

On-line Table 1: Summary of inclusion and exclusion criteria for Clinical Trial NCT01182350^a

Criteria for Inclusion	Criteria for Exclusion
Newly diagnosed nondisseminated DIPG based on imaging	Presence of other significant medical illness that would compromise receiving medical therapy (determined by investigator)
No prior treatment	Concurrent use of other anticancer or experimental therapy
Age between 3 and 18 years	Patient with disseminated tumor to the brain or spine
Karnofsky scale >50 for children older than 12 years or Lansky Performance score >50 for children younger than 12 years	Use of medications or substances that are strong/intermediate inhibitors or inducers of cytochrome P450 (CYP450), cytochrome P3A4(CYP3A4), or cytochrome 1A2 (CYP1A2)
Normal visceral organ and bone marrow function	Use of hematopoietic growth factors 2 weeks prior to initiation of therapy
Willingness to use birth control methods	Evidence of spontaneous (nonsurgical) hemorrhage of >0.5 cm
	Acute uncontrolled illnesses (eg, infection, congestive heart failure, cardiac arrhythmia)
	Pregnancy

^a More details can be found at <https://clinicaltrials.gov/ct2/show/NCT01182350>.

On-line Table 2: Univariate Cox proportional hazards regression analysis to test association of imaging predictors with OS and PFS

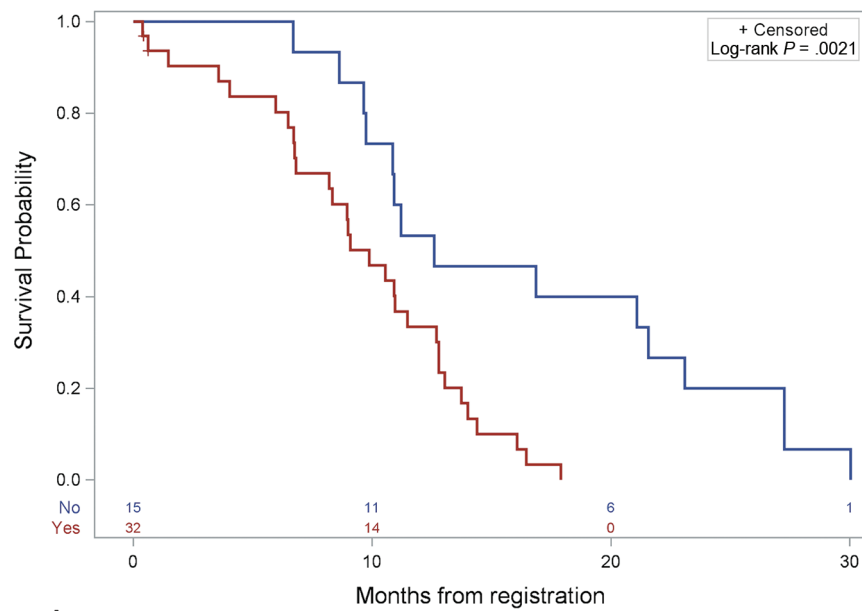
Imaging Predictor	OS			PFS		
	No.	Hazard Ratio (95% CI)	P Value	No.	Hazard Ratio (95% CI)	P Value
T2-FLAIR/T2 tumor volume (mL)	49	1.01 (0.99–1.03)	.4	49	1.02 (0.999–1.04)	.07
Tumor volume cyst/necrosis (mL) in patients with cyst/necrosis	23	0.96 (0.8–1.2)	.8	23	1.2 (0.9–1.5)	.2
Presence of necrosis (yes vs no) in patients with enhancing tumor volume >0	32	1.3 (0.5–3.0)	.6	32	1.0 (0.4–2.3)	.98
Tumor volume enhancing (mL) in patients with enhancing tumor volume >0	32	1.1 (0.97–1.2)	.2	32	1.1 (1.02–1.3)	.02
Presence of enhancement (yes vs no)	47	3.2 (1.5–7.0)	.003 ^a	47	1.8 (0.98–3.5)	.06
Mean ADC_FLAIR $\times 10^{-6}$ mm ² /s	46	0.999 (0.998–1.0)	.1	46	0.9998 (0.999–1.001)	.7
Median ADC_FLAIR $\times 10^{-6}$ mm ² /s	46	0.999 (0.998–1.0)	.1	46	0.9996 (0.999–1.001)	.5
Mode ADC_FLAIR $\times 10^{-6}$ mm ² /s	46	0.999 (0.998–1.0)	.07	46	0.999 (0.999–1.0004)	.2
Mean (PG) ADC-enhancement $\times 10^{-6}$ mm ² /s	28	1.0005 (0.999–1.002)	.5	28	0.9999 (0.999–1.001)	.9
Median (PG) ADC-enhancement $\times 10^{-6}$ mm ² /s	28	1.0005 (0.999–1.002)	.5	28	0.9998 (0.998–1.001)	.9
Mode (PG) ADC-enhancement $\times 10^{-6}$ mm ² /s	28	1.0007 (0.999–1.003)	.5	28	1.00004 (0.998–1.002)	.96

^a Test is significant after FDR adjustment of <0.1.

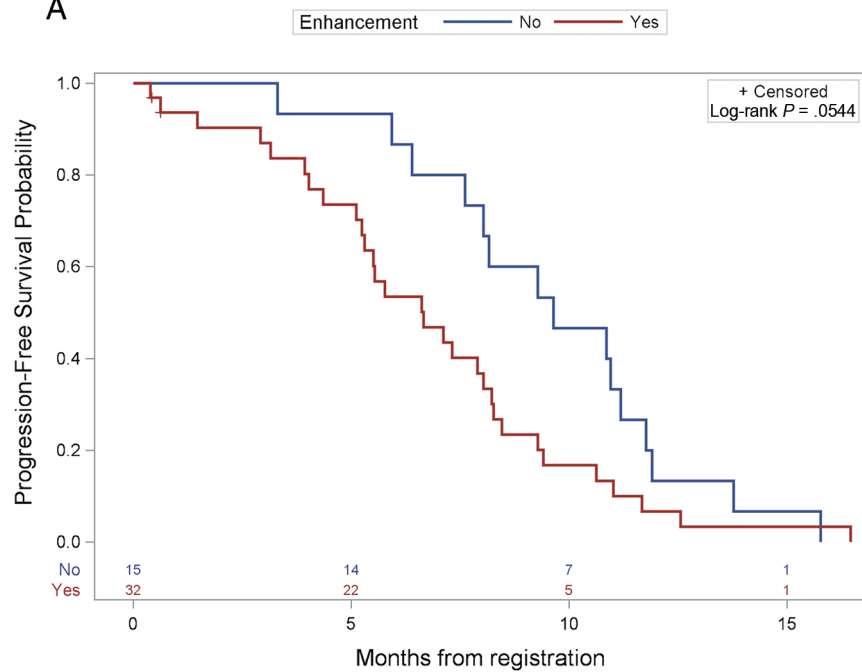
On-line Table 3: Association of imaging predictors and molecular subgroups (n=48)

Imaging Parameters (Median) (Range)	No.	Molecular Subgroup				Kruskal-Wallis P Value
		MGMT−/EGFR− (n = 28)	MGMT−/EGFR+ (n = 14)	MGMT+/EGFR− (n = 3)	MGMT+/EGFR+ (n = 3)	
FLAIR/T2 tumor volume (mL)	47	33.4 (10.7–54.3)	36.2 (24.7–70.9)	35.1 (29–40.8)	41.2 (40.8–47.1)	.2
Tumor volume cyst/necrosis (mL) in patients with cyst/necrosis	22	1.3 (0.07–4.1) (n = 12)	0.7 (0.08–1.2) (n = 6)	4.3 (0.5–8.1) (n = 2)	1.1 (0.1–2.1) (n = 2)	.6
Presence of necrosis (yes vs no) in patients with enhancing tumor volume >0	30	12/14 (86%)	6/10 (60%)	2/3 (67%)	2/3 (67%)	.5 ^a
Tumor volume enhancing (mL) in patients with enhancing tumor volume >0	30	3.6 (0.08–11.1) (n = 14)	1.6 (0.3–6.9) (n = 10)	12.4 (6.9–15.2) (n = 3)	0.5 (0.1–3.8) (n = 3)	.04
Presence of enhancement (yes vs no)	47	14/26 (54%)	10/13 (77%)	3/3 (100%)	3/3 (100%)	.2 ^a
Mean ADC_FLAIR × 10 ^{−6} mm ² /s	44	1377 (898.9–2098.3)	1331 (1019–1915.2)	1303 (1273.9–1375.1)	1447 (1360.3–1469.3)	.8
Median ADC_FLAIR × 10 ^{−6} mm ² /s	44	1363 (906.7–2146)	1313 (1038.5–1913)	1257 (1243.6–1319.2)	1425 (1309–1473.2)	.8
Mode ADC_FLAIR × 10 ^{−6} mm ² /s	44	1339 (895.5–2214.4)	1321 (1046–1886.4)	1297 (1052.6–1299.9)	1388 (1150.8–1497.3)	.7
Skewness ADC_FLAIR	42	0.5 (−1.3–2.8)	0.7 (−0.6–2.0)	1.1 (0.2–1.1)	0.9 (0.2–1.2)	.6
Kurtosis ADC_FLAIR	42	0.8 (−1.1–8.9)	1.5 (−0.6–9.0)	1.6 (0.4–2.9)	2.0 (1.1–3.8)	.7
Mean (PG) ADC-enhancement × 10 ^{−6} mm ² /s	26	1349 (773–1820.7)	1147 (779.4–1458.9)	1274 (1099.5–1357.7)	1505 (1329.2–1538)	.3
Median (PG) ADC-enhancement × 10 ^{−6} mm ² /s	26	1333 (786.2–1773.1)	1135 (789.1–1364.3)	1171 (1068.1–1351.5)	1486 (1305.2–1530)	.2
Mode (PG) ADC-enhancement × 10 ^{−6} mm ² /s	26	1247 (778.3–1622)	1111 (812.9–1313.5)	1064 (978.4–1298.4)	1400 (1218.5–1477.4)	.2
Skewness (PG) ADC-enhancement	22	0.7 (−0.08–1.1)	0.6 (0.1–1.4)	1.0 (0.3–1.2)	0.3 (−0.3–1.8)	.9
Kurtosis (PG) ADC-enhancement	22	0.8 (−1.0–2.3)	0.09 (−1.2–3.5)	1.0 (0.1–1.7)	0.5 (−0.5–4.9)	.7

^a Fisher exact test P value.



A



B

ON-LINE FIGURE. Prognostic differences in tumors with enhancement ($n=32$) versus no enhancement ($n=15$). A, Kaplan-Meier curve shows significant differences in OS between tumors with enhancement versus no enhancement. B, The Kaplan-Meier curve shows a trend that approaches significance in PFS between tumors with enhancement versus no enhancement.