Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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Sample Information

Patient Name: 張明焜
Gender: Male
ID No.: Q121603916
History No.: 48753259
Age: 63

Ordering Doctor: DOC5636D 吳紋綺
Ordering REQ.: 0BWZSHC
Signing in Date: 2022/07/07

Path No.: S111-99726
MP No.: F22068
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S111-70847H
Percentage of tumor cells: 80%

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

Note:

Sample Cancer Type: Melanoma

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Relevant Melanoma Variants

Gene	Finding
BRAF	None detected
KIT	None detected
NRAS	None detected
NTRK1	None detected
NTRK2	None detected
NTRK3	None detected

Relevant Biomarkers

No relevant biomarkers found in this sample.

Prevalent cancer biomarkers without relevant evidence based on included data sources
GNA11 p.(R183C) c.547C>T

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
GNA11	p.(R183C)	c.547C>T	COSM21651	chr19:3115012	38.34%	NM_002067.5	missense	1985
FGFR4	p.(A161=)	c.483A>G	.	chr5:176517985	17.20%	NM_213647.3	synonymous	2000
MAP2K2	p.(E66K)	c.196G>A	.	chr19:4117524	9.55%	NM_030662.4	missense	1999

Biomarker Descriptions

GNA11 (G protein subunit alpha 11)

Background: The GNA11 gene encodes an alpha subunit of heterotrimeric guanine nucleotide-binding proteins (G-proteins). G-protein alpha subunits bind guanine nucleotide, hydrolyze GTP, and interact with specific receptor and effector molecules. GNA11 is closely related to GNAQ, another G-protein alpha subunit.

Alterations and prevalence: Somatic activating mutations in GNA11 and GNAQ at amino acids R183 and Q209 are common in uveal melanoma and are mutually exclusive. These mutations render the G protein constitutively active leading to the stimulation of MAP kinases, PI3K/AKT, and protein kinase C, which promote tumor growth and proliferation[1,2,3]. Approximately 45% of uveal melanoma cases contain activating mutations in GNA11 and up to 50% of cases contain activating mutations in GNAQ[4,5,6]. By contrast, GNA11 and GNAQ mutations are infrequent in cutaneous melanoma, with a combined prevalence of approximately 1%, and are infrequently observed in other cancers[5,6].

Potential relevance: Currently, no therapies are approved for GNA11 aberrations. In a randomized phase II clinical trial of MEK inhibitor selumetinib versus chemotherapy, GNA11 and GNAQ positive uveal melanoma patients demonstrated a median progression-free survival (PFS) of 15.9 weeks versus 7 weeks, respectively[7]. However, no statistically significant improvement in overall survival (OS) was observed and the improvement in outcomes was associated with a high rate of adverse events[7].

Clinical Trials in Taiwan region:

Signatures

Testing Personnel: 

2022.07.08
09:54:40 +08'00'

Laboratory Supervisor: 
2022.07.08
09:54:53 +08'00'

Pathologist: 
2022.07.08
09:55:06 +08'00'

References

1. Luke et al. Biology of advanced uveal melanoma and next steps for clinical therapeutics. Pigment Cell Melanoma Res. 2015 Mar;28(2):135-47. PMID: 25113308
2. Amaro et al. The biology of uveal melanoma. Cancer Metastasis Rev. 2017 Mar;36(1):109-140. PMID: 28229253
3. Parish et al. GNAS, GNAQ, and GNA11 alterations in patients with diverse cancers. Cancer. 2018 Oct 15;124(20):4080-4089. PMID: 30204251
4. Van et al. Mutations in GNA11 in uveal melanoma. N. Engl. J. Med. 2010 Dec 2;363(23):2191-9. PMID: 21083380
5. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. Nat. Genet. 2013 Oct;45(10):1113-20. PMID: 24071849
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7. Carvajal et al. Effect of selumetinib vs chemotherapy on progression-free survival in uveal melanoma: a randomized clinical trial. JAMA. 2014 Jun 18;311(23):2397-405. PMID: 24938562