



Lorlatinib with or without chemotherapy in ALK-driven refractory/relapsed neuroblastoma: phase 1 trial results

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Supplementary Table 1. Tumor Tissue Verses ctDNA Baseline ALK Results

Best overall response	Tumor ALK	Tumor source/ timepoint	ctDNA baseline	Prior ALK inhibitor
PD (Course 1)	F1174L	Bone/Relapse	F1174 F1245 R1275	Alectinib + Chemotherapy
PR (27 Courses)	D1276_R1279>E	Soft tissue/Relapse	D1276_R1279>E G1202R	Crizotinib x 3 years
PD (Course 2)	ALK Amplification	Soft tissue/Refractory	ALK Amplification F1174L	No Prior ALK TKI

Supplementary Table 2. MIBG Curie Scores at enrollment and Best Overall Response

Patient ID	32	10	30	12	9	26	40	17	3	11	21	25	2	38	31
Enrollment Curie	2	4	5	6	10	11	10	15	18	1	3	2	5	3	3
Minimum Curie	14	6	7	8	9	9	3	2	1	0	0	0	0	0	0
Best overall response	PD	PD	PD	PD	PD	PD	MR	MR	PR	SD	SD	SD	MR	PR	CR
Curie Score Percent Change	600	50	40	33.33	-10	-18.18	-70	-86.66	-94.44	-100	-100	-100	-100	-100	-100

PD; Progressive disease, SD; Stable disease, MR; Minimal response, PR; Partial response, CR; Complete response

Supplementary Table 3: Neuropsychological Administration Procedures by Age Group

Age at Testing (Years: Months)	Patient Testing/Self Report	Parent Report	Duration of Testing for Parents	Duration of Testing for Patients
1:1 to 1:11	1. Bayley-III (only at <u>baseline, course 2, and every 6 months</u> for duration of treatment- e.g., course 8, 14, etc.)	1. ABAS-3 Parent/Primary Caregiver Form (Ages 0-5) 2. PedsQL Infant Scales (13-24 months)	~ 20 minutes	~ 60 - 90 minutes
2:0 – 2:11	1. Bayley-III (only at <u>baseline, course 2, and every 6 months</u> for duration of treatment- e.g., course 8, 14, etc.)	1. ABAS-3 Parent/Primary Caregiver Form (Ages 0-5) 2. BASC-3 Parent Rating Scales-Preschool (Ages 2-5) 3. BRIEF- Preschool Version 4. PedsQL Generic Version – Parent Report for Toddlers (Ages 2-4) 5. PedsQL Multidimensional Fatigue Parent Report for Toddlers (Ages 2-4)	~ 50 minutes	~ 60 - 90 minutes
3:0 – 4:11	1. Cogstate (Detection, Identification)	1. ABAS-3 Parent/Primary Caregiver Form (Ages 0-5) 2. BASC-3 Parent Rating Scales-Preschool (Ages 2-5) 3. BRIEF- Preschool Version 4. PedsQL Generic Version – Parent Report for Toddlers (Ages 2-4) 5. PedsQL Multidimensional Fatigue – Parent Report for Toddlers (Ages 2-4)		~ 10 minutes
5:0 – 5:11	1. Cogstate (Detection, Identification)	1. ABAS-3 Parent/Primary Caregiver Form (Ages 0-5) 2. BASC-3 Parent Rating Scales-Preschool (Ages 2-5) 3. BRIEF- Preschool Version 4. PedsQL Generic Version – Parent Report for Young Children (Ages 5-7) 5. PedsQL Multidimensional Fatigue – Parent Report for Young Children (Ages 5-7) 6.		

6:0 – 6:11	1. Cogstate (<i>Detection, Identification, One Card Learning, One Back, Groton Maze Learning Task</i>)	1. ABAS-3 Parent Form (Ages 5-21) 2. BASC-3 Parent Rating Scales-Child (Ages 6-11) 3. BRIEF 4. PedsQL Generic Version – Parent Report for Young Children (Ages 5-7) 5. PedsQL Multidimensional Fatigue – Parent Report for Young Children (Ages 5-7)	~ 50 minutes	
7:0-7:11	1. Cogstate (<i>Detection, Identification, One Card Learning, One Back, Groton Maze Learning Task</i>)	1. ABAS-3 Parent Form (Ages 5-21) 2. BASC-3 Parent Rating Scales-Child (Ages 6-11) 3. BRIEF 4. PedsQL Generic Version – Parent Report for Young Children (Ages 5-7) 5. PedsQL Multidimensional Fatigue – Parent Report for Young Children (Ages 5-7) 6. CSSRS – Children’s Version		
8:0-9:11	1. Cogstate (<i>Detection, Identification, One Card Learning, One Back, Groton Maze Learning Task</i>)	1. ABAS-3 Parent Form (Ages 5-21) 2. BASC-3 Parent Rating Scales-Child (Ages 6-11) 3. BRIEF 4. PedsQL Generic Version – Parent Report for Children (Ages 8-12) 5. PedsQL Multidimensional Fatigue – Parent Report for Children (Ages 8-12) 6. CSSRS – Children’s Version	~ 50 – 55 minutes	~ 30-40 minutes
10:0-11:11	1. Cogstate (<i>International Shopping List, Detection, Identification, One Card Learning, One Back, Groton Maze Learning Task, International Shopping List Delayed</i>)	1. ABAS-3 Parent Form (Ages 5-21) 2. BASC-3 Parent Rating Scales-Child (Ages 6-11) 3. BRIEF 4. PedsQL Generic Version – Parent Report for Children (Ages 8-12) 5. PedsQL Multidimensional Fatigue – Parent Report for Children (Ages 8-12) 6. CSSRS – Children’s Version		~ 35-45 minutes
12:0 – 12:11	1. Cogstate (<i>International Shopping List, Detection, Identification, One Card Learning, One Back, Groton</i>)	1. ABAS-3 Parent Form (Ages 5-21)		

	<i>Maze Learning Task, International Shopping List Delayed)</i>	<ol style="list-style-type: none"> 2. BASC-3 Parent Ratings Scales – Adolescent (Ages 12-21) 3. BRIEF 4. PedsQL Generic Version – Parent Report for Children (Ages 8-12) 5. PedsQL Multidimensional Fatigue – Parent Report for Children (Ages 8-12) 6. CSSRS 	~ 50-55 minutes	~ 35-45 minutes
13:0 – 17:11	<ol style="list-style-type: none"> 1. Cogstate (International Shopping List, Detection, Identification, One Card Learning, One Back, Groton Maze Learning Task, International Shopping List Delayed) 	<ol style="list-style-type: none"> 1. ABAS-3 Parent Form (Ages 5-21) 2. BASC-3 Parent Ratings Scales – Adolescent (Ages 12-21) 3. BRIEF 4. PedsQL Generic Version – Parent Report for Teens (Ages 13-18) 5. PedsQL Multidimensional Fatigue – Parent Report for Teens (Ages 13-18) 6. CSSRS 		
18:0 – 25:11	<ol style="list-style-type: none"> 1. Cogstate (International Shopping List, Detection, Identification, One Card Learning, One Back, Groton Maze Learning Task, International Shopping List Delayed) 2. ABAS-3 Adult Self-Report Form (Ages 16-89) 3. BASC-3 Self-Report College (Ages 18-25) 4. BRIEF - Adult Self Report 5. PedsQL Generic Version - Young Adult Report (Ages 18-25) 6. PedsQL Multidimensional Fatigue - Young Adult Report (Ages 18-25) 7. BDI-II 8. CSSRS 	No Parent Reports	N/A	~80-90 minutes
≥26:0	<ol style="list-style-type: none"> 1. Cogstate (International Shopping List, Detection, Identification, One Card Learning, One Back, Groton Maze Learning Task, International Shopping List Delayed) 2. ABAS-3 Adult Self-Report Form (Ages 16-89) 3. BRIEF - Adult Self Report 4. PedsQL Generic Version - Adult Report (Ages ≥26) 5. PedsQL Multidimensional Fatigue - Adult Report (Ages ≥26) 6. BDI-II 7. CSSRS 			

Supplementary Figure 1. Responses on cohort A1 by age at enrollment. Statistically evaluated using two-sided T-Test.

Cohort	n	Mean Age (range) [n] for CR+PR+MR	Mean Age (range) [n] for SD+PD	t-test p-value
A1	23	10.5 (6-17) [7]	5.12 (2-9) [16]	0.0006

