023. Treatment-related mortality in children with cancer in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet Oncol*, 24(9):967-977. doi: 10.1016/S1470-2045(23)00318-2.

Enneking WF. 1987. Modification of the system for functional evaluation of surgical management musculoskeletal tumors. In: Enneking WF. *Limb Salvage in Musculoskeletal Oncology*. New York: Churchill Livingstone; p.626-39.

Erdlenbruch B, Pekrun A, Roth C, Grunewald RW, Kern W, Lakomek M. 2001. Cisplatin nephrotoxicity in children after continuous 72-h and 3×1-h infusions. *Pediatric Nephrology*,16(7):586-593. doi:10.1007/s004670100610.

Evans DR, Lazarides AL, Visgauss JD, Somarelli JA, Blazer DG 3rd, Brigman BE, Eward WC. 2020. Limb salvage versus amputation in patients with osteosarcoma of the extremities: an update in the modern era using the National Cancer Database. *BMC Cancer*,20(1):995. doi: 10.1186/s12885-020-07502-z. PMID: 33054722; PMCID: PMC7557006.

Evans WE, Pratt CB, Taylor RH, Barker LF, Crom WR. 1979. Pharmacokinetic monitoring of high-dose methotrexate. Early recognition of high-risk patients. *Cancer Chemother Phar- macol*, 3:161-166.

Fan TM, Roberts RD, Lizardo MM. 2020. Understanding and Modeling Metastasis Biology to Improve Therapeutic Strategies for Combating Osteosarcoma Progression. *Front Oncol*,10. Available at: <https://doi.org/10.3389/fonc.2020.00013>.

Ferrari S, Sassoli V, Orlandi M, Strazzari S, Puggioli C, Battistini A, Bacci G. 1993. Serum methotrexate (MTX) concentrations and prognosis in patients with osteosarcoma of the extremities treated with a multidrug neoadjuvant regimen. *J Chemother*,5(2):135-41. doi: 10.1080/1120009x.1993.11739222. PMID: 8515297.

Finlay-Schultz J, Sartorius CA. 2015. Steroid hormones, steroid receptors, and breast cancer stem cells. *J Mammary Gland Biol Neoplasia*, 20(1-2):39-50. doi: 10.1007/s10911-015-9340-5. Epub 2015 Aug 12. PMID: 26265122; PMCID: PMC4666507.

Fletcher CDM, Bridge JA, Hogendoorn PCW MF, ed. WHO Classification of Tumours of Soft Tissue and Bone. 4th ed. World Health Organization; 2013.

Freedman JL, Beeler DM, Bowers A, Bradford N, Cheung YT, Davies M, Dupuis LL, Elgarten CW, Jones TM, Jubelirer T, Miller TP, Patel P, Phillips CA, Wardill HR, Orsey AD. 2023. Supportive Care in Pediatric Oncology: Opportunities and Future Directions. *Cancers (Basel)*,15(23):5549. doi: 10.3390/cancers15235549. PMID: 38067252; PMCID: PMC10705083.

Friedrich P, Ortiz R, Fuentes S, Gamboa Y, Ah Chu-Sanchez MS, Arambú IC, Montero M, Báez F, Rodríguez-Galindo C, Antillón-Klussmann F; Central American Association of Pediatric Hematologists and Oncologists (AHOPCA). 2014. Barriers to effective treatment of pediatric solid tumors in middle-income countries: can we make sense of the spectrum of nonbiologic factors that influence outcomes? *Cancer*,120(1):112-25. doi: 10.1002/cncr.28339. Epub 2013 Oct 16. PMID: 24132910; PMCID: PMC3934757.

Frisch SM, Francis H. 1994. Disruption of epithelial cell-matrix interactions induces apoptosis. *J Cell Biol*,124(4):619-26. doi: 10.1083/jcb.124.4.619. PMID: 8106557; PMCID: PMC2119917.

Fry DW, Anderson LA, Borst M, Goldman ID. 1983. Analysis of the role of membrane transport and polyglutamation of methotrexate in gut and the Ehrlich tumor in vivo as factors in drug sensitivity and selectivity. *Cancer Res*,43(3):1087-92. PMID: 6186369.

Fu P, Shi Y, Chen G, Fan Y, Gu Y, Gao Z. 2020. Prognostic Factors in Patients With Osteosarcoma With the Surveillance, Epidemiology, and End Results Database. *Technol Cancer Res Treat*,19:1533033820947701. doi: 10.1177/1533033820947701. PMID: 32787692; PMCID: PMC7427153.

Gallo N, Czuppon K, Tomsits E, Garami M, Hauser P, Jakab Z, Nagy K, Kovacs GT. 2022. The Effect of Nutritional Support on the Disease Progression and Survival in Pediatric Patients with Solid Tumors. *Nutr Cancer*,74(1):184-192. doi: 10.1080/01635581.2020.1869275. Epub 2021 Jan 12. PMID: 33432830.

Gándara-Mireles JA, Lares-Asseff I, Reyes Espinoza EA, Córdova Hurtado LP, Payan Gándara H, Botello Ortiz M, et al. 2024. Nutritional Status as a Risk Factor for

Doksorubisin Cardiotoxicity in Mexican Children with Acute Lymphoblastic Leukemia. *Nutr Cancer*, 76(10):952-962. doi: 10.1080/01635581.2024.2378502.

Garófolo A, Lopez FA, Petrilli AS. 2005. High prevalence of malnutrition among patients with solid non-hematological tumors as found by using skinfold and circumference measurements. *Sao Paulo Med J*, 123(6):277-81. doi: 10.1590/s1516-31802005000600005. Epub 2006 Jan 20. PMID: 16444387; PMCID: PMC11060350.

Geller DS, Gorlick R. 2010. Osteosarcoma: a review of diagnosis, management, and treatment strategies. *Clin Adv Hematol Oncol*, 8(10):705-18. PMID: 21317869.

Giovannetti E, Ugrasena DG, Supriyadi E, Vroling L, Azzarello A, de Lange D, Peters GJ, Veerman AJ, Cloos J. 2008. Methylenetetrahydrofolate reductase (MTHFR) C677T and thymidylate synthase promoter (TSER) polymorphisms in Indonesian children with and without leukemia. *Leuk Res*, 32(1):19-24. doi: 10.1016/j.leukres.2007.02.011. Epub 2007 Mar 28. PMID: 17395259.

Gok Durnali, A.; Paksoy Turkoz, F.; Ardic Yukruk, F.; Tokluoglu, S.; Yazici, O.K.; Demirci, A.; Bal, O.; Gundogdu Buyukbas, S.; Esbah, O.; Oksuzoglu, B.; et al. 2016. Outcomes of Adolescent and Adult Patients with Lung Metastatic Osteosarcoma and Comparison of Synchronous and Metachronous Lung Metastatic Groups. *PLoS ONE* 2016, 11, e0152621.

Goldin A, Venditti JM, Kline I, Mantel N. 1966. Eradication of leukaemic cells (L1210) by methotrexate and methotrexate plus citrovorum factor. *Nature*, 212(5070):1548-50. doi: 10.1038/2121548a0. PMID: 21105503.

Goorin AM, Shuster JJ, Baker A, Horowitz ME, Meyer WH, Link MP. 1991. Changing pattern of pulmonary metastases with adjuvant chemotherapy in patients with osteosarcoma: results from the multiinstitutional osteosarcoma study. *J Clin Oncol*, 9(4):600-5. doi: 10.1200/JCO.1991.9.4.600. PMID: 2066757.

Goorin AM, Schwartzentruber DJ, Devidas M, Gebhardt MC, Ayala AG, Harris MB, Helman LJ, Grier HE, Link MP; Pediatric Oncology Group. 2003. Presurgical chemotherapy compared with immediate surgery and adjuvant chemotherapy for nonmetastatic osteosarcoma: Pediatric Oncology Group Study POG-8651. *J Clin Oncol*, 21(8):1574-80. doi: 10.1200/JCO.2003.08.165. PMID: 12697883.

Gorlick R, Goker E, Trippett T, Waltham M, Banerjee D, Bertino JR. 1996. Intrinsic and acquired resistance to methotrexate in acute leukemia. *N Engl J Med*, 335(14):1041-8. doi: 10.1056/NEJM199610033351408. PMID: 8793930.

Grimer RJ, Taminiu AM, Cannon SR; Surgical Subcommitte of the European Osteosarcoma Intergroup. 2002. Surgical outcomes in osteosarcoma. *J Bone Joint Surg Br*, 84(3):395-400. doi: 10.1302/0301-620x.84b3.12019. PMID: 12002500.

Gürlek Gökçebay D, Emir S, Bayhan T, Demir HA, Gunduz M, Tunc B. 2015. Assessment of Nutritional Status in Children With Cancer and Effectiveness of Oral Nutritional Supplements. *Pediatr Hematol Oncol*, 32(6):423-32. doi: 10.3109/08880018.2015.1065303. PMID: 26418028.

Guo C, Hu B, Guo C, Meng X, Kuang Y, Huang L, Wang D, Xu K, Zhao Y, Yang G, Cai W, Shu Y. 2021. A Survey of Pharmacogenomics Testing Among Physicians, Pharmacists, and Researchers From China. *Front Pharmacol*, 12:682020. doi: 10.3389/fphar.2021.682020. PMID: 34322018; PMCID: PMC8311355.

Gougelet A, Pissaloux D, Besse A, Perez J, Duc A, Dutour A, Blay JY, Alberti L. 2011. Micro-RNA profiles in osteosarcoma as a predictive tool for ifosfamide response. *Int J Cancer*, 129(3):680-90. doi: 10.1002/ijc.25715. Epub 2010 Nov 23. PMID: 20949564.

Gupta SK, Singh P, Ali V, Verma M. 2020. Role of membrane-embedded drug efflux ABC transporters in the cancer chemotherapy. *Oncol Rev*, 14(2):448. doi: 10.4081/oncol.2020.448. PMID: 32676170; PMCID: PMC7358983.

Hagleitner MM, Hoogerbrugge PM, van der Graaf WT, Flucke U, Schreuder HW, te Loo DM. 2011. Age as prognostic factor in patients with osteosarcoma. *Bone*, 49(6):1173-7. doi: 10.1016/j.bone.2011.08.014.

Halalsheh H, Ismael T, Boheisi M, Shehadeh A, Sultan I. 2024. Impact of delay of local control in nonmetastatic extremity primary osteosarcoma. *Pediatr Blood Cancer*, 71(1):e30752. doi: 10.1002/pbc.30752. Epub 2023 Oct 30. PMID: 37902470.

Hang JF, Chen PCH. 2014. Parosteal osteosarcoma. *Arch Pathol Lab Med*, 138:694-9. Available at: <https://doi.org/10.5858/arpa.2013-0030-RS>.

Hao T, Feng W, Zhang J, Sun YJ, Wang G. 2012. Association of four ERCC1 and ERCC2 SNPs with survival of bone tumour patients. *Asian Pac J Cancer Prev*, 13(8):3821-4. doi: 10.7314/apjcp.2012.13.8.3821. PMID: 23098477.

Harting MT, Lally KP, Andrassy RJ, Vaporciyan AA, Cox CS Jr, Hayes-Jordan A, Blakely ML. 2010. Age as a prognostic factor for patients with osteosarcoma: an analysis of 438 patients. *J Cancer Res Clin Oncol*, 136(4):561-70. doi: 10.1007/s00432-009-0690-5. Epub 2009 Sep 27. PMID: 19784847.

Hattinger CM, Reverter-Branchat G, Remondini D, Castellani GC, Benini S, Pasello M, Manara MC, Scotlandi K, Picci P, Serra M. 2003. Genomic imbalances associated with methotrexate resistance in human osteosarcoma cell lines detected by comparative genomic hybridization-based techniques. *Eur J Cell Biol*, 82(9):483-93. doi: 10.1078/0171-9335-00336. PMID: 14582536.

Hattinger, C.M., Patrizio, M.P, Luppi, S., Serra M. 2020. Pharmacogenomics and Pharmacogenetics in Osteosarcoma: Translational Studies and Clinical Impact. *Int. J. Mol. Sci*, 21: 4659. doi: 10.3390/ijms21134659.

Haydon, R.C., Deyrup, A., Ishikawa, A., Heck, R., Jiang, W., Zhou, L., Feng, T., King, D., Cheng, H., Breyer, B., Peabody, T., Simon, M.A., Montag, A.G., He, T.C. 2002. Cytoplasmic and/or Nuclear Accumulation of the  $\beta$ -catenin Protein is a Frequent in Human Osteosarcoma. *Int. J. Cancer*, 102, 338-342. doi: 10.1002/ijc.10719.

He H, Ni J, Huang J. 2014 Molecular mechanisms of chemoresistance in osteosarcoma (Review). *Oncol Lett*, 7(5):1352-1362. doi: 10.3892/ol.2014.1935. Epub 2014 Mar 4. PMID: 24765137; PMCID: PMC3997672.

Heck RK, Stacy GS, Flaherty MJ, Montag AG, Peabody TD, Simon MA. 2003. A Comparison Study of Staging Systems for Bone Sarcomas. *Clin Orthop Relat Res*, vol.415, Lippincott Williams and Wilkins; p. 64–71. Available at: <https://doi.org/10.1097/01.blo.0000093898.12372.6c>.

Hegy M, Gulácsi A, Cságoly E, Csordás K, Eipel OT, Erdélyi DJ, Müller J, Nemes K, Lautner-Csorba O, Kovács GT. 2012. Clinical relations of methotrexate pharmacokinetics in the treatment for pediatric osteosarcoma. *J Cancer Res Clin Oncol*, 138(10):1697-702. doi: 10.1007/s00432-012-1214-2. Epub 2012 Jun 1. PMID: 22652833.

Holmboe L, Andersen AM, Mørkrid L, Slørdal L, Hall KS. 2012. High dose methotrexate chemotherapy: pharmacokinetics, folate and toxicity in osteosarcoma patients. *Br J Clin Pharmacol*, 73(1):106-14. doi: 10.1111/j.1365-2125.2011.04054.x. PMID: 21707700; PMCID: PMC3248260.

Howard, S.C., McCormick, J., Pui, C.H., Buddington, R.K., Harvey, R.D. 2015. Preventing and Managing Toxicities of High-Dose Methotrexate. *The Oncologist*, 21:1471-1482. Available at: <http://dx.doi.org/10.1634/theoncologist.2015-0164>.

Howard SC, Pedrosa M, Lins M et al. 2004. Establishment of a pediatric oncology program and outcomes of childhood acute lymphoblastic leukemia in a resource-poor area. *JAMA*, 291:2471–2475.

Hu, L., Yin, C., Zhao, F., Ali, A., Ma, J., Qian, A. 2018. Mesenchymal Stem Cells: Cell Fate Decision to Osteoblast or Adipocyte and Application in Osteoporosis Treatment. *Int. J. Mol. Sci*, 19, 360. doi: 10.3390/ijms19020360.

Huang G, Mills L, Worth LL. 2007. Expression of human glutathione S-transferase P1 mediates the chemosensitivity of osteosarcoma cells. *Mol Cancer Ther*, 6(5):1610-9. doi: 10.1158/1535-7163.MCT-06-0580. PMID: 17513610.

Huang J, Ni J, Liu K, Yu Y, Xie M, Kang R, Vernon P, Cao L, Tang D. 2012. HMGB1 promotes drug resistance in osteosarcoma. *Cancer Res*, 72(1):230-8. doi: 10.1158/0008-5472.CAN-11-2001. Epub 2011 Nov 18. PMID: 22102692.

Houghton PJ, Morton CL, Kolb EA, Gorlick R, Lock R, Carol H, Reynolds CP, Maris JM, Keir ST, Billups CA, Smith MA. 2008. Initial testing (stage 1) of the mTOR inhibitor rapamycin by the pediatric preclinical testing program. *Pediatr Blood Cancer*, 50(4):799-805. doi: 10.1002/pbc.21296. PMID: 17635004.

Isakoff MS, Barkauskas DA, Ebb D, Morris C, Letson GD. 2012. Poor survival for osteosarcoma of the pelvis: A report from the children's oncology group. *Clin Orthop Relat*, 470:2007–13. Available at: <https://doi.org/10.1007/s11999-012-2284-9>.

Iurlaro R, León-Annicchiarico CL, Muñoz-Pinedo C. 2014. Regulation of cancer metabolism by oncogenes and tumor suppressors. *Methods Enzymol*,542:59-80. doi: 10.1016/B978-0-12-416618-9.00003-0. PMID: 24862260.

Izraeli S, Vora A, Zwaan CM, Whitlock J. 2014. How I treat ALL in Down's syndrome: pathobiology and management. *Blood*,123(1):35-40. doi: 10.1182/blood-2013-07-453480. Epub 2013 Nov 14. PMID: 24235135.

Jain A, Jahagirdar D, Nilendu P, Sharma NK. 2017. Molecular approaches to potentiate cisplatin responsiveness in carcinoma therapeutics. *Expert Rev Anticancer Ther*,17:815–25. <https://doi.org/10.1080/14737140.2017.1356231>.

Janeway KA, Barkauskas DA, Krailo MD, Meyers PA, Schwartz CL, Ebb DH, Seibel NL, Grier HE, Gorlick R, Marina N. 2012. Outcome for adolescent and young adult patients with osteosarcoma: a report from the Children's Oncology Group. *Cancer*,118(18):4597-605. doi: 10.1002/ncr.27414. Epub 2012 Jan 17. PMID: 22252521; PMCID: PMC4008337.

Jawad MU, Scully SP. 2010. Classifications in brief: Enneking classification: Benign and malignant tumors of the musculoskeletal system. *Clin Orthop Relat Res*,468:2000–2. Available at: <https://doi.org/10.1007/s11999-010-1315-7>.

Jiang Y, Wang T, Wei Z. 2020. Construction and Validation of Nomograms for Predicting the Prognosis of Juvenile Osteosarcoma: A Real-World Analysis in the SEER Database. *Technology in Cancer Research & Treatment*. Available at: doi:[10.1177/1533033820947718](https://doi.org/10.1177/1533033820947718)

Jones RD, Reid R, Balakrishnan G, Barrett A. 1993. Multifocal synchronous osteosarcoma: the Scottish Bone Tumour Registry experience. *Med Pediatr Oncol*, 21(2):111-6. doi: 10.1002/mpo.2950210206. PMID: 8433676.

Jordan K, Feyer P, Höller U, Link H, Wörmann B, Jahn F. 2017. Supportive Treatments for Patients with Cancer. *Dtsch Arztebl Int*, 114(27-28):481-487. doi: 10.3238/arztebl.2017.0481. PMID: 28764837; PMCID: PMC5545632.

Kalim D. 2020. Epidemiology of Osteosarcoma : Single Center Study in Indonesia. *Int J Pharmtech Res*,13:105–8. <https://doi.org/10.20902/IJPTR.2019.130112>.

Kaneuchi, Y.; Hakozaiki, M.; Yamada, H.; Hasegawa, O.; Yamada, S.; Oka, Y.; Watanabe, K.; Konno, S. 2020. Very Late Relapse of High-Grade Osteosarcoma: A Case Report and Review of the Literature. *Medicine*, e21206.

Kemenkes RI. 2019. Pedoman Nasional Pelayanan Kedokteran Tatalaksana Osteosarkoma.

Kamen, B.A., Winick, N.J. 1988. Commentary High Dose Methotrexate therapy: insecure rationale? *Biochemical Pharmacology*, 37(14):2713-2715. [https://doi.org/10.1016/0006-2952\(88\)90032-9](https://doi.org/10.1016/0006-2952(88)90032-9).

Kaneuchi Y, Yoshida S, Fujiwara T, Evans S, Abudu A. 2022. Limb salvage surgery has a higher complication rate than amputation but is still beneficial for patients younger than 10

years old with osteosarcoma of an extremity. *J Pediatr Surg*, 57(11):702-709. doi: 10.1016/j.jpedsurg.2022.04.001. Epub 2022 Apr 8. PMID: 35490054.

Karalexi MA, Markozannes G, Tagkas CF, Katsimpris A, Tseretopoulou X, Tsilidis KK, Spector LG, Schüz J, Siahaniidou T, Petridou ET, Ntzani EE. 2022. Nutritional Status at Diagnosis as Predictor of Survival from Childhood Cancer: A Review of the Literature. *Diagnostics (Basel)*, 12(10):2357. doi: 10.3390/diagnostics12102357. PMID: 36292046; PMCID: PMC9600212.

Kaseta MK, Khaldi L, Gomatos IP, Tzagarakis GP, Alevizos L, Leandros E, Papagelopoulos PJ, Soucacos PN. 2008. Prognostic value of bax, bcl-2, and p53 staining in primary osteosarcoma. *J Surg Oncol*, 97(3):259-66. doi: 10.1002/jso.20913. PMID: 18161867.

Katagiri, T. and Takahashi, N. 2002. Regulatory mechanism of osteoblas and osteoclast differentiation. *Oral Disease*, 8:147-159. Available at <http://www.blackwellmunksgaard.com>.

Kementerian Kesehatan Republik Indonesia. 2019. Keputusan Menteri Kesehatan Republik Indonesia No. HK.01.07/MENKES/88/2019.

Kim, E.K., Lim, S., Park, J.M., Seo, J.K., Kim, J.H., Kim, K.T., Ryu, S.H., Suh, P.G. 2012. Human Mesenchymal Stem Cell Differentiation to the Osteogenic or Adipogenic Lineage is Regulated by AMP-Activated Protein Kinase. *J. Cell Physiol*, 227: 1680-1687.

Kim MS, Lee SY, Lee TR, Cho WH, Song WS, Koh JS, Lee JA, Yoo JY, Jeon DG. 2009. Prognostic nomogram for predicting the 5-year probability of developing metastasis after neo-adjuvant chemotherapy and definitive surgery for AJCC stage II extremity osteosarcoma. *Ann Oncol*, 20(5):955-60. doi: 10.1093/annonc/mdn723. Epub 2009 Jan 19. PMID: 19153123.

Kim, W.; Han, I.; Lee, J.S.; Cho, H.S.; Park, J.W.; Kim, H.S. 2018. Postmetastasis survival in high-grade extremity osteosarcoma: A retrospective analysis of prognostic factors in 126 patients. *J. Surg. Oncol*, 117, 1223–1231.

Korsmeyer SJ. 1999. BCL-2 gene family and the regulation of programmed cell death. *Cancer Res*, 59(7 Suppl):1693s-1700s. PMID: 10197582.

Kouwenberg TW, van Dalen EC, Feijen EAM, Netea SA, Bolier M, Slieker MG, et al. 2023. Acute and early-onset cardiotoxicity in children and adolescents with cancer: a systematic review. *BMC Cancer*, 23(1):866. doi: 10.1186/s12885-023-11353-9.

Kukurba, K.R.; Parsana, P.; Balliu, B.; Smith, K.S.; Zappala, Z.; Knowles, D.A.; Favé, M.-J.; Davis, J.R.; Li, X.; Zhu, X.; et al. 2016. Impact of the X chromosome and sex on regulatory variation. *Genome Res*, 26, 768–777.

Krischer JP, Epstein S, Cuthbertson DD, Goorin AM, Epstein ML, Lipshultz SE. 1997. Clinical cardiotoxicity following anthracycline treatment for childhood cancer: the Pediatric Oncology Group experience. *J Clin Oncol*, 15(4):1544-52. doi: 10.1200/JCO.1997.15.4.1544.

Kwon H, Schafer JM, Song NJ, Kaneko S, Li A, Xiao T, Ma A, Allen C, Das K, Zhou L, Riesenberg B, Chang Y, Weltge P, Velegraki M, Oh DY, Fong L, Ma Q, Sundi D, Chung D, Li X, Li Z. 2020. Androgen conspires with the CD8(+) T cell exhaustion program and contributes to sex bias in cancer. *Sci Immunol*, 7:eabq2630. Available at: <https://doi.org/10.1126/sciimmunol.abq2630>.

Laitinen, M.K.; Albergo, J.I.; Stevenson, J.D.; Farfalli, G.L.; Aponte-Tinao, L.A.; Grimer, R.J.; Jeys, L.M.; Parry, M.C. 2020. Female gender in the hormonally active age group plays a major role in high-grade chondrosarcoma survival. *Acta Oncol*, 59, 242–246.

Lambert LA, Qiao N, Hunt KK, Lambert DH, Mills GB, Meijer L, Keyomarsi K. 2008. Autophagy: a novel mechanism of synergistic cytotoxicity between doxorubicin and roscovitine in a sarcoma model. *Cancer Res*, 68(19):7966-74. doi: 10.1158/0008-5472.CAN-08-1333. PMID: 18829554; PMCID: PMC2561224.

Lamora A, Talbot J, Mullard M, Brounais-Le Royer B, Redini F, Verrecchia F. 2016. TGF- $\beta$  Signaling in Bone Remodeling and Osteosarcoma Progression. *J Clin Med*, 5. <https://doi.org/10.3390/jcm5110096>.

Laverdière C, Chiasson S, Costea I, Moghrabi A, Krajcinovic M. 2002. Polymorphism G80A in the reduced folate carrier gene and its relationship to methotrexate plasma levels and outcome of childhood acute lymphoblastic leukemia. *Blood*, 100(10):3832-4. doi: 10.1182/blood.V100.10.3832. PMID: 12411325.

Lee JA, Kim DH, Lim JS, Park KD, Song WS, Lee SY, Jeon DG. 2007. The survival of osteosarcoma patients 10 years old or younger is not worse than the survival of older patients: a retrospective analysis. *Cancer Res Treat*, 39(4):160-4. doi: 10.4143/crt.2007.39.4.160. Epub 2007 Dec 31. PMID: 19746238; PMCID: PMC2739368.

Li H, Jiang W, Liu S, Yang M, Chen S, Pan Y, Cui M. 2024. Connecting the mechanisms of tumor sex differences with cancer therapy. *Mol Cell Biochem*, 479(2):213-231. doi: 10.1007/s11010-023-04723-1. Epub 2023 Apr 7. PMID: 37027097.

Li Y, Lu Z, Ma A, Yao W, Dong R, Li K, Wu M, Dong K, Qian T. 2024. Nutritional status associated with clinical outcomes in children with solid tumors: A retrospective cohort study from China. *Cancer Med*, 13(1):e6798. doi: 10.1002/cam4.6798. Epub 2023 Dec 18. PMID: 38111308; PMCID: PMC10807599.

Li Z, Xu B, Cai J, Zha Z. 2023. Cancer-Specific Survival after Limb Salvage versus Amputation in Children and Adolescents with Osteosarcoma: A Population-Based Analysis with Propensity Score Matching. *J Oncol*, 2023:8635829. doi: 10.1155/2023/8635829. PMID: 37089259; PMCID: PMC10118882.

Libert, C.; Dejager, L.; Pinheiro, I. 2010. The X chromosome in immune functions: When a chromosome makes the difference. *Nat. Rev. Immunol.* 2010, 10, 594–604.

Lindsay AD, Haupt EE, Chan CM, Spiguel AR, Scarborough MT, Zlotecki RA, Gibbs PC. 2018. Treatment of Sarcoma Lung Metastases with Stereotactic Body Radiotherapy.

*Sarcoma*, 2018:9132359. doi: 10.1155/2018/9132359. PMID: 29808081; PMCID: PMC5901828.

Lipshultz SE, Miller TL, Lipsitz SR, Neuberger DS, Dahlberg SE, Colan SD, et al. 2012. Continuous versus Bolus infusion of doxorubicin in children with ALL: longterm cardiac outcomes. *Pediatrics*, 130(6):1003e11.

Liu B, Liu G, Liu B, Guo Y, Peng N, Li T. 2024. Correlation between gene polymorphism and adverse reactions of high-dose methotrexate in osteosarcoma patients: a systematic review and meta-analysis. *World J Surg Oncol*, 22(1):19. doi: 10.1186/s12957-023-03287-0. PMID: 38212758; PMCID: PMC10782754.

Liu JJ, Liu S, Wang JG, Zhu W, Hua YQ, Sun W, Cai ZD. 2013. Telangiectatic osteosarcoma: a review of literature. *Onco Targets Ther*, 6:593-602. doi: 10.2147/OTT.S41351. PMID: 23745051; PMCID: PMC3671797.

Liu T, Cui L, He Z, Chen Z, Tao H, Yang J. 2023. Epidemiology and nomogram of pediatric and young adulthood osteosarcoma patients with synchronous lung metastasis: A SEER analysis. *PLoS One*, 18(7):e0288492. doi: 10.1371/journal.pone.0288492. PMID: 37437020; PMCID: PMC10337906.

Loh AH, Navid F, Wang C, Bahrami A, Wu J, Neel MD, Rao BN. 2014. Management of local recurrence of pediatric osteosarcoma following limb-sparing surgery. *Ann Surg Oncol*, 21(6):1948-55. doi: 10.1245/s10434-014-3550-8.

Luetke A, Meyers PA, Lewis I, Juergens H. 2014. Osteosarcoma treatment - where do we stand? A state of the art review. *Cancer Treat Rev*, 40(4):523-32. doi: 10.1016/j.ctrv.2013.11.006. Epub 2013 Nov 27. PMID: 24345772.

Lowenberg D, Thorn CF, Desta Z, Flockhart DA, Altman RB, Klein TE. 2014. PharmGKB summary: ifosfamide pathways, pharmacokinetics and pharmacodynamics. *Pharmacogenet Genomics*, 24(2):133-8. doi: 10.1097/FPC.000000000000019. PMID: 24401834; PMCID: PMC4084804.

Mailankody, S., Kumar, V.S., Khan, S.A., Banavali, S.D., Bajpai, J. 2022. Resources-appropriate selection of osteosarcoma treatment protocols in low-and middle-income countries. *Pediatr Blood Cancer*, 69:e29540. Available at: <https://doi.org/10.1002/pbc.29540>.

Makino S. 1959. The role of tumor stem-cells in regrowth of the tumor following drastic applications. *Acta Unio Int Contra Cancrum*, 15(Suppl 1):196-8. PMID: 14420161.

Malhas AM, Sumathi VP, James SL, Menna C, Carter SR, Tillman RM, Jeys L, Grimer RJ. 2012. Low-grade central osteosarcoma: a difficult condition to diagnose. *Sarcoma*, 2012:764796. doi: 10.1155/2012/764796. Epub 2012 Jul 16. PMID: 22851905; PMCID: PMC3407619.

Mankin HJ, Hornicek FJ, Rosenberg AE, Harmon DC, Gebhardt Mc. 2004. Survival data for 648 patients with osteosarcoma treated at one institution. *Clin Orthop Relat Res*, 286-291.

Marina N, Bielack S, Whelan J, Smeland S, Krailo M, Sydes MR, Butterfass-Bahloul T, Calaminus G, Bernstein M. 2009. International collaboration is feasible in trials for rare conditions: the EURAMOS experience. *Cancer Treat Res*, 152:339-53. doi: 10.1007/978-1-4419-0284-9\_18. PMID: 20213400.

Marina NM, Smeland S, Bielack SS, Bernstein M, Jovic G, Krailo MD, *et al.* 2016. Comparison of MAPIE versus MAP in patients with a poor response to preoperative chemotherapy for newly diagnosed high-grade osteosarcoma (EURAMOS-1): an open-label, international, randomised controlled trial. *Lancet Oncol*, 17(10):1396-1408. doi: 10.1016/S1470-2045(16)30214-5. Epub 2016 Aug 25. PMID: 27569442; PMCID: PMC5052459.

Marko TA, Diessner BJ, Spector LG. 2016. Prevalence of Metastasis at Diagnosis of Osteosarcoma: An International Comparison. *Pediatr Blood Cancer*, 63(6):1006-11. doi: 10.1002/pbc.25963. Epub 2016 Feb 29. PMID: 26929018; PMCID: PMC4833631.

Masson E, Relling MV, Synold TW, Liu Q, Schuetz JD, Sandlund JT, Pui CH, Evans WE. 1996. Accumulation of methotrexate polyglutamates in lymphoblasts is a determinant of antileukemic effects in vivo. A rationale for high-dose methotrexate. *J Clin Invest*, 97(1):73-80. doi: 10.1172/JCI118409. PMID: 8550853; PMCID: PMC507064.

Matherly LH, Taub JW, Ravindranath Y, Proefke SA, Wong SC, Gimotty P, Buck S, Wright JE, Rosowsky A. 1995. Elevated dihydrofolate reductase and impaired methotrexate transport as elements in methotrexate resistance in childhood acute lymphoblastic leukemia. *Blood*, 85(2):500-9. PMID: 7812005.

McDonald J, DenOtter TD. 2023. Codman Triangle In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK549764/>

McGowan, J.V., Chung, R., Maulik, A., Piotrowska, I., Walker, J.M., Yellon, D.M. 2017. Review Article-Anthracycline Chemotherapy and Cardiotoxicity. *Cardiovasc Drugs Ther*, 63-75. doi: 10.1007/s10557-016-6711-0.

Mialou V, Philip T, Kalifa C, Perol D, Gentet JC, Marec-Berard P, Pacquement H, Chastagner P, Defaschelles AS, Hartmann O. 2005. Metastatic osteosarcoma at diagnosis: prognostic factors and long-term outcome--the French pediatric experience. *Cancer*, 104(5):1100-9. doi: 10.1002/cncr.21263. PMID: 16015627.

Mikkelsen TS, Thorn CF, Yang JJ, Ulrich CM, French D, Zaza G, Dunnenberger HM, Marsh S, McLeod HL, Giacomini K, Becker ML, Gaedigk R, Leeder JS, Kager L, Relling MV, Evans W, Klein TE, Altman RB. 2011. PharmGKB summary: methotrexate pathway. *Pharmacogenet Genomics*, 21(10):679-86. doi: 10.1097/FPC.0b013e328343dd93. PMID: 21317831; PMCID: PMC3139712.

Mirabello L, Troisi RJ, Savage SA. 2009. Osteosarcoma incidence and survival rates from 1973 to 2004: data from the Surveillance, Epidemiology, and End Results Program. *Cancer*, 115(7):1531-43. doi: 10.1002/cncr.24121. PMID: 19197972; PMCID: PMC2813207.

Miranda M, Nadel S. 2023. Pediatric Sepsis: a Summary of Current Definitions and Management Recommendations. *Curr Pediatr Rep*, 11(2):29-39. doi: 10.1007/s40124-023-00286-3. Epub 2023 May 9. PMID: 37252329; PMCID: PMC10169116.

Misaghi A, Goldin A, Awad M, Kulidjian AA. 2018. Osteosarcoma: a comprehensive review. *SICOT J*, 4:12. doi: 10.1051/sicotj/2017028. Epub 2018 Apr 9. PMID: 29629690; PMCID: PMC5890448.

Mohamed, A.M. 2008. Review article An Overview of Bone Cells and Their Regulating Factors of Differentiation. *Malaysian Journal of Medical Sciences*, 15;1:4-12.

Monsereenusorn C, Alcasabas AP, Loh AHP, Soh SY, Leung KWP, Dhamne C, Blair S, Lam C, Rujkijyanont P, Traivaree C, Photia A, Veerapan P, Puhaindran ME, Oh BLZ, Wang E, Rodriguez-Galindo C. 2022. Predictors and Treatment Outcomes of Pediatric Osteosarcoma in Diverse Socioeconomic Backgrounds in Southeast Asia: A Retrospective Multicenter Study. *Asian Pac J Cancer Prev*, 23(2):631-640. doi: 10.31557/APJCP.2022.23.2.631. PMID: 35225476; PMCID: PMC9272642.

Monjanel S, Rigault JP, Cano JP, Carcassonne Y, Favre R. 1979. High-dose methotrexate: preliminary evaluation of a pharmacokinetic approach. *Cancer Chemother Pharmacol*;3(3):189-96. doi: 10.1007/BF00262421. PMID: 527209.

Mu X, Isaac C, Schott T, Huard J, Weiss K. 2013. Rapamycin Inhibits ALDH Activity, Resistance to Oxidative Stress, and Metastatic Potential in Murine Osteosarcoma Cells. *Sarcoma*, 2013:480713. doi: 10.1155/2013/480713. Epub 2013 Feb 14. PMID: 23476113; PMCID: PMC3586506.

Nagamine A, Araki T, Yashima H, Kamimura A, Shiraishi T, Yanagawa T, Obayashi K, Yamamoto K. 2022. Target concentration achievement for efficacy and safety of patients with osteosarcoma treated with high-dose methotrexate based on individual pharmacokinetics: A retrospective study. *Oncol Lett*;25(2):70. doi: 10.3892/ol.2022.13656. PMID: 36688106; PMCID: PMC9843304.

Nakajima H, Sim FH, Bond JR, Unni KK. 1997. Small cell osteosarcoma of bone. Review of 72 cases. *Cancer*;79(11):2095-106. doi: 10.1002/(sici)1097-0142(19970601)79:11<2095::aid-cnrcr6>3.0.co;2-o. PMID: 9179055.

Odri GA, Tchicaya-Bouanga J, Yoon DJY, Modrowski D. 2022. Metastatic Progression of Osteosarcomas: A Review of Current Knowledge of Environmental versus Oncogenic Drivers. *Cancers (Basel)*, 14(2):360. doi: 10.3390/cancers14020360. PMID: 35053522; PMCID: PMC8774233.

Ogura K, Fujiwara T, Yasunaga H, Matsui H, Jeon DG, Cho WH, Hiraga H, Ishii T, Yonemoto T, Kamoda H, Ozaki T, Kozawa E, Nishida Y, Morioka H, Hiruma T, Kakunaga S, Ueda T, Tsuda Y, Kawano H, Kawai A. 2015. Development and external validation of nomograms predicting distant metastases and overall survival after neoadjuvant chemotherapy and surgery for patients with nonmetastatic osteosarcoma: A multi-institutional study. *Cancer*;121(21):3844-52. doi: 10.1002/cncr.29575. Epub 2015 Jul 20. PMID: 26194185; PMCID: PMC5034754.

Okada K, Unni KK, Swee RG, Sim FH. 1999. High grade surface osteosarcoma: a clinicopathologic study of 46 cases. *Cancer*;85(5):1044-54. doi: 10.1002/(sici)1097-0142(19990301)85:5<1044::aid-cncr6>3.0.co;2-a. PMID: 10091787.

Oliveira CS, Leeuwenburgh S, Mano JF. 2021. New insights into the biomimetic design and biomedical applications of bioengineered bone microenvironments. *APL Bioeng*;5(4):041507. doi: 10.1063/5.0065152. PMID: 34765857; PMCID: PMC8568480.

Ornos ED, Cando LF, Catral CD, Quebral EP, Tantengco OA, Arevalo MVP, Dee EC. 2023. Molecular basis of sex differences in cancer: Perspective from Asia. *iScience*, 26(7):107101. doi: 10.1016/j.isci.2023.107101. PMID: 37404373; PMCID: PMC10316661.

Ozaki T, Flege S, Kevric M, Lindner N, Maas R, Delling G, Schwarz R, von Hochstetter AR, Salzer-Kuntschik M, Berdel WE, Jürgens H, Exner GU, Reichardt P, Mayer-Steinacker R, Ewerbeck V, Kotz R, Winkelmann W, Bielack SS. 2003. Osteosarcoma of the pelvis: experience of the Cooperative Osteosarcoma Study Group. *J Clin Oncol*;21(2):334-41. doi: 10.1200/JCO.2003.01.142. PMID: 12525527.

Pakos EE, Nearchou AD, Grimer RJ, Koumoullis HD, Abudu A, Bramer JA, Jeys LM, Franchi A, Scoccianti G, Campanacci D, Capanna R, Aparicio J, Tabone MD, Holzer G, Abdolvahab F, Funovics P, Dominkus M, Ilhan I, Berrak SG, Patino-Garcia A, Sierrasesumaga L, San-Julian M, Garraus M, Petrilli AS, Filho RJ, Macedo CR, Alves MT, Seiwerth S, Nagarajan R, Cripe TP, Ioannidis JP. 2009. Prognostic factors and outcomes for osteosarcoma: an international collaboration. *Eur J Cancer*;45(13):2367-75. doi: 10.1016/j.ejca.2009.03.005. Epub 2009 Apr 6. PMID: 19349163.

Papakonstantinou E, Stamatopoulos A, I Athanasiadis D, Kenanidis E, Potoupnis M, Haidich AB, Tsiridis E. 2020. Limb-salvage surgery offers better five-year survival rate than amputation in patients with limb osteosarcoma treated with neoadjuvant chemotherapy. A systematic review and meta-analysis. *J Bone Oncol*;25:100319. doi: 10.1016/j.jbo.2020.100319. PMID: 33088699; PMCID: PMC7567946.

Peled Y, Levin D, Manisterski M, Kollander N, Shukrun R, Elhasid R. 2024. Weight loss and response to chemotherapy in pediatric patients with osteosarcoma. *Eur J Clin Nutr*, 78(6):541-543. doi: 10.1038/s41430-024-01404-0. Epub 2024 Jan 18. PMID: 38238462.

Picci P, Sangiorgi L, Rougraff BT, Neff JR, Casadei R, Campanacci M. 1994. Relationship of chemotherapy-induced necrosis and surgical margins to local recurrence in osteosarcoma. *J Clin Oncol*;12(12):2699-705. doi: 10.1200/JCO.1994.12.12.2699. PMID: 7989947.

Picci P. 2007. Osteosarcoma (osteogenic sarcoma). *Orphanet J Rare Dis*;2:6. doi: 10.1186/1750-1172-2-6. PMID: 17244349; PMCID: PMC1794406.

Piperno-Neumann S, Ray-Coquard I, Ocean BV, Laurence V, Cupissol D, Perrin C, Penel N, Bompas E, Rios M, Le Cesne A, Italiano A, Anract P, de Pinieux G, Collard O, Bertucci F, Duffaud F, Le Deley MC, Delays J, Brugieres L, Blay JY. 2020. Results of API-AI based regimen in osteosarcoma adult patients included in the French OS2006/Sarcome-09

study. *Int J Cancer*;146(2):413-423. doi: 10.1002/ijc.32526. Epub 2019 Jul 19. PMID: 31246277.

Prabowo Y, Kamal AF, Kodrat E, Prasetyo M, Maruanaya S, Efar TS. 2020. Parosteal Osteosarcoma: A Benign-Looking Tumour, Amenable to a Variety of Surgical Reconstruction. *Int J Surg Oncol*;2020:4807612. doi: 10.1155/2020/4807612. PMID: 32550023; PMCID: PMC7275216.

Puri A, Byregowda S, Gulia A, Crasto S, Chinaswamy G. 2018. A study of 853 high grade osteosarcomas from a single institution-Are outcomes in Indian patients different? *J Surg Oncol*;117(2):299-306. doi: 10.1002/jso.24809. Epub 2017 Aug 22. PMID: 28833209.

Qi L, Ren X, Liu Z, Li S, Zhang W, Chen R, Chen C, Tu C, Li Z. 2020. Predictors and Survival of Patients with Osteosarcoma After Limb Salvage versus Amputation: A Population-Based Analysis with Propensity Score Matching. *World J Surg*;44(7):2201-2210. doi: 10.1007/s00268-020-05471-9. PMID: 32170370.

Rastogi S, Aggarwal A, Tiwari A, Sharma V. 2018. Chemotherapy in Nonmetastatic Osteosarcoma: Recent Advances and Implications for Developing Countries. *J Glob Oncol*;4:1-5. doi: 10.1200/JGO.2016.007336. Epub 2017 Jan 18. PMID: 30241154; PMCID: PMC6180788.

Rathore R, Van Tine BA. 2021. Pathogenesis and Current Treatment of Osteosarcoma: Perspectives for Future Therapies. *J Clin Med*;10(6):1182. doi: 10.3390/jcm10061182. PMID: 33809018; PMCID: PMC8000603.

Ren HY, Sun LL, Li HY, Ye ZM. 2015. Prognostic Significance of Serum Alkaline Phosphatase Level in Osteosarcoma: A Meta-Analysis of Published Data. *Biomed Res Int*;2015:160835. doi: 10.1155/2015/160835. Epub 2015 Nov 4. PMID: 26618165; PMCID: PMC4649087.

Renard AJ, Veth RP, Schreuder HW, van Loon CJ, Koops HS, van Horn JR. 2000. Function and complications after ablative and limb-salvage therapy in lower extremity sarcoma of bone. *J Surg Oncol*;73(4):198-205. doi: 10.1002/(sici)1096-9098(200004)73:4<198::aid-jso3>3.0.co;2-x. PMID: 10797332.

Righi A, Gambarotti M, Longo S, Benini S, Gamberi G, Cocchi S, Vanel D, Picci P, Bertoni F, Simoni A, Franchi A, Dei Tos AP. 2015. Small cell osteosarcoma: clinicopathologic, immunohistochemical, and molecular analysis of 36 cases. *Am J Surg Pathol*;39(5):691-9. doi: 10.1097/PAS.0000000000000412. PMID: 25723116.

Ritacco LE, Milano FE, Farfalli GL, Ayerza MA, Muscolo DL, Aponte-Tinao LA. 2013. Accuracy of 3-D planning and navigation in bone tumor resection. *Orthopedics*;36. <https://doi.org/10.3928/01477447-20130624-27>.

Riza M, Salimo H, Wasita B, Idulhaq M, Saputra R, Widyaningsih V, Soestrisno S, Zahidah F, Wayanshakty J. 2024. Survival and prognostic factors in pediatric osteosarcoma: A 5-year single-center experience in Central Java, Indonesia. *PI [Internet]*;64(1):10-. Available from:

<https://www.paediatricaindonesiana.org/index.php/paediatricaindonesiana/article/view/3448>

Robien K, Ulrich CM. 2003. 5,10-Methylenetetrahydrofolate reductase polymorphisms and leukemia risk: a HuGE minireview. *Am J Epidemiol*;157(7):571-82. doi: 10.1093/aje/kwg024. PMID: 12672676.

Rosen G, Marcove RC, Huvos AG, Caparros BI, Lane JM, Nirenberg A, Cacavio A, Groshen S. 1983. Primary osteogenic sarcoma: eight-year experience with adjuvant chemotherapy. *J Cancer Res Clin Oncol*;106 Suppl:55-67. doi: 10.1007/BF00625054. PMID: 6604058.

Rothzerg E, Xu J, Wood D. 2023. Different Subtypes of Osteosarcoma: Histopathological Patterns and Clinical Behaviour. *Journal of Molecular Pathology*;4:99-108. <https://doi.org/10.3390/jmp4020011>.

Rougraff BT, Simon MA, Kneisl JS, Greenberg DB, Mankin HJ. 1994. Limb salvage compared with amputation for osteosarcoma of the distal end of the femur. A long-term oncological, functional, and quality-of-life study. *J Bone Joint Surg Am*;76(5):649-56. doi: 10.2106/00004623-199405000-00004. PMID: 8175811.

Rubio R, Gutierrez-Aranda I, Sáez-Castillo AI, Labarga A, Rosu-Myles M, Gonzalez-Garcia S, Toribio ML, Menendez P, Rodriguez R. 2013. The differentiation stage of p53-Rb-deficient bone marrow mesenchymal stem cells imposes the phenotype of in vivo sarcoma development. *Oncogene*;32(41):4970-80. doi: 10.1038/onc.2012.507. Epub 2012 Dec 10. PMID: 23222711.

Rykov, Maxim & Sengapova, Elmira. 2019. Treatment of Children with Osteosarcoma. doi: 10.5772/intechopen.83756.

Sadikovic B, Thorner P, Chilton-Macneill S, Martin JW, Cervigne NK, Squire J, Zielenska M. 2010. Expression analysis of genes associated with human osteosarcoma tumors shows correlation of RUNX2 overexpression with poor response to chemotherapy. *BMC Cancer*;10:202. doi: 10.1186/1471-2407-10-202. PMID: 20465837; PMCID: PMC2875220.

Saeter G, Elomaa I, Wahlqvist Y, Alvegård TA, Wiebe T, Monge O, Forrestier E, Solheim OP. 1997. Prognostic factors in bone sarcomas. *Acta Orthop Scand Suppl*;273:156-60. doi: 10.1080/17453674.1997.11744723. PMID: 9057608.

Saito Y, Kumamoto T, Makino Y, Tamai I, Ogawa C, Terakado H. 2016. A retrospective study of treatment and prophylaxis of ifosfamide-induced hemorrhagic cystitis in pediatric and adolescent and young adult (AYA) patients with solid tumors. *Jpn J Clin Oncol*;46(9):856-61. doi: 10.1093/jjco/hyw093. Epub 2016 Jul 5. PMID: 27380806.

Salunke AA, Chen Y, Tan JH, Chen X, Khin LW, Puhaindran ME. 2014. Does a pathological fracture affect the prognosis in patients with osteosarcoma of the extremities?: A systematic review and meta-analysis. *Bone Joint J*;96-B:1396-403. doi: 10.1302/0301-620X.96B10.34370.

Sari NM, Rakhmilla LE, Bashari MH, Zazuli Z, Suryawan N, Susannah S, Reniarti L, Raspati H, Supriyadi E, Kaspers GJL, Idjradinata P. 2021. Monitoring Of High-Dose Methotrexate (Mtx)-Related Toxicity and Mtx Levels in Children with Acute Lymphoblastic Leukemia: A Pilot-Study in Indonesia. *Asian Pac J Cancer Prev*, 1;22(7):2025-2031. doi: 10.31557/APJCP.2021.22.7.2025.

Schmiegelow K. 2009. Advances in individual prediction of methotrexate toxicity: a review. *Br J Haematol*;146(5):489-503. doi: 10.1111/j.1365-2141.2009.07765.x. Epub 2009 Jun 15. PMID: 19538530.

Sethi SK, Bunchman T, Chakraborty R, Raina R. 2021. Pediatric acute kidney injury: new advances in the last decade. *Kidney Res Clin Pract*;40(1):40-51. doi: 10.23876/j.krcp.20.074. Epub 2021 Mar 3. PMID: 33663033; PMCID: PMC8041642

Setiawati, R. and Rahardjo, P. 2018. Bone Development and Growth. *Intech Open*;64747. doi: 10.5772/intechopen.82452.

Shi Y, He G, Lee W-C, McKenzie JA, Silva MJ, Long F. 2017. Gli1 identifies osteogenic progenitors for bone formation and fracture repair. *Nat Commun*;8:2043. <https://doi.org/10.1038/s41467-017-02171-2>.

Shulman DS, Klega K, Imamovic-Tuco A, Clapp A, Nag A, Thorner AR, et al. 2018. Detection of circulating tumour DNA is associated with inferior outcomes in Ewing sarcoma and osteosarcoma: a report from the Children's Oncology Group. *Br J Cancer*, 119:615–21. <https://doi.org/10.1038/s41416-018-0212-9>.

Siegel RL, Miller KD, Fuchs HE, Jemal A. 2022. Cancer statistics, 2022. *CA Cancer J Clin*;72(1):7-33. doi: 10.3322/caac.21708. Epub 2022 Jan 12. PMID: 35020204.

Siu LL, Moore MJ. 1998. Use of mesna to prevent ifosfamide-induced urotoxicity. *Support Care Cancer*;6(2):144-54. doi: 10.1007/s005200050149. PMID: 9540174.

Simpson E, Brown HL. 2018. Understanding osteosarcomas. *JAAPA*;31(8):15-19. doi: 10.1097/01.JAA.0000541477.24116.8d. PMID: 29979330.

\ Sjakti H, Putri I, Windiastuti E. 2021. Survival rate of pediatric osteosarcoma in Indonesia: a single center study. *PI [Internet]*;62(1):27-1. Available from: <https://www.paediatricaindonesiana.org/index.php/paediatricaindonesiana/article/view/2550>.

Smeland S, Muller C, Alvegard TA, et al. 2003. Scandinavian Sarcoma Group Osteosarcoma Study SSG VIII: prognostic factors for outcome and the role of replacement salvage chemotherapy for poor histological responders. *Eur J Cancer*, 39:488-494.

Smeland S, Bruland OS, Hjorth L, Brosjö O, Bjerkehagen B, Osterlundh G, Jakobson A, Hall KS, Monge OR, Björk O, Alvegaard TA. 2011. Results of the Scandinavian Sarcoma Group XIV protocol for classical osteosarcoma: 63 patients with a minimum follow-up of 4 years. *Acta Orthop*;82(2):211-6. doi: 10.3109/17453674.2011.566141. Epub 2011 Mar 24. PMID: 21434784; PMCID: PMC3235293.

Song B, Wang Y, Xi Y, Kudo K, Bruheim S, Botchkina GI, Gavin E, Wan Y, Formentini A, Kornmann M, Fodstad O, Ju J. 2009. Mechanism of chemoresistance mediated by miR-140 in human osteosarcoma and colon cancer cells. *Oncogene*, 28(46):4065-74. doi: 10.1038/onc.2009.274. Epub 2009 Sep 7. PMID: 19734943; PMCID: PMC2783211.

Song B, Wang Y, Titmus MA, Botchkina G, Formentini A, Kornmann M, Ju J. 2010. Molecular mechanism of chemoresistance by miR-215 in osteosarcoma and colon cancer cells. *Mol Cancer*, 9:96. doi: 10.1186/1476-4598-9-96. PMID: 20433742; PMCID: PMC2881118.

Song Z, Hu Y, Liu S, Jiang D, Yi Z, Benjamin MM, Zhao R. 2021. The Role of Genetic Polymorphisms in High-Dose Methotrexate Toxicity and Response in Hematological Malignancies: A Systematic Review and Meta-Analysis. *Front Pharmacol*;12:757464. doi: 10.3389/fphar.2021.757464. PMID: 34744734; PMCID: PMC8570281.

Strauss SJ, Whelan JS. 2018. Current questions in bone sarcomas. *Curr Opin Oncol*;30(4):252-259. doi: 10.1097/CCO.0000000000000456. PMID: 29782347.

Sun, T., Zhong, X., Song, H. et al. 2019. Anoikis resistant mediated by FASN promoted growth and metastasis of osteosarcoma. *Cell Death Dis*;10:298. <https://doi.org/10.1038/s41419-019-1532-2>.

Taccone A, Di Stadio M, Oliveri M, Oddone M, Occhi M. 1995. Multifocal synchronous osteosarcoma. *Eur J Radiol*;20(1):43-5. doi: 10.1016/0720-048x(95)00624-y. PMID: 7556252.

Tam, W.L.; Luyten, F.P.; Roberts, S.J. 2018. From skeletal development to the creation of pluripotent stem cell-derived bone-forming progenitors. *Philos. Trans. R. Soc. B Biol. Sci*;373, 1–11. <http://dx.doi.org/10.1098/rstb.2017.0218>.

Tan VZZ, Chan NM, Ang WL, Mya SN, Chan MY, Chen CK. 2021. Cardiotoxicity After Anthracycline Chemotherapy for Childhood Cancer in a Multiethnic Asian Population. *Front Pediatr*, 3(9):639603. doi: 10.3389/fped.2021.639603.

Taran SJ, Taran R, Malipatil NB. 2017. Pediatric Osteosarcoma: An Updated Review. *Indian J Med Paediatr Oncol*;38(1):33-43. doi: 10.4103/0971-5851.203513. PMID: 28469335; PMCID: PMC5398104.

Tiwari P, Thomas MK, Pathania S, Dhawan D, Gupta YK, Vishnubhatla S, Bakhshi S. 2015. Serum Creatinine Versus Plasma Methotrexate Levels to Predict Toxicities in Children Receiving High-dose Methotrexate. *Pediatr Hematol Oncol*;32(8):576-84. doi: 10.3109/08880018.2015.1087612. Epub 2015 Nov 11. PMID: 26558505.

Traivaree C, Likasitthananon N, Monsereenusorn C, Rujkijyanont P. 2018. The effect of intravenous hydration strategy on plasma methotrexate clearance during intravenous high-dose methotrexate administration in pediatric oncology patients. *Cancer Manag Res*;10:4471-4478. doi: 10.2147/CMAR.S172117. PMID: 30349379; PMCID: PMC6188117.

Treon SP, Chabner BA. 1996. Concepts in use of high-dose methotrexate therapy. *Clin Chem*;42(8 Pt 2):1322-9. PMID: 8697606.

Treviño LR, Shimasaki N, Yang W, Panetta JC, Cheng C, Pei D, Chan D, Sparreboom A, Giacomini KM, Pui CH, Evans WE, Relling MV. 2009. Germline genetic variation in an organic anion transporter polypeptide associated with methotrexate pharmacokinetics and clinical effects. *J Clin Oncol*;27(35):5972-8. doi: 10.1200/JCO.2008.20.4156. Epub 2009 Nov 9. PMID: 19901119; PMCID: PMC2793040.

Tübel J, Kuntz L, Marthen C, Schmitt A, Wiest I, VON Eisenhart-Rothe R, Jeschke U, Burgkart R. 2016. Methylation of the ER-alpha Promoter Is Influenced by its Ligand Estrogen in Osteosarcoma Cells SAOS-2 In Vitro. *Anticancer Res*, 36(6):3199-204. PMID: 27272849.

Vaishnavi K, Bansal D, Trehan A, Jain R, Attri SV. 2018. Improving the safety of high-dose methotrexate for children with hematologic cancers in settings without access to MTX levels using extended hydration and additional leukovorin. *Pediatr Blood Cancer*;65(12):e27241. doi: 10.1002/pbc.27241. Epub 2018 May 16. PMID: 29768710.

Vale SS, Castro R, Andrade A, Faleiro J, Abreu N, Mendes C, Gonçalves JP. 2025. Amputation Versus Limb-Salvage Surgery as Treatments for Pediatric Bone Sarcoma: A Comparative Study of Survival, Function, and Quality of Life. *Cureus*, 17(2):e78543. doi: 10.7759/cureus.78543. PMID: 40062064; PMCID: PMC11887411.

van Dalen EC, van As JW, de Camargo B. 2011. Methotrexate for high-grade osteosarcoma in children and young adults. *Cochrane Database Syst Rev*, 2011(5):CD006325. doi: 10.1002/14651858.CD006325.pub3. PMID: 21563152; PMCID: PMC6466691.

Vasiliadis HS, Arnaoutoglou C, Plakoutsis S, Doukas M, Batistatou A, Xenakis TA. 2013. Low-grade central osteosarcoma of distal femur, resembling fibrous dysplasia. *World J Orthop*;4(4):327-32. doi: 10.5312/wjo.v4.i4.327. PMID: 24147271; PMCID: PMC3801255.

Vasquez, L., Tarillo, F., Oscanoa, M., Maza, I., Geronimo, J., Paredes, G., Silva, J.S., Sialer, L. 2016. Analysis of Prognostic Factors in High-Grade Osteosarcoma of the Extremities in Children: A 15-Year Single-Institution Experience. *Front. Oncol*;6:22. doi: 10.3389/fonc.2016.00022.

Vasquez, L.; Silva, J.; Chavez, S.; Zapata, A.; Diaz, R.; Tarrillo, F.; Maza, I.; Sialer, L.; García, J. 2020. Prognostic Impact of Diagnostic and Treatment Delays in Children with Osteosarcoma. *Pediatric Blood Cancer*, 67, e28180.

Villanueva F, Araya H, Briceño P, Varela N, Stevenson A, Jerez S, Tempio F, Chnaiderman J, Perez C, Villarroel M, Concha E, Khani F, Thaler R, Salazar-Onfray F, Stein GS, van Wijnen AJ, Galindo M. 2019. The cancer-related transcription factor RUNX2 modulates expression and secretion of the matricellular protein osteopontin in osteosarcoma cells to promote adhesion to endothelial pulmonary cells and lung metastasis. *J Cell Physiol*;234(8):13659-13679. doi: 10.1002/jcp.28046. Epub 2019 Jan 13. PMID: 30637720.

Voelcker G. 2018. Influence of the alkylating function of aldo-Ifosfamide on the anti-tumor activity. *Anticancer Drugs*;29(1):75-79. doi: 10.1097/CAD.0000000000000569. PMID: 29219879.

Wang B, Yao H, Xie X, Yin J, Zou C, Huang G, Shen J. 2018. Relationship of peak serum methotrexate concentration to prognosis and drug tolerance in non-metastatic extremity osteosarcomas. *Cancer Chemother Pharmacol*;82(2):221-227. doi: 10.1007/s00280-018-3592-x. Epub 2018 May 28. PMID: 29808416.

Wang D, Luo M, Kelley MR. 2004. Human apurinic endonuclease 1 (APE1) expression and prognostic significance in osteosarcoma: enhanced sensitivity of osteosarcoma to DNA damaging agents using silencing RNA APE1 expression inhibition. *Mol Cancer Ther*, 3(6):679-86. PMID: 15210853.

Wang ZX, Yang JS, Pan X, Wang JR, Li J, Yin YM, De W. 2010. Functional and biological analysis of Bcl-xL expression in human osteosarcoma. *Bone*, 47(2):445-54. doi: 10.1016/j.bone.2010.05.027. Epub 2010 May 23. PMID: 20580954.

Wang J, Ni XZ, Yang ML, Huang X, Hou SM, Peng C, Cao JS, Liu TL. 2023. Prognostic factors and treatment outcomes of spinal osteosarcoma: Surveillance, epidemiology, and end results database analysis. *Front Oncol*, 13:1083776. doi: 10.3389/fonc.2023.1083776. PMID: 36937397; PMCID: PMC10014918.

Wang YH, Han XD, Qiu Y, Xiong J, Yu Y, Wang B, Zhu ZZ, Qian BP, Chen YX, Wang SF, Shi HF, Sun X. 2012. Increased expression of insulin-like growth factor-1 receptor is correlated with tumor metastasis and prognosis in patients with osteosarcoma. *J Surg Oncol*, 105(3):235-43. doi: 10.1002/jso.22077. Epub 2011 Aug 22. PMID: 21866554.

Weinstein RS, Kuzak JR, Kluskens LF, Coon JS. 1990. P-glycoproteins in pathology: the multidrug resistance gene family in humans. *Hum Pathol*, 21(1):34-48. doi: 10.1016/0046-8177(90)90073-e. PMID: 1967244.

Weiss L, Dimitrov DS. 1984. A fluid mechanical analysis of the velocity, adhesion, and destruction of cancer cells in capillaries during metastasis. *Cell Biophys*, 6(1):9-22. doi: 10.1007/BF02788577. PMID: 6204763.

Weiss A, Khoury JD, Hoffer FA, Wu J, Billups CA, Heck RK, Quintana J, Poe D, Rao BN, Daw NC. 2007. Telangiectatic osteosarcoma: the St. Jude Children's Research Hospital's experience. *Cancer*, 109(8):1627-37. doi: 10.1002/cncr.22574. PMID: 17351949.

Whelan JS, Bielack SS, Marina N, Smeland S, Jovic G, Hook JM, *et al.* 2015. EURAMOS-1, an international randomised study for osteosarcoma: results from pre-randomisation treatment. *Ann Oncol*;26(2):407-14. doi: 10.1093/annonc/mdu526.

Widemann BC, Balis FM, Kempf-Bielack B, Bielack S, Pratt CB, Ferrari S, *et al.* 2004. High-dose methotrexate-induced nephrotoxicity in patients with osteosarcoma. *Cancer*, 100(10):2222-32. doi: 10.1002/cncr.20255.

Williams LA, Barragan S, Lu Z, Weigel BJ, Spector LG. 2024. Sex differences in osteosarcoma survival across the age spectrum: A National Cancer Database analysis

(2004-2016). *Cancer Epidemiol*, 92:102565. doi: 10.1016/j.canep.2024.102565. Epub 2024 Apr 4. PMID: 38575425.

Williams LA, Spector LG. 2019. Survival Differences Between Males and Females Diagnosed With Childhood Cancer. *JNCI Cancer Spectr*, 3(2):pkz032. doi: 10.1093/jncics/pkz032. Epub 2019 May 11. PMID: 31259303; PMCID: PMC6580869

Wiromrat P, Jetsrisuparb A, Komvilaisak P, Sirichativapee W, Kamsa-Ard S, Wiangnon S. 2012. Incidence and survival rates among pediatric osteogenic sarcoma cases in Khon Kaen, Thailand, 1985-2010. *Asian Pac J Cancer Prev*;13(9):4281-4. doi: 10.7314/apjcp.2012.13.9.4281. PMID: 23167328.

Worch J, Matthay KK, Neuhaus J, Goldsby R, DuBois SG. 2010. Osteosarcoma in children 5 years of age or younger at initial diagnosis. *Pediatr Blood Cancer*;55(2):285-9. doi: 10.1002/pbc.22509. PMID: 20582978; PMCID: PMC2917386.

Wong KC, Niu X, Xu H, Li Y, Kumta S. 2018. Computer Navigation in Orthopaedic Tumour Surgery. *Adv Exp Med Biol*;1093:315-326. doi: 10.1007/978-981-13-1396-7\_24. PMID: 30306491.

Wong RP, Tsang WP, Chau PY, Co NN, Tsang TY, Kwok TT. 2007. p53-R273H gains new function in induction of drug resistance through down-regulation of procaspase-3. *Mol Cancer Ther*, 6(3):1054-61. doi: 10.1158/1535-7163.MCT-06-0336. PMID: 17363498.

World Bank. 2021. World Development Indicators. World Bank 2021. <https://databank.worldbank.org/reports.aspx?source=2&country=LMY> (accessed July 24, 2024).

Wu H, Li S, Lin Y, Wang J, Chekhonin VP, Peltzer K, Baklaushev VP, Abbas KS, Zhang J, Li H, Zhang C. 2022. Association between malnutrition and leucopenia in patients with osteosarcoma. *Front Nutr*, 9:899501. doi: 10.3389/fnut.2022.899501. PMID: 35967822; PMCID: PMC9366299.

Wu X, Cai ZD, Lou LM, Zhu YB. 2012. Expressions of p53, c-MYC, BCL-2 and apoptotic index in human osteosarcoma and their correlations with prognosis of patients. *Cancer Epidemiol*, 36(2):212-6. doi: 10.1016/j.canep.2011.08.002. Epub 2011 Sep 3. PMID: 21890444.

Wu X, Ma S, Wu Z, Zhao Q. 2023. Global scientific trends on matrix metalloproteinase and osteosarcoma: A bibliometric and visualized analysis. *Front Oncol*;13:1064815. doi: 10.3389/fonc.2023.1064815. PMID: 36814819; PMCID: PMC9939641.

Xin S, Wei G. 2020. Prognostic factors in osteosarcoma: A study level meta-analysis and systematic review of current practice. *J Bone Oncol*;21:100281. doi: 10.1016/j.jbo.2020.100281. PMID: 32140401; PMCID: PMC7047183.

Xu, Jiahai., Li, Zhanghua, Hou, Y., Fang, W. 2015. Review article Potential mechanisms underlying the Runx2 induced osteogenesis of bone marrow mesenchymal stem cells. *Am. J. Transl*; 7(12):2527-2535.

Yang F, Teves SS, Kemp CJ, Henikoff S. 2014. Doksorubisin, DNA torsion, and chromatin dynamics. *Biochim Biophys Acta*;1845(1):84-9. doi: 10.1016/j.bbcan.2013.12.002. Epub 2013 Dec 19. PMID: 24361676; PMCID: PMC3927826.

Yin, Y.H.; Li, Y.Y.; Qiao, H.; Wang, H.C.; Yang, X.A.; Zhang, H.G.; Pang, X.-W.; Zhang, Y.; Chen, W.-F. 2005. TSPY is a cancer testis antigen expressed in human hepatocellular carcinoma. *Br. J. Cancer*, 93, 458–463.

Yoshida T, Niho S, Toda M, Goto K, Yoh K, Umemura S, Matsumoto S, Ohmatsu H, Ohe Y. 2014. Protective effect of magnesium preloading on cisplatin-induced nephrotoxicity: a retrospective study. *Jpn J Clin Oncol*;44(4):346-54. doi: 10.1093/jjco/hyu004. Epub 2014 Feb 5. PMID: 24503028.

Zhao R, Goldman ID. 2003. Resistance to antifolates. *Oncogene*;22(47):7431-57. doi: 10.1038/sj.onc.1206946. PMID: 14576850.

Zhang B, Zhang Y, Li R, Li J, Lu X, Zhang Y. 2020. The efficacy and safety comparison of first-line chemotherapeutic agents (high-dose methotrexate, doksorubisin, cisplatin, and ifosfamide) for osteosarcoma: a network meta-analysis. *J Orthop Surg Res*;15(1):51. doi: 10.1186/s13018-020-1576-0. PMID: 32054494; PMCID: PMC7020590.

Zheng, Y., Wang, G., Chen, R., Hua, Y., Cai, Z. 2018. Mesenchymal stem cells in the osteosarcoma microenvironment: their biological properties, influence on tumor growth, and therapeutic implications. *Stem Cell research & Therapy*;9:22. Doi: 10.1186/s13045-016-0373-z.

Zhong W, Luo W, Lin Z, Wu Z, Yuan Y, He Y. 2023. Prognostic analysis of telangiectatic osteosarcoma of the extremities. *Front Oncol*;12. <https://doi.org/10.3389/fonc.2022.1105054>.

Zou C, Huang R, Lin T, Wang Y, Tu J, Zhang L, Wang B, Huang J, Zhao Z, Xie X, Huang G, Wang K, Yin J, Shen J. 2024. Age-dependent molecular variations in osteosarcoma: implications for precision oncology across pediatric, adolescent, and adult patients. *Front Oncol*, 14:1382276. doi: 10.3389/fonc.2024.1382276. PMID: 38841159; PMCID: PMC11150704.