DOI: 10.4274/jbuch.galenos.2026.25826
J Dr Behcet Uz Child Hosp 2026;16(2):120-126

Original Article

High Mobility Group Box 1 Expression in Wilms Tumor: Stage-stratified Survival Analysis in 46 Cases

Wilms Tümöründe High Mobility Grup Box 1 Ekspresyonu: 46 Olguda Evreye Göre Tabakalandırılmış Sağkalım Analizi

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ABSTRACT

Objective: To investigate High Mobility Group Box 1 (HMGB1) expression in Wilms tumors and determine its relationship with clinicopathological factors and overall survival (OS), including stage-stratified survival analyses.

Method: Forty-six Wilms tumor cases were retrospectively evaluated. Immunohistochemical expression of HMGB1 was recorded as the percentage of HMGB1-positive tumor cells. Associations with clinicopathological parameters were tested using chi-square/Fisher's exact and non-parametric tests. OS was assessed with Kaplan-Meier analysis and log-rank testing. Exploratory analyses included HMGB1 tertiles and a simplified "HMGB1-low" vs. "HMGB1-other" grouping. Stage was analyzed as low stage (1-2) vs. high stage (3-5).

Results: HMGB1 dichotomized using 5% and 10% cut-offs showed no significant associations with clinicopathological variables or OS (p-value>0.05). Stage 3-5 cases had significantly worse OS compared with stage 1-2 (log-rank p-value=0.049). In stage 1-2 tumors, very low HMGB1 expression (1-4%) was associated with significantly worse OS compared with HMGB1expression of ≥5% (log-rank p-value=0.024). This association was not observed in stage 3-5 tumors (log-rank p=0.858).

Conclusion: In this study, HMGB1 expression was not an independent prognostic marker in the overall cohort. However, very low HMGB1 expression may identify a subgroup of early-stage Wilms tumor patients with unfavorable survival and deserves validation in larger-scale studies.

Keywords: Wilms tumor, nephroblastoma, HMGB1, immunohistochemistry, prognosis, overall survival, stage-stratified analysis

ÖZ

Amaç: Bu çalışmada, Wilms tümörlerinde High Mobility Group Box 1 (HMGB1) ekspresyonunun araştırılması ve evreye göre tabakalandırılmış sağkalım analizleri de dahil olmak üzere, klinikopatolojik faktörler ve genel sağkalım (OS) ile ilişkisinin belirlenmesi amaçlandı.

Yöntem: Kırk altı Wilms tümörü olgusu retrospektif olarak değerlendirildi. HMGB1 immünohistokimyasal ekspresyonu, pozitif tümör hücrelerinin yüzdesi olarak kaydedildi. Klinikopatolojik parametrelerle ilişkiler ki-kare/Fisher'ın kesin testi ve non-parametrik testler kullanılarak analiz edildi. OS Kaplan-Meier analizi ve log-rank testi ile değerlendirildi. Keşifsel analizler kapsamında HMGB1 tertilleri ve basitleştirilmiş "HMGB1-düşük" ile "HMGB1-diğer" gruplaması kullanıldı. Evre, düşük evre (1-2) ve yüksek evre (3-5) olarak analiz edildi.

Bulgular: %5 ve %10 eşik değerleri kullanılarak dikotomize edilen HMGB1 ekspresyonu ile klinikopatolojik değişkenler veya OS arasında anlamlı ilişki saptanmadı (p-değeri>0,05). Evre 3-5 olguların OS, evre 1-2 olgulara kıyasla anlamlı derecede daha kötü bulundu (log-rank p-değeri=0,49). Evre 1-2 tümörlerde, çok düşük HMGB1 ekspresyonu (%1-4), ≥%5 ekspresyona kıyasla anlamlı derecede daha kötü OS ile ilişkiliydi (log-rank p-değeri=0,024). Bu ilişki evre 3-5 tümörlerde gözlenmedi (log-rank p-değeri=0,858).

Sonuç: Bu çalışmada, HMGB1 ekspresyonu tüm kohortta bağımsız bir prognostik belirteç olarak saptanmadı. Ancak çok düşük HMGB1 ekspresyonu, erken evre Wilms tümörü hastalarında olumsuz sağkalıma sahip bir alt grubu tanımlayabilir ve daha geniş serilerde doğrulanmayı gerektirir.

Anahtar kelimeler: Wilms tümörü, nefroblastom, HMGB1, immünohistokimya, prognoz, genel sağkalım, evreye göre tabakalandırılmış analiz

Received: 09.04.2026
Accepted: 01.06.2026
Publication Date: 21.08.2026

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Cite as: Diniz G, Aktaş S, Ortaç R. High mobility group box 1 expression in Wilms tumor: stage-stratified survival analysis in 46 cases. J Dr Behcet Uz Child Hosp. 2026;16(2):120-126

INTRODUCTION

Wilms tumor (also known as nephroblastoma) is the most common malignant renal tumor of childhood, typically occurring before the age of five[1]. It arises from persistent embryonal renal tissue and is classically characterized by a triphasic histology composed of blastemal, epithelial, and stromal elements, although monophasic variants may occur[2]. Clinically, patients often present with an asymptomatic abdominal mass, sometimes accompanied by hematuria, hypertension, or abdominal pain. Genetic alterations frequently involve the *Wilms Tumor 1 (WT1)* gene and other loci associated with renal development[1-3]. Prognosis is generally favorable with modern multimodal therapy, including surgery, chemotherapy, and, in selected cases, radiotherapy; however, histological subtype (especially anaplastic type) and stage remain critical determinants of outcome[4,5]. Although outcomes are generally favorable, a subset of patients experience relapses, treatment resistance, and fatal outcomes[1-3]. Therefore, there is ongoing interest in biomarkers that complement established risk factors such as stage and histology[4,5].

High mobility group box (HMGB) proteins are non-histone nuclear proteins that play key roles in multiple cellular processes[6,7]. The HMGB family comprises HMGB1, HMGB2, and HMGB3. Among these, HMGB1 is ubiquitously expressed in the nuclei of most eukaryotic cells, whereas HMGB2 and HMGB3 show more restricted expression patterns[8-10]. HMGB1 is primarily localized in the nucleus, where it participates in chromatin organization, DNA replication, repair, and transcriptional regulation. However, post-translational modifications such as acetylation, phosphorylation, and methylation can induce its translocation from the nucleus to the cytoplasm. In addition, HMGB1 may be released into the extracellular environment under certain conditions such as hypoxia or during chemoradiotherapy, either actively from immune cells or passively from necrotic or apoptotic cells. Extracellular HMGB1 functions as a cytokine-like mediator, signaling tissue injury and promoting inflammatory responses[10-14].

In cancer biology, HMGB1 contributes to tumor progression through several mechanisms. It supports survival and proliferation of tumor cells by enhancing DNA repair and replication, promotes angiogenesis, modulates immune responses to facilitate immune evasion, and increases the invasive and metastatic capacity of tumor cells[8-10]. Clinically, increased HMGB1 expression is often associated with adverse prognostic features, including higher tumor grade and greater metastatic potential. Given these roles, HMGB1 has emerged as a potential therapeutic target, with current approaches focusing on inhibiting its extracellular signaling or downregulating its expression to limit tumor growth and dissemination[15-19].

This study aimed to evaluate HMGB1 expression in Wilms tumor tissue and to assess its association with clinicopathological variables, overall survival (OS) and its utilization in exploratory stage-stratified analyses.

MATERIALS and METHODS

Study Design and Patients

This retrospective study included 46 patients diagnosed with Wilms tumor. Clinical and pathological data were retrieved from institutional records. The Local Ethics Committee of Buca Seyfi Demirsoy Training and Research Hospital Research and Training Hospital approved this project (decision no: 2024/305, dated: 26.06.2024).

Immunohistochemistry (IHC)

HMGB1 IHC was performed on representative formalin-fixed paraffin-embedded tumor sections using standard staining protocols. Positive and negative controls were included in the analyses. Archival slides stained with hematoxylin and eosin were reassessed for detecting the viable tumor regions and selecting suitable paraffin blocks. IHC was then carried out using diluted monoclonal rabbit antibodies against HMGB1 (Atlas, ATL-HPA049521, USA) at a dilution of 1:500. The pathologists blinded to the patients' clinical characteristics analyzed the slides, and classified staining patterns based on their staining intensities. Diffuse nuclear and/or cytoplasmic staining of the tumor cells was considered HMGB1 positivity, and the number of positive cells was recorded (Figure 1). Furthermore, we assessed whether inflammatory cells that were HMBG1-positive had invaded the tumors and whether HMGB1 was expressed extracellularly.

HMGB1 Scoring

HMGB1 expression was recorded as the percentage of positive tumor cells. HMGB1 was analyzed (i) as a continuous variable, (ii) dichotomized using 5% and 10% cut-offs, and (iii) categorized into tertiles based on its distribution. Exploratory analyses suggested an early-stage survival signal among tumors with very low HMGB1 expression; therefore, tertiles were additionally simplified into HMGB1-low (1-4%) versus HMGB1-other (≥5%).

Follow-up and Outcome Definition

OS was defined as the time from diagnosis to death or last follow-up, expressed in months. Death was considered an event?, Patients alive at last follow-up or lost to follow-up were censored.

Statistical Analysis

Categorical variables were compared using chi-square or Fisher's exact test, as appropriate. Continuous variables were compared using Mann-Whitney U or Kruskal-Wallis tests. OS was analyzed using Kaplan-Meier estimates with log-rank testing. Cox proportional hazards regression models were used for univariate and multivariate analyses. Disease stages were additionally classified as low stage (1-2) versus high stage (3-5) to increase statistical power. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Clinicopathological Characteristics

A total of 46 patients were included in the study, with an equal sex distribution (23 males and 23 females). The mean age was 3.35±2.07 years. The majority of tumors were unilateral, located on the right side in 47.8% and on the left in 39.1% of the cases, while 13.0% of them were bilateral (Stage V). According to stage distribution, most frequently (37.0%) stage II tumors were detected, followed by stage I (23.9%), stage III (15.2%), stage V (13.0%), and stage IV (10.9%) tumors. When grouped, 60.9% of cases were classified as low stage and 39.1% as high stage. Favorable histology was observed in 76.1% of patients, while 23.9% had unfavorable histology. Clinically, 71.7% of patients had no evidence of relapse, 21.7% experienced relapse, and in 6.5% the outcome was unknown. The average tumor size was 9.13±3.02 cm, and the mean tumor weight was 481.0±321.1 g. The mean overall, and median survival (OS) were 58.76±5.5 and 51.5 months, respectively. There were 11 death events in the cohort.

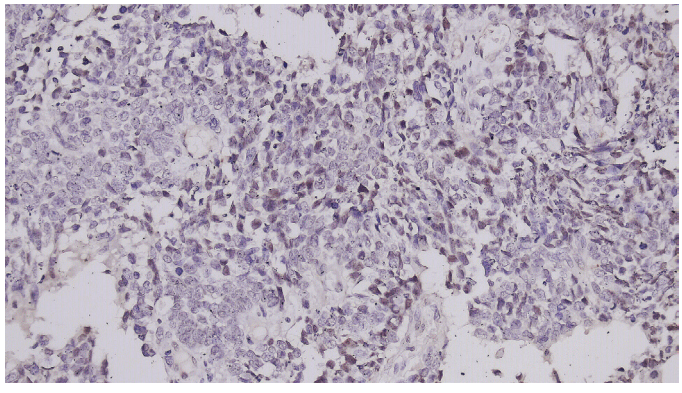

Figure 1. Strong nuclear expression of HMGB1 in some tumor cells (DAB x200)

DAB: 3,3'-diaminobenzidine

HMGB1 Expression and Clinicopathological Correlations

HMGB1 expression detected in tumor cells was limited to the nucleus; no cytoplasmic or extranuclear expression was detected. No difference in HMGB1 expression was found among tumor components. In addition, HMGB1 expression was also present in inflammatory cells in the tumor microenvironment in all tumors. The mean HMGB1 expression level was 15.26±22.21%. Using dichotomized cut-offs of 5% and 10%, HMGB1 expression was not significantly associated with stage grouping, histological subtype, or outcome categories (all p-value>0.05).

Survival Analysis

In Kaplan-Meier analysis, stage 3-5 tumors demonstrated significantly worse OS compared with stage 1-2 tumors (log-rank p-value=0.049) (Figure 2). HMGB1 expression dichotomized at 5% and 10% did not show a significant association with OS (p-value>0.05).

Exploratory tertile-based survival analysis suggested that very low HMGB1 expression (1-4%) might be associated with worse survival. Therefore, tertiles were simplified to HMGB1-low (1-4%) versus HMGB1-other (≥5%) categories. In stage 1-2 tumors, HMGB1-low cases had significantly worse OS compared with HMGB1-other cases (log-rank p=0.024) (Figure 3). This association was not observed in stage 3-5 tumors (log-rank p-value=0.858). The findings of stage-stratified survival analysis for HMGB1-low vs. HMGB1-other are shown in Table 1.

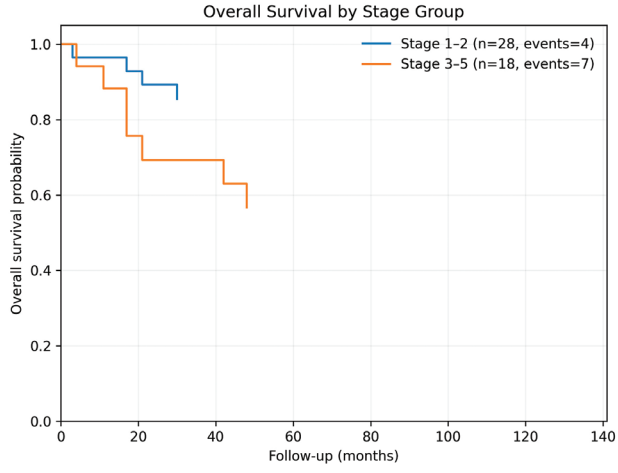

Figure 2. Kaplan-Meier OS curves by stage groups (1-2 vs. 3-5)

OS: Overall survival

Cox Regression Analysis

In multivariate Cox regression analyses of HMGB1 expression (log-transformed), age, stage group (3-5 vs. 1-2), and histology, HMGB1 expression was not independently associated with OS, whereas the stage group showed a borderline association with OS, consistent with the limited number of events.

DISCUSSION

In this retrospective series of 46 Wilms tumor cases with a median survival of 51.5 months also including 11 death events, we evaluated the prognostic impact of HMGB1 immunohistochemical expression using multiple analytic approaches, including conventional dichotomization, tertile categorization, and exploratory stage-stratified survival analyses. The key findings of this study can be summarized as follows: (i) in the overall cohort, HMGB1 expression was not significantly associated with clinicopathological variables or OS when analyzed using 5% and 10% cut-offs; (ii) stage remained a dominant clinical determinant of survival, as stage 3-5 tumors demonstrated significantly inferior OS compared with stage 1-2 disease (log-rank p-value=0.049); and (iii) notably, within early-stage tumors (stage 12), very low HMGB1 expression (1-4%) was associated with significantly worse OS compared with ≥5% expression (log-rank p-value=0.024), whereas this association was not observed in advanced-stage tumors (log-rank p-value=0.858). Collectively, these results suggest that HMGB1 is unlikely to serve as a universal prognostic biomarker across all Wilms tumor patients; however, very low expression may identify a biologically distinct subgroup of early-stage cases with unfavorable survival. Recognizing this subgroup may have clinical implications, as these patients—despite presenting at an early stage—could be considered for the implementation of more intensive and tailored therapeutic strategies[20,21].

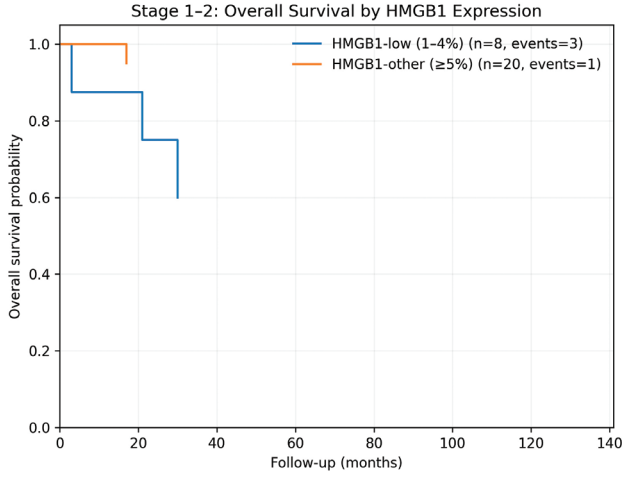

Figure 3. Kaplan-Meier OS curves in stage 1-2 tumors by HMGB1-low vs. HMGB1-other

OS: Overall survival, HMG1: High Mobility Group Box 1

Wilms tumor remains the most common malignant renal tumor of childhood and, despite excellent overall outcomes in contemporary treatment protocols, a clinically meaningful proportion of patients still experience relapse, treatment resistance, and fatal outcomes. Current management is guided by risk-adapted strategies shaped by Children's Oncology Group (COG/NWTS) and International Society of Paediatric Oncology (SIOP) approaches[22]. Although these protocols differ in the timing of surgery and the use of preoperative chemotherapy, both emphasize the prognostic relevance of stage and histologic risk group, together with surgical factors such as tumor spill, margin status, and lymph node evaluation. In agreement with this established framework, the present study confirmed that stage retains significant prognostic importance. The observed survival disadvantage in stage 3-5 patients (log-rank p-value=0.049) reinforces that tumor burden, local extension, nodal involvement, and metastatic spread remain major determinants of outcome even in the modern multimodal treatment era. Importantly, modern treatment protocols of Wilms tumor increasingly seek to balance cure rates with minimization of late toxicities. This has led to treatment de-escalation attempts in clearly

Table 1. Stage-stratified survival analysis for HMGB1-low vs. HMGB1-other

Stage group	HMGB1 group	n	Deaths (events)	Censored
Stage 1-2	HMGB1-low (T1: 1-4%)	8	3	5
Stage 1-2	HMGB1-other (T2+T3: ≥5%)	20	1	19
Stage 3-5	HMGB1-low (T1: 1-4%)	7	3	4
Stage 3-5	HMGB1-other (T2+T3: ≥5%)	11	4	7

Log-rank p-values: Stage 1-2: p-value=0.024; Stage 3-5: p-value=0.858
HMG1: High Mobility Group Box 1

favorable subgroups; however, a persistent challenge is that a small fraction of "clinically favorable" early-stage patients may still relapse or die. Therefore, biomarkers capable of refining prognosis within early-stage disease—where baseline survival is expected to be high—could be clinically meaningful. Our stage-stratified findings support this concept by suggesting that very low HMGB1 expression may identify a subset of stage 1-2 patients with unexpectedly unfavorable OS[20-22].

HMGB1 is a multifunctional non-histone chromatin-binding protein involved in transcriptional regulation, chromatin remodeling, and DNA damage response (DDR). Beyond its nuclear role, HMGB1 can be actively secreted or passively released and acts extracellularly as a damage-associated molecular pattern, thereby modulating innate immune responses and shaping the tumor microenvironment through inflammatory signaling. This dual intracellular-extracellular biology has driven considerable interest in HMGB1 as both a prognostic biomarker and a therapeutic target in multiple tumor types. However, the direction of HMGB1-prognosis association varies widely across cancers, likely reflecting differences in tumor context, immune microenvironment, treatment exposures, and especially HMGB1 compartmentalization and post-translational modifications. A critical interpretative aspect is HMGB1 localization. Physiologically, HMGB1 is predominantly nuclear; however, cancer-related stress responses may drive nuclear-to-cytoplasmic translocation and/or extracellular release. Cytoplasmic accumulation is frequently interpreted as a proxy for HMGB1 mobilization and active inflammatory signaling. Conversely, decreased nuclear HMGB1 (or low overall expression) levels in certain contexts may reflect altered chromatin states, impaired DDR programs, or dedifferentiation-related transcriptional changes. In the present study, HMGB1 expression was consistently observed in association with nuclear localization in tumor cells, and evaluation was based on this nuclear positivity. Therefore, the absence of distinct nuclear-cytoplasmic expression patterns reported in the literature may partly explain the lack of a significant association in the overall cohort[20-22].

In the overall cohort, HMGB1 expression did not show prognostic relevance when dichotomized at 5% and 10%. This negative finding suggests that HMGB1 is not a strong standalone prognostic marker across unselected Wilms tumor cases, and it also highlights an important methodological issue namely HMGB1 biology may not be adequately captured using simple percent-positivity scoring alone. In addition, Wilms tumor is heterogeneous in both histologic composition and molecular drivers; thus, biomarker effects may be context-dependent and clinically visible only in selected subgroups rather than uniformly across all stages[5,14].

The most clinically notable observation of this study is the early-stage survival signal. Among stage 1-2 tumors, HMGB1-low cases (1-4%) demonstrated significantly worse OS than HMGB1-other tumors (≥5%). Interestingly, this association was absent in stage 3-5 tumors. One plausible explanation is that in advanced-stage disease, the adverse prognostic impact of stage dominates outcomes and may obscure smaller biomarker effects. In contrast, early-stage disease provides a "low-noise" prognostic setting where biological differences can emerge more clearly. Therefore, expression of low levels of HMGB1 may represent a hidden biological risk factor that is clinically detectable only for early-stage disease. Several mechanistic hypotheses may be considered. First, very low HMGB1 expression might correlate with unfavorable molecular programs affecting DDR, potentially contributing to treatment resistance or genomic instability. Second, HMGB1 deficiency may influence the immunologic contexture of the tumor microenvironment, reducing immunogenic signaling and limiting immune surveillance. Third, HMGB1 expression could reflect broader differentiation status and embryonal programs within Wilms tumor. Importantly, these mechanistic interpretations remain speculative in the present study and should be validated by future studies combining HMGB1 scoring with molecular profiling and assessment of immune micro environment[6-10].

In multivariable Cox regression models analyzing HMGB1 expression (log-transformed), age, stage group, and histology, HMGB1 did not retain independent prognostic significance, whereas stage showed a borderline association with OS. This result is expected given the limited number of death events (n=11), which constrains statistical power and increases the risk of imprecise hazard estimates in multivariate models. Therefore, while the Kaplan-Meier stage-stratified findings are compelling, they should be interpreted as hypothesis-generating data which should be subjected to external validation[6].

Study Limitations

The present study has limitations. The retrospective single-center design may introduce selection bias and restrict completeness of treatment and molecular data? The sample size is modest and event number limited, reducing power for subgroup analyses and multivariate modeling.

Treatment protocol variables (e.g., COG vs. SIOP-based risk-adapted strategies, radiotherapy exposure, intensity of chemotherapy) were not incorporated which could modify observed associations. In addition, unfortunately the HMGB1 scoring method relied only on percent-positivity without detailed evaluation of staining intensity or intensity of different tumoral components which are key determinants of HMGB1 functional biology. Finally, the HMGB1-low cut-off (1-4%) was derived through exploratory tertile analyses and should not be considered as definitive criteria prior to validation. Despite these limitations, this study provides stage-stratified evidence suggesting that very low HMGB1 expression may be clinically relevant in early-stage Wilms tumor. Future multi-institutional studies with standardized HMGB1 staining/scoring (including localization-based assessment) and integration of molecular risk factors are warranted. If confirmed, HMGB1-low expression may represent a practical biomarker for identifying a small subgroup of early-stage Wilms tumor patients who may require closer surveillance or therapy adjustment[15-19].

CONCLUSION

In conclusion, HMGB1 expression did not emerge as an independent prognostic marker in the overall Wilms tumor cohort; however, very low HMGB1 expression (1-4%) was associated with inferior OS in stage 1-2 tumors, suggesting a potential subgroup effect. This finding supports the broader concept that biomarker discovery in Wilms tumor may benefit from stage-specific evaluation, and that selected early-stage patients may harbor adverse tumor biology not captured by stage alone.

Ethics

Ethics Committee Approval: The Local Ethics Committee of Buca Seyfi Demirsoy Training and Research Hospital Research and Training Hospital approved this project (decision no: 2024/305, dated: 26.06.2024).

Informed Consent: Retrospective study.

Declaration of AI Use: ChatGPT (OpenAI) was used solely to assist in drafting the Main Points section requested by the journal.

Footnotes

Author Contributions

Surgical and Medical Practices: G.D., S.A., Concept: G.D., S.A., R.O., Design: G.D., S.A., Data Collection or Processing: G.D., S.A., R.O., Analysis or Interpretation: G.D., R.O., Literature Search: G.D., Writing: G.D., S.A.

Conflict of Interest: The authors declare no conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Neagu MC, David VL, Iacob ER, Chiriac SD, Muntean FL, Boia ES. Wilms' tumor: a review of clinical characteristics, treatment advances, and research opportunities. Medicina (Kaunas). 2025;61(3):491. doi: 10.3390/medicina61030491.
2. Benedetti DJ, Cost NG, Ehrlich PF, Evageliou N, Fialkowski E, Parsons LN, et al. Updated favourable-histology Wilms tumour risk stratification: rationale for future children's oncology group clinical trials. Nat Rev Urol. 2025;22(11):775-88. doi: 10.1038/s41585-025-01055-1.
3. Vujanić GM, Graf N, D'Hooghe E, Pritchard-Jones K, Bergeron C, van Tinteren H, et al.; International Society of Paediatric Oncology Renal Tumour Study Group (SIOP-RTSG). Omission of adjuvant chemotherapy in patients with completely necrotic Wilms tumor stage I and radiotherapy in stage III: the 30-year SIOP-RTSG experience. Pediatr Blood Cancer. 2024;71(3):e30852. doi: 10.1002/pbc.30852.
4. Jhaveri HF, Sarantos N, Aitelli A, Kaplan S, Routh JC. Current clinical and surgical insights in the workup and management of Wilms tumor (nephroblastoma). Curr Opin Pediatr. 2025;37(5):488-94. doi: 10.1097/MOP.0000000000001490.
5. Puchertova M, Rychly B, Kolenova A, Vujanic GM. Navigating the complexity of Wilms tumors in pediatrics: diagnostic challenges for better treatment. Surg Exp Pathol. 2024;7:23. doi:10.1186/s42047-024-00166-0.
6. Tang D, Kang R, Zeh HJ, Lotze MT. The multifunctional protein HMGB1: 50 years of discovery. Nat Rev Immunol. 2023;23(12):824-41. doi: 10.1038/s41577-023-00894-6.
7. Wang S, Zhang Y. HMGB1 in inflammation and cancer. J Hematol Oncol. 2020;13(1):116. doi: 10.1186/s13045-020-00950-x.
8. Shao L, Zhu L, Wang M, Ning Y, Chen F, Gao X, et al. Mechanisms involved in the HMGB1 modulation of tumor multidrug resistance (review). Int J Mol Med. 2023;52(2):69. doi: 10.3892/ijmm.2023.5272.
9. Idoudi S, Bedhiafi T, Pedersen S, Elahtem M, Alremawi I, Akhtar S, et al. Role of HMGB1 and its associated signaling pathways in human malignancies. Cell Signal. 2023;112:110904. doi: 10.1016/j.cellsig.2023.110904.
10. Fan J, He K, Zhang Y, Li R, Yi X, Li S. HMGB1: new biomarker and therapeutic target of autoimmune and autoinflammatory skin diseases. Front Immunol. 2025;16:1569632. doi: 10.3389/fimmu.2025.1569632.
11. Chen R, Zou J, Zhong X, Li J, Kang R, Tang D. HMGB1 in the interplay between autophagy and apoptosis in cancer. Cancer Lett. 2024;581:216494. doi: 10.1016/j.canlet.2023.216494.
12. Guo L, Wang D, Jiang X, He G. HMGB1: from molecular functions to clinical applications in cancer and inflammatory diseases. Med Res Rev. 2026;46(2):408-44. doi: 10.1002/med.70017.
13. Pilzweger C, Holdenrieder S. Circulating HMGB1 and RAGE as clinical biomarkers in malignant and autoimmune diseases. Diagnostics. 2015;5(2):219-53. doi: 10.3390/diagnostics5020219.

14. Wu T, Zhang W, Yang G, Li H, Chen Q, Song R, et al. HMGB1 overexpression as a prognostic factor for survival in cancer: a meta-analysis and systematic review. Oncotarget. 2016;7(31):50417-27. doi: 10.18632/oncotarget.10413.

15. Li D, Lei X, Zhao L, Fu Q, Chen Y, Yang X. Mechanism of action of HMGB1 in urologic malignancies. Front Oncol. 2025;15:1593157. Erratum in: Front Oncol. 2025;15:1735134. doi: 10.3389/fonc.2025.1735134.

16. Patra S, Roy PK, Dey A, Mandal M. Impact of HMGB1 on cancer development and therapeutic insights focused on CNS malignancy. Biochim Biophys Acta Rev Cancer. 2024;1879(3):189105. doi: 10.1016/j.bbcan.2024.189105.

17. Dong H, Zhang L, Liu S. Targeting HMGB1: an available therapeutic strategy for breast cancer therapy. Int J Biol Sci. 2022;18(8):3421-34. doi: 10.7150/ijbs.73504.

18. Shen W, Lyu Q, Yi R, Sun Y, Zhang W, Wei T, et al. HMGB1 promotes chemoresistance in small cell lung cancer by inducing PARP1-related nucleophagy. J Adv Res. 2024;66:165-80. doi:10.1016/j.jare.2023.12.020.

19. Cheng KJ, Alshawsh MA, Mejia Mohamed EH, Thavagnanam S, Sinniah A, Ibrahim ZA. HMGB1: an overview of its versatile roles in the pathogenesis of colorectal cancer. Cell Oncol (Dordr). 2020;43(2):177-93. doi: 10.1007/s13402-019-00477-5.

20. Gratias EJ, Jennings LJ, Anderson JR, Dome JS, Grundy P, Perlman EJ. Gain of 1q is associated with inferior event-free and overall survival in patients with favorable histology Wilms tumor: a report from the children's oncology group. Cancer. 2013119(21):3887-94. doi: 10.1002/cncr.28239.

21. Messahel B, Williams R, Ridolfi A, A'hern R, Warren W, Tinworth L, et al.; Children's Cancer and Leukaemia Group (CCLG). Allele loss at 16q defines poorer prognosis Wilms tumour irrespective of treatment approach in the UKW1-3 clinical trials: a children's cancer and leukaemia group (CCLG) study. Eur J Cancer. 2009;45(5):819-26. doi: 10.1016/j.ejca.2009.01.005.

22. Dome JS, Perlman EJ, Graf N. Risk stratification for Wilms tumor: current approach and future directions. Am Soc Clin Oncol Educ Book. 2014:215-23. doi: 10.14694/EdBook_AM.2014.34.215.