

TABLE 1 – PATIENT CHARACTERISTICS

Pt.	Age	Sex	Location	Pathology	MAPK Pathway alteration	Additional tumor Genetics	Tx lin e	Drug	Tx duration	Combo duration
1	3	<i>f</i>	Multi-system	LCH	Val600Glu	FGFR & EGFR mutation	3	Dabrafenib \\Zelboraf	37	-
2	14	<i>f</i>	Medulla	JPA	Val600Glu	Monosomy 7	2	Dabrafenib	46	-
3	4	<i>f</i>	Optic Tract	JPA	Val600Glu	-	2	Dabrafenib	36	-
4	19	<i>m</i>	Frontal lobe	Epithelioid GBM	Val600Glu	MGMT	2	Dabrafenib	33	-
5	9	<i>f</i>	Temporo-occiput	PXA grade 2	Val600Glu	CDK2N deletion	1	Dabrafenib	31	-
6	10	<i>m</i>	Cervico-medulla	GG grade 1	Val600Glu	-	1	Dabrafenib	19	-
7	15	<i>m</i>	Temporo-parietal lobes	PXA grade 3	Val600Glu	EGFR, MDM2 & P53 mutations	3	Dabrafenib \\Zelboraf	32	-
8	16	<i>m</i>	Mandible	Ameloblastoma	Val600Glu	-	1	Dabrafenib	26	-
9	14	<i>m</i>	Mandible	Ameloblastoma	Val600Glu	-	1	Dabrafenib	19	-
10	11	<i>m</i>	Mandible	Ameloblastoma	Val600Glu	-	1	Dabrafenib	10	-
11	6	<i>m</i>	Medulla	GG grade 1	Val600Glu	Germ line BRACA1	1	Dabrafenib	9	-
12	8	<i>m</i>	Temporal	PXA grade	Val600Glu	CDK2N	1	Combo	28	27

			lobe	2		deletion				
13	11	<i>f</i>	Parietal lobe	PXA grade 3	Val600Glu	CDK2N deletion	2	Combo	3	1
14	9	<i>m</i>	Optic Tract	JPA	Val600Glu	-	2	Combo	17	12
15	3	<i>m</i>	Optic Tract	JPA	Val600Glu	CDK2N deletion	4	Combo	23	18
16	11	<i>m</i>	Right arm	Plexiform neurofibroma	NF1	-	1	Trametinib	39	-
17	4	<i>m</i>	Medulla	JPA	BRAF\ KIAA	Monosomy 7	4	Trametinib	15	-
18	14	<i>f</i>	Supra-Sellar	JPA+LMS	BRAF\ KIAA	-	5	Trametinib	15	-
19	16	<i>m</i>	Vertebra C2	Low grade sarcoma	PIB1\ BRAFusion	-	1	Trametinib	12	-
20	11	<i>f</i>	Optic Tract	JPA	NF1	-	3	Trametinib	37	-
21	14	<i>m</i>	Pons	NR	NO BIOPSY	No biopsy	2	Trametinib	12	-
21	14	<i>m</i>	Optic Tract	JPA	BRAF\ KIAA	-	4	Trametinib	9	-

2 Pt.-patient number; Tx-treatment; MAPK- Mitogen activated protein kinase; GG- Ganglioglioma; Combo –
3 combination of dabrafenib and trametinib; LMS- Leptomeningeal spread; NF1- Neurofibromatosis type 1 JPA-
4 Juvenile pilocytic astrocytoma; LCH- Langerhans cell histiocytosis; PXA- Pleomorphic Xanthoastrocytoma
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TABLE 2 – PATIENTS CHARACTERISTICS - ADVERSE EVENTS

Pt.	Drug	Adverse Event	CTCAE grade or SEA	SEA Management
1	Zelboraf	Altered liver enzymes	4	Drug changed to Dabrafenib
2	Dabrafenib	Hyperkeratosis & hyperhidrosis	1	-
3	Dabrafenib	Hair changes & dermatitis	1	-
4	Dabrafenib	Acne	1-2	-
5	Dabrafenib	Hair changes	1	-
6	Dabrafenib	-	-	-
7	Zelboraf	Acneiform rash	1	Drug changed to Dabrafenib
		Erythema Nodosum	3	
8	Dabrafenib	Hair changes & fever	1	-
9	Dabrafenib	Acne	1-2	-
10	Dabrafenib	Erythema Nodosum	SEA	Failed re-challenge - Dabrafenib not renewed
11	Dabrafenib	Sarcoid-like pulmonary lymphadenopathy	3	Steroid treatment. Failed re-challenge - Dabrafenib discontinued
12	Combo	Grade 1 CPK elevation	2	-
13	Combo	Keratosis, Pilaris-like rash	1	Trametinib discontinued, Dabrafenib continued
		Retinal pigment epithelial irregularity	SEA	
14	Combo	-	-	-
15	Combo	-	-	-
16	Trametinib	CPK elevation	3	

				Treatment renewed after resolution to grade 1
		Paronychia, Acne	1-2	
17	Trametinib	Folliculitis, Keratosis, Pilaris-like rash, Paronychia, Fever, CPK & LDH elevation	1-2	-
18	Trametinib	Pustular rash	1-2	-
		CPK elevation	3	Treatment renewed after resolution to grade 1
19	Trametinib	Osteoporosis	3	Trametinib discontinued
		Asymptomatic decrease in SF Acne	1-2	
20	Trametinib	Acne & CPK elevation	1-2	-
21	Trametinib	Acne & Paronychia	1-2	-
22	Trametinib	Grade 1 CPK elevation, Paronychia, Hair loss, asymptomatic decrease in SF	1-2	
		Grade 3 PLEVA-like rash	3	Trametinib renewed at 50% dose

11 SF= Shortening fraction on Echocardiography; SEA-severe adverse event; PLEVA- pityriasis lichenoides et

12 varioliformis acuta; Combo – combination of dabrafenib and trametinib;

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17 **TABLE 3- MAIN ADVERSE EVENTS SUMMERY**

Event	Number of events	Percentage (%)	Drug
All AE	19	86	-
Dermatological AE	15	68	-
Grade 3 PLEVA-like rash	1	-	Trametinib
Acneiform rash	7	32	Zelboraf
Paronychia	4	18	Trametinib
Hair change- straight to curly	2	9	Dabrafenib
Hair loss	1	-	Trametinib
CTCAE grade 3/4 or Clinically Severe (SEA)	8	36	-
PLEVA-like rash	1	-	Trametinib
Osteoporosis	1	-	Dabrafenib
Retinal pigment epithelial changes	1	-	Trametinib (combination therapy)
Elevated liver enzymes	1	-	Zelboraf
Sarcoid-like pulmonary massive lymphadenopathy	1	-	Dabrafenib
Erythema Nodosum	2	9	Zelboraf and Dabrafenib
Elevated CPK	1	-	Trametinib