TABLE 1. Patient characteristics.

	Stratum I (N = 21)		***Stratum II (N = 14)***	
AGE (Years)	At Initial Diagnosis	At Study Entry	At Initial Diagnosis	At Study Entry
Median	9.1	11.9	7.9	12.8
Minimum	3.5	4.9	0.8	6.3
Maximum	16.4	21.1	15.1	21.6
	Number	***Percentage***	***Number***	***Percentage***
SEX				
Female	9	42.9	3	21.4
Male	12	57.1	11	78.6
ETHNICITY				
Hispanic or Latino	5	23.8	3	21.4
Not Hispanic or Latino	13	61.9	7	50.0
Unknown	3	14.3	4	28.6
RACE				
American Indian or Alaska Native	0	0.0	1	7.1
Asian	3	14.3	0	0.0
Black or African American	2	9.5	2	14.3
Multiracial	1	4.8	0	0.0
White	13	61.9	10	71.4
Unknown	2	9.5	1	7.1
CURRENT DIAGNOSIS				
Anaplastic astrocytoma	3	14.3	0	0.0
CNS primary tumor, NOS	1	4.8	1	7.1
Choroid plexus carcinoma	0	0.0	1	7.1
DIPG*	7	33.3	1	7.1
Ependymoma, NOS	3	14.3	7	50.0
Glioblastoma multiforme	6	28.6	0	0.0
High-grade astrocytoma, NOS	1	4.8	0	0.0
Medulloblastoma*	0	0.0	4	28.6

Tumor types with an asterisk did not require immunohistochemistry for Rb; all other tumor types were screened and tested positive for Rb expression based on immunohistochemistry. NOS, not otherwise specified.

TABLE 2. DLT summary.

Dose Level (mg/m2/ dose)	Stratum	Number of Enrolled Patients	Number of Evaluable Patients	Number of Patients with DLTs	Description of DLTs
75	I	12	12	2	Grade 3 dehydration (n=1) Grade 4 neutrophil count decreased (n=1)
75	II	10	7	1	Grade 3 platelet count decreased (n=1)
95	I	6	4	2	Grade 4 neutrophil count decreased (n=2)

TABLE 3. Type and grade of adverse events experienced by ≥10% of Stratum I patients. Represents 21 patients and 56 courses.

	Grade				
Adverse Event	**1**	**2**	**3**	**4**	**Overall**
White blood cell decreased	14(9)	37(14)	19(3)		70(17)
Neutrophil count decreased	8(5)	26(7)	27(9)	3(3)	64(15)
Lymphocyte count decreased	22(8)	17(4)	12(7)		51(13)
Platelet count decreased	28(10)				28(10)
Fatigue	7(7)	3(3)			10(9)
Mucositis oral	5(2)	5(2)			10(3)
Anemia	7(5)	2(2)			9(7)
Constipation	8(6)				8(6)
Vomiting	5(4)	1(1)	1(1)		7(5)
Headache	4(3)	3(2)			7(4)
Hypokalemia	5(4)	1(1)			6(5)
Nausea	4(3)	1(1)	1(1)		6(3)
Ataxia	1(1)	3(3)	1(1)		5(5)
Alanine aminotransferase increased	4(4)				4(4)
Diarrhea	4(3)				4(3)
Dry skin	3(3)				3(3)
Gait disturbance		2(2)	1(1)		3(3)
Muscle weakness left-sided			3(3)		3(3)

The first number in each cell represents the number of episodes for each adverse event and the number in parentheses represents the number of patients for whom the adverse event was reported. All adverse events were reported regardless of attribution to palbociclib.

TABLE 4. Type and grade of adverse events experienced by ≥10% of Stratum II patients. Represents 13 patients and 28 courses.

	Grade				
Adverse Event	**1**	**2**	**3**	**4**	**Overall**
Neutrophil count decreased	6(4)	19(10)	13(9)	1(1)	39(11)
White blood cell decreased	13(5)	18(9)	7(6)		38(11)
Platelet count decreased	16(8)	5(3)	2(2)	1(1)	24(8)
Anemia	17(9)	3(3)			20(10)
Lymphocyte count decreased	10(5)	6(3)	3(3)		19(7)
Vomiting	5(3)		1(1)		6(4)
Fatigue	2(2)	2(2)			4(4)
Headache	1(1)	1(1)	2(2)		4(4)
Dizziness	3(2)	1(1)			4(3)
Anorexia	3(3)				3(3)
Hypokalemia	3(3)				3(3)
Seizure			3(3)		3(3)
Alanine aminotransferase increased	3(2)				3(2)
Constipation	1(1)	2(1)			3(2)
Electrocardiogram qt corrected interval prolonged	3(2)				3(2)
Aspartate aminotransferase increased	2(2)				2(2)
Hypercalcemia	2(2)				2(2)
Hyperkalemia	2(2)				2(2)
Mucositis oral	1(1)	1(1)			2(2)
Pain	1(1)		1(1)		2(2)

The first number in each cell represents the number of episodes for each adverse event and the number in parentheses represents the number of patients for whom the adverse event was reported. All adverse events were reported regardless of attribution to palbociclib.

TABLE 5. Number of patients in each course receiving palbociclib.

Stratum I

Dose	Course												
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**...**	**17**	**18**
	N	N	N	N	N	N	N	N	N	N	N	N	N
50 mg/m^2/day	3	2	1	1	0	0	0	0	0	0	0	0	0
75 mg/m^2/day	12	8	2	2	2	2	1	1	1	1	1	1	1
95 mg/m^2/day	6	3	0	0	0	0	0	0	0	0	0	0	0

Stratum II

Dose	Course			
	1	**2**	**3**	**4**
	N	N	N	N
50 mg/m^2/day	4	3	2	2
75 mg/m^2/day	9	6	1	1

TABLE 6. Pharmacokinetic parameters of palbociclib after single dose (Day 1) and repeated oral doses (Day 21)

		Parameters†				
Dosage	**Day**	**C_{max} (ng/mL)**	**T_{max} (h)**	**$AUC_{0\text{-}Tlast}$ (h·ng/mL)**	**CL/F ($L/h/m^2$)**	**Half-life (h)**
50 mg/m^2	Day 1 (N= 7)	69.3 ± 43.7 54.9 (35.8-135)	6.6 ± 2.5 8.0 (2.0-8.0)	1327 ± 721 1156 (747-2834)	39.9 ± 15.1 36.3 (16.9-64)	14.4 ± 3.9 13.0 (9.9-22)
	Day 21 (N=6)	90.0 ± 62.7 77.2 (32.3-210)	5.3 ± 2.1 4.0 (4.0-8.0)	1517 ± 975 1227 (559-3301)	26.8 ± 20.0 19.5 (9.7-64)	19.5 ± 7.7 17.4 (10.5-30)
75 mg/m^2	Day 1 (N=21)	92.0 ± 34.9 94.0 (17.9-148)	5.2 ± 2.2 4.0 (2.0-10)	1872 ± 716 1831 (189-2951)	52.6 ± 71.3 35.2 (11.7-355)	16.6 ± 9.5 13.3 (7.1-49)
	Day 21 (N=17)‡	139.9 ± 67.1 137 (31.8-286)	4.9 ± 2.5 4.0 (2.0-8.0)	2219 ± 1086 2269 (521-4253)	30.5 ± 23.1 22.1 (12.1-100)	15.8 ± 7.9 14.4 (6.5-42)
95 mg/m^2	Day 1 (N=6)	132.5 ± 33.4 122 (98.1-180)	5.0 ± 2.5 4.0 (2.0-8.0)	2375 ± 820 2407 (1485-3252)	36.3 ± 16.6 33.7 (17.3-63)	15.9 ± 7.5 14.6 (8.4-30)
	Day 21 (N=2)‖	190 ± 29.1 183 (165-222)	6.0 ± 3.5 8.0 (2.0-8.0)	2294 ± 828 2193 (1520-3168)	28.1 ± 10.3 28.1 (20.8-35)	11.3 ± 2.1 11.3 (9.8-13)_

C_{max}: maximum concentration, T_{max}: time to reach C_{max}, $AUC_{0\text{-}Tlast}$: area under the concentration curve from zero to the last measurable time-point, CL/F: apparent oral clearance.

†The parameters are reported as mean ± standard deviation (first row) and median (range) (second row).

‡N = 18 patients receiving 75 mg/m^2 palbociclib had samples collected and analyzed for Day 21 pharmacokinetics. However, one patient had 4 concentrations below the limit of quantification. Thus, this patient was excluded from the non-compartmental analysis.

‖N = 3 patients receiving 95 mg/m^2 palbociclib had samples collected and analyzed for Day 21 pharmacokinetics. However, one patient had only 3 samples collected at times 2, 4, and 8 hours. Thus, this patient was excluded from the non-compartmental analysis.