Supplementary Materials for Chi, SN et al. Tazemetostat for Tumors Harboring SMARCB1/SMARCA4 or EZH2 Alterations: Results from NCI-COG Pediatric MATCH APEC1621C

Supplementary Table 1. Designated actionable tumor alterations for Pediatric MATCH Arm C.

Gene Name	Variant ID	Variant Type	Actionable mutation
SMARCB1	N/A	N/A	Two deleterious (inactivating) mutations or protein loss by IHC
SMARCA4	N/A	N/A	Two deleterious (inactivating) mutations or protein loss by IHC
EZH2	COSM37032	SNV	p.Y646C
EZH2	COSM37028	SNV	p.Y646F
EZH2	COSM37030	SNV	p.Y646H
EZH2	COSM37031	SNV	p.Y646N
EZH2	COSM37029	SNV	p.Y646S
EZH2	COSM220386	SNV	p.A682G
EZH2	COSM1315851	SNV	p.A682V
EZH2	COSM220529	SNV	p.A692V
IHC, immunohistochemistry; SNV, single nucleotide variant.			

Supplementary Table 2. Prior Therapy of Patients Treated on APEC1621C.

Patient ID	Diagnosis	Multi-Agent Chemotherapy	Autologous Stem Cell Transplant	Radiation Therapy	Other*
1	Ewing Sarcoma	X	--	X	--
2	Hepatocellular carcinoma	X	--	X	X
3	Non-LCH	X	--	--	X
4	ES	X	--	X	--
5	ATRT	X	X	--	--
6	RMC	X	--	--	--
7	ES	X	--	--	--
8	ATRT	X	X	X	X
9	ATRT	X	X	X	X
10	Ependymoma	X	--	X	X
11	ATRT	X	--	X	--
12	MRT	X	--	--	--
13	ATRT	X	--	X	--
14	ATRT	X	X	X	X
15	ATRT	X	--	X	--
16	ATRT	X	X	X	X
17	MRT	X	--	X	--
18	Ewing sarcoma	X	--	--	--
19	MRT	X	--	--	--
20	MRT	X	--	--	--

*Other: including experimental, maintenance, or immune therapies. ATRT, atypical teratoid rhabdoid tumor; RMC, renal medullary carcinoma; ES, epithelioid sarcoma; LCH, Langerhans cell histiocytosis.

Supplementary Table 3. Diagnoses and detailed genomic test results of 20 treated patients.

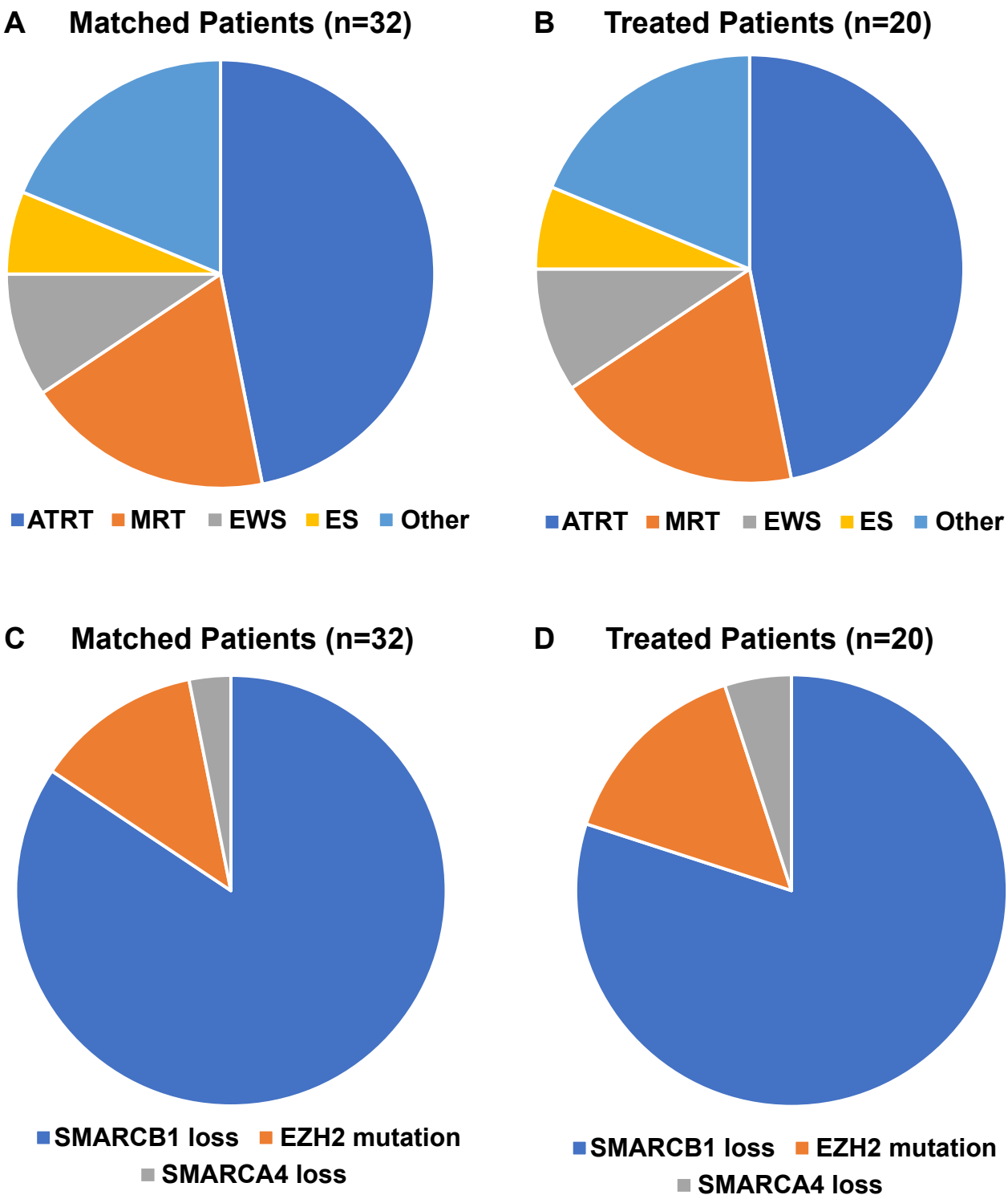
Patient ID	Age (yrs)	Sex	Diagnosis	Actionable tumor mutation(s)	Other tumor cancer gene mutations detected	Germline mutation detected
5	1	Male	ATRT	SMARCB1 loss by IHC	--	--
15	3	Female	ATRT	SMARCB1 loss by IHC	--	--
14	3	Female	ATRT	SMARCB1 loss by IHC; SMARCB1 p.Tyr47Ter (0.94)	TP53 c.796G>A, p.Gly266Arg (0.155)	SMARCB1 p.Tyr47Ter (0.52)
11	3	Female	ATRT	SMARCB1 loss by IHC; SMARCB1 p.Arg201Ter (0.79)	TSC1 p.Gln897fs (0.50)	--
8	4	Male	ATRT	SMARCB1 loss by IHC	NRAS p.Gln61Arg (0.33); TP53 p.Leu130fs (0.49)	--
13	5	Male	ATRT	SMARCB1 loss by IHC	--	--
16	5	Male	ATRT	SMARCB1 loss by IHC	--	--
9	20	Female	ATRT	SMARCB1 loss by IHC	--	--
17	1	Female	MRT	SMARCB1 loss by IHC; SMARCB1 p.Arg201Ter (0.65)	--	--
12	2	Male	MRT	SMARCB1 loss by IHC	--	--
20	3	Female	MRT	SMARCB1 loss by IHC	--	--
19	3	Male	MRT	SMARCB1 loss by IHC	--	--
7	15	Male	ES	SMARCB1 loss by IHC	--	--
4	18	Male	ES	SMARCB1 loss by IHC	--	--
6	19	Male	RMC	SMARCB1 loss by IHC	--	--
2	10	Male	Hepatocellular carcinoma	SMARCB1 loss by IHC	CHEK2 p.Thr367fs (0.52); DNAJB1-PRKACA fusion	CHEK2 p.Thr367fs (0.49)
3	10	Male	Non-LCH	SMARCA4 loss by IHC	--	--
18	17	Female	Ewing sarcoma	EZH2 p.Ala682Gly (0.12)	--	--
1	17	Male	Ewing sarcoma	EZH2 p.Tyr646Phe (0.14)	--	--
10	15	Male	Ependymoma	EZH2 p.Ala692Val (0.52)	--	--

NOTE: Age as reported at screening protocol study enrollment. Variant allele fractions (VAFs) for mutations are provided in parentheses. IHC, immmunohistochemistry; fs, frameshift. ATRT, atypical teratoid rhabdoid tumor; RMC, renal medullary carcinoma; ES, epithelioid sarcoma; LCH, Langerhans cell histiocytosis.

Supplementary Table 4. All Grade 3 or above adverse events potentially associated with the protocol treatment (with attribution Possible, Probable, or Definite) as per CTCAE v5.0.

Patient ID	Dose Level (mg/m^2)	Reporting period	Adverse event	Grade	Attribution
2	1200	Follow-Up Period (30-day)	Alkaline phosphatase increased	3	Possible
9	1200	Cycle 1	Dyspnea	3	Possible
9	1200	Cycle 1	Alanine aminotransferase increased	3	Probable
9	1200	Cycle 1	Abdominal pain	3	Probable
9	1200	Cycle 1	Platelet count decreased	3	Probable
9	1200	Follow-Up Period (30-day)	GGT increased	3	Possible
11	1200	Cycle 5	Anemia	3	Possible
16	1200	Cycle 1	Intracranial hemorrhage	3	Possible
17	520	Cycle 1	Lung infection	3	Possible
19	520	Cycle 1	Anemia	3	Probable

Supplementary Figure 1



Supplementary Figure 1. Histologic diagnoses and distribution of actionable alterations of all 32 matched patients (A, C) and 20 treated patients (B, D) on arm C.