Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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Sample Information

Patient Name: 張千金
Gender: Female
ID No.: A222972535
History No.: 48041652
Age: 54

Ordering Doctor: DOC6428J 高士勛
Ordering REQ.: 0CLLSKH
Signing in Date: 2023/06/01

Path No.: M112-00
MP No.: F23041
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S112-23973A+B
Percentage of tumor cells: 30%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	None detected	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*AR amplification* androgen receptor	None	hormone therapy	0

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

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

Copy Number Variations

Gene	Locus	Copy Number
AR	chrX:66776186	8.1

Biomarker Descriptions

AR (androgen receptor)

Background: The AR gene encodes the androgen receptor protein (AR), a ligand-activated transcription factor regulated by the binding of the hormones testosterone and dihydrotestosterone[1,2]. Hormone binding to AR results in receptor dimerization, nuclear translocation, and target gene transcription, thus activating the RAS/RAF/MEK/ERK and PI3K/AKT/MTOR signaling pathways, which promote cell proliferation and survival[2,3,4].

Alterations and prevalence: Alterations in AR function can result from overexpression, gene amplification, or mutations. AR mutations, including L702H, W742C/L, H875Y, and T878A, are commonly observed in 10-30% of castration-resistant prostate cancer and result in decreased ligand specificity, allowing other nuclear hormones to activate AR[5]. Androgen receptor splice variants have been reported in castration resistant prostate cancer[6,7]. The androgen receptor splice variant 7 (AR-V7) is a result of aberrant mRNA splicing of AR exons 1-3 and a cryptic exon 3, resulting in the expression of a constitutively active protein[7].

Potential relevance: The FDA has granted fast track designation (2022) to the selective androgen receptor targeting agonist, enobosarm, for the treatment of patients with androgen AR-positive, estrogen receptor (ER)-positive, HER2-negative metastatic breast cancer[8]. The FDA also granted fast track designation (2016) to the small-molecule CYP17 lyase-selective inhibitor, seviteronel, for AR-positive triple-negative breast cancer (TNBC) patients[9]. Androgen deprivation therapy (ADT) such as abiraterone[10] (2011) and enzalutamide[11] (2011) are FDA approved for use in locally advanced and metastatic prostate cancers. Other ADT therapies including leuprolide and bicalutamide are specifically recommended in AR+ unresectable metastatic salivary gland tumors[12]. Although many men initially respond to ADT, most will develop hormone resistance. Resistance to ADT is also associated with other aberrations of the AR gene including mutations within the ligand binding domain and gene amplification[5,13,14]. The androgen receptor splice variant, AR-V7, lacks the ligand binding domain, resulting in constitutive activation and is associated with resistance to androgen deprivation therapy (ADT) in advanced prostate cancer[6].

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

AR amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bicalutamide	✖	○	✖	✖	✖
leuprorelin	✖	○	✖	✖	✖

Relevant Therapy Details

Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

NCCN information is current as of 2023-03-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

AR amplification

○ bicalutamide

Cancer type: Head and Neck Cancer **Variant class:** AR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2023]

○ leuprorelin

Cancer type: Head and Neck Cancer **Variant class:** AR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2023]

Clinical Trials in Taiwan region:

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2023-03-15. For the most up-to-date information, search www.fda.gov.

AR amplification

enobosarm

Cancer type: Breast Cancer **Variant class:** AR positive

Other criteria: ERBB2 negative, ER positive

Supporting Statement:
The FDA has granted Fast Track Designation to enobosarm for AR+/ER+/HER2- in metastatic breast cancer.

Reference:

https://www.cancernetwork.com/view/fda-grants-fast-track-designation-to-enobosarm-in-ar-er-her2--metastatic-breast-cancer

seviteronel

Cancer type: Triple Negative Breast Cancer **Variant class:** AR positive

Supporting Statement:

The FDA has granted Fast Track Designation to the small-molecule CYP17 lyase-selective inhibitor, seviteronel, for:

- Androgen receptor (AR) positive advanced triple negative breast cancer (TNBC).
- Estrogen receptor (ER) positive advanced breast cancer.

Reference:

https://www.businesswire.com/news/home/20160106006206/en/Innocrin-Pharmaceuticals-Granted-Fast-Track-Designation-FDA

References

1. Lu et al. International Union of Pharmacology. LXV. The pharmacology and classification of the nuclear receptor superfamily: glucocorticoid, mineralocorticoid, progesterone, and androgen receptors. Pharmacol. Rev. 2006 Dec;58(4):782-97. PMID: 17132855
2. Davey et al. Androgen Receptor Structure, Function and Biology: From Bench to Bedside. Clin Biochem Rev. 2016 Feb;37(1):3-15. PMID: 27057074
3. Crumbaker et al. AR Signaling and the PI3K Pathway in Prostate Cancer. Cancers (Basel). 2017 Apr 15;9(4). PMID: 28420128
4. Leung et al. Non-Genomic Actions of the Androgen Receptor in Prostate Cancer. . Front Endocrinol (Lausanne). 2017 Jan 17;8:2. . PMID: 28144231
5. Waltering et al. Androgen receptor (AR) aberrations in castration-resistant prostate cancer. Mol. Cell. Endocrinol. 2012 Sep 5;360(1-2):38-43. PMID: 22245783
6. Antonarakis et al. AR-V7 and resistance to enzalutamide and abiraterone in prostate cancer. N. Engl. J. Med. 2014 Sep 11;371(11):1028-38. PMID: 25184630
7. Zhu et al. Novel Junction-specific and Quantifiable In Situ Detection of AR-V7 and its Clinical Correlates in Metastatic Castration-resistant Prostate Cancer. Eur. Urol. 2018 May;73(5):727-735. PMID: 28866255
8. https://www.cancernetwork.com/view/fda-grants-fast-track-designation-to-enobosarm-in-ar-er-her2--metastatic-breast-cancer
9. https://www.businesswire.com/news/home/20160106006206/en/Innocrin-Pharmaceuticals-Granted-Fast-Track-Designation-FDA
10. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/202379s035lbl.pdf
11. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/203415s019,213674s006lbl.pdf
12. NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2023]
13. Lallous et al. Functional analysis of androgen receptor mutations that confer anti-androgen resistance identified in circulating cell-free DNA from prostate cancer patients. Genome Biol. 2016 Jan 26;17:10. PMID: 26813233
14. Robinson et al. Integrative clinical genomics of advanced prostate cancer. Cell. 2015 May 21;161(5):1215-1228. PMID: 26000489