UNDERSTANDING THE ROLE OF BRAF MUTATIONS IN METASTATIC MELANOMA

Melanoma is a form of skin cancer that develops when unrepaired DNA damage to skin cells triggers mutations that may lead them to multiply and form "malignant," or cancer-causing, tumors.¹







The incidence of melanoma has MORE THAN DOUBLED in the past 40 years.³

Metastatic melanoma is the most serious and life-threatening type of skin cancer and is associated with low survival rates.^{3,4}

BRAF-Mutant Metastatic Melanoma



BRAF

A variety of genetic mutations can lead to metastatic melanoma, but the most common is *BRAF*.^{1,5}



~50%

of metastatic melanoma cases have the *BRAF* GENE MUTATION, a key target in the treatment of metastatic melanoma.⁵

Role of BRAF and the MAPK Signaling Pathway

The majority of melanomas have mutations associated with the mitogen-activated protein kinase (MAPK) pathway, which is involved in cancer cell growth, differentiation and survival.⁵



BRAF and MEK are key protein kinases in the MAPK signaling pathway (RAS-RAF-MEK-ERK). Clinicians target this pathway to treat advanced melanoma.⁶



Targeted therapy with BRAF and MEK inhibitors has evolved to become a standard of care for patients with advanced or metastatic *BRAF*-mutant melanoma.⁷



- [1] American Cancer Society. What Causes Melanoma Skin Cancer? 2016. https://www.cancer.org/cancer/melanoma-skin-cancer/causes-risks-prevention/what-causes.html.
- [2] American Cancer Society. Cancer Facts & Figures 2018. Atlanta, GA: American Cancer Society; 2018. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures-2018.pdf
- [3] National Cancer Institute. Surveillance, Epidemiology, and End Results (SEER) Cancer Stat Facts: Melanoma of the Skin. Bethesda, MD: National Cancer Institute. https://seer.cancer.gov/statfacts/html/melan.html.
 - 4] American Cancer Society, Survival Rates for Melanoma Skin Cancer, by Stage. 2016. https://www.cancer.org/cancer/melanoma-skin-cancer/detection-diagnosis-staging/survival-rates-for-melanoma-skin-cancer-by-stage.html
- [5] Cheng L, Lopez-Beltran A, Massari F, MacLennan GT, Montironi R. Molecular testing for BRAF mutations to inform melanoma treatment decisions: a move toward precision medicine. Mod Pathol. 2018;3(1):24-38.
- [6] Wang AX, Qi XY. Targeting RAS/RAF/MEK/ERK signaling in metastatic melanoma. IUBMB Life. 2013;65(9):748-758.
- [7] Luke JJ, Flaherty KT, Ribas A, Long GV. Targeted agents and immunotherapies: optimizing outcomes in melanoma. Nat Rev Clin Oncol. 2017;14(8):463-482.