GENOMIC PROFILING OF PEDIATRIC TUMORS: A SINGLE INSTITUTION EXPERIENCE

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PURPOSE

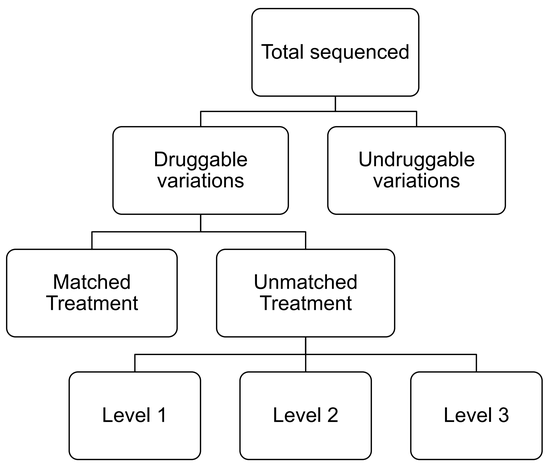
- The goal of this project is to study the prevalence of oncogenic variants and potential utility of targeted therapy among pediatric cancers.

BACKGROUND

- Outcomes remain poor for relapsed malignancies.
- Whole genome sequencing in an emerging tool to identify driver genetic alterations.[1-5]

METHODS

- Retrospective chart review was conducted on 82 patients (2013-2019) at Cook Children's Medical Center.
- Tumor samples were sent to Foundation Medicine, Inc., which identified:
  - Genetic variants and available targeted therapies
  - Programmed death-ligand 1 (PD-L1) expression
  - Tumor mutation burden (TMB)
  - Microsatellite instability (MSI)
- The druggable recommendations were then stratified by clinical significance to level 1, 2, and 3.



RESULTS

- 82 total patients
- Gender
  - 49 males (60%)
  - 33 females (40%)
- Age at diagnosis:
  - Median: 6.92 years
  - Range: 0.01-40.33 years
- Ethnicity
  - 37 (45%) White
  - 14 (17%) Black
  - 26 (32%) Hispanic
  - 3 (4%) Asian
  - 2 (2%) Unknown

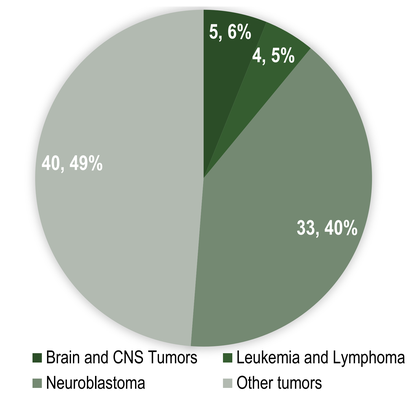


Fig. 1: Pie graph of represented patient diagnoses.

Table 1. Descriptive statistics for diagnostic and treatment variables stratified by alteration group

Variable	Level	Total (N=82)	Druggable (N=35)		Undruggable (N=47)
			Unmatched (N=22)	Matched (N=13)	
Diagnosis	Brain/CNS Tumors	5 (6%)	4 (18%)	0 (0%)	1 (2%)
	Leukemia/Lymphoma	4 (5%)	2 (9%)	0 (0%)	2 (4%)
	Neuroblastoma	33 (40%)	5 (23%)	6 (46%)	22 (47%)
	Other Tumors	40 (49%)	11 (50%)	7 (54%)	22 (47%)
Prior Relapse	Yes	30 (37%)	10 (45%)	6 (46%)	14 (30%)
	No	52 (63%)	12 (55%)	7 (54%)	33 (70%)
Prior Lines of Therapy	0	36 (44%)	10 (48%)	4 (31%)	22 (47%)
	1	24 (30%)	5 (24%)	4 (31%)	15 (32%)
	2+	21 (26%)	6 (29%)	5 (38%)	10 (21%)

Table 2. Biomarker Results

Variable	How many were tested?	Result	
PD-L1	34	Positive	6 (18%)
		Negative	28 (82%)
TMB	51	Low	44 (86%)
		Intermediate	7 (14%)
MSI	41	Stable	41 (100%)
		Unstable	0 (0%)

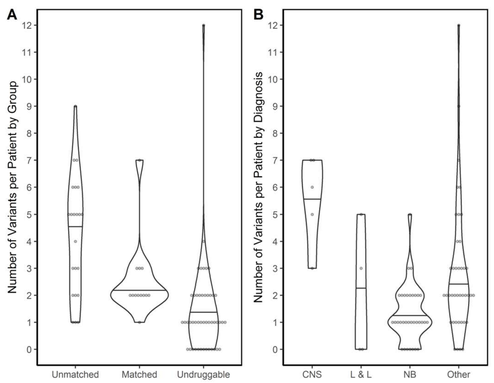


Fig. 2: Violin and dot plots of number of mutations per patient stratified by (A) mutation group and (B) diagnosis. Horizontal lines indicate median values.

NB: Neuroblastoma
L & L: Leukemia and lymphoma
CNS: CNS and brain tumors
Other: Other solid tumors

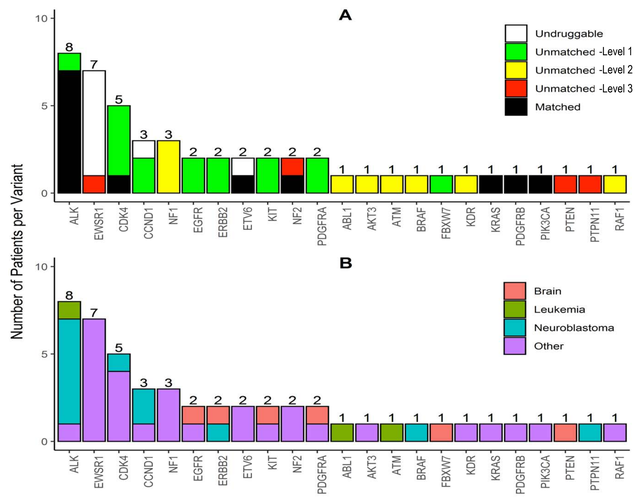


Fig. 3: Bar plot of number of patients per mutation stratified by (A) Alteration group and (B) Diagnosis for all druggable mutations.

RESULTS

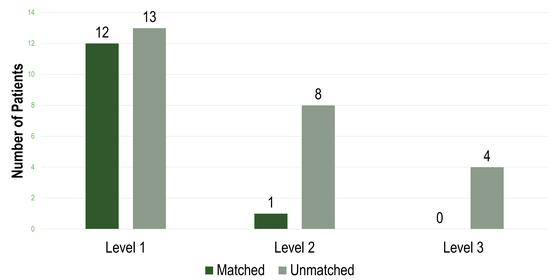


Fig. 4: Bar plot of matched and unmatched variants stratified by level 1, 2, and 3.

DISCUSSION

- Our study showed 35 of 82 (43%) patients had ≥ 1 potentially targetable alterations, which is comparable to results from other pediatric studies[6-11].
- 13 patients received targeted therapy; 12/13 were Level 1 recommendations, and all were off-label drug use.
- Three patients experienced adverse effects from targeted therapy.
- Of those positive for PD-L1, only one patient received pembrolizumab.

CONCLUSION

- This study highlights how tumor profiling can be utilized to identify potential molecular targets and biomarkers in pediatric cancers.

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