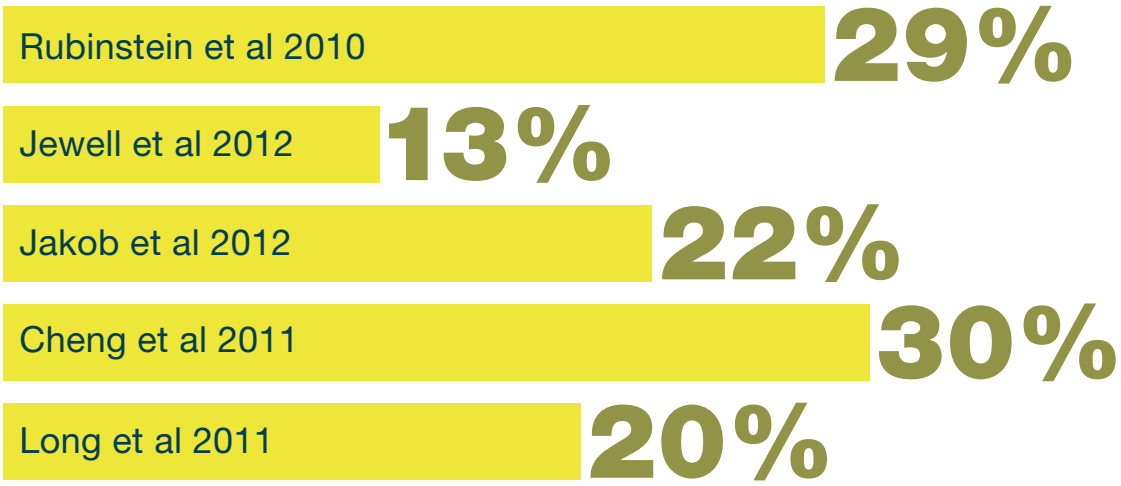
# BRAF STATUS +

# V600K mutations: common, critical, and often undetected

## V600K mutations are the second most common *BRAF* mutation in melanoma[1]

**V600K mutations may account for more than 20% of *BRAF* V600 mutations[2-6]**




**Like other V600 mutations, the V600K mutation is an important driver of aggressive melanoma[7]**

Despite their prevalence, V600K mutations often go undetected[8]

**In a study that assessed the quality of *BRAF* mutation testing in melanomas...**

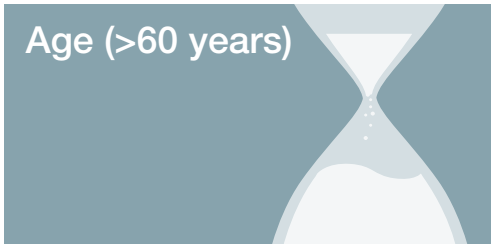
**V600K mutations were missed 21x more often than V600E**

(12.6% failure-to-detect rate in V600K mutations vs 0.6% in V600E mutations[8])

# V600K mutations are more likely to occur in older, traditionally underserved patient populations[3,9,10]

- Older patients with *BRAF*-mutated melanoma are more likely than younger patients to carry a V600K mutation[3,9]
- All patients at risk should be screened but certain factors are more commonly associated with V600K mutations than with V600E mutations[3]

## Independent factors associated with V600K mutations[3,9]







## *BRAF* mutation testing should include accurate detection of V600K[9,11]

- Precision testing methods are critical to ensuring comprehensive mutation detection[9,11]
- Missed V600K mutations can result in failure to treat with targeted therapies that may be most effective in these patients[9,11]

## Choose the most accurate *BRAF* mutation testing methods to guide selection of the most appropriate treatment option for your advanced melanoma patients[9,11]

**For more information, please visit www.brafV600.com**

**References: 1.** Hauschild A, Grob J-J, Demidov LV, et al. Dabrafenib in *BRAF*-mutated metastatic melanoma: a multicentre, open-label, phase 3 randomised controlled trial [published online ahead of print June 25, 2012]. *Lancet*. 2012;380:358-365. doi:10.1016/S0140-6736(12)60868-X. **2.** Rubinstein JC, Sznol M, Pavlick AC, et al. Incidence of the V600K mutation among melanoma patients with BRAF mutations, and potential therapeutic response to the specific BRAF inhibitor PLX4032. *J Transl Med.* 2010;8:67. doi:10.1186/1479-5876-8-67. **3.** Jewell R, Chambers P, Harland M, et al. Clinicopathologic features of V600E and V600K melanoma—letter [published online ahead of print November 20, 2012]. *Clin Cancer Res*. 2012;18:6792. doi:10.1158/1078-0432.CCR-12-2974. **4.** Jakob JA, Bassett RL Jr, Ng CS, et al. *NRAS* mutation status is an independent prognostic factor in metastatic melanoma. *Cancer*. 2012;118:4014-4023. **5.** Cheng S, Chu P, Hinshaw M, Smith K, Maize J, Sferruzza A. Frequency of mutations associated with targeted therapy in malignant melanoma patients. *J Clin Oncol.* 2011;29(suppl; ASCO Meeting Abstracts Part 1):8597. **6.** Long GV, Menzies AM, Nagrial AM, et al. Prognostic and clinicopathologic associations of oncogenic *BRAF* in metastatic melanoma. *J Clin Oncol.* 2011:29:1239-1246. **7.** Ellerhorst JA, Greene VR, Ekmekcioglu S, et al. Clinical correlates of *NRAS* and *BRAF* mutations in primary human melanoma. *Clin Cancer Res*. 2011;17:229-235. **8.** Emile J-F, Tisserand J, Bergougnoux L, et al; and BRAF EQA Group. Improvement of the quality of *BRAF* testing in melanomas with nationwide external quality assessment, for the BRAF EQA group. *BMC Cancer.* 2013;13:472. doi:10.1186/1471-2407-13-472. **9.** Menzies AM, Haydu LE, Visintin L, et al. Distinguishing clinicopathologic features of patients with V600E and V600K *BRAF*-mutant metastatic melanoma. *Clin Cancer Res*. 2012;18:3242-3249. **10.** Bhatt VR, Shrestha R, Krishnamurthy J, et al. Clinicopathologic characteristics and management trends of cutaneous invasive and *in situ* melanoma in older patients: a retrospective analysis of the National Cancer Data Base. *Ther Adv Med Oncol*. 2015;7:4-11. **11.** Heinzerling L, Kühnapfel S, Meckbach D, et al. Rare BRAF mutations in melanoma patients: implications for molecular testing in clinical practice. *Br J Cancer.* 2013;108:2164–2171.

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