

Supplementary Table no. 1: method for comprehensive literature collection on liquid biopsy investigation within pediatric solid tumors.

Studies were collected through an advanced search on pubmed using two search strategies (below). Articles from the year 1989 up and until December 2023 were considered.			
Advanced Pubmed search A			
Step 1	Search parameter	Search words	
	title/abstract	Neuroblastoma* OR wilms* OR nephoblastoma* OR malignant rhabdoid* OR renal cell carcinoma* OR renal medullary carcinoma* OR clear cell carcinoma of the kidney* OR congenital mesoblastic nephroma* OR germ cell tumor* OR teratoma* OR germinoma* OR dysgerminoma* OR embryonal carcinoma* OR yolk sac* OR seminoma* OR non-seminoma* OR choriocarcinoma* OR osteosarcoma* OR rhabdomyosarcoma* OR synovial sarcoma* OR malignant peripheral nerve sheath tumor* OR peripheral nerve sheath tumor* OR MPNST* OR PNST* OR Desmoplastic Small Round Cell Tumo* OR DSRCT* OR (Malignant rhabdoid tumor* AND soft tissue*) OR MRT* OR Alveolar Soft Part Sarcoma* OR ASPS* OR Clear Cell Sarcoma of the soft tissue* OR CCS* OR Epithelioid sarcoma* OR Ewing sarcoma* OR hepatoblastoma* OR hepatocellular carcinoma*	
	title/abstract	cancer* OR tumor* OR tumour*	
	title/abstract	blood* OR serum* OR plasma* OR urin* OR cerebrospinal fluid* OR bone marrow* OR CSF* OR saliva* OR sputum* OR ascite* OR pleural effus* OR fluid*	
	title/abstract	circulating tumor DNA* OR ctDNA* OR cell free DNA* OR cell-free DNA* OR cfDNA OR microRNA* OR miRNA* OR mRNA* OR circulating tumor cell* OR circulating tumour cell* OR CTC* OR vesicle* protein* OR platelet* OR fibroblast*	
	title/abstract	marker* OR liquid biops*	
	all fields	pediatric* OR paediatric* OR prepubertal* OR child* OR adolescent*	
Advanced Pubmed search B			
Step 2	Search parameter	Search words	
	title/abstract	Neuroblastoma* OR wilms* OR nephoblastom* OR malignant rhabdoid* OR renal cell carcinoma* OR renal medullary carcinoma* OR clear cell carcinoma of the kidney* OR congenital mesoblastic nephroma* OR germ cell tumor* OR teratoma* OR germinoma* OR dysgerminoma* OR embryonal carcinoma* OR yolk sac* OR seminoma* OR non-seminoma* OR choriocarcinoma* OR osteosarcoma* OR rhabdomyosarcoma* OR synovial sarcoma* OR malignant peripheral nerve sheath tumor* OR peripheral nerve sheath tumor* OR MPNST* OR PNST* OR Desmoplastic Small Round Cell Tumo* OR DSRCT* OR (Malignant rhabdoid tumor* AND soft tissue*) OR MRT* OR Alveolar Soft Part Sarcoma* OR ASPS* OR Clear Cell Sarcoma of the soft tissue* OR CCS* OR Epithelioid sarcoma* OR Ewing sarcoma* OR hepatoblastoma* OR hepatocellular carcinoma*	
	all fields	liquid biops*	
	Review articles were collected using similar strategies, with the following exceptions: using 'all fields' instead of 'title/abstract' for all search parameters in search A, and including the (pediatric* OR paediatric* OR prepubertal* OR child* OR adolescent*) search words (all fields) in search B.		
	Step 3	Titles and abstracts of identified articles (studies and reviews) were checked. Articles that focussed on liquid biopsies in one or more pediatric solid tumors were included in our initial collection. The most common exclusion criteria are indicated below.	
		Common exclusion criteria:	Articles did not focus on liquid biopsies.
			Articles were not in english.
			Articles did not focus on pediatric tumor types.
Articles focussed on haematological or brain tumors.			
Step 4	Review articles passing the previous criteria (61 passed) were included in our initial collection, and checked for additional studies that did not show up during step 1. When found, these additional studies were included in our initial collection.		
Step 5	For studies focussing on pediatric tumor types that are also common in adults (renal cell carcinoma, osteosarcoma, germ cell tumors, hepatocellular carcinoma, and non-rhabdomyosarcoma soft tissue sarcoma), we checked the patient cohort and excluded articles that focussed on adults.		
Step 6a	The remaining studies (283) formed our final collection and were comprehensively analysed (identification of pediatric patient cohort and involved tumor types, investigated liquid biopsy biomarkers, detection methods, analytes, matrices, and suggested application of the respective biomarkers). The Neuroblastoma and osteosarcoma tables (S2 and S5) are the only exceptions and more generic tables are provided instead.		
Step 6b	Studies were organized in tables according to tumor type (Tables S2-S9), and included in Table 1 and Figures 2A and 2B.		
Step 6c	Reviews were included in Table 1, Figure 2A, and Table S10		
Abbreviations: PB = peripheral blood, BM = bone marrow. All other abbreviations are provided in the main text.			

Supplementary Table no. 2: overview of commonly investigated ctDNA-based biomarkers in pediatric NB patients and involved studies and methods.

Biomarker in ctDNA	Methods	References
MYCN amplification	qPCR, ddPCR, WES, WGS	140,142,144,145,335,357,380-393
ALK amplification/ mutation	qPCR, ddPCR, WES, WGS	142,235,357,380,392-395
Chromosome copy number profiling (1p and 11q loss, 17q gain)	Arrays (oncoscan, CGH, SNP, methylation), MLPA, microsatellite analysis, WGS, WES, EM-seq, ddPCR	140,144,148,152,357,386,391,395-397
Targeted genomic marker panel	targeted sequencing, qPCR, ddPCR, arrays	145-147,149,357,398,399,401,402,404
Comprehensive genome analysis	WES, WGS	235,357,391,403,404
Total ctDNA levels	WGS, qPCR, Qubit assay	138-140,235,392,405-409
Targeted methylation profiling (RAS5F1A and DCR2)	methylation specific PCR, qPCR, EM-seq, ddPCR, nano-hmC-Seal	145,153,406,410,411,446
Comprehensive methylome analysis	EM-seq, WGBS, cRRBS	152,153,236
List of studies investigating non ctDNA-derived biomarkers such as CTCs and derived material (e.g. mRNA, miRNA, nucleosomes, EVs):		51-123,400

Supplementary Table no. 3: comprehensive overview of studies involving analysis of liquid biopsy-based biomarkers in pediatric renal tumor patients.

Study and reference	Renal tumor type	Biomarker	Detection methods	Analyte	Matrix	Population	Suggested application
Schmitt et al. (2012) ¹⁸³	WT	miRNA panel	RT-qPCR, array	miRNA	PB	43	Diagnosis
Charlton et al. (2014) ⁴¹²	WT	Methylated DMR-2	Bisulfite sequencing	cfDNA	Serum	10	Tumor response during treatment
Murray et al. (2015) ¹⁰⁶	WT	miR-143-3p	RT-qPCR	miRNA	Serum	7	Differential diagnosis
Ludwig et al. (2015) ¹⁸²	WT	miRNA panel	RT-qPCR	miRNA	Serum	43	Diagnosis
Kurihara et al. (2015) ²³⁵	WT, MRTK	WT1 and SMRKC81 mutations	NGS, dPCR	cfDNA	Plasma	5	Diagnosis, treatment efficacy
Klega et al. (2018) ¹³⁹	WT	ctDNA levels, CNAs	ULP-WGS	ctDNA	Plasma	8	Disease response and genomic subclassifier identification
Biderman Waberski et al. (2018) ⁴¹⁴	WT	PIK3CA	ddPCR	cfDNA	Plasma, urine	8	Diagnosis
Ueno-Yokohata et al. (2018) ⁴¹³	CCSK	BCOR-ITD	PCR	cfDNA	Plasma	3	Diagnosis
Treger et al. (2018) ⁴¹⁵	WT	ctDNA concentration, TP53 status	ddPCR	ctDNA	Plasma, serum, urine	4	Risk stratification and surveillance
Chen et al. (2019) ⁴¹⁶	RCC	Somatic mutations	targeted sequencing, WES	ctDNA	Plasma	1	Mutation detection
Jiménez et al. (2019) ¹⁷⁹	WT, CCSK, RCC	CNAs and SNVs	WES	ctDNA	Plasma	18	Treatment guidance, disease monitoring, follow-up
Ortiz et al. (2019) ¹⁹⁰	MRTK, CCSK, RCC, WT	Protein panel (prohibitin)	HR-MS, ELISA	Protein	Urine	139	Early diagnosis, therapy stratification, treatment response
Miguez et al. (2020) ¹⁸⁰	WT	Somatic mutations	Targeted sequencing, WES	cfDNA	Plasma, urine	5	Monitoring treatment response
Rossi et al. (2020) ⁴¹⁷	RCC	Counts, c-MET expression	CellSearch system	CTCs, CECs	PB	2	Prognostic marker and follow-up
He et al. (2021) ¹⁸¹	WT	XIST	Array, RT-qPCR	lncRNA	PB	49	Prognostic marker
van Zogchel et al. (2021) ¹⁴¹	WT	ctDNA levels and hypermethylated RASSF1A	ddPCR	ctDNA	Plasma	13	Pan-tumor marker
van Paemel et al. (2021) ²³⁶	WT, MRTK, CCSK	Methylation profiling	cRRBS	cfDNA	Plasma	19	Diagnosis
van Paemel et al. (2022) ¹⁴⁸	WT	CNAs	sWGS	cfDNA	Plasma	19	Prognostic classification, therapeutic stratification, tumor heterogeneity
Madanat-Harjuoja et al. (2022) ¹⁷⁸	WT	ctDNA levels, CNAs	ULP-WGS, targeted sequencing	ctDNA	Serum, urine	50	Prognostic marker, tumor heterogeneity
Christodoulou et al. (2023) ⁹	WT, CCSK, CMN	CNA detection	Targeted sequencing, LP-WGS	cfDNA	Plasma	12	Patient monitoring for diagnosis, treatment, and recurrence
Ruas et al. (2023) ¹⁴⁰	WT	ctDNA levels, CNAs	dPCR	cfDNA	Plasma	14	Diagnosis, monitoring disease response

Supplementary Table no. 4: comprehensive overview of studies involving analysis of liquid biopsy-based biomarkers in pediatric MGCT patients.

Study and reference	GCT type	Biomarker	Detection method	Analyte	Matrix	Population	Suggested application
Murray et al. (2011) ²⁰⁹	YST	miR-371,372,373 and 302 clusters	RT-qPCR	miRNA	Serum	1	Diagnosis and disease monitoring
Murray et al. (2016) ²¹³	YST, MMGCT, eMGCT, iMGCT	miR-371a-3p, miR-372-3p, miR-373-3p	RT-qPCR	miRNA	Serum, CSF	25	Diagnosis and disease monitoring
Murray et al. (2020) ²¹⁴	iMGCT	miR-371a-3p	RT-qPCR	miRNA	Serum, CSF	4	Diagnosis, prognostication, and patient management
Murray et al. (2021) ¹⁹⁶	Choriocarcinoma	miR-371a-3p, and several within the C19MC cluster	RT-qPCR	miRNA	Serum, CSF	1	Patient management
Christodoulou et al. (2023) ⁹	Not specified	CNAs (1 and 12p gain)	LP-WGS and targeted sequencing	ctDNA	Plasma	10	Diagnosis and evaluating clonal evolution
Schonberger et al. (2023) ²¹⁵	iMGCT (both non-germinoma and germinoma)	miR-371a-3p, miR-372-3p, miR-367, miR-302a, miR-302d-3p	RT-qPCR	miRNA	Serum and CSF	8	iGCT discrimination, monitor therapy response, and early relapse detection
Saliyeva et al. (2023) ²³⁶	Various types	miR-302/367 and 371-373 clusters	RT-qPCR	miRNA	Serum	20	Diagnosis and follow-up

Supplementary Table no. 5: overview of commonly investigated liquid biopsy analytes in pediatric osteosarcoma patients and involved targets, methods, and studies.

Liquid biopsy analyte	Targets	Methods	References
ctDNA	Quantification, somatic alterations (CNAs, SNVs, INDELS, SVs, translocations), methylation profiling	Targeted sequencing, ULP-WGS, sWGS CAPP-seq, ddPCR, cRRBS	9,139,140,148,149,232,234-238, 336
CTCs	Identification and quantification, classification/ characterization, epithelial cell adhesion molecule expression	RNA-ISH, flow-cytometry, microfluidics, IMC, CanPatrol CTC technology, immunofluorescence imaging, FISH, iFISH	240,241,243-245,306,335,418-424
miRNA	Expression levels	RT-qPCR, dPCR, arrays, RNA-seq	306,347,263,425-482
lncRNA	Expression levels	RT-qPCR, dPCR, arrays, RNA-seq	483-496
EVs	Cargo analysis (proteins, RNA, ligands)	Immunogold labeling, ELISA, LC-MS, immunoblots, MALDI-TOF MS, SERS, RNA seq	233,497-500

Supplementary Table no. 6: comprehensive overview of studies involving analysis of liquid biopsy-based biomarkers in pediatric EWS patients.

Study and reference	Biomarker	Detection method	Analyte	Matrix	Population	Suggested implementation
West et al. (1997) ²⁶⁴	EWS-FU1 fusion transcripts	RT-PCR	CTC derived RNA	BM and PB	28	MRD monitoring
Zoubek et al. (1998) ²⁶⁵	EWS-ETS fusion transcripts	RT-PCR	CTC derived RNA	BM	35	Prognostic
Fagnou et al. (1998) ²⁶⁶	EWS-FU1/ERG fusion transcripts	RT-PCR	CTC derived RNA	BM and PB	67	Staging and diagnosis
De Alava et al. (1998) ²⁶⁷	EWS-FU1/ERG fusion transcripts	RT-PCR	CTC derived RNA	PB	28	Therapy monitoring and prediction of disease progression
Thomson et al. (1999) ³⁰¹	t(11;22) translocations	RT-PCR	CTCs	PB and BM	9	Disease clearance
Gattenloehner et al. (1999) ³²²	Myogenin	RT-PCR	mRNA	BM	5	MRD detection
Athale et al. (2001) ³³⁸	EWS-FU1/ERG fusion transcripts	RT-PCR	CTC derived RNA	BM and PB	31	Disease staging, follow-up, and MRD detection
Schleiermacher et al. (2003) ³⁶⁹	EWS-FU1/ERG fusion transcripts	RT-PCR	CTC derived RNA	BM and PB	172	Prognostic
Yu et al. (2012) ⁵⁰²	Ccf-mtDNA levels	RT-qPCR	Ccf-mtDNA	Serum	25	Diagnosis and patient management
Nie et al. (2015) ⁵⁰³	miR-125b	RT-qPCR	miRNA	Serum	63	Diagnosis
Murray et al. (2015) ¹⁰⁶	miR-214-3/5p, miR-92b-3p	RT-qPCR	miRNA	Serum	2	Diagnosis
Krumbholz et al. (2016) ⁵⁰⁴	EWSR1 fusions, ctDNA levels	ddPCR	ctDNA	Plasma	20	Therapy response
Hayashi et al. (2016) ³⁰⁵	EWS-ETS breakpoints	ddPCR	ctDNA	Plasma	3	Relapse detection
Shukla et al. (2017) ³²¹	EWSR1 fusions	ddPCR	cfDNA	Plasma	17	Disease monitoring
Hayashi et al. (2017) ³⁰⁶	CTC detection and quantification, EWS-FU1 translocation, P53 mutation	CellSieve size-based low pressure microfiltration system	CTC and derived mRNA	PB	9	Disease monitoring and relapse prediction
Klega et al. (2018) ³³⁹	EWSR1 translocation, ctDNA levels	Targeted sequencing	ctDNA	Plasma	11	track disease response and identify genomic subclassifiers of disease
Lee et al. (2018) ⁵⁰⁶	type 1 EWS-FU1 translocation	RT-qPCR	CTC derived RNA	Plasma	1	Therapy response and prognosis prediction
Shulman et al. (2018) ²³⁸	ctDNA levels	targeted sequencing, ULP-WGS	ctDNA	Plasma	94	Diagnosis, risk stratification, monitor clonal evolution
Allegretti et al. (2018) ²⁷⁴	type 1 and 2 EWS-FU1 fusion transcripts	RT-qPCR and dPCR	ctRNA	Plasma	4	Patient monitoring and management
Benini et al. (2018) ³⁰⁷	EWSR1-FU1/ETS fusion transcripts	Immunoseparation, RT-dPCR	CTCs and derived RNA	PB	18	Prognostic and predictive purposes
Schmidkonz et al. (2020) ²⁷²	ctDNA levels	ddPCR	ctDNA	Plasma	20	Treatment response monitoring and relapse detection
Samuel et al. (2020) ²⁷⁵	sEV mRNA cargo (EWS-ETS transcripts)	RT-qPCR	sEV-derived mRNA	Plasma	10	Diagnostic and prognostic
Tombolan et al. (2020) ³³⁶	Membrane-bound EpCAM expression	EPCAM-based CellSearch platform	CTCs	PB	2	Disseminated disease assessment
Peneder et al. (2021) ³³⁵	EWS-ETS fusions, fragmentation patterns, CNA profiling	WGS, ddPCR, cRRBS	ctDNA	PB	95	Prognostic
Bodlak et al. (2021) ²⁷⁶	EWS-FU1/ERG fusions	ddPCR	ctDNA, ctRNA	Plasma	5	MRD detection
Krumbholz et al. (2021) ²⁷¹	EWSR1 fusions	ddPCR	ctDNA	Plasma	102	Early risk stratification and early prediction of treatment response
Shah et al. (2021) ²³⁷	translocations, ctDNA levels	WGS, CAPP-seq	ctDNA	Plasma	8	Diagnosis, monitoring, and early relapse detection
van Paemel et al. (2021) ²³⁶	Methylation profiling	cRRBS	cfDNA	Plasma	6	Diagnosis
van Paemel et al. (2022) ³⁴⁸	CNA profiling	sWGS	cfDNA	Plasma	9	Complementary assay for tissue analysis
Seidel et al. (2022) ²⁷³	EWS-FU1 fusion breakpoints, ctDNA levels	ddPCR and WGS	ctDNA	Plasma	6	MRD monitoring and treatment stratification
Crow et al. (2022) ³⁶³	miRNA profiling	miRNAseq	exosome and cell derived miRNA	Plasma	8	Diagnosis and disease monitoring
Subhash et al. (2022) ³²³	CTC quantification, EWS fusion transcripts	WGS, qPCR, ddPCR	CTC	BM and PB	6	Monitoring treatment response
Cahn et al. (2022) ³⁴⁹	SVs and mutations	Targeted seq	cfDNA	Plasma	5	Molecular profiling
Christodoulou et al. (2023) ⁹	EWSR1 fusions, ctDNA levels	Targeted seq, LP-WGS	cfDNA	Plasma	12	Patient evaluation
Ruas et al. (2023) ³⁴⁰	Amount, CNA profiling	dPCR	cfDNA	Plasma	4	Diagnosis, disease response monitoring
Turaga et al. (2023) ⁵⁰⁸	UGT3A2	LC-MS, ELISA, Western blot	sEV-derived protein	Plasma	16	Diagnosis
van Zogchel et al. (2023) ³⁴⁶	Patient specific breakpoints	SNP-array, RT-qPCR, ddPCR	cfDNA	Plasma	1	MRD detection
Gelineau et al. (2023) ³⁴⁵	Methylome profiling	cRRBS	cfDNA	Plasma	1	Metastatic status determination, prognostication, and monitoring of MRD

Supplementary Table no. 7: comprehensive overview of studies involving analysis of liquid biopsy-based biomarkers in pediatric RMS patients.

Study and reference	RMS type	Biomarker	Detection method	Analyte	Matrix	Population	Suggested application
Thomson et al. (1999) ³⁰¹	ARMS	t(2;13) translocations	RT-PCR	CTCs	PB and BM	3	Disease clearance
Gattenloehner et al. (1999) ³²²	ARMS	AChR	RT-PCR	mRNA	BM	5	MRD detection
Athale et al. (2001) ³³⁸	ARMS	PAX3/7-FKHR fusion transcripts	RT-PCR	CTC derived RNA	BM and PB	13	Disease staging, follow-up, and MRD detection
Michelagnoli et al. 2003 ²⁹⁶	ARMS, ERMS	MyoD1, myogenin	RT-PCR	mRNA	PB and BM	20	Diagnosis and small volume disease detection
Gallego et al. (2006) ²⁹⁷	ARMS, ERMS	MyoD1, AChR, PAX3/7-FKHR	RT-PCR	mRNA	PB and BM	16	MRD detection
Sartori et al. (2006) ²⁹⁸	ARMS, ERMS	MyoD1, myogenin, PAX-FKHR transcripts	RT-PCR	mRNA	BM	40	MDD detection
Miyachi et al. (2010) ⁵⁰⁹	Not specified	miR-206	RT-PCR	miRNA	Serum	10	RMS detection
Krsková et al. (2010) ²⁹⁹	ARMS	PAX3/7-FKHR, MyoD1	RT-qPCR	mRNA	PB and BM	33	MDD detection
Murray et al. (2015) ¹⁰⁶	ERMS	miR panel	RT-qPCR	miRNA	Serum	3	Diagnosis
Hayashi et al. (2017) ³⁰⁶	ARMS, ERMS	CTC amount	CellSieve, single cell RNA-seq	CTCs	PB	4	Disease response monitoring, prediction of metastatic relapse
Klega et al. (2018) ³³⁹	ARMS	ctDNA levels	ULP-WGS	ctDNA	Plasma	7	Monitoring disease response, identification of genomic subclassifiers
Eguchi-Ishimae et al. (2019) ³⁰⁷	ARMS	PAX3-FOXO1 fusion gene	qPCR	ctDNA and CTCs	PB and BM	1	Monitoring tumor burden
Ghamloush et al. (2019) ⁵¹⁰	ARMS, ERMS	miR-486-5p	Microarray	Exosomal miRNA	Serum	Not specified	RMS detection
Tombolan et al. (2020) ⁵¹¹	ARMS, ERMS	miR-26a	RT-qPCR, ddPCR	miRNA	Plasma	30	Diagnostic, prognostic
Poli et al. (2020) ³⁰³	ARMS, ERMS	IGFBP2 protein and autoantibodies	Direct and indirect ELISA	circulating protein	Plasma	114	Diagnostic, prognostic
Tombolan et al. (2020) ³³⁶	ARMS, ERMS	Membrane-bound EpCAM expression	EPCAM-based CellSearch platform	CTCs	PB	7	Disseminated disease assessment
van Zogchel et al. (2021) ³⁴¹	Not specified	Hypermethylated RASSF1A	ddPCR	cfDNA	Plasma	14	RMS detection
Shah et al. (2021) ²³⁷	ARMS	Recurrent translocation breakpoints	CAPP-seq	ctDNA	Plasma	4	Diagnosis, monitoring, early relapse detection
Peneder et al. (2021) ³³⁵	ARMS, ERMS	WGS, ddPCR, cRRBS	EWS-ETS fusions, fragmentation patterns, CNA profiling	ctDNA	PB	12	prognostic
Lak et al. (2021) ²⁸⁹	ARMS, ERMS	Targeted marker panel	RT-qPCR	CTC derived mRNA	PB and BM	99	Disseminated disease detection at diagnosis, conventional risk stratification
van Paemel et al. (2021) ²³⁶	ARMS, ERMS	Methylation profiling	cRRBS	cfDNA	Plasma	17	Diagnosis

van Paemel et al. (2022) ¹⁴⁸	Not specified	CNA profiling	sWGS	cfDNA	Plasma	10	Prognostic classification, therapeutic stratification, tumor heterogeneity
Tombolan et al. (2022) ³⁰⁸	ARMS, ERMS	CTC and DCT amount, patient specific somatic variants	EpCAM-based CellSearch platform, WES, ddPCR	CTCs, DCTs, cfDNA	PB and BM	17	Disseminated disease assessment, longitudinal patient monitoring
Cahn et al. (2022) ¹⁴⁹	Not specified	SVs and mutations	Targeted seq	cfDNA	Plasma	3	Molecular profiling
Ruhen et al. (2022) ³⁰⁰	ARMS, ERMS	ctDNA levels	ddPCR, targeted sequencing, WES	ctDNA	Plasma	28	Disease burden, treatment response
Uria et al. (2022) ³⁰⁴	ARMS, ERMS	TKTL1, APO10	EDIM, flow-cytometry	Monocytes	PB	29	Therapeutic guidance, monitoring of recurrence
Stegmaier et al. (2022) ³⁰⁹	ARMS	PAX3/7-FOXO1 fusion transcripts	RT-qPCR	Exosomal cfRNA	Plasma	65	Diagnosis, monitoring
Lak et al. (2023) ³⁰²	ARMS, ERMS	Methylation profiling, ctDNA amount, RASSF1A hypermethylation, RNA marker panel	shWGS, cfRRBS, ddPCR	ctDNA	Plasma	57	Diagnosis, prognosis
Christodoulou et al. (2023) ⁹	ARMS, ERMS	Patient specific genome-wide CNAs and fusion genes	lp-WGS, targeted sequencing	cfDNA	Plasma	5	Patient monitoring for diagnosis, treatment, and recurrence
Ruas et al. (2023) ¹⁴⁰	Not specified	cfDNA levels, CNAs	ddPCR	cfDNA	Plasma	4	Monitoring disease response
van Zogchel et al. (2023) ¹⁴⁶	ARMS	Patient-specific markers for cfDNA detection	TLA, TLC, ddPCR	cfDNA	Plasma	2	MRD detection
Abbou et al. (2023) ³⁰¹	ARMS, ERMS	ctDNA levels, CNAs, patient-specific rearrangements and SNVs	ULP-WGS, targeted sequencing	ctDNA	Serum	124	Prognosis
Gelineau et al. (2023) ¹⁴⁵	ERMS	Targeted marker panel	RT-qPCR, ddPCR, cfRRBS	cfDNA	PB and BM	2	Metastatic status, prognostication, and disease response monitoring
de Traux de Wardin et al. (2023) ³⁰⁵	ARMS, ERMS	Targeted marker panel (SNVs, fusion genes, CNAs)	Targeted seq, WES, WGS	ctDNA	Plasma	10	Disease response monitoring

Supplementary Table no. 8: comprehensive overview of studies involving analysis of liquid biopsy-based biomarkers in pediatric NRSTS tumors.

Reference	NRSTS subtype	Marker	Methods	Analyte	Matrix	Population	Suggested application
Athale et al. (2001) ²⁶⁸	DSRCT	EWS-WT1 fusion transcript	RT-PCR	CTC derived RNA	BM and PB	3	Disease staging, follow-up, and MRD detection
Colletti et al. (2019) ³³⁴	DSRCT	miRNA panel	RT-qPCR	miRNA	Exosomes	3	DSRCT disease status and therapeutic response
Tombolan et al. (2020) ³³⁶	SS	Membrane-bound EpCAM expression	EPICAM-based CellSearch platform, RT-qPCR	CTCs	PB	1	N/A (no liquid biopsy signal)
Peneder et al. (2021) ³³⁵	SS	SVs	WGS, ddPCR, cfRRBS	cfDNA	PB	3	N/A (no elaboration on results)
Shah et al. (2021) ²³⁷	SS	Translocations (SSX1-SS18), ctDNA levels	WGS, CAPP-seq	ctDNA	Plasma	1	N/A (no liquid biopsy signal)
Stegmaier et al. (2022) ³⁰⁹	SS	SVT-SSX fusion transcripts	RT-qPCR	Cell-free exosomal RNA	Plasma	15	N/A (no liquid biopsy signal)
Cahn et al. (2022) ¹⁴⁹	Five subtypes	SVs and mutations	Targeted seq	cfDNA	Plasma	6	Molecular profiling
Ruas et al. (2023) ¹⁴⁰	Leiomyosarcoma	cfDNA levels, CNAs	ddPCR	cfDNA	Plasma	1	N/A (no elaboration on results)
Christodoulou et al. (2023) ⁹	SS, MPNST	CNAs, and mutations	Targeted seq, LP-WGS	cfDNA	Plasma	4	Patient evaluation

Supplementary Table no. 9: comprehensive overview of studies involving analysis of liquid biopsy-based biomarkers in pediatric liver cancer patients.

Study and reference	Liver tumor type	Biomarker	Detection method	Analyte	Matrix	Population	Suggested application
Murray et al. (2015) ¹⁰⁶	HB	miR-122-5p, miR-483-3p and miR-205-5p	RT-qPCR	miRNA	Serum	4	Diagnosis
Zhao et al. (2015) ³⁴⁹	HB	Apo A-I	qPCR, ELISA	Protein	Serum	30	Diagnosis
Kurihara et al. (2015) ²³⁵	HB	CTNNB1 and APC mutations	Targeted seq, dPCR	cfDNA	Plasma	6	Diagnosis, treatment efficacy
Liu et al. (2016) ³⁴⁶	HB	miR-21	RT-qPCR	miRNA	Whole blood	32	Diagnosis and prognosis
Jiao et al. (2017) ³⁴⁷	HB	miR-34a, miR-34b, and miR-34c	RT-qPCR	miRNA	Whole blood	89	Diagnosis and prognosis
Kahana-Edwin et al. (2020) ³⁵⁰	HB	CTNNB1	ddPCR	ctDNA	Plasma	3	Treatment response
Christodoulou et al. (2023) ⁹	HB	CNA detection	Targeted seq, LP-WGS	cfDNA	Plasma	3	Patient monitoring for diagnosis, treatment, and recurrence
Espinoza et al. (2023) ^{343a}	HB and HCC (including FLC subtype)	Quantification	Fluorescence microscopy and flow cytometry	CTC	Whole blood	14	Prognostication

*: at time of publication, this article is in a preprint and has not been peer-reviewed yet.

Supplementary Table no. 10: comprehensive overview of review articles focussing on liquid biopsy-based biomarkers in pediatric cancer patients.

Study and reference	Title
Zhenjian et al. (2022) ¹²⁴	Advances in liquid biopsy in neuroblastoma
Almstrup et al. (2020) ²⁰⁰	Application of miRNAs in the diagnosis and monitoring of testicular germ cell tumours.
Li et al. (2018) ⁵¹²	Application of liquid biopsy in bone and soft tissue sarcomas: Present and future.
Abbou et al. (2018) ¹²⁵	Assessment of circulating tumor DNA in pediatric solid tumors: The promise of liquid biopsies.
Murray et al. (2015) ⁵¹³	Biology of childhood germ cell tumours, focussing on the significance of microRNAs
Zheng et al. (2023) ¹⁴⁵	Biomarkers for patients with Wilms tumor: a review
Takami et al. (2022) ⁵¹⁴	Biomarkers for risk-based treatment modifications for CNS germ cell tumors: Updates on biological underpinnings, clinical trials, and future directions
Charlton et al. (2015) ³⁰⁴	Biomarkers to detect Wilms tumors in pediatric patients: where are we now?
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