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RESEARCH ARTICLE

Challenges in Launching a Precision Pediatric Oncology Program in Argentina

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ABSTRACT

Background/Objectives: Advances in pediatric cancer care have underscored the importance of tumor sequencing for diagnosis and treatment selection. However, access to genomic diagnostics in Latin America remains limited. The COPPA Project, an initiative based in Argentina, was conceived to assess the feasibility of delivering clinically useful genomic sequencing for childhood cancers at no cost while maximizing the clinical value of genomic data through multidisciplinary molecular tumor boards (MTBs).

Design/Methods: Project planning involved securing funding, establishing a sequencing facility, selecting and optimizing an NGS panel, training technical staff in sequencing and interpretation, addressing sample transportation logistics, recruiting oncologists from multiple institutions, and promoting the establishment and participation in a virtual MTB. Tumors underwent sequencing using the Illumina Cancer Childhood Panel. Results were reported and discussed with the treating physicians and during MTB meetings. A survey was administered to MTB participants to assess perceived barriers and facilitators related to the project.

Results: A total of 38 tumors were analyzed, 24 of which were sequenced in-house. Genomic findings were considered to have clinical utility in 67% of cases. Barriers such as a low demand for studies and oncologists' lack of time for MTBs were identified. Survey responses highlighted the educational value of the MTBs, with all respondents reporting increased knowledge of precision medicine and greater motivation to adopt genomic testing in clinical practice.

Abbreviations: CCP, Illumina Cancer Childhood Panel; CNA, copy-number alteration; COPPA, Colaboración en Oncología Pediátrica de Precisión Argentina—Argentinian Collaboration on Precision Medicine for Pediatric Oncology; FFPE, formalin-fixed paraffin-embedded; Indel, short insertions and deletions; IRB, Institutional review board; LMIC, Low- and middle-income countries; MTB, molecular tumor board; NGS, next-generation sequencing; SNV, single-nucleotide variation; VAF, variant allelic frequency.

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Conclusion: This study identifies key barriers and facilitators encountered in a middle-income setting. These findings may inform future efforts to implement precision medicine approaches for pediatric cancer in the region.

1 | Introduction

Several initiatives have demonstrated the value of genomic sequencing for pediatric tumor characterization and treatment [1–5]. In Latin America, such efforts have been scarce, due mainly to a general lack of understanding of the value of genomic evidence among health professionals, and the high costs of reagents and equipment [6]. However, for optimizing the clinical management, pediatric tumor sequencing has proved to be of utmost importance in LMICs [7–9].

As opposed to adult cancers, pediatric tumors have shown a low mutation rate and a relatively higher proportion of driver chromosomal abnormalities (such as copy-number alterations and fusions) [10, 11]. Hence, a comprehensive, three-platform, next-generation sequencing (NGS) approach that integrates whole-genome, whole-exome, and RNA sequencing has been proposed as the gold standard for clinical use [2]. However, this approach is costly and requires a team of several specialists to analyze and timely interpret their results, which are seldom available in low- and middle-income countries (LMIC) [12]. In these settings, small NGS panels focused on actionable findings [13, 14] may be an alternative to replace more costly options [15]. In Mexico, a pilot experience showed successful NGS testing at INMEGEN using a locally developed 200-gene panel [16]. In Malawi, a panel run in the NanoString nCounter system provided clinically important diagnostic information [17]. Additionally, the Make-an-IMPACT philanthropic effort has enabled genomics diagnosis in 11 LMIC, but with no local implementation actions [18]. In all these experiences, international partnerships consistently emerged as critical enablers, showing that fully local initiatives are still difficult to carry out.

In spite of the advantages of using genomic sequencing, the absence of genomics-oriented curricula in medical education has been recognized as a widespread barrier to its adoption, with LMICs showing a pronounced lag in this regard [19, 20]. Evidence has shown that multidisciplinary molecular tumor boards (MTBs) could be an educational tool for oncologists to gain a proper understanding of the clinical utility of genomic information [21]. To set up the basis for promoting the inclusion of genomic sequencing in the clinical management of pediatric tumors in Argentina, we established the COPPA Project (Argentinian Collaboration on Precision Medicine for Pediatric Oncology). The COPPA Project was built on three pillars: first, building and sustaining a community of experts in different disciplines related to the clinical use of sequencing information for childhood cancer. Second, reducing access barriers by securing (a) a proper infrastructure and expertise for genomic sequencing, (b) a low-cost approach (i.e., NGS panel instead of multiomics) that could be offered at no cost to the patients with a reasonable clinical utility, and (c) logistic resources for samples coming from different parts of the country. The third pillar addressed the uncertainties of oncologists regarding the clinical use of genomic information by means of an MTB-mediated educational approach.

2 | Methods

2.1 | Planning and Building the COPPA Project

A multidisciplinary team with established experience in collaborative translational research oversaw the management of the COPPA Project. Planning involved seven key factors: (1) setting up the project as a translational research project to secure funding, (2) setting up a sequencing facility, (3) selecting and optimizing the use of a NGS panel, (4) training the technical staff in NGS sequencing and interpretation, (5) solving sample transportation logistics, (6) inviting pediatric oncologists from different hospitals for participation in the project, and (7) promoting the constitution and attendance of a virtual molecular tumor board among the participating oncologists and other health professionals.

The COPPA core group included two basic researchers and two bioinformaticians from a national research institute and three pediatric oncologists, a pathologist, and a geneticist from a university hospital. A dedicated doctoral fellow was recruited. A partnership with Natalie Dafne Flexer Foundation (FNDF), a patient advocacy group, was established that provided access to funding and support for the logistics of sample arrival to the sequencing center.

The COPPA core group established a collaboration with St Jude's Children Research Hospital (Memphis) and Sant Joan de Déu Hospital (Barcelona) for training of one bioinformatician in NGS sequencing analysis and interpretation.

A call for participation was issued to members of seven different hospitals and health institutions. Although oncologists from five institutions joined the project, the two major national referral centers, which together manage about one third of Argentine pediatric oncology patients, decided not to participate in the program and developed their own internal programs.

The core group was first awarded a national public competitive grant that secured funding for setting up the sequencing facility. An Illumina NextSeq 550 equipment was set up at Instituto de Investigaciones en Medicina Traslacional (IIMT), a unit based at Hospital Universitario Austral (HUA), a not-for-profit university hospital in Buenos Aires province of Argentina. Later on, the group, along with FNDF, was awarded an international innovation prize that helped launch the sequencing service. With this funding, we were able to run the pilot sequencing cases that are described in this manuscript, so that the cost barrier was not an issue.

Guidelines for specimen procurement were established so that the obtained material presented the necessary quality standards. Infographics about sample handling procedures were delivered to the participating hospitals. Participants were trained for the collection of fresh specimens if necessary.

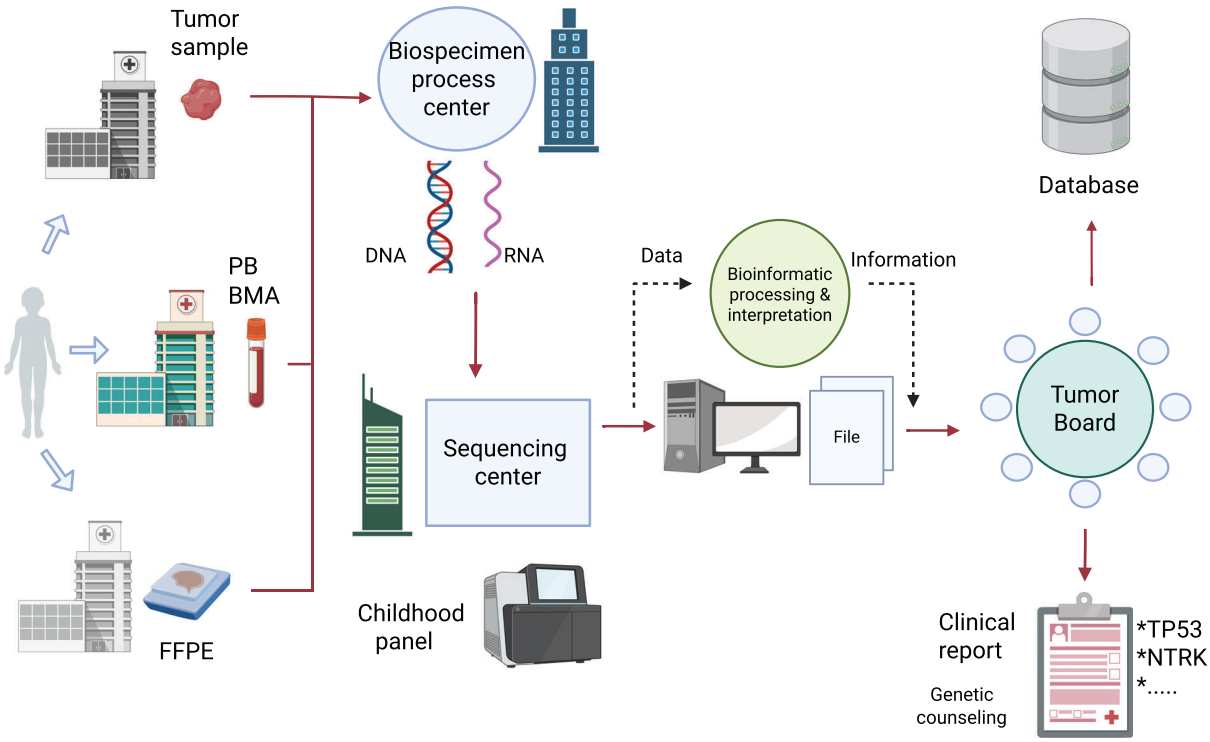

FIGURE 1 | Schematics of the project setup. Different types of samples were collected from the affiliated hospitals and carried to the processing center, producing targeted panel libraries from QC-verified extracted DNA and RNA. Libraries were sequenced in an Illumina NextSeq550. Raw sequencing data were processed with the vendor's dedicated pipeline, and variant calling and interpretation were performed. Manually curated variants were discussed in a molecular tumor board and/or with the attending physician. Clinical reports were elaborated afterward, and the treating oncologist (in collaboration with a genetic counselor whenever necessary) advised the patient about further therapeutic decisions. BMA: bone marrow aspirate; PB: peripheral blood; FFPE: formalin-fixed paraffin-embedded tissue. Figure created with BioRender.com.

The COPPA objectives were promoted in different instances, including presentations in hospital seminars, course classes promoted by the pharmaceutical industry, tumor symposiums, national, and international congresses, and in informal conversations with different actors involved in pediatric cancer care.

Figure 1 illustrates the workflow for receiving and processing samples, the interpretation of sequencing results, and the discussion of the findings in the context of the COPPA MTB. For the inclusion of patients, the COPPA team adopted a passive role, awaiting contact from interested physicians who initiated requests for genomic sequencing on behalf of their patients. Once the case was deemed eligible, the participating physician took care of the patient recruitment while the COPPA team handled the logistics of sample collection, transport, and reception with the help of FNDF. In parallel, at the beginning of 2022, the core group issued an open invitation to a broad community of pediatric oncologists from the region (i.e., Argentina, Chile, Uruguay, and Brazil) to discuss any challenging tumor cases with available molecular information (being or not sequenced by COPPA) in a virtual molecular tumor board, the COPPA MTB. Each COPPA MTB was held every 1 or 2 months, lasting approximately an hour. If an oncologist wanted to participate, the case was assigned to a specific session, ensuring that no more than two cases were discussed per session. The genomic and molecular findings (either from COPPA sequencing or from external sources) were analyzed in the context of the disease by the core group.

2.2 | Patient Inclusion Criteria for the COPPA Project

The COPPA protocol was approved by the HUA institutional review board in February 2022 under the number P22-002. No clinical study registration number was assigned to this study. The first specimen for study was received in April 2022. Exclusion criteria for this study included age over 18 years, lack of availability of biospecimens for diagnosis, and lack of written informed consent.

2.3 | Sequencing Approach

Tumor-derived nucleic acids were sequenced using the Illumina Ampliseq Childhood Cancer Panel. This hybrid panel (DNA and RNA) includes the analysis of single-nucleotide variants (SNVs), insertions/deletions (indels) for 186 genes, copy-number aberrations (CNAs) for 23 genes, and fusions for 92 genes. Our approach allowed running 24 samples per flowcell, which was considered a low-enough cost alternative in our local setting.

Genetic material (DNA and RNA) was processed as described in detail in Supplementary Materials. Quality control steps included the use of Horizon reference standards for sensibility and sensitivity analysis (https://horizondiscovery.com/; Supplementary Materials). Variant interpretation was manually performed with the help of online classification tools and databases and the available bibliography at the moment (see Supplementary Materials for details). Standard operating procedures describing all the

processes involved in sample processing at the sequencing center were carefully followed, and the variant interpretation process was detailed in every report issued to the attending oncologist.

2.4 | Report of the Information to the Attending Oncologists

For COPPA-sequenced cases, the generated report was discussed in the context of the pathology in a virtual or in-person meeting with the treating oncologist. The actual clinical utility, defined as "the ability to confirm or improve diagnosis, prognosis or risk classification, define or confirm treatment, or suggest the need for genetic counseling" [22, 23], was identified at those meetings. After that discussion, the physician was invited to present the case in the MTB, which the physician could accept or not. The treating oncologist communicated the results and treatment plan to the families with the support of a genetic counselor if appropriate.

2.5 | Survey Data Collection

Approximately 2 years after the COPPA Project initiation, we conducted an anonymous self-administered survey using an open-ended questionnaire. This survey explored different dimensions related to the barriers and facilitators addressed by the COPPA Project, including the accessibility to genomic testing prior to the project being established, the perceived advantages of and barriers to participation in the MTBs, and the potential improvements to ensure sustainability of the program. Eligibility for this survey was that the physician attended MTBs for more than 2 sessions and presented at least one case in the MTB. Most questions presented a preselected response option and one free-text field (i.e., "Other") to record options that were not among the preselected. In all of these questions, respondents could select more than one option. Results are presented with descriptive analysis as frequencies. Free text responses were analyzed with a qualitative approach using thematic analysis to identify physicians' perceptions regarding the COPPA Project.

2.6 | Ethical Statement

Written informed consent for the use of genomic and clinical information was obtained from the patient's legal guardians and appropriately documented. All procedures were conducted in accordance with established ethical standards for research involving human subjects, ensuring the protection of patient privacy and confidentiality.

3 | Results

3.1 | Case Selection

From April 2022 to December 2024, five oncologists presented 29 eligible pediatric patients with cancer for enrollment in the COPPA Project. Twenty-eight patients and their families (96.6%) agreed to participate and signed a written informed consent; 1 (3.5%) declined. From the 28 recruited cases, we could not retrieve DNA or RNA from the available specimens in four cases, leaving 24 cases for analysis.

In addition to cases sequenced by the COPPA Project, 14 cases coming from external diagnostic or sequencing services were discussed in the COPPA MTB. A summary of the 38 cases analyzed in the context of this initiative, both internally and externally analyzed, is presented in Figure 2.

3.2 | Clinical Utility of the COPPA Sequencing Approach

Mutations, including SNVs, indels, CNAs, and/or gene fusions, were detected in 88% of the tumors internally sequenced by COPPA (21/24 cases). The summary of the sequencing results, along with the complementarity with other findings and the resulting clinical utility, is shown in Table 1. As expected, according to the pathologies registered, MYC/MYCN amplification and TP53 mutations were the most represented, with a prevalence of 25% and 13%, respectively (Supplementary Figure S1). The heterogeneity of the type of tumors studied makes it difficult to define the overall diagnostic yield, as different types of alterations were expected in different tumors. Of the 24 cases, 9 were considered to have undergone complete analysis. In 9 additional cases, partial findings complemented other studies, enabling an adequate diagnosis. Three of the 24 cases lacked detectable mutations in the genes covered by the panel, and the other three presented findings that were neither actionable nor clarified the molecular diagnosis (Table 1).

According to the extended definition mentioned in Methods, clinical utility was demonstrated in 67% (16/24) of the internally sequenced and 93% (13/14) of the externally analyzed cases (Table 1). In 9 out of 38 total cases, no additional clinical applicability was found (Table 1). Most studied cases involved solid tumors where the available pathological studies were insufficient to classify the tumor, and in many of those, the NGS results provided information about the molecular characteristics of the disease. Evidence of therapeutic actionability was more limited because of the scarcity of targeted/specific treatment for the mutations found and the lack of available clinical trials in our setting. The following are examples of different clinical uses of alterations found: PO93, a case of B-cell acute lymphoblastic leukemia, confirmed the coexistence of a JAK2 mutation with a P2RY8::CRLF2 fusion, which validated the use of ruxolitinib as a targeted therapy. In case RC76, an angiomatoid fibrous histiocytoma, the detection of the EWSR1::CREB1 fusion supported the final differential diagnosis from other sarcomas. Case DL13 revealed DICER1 biallelic mutations, broadly described in pleuropulmonary blastoma, aiding the differential diagnosis, and strongly indicating the need for genetic counseling.

3.3 | Clinical Utility in the Context of the COPPA Virtual MTB: Understanding the Role of Molecular Findings

A total of 24 MTB sessions were held between January 2022 and May 2025. Forty-seven medical professionals from more

TABLE 1 | Detailed description of cases analyzed by COPPA sequencing and external cases presented in MTB.

Patient ID	Tumor	Reportable findings	Clinical yield[#]	Clinical utility (if any)
Patients sequenced by COPPA (ID)				
QP34	Relapsed B-cell acute lymphoblastic leukemia (B-ALL)	CCDC6::RET fusion	C	Novel description of the association of this mutation with ALL refractory to standard treatments—crizotinib considered as compassionate use. No BCR::ABL, TEL::AML1, KMT2A, or E2A alterations detected by FISH.
RC76	**Angiomatoid fibrous histiocytoma (AFH)**	EWSR1::CREB1 fusion TPMT polymorphism	C	Supported the final differential diagnosis from other sarcomas. EWSR1 rearrangement confirmed by FISH.
VT33	**Neuroblastoma**	PTPN11 Glu69Lys	P	Redefined the risk of the underlying disease. Genetic counseling advised (Noonan syndrome). Deletion of the 1p36 region detected by other methodologies. Deletion for the 11q region and MYCN amplification not detected.
ON67	**Hepatoblastoma**	CTNNB1 Ile35Ser Chromosome 1q gain	P	Supported diagnosis (consistent with the clinical evolution). Beta-catenin is positive in the membrane and the nucleus by immunostaining.
PO93[##]	**Relapsed B-cell acute lymphoblastic leukemia**	P2RY8::CRLF2 fusion JAK2 Arg683Gly KMT2D Glu2678fsTer14	C	Validated the use of ruxolitinib as a target therapy together with immunotherapy, allowing disease control and prolonged disease-free survival. Rearrangement of CRLF2 and deletion of P2RY8, suggesting P2RY8::CRLF2 fusion confirmed by FISH.
DL13	**Pleuropulmonary blastoma**	TP53 Val122fs DICER1 Ile582LeufsTer5 DICER1 Glu1705Val Chromosome 8 gain TP53 LOH	C	Supported differential diagnosis and indicated the need for confirmation of the germline mutation and genetic counseling (DICER1 syndrome). Patient progressed rapidly and died.
ZL69	**Renal cell carcinoma**	FBXW7 Arg479Pro CDKN2A c.-34G>T TP35 Arg175His	P	Unusual genomic findings for this entity—Genetic counseling advised for DEDHIL, Li–Fraumeni, melanoma predisposition, melanoma-pancreatic cancer, and melanoma-neural system tumor syndromes. ALK and TFE3 rearrangement not detected by FISH.
EO28	Acute myeloid leukemia	NRAS Gly12Ala	P	Although RNA could not be studied by NGS, the association with KMT2A/ELL detected from another study defined consolidation with allogeneic bone marrow transplant in first remission.
JF85	Relapsed chondrosarcoma	None	N	No NGS findings. A 22q12 rearrangement involving the EWSR1 gene was detected by another methodology. No independent IDH analysis was reported.

(Continues)

TABLE 1 | (Continued)

Patient ID	Tumor	Reportable findings	Clinical yield[#]	Clinical utility (if any)
TM77	High-grade undifferentiated neoplasia	MYC gain	I	Patient progressed rapidly and died. EWSR1 and SYT rearrangement not detected by FISH.
GU72	Gastrointestinal clear cell sarcoma	PTEN Thr319_Leu320delinsTer	P	Redefined prognosis.
AI69	Inflammatory myofibroblastic tumor	ARID1B Gln195ProfsTer67 ATRX Lys1408GlufsTer13	P	No actionable mutations. Dot patterns in IHC suggested an ALK alteration. RNA could not be studied by NGS.
QV48	Neuroblastoma	MYCN amplification	C	Allowed better risk stratification. MYCN amplification confirmed by FISH.
YI23	Infant fibrosarcoma	PHF6 Cys28TrpfsTer7 SMARCA4 Thr910Met TPMT polymorphism MYCN gain Chromosome 8q gain	P	Sequencing did not add clinical utility to the ETV6 rearrangement detected by another methodology. RNA could not be studied by NGS.
LW63	**B-cell acute lymphoblastic leukemia**	NRAS Gln61Leu KRAS Gly13Asp	C	Explained the high-risk clinical behavior of this patient. Genetic counseling advised (Noonan and Cardiofaciocutaneous syndrome). No BCR::ABL, KMT2A, TEL:: AML1, cMYC, TCF3, P2RY8::CFRL2, ERG alterations were detected by FISH.
SY60	**Relapsed B-cell acute lymphoblastic leukemia**	NSD2 Glu1099Lys TCF3::PBX1 fusion TPM3::ROS1 fusion KIF5B::ALK fusion	C	Novel description of the association of this mutation with ALL refractory to standard treatments—crizotinib considered as compassionate use. Rearrangement of the TCF3 gene confirmed by other methodology.
SS50	Gliosarcoma	No	N	No findings. H3K27 not altered and BRAFV600E not detected by IHC.
JD80	Neuroblastoma	MYCN amplification TPMT polymorphism	C	Allowed better risk stratification. MYCN amplification confirmed by other methodology.
QF89	Medulloblastoma	Possible MYCN gain	I	Confirmation with another method was suggested due to a low-quality call. No MYCN amplification by CISH (2-6 signals per nucleus).
QS55	Neuroblastoma	MYCN gain	I	Feature of uncertain significance in the context of the pathology. No MYCN amplification detected by CISH.
DV56	**Fusocellular high-grade sarcoma**	PTEN p.Val175Met TP53 p.Cys141Tyr PTEN p.Pro96Leu	P	Confirmed a poor outcome scenario and helped to consider palliative therapy in the face of refractoriness. Genetic counseling advised (Li–Fraumeni syndrome).

(Continues)

TABLE 1 | (Continued)

Patient ID	Tumor	Reportable findings	Clinical yield[#]	Clinical utility (if any)
DR80	Inflammatory myofibroblastic tumor	No	N	No findings—ALK alterations had been ruled out by another methodology.
GZ74	**Wilms tumor**	WT1:c.1447+1G>A	C	Genetic counseling advised (Frasier syndrome). Suggested follow-up for patients with a predisposition to cancer.
MF90	**Angioimmunoblastic T-cell lymphoma**	SMARCA4 Glu579Argfs*34 TET2 Gln860*	P	Confirmed a poor outcome scenario. The patient was offered enrollment in a clinical trial. ALK alterations had been ruled out by another methodology.
Patients externally sequenced and presented in MTB				
MTB 1	Wilms tumor	TP53 Ser106fs*1	N/A	Genetic counseling advised. The patient rapidly progressed and died.
MTB 2	Gastrointestinal stromal tumor (GIST)	KIT Lys558delinsAsnPro SETD2 Gln7*	N/A	Guided oncologic management and follow-up.
MTB 3	Ewing-like sarcoma	CDKN2A/B CDKN2A loss CDKN2B loss	N/A	Feature of uncertain significance in the context of the pathology. BCOR rearrangement detected by immunostaining and ETV6 rearrangement ruled out by FISH.
MTB 4	Fusocellular undifferentiated high-grade sarcoma	TP53 Pro153fs*28	N/A	Genetic counseling advised. Tested for TP53 germline status with negative results. No changes in treatment.
MTB 5	Primitive myxoid mesenchymal tumor of infancy (PMMTI)	BCOR Pro1712_Ser1713ins22 (ITD)	N/A	Allowed better risk stratification. Chemotherapy was adapted to prognostic implications.
MTB 6	Neuroblastoma	ALK Phe1174Val PIK3CA Glu545Lys MYCN amplification NTRK1 amplification, rearrangement intron 1 CREBBP duplication exons 4–10 ERBB4 Asn1224Lys PTPN11 Asp61Gly SRC Glu527Lys	N/A	Validated the use of ALK inhibitors. However, the patient rapidly progressed and died.
MTB 7	Inflammatory myofibroblastic tumor	ROS1 fusion	N/A	Validated the use of crizotinib as a target therapy, allowing disease control and prolonged disease-free survival. ALK alterations and ETV6-NTRK3 ruled out by PCR.

(Continues)

TABLE 1 | (Continued)

Patient ID	Tumor	Reportable findings	Clinical yield[#]	Clinical utility (if any)
MTB 8[##]	Relapsed Ewing-like sarcoma	BCOR rearrangement	N/A	Confirmed diagnosis. ALK and ROS1 rearrangement not detected by RT-PCR.
MTB 8bis		Polymorphisms with no clinical impact	N/A	New relapse—no actionable mutations.
MTB 9	Post-radiation high-grade glioma	MUTYH Gly382Asp PDGFRA amplification PTPN11 Asn58Lys FGFR4 Arg78His	N/A	Enrolled in a clinical trial for the FGFR4 Arg78His mutation but patient progressed rapidly and died. Alterations in H3K27M and IDH ruled out by immunohistochemistry. Family genetic counseling recommended because of the risk of colorectal cancer.
MTB 10	Primitive myxoid mesenchymal tumor of infancy	BCOR *1722Leuext*33 (ITD)	N/A	Confirmed diagnosis. Allowed better risk stratification.
MTB 11	Secretory carcinoma of the breast	ETV6::NTRK3 fusion	N/A	Validated the putative use of TRK inhibitors in case of disease recurrence.
MTB 12	Peritoneal mesothelioma	SQSTM1::ALK fusion	N/A	Validated the putative use of ALK inhibitors in case of disease recurrence.
MTB 13	B-cell acute lymphoblastic leukemia	IKZF1 and PAX5 deletion PSMB5, DICER1 and AKT1 one copy gain	N/A	Allowed better molecular classification and risk stratification.
MTB 14	Sclerosing epithelioid fibrosarcoma	EWSR1::CREB3L1 fusion TP53 Arg248Gln	N/A	Supported correct diagnosis and therapeutic decision. Currently under active follow-up.

COPPA sequenced cases presented in MTB are highlighted in bold. IHC, immunohistochemistry.

[#]Clinical yield of COPPA sequencing. C: the results of the sequence represented a complete genomic characterization of the sample; P: sequencing only yielded partial genomic information, although in many cases, it got complemented by other molecular findings to provide a complete characterization of the tumor; I: insufficient (findings neither were actionable nor clarified the molecular diagnosis); N: no findings. The externally studied cases of the MTB were not assessed for clinical yield and were labeled "not applicable" (N/A).

Presented on two occasions in MTB.

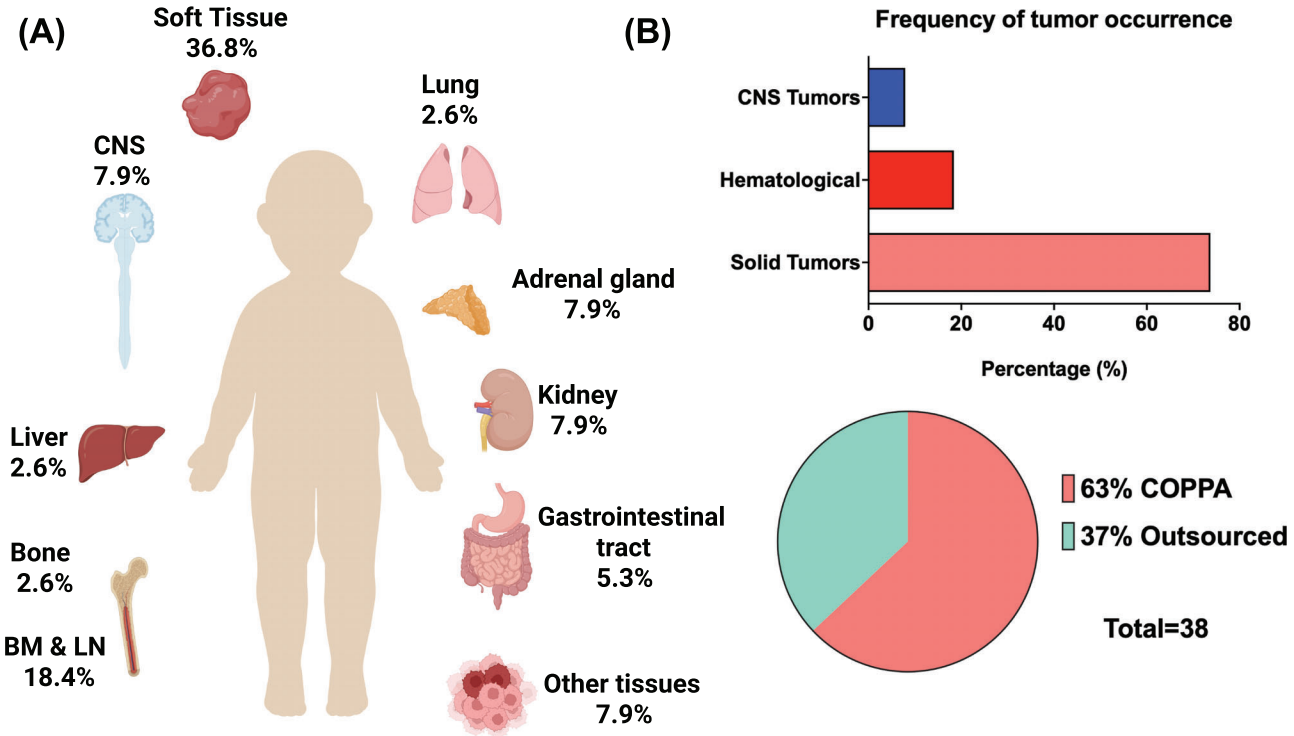

FIGURE 2 | (A) Distribution by tumor localization of the cases included in the study cohort, both externally ($n = 14$) and internally ($n = 24$) analyzed. (B) Summary of main tumor categories included in this study. (C) Source of molecular studies used in the study cohort. Internal sequencing was performed in our facilities with the Illumina Childhood Cancer Panel (COPPA); the rest of the cases were analyzed by different commercial companies, including regional providers. CNS: central nervous system, BM: bone marrow, LN: Lymph nodes. Figure created with BioRender.com.

than 10 institutions were invited to participate in the MTB, and a total of 20 attended at least one MTB meeting. Each session was attended by between 8 and 20 participants. Eighteen (38%) attended the MTB regularly, being 78% oncologists and hemato-oncologists, representative of more than 5 institutions, and 22% pathologists; 10 of these regular attendees presented at least one case. Even though this was initially considered a local project limited to Argentina, the COPPA virtual MTB attracted other groups in Latin America that were also starting their sequencing projects. Hence, colleagues from Brazil, Chile, and Uruguay also joined these virtual sessions. A total of 25 cases were presented (including 11 COPPA cases and 14 with molecular information from other sources) (Table 1). For the COPPA cases, the recommendation given in the MTB was included in the final report.

In terms of the MTB clinical utility, the interaction between the COPPA team and the attending doctors allowed to either confirm or improve diagnosis, prognosis, or risk classification in 39% of the cases (15/38), and in 42% (16/38) allowed to define or confirm treatment and/or follow-up. In 26% of the patients (10/38), genetic counseling was advised (Table 1).

3.4 | Barriers Detected During the COPPA Project

The number of sequencing requests (29 cases over the 34-month period from initial protocol activation to project completion) was substantially lower than anticipated. Over the course of the COPPA Project, we empirically identified several reasons, including institutional constraints that limited participation in a research-based protocol, physician reluctance to refer patients in the absence of clear expectations regarding clinical utility, and competing demands for tumor samples, which in some instances were prioritized for additional testing at reference pathology laboratories. Because sequencing costs were optimized for batches of 24 samples, the intention to accumulate a sufficient number of cases before initiating a sequencing run led to prolonged turnaround times, ranging from 1 to 7 months, with one outlier case delayed by 13 months. Ultimately, four sequencing runs were performed well below capacity, resulting in increased per-sample costs and reduced capacity for timely clinical intervention.

Technical barriers also impacted the project's success. Although not frequent, suboptimal pathology workflows in some institutions—stemming from limited personnel and inadequate equipment—compromised DNA/RNA quality, reducing sequencing success rates (see Supplementary Information for details).

Human resource retention poses another systemic challenge: specialists trained in molecular interpretation require long preparation periods but are difficult to retain due to unfavorable working conditions in the public health sector, prompting migration to the private sector or abroad.

3.5 | Analysis of the Perceptions and Opinions of the MTB Attendants Towards the COPPA Project

Ten participants were invited to respond to the self-administered questionnaire, and the response rate was 80%. Regarding the

accessibility of genomic testing prior to the COPPA Project, respondents referred to various, concomitant barriers that hindered the adoption of genomic testing: two of 8 (25%) reported not knowing where to send samples for analysis; 3 of 8 (38%) described difficulties or delays in obtaining or shipping samples, and half of them reported conflicts with other institutions over sample availability. Three of 8 (38%) indicated a lack of financial resources to perform genomic testing, and 1 of 8 (13%) stated not knowing how to select the most appropriate study. Regarding the impacts of introducing the COPPA program, we first interrogated whether participants encountered barriers in sending the sample for analysis, to which all participants responded "No." Regarding advantages/improvements derived from participation in the MTB, all respondents (100%) considered that the MTB increased their knowledge of precision medicine and encouraged the adoption of genomic testing. Seven of 8 (88%) reported "learned to interpret variants in a tumor context," 5 of 8 (63%) "learned about the existence of different molecular analysis," 5 of 8 (63%) "learned about the utility of the used methodologies," 6 of 8 (75%) "learned about the limitations of the used technologies," and 6 of 8 (75%) "learned about the evaluation of potential germinal variants in the context of a tumor sequencing." Among the difficulties that arose during the implementation of the COPPA Project, we detected a decrease in attendance over time. We therefore asked specifically about the perceived barriers to participation. Six of 8 (75%) cited inconvenient meeting times, 2 of 8 (25%) reported work overload and lack of protected time, 1 of 8 (13%) indicated difficulty actively participating when both solid and hematologic tumors were discussed, 1 of 8 (13%) reported challenges understanding the molecular discussion, and 1 of 8 (13%) mentioned the existence of other competing tumor boards or seminars. All respondents expressed willingness to continue attending, either always (5 of 8, 63%) or sometimes (3 of 8, 38%); none selected "never." Open-ended comments highlighted strong support for continuing the MTB, including: "I hope the MTB continues," "they are very useful," and "they should continue, as they greatly help professionals working in remote regions." Participants' suggestions for future planning included improving meeting times, providing more technical explanations of molecular tests during presentations, sending the case notes in advance for analysis, and exploring the possibility of conducting molecular studies in other countries.

4 | Discussion

While several precision medicine programs have been developed for pediatric patients in developed countries [24], evidence on such programs in LMIC remains scarce. This study presents a pioneering, fully local initiative in Latin America to promote the adoption of genomic testing for pediatric cancer in Argentina. To our knowledge, no reports of such initiatives in the region were published.

The COPPA Project's sequencing strategy successfully provided complete or partial molecular diagnoses for over two-thirds of patients, a performance comparable to high-income reference programs [3, 24]. However, low initial demand and the technical need to batch samples for cost-efficiency hindered timely clinical use. These challenges underscore the need of testing other technical alternatives that, for example, might not be affected by the number of cases available for sequencing, such as Nanopore-based sequencing [25]. If these low-cost approaches are optimized, the "no-cost-to-the-patient" model could remain sustainable beyond research-based funding through targeted fundraising.

The COPPA Project also generated insights into barriers and facilitators that might affect both the adoption and sustainability of this strategy. A primary facilitator for adoption was the COPPA MTB. Its virtual modality reduced geographic and logistical barriers, fostering participation across Argentina and neighboring countries. Crucially, the MTBs addressed a significant gap in genomic education for oncologists who often lack formal training in this field and have limited opportunities for continuing education, as available genomics training is often primarily targeted to molecular biologists or geneticists. By lowering the perceived complexity of genomic medicine, the MTB encouraged clinicians to engage more frequently, eventually increasing sample volumes.

The planning phase was essential for building a cooperative network of diverse key actors. For example, the cooperation with FNDF made possible nationwide sample transportation, lowering one of the perceived adoption barriers, as reflected in the survey responses. Another facilitator of adoption was the high uptake of genomic testing by families, nearly all of whom provided consent, indicating strong trust in the value of genomic data.

The educational benefit of the MTB was also a key factor for long-term sustainability. In Latin America, where commercial reports may contain misinterpretations, the MTB helped prevent inappropriate clinical actions. It also raised awareness regarding familial or hereditary syndromes, as somatic sequencing can reveal germinal variants in cases where clinical evidence was not previously obvious. This is particularly important in syndromes with low genetic penetrance or mild phenotypes that can easily go unnoticed [26]. All surveyed participants expressed willingness to continue attending the MTB—either regularly or occasionally—indicating strong commitment and perceived relevance, two essential components for sustainability.

Several barriers limited the participation of health professionals. In addition to the initial hesitance of oncologists in the value of genomic medicine in oncopediatrics, clinicians cited meeting times that conflicted with clinical duties and a lack of "protected time" as major hurdles. Competing commitments with other tumor boards also reduced attendance. Overall, a significant limitation of the COPPA Project design was its reliance on individual participant commitment rather than sustained institutional support. In this sense, pediatric care institutions are encouraged to foster multicenter, multidisciplinary MTBs and provide the necessary resources and time for meaningful professional participation. Also, a more permissive "genomic ecosystem" is required, as current national pediatric oncology policies do not prioritize precision diagnostics as a strategic necessity. This lack of framework fails to mitigate high sequencing costs or address limited commercial incentives for small patient populations.

4.1 | Overall Implications

Overall, the COPPA Project provided practical insights into the integration of genomic diagnostics into pediatric oncology care in a middle-income setting. Our experience suggests that medical education in genomics is not ancillary but rather a core component of successful implementation. Furthermore, the use of a comprehensive yet relatively low-cost NGS strategy, with ongoing refinements, may help reduce accessibility barriers and support the continued subsidization of genomic testing for a majority of patients unable to afford out-of-pocket costs. Because genomic testing is a small fraction of overall treatment costs, it should be viewed as a strategic investment by health authorities to improve diagnostic precision. A word of caution is necessary: sequencing-based diagnostics cannot be fully evaluated through cost-effectiveness analyses until operational challenges—turnaround time, sample flow, workflow reliability, and a steady demand—are addressed. Implementation must be grounded in local standards of care and tailored to the therapeutic options realistically available in the region [27].

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Conflicts of Interest

The authors have no competing interests to declare.

Ethics Statement

The COPPA protocol was approved by the HUA institutional review board in February 2022 under the number P22-002.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supporting File 1: pbc70290-sup-0001-SuppMat.pdf