سدرة للطب
Sidra Medicine

PEDIATRIC ONCOLOGY REPORT 2024

Data from 2019 - 2024

SPOQ
Sidra Pediatric Oncology Qatar

وزارة الصحة العامة
Ministry of Public Health
State of Qatar • دولة قطر

Qatar Cancer Society
الجمعية القطرية للسرطان

QPHI
معهد قطر للرعاية الصحية الدقيقة
Qatar Precision Health Institute

SIDRA MEDICINE
Pediatric Oncology Report 2024

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Division Chief
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Dr. Wouter Hendrickx
Director - Translational Research Program:
Sidra Pediatric Oncology Qatar
Principal Investigator Tumor Biology &
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WELCOME MESSAGE

We are pleased to bring to you Sidra Medicine's 2024 Annual Pediatric Oncology Report featuring key updates on Pediatric Cancer and Precision Pediatric Oncology in Qatar over the past six years.

By sharing data from 2019 to 2024, we aim to highlight how these efforts help our clinicians detect rare, actionable somatic mutations and connect patients to global clinical trials. This information opens the door to discovering new molecular targets in specific groups of patients, driving the identification of emerging biomarkers and innovative therapeutic approaches.

This year's report is a joint effort from the Oncology and Hematology Division, the Anatomical Pathology Division, the Hematopathology Division, the Neurosurgery Division and the Translational Research Program: Sidra Pediatric Oncology Qatar at Sidra Medicine.

Our close collaboration between clinical and research teams allows us to deeply understand both the unique characteristics and needs of our patient population, while also designing individualized precision medicine protocols. This teamwork has given rise to two key resources: the Qatar Pediatric Cancer Registry and the Sidra Pediatric Cancer Biorepository. The registry gathers extensive clinical data, and the biorepository seeks patient consent to donate leftover diagnostic materials, supporting research tailored to our community. Built on years of focused expertise, these resources now serve as the foundation for advancing precision pediatric oncology in Qatar.

Last year we presented data on Central Nervous System (CNS) tumor and Leukemia in detail. This year we include details on three additional cancer types - Neuroblastoma, Germ cell tumors and Lymphoma. Our report highlight that these cancers are the five most prevalent in Qatar and make up over 70 percent of pediatric cancers.

Worldwide, the incidence rates of childhood cancer range between 50 and 200 per million children. In Qatar, the rate is 126 per million children. The patient population at Sidra Medicine primarily consists of individuals of Arab and Asian descent, constituting 59 percent and 31 percent of our patients, respectively.

The most common diagnoses are Leukemia (24%), Central Nervous System malignancies (23%), Lymphoma (10%), Neuroblastoma (7%), Germ cell tumors (7%), and Sarcomas.

Since the inauguration of our main hospital in 2018, Sidra Medicine has emerged as the nation's exclusive healthcare provider for the diagnosis and treatment of pediatric and adolescent cancer patients. Sidra Medicine started the Pediatric Precision Oncology Program in 2019, integrating it with pediatric cancer services. Funded by Sidra Medicine Research Branch IRF and QRDI PPM5, this program is now part of the Translational Research Programs strategy.

As one of the leading institutions in the region, Sidra Medicine is proud that through our Translational Research Programs, we can offer each child with cancer in Qatar, molecular profiling at the point of diagnosis. This results in the most accurate diagnostic methodology available today and a wealth of research data.

In addition to activities in the diagnostic field, we are developing pharmacogenomics services aimed at optimizing drug dosages based on patients' genetic profiles. This approach seeks to enhance medication response and reduce toxicity. Progress has also been made in advanced therapeutics, with our Advanced Cell Therapy Core team currently investigating CAR-T cell manufacturing.

This year's report is a strong reflection of our strategy to align people and technologies, ensuring harmony between clinical prowess, research innovation, and patient care; an equally challenging and rewarding endeavor.

We remain committed to personalizing precision medicine for every pediatric cancer patient in Qatar. By enhancing understanding and improving cancer care outcomes through shared knowledge, we are ensuring a brighter future for our children.

Dr. Wouter Hendrickx
Director - Translational Research Program:
Sidra Pediatric Oncology Qatar

MEET THE TEAM

Oncology Team

- Dr. Ayman Saleh
- Dr. Chiara Cugno
- Dr. Ata Maaz
- Dr. Tayseer Alsaad
- Dr. Wafaa Abdelghany
- Dr. Naima Al Mulla

Director
Sidra Pediatric Oncology Qatar: Translational Research Program

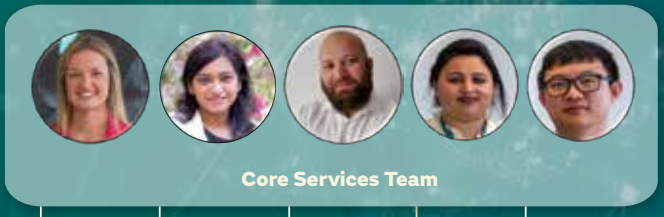
- Dr. Wouter Hendrickx

Wet Lab Team

- Dr. Christophe Raynaud
- Dr. Tracy Augustine
- Apryl Sanchez
- Adithya Suresh

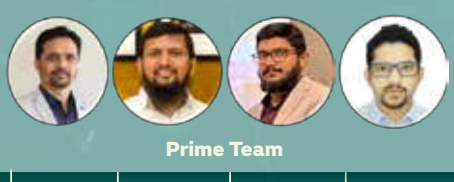
CRC Team

- Blessing Dason
- Aisha Khalifa
- Asma Jamil



Core Services Team

- Dr. Sara Tomei
- Dr. Abbirami Sathappan
- Dr. Oleksandr Soloviov
- Lisa Sara Mathew
- Kun Wang



Prime Team

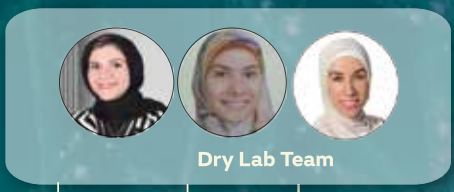
- Shafqat Baig
- Mohammedhusen Khatib
- Mehshad Hamza
- Shibin Poolat

Anatomical Pathology Team

- Dr. Erdener Ozer
- Dr. Sergey Popov
- Dr. Gordon Vujanic
- Dr. Fouad Alchami
- Joana Moreira

Hematopathology Team

- Dr. Mohammed Yousuf Karim
- Dr. Jason Ford
- Dr. MHD Sadek Almiski



Dry Lab Team

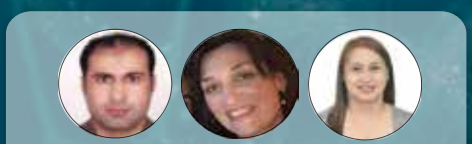
- Dr. Shimaa Sherif
- Rania Alanany
- Dr. Heba Saadeh

Surgical Team

- Dr. Ian Pople
- Dr. Khalid Al-Kharazi

Bioinformatics Team

- Dr. Abdul Rahman Salhab
- Sahin Sarihan



Nursing Team

- Mohammed Anas
- Rachel Park
- Arianne Alejo

INSIGHTS IN FOCUS

Precision Medicine in Pediatric Cancer Care: Clinical Genomics Core

Sidra Medicine's Clinical Genomics Core plays a vital role in supporting both clinical and translational research in pediatric oncology through advanced next-generation sequencing (NGS) technologies.

Dr. Oleksandr Soloviov, Lab Manager of the Clinical Genomics Laboratory; Lisa Sara Mathew, Lead of Library Preparation and Kun Wang, Lead of Sequencing at the Genomics Core at Sidra Medicine provide their perspectives on the clinical genomics core services.

Dr. Oleksandr is responsible for overseeing the entire genomic testing process, while Lisa oversees the implementation and optimization of various NGS workflows that form the backbone of genomic testing for pediatric cancer patients.

Dr. Oleksandr explains: "Cancer samples, particularly in pediatric oncology, are often challenging due to low nucleic acid yield or poor DNA and RNA quality, which makes the continuous optimization of laboratory workflows an essential part of our work. He highlights the team's commitment to quality: "Regardless of whether the samples are intended for cancer diagnostics or research applications, we ensure that each specimen, especially those that are technically challenging, receives careful handling and optimal processing to deliver the highest quality results."

Lisa says: "For whole genome sequencing (WGS), we use a polymerase chain reaction free (PCR-free) to ensure unbiased coverage of the entire genome from both tumor tissue and matched blood samples. This is essential for detecting structural variants, copy number alterations, non-coding mutations, and other genomic changes that drive pediatric cancers, which typically have a low somatic mutation burden."

In addition to WGS, the team performs total RNA sequencing (RNA-seq) for transcriptomic profiling.

Lisa highlights the importance of RNA-seq in pediatric oncology: "Many childhood cancers are driven by gene fusions rather than high mutational loads. Through RNA-seq, we can detect clinically significant fusion genes which are critical for accurate diagnosis, risk stratification, and guiding targeted therapy. RNA-seq also provides insights into gene expression profiles and alternative splicing patterns, further refining tumor classification and supporting precision medicine."

Recognizing the challenges of working with formalin-fixed paraffin-embedded (FFPE) tissues, which are often the only available material for molecular testing in pediatric oncology, Dr. Oleksandr and his team have adopted Watchmaker's DNA and RNA library preparation kits, specifically optimized for FFPE-derived and low-input samples. These kits are designed to address the inherent difficulties of working with fragmented and chemically modified nucleic acids, which is a common limitation when processing FFPE specimens.

Lisa said: "FFPE samples frequently yield degraded or

chemically DNA and RNA, making it essential to use workflows that incorporate enzymes capable of repairing oxidative DNA damage, along with ribosomal RNA depletion and random priming, to ensure successful library construction. By implementing these optimized workflows, we have been able to recover valuable genomic and transcriptomic data even from highly challenging FFPE pediatric tumor specimens, thereby expanding the molecular diagnostic capabilities available for children with cancer."

Lisa continues: "The team's approach has been validated by the bioinformatics team, confirming that fusion genes identified through RNA-seq often align with histopathological findings, reinforcing the robustness and clinical relevance of these protocols," continued Lisa.

Kun's role is central to ensuring the success of the sequencing process and once libraries are prepared, he is responsible for performing library quantification, pooling, and loading samples onto the sequencers, followed by continuous monitoring of sequencing run quality.

During the sequencing, Kun evaluates key quality metrics such as Q30 scores, depth of coverage, and adapter contamination levels. For RNA sequencing, he closely monitors mapping rates and alignment quality, which can be significantly impacted in degraded FFPE samples. After sequencing, the bioinformatics team confirms the detection of important molecular targets, such as clinically significant fusion genes, ensuring that the genomic results are robust and reliable for downstream clinical interpretation and reporting.

In pediatric oncology, rapid turnaround time is critical for enabling timely clinical decisions. One of the key challenges the team has faced is the batching requirement for high-throughput sequencers. To address this, the team is strategically transitioning to lower-throughput flow cells for expedited pediatric cases. This shift minimizes the need to wait for large batch completion and accelerates sequencing for time-sensitive cases.

As a key goal for this year, Dr. Oleksandr highlights that, "We are working to evaluate and implement library preparation protocols that allow DNA and RNA libraries to be pooled together for sequencing. Previously, we relied on separate protocols and indexing strategies, which made co-sequencing difficult and led to delays, particularly for urgent pediatric cancer cases. To streamline this process, the team has begun adopting shared indexing through Watchmaker's library preparation system.

This innovation allows simultaneous sequencing of DNA and RNA libraries, significantly improving workflow efficiency and reducing turnaround time."

Dr. Oleksandr further emphasizes that, "Our overarching goal is to complete sequencing preparation within one week and to deliver the final genomic results, including bioinformatics analysis, within two weeks. This ensures that our clinicians receive timely, actionable data to support decision-making in pediatric oncology." For expedited genomic oncology program (eGOP) samples, where timely results are critical, the team places special emphasis on monitoring fragment size variation and minimizing unnecessary DNA shearing to preserve sample integrity and ensure high-quality sequencing outcomes.

Looking ahead, Dr. Oleksandr envisions significant advancements in genomic diagnostics that will further enhance the care of pediatric oncology patients. The team is working toward the development of a unified workflow capable of extracting and integrating genome, transcriptome, and epigenome data from a single sample.

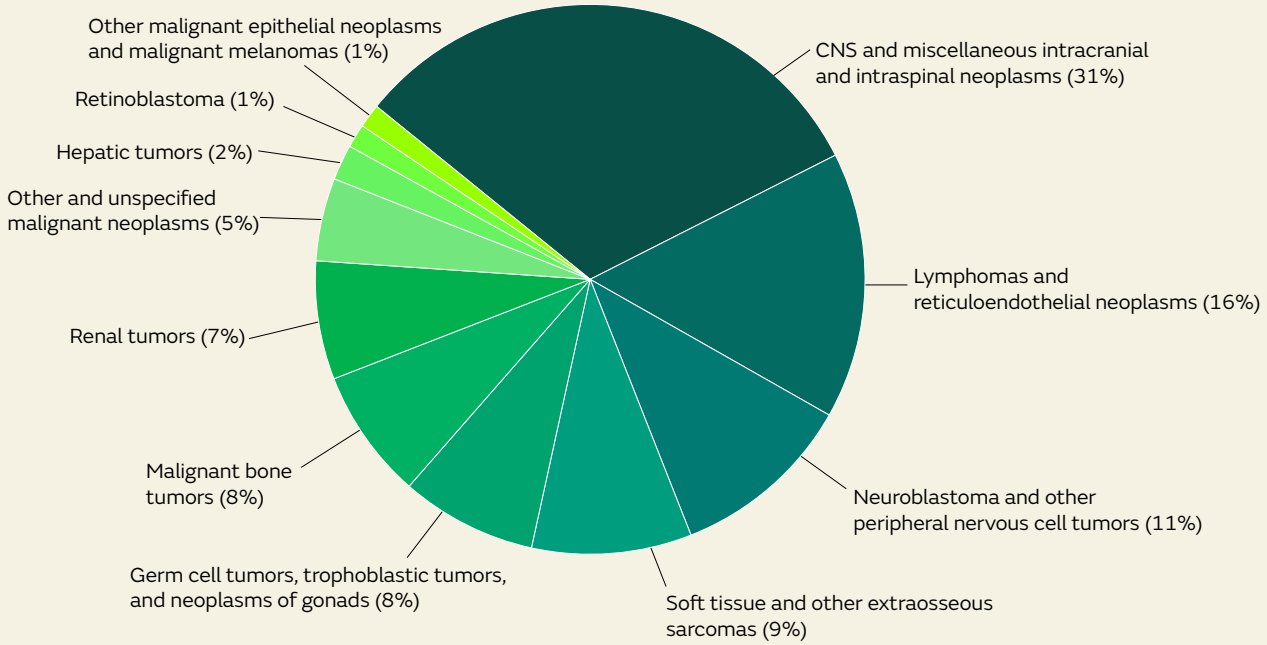
Dr. Oleksandr notes: "Emerging long-read sequencing technologies hold promise for achieving this integration by enabling simultaneous detection of structural variants, methylation patterns, and gene expression within the same assay. The team also continues to pursue innovative, less invasive approaches, including the use of cerebrospinal fluid (CSF) as a source of both tumor DNA and RNA, which could allow for non-invasive molecular profiling. If successful, this could potentially eliminate the need for repeat biopsies in pediatric patients, significantly reducing clinical burden.", Dr. Oleksandr explains.

Dr. Oleksandr highlights that every new challenge is addressed through a spirit of collaboration and innovation. He adds that Dr. Wouter, in collaboration with the omics and bioinformatics teams, is actively exploring such integrated multi-omics solutions.

"If Dr. Wouter proposes a new idea, the team works together to explore and implement a feasible solution. Our approach is dynamic, data-driven, and deeply patient-focused, with the shared goal of continuously advancing precision diagnostics in pediatric oncology. This collaborative ethos ensures that the team remains at the forefront of molecular innovation, always striving to deliver timely, accurate, and meaningful genomic insights to improve outcomes for children with cancer."

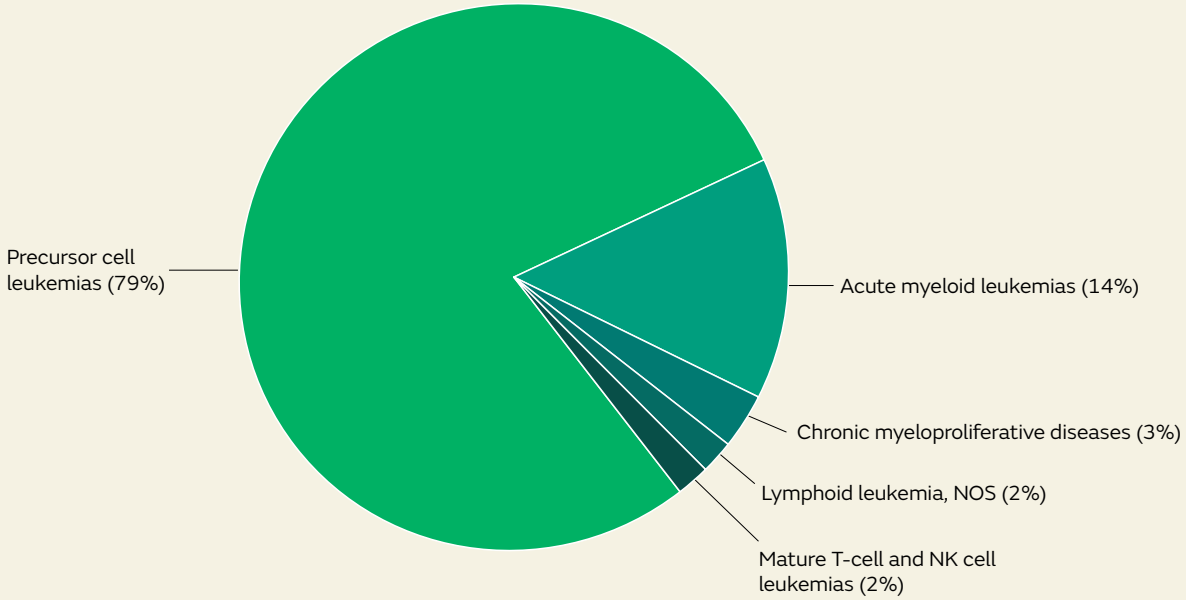
SIDRA MEDICINE PEDIATRIC CANCER REGISTRY

Types of pediatric solid cancer presented at Sidra Medicine (65%)



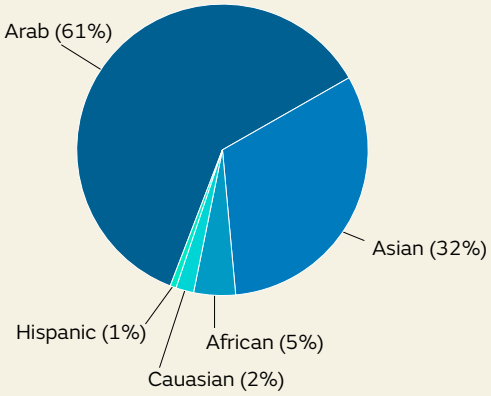
The types of solid tumor, presenting at Sidra Medicine classified according to the International Classification of Childhood Cancer, Third Edition, Level 1

Types of pediatric non-solid cancer presented at Sidra Medicine (35%)

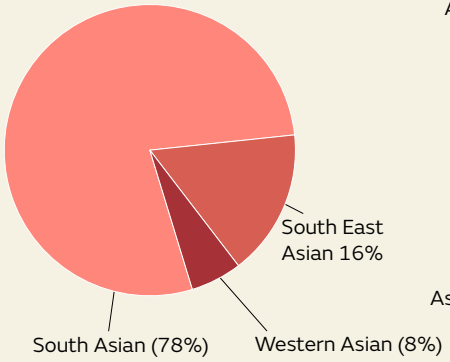


The types of hematologic cancer, presenting at Sidra Medicine classified according to the International Classification of Childhood Cancer, Third Edition, Level 3

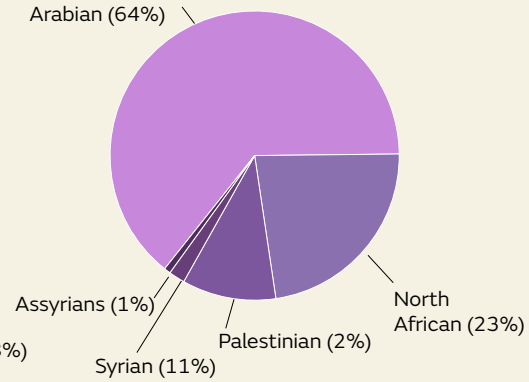
Ethnicity of our patients



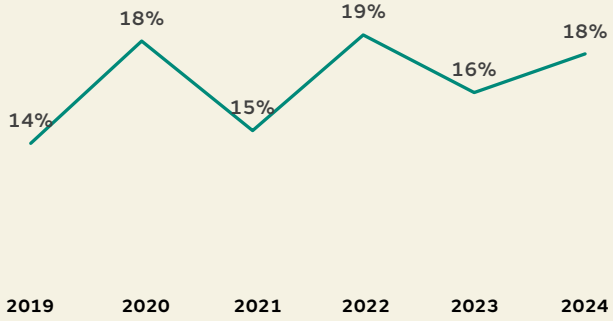
Asian population



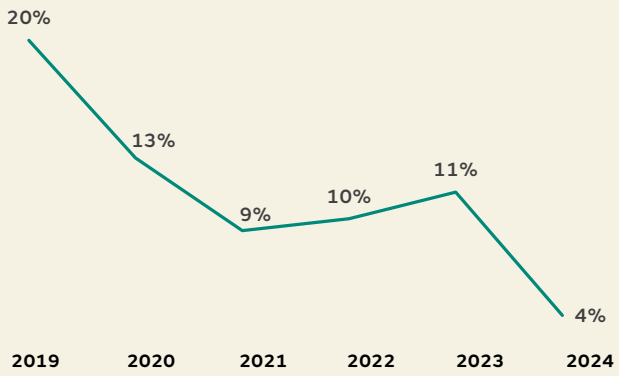
Arab population



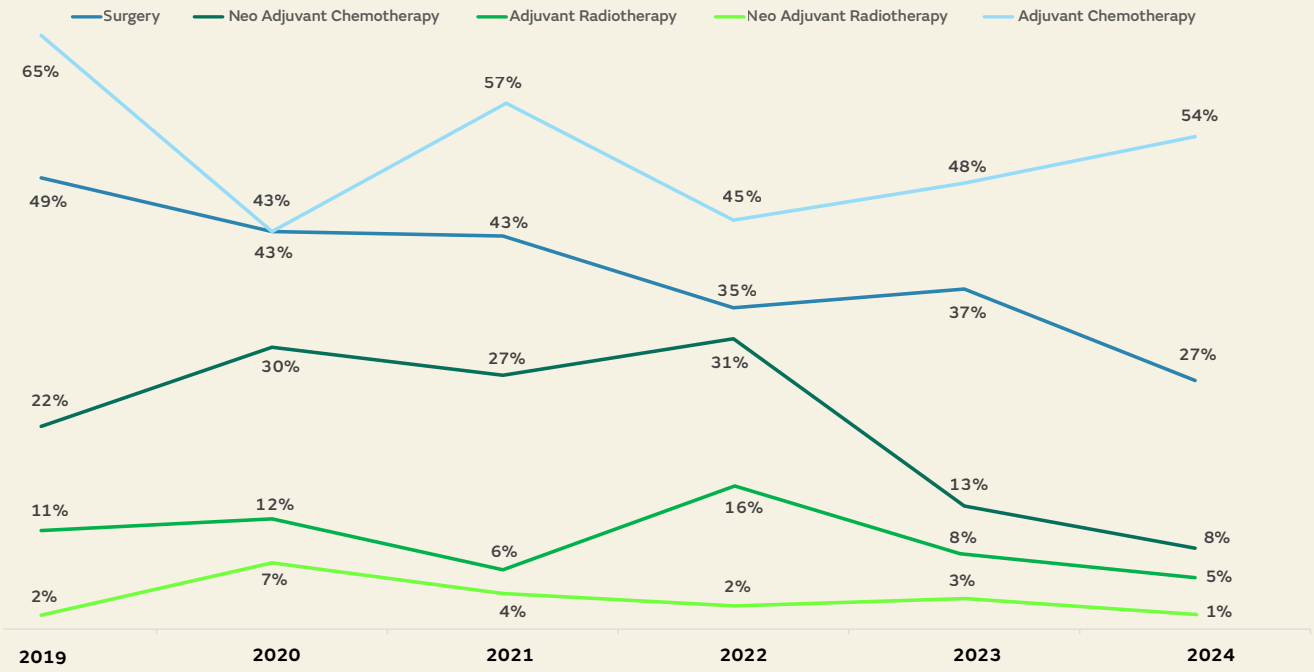
Patients with metastasis at diagnosis



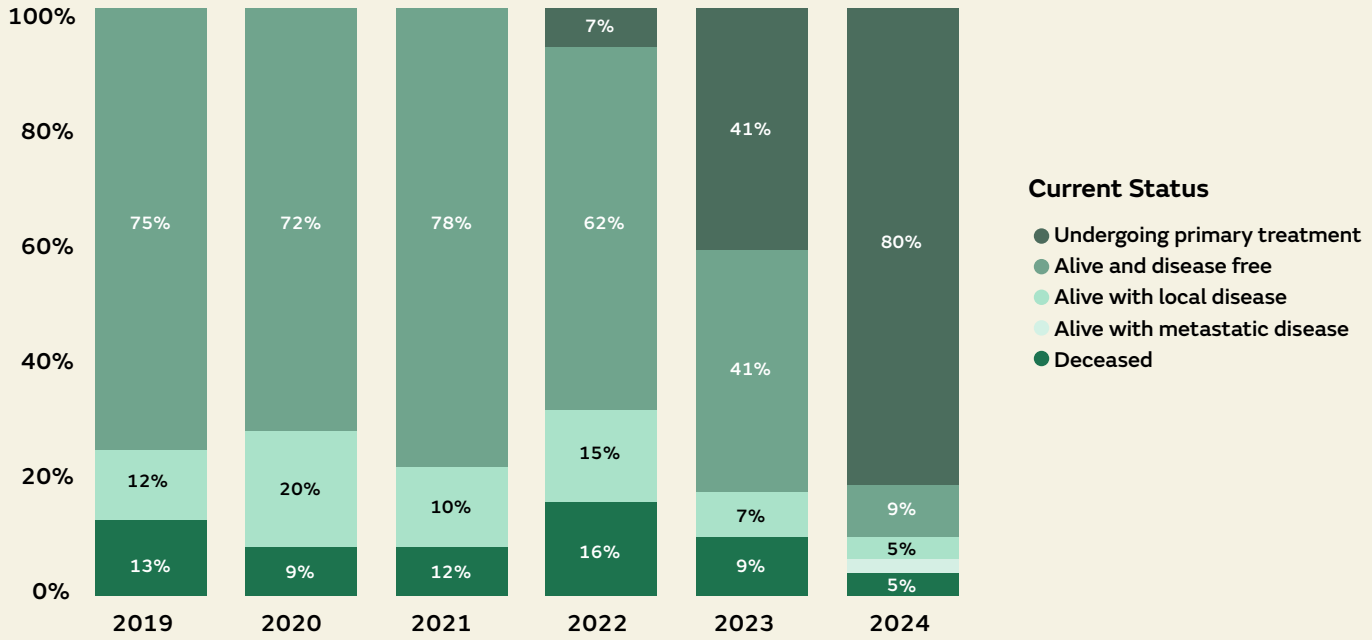
Treated abroad by year



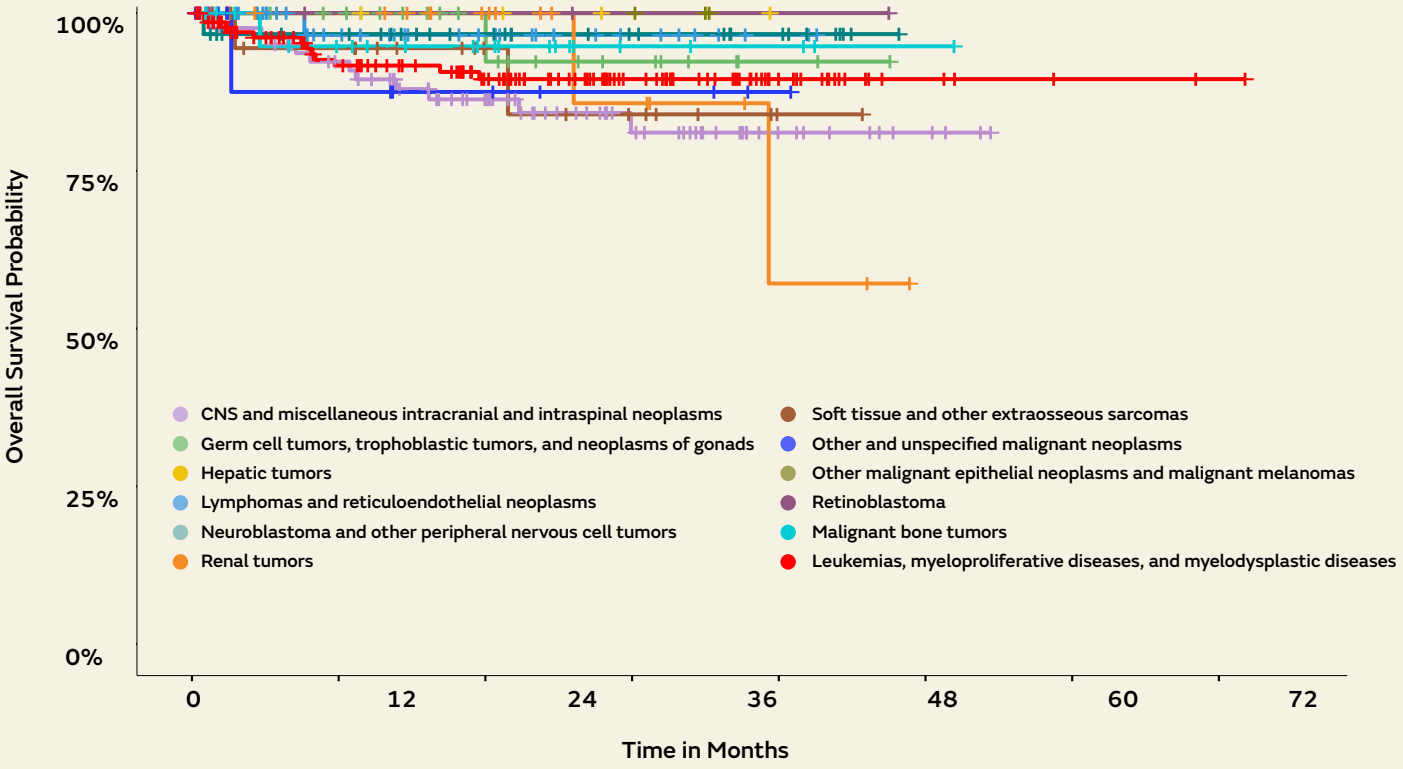
Evolution of the modalities of treatments applied at Sidra Medicine



Status of Patients by their Year of Diagnosis

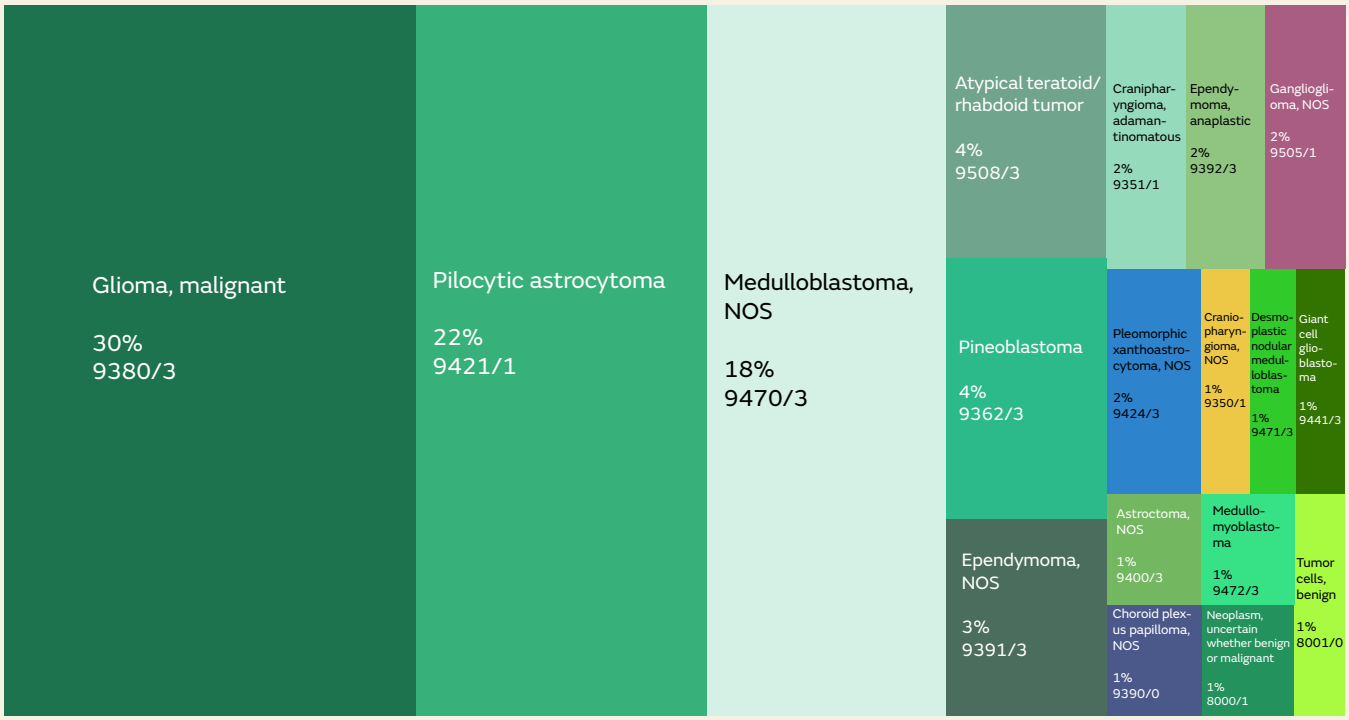


Traditional Kaplan Meir Survival Plot of Our Patient's Population by Cancer Type, by International Classification of Childhood Cancer, Third Edition, Level 1

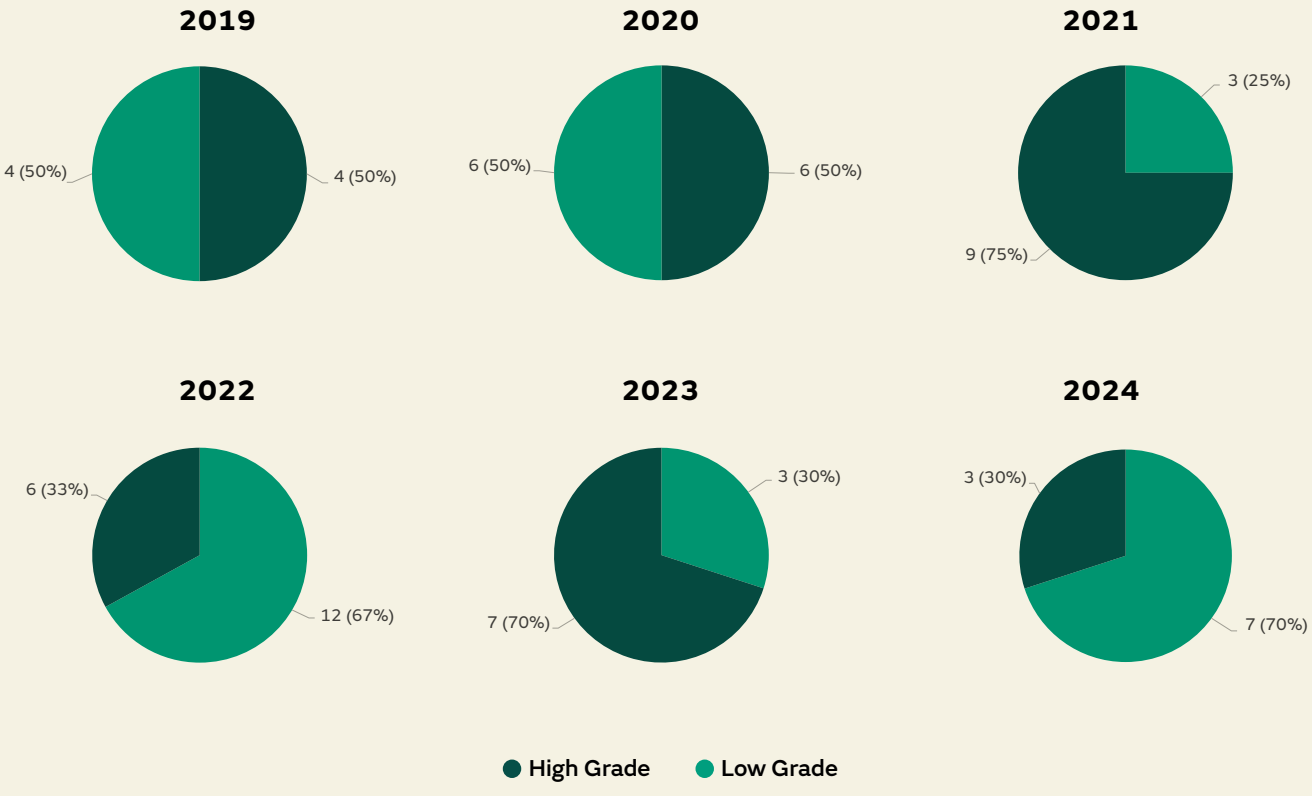


CENTRAL NERVOUS SYSTEM (CNS) TUMORS

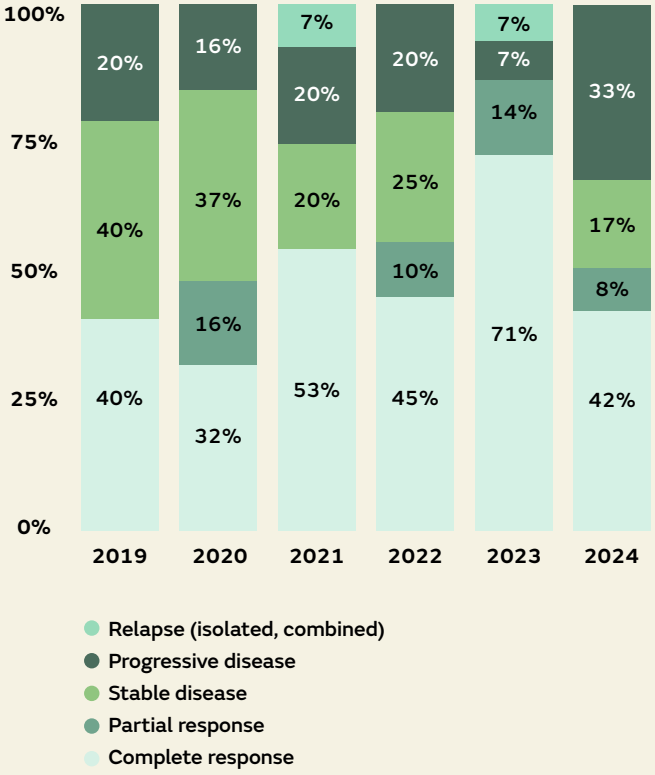
Distribution of ICDO3 codes of our CNS patients



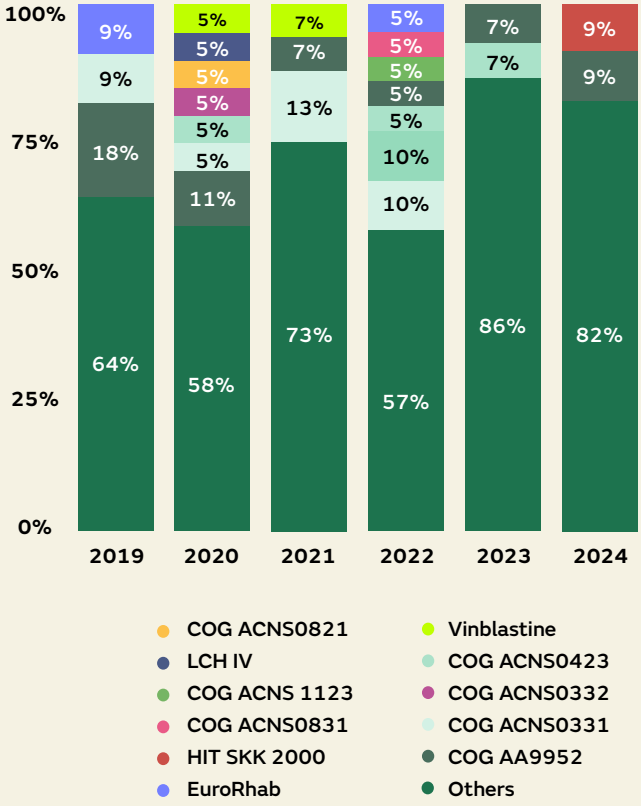
Cancer grade of CNS tumors at diagnosis by year



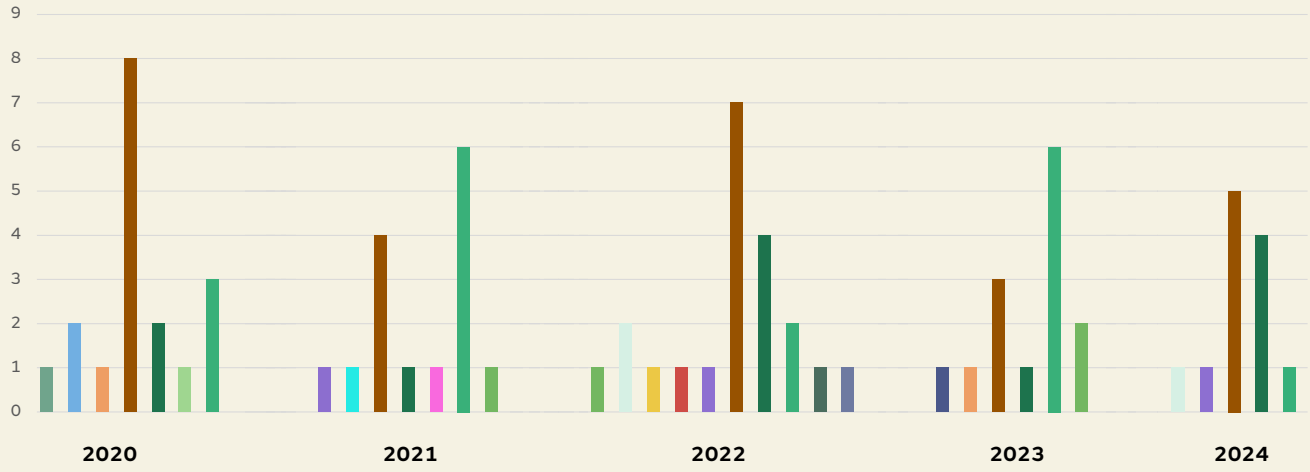
Response of our CNS patients after finishing primary treatment



Treatment protocols applied to our patient population by year of diagnosis



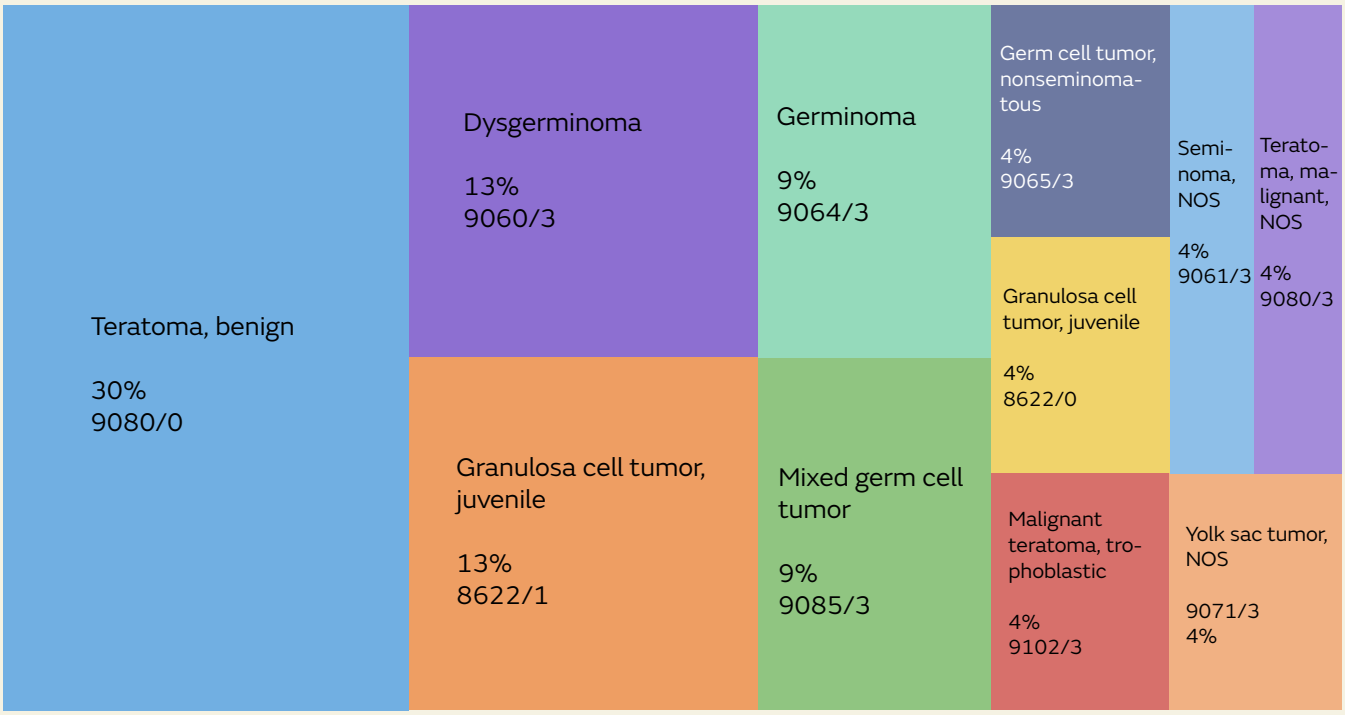
ICDO3 codes by year of diagnosis



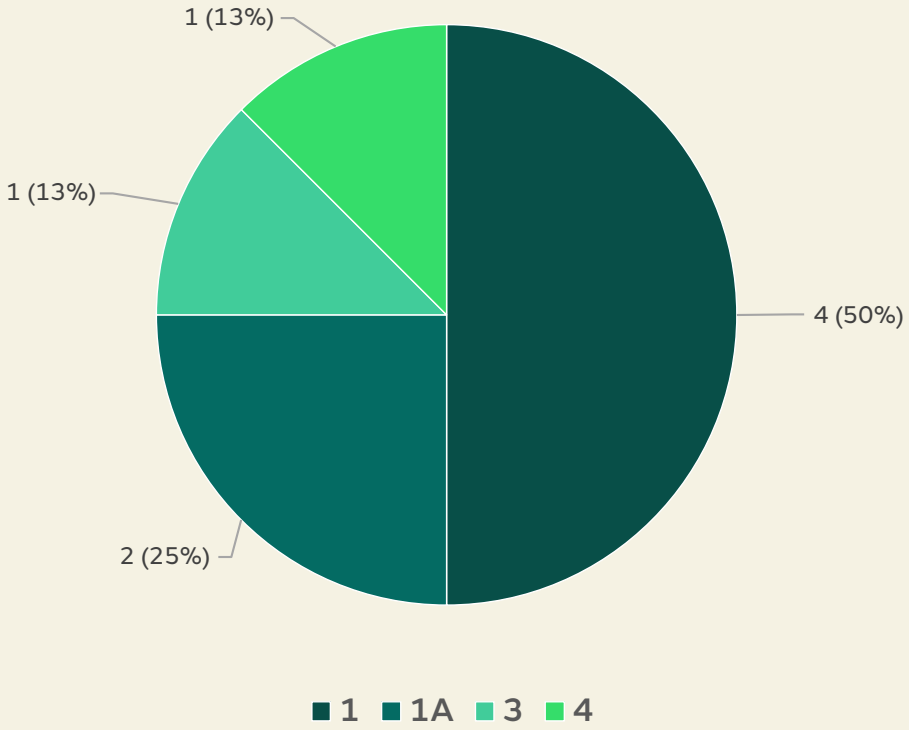
- Astrocytoma, NOS
- Atypical teratoid/rhabdoid tumor
- Choroid plexus papilloma, NOS
- Craniopharyngioma, adamantinomatous
- Craniopharyngioma, NOS
- Desmoplastic nodular medulloblastoma
- Ependymoma, anaplastic
- Ependymoma, NOS
- Ganglioglioma, NOS
- Giant cell glioblastoma
- Glioma, malignant
- Medulloblastoma, NOS
- Medullomyoblastoma
- Neoplasm, malignant
- Neoplasm, uncertain whether benign or malignant
- Pilocytic astrocytoma
- Pineoblastoma
- Pleomorphic xanthoastrocytoma, NOS
- Tumor cells, benign

GERM CELL TUMORS, TROPHOBLASTIC TUMORS AND NEOPLASMS OF GONADS

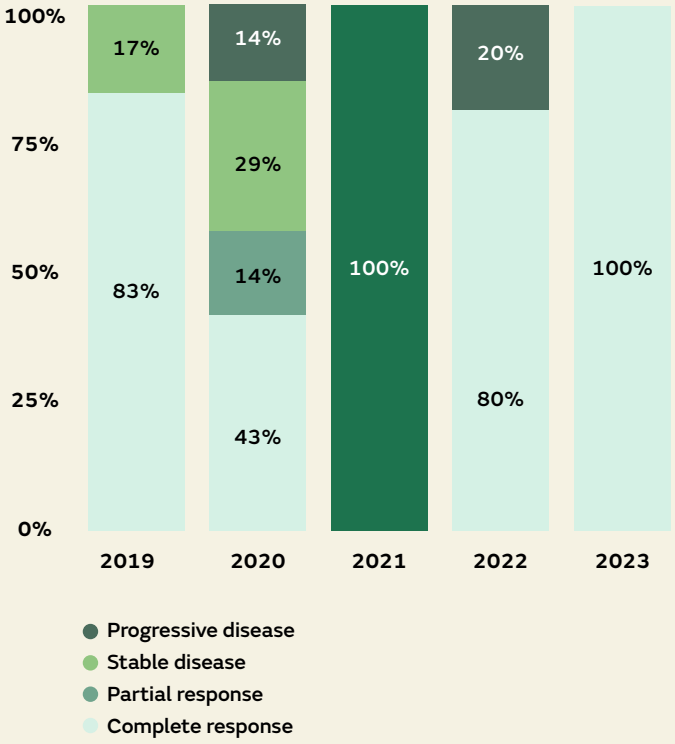
Distribution of ICDO3 codes of our patients



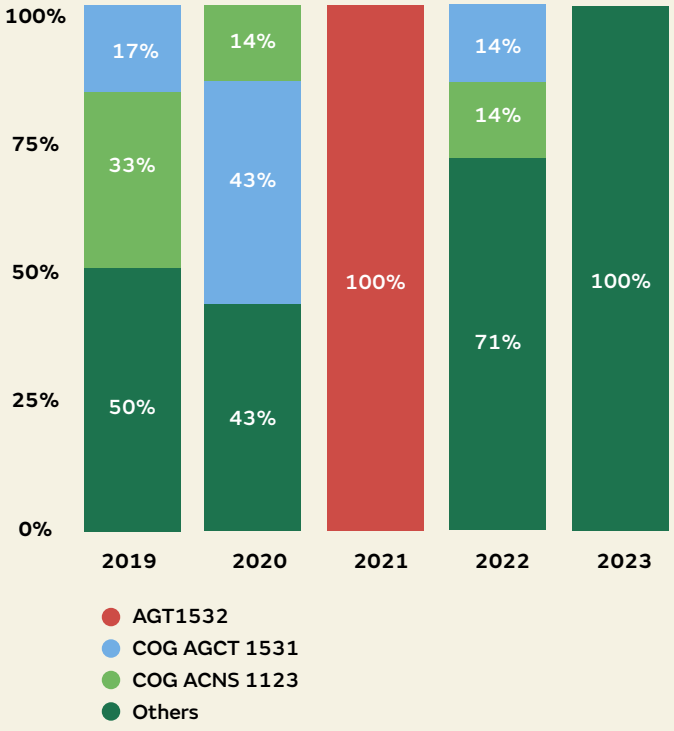
Cancer stage of tumors at diagnosis from 2019 - 2023



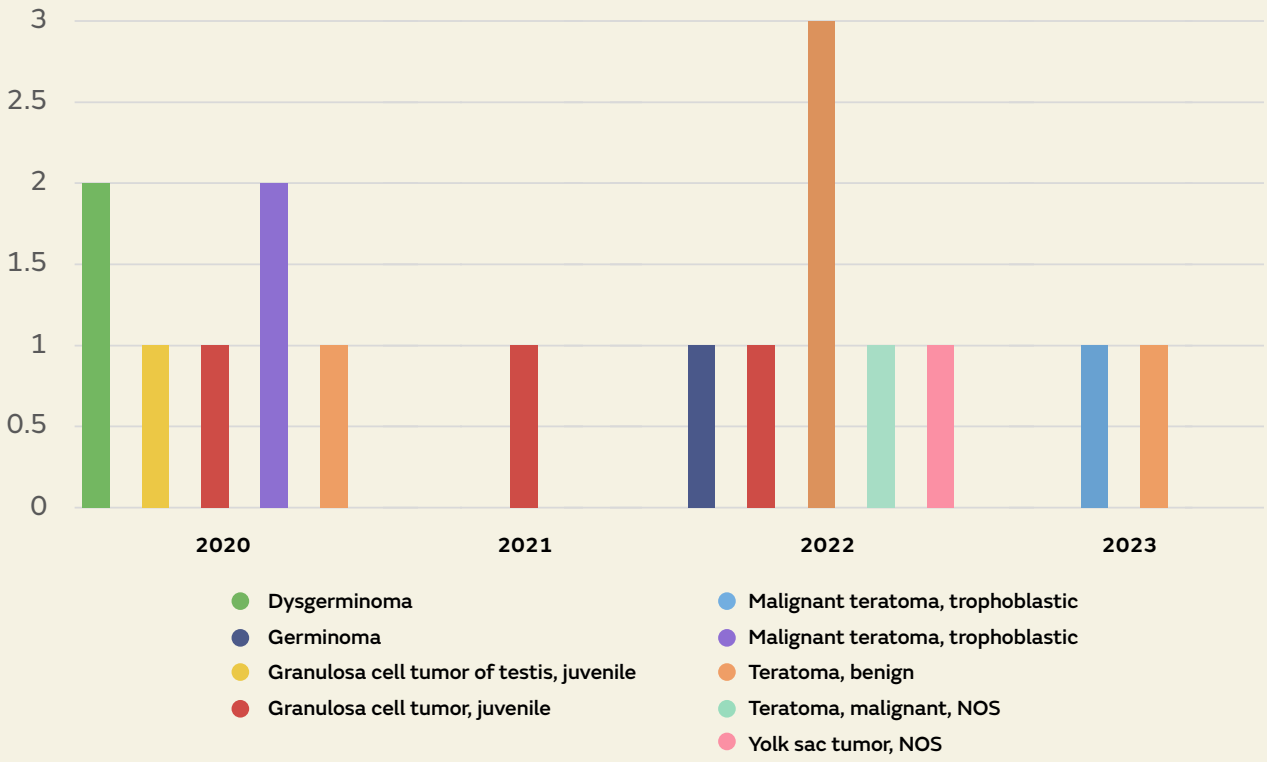
Response of our tumour patients after finishing primary treatment



Treatment protocols applied to our patient population by year of diagnosis

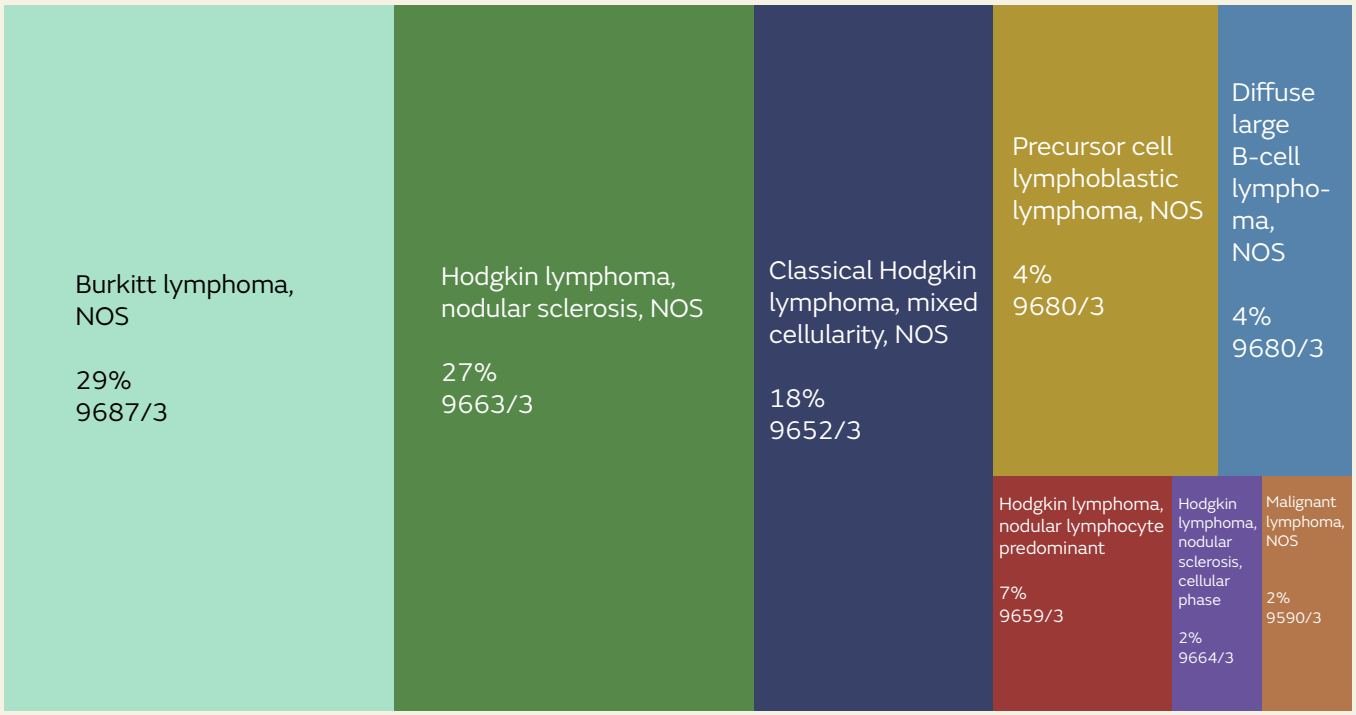


ICDO3 codes by year of diagnosis

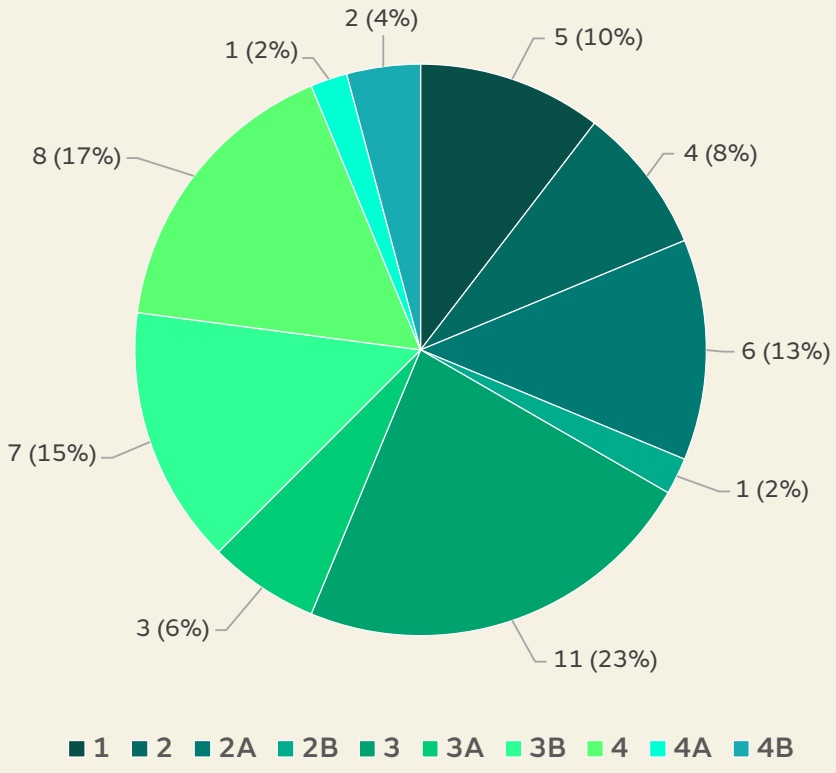


LYMPHOMAS AND RETICULOENDOTHELIAL NEOPLASMS

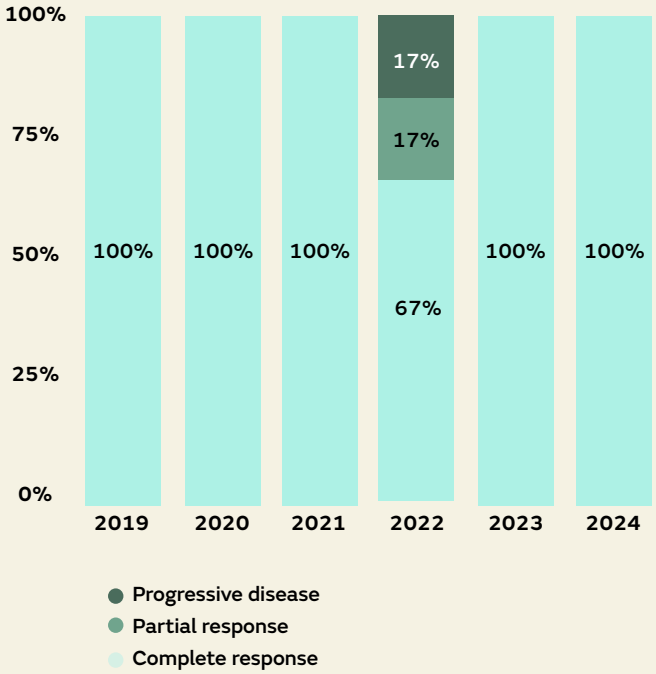
Distribution of ICDO3 codes of our patients



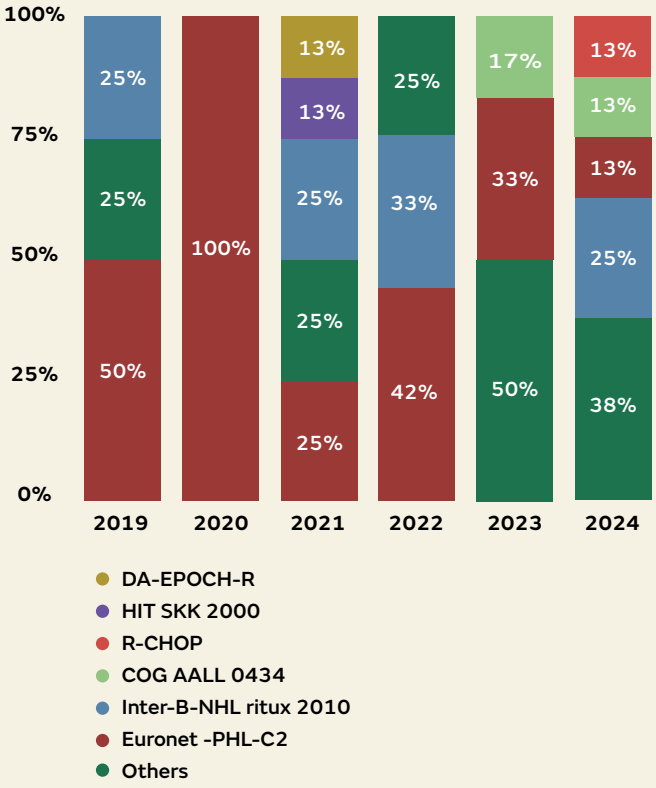
Cancer stage of tumors at diagnosis from 2019 - 2024



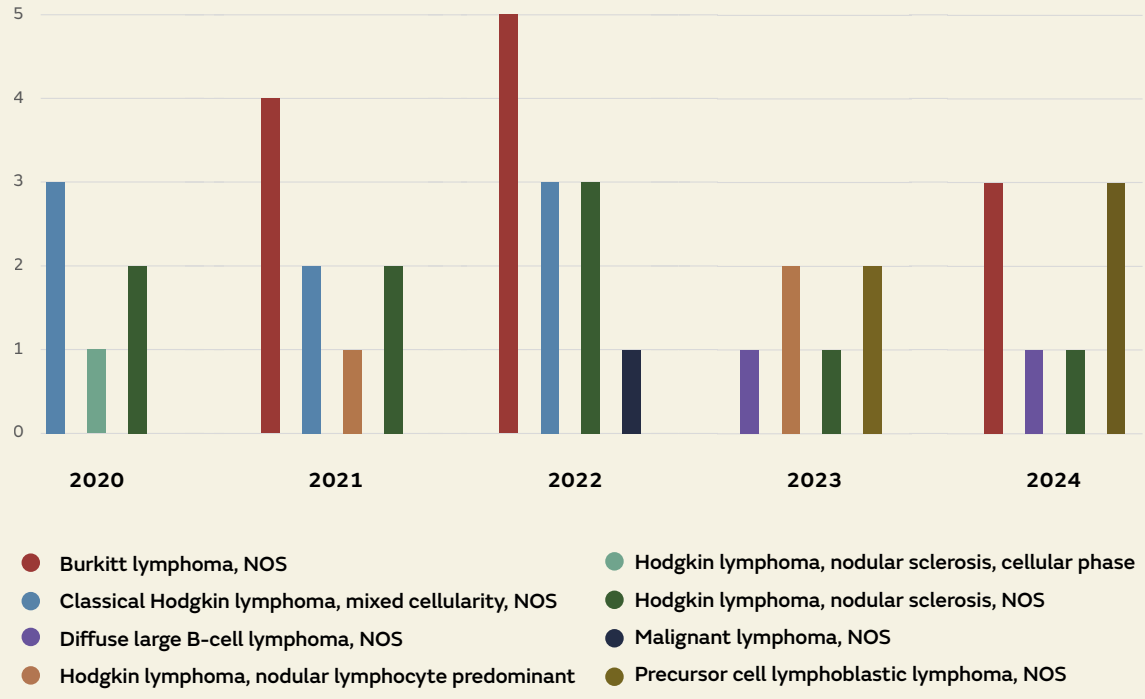
Response of our tumor patients after finishing primary treatment



Treatment protocols applied to our patient population by year of diagnosis

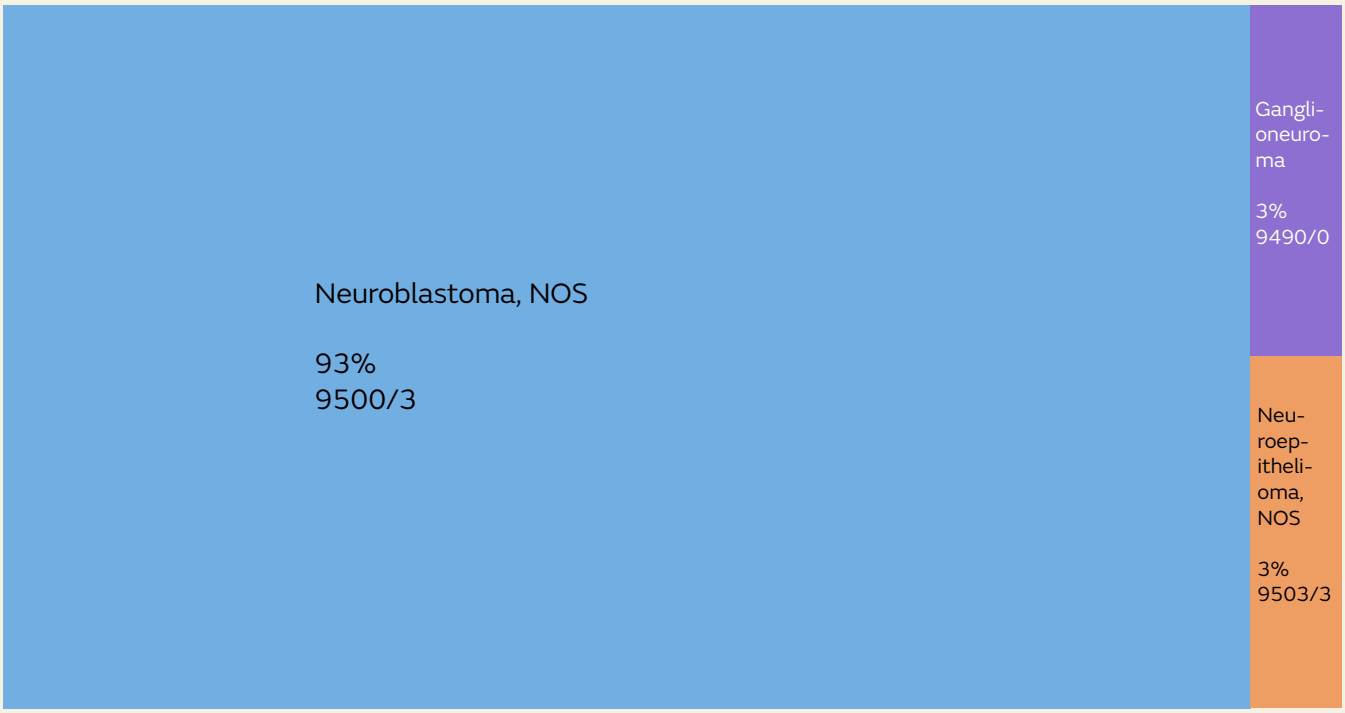


ICDO3 codes by year of diagnosis

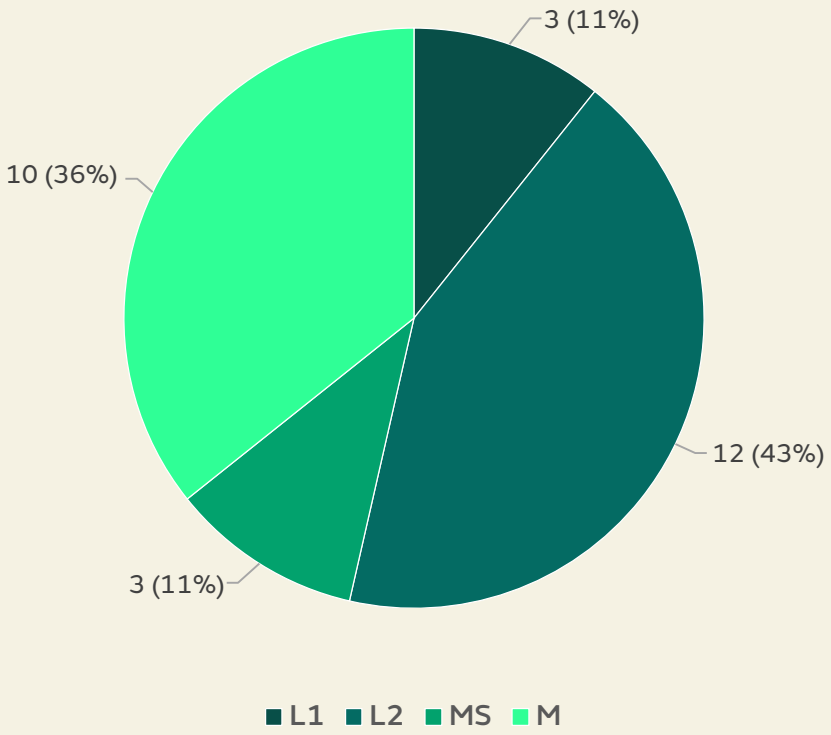


NEUROBLASTOMAS AND PERIPHERAL CELL TUMORS

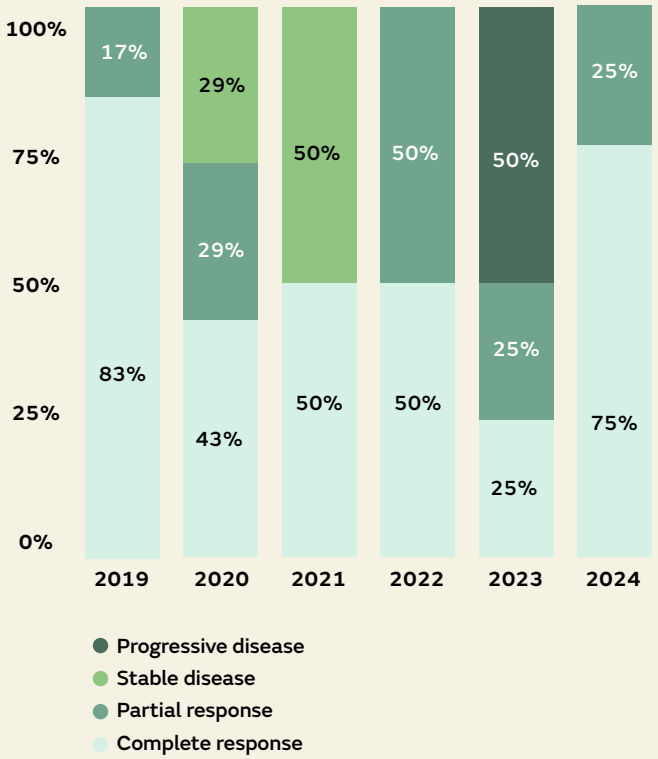
Distribution of ICDO3 codes of our patients



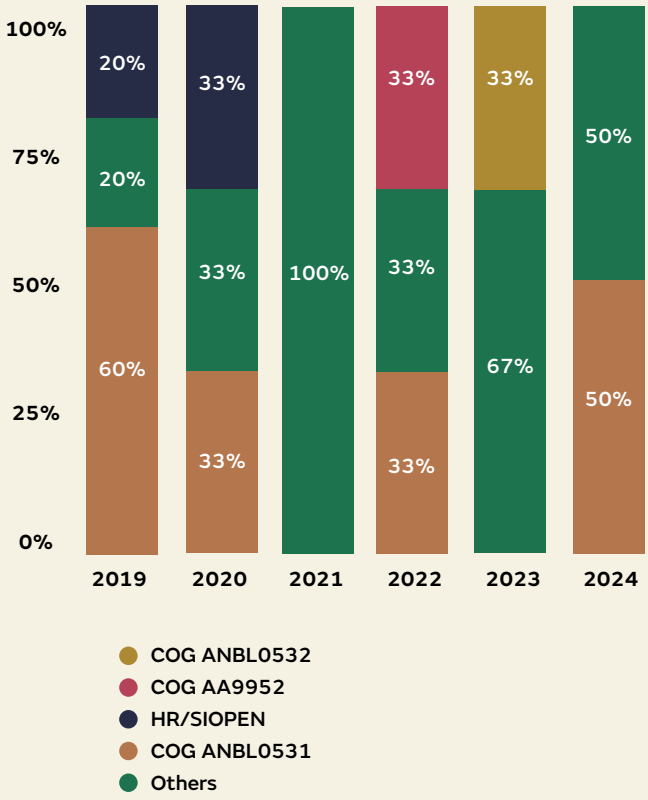
Cancer stage of tumors at diagnosis from 2019 - 2024



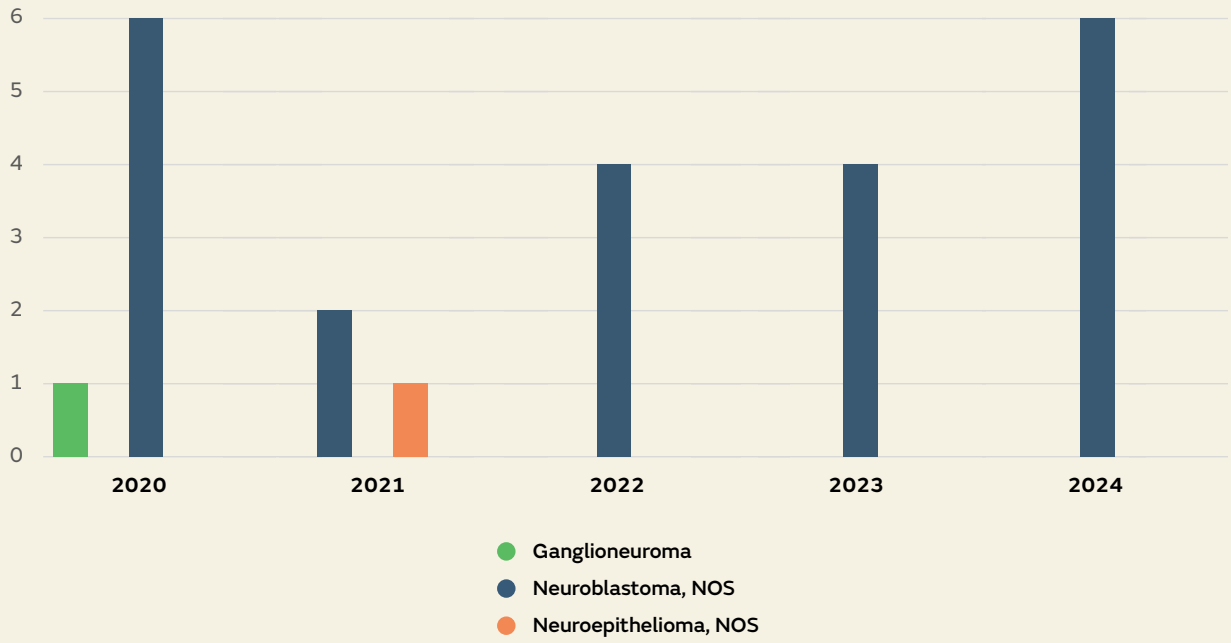
Response of our tumor patients after finishing primary treatment



Treatment protocols applied to our patient population by year of diagnosis

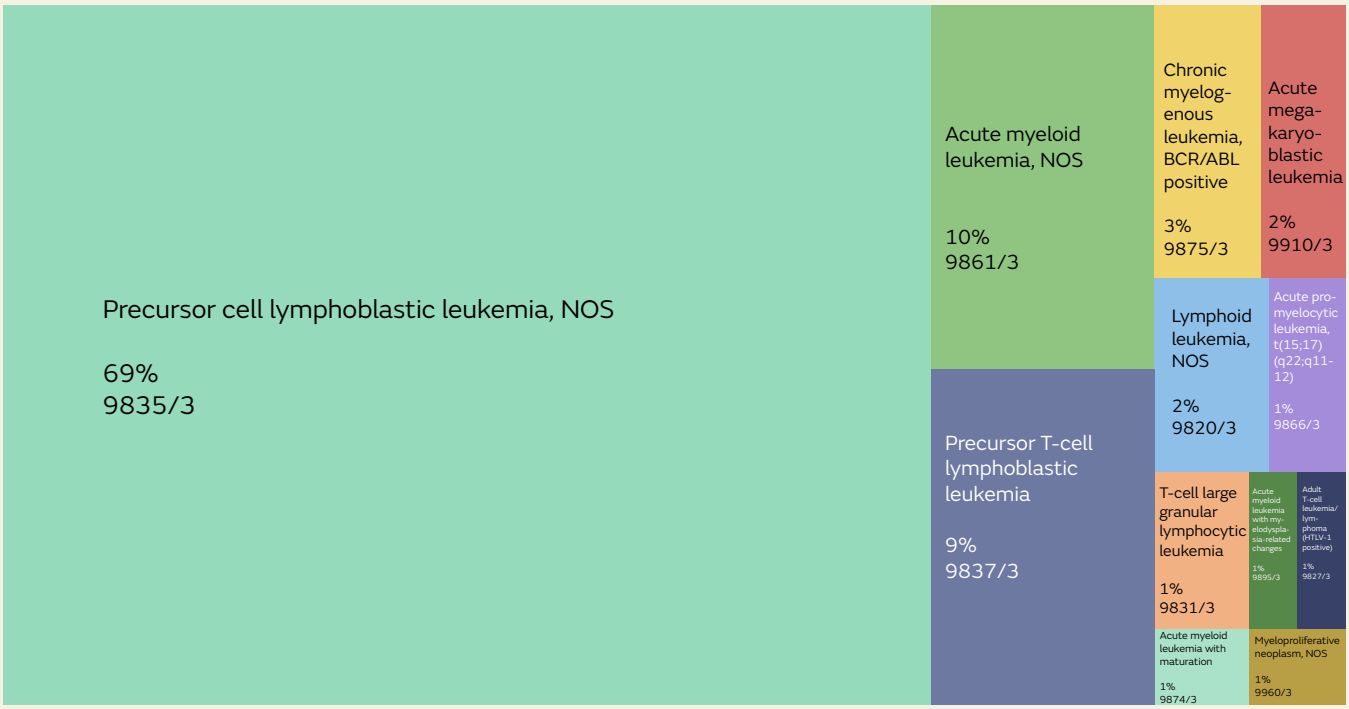


ICDO3 codes by year of diagnosis

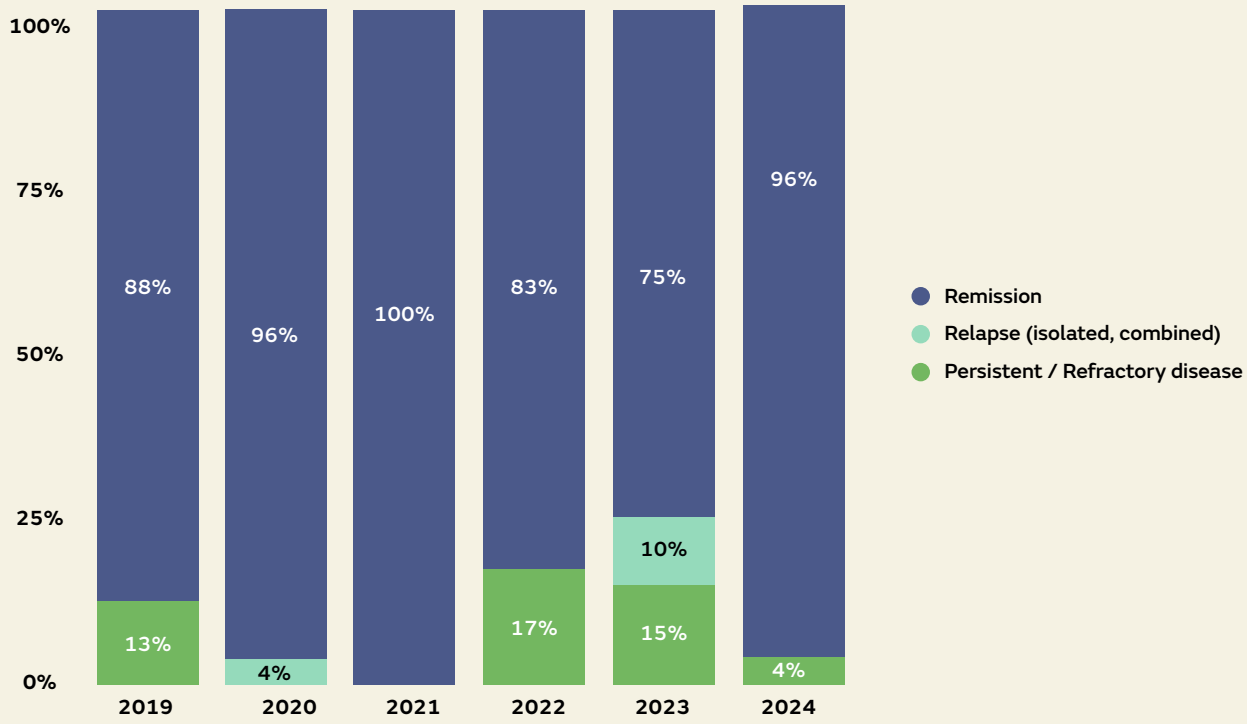


LEUKEMIA, MYELOPROLIFERATIVE DISEASES AND MYELODYSPLASTIC DISEASES

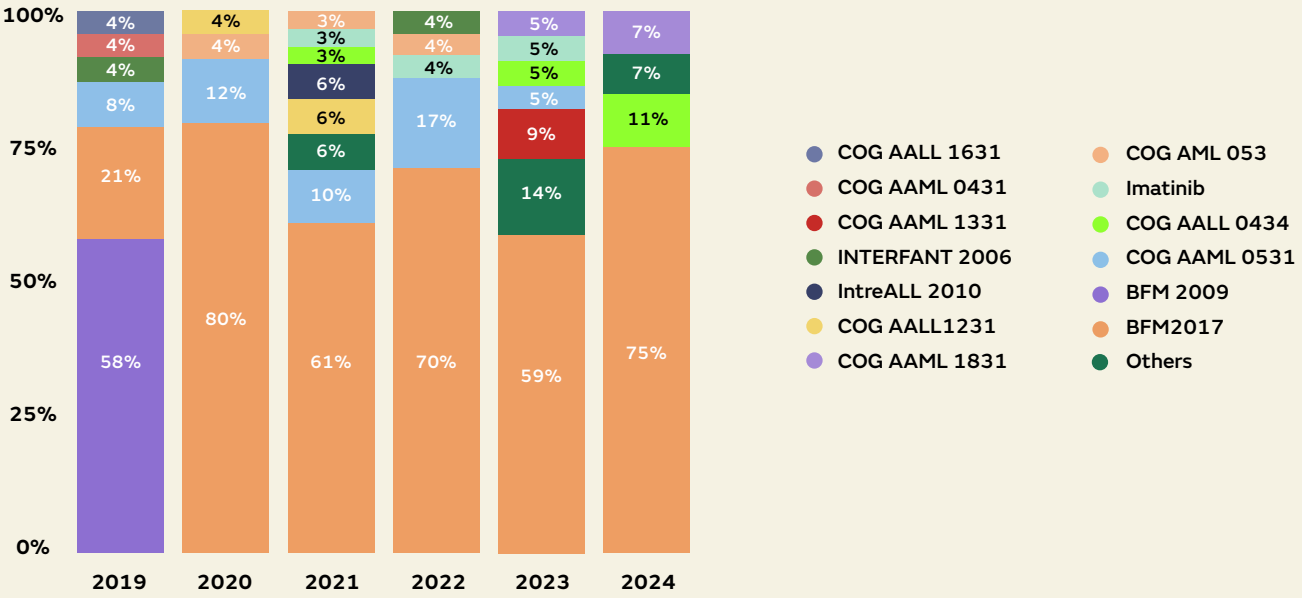
Distribution of ICDO3 codes of our patients



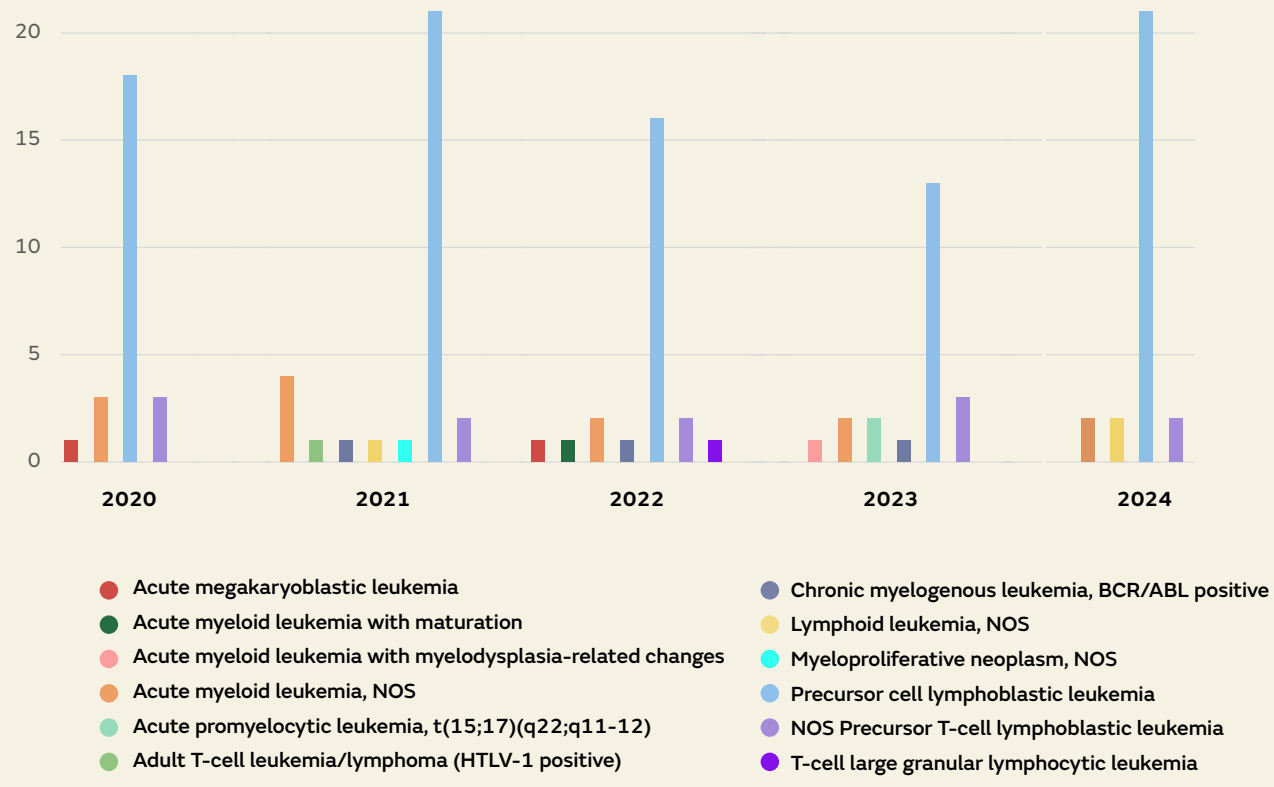
Response of our tumor patients after finishing primary treatment



Treatment protocols applied to our patient population by year of diagnosis



ICDO3 codes by year of diagnosis



REFLECTIVE INSIGHTS

A talk with Khadra Abdi, Lead, Institutional Review Board (IRB), Sidra Medicine

At Sidra Medicine, the Institutional Review Board (IRB) Office plays a pivotal role in ensuring that oncology research progresses ethically, safely, and in accordance with both national and international standards. Khadra Abdi, the IRB Office Lead, who has been with Sidra Medicine since 2014, describes her role as a balance between protecting patients and enabling cutting-edge research.

"As the IRB Office Lead at Sidra Medicine, my role is to ensure that every protocol aligns with ethical standards such as the Belmont Report principles, Good Clinical Practice (GCP), and the Ministry of Public Health (MoPH) guidelines," Khadra Abdi explains. This oversight includes a detailed review of scientific rationale, methodology, risk-benefit assessments, and participant eligibility, especially in high-risk cancer studies and integration with the research Project Management Office.

The process is highly collaborative and involves working closely with oncology experts to scrutinize novel interventions. "We conduct rigorous reviews of oncology protocols and consent materials, and we prioritize patient safety through adverse event oversight," Khadra adds. "This ensures that cancer research at Sidra Medicine advances safely, ethically, and in full compliance with global best practices."

The IRB follows a structured review pathway that begins with a full submission check by the IRB Office, followed by expert assignment (IRB Member), a strict evaluation of the risk-benefit ratio. Oncology protocols receive special attention due to the vulnerable nature of the patient population and the high complexity of proposed interventions. Khadra remarks that, "We pay special attention to informed consent clarity and ensure robust safety oversight. Even after the IRB grants approval, we continue monitoring safety reports, protocol amendments, enrollments, and annual reviews."

Given the complexity and urgency of oncology studies, timeliness is critical. "Oncology protocols are known for their complexity and high stakes, so timely, yet thorough reviews are a top priority," says Khadra Abdi. "We achieve this by combining structured workflows, oncology expertise, and proactive quality oversight." Sidra Medicine's IRB integrates early support for investigators, enables parallel review processes, and continuously monitors study progress. "This allows us to meet research timelines without compromising ethical review, ultimately enabling the rapid advancement of critically important cancer studies with participant safety firmly at the center."

Despite the structured approach, oncology research presents unique and demanding challenges. "Patients in these studies often have limited treatment options, and the trials involve potentially toxic interventions," Khadra notes. This requires "more stringent scientific and ethical review, robust and transparent consent processes, and enhanced safety monitoring systems."

Nevertheless, the IRB views this responsibility as essential to advancing hope and therapeutic options for cancer patients. Protocols of the Sidra Pediatric Oncology Qatar program bring a different layer of complexity compared to standard research studies. "These involves collecting, processing, and biobanking tissues, like tumor, blood, and bone marrow, for future molecular research," Khadra explains. "This adds operational and ethical demands that go beyond typical observational studies."

Handling, freezing, tracking, and disposal of biological materials, all require detailed SOPs approved by the IRB. Additionally, consent for biobanking extends beyond a single study and must account for future, unspecified research. "Registries, on the other hand, involve longitudinal clinical and genomic data that can span decades. This demands more stringent data governance and continuous compliance."

Unlike discrete clinical trials, biobanks and registries operate continuously, which requires annual renewals, storage monitoring and regular ethics checks. "The IRB must monitor recruitment procedures, manage withdrawals, oversee policy changes, and ensure long-term compliance with evolving regulations."

Through structured processes, close collaboration, and a commitment to ethical integrity, Khadra Abdi and the IRB team at Sidra Medicine ensure that oncology research is conducted responsibly while fostering breakthroughs that hold promise for patients in Qatar and beyond.

PERSPECTIVES IN FOCUS

Discussion with Farhan Mohammad Naim, Program Manager, Project Management Office (PMO), Sidra Medicine

In the evolving landscape of precision medicine, the integration of biobanking and oncology research requires meticulous coordination, regulatory compliance, and unwavering support for investigators. At Sidra Medicine, Farhan Mohammad Naim, Manager of the Project Management Office (PMO), plays a pivotal role in orchestrating these efforts.

From project registration to final reporting, the PMO manages the complete lifecycle of research studies. This includes ensuring timely initiation, securing regulatory approvals, and monitoring progress toward defined milestones."

"My main role is to oversee the daily operations of the research Project Management Office, or PMO," Farhan explains. "The PMO is the entry point for any researcher wanting to conduct research at Sidra Medicine. To facilitate the entire PMO lifecycle, we operate a database, PMO REDCap, that serves as a central repository of key project information. It houses project team rosters, sample storage logs, research protocols, regulatory documentation and project outcomes like patents of publications."

A notable share of Sidra Medicine's research efforts, approximately 15 percent, are focused on oncology, particularly in the domain of precision oncology, which relies heavily on well-curated, longitudinal clinical and biological datasets. "Precision oncology is one of the most promising fields in precision medicine," says Farhan.

"High-quality datasets linked to biobanked biological specimens are its backbone." This has led the PMO to dedicate significant resources to the onboarding and support of oncology projects, ensuring they are effectively launched and closely monitored.

Handling a diverse and high-stakes research portfolio demands a nuanced approach to coordination. Farhan emphasizes the importance of communication and flexibility in working with principal investigators (PIs) and their teams. "The key is maintaining clear and open communication with Lead PIs through all stages of the project lifecycle. Each project is unique, with its own targets, deadlines, and

funding implications." Instead of traditional prioritization, the PMO employs a collaborative model that adjusts timelines based on feasibility and readiness, while treating all research initiatives with equal importance. "We try to avoid the word 'prioritization' because all research is important. Our goal is to provide equitable support to all investigators."

Research in oncology, especially involving rare tumors and biobanking, is not without its challenges. Recruitment and sample collection can be particularly complex in pediatric oncology settings. "Cancer patients, especially those with very rare tumors, are often the most sick patients we see. This can make enrollment and sample collection difficult, which in turn affects the ability to meet project milestones." Despite these hurdles, Farhan is optimistic about the transformative potential of Sidra Medicine's research initiatives. "Some of our promising diagnostic marker discovery research may lead to the development of therapeutic candidates. These could eventually move into clinical trials and perhaps become part of our standard of care."

At Sidra Medicine, the PMO is actively working to reduce administrative friction and enable investigators to focus on science. "Good, high-quality project management can make researchers' lives much easier," Farhan notes. "That's what

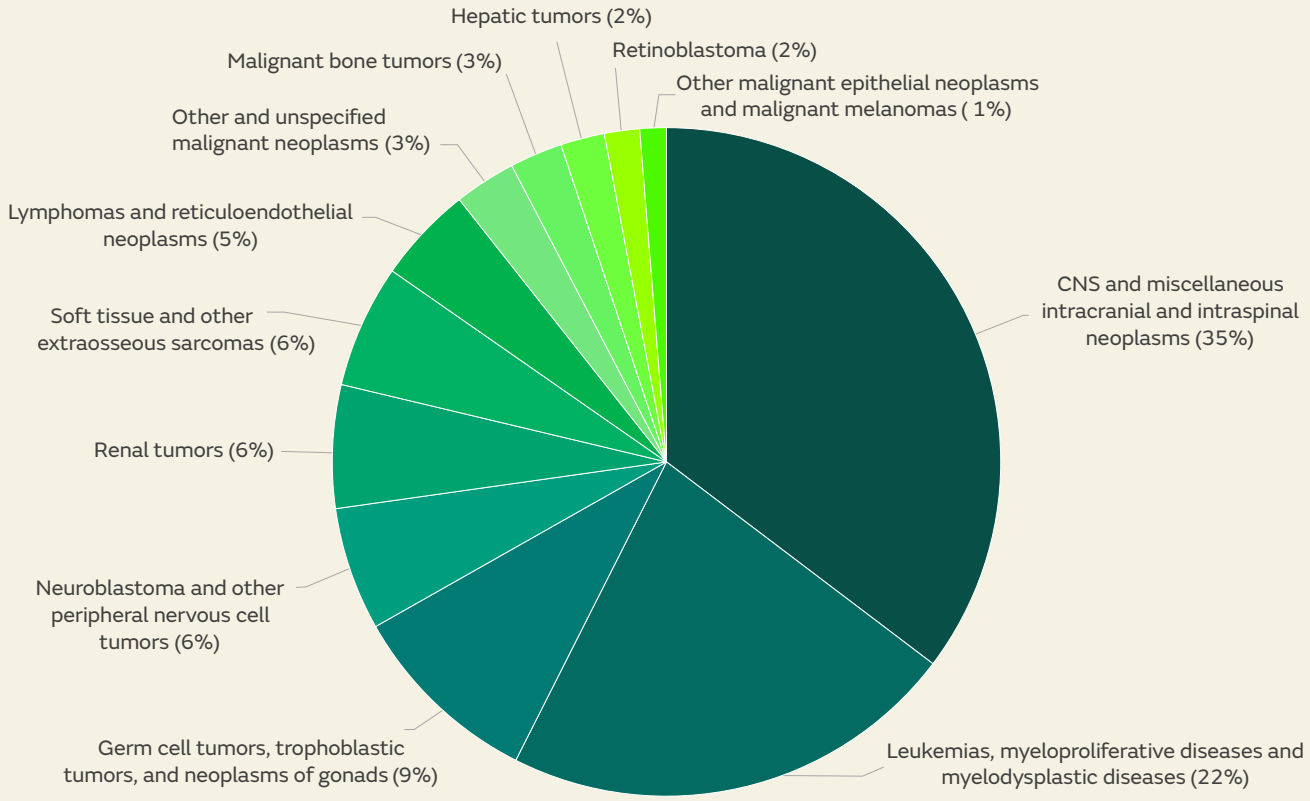
we aspire to, in order to streamline research and remove the drudgery so that our PIs can concentrate on discovery and invention." To institutionalize this approach, the PMO has developed a comprehensive two-year strategic plan aimed at innovating research infrastructure and support. As part of its strategic shift, the PMO is adopting a programmatic support model, Translational Research Programs or TRP. Each major research domain will have dedicated personnel providing tailored support, backed by data-driven tools.

"For the Sidra Pediatric Oncology Qatar (SPOQ) TRP this means access to a single point of contact in the PMO who can provide real-time data on project performance, risks, and issues," Farhan explains. "We've already begun developing a dashboard that gives TRP directors instant visibility into the research activities within their domain." When managing biobanking and personalized medicine projects, feasibility assessments are crucial. "We need to ensure that recruitment timelines are realistic, sample numbers are achievable, and resources, like freezer and bench space, are available before we initiate a project." These foresight-driven considerations form the foundation of sustainable and impactful research practices.

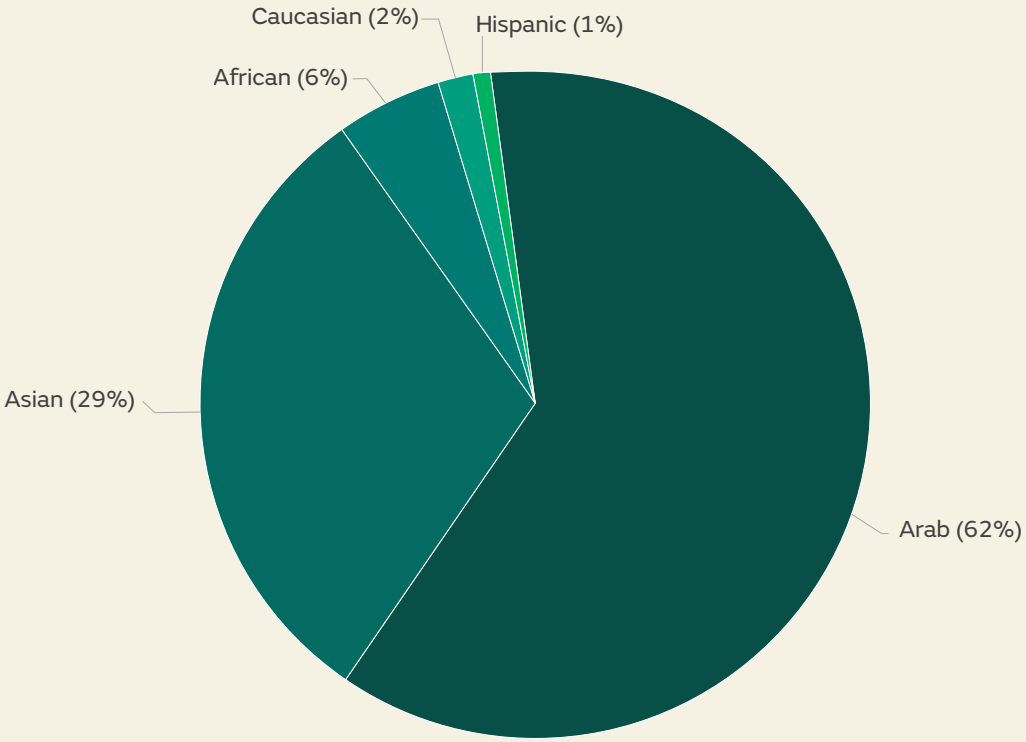
Farhan's perspective underscores how integrated project management acts as a cornerstone of Sidra Medicine's research environment, particularly in high-impact fields like oncology and precision medicine. By pairing strategic oversight with tailored operational support, the PMO empowers researchers to pursue discovery with efficiency and confidence.

SIDRA MEDICINE PEDIATRIC CANCER BIOBANK OVERVIEW

Types of pediatric solid and non-solid cancer in the biobank

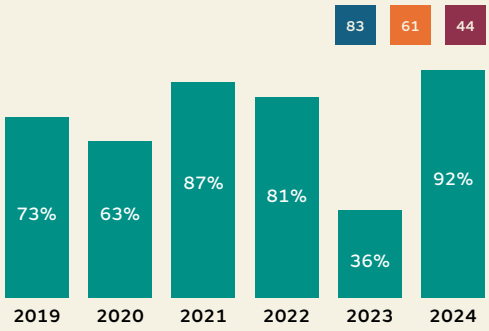


Biobank ethnicity

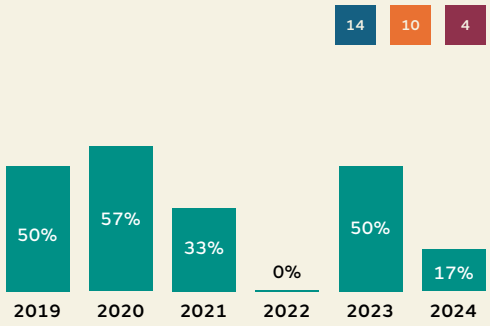


Consents and overall sampling rates per cancer type per year of diagnosis

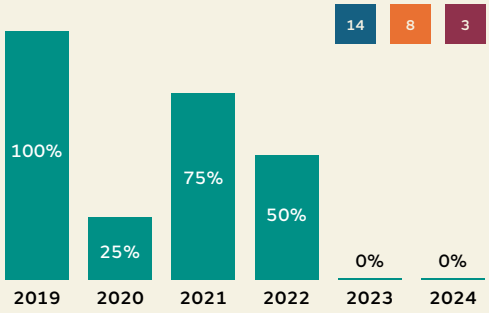
Consent rate for CNS and miscellaneous intracranial and intraspinal neoplasms



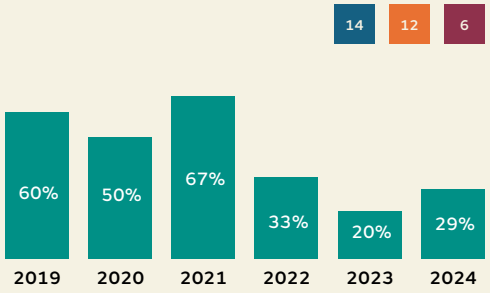
Consent rate for neuroblastoma and other peripheral nervous cell tumors



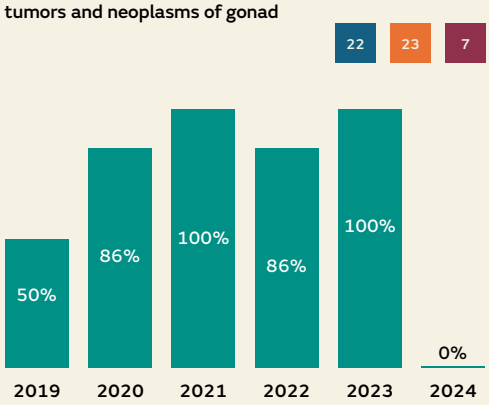
Consent rate for renal tumors



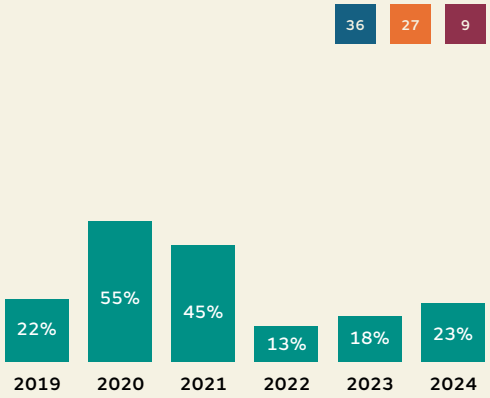
Consent rate for soft tissue and other extraosseous sarcomas



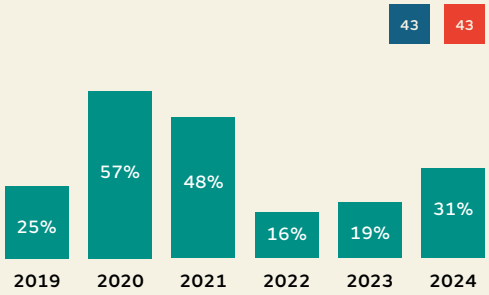
Consent rate for germ cell tumors, trophoblastic tumors and neoplasms of gonad



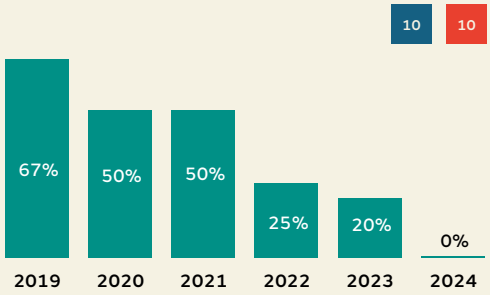
Consent rate for other solid tumors



Consent rate for lymphoid leukemias



Consent rate for acute myeloid leukemias

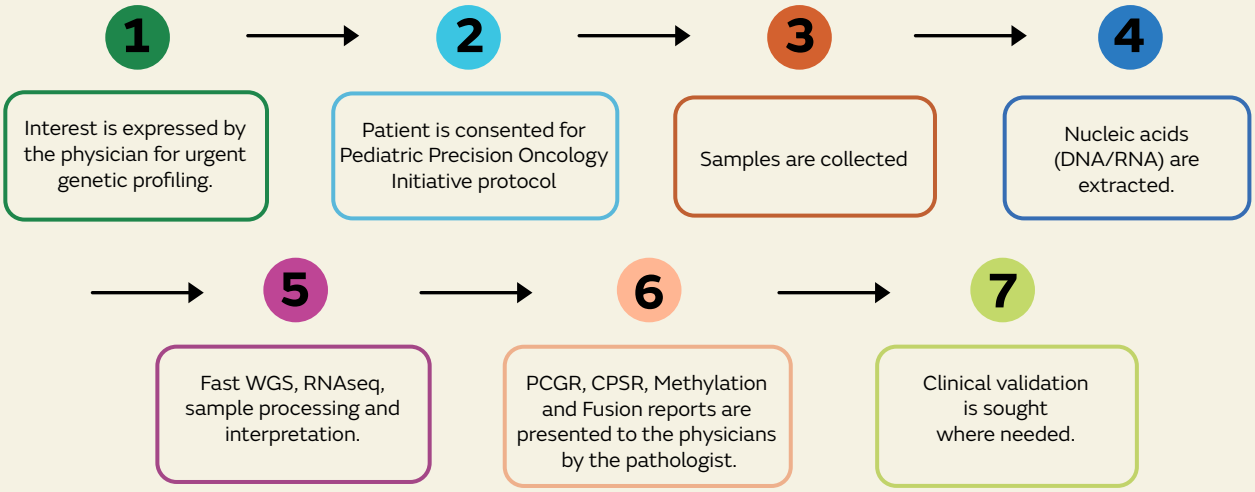


Total consented | Blood WGS | Tumor WGS | Blood/bone marrow sample

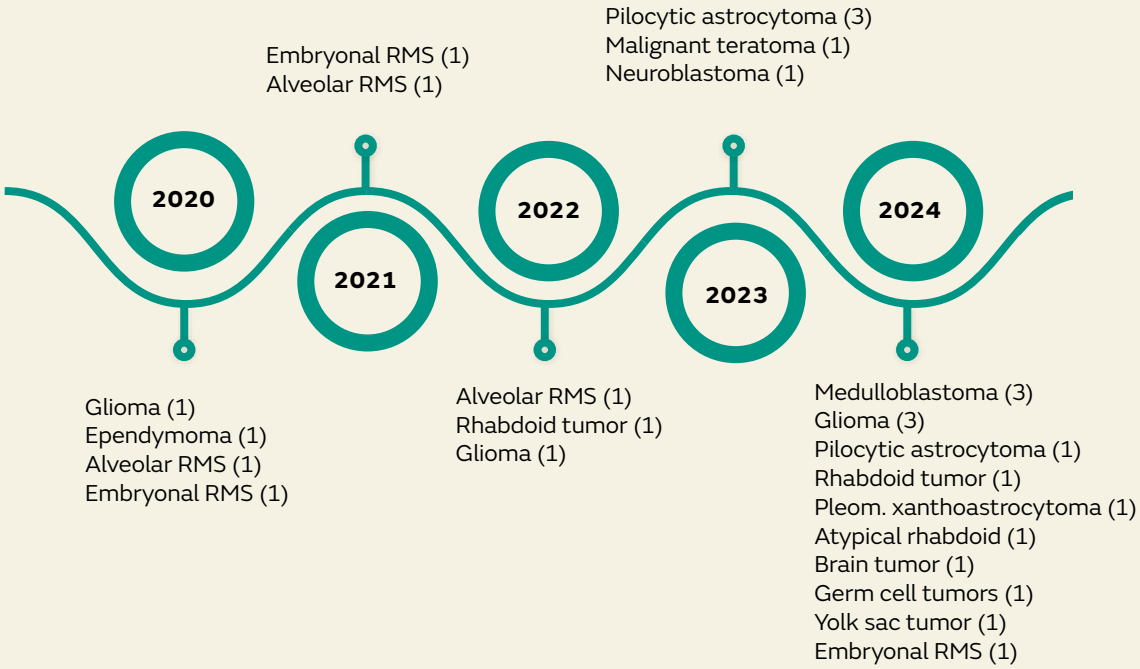
eXPEDITED GENOMIC ONCOLOGY PROFILING (eGOP)

The expedited Genomic Oncology Profiling (eGOP) procedure has been available since October 2020. This protocol is activated whenever the clinician (oncologist or pathologist) feels the need for an urgent molecular characterization to guide diagnosis and treatment. The eGOP procedure is typically requested for patients with extremely aggressive/relapsed cases and poor prognoses. The pipeline includes the rapid transfer of samples to research, DNA and RNA extraction, next-generation sequencing, variant annotation, and generating the "Personal Cancer Genome Report" (PCGR) and Cancer Predisposition Sequencing Report (CPSR), the Methylation Classification Reports Molecular Neuropathology (MNP) and National Institutes of Health (NIH) and the fusion genes report to clinicians within 2-3 weeks.

eGOP mechanism



eGOP patients

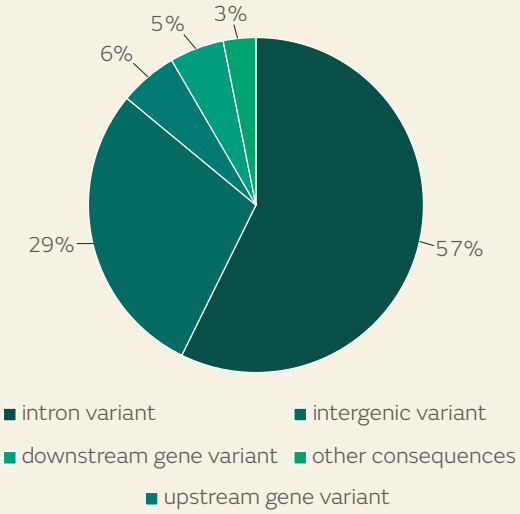


SNAPSHOTS OF PATIENTS' REPORTS

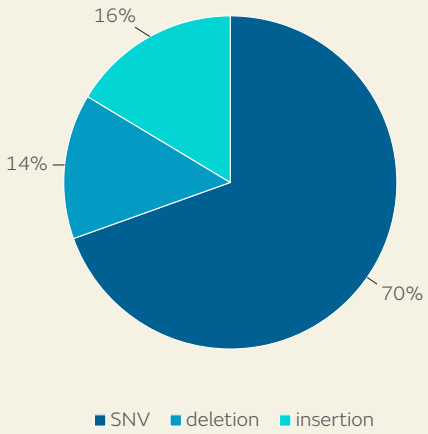
1- Personal Cancer Genome Reporter (PCGR) v.2.2.1

Somatic mutations are changes to a person's DNA that occurs after conception to any cell that isn't a germ cell (egg or sperm cell). Somatic or acquired genomic variants are the most common cause of cancer. In the SPCB, we are generating a PCGR report for each patient that interprets both somatic SNVs/InDels and copy number aberrations. PCGR implements standard operating procedures for oncogenicity evaluation developed by ClinGen/CGC/VICC. This classification is based on multiple properties of variants (hotspot occurrence, variant consequence (i.e. loss-of-function), population frequency etc.).

Variant statistics | any consequence type



Variant statistics | type



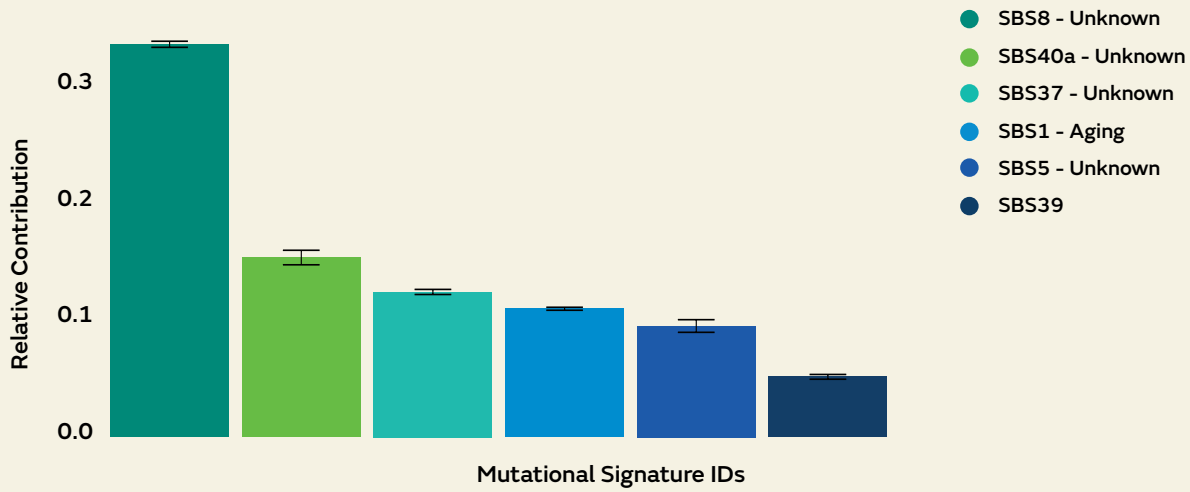
Clinical significance of somatic mutations

Symbol	Alteration	Gene name	Consequence	Oncogenicity	Protein Domain
TP53	c.782+1G>A	tumor.protein p53	splice_donor_variant	Oncogenic	N/A
ATRX	p.Gly2110Ter	ATRX chromatin remodeler	splice_region_variant, stop_gained	Oncogenic	Helicase conserved C-terminal domain
H3-3A	p.Lys28Met	H3.3 histone A	missense_variant	Likely_Oncogenic	Core histone H2A/ H2B/H3/H4
SLC4A4	p.Ala360Gly	solute carrier family 4 member 4	missense_variant	VUS	Band 3 cytoplasmic domain
TCEA1	p.Lys265Arg	transcription elonga-tion factor A1	missense_variant	VUS	Transcription factor S-II (TFIIS)
RUNX2	p.Arg519Ter	RUNX family tran-scription factor 2	stop_gained	VUS	Runx inhibition do-main

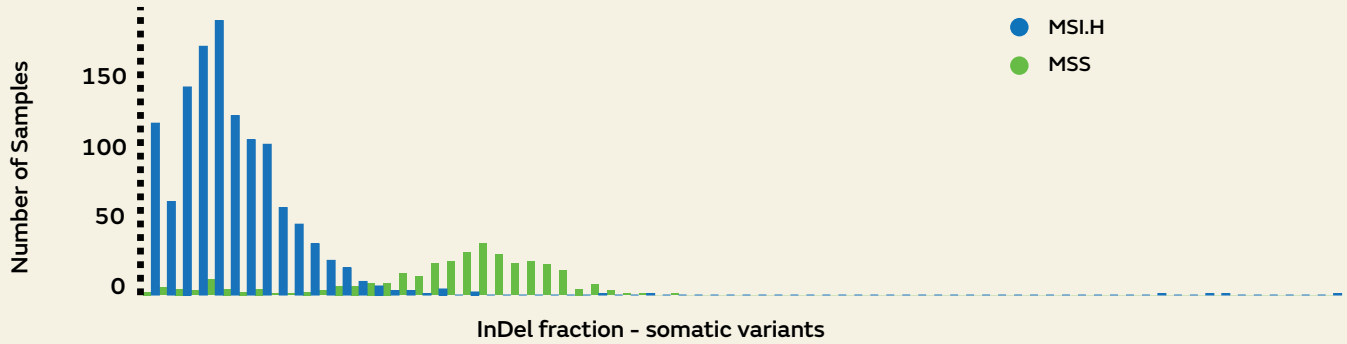
Clinical significance of somatic mutations

Molecular Alteration	Gene name	Vaf Tumor	Biomarker Evidence	Protein Domain
H3-3A missense_variant - ENST00000366815.10:c.83A>T-p.K28M	H3.3 histone A	0.421	- CNS/Brain: Diagnostic | Positive - CNS/Brain: Prognostic | Poor Outcome	Core histone H2A/H2B/H3/H4
ATRX splice_region_variant, stop_gained - ENST00000373344.11:c.6328G>T-p.G2110x	ATRX chromatin remodeler	0.454	- CNS/Brain: Diagnostic | Positive	Helicase conserved C- terminal domain

Mutational signatures



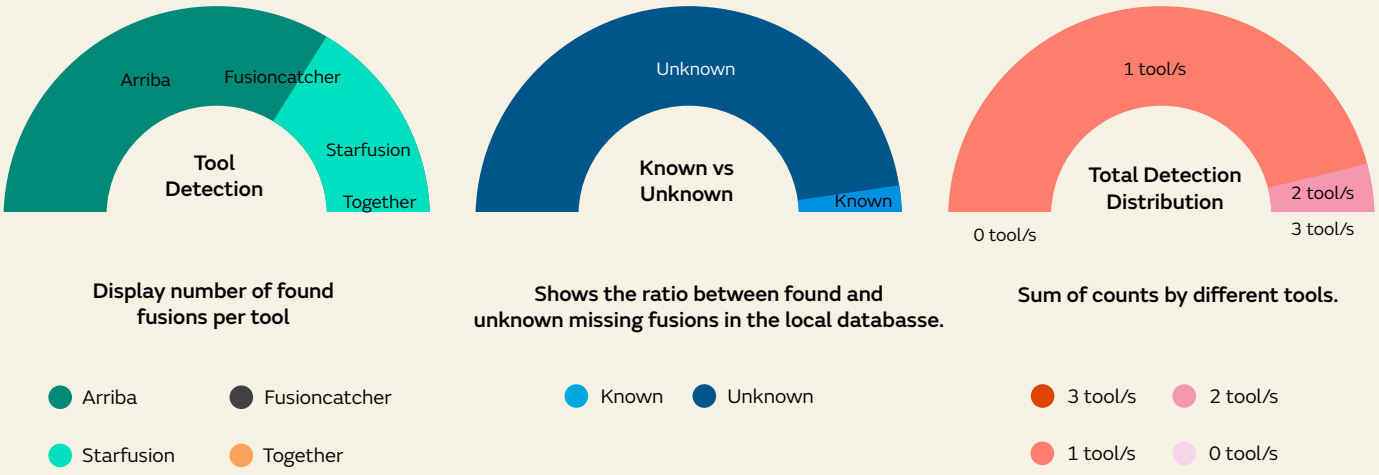
Microsatellite instability (MSI) status



2- Fusion reports

A fusion gene is defined as two genes that are joined so that they are transcribed and translated as a single unit. Fusion proteins produced by this change may lead to the development of some types of cancer.

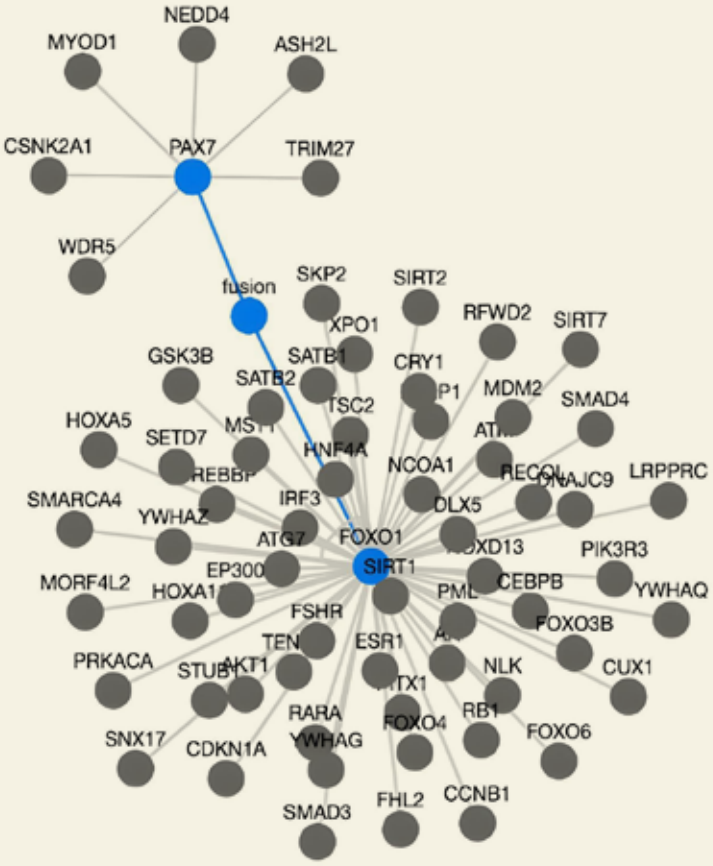
For the SPCB, we are generating a fusion report for each patient through implementing a bioinformatics analysis pipeline for RNA sequencing using list of tools for detecting and visualizing fusion genes.



List of detected fusions

Fusion Gene	Found in DB	Arriba	Fusioncatcher	Starfusion	Tool Hits	Score
PAX7--F0X01	FusionGDB	✓	✗	✓	2	0.243
SETBP1--AL35709.1	Not Found	✓	✗	✓	2	0.143
KANSL1--ARL17B	Not Found	✗	✗	✓	1	0.071
AC09269.1--LSAMP	Not Found	✗	✗	✓	1	0.071

Chimeric Protein-Protein interactions



Related diseases

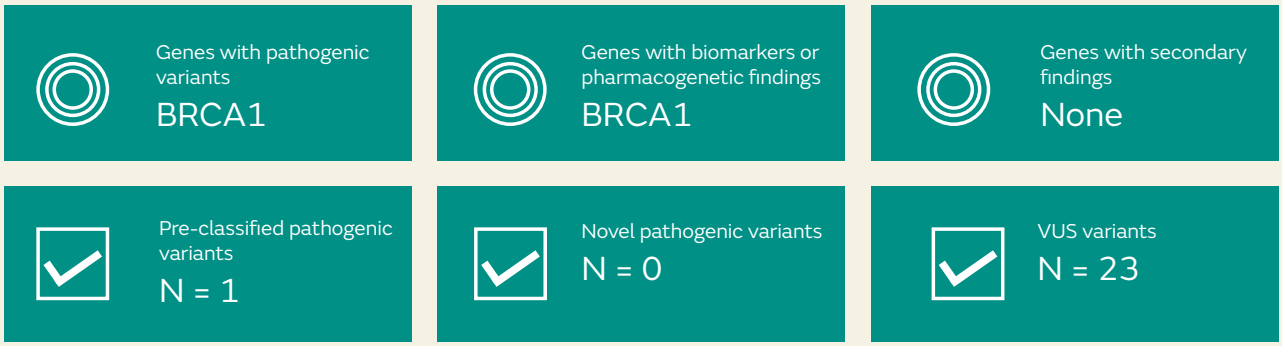
Gene (Disease ID)	Disease Description	Disease Probaility (%)	Disease Publications	Disease Source
FOX01 (C0206655)	Alveolar rhabdomyosarcoma	64.6082322861215	0	CTD_human, HPO, ORPHANET
PAX7 (C0206655)	Alveolar rhabdomyosarcoma	61.8377983787643	0	CTD_human, HPO, ORPHANET
FOX01 (C0023467)	Leukemia, Myelocytic, Acute	20.328236603323997	1	CTD_human
FOX01 (C0022578)	Keratoconus	20.1098907136852	1	CTD_human

3- Cancer Predisposition Sequencing Reporter (CPSR)

Cancer predisposition gene is a term used to describe a gene that may increase a person's risk of developing some types of cancer if it has certain mutations (changes). For the SPCB, we are generating a CPSR for each patient. The CPSR is a computational workflow that interprets and classifies germline DNA variants identified from next-generation sequencing in the context of cancer predisposition and inherited cancer syndromes.

Variants classification
Pathogenic variant is a genetic alteration that increases an individual's susceptibility or predisposition to a certain disease or disorder.
Variants are classified based on the pathogenicity into different classes ordered by highest pathogenicity:

Summary of findings



1- Pathogenic variants
2- Likely Pathogenic variants
3- Variants of Uncertain Significance (VUS)
4- Likely Benign variants
5- Benign variants

Symbol	Clinvar Phenotype	Consequence	Alteration	Genotype	Gene name
BRCA1	Hereditary cancer- predisposing syndrome; Hereditary breast ovarian cancer syndrome; Breast- ovarian cancer, familial, susceptibility to, 1; not provided	splice_donor_variant	c.441+1G>A	het	BRCA1 DNA repair associated

Predictive markers

Symbol	Gene name	Alteration	Consequence	Bm-Evidence Level
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	A: Validated
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	A: Validated
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	A: Validated
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	A: Validated
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	A: Validated
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	B: Clinical Evidence

Prognostic markers

Symbol	Gene name	Alteration	Consequence	Bm-Evidence Level
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	B: Clinical Evidence
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	B: Clinical Evidence
BRCA1	BRCA1 DNA repair associated	c.441+1G>A	splice_donor_variant	B: Clinical Evidence

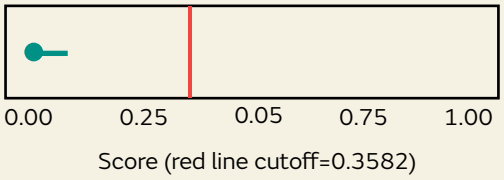
4- Methylation classification report (MNP report)

Version 12.8 of the brain classifier results

Methylation Classes (Highest level >= 0.3, lower levels >= 0.1, all of lowest level)	Calibrated Score	Interpretation	
Low Grade Glial/glioneuronal/neuroepithelial Tumours	0.99	match	✓
Pilocytic Astrocytoma	0.99	match	✓
Supratentorial Midline Pilocytic Astrocytoma	0.99	match	✓
Mc Pilocytic Astrocytoma, Midline	0.99	match	✓

Legend: ✓ Match (score >= 0.9) ✗ No match (score < 0.9): possibly still relevant for low tumor content and low DNA quality cases.

MGMT promotor status prediction



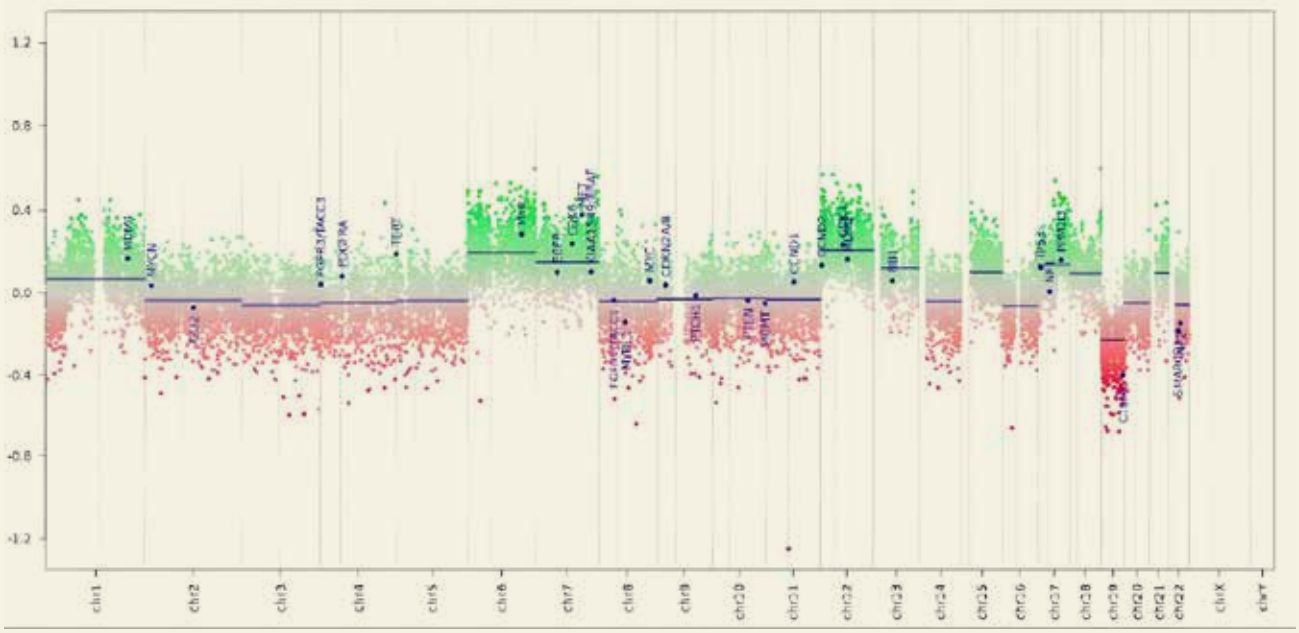
Score (red line cutoff=0.3582)

Status	Estimated	CI lower	CI upper
unmethylated	0.01164	0.00138	0.09105

Class Descriptions

MC Pilocytic astrocytoma, midline: The “msc Supratentorial midline pilocytic astrocytoma” represents pilocytic astrocytoma and can also comprise tumors previously designated as pilomyxoid astrocytoma. They are located in supratentorial midline structures (thalamus, optic pathway, 3rd ventricle). These tumours typically carry MAPK pathway alterations, most commonly KIAA1549:BRAF fusion, but also some others (for example FGFR1 mutation is recurrently observed in this class and NF1-associated OPGs typically belong to this category). In case of high quality data the BRAF duplication can be appreciated on chromosome 7q (present in more than 60% of the reference cases). Besides this, most cases show a flat profile in copy number analysis.

Copy Number Profile



Methylation classification report (NIH report)

Top Hit Classifiers Results

	Best.match	Scores	Comment
Family	Neuroblastic_embryo-nal_tumors	0.993	Matched
Class	MB_SHH_1	0.969	Matched

MGMT Status

Promoter Status	Status	Pred
MGMT	Unmethylated	0.00941708241639341

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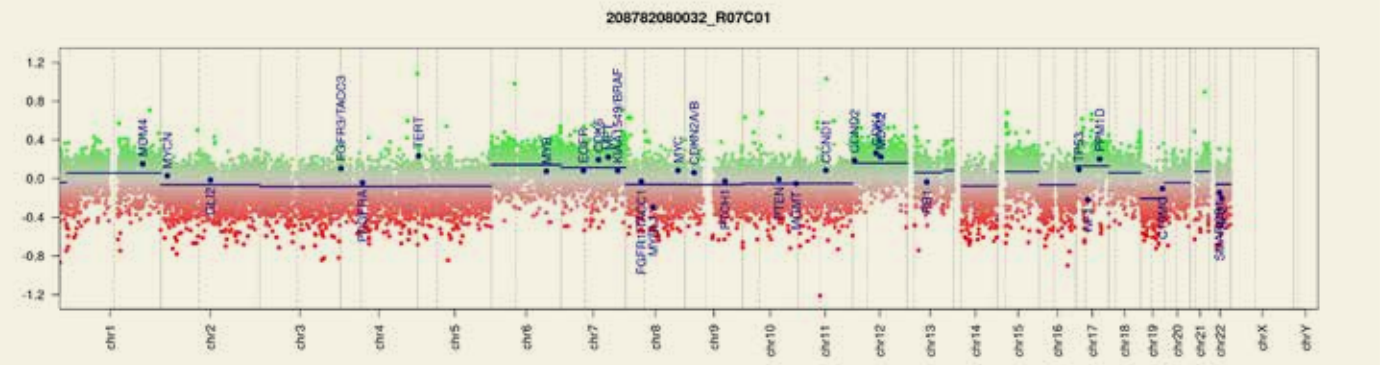
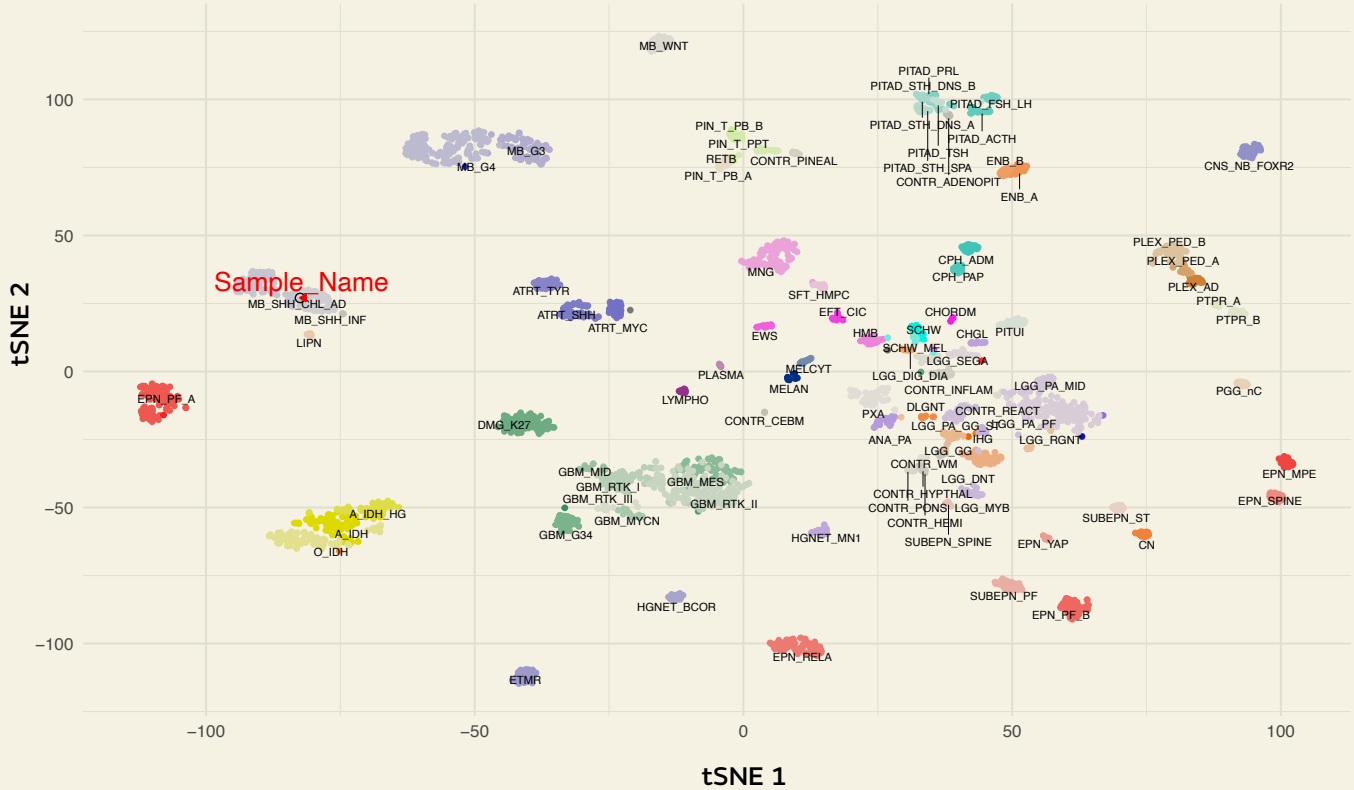


UMAP of the reference dataset used for training eNeural network model for the Bethesda classifier



PUBLICATION HIGHLIGHT 2024

In September 2024, the team published in Frontiers Genetics a collaboration between Ospedale Centrale Bolzano in Italy, Hamad Bin Khalifa University, Qatar and Queen Mary University, UK.

Multi-omic analysis of longitudinal acute myeloid leukemia patient samples reveals potential prognostic markers linked to disease progression

Relapse remains a determinant of treatment failure and contributes significantly to mortality in acute myeloid leukemia (AML) patients. Despite efforts to understand AML progression and relapse mechanisms, findings on acquired gene mutations in relapse vary, suggesting inherent genetic heterogeneity and emphasizing the role of epigenetic modifications. We conducted a multi-omic analysis using Omni-C, ATAC-seq, and RNA-seq on longitudinal samples from two adult AML patients at diagnosis and relapse. Herein, we characterized genetic and epigenetic changes in AML progression to elucidate the underlying mechanisms of relapse. Differential interaction analysis showed significant 3D chromatin landscape reorganization between relapse and diagnosis samples. Comparing global open chromatin profiles revealed that relapse samples had significantly fewer accessible chromatin regions than diagnosis samples. In addition, we discovered that relapse-related upregulation was achieved either by forming new active enhancer contacts or by losing interactions with poised enhancers/potential silencers. Altogether, our study highlights the impact of genetic and epigenetic changes on AML progression, underlining the importance of multi-omic approaches in understanding disease relapse mechanisms and guiding potential therapeutic interventions.

DOI: 10.3389/fgene.2024.1442539

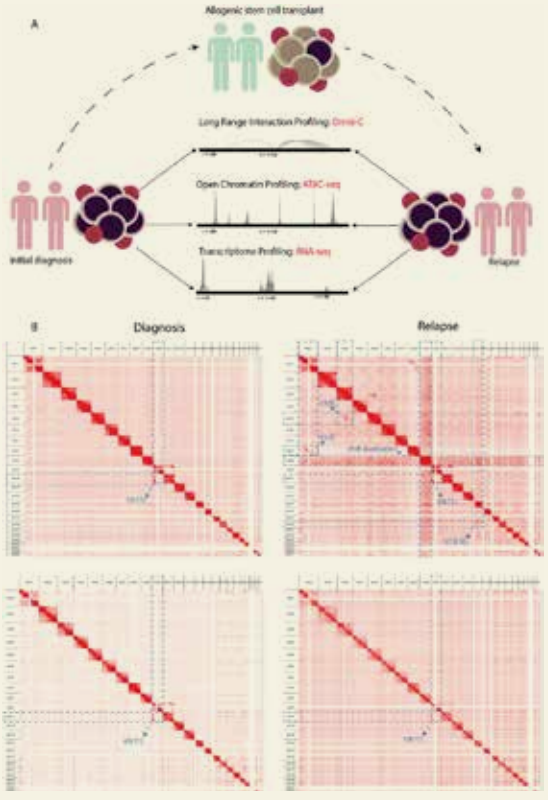
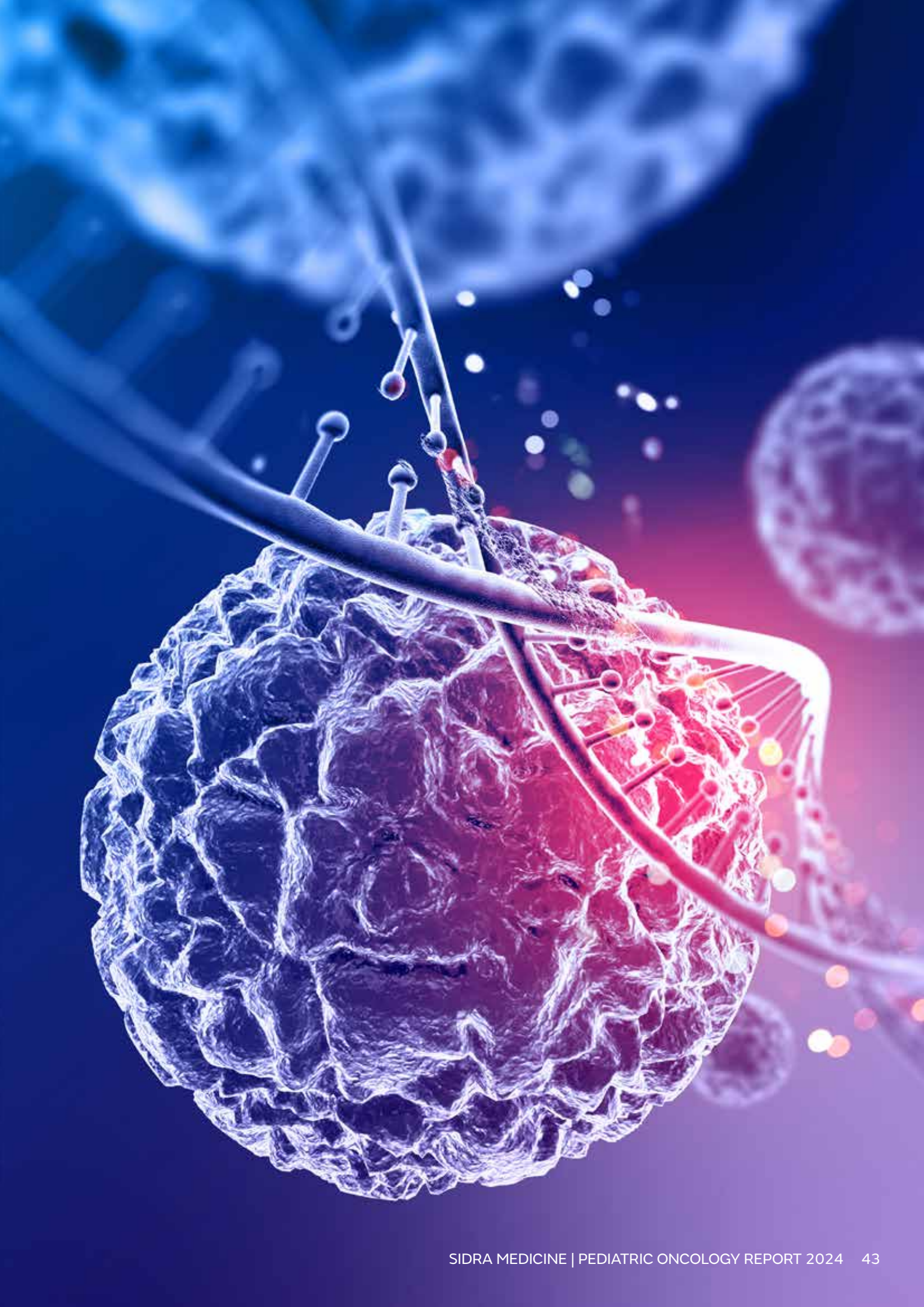
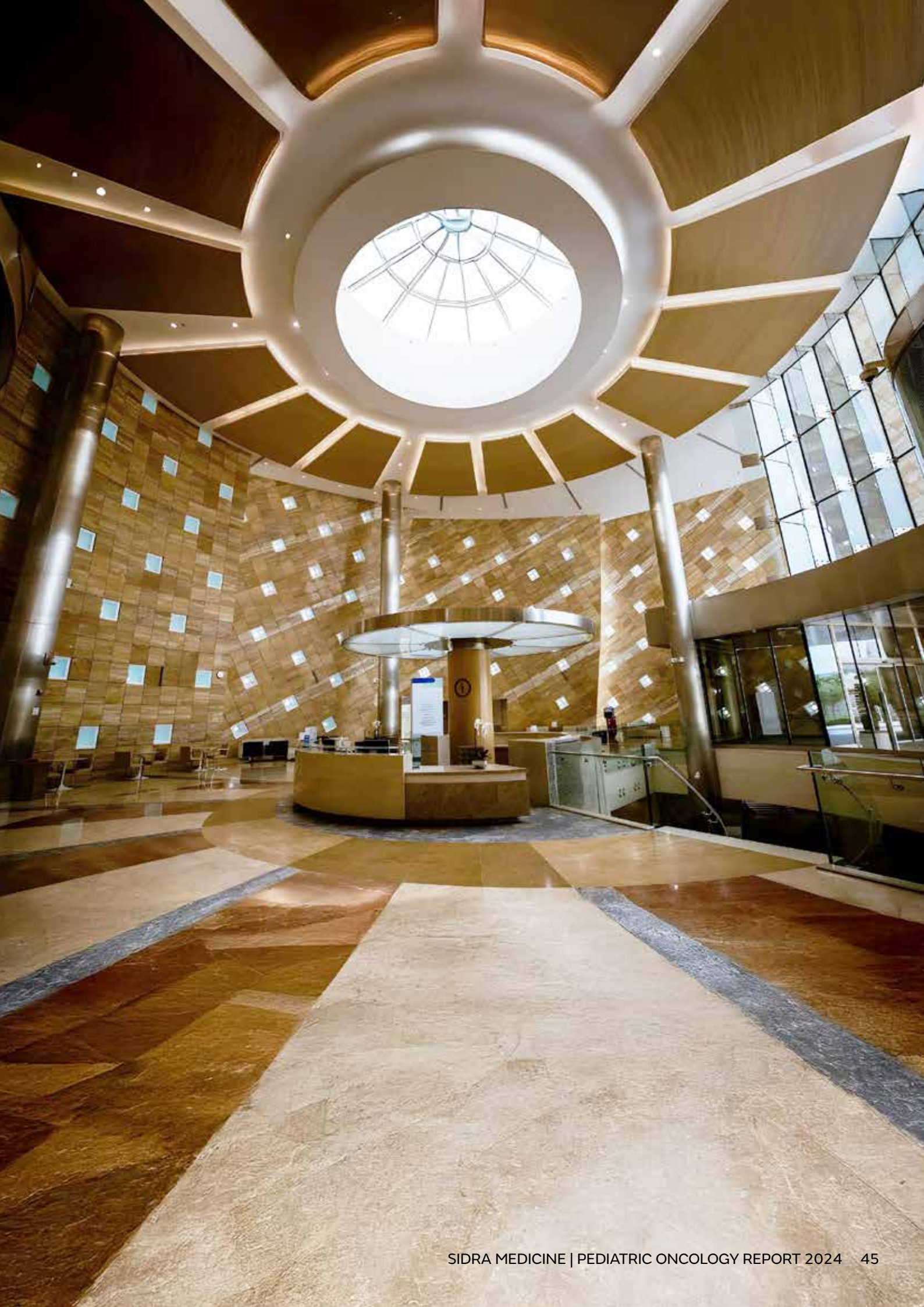


Figure 1. (A) Schematics showing the experimental workflow where PBMCs obtained from adult AML samples at initial diagnosis underwent NGS library preparation for Omni-C, ATAC-seq, and RNA-seq analyses. Subsequently, the same NGS libraries were prepared from samples upon relapse following allogenic stem cell transplantation. (B) Contact maps derived from the Omni-C dataset, depicting the chromosomal architecture of diagnosis samples (left) compared with relapse samples (right). The blue dotted lines show the chromosomal abnormalities each sample contains genome wide.



CANCER GRANT AWARDS

#	Funding	Awarded Year	Start Date	End Date	Awarding Institution	LPI	Title
1	GREX (External-International)	2024	14-Nov-24	14-May-26	Sidra Medicine	Sara Deola	Pre-clinical development and regulatory filing of Qatar's first CAR-T cell therapy.
2	IRF24 (Internal)	2024	3-Jul-24	2-Jul-25	Sidra Medicine	Erdener Ozer	Integrative Application of High-Resolution Single-Cell ATAC and RNA Sequencing in Clinical Decision-Making of Neuroblastoma Patients.
3	IRF24 (Internal)	2024	10-May-22	10-May-26	Sidra Medicine	Christophe Raynaud	Prognostic and Therapeutic Potential of SLFN11 in Pediatric Solid Tumors.
4	HSREP06-0429-240024 (External-QRDI)	2024	15-Jan-25	15-Jan-26	Sidra Medicine	Ajaz Bhat	Precision Attack: Targeting Glutaminase to Enhance Cisplatin Efficacy in Colorectal Cancer Treatment.
5	UREP31-181-1-037 (External-QRDI)	2024	15-Jan-25	15-Jan-26	Qatar University	Sahar Daas	Engineered Bioactive Peptides: An Alternative Therapeutic Approach for Colorectal Cancer Management.
6	ARG01-0507-230085 (External-QRDI)	2023	1-Apr-24	6-Nov-25	Sidra Medicine	Wouter Hendrickx	Recapitulation of the human microbiome risk score in mice to elucidate its mechanism of action.
7	ARG01-0516-230187 (External-QRDI)	2023	1-Apr-24	1-Apr-27	HBKU	Wouter Hendrickx	Towards better cancer care in pediatric oncology: exploring the biomarker and therapeutic potential of cancer testis antigens.
8	IRF22 (Internal)	2022	9-May-21	9-May-25	Sidra Medicine	Wouter Hendrickx	Implementation of Spatially Resolved Transcriptomics in Pediatric Brain Tumors: Toward Advanced Diagnostics Enabling Precision Immunotherapeutic Approaches.
9	IRF22 (Internal)	2022	1-Apr-22	31-Dec-25	Sidra Medicine	Wouter Hendrickx	Pediatric solid tumor heterogeneity and clinical impact by multi-regional NGS @ Sidra Medicine.
10	GSRA8-L-1-0506-21033 (External-QRDI)	2021	1-Sep-21	1-Jan-26	Sidra Medicine	Alex Issam Tout	Colorectal Cancer Stem Cells Immune Signature and Its Implications in Cancer Therapy.
11	PPM 05-0316-210001 (External-QRDI)	2021	12-Feb-23	12-Feb-27	Sidra Medicine	Wouter Hendrickx	Multiregional genomic sequencing of pediatric cancer patients from Qatar, solid tumor heterogeneity and clinical impact.
12	NPRP13S-0107-200023 (External-QRDI)-0107-200023 (External-QRDI)	2020	2-May-21	6-Nov-25	Sidra Medicine	Sara Deola	Mapping the road of GVHD and GVT. Multicenter Prospective Study of the "Transcriptome Fingerprinting" Post Allogeneic Hematopoietic Stem Cell Transplantation Using System Immunology Approach.
13	PPM 04-0128-200014 (External-QRDI)	2020	1-Jan-21	31-Mar-25	Sidra Medicine	Naima Al Mulla	Pharmacogenetics in childhood acute lymphoblastic leukemia: from variants identification to clinical implementation.



CANCER PUBLICATIONS LIST 2022 - 2024

Pediatric Cancer

Sherif S, Hendrickx WRL, Raynaud CM, Mifsud W, Bedognetti D, Maaz AUR.
Identification of an unusual combination of actionable mutations through genomic profiling in a child with an aggressive sarcoma.
Pediatric Blood & Cancer, 2024
PMID: 37845795

Vujanić GM, Graf N, D'Hooghe E, Pritchard-Jones K, Bergeron C, Tinteren HV, Furtwängler R, 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.
Pediatric Blood & Cancer, 2024
PMID: 38185745

Vujanić GM, Mifsud W.
Anaplasia in Wilms tumor: A critical review.
Pediatric Blood & Cancer, 2024
PMID: 38605554

Kiss R, Micsik T, Bedics G, Papp G, Csóka M, Jenővári Z, Szabó S, Tornóczki T, Vujanic G, Kuthi L.
Pediatric thyroid-like follicular renal cell carcinoma-a post-neuroblastoma case with comprehensive genomic profiling data.
Virchows Archiv, 2024
PMID: 38990362

Ahmed N, Cavattoni I, Villiers W, Cugno C, Deola S, Mifsud B.
Multi-omic analysis of longitudinal acute myeloid leukemia patient samples reveals potential prognostic markers linked to disease progression.
Frontiers in Genetics, 2024
PMID: 39399221

Shimaa Sherif, Wouter R. L. Hendrickx, Christophe Michel Raynaud, William Mifsud, Davide Bedognetti, Ata Ur Rehman Maaz
Identification of an unusual combination of actionable mutations through genomic profiling in a child with an aggressive sarcoma
Pediatric Blood & Cancer, 2023
PMID: 37845795

Muhammad Saghir Khan , Ata Ur Rehman Maaz , Abid Quddus Qazi , Sophia Aslam, Shazia Riaz , Ayesha Saeed Malik , Najma Shaheen
Prognostic impact of pre-referral tumor resection in unilateral Wilms tumor: A single-institute experience from a lower middle-income country
Pediatric Blood & Cancer, 2023
PMID: 37962283

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Histopathology, 2023
PMID: 38084641

Ellen D'Hooghe, Rhoikos Furtwängler, Tanzina Chowdhury, Christian Vokuhl, Reem Al-Saadi, Kathy Pritchard-Jones, Norbert Graf, Gordan M Vujanić
Stage I epithelial or stromal type Wilms tumors are low risk tumors: An analysis of patients treated on the SIOP-WT-2001 protocol in the UK-CCLG and GPOH studies (2001-2020).
Cancer, 2023
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Shimaa Sherif, Jessica Roelands, William Mifsud, Eiman I Ahmed, Christophe M Raynaud, Darawan Rinchai, Abbirami Sathappan, Ata Maaz, Ayman Saleh, Erdener Ozer, Khalid A Fakhro, Borbala Mifsud, Vésteinn Thorsson, Davide Bedognetti, Wouter R L Hendrickx
The immune landscape of solid pediatric tumors
Journal Of Experimental & Clinical Cancer Research, 2022
PMID35690832

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Characteristics and outcomes of preoperatively treated patients with anaplastic Wilms tumors registered in the UK SIOP-WT-2001 and IMPORT study cohorts (2002-2020)
Cancer, 2022
PMID35119702

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European Journal Of Cancer, 2022
PMID35255331

Vujanić GM, Parsons LN, D'Hooghe E, Treece AL, Collini P, Perlman EJ.
Pathology of Wilms' tumour in International Society of Paediatric Oncology (SIOP) and Children's oncology group (COG) renal tumour studies: Similarities and differences
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Bioinformatics Analysis Reveals FOXM1/BUB1B Signaling Pathway as a Key Target of Neosetophomone B in Human Leukemic Cells: A Gene Network-Based Microarray Analysis
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Renal cell carcinoma in children and adolescents: a retrospective study of a French-Italian series of 93 cases
Histopathology, 2022
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How we approach paediatric renal tumour core needle biopsy in the setting of preoperative chemotherapy: A Review from the SIOP Renal Tumour Study Group
Pediatric Blood & Cancer, 2022
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Journal Of Pediatric Hematology Oncology, 2022
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Anticancer activity of Neosetophomone B by targeting AKT/SKP2/MTH1 axis in leukemic cells
Biochemical And Biophysical Research Communications, 2022
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Cancer Immunology and Immunotheraphy

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Frontiers in Molecular Biosciences, 2024
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Location matters: spatial dynamics of tumor-infiltrating T cell subsets is prognostic in colon cancer.
Frontiers in Immunology, 2024
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Signal Transduction and Targeted Therapy, 2024
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Biomedicine & Pharmacotherapy, 2024
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Cureus, 2024
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Exploring the in vivo anti-cancer potential of Neosetophomone B in leukemic cells using a zebrafish xenograft model.

Experimental Cell Research, 2024
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Immunologic constant of rejection as a predictive biomarker of immune checkpoint inhibitors efficacy in non-small cell lung cancer.
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PMID: 37726776

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Stressed target cancer cells drive nongenetic reprogramming of CAR T cells and solid tumor microenvironment.
Nature Communications, 2023
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Small Methods, 2023
PMID: 37291737

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Molecular Cancer, 2023
PMID: 36717905

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Cureus, 2024
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Exploring the Role of microRNAs in Glioma Progression, Prognosis, and Therapeutic Strategies.
Cancers, 2023
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Metabolic and physiologic magnetic resonance imaging in distinguishing true progression from pseudoprogression in patients with glioblastoma
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Breast Cancer

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Cancer Cell International, 2023
PMID: 38001424

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Tyrosine kinase inhibitors and human epidermal growth factor receptor-2 positive breast cancer
World Journal of Clinical Oncology 2023
PMID: 37275938

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Clinical Breast Cancer, 2022
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Jco Precision Oncology, 2022
PMID: 34768233

Kannan S, Shailesh H, Mohamed H, Souchelnytskyi N, Souchelnytskyi S.
A long-term 10G-hypergravity exposure promotes cell-cell contacts and reduces adhesiveness to a substrate, migration, and invasiveness of MCF-7 human breast cancer cells.
Experimental Oncology, 2022
PMID: 35548967

Ovarian, Endometrial, and Cervical Cancer

Therachiyil L, Anand A, Azmi A, Bhat A, Korashy HM, Uddin S.
Role of RAS signaling in ovarian cancer
F100 Research, F1000 Research, 2022
PMID: 36451660

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Journal Of Translational Medicine, 2022
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Advances in Protein Chemistry and Structural Biology, 2022
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Other Cancers

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Journal of Translational Medicine, 2024
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Integrating network analysis with differential expression to uncover therapeutic and prognostic biomarkers in esophageal squamous cell carcinoma.
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Frontiers in Bioscience-Landmark, 2024
PMID: 38287817

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PMID: 38567100

Renal Tumour Study Group
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Diagnosis and management of neurofibromatosis type 1 in Arabian Gulf Cooperation Council Region: challenges and recommendations.
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