

Clinical studies

Study reference	Reason for exclusion
Anwar, Muhammad Ahmed Farooq, Murad, Fadi, Dawson, Erin et al. (2016) Immunohistochemistry as a reliable method for detection of BRAF-V600E mutation in melanoma: a systematic review and meta-analysis of current published literature. The Journal of surgical research 203(2): 407-15	- Systematic review used as source of primary studies
Arenberger, P, Arenbergerova, M, Vohradnikova, O et al. (2008) Early detection of melanoma progression by quantitative real-time RT-PCR analysis for multiple melanoma markers. The Keio journal of medicine 57(1): 57-64	- Did not look at relevant genes

Study reference	Reason for exclusion
Barbano, Raffaella, Pasculli, Barbara, Coco, Michelina et al. (2015) Competitive allele-specific TaqMan PCR (Cast-PCR) is a sensitive, specific and fast method for BRAF V600 mutation detection in Melanoma patients. Scientific reports 5: 18592	- Reference standard did not meet inclusion criteria
Boursault, Lucile, Haddad, Veronique, Vergier, Beatrice et al. (2013) Tumor homogeneity between primary and metastatic sites for BRAF status in metastatic melanoma determined by immunohistochemical and molecular testing. PloS one 8(8): e70826	- Reference standard did not meet inclusion criteria
Bruno, William, Martinuzzi, Claudia, Andreotti, Virginia et al. (2017) Heterogeneity and frequency of BRAF mutations in primary melanoma: Comparison between molecular methods and immunohistochemistry. Oncotarget 8(5): 8069-8082	- Could not create 2 x 2 table for relevant study population
Calbet-Llopart, N., Potrony, M., Tell-Marti, G. et al. (2020) Detection of cell-free circulating BRAFV 600E by droplet digital polymerase chain reaction in patients with and without melanoma under dermatological surveillance. British Journal of Dermatology 182(2): 382-389	- Outcome did not meet protocol
Chen, Qiongrong, Xia, Chunjiao, Deng, Yunte et al. (2014) Immunohistochemistry as a quick screening method for clinical detection of BRAF(V600E) mutation in melanoma patients. Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine 35(6): 5727-33	- Reference standard did not meet inclusion criteria
Chen, Tai-Long, Chang, John Wen-Cheng, Hsieh, Jia-Juan et al. (2016) A Sensitive Peptide Nucleic Acid Probe Assay for Detection of BRAF V600 Mutations in Melanoma. Cancer genomics & proteomics 13(5): 381-6	- Did not look at immunohistochemistry
Cheng, Liang, Lopez-Beltran, Antonio, Massari, Francesco et al. (2018) Molecular testing for BRAF mutations to inform melanoma treatment decisions: a move toward precision medicine. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc 31(1): 24-38	- Did not look at immunohistochemistry
Colomba E, Hélias-Rodzewicz Z, Von Deimling A et al. (2013) Detection of BRAF p.V600E mutations in melanomas: comparison of four methods argues for sequential use of immunohistochemistry and pyrosequencing. The Journal of molecular diagnostics : JMD 15(1): 94-100	- Reference standard did not meet inclusion criteria
Colombino, Maria, Rozzo, Carla, Paliogiannis, Panagiotis et al. (2020) Comparison of BRAF Mutation Screening Strategies in a Large Real-Life Series of Advanced Melanoma Patients. Journal of clinical medicine 9(8)	- Did not look at immunohistochemistry
Corean, J.L.E., George, T.I., Patel, J.L. et al. (2019) Bone marrow findings in metastatic melanoma, including role of BRAF immunohistochemistry. International Journal of Laboratory Hematology 41(4): 550-560	- Reference standard did not meet inclusion criteria
Emile, Jean-Francois, Tisserand, Julie, Bergougnoux, Loic et al. (2013) Improvement of the quality of BRAF testing in melanomas with nationwide external quality assessment, for the BRAF EQA group. BMC cancer 13: 472	- Did not look at immunohistochemistry
Eriksson, H., Zebary, A., Vassilaki, I., Omholt, K., Ghaderi, M., & Hansson, J. (2015). BRAFV600E protein expression in primary cutaneous malignant melanomas and paired metastases. JAMA dermatology, 151(4), 410-416.	- Reference standard did not meet inclusion criteria
Etienne, M., Oca, F., Prunier-Mirebeau, D. et al. (2018) Immunohistochemistry using clone VE1 is an economic,	- Non-English language paper

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specific and sensitive method for detecting the presence of BRAFV600E mutations in melanoma. <i>Annales de Dermatologie et de Venereologie</i> 145(3): 159-165	
Fatnassi-Mersni, G., Arfaoui, A.T., Cherni, M. et al. (2020) Molecular and Immunohistochemical Analysis of BRAF gene in Primary Cutaneous Melanoma: Discovery of novel mutations. <i>Journal of cutaneous pathology</i>	- Reference standard did not meet inclusion criteria
Garg, S., Grenier, S., Misyura, M. et al. (2020) Assessing the Diagnostic Yield of Targeted Next-Generation Sequencing for Melanoma and Gastrointestinal Tumors. <i>Journal of Molecular Diagnostics</i> 22(4): 467-475	- Did not look at immunohistochemistry
Harle, Alexandre, Salleron, Julia, Franczak, Claire et al. (2016) Detection of BRAF Mutations Using a Fully Automated Platform and Comparison with High Resolution Melting, Real-Time Allele Specific Amplification, Immunohistochemistry and Next Generation Sequencing Assays, for Patients with Metastatic Melanoma. <i>PLoS one</i> 11(4): e0153576	- Same sample used in another included study
How-Kit, Alexandre, Lebbe, Celeste, Bousard, Aurelie et al. (2014) Ultrasensitive detection and identification of BRAF V600 mutations in fresh frozen, FFPE, and plasma samples of melanoma patients by E-ice-COLD-PCR. <i>Analytical and bioanalytical chemistry</i> 406(22): 5513-20	- Did not look at immunohistochemistry
Huang, Wen-Kuan, Kuo, Tseng-Tong, Wu, Chiao-En et al. (2016) A comparison of immunohistochemical and molecular methods used for analyzing the BRAF V600E gene mutation in malignant melanoma in Taiwan. <i>Asia-Pacific journal of clinical oncology</i> 12(4): 403-408	- Reference standard did not meet inclusion criteria
Ihle, Michaela Angelika, Fassunke, Jana, Konig, Katharina et al. (2014) Comparison of high resolution melting analysis, pyrosequencing, next generation sequencing and immunohistochemistry to conventional Sanger sequencing for the detection of p.V600E and non-p.V600E BRAF mutations. <i>BMC cancer</i> 14: 13	- Could not separate out melanoma population from overall cohort
Jabbar KJ, Luthra R, Patel KP et al. (2015) Comparison of next-generation sequencing mutation profiling with BRAF and IDH1 mutation-specific immunohistochemistry. <i>The American journal of surgical pathology</i> 39(4): 454-461	- Could not separate out melanoma population from overall cohort
Jurkowska, Monika, Gos, Aleksandra, Ptaszynski, Konrad et al. (2015) Comparison between two widely used laboratory methods in BRAF V600 mutation detection in a large cohort of clinical samples of cutaneous melanoma metastases to the lymph nodes. <i>International journal of clinical and experimental pathology</i> 8(7): 8487-93	- Did not look at immunohistochemistry
Just PA, Audebourg A, Pasmant E et al. (2014) Immunohistochemistry versus next-generation sequencing for the routine detection of BRAF V600E mutation in melanomas. <i>Human pathology</i> 45(9): 1983-1984	- Letter to editor
Kakavand, Hojabr, Walker, Emily, Lum, Trina et al. (2016) BRAF(V600E) and NRAS(Q61L/Q61R) mutation analysis in metastatic melanoma using immunohistochemistry: a study of 754 cases highlighting potential pitfalls and guidelines for interpretation and reporting. <i>Histopathology</i> 69(4): 680-6	- Reference standard did not meet inclusion criteria
Knol, A.-C., Pandolfino, M.-C., Vallee, A. et al. (2015) Comparative analysis of BRAF, NRAS and c-KIT mutation status between tumor tissues and autologous tumor cell-lines	- Reference standard did not meet inclusion criteria

Study reference	Reason for exclusion
of stage III/IV melanoma. <i>Experimental Dermatology</i> 24(1): 70-73	
Lamy, Pierre-Jean, Castan, Florence, Lozano, Nicolas et al. (2015) Next-Generation Genotyping by Digital PCR to Detect and Quantify the BRAF V600E Mutation in Melanoma Biopsies. <i>The Journal of molecular diagnostics : JMD</i> 17(4): 366-73	- Reference standard did not meet inclusion criteria
Leblond, Anne-Laure, Rechsteiner, Markus, Jones, Amy et al. (2019) Microfluidic-Based Immunohistochemistry Combined With Next-Generation Sequencing on Diagnostic Tissue Sections for Detection of Tumoral BRAF V600E Mutation. <i>American journal of clinical pathology</i> 152(1): 59-73	- Could not separate out melanoma population from overall cohort
Loes, Inger Marie, Immervoll, Heike, Angelsen, Jon-Helge et al. (2015) Performance comparison of three BRAF V600E detection methods in malignant melanoma and colorectal cancer specimens. <i>Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine</i> 36(2): 1003-13	- Reference standard did not meet inclusion criteria
Long, E, Ilie, M, Lassalle, S et al. (2015) Why and how immunohistochemistry should now be used to screen for the BRAFV600E status in metastatic melanoma? The experience of a single institution (LCEP, Nice, France). <i>Journal of the European Academy of Dermatology and Venereology : JEADV</i> 29(12): 2436-43	- Reference standard did not meet inclusion criteria
Loo, Eric, Khalili, Parisa, Beuhler, Karen et al. (2018) BRAF V600E Mutation Across Multiple Tumor Types: Correlation Between DNA-based Sequencing and Mutation-specific Immunohistochemistry. <i>Applied immunohistochemistry & molecular morphology : AIMM</i> 26(10): 709-713	- Reference standard did not meet inclusion criteria
Liu, Hui, Li, Zhongwu, Wang, Yan et al. (2014) Immunohistochemical detection of the BRAF V600E mutation in melanoma patients with monoclonal antibody VE1. <i>Pathology international</i> 64(12): 601-6	- Reference standard did not meet inclusion criteria
Malicherova, B., Burjanivova, T., Grendar, M. et al. (2018) Droplet digital PCR for detection of BRAF V600E mutation in formalin-fixed, paraffin-embedded melanoma tissues: A comparison with Cobas 4800, sanger sequencing, and allele-specific PCR. <i>American Journal of Translational Research</i> 10(11): 3773-3781	- Could not create 2 x 2 table for relevant study population
Mancini, I., Simi, L., Salvianti, F. et al. (2019) Analytical evaluation of an NGS testing method for routine molecular diagnostics on melanoma formalin-fixed, paraffin-embedded tumor-derived DNA. <i>Diagnostics</i> 9(3): 117	- Did not look at immunohistochemistry
Manfredi, Laure, Meyer, Nicolas, Tournier, Emilie et al. (2016) Highly Concordant Results Between Immunohistochemistry and Molecular Testing of Mutated V600E BRAF in Primary and Metastatic Melanoma. <i>Acta dermato-venereologica</i> 96(5): 630-4	- Reference standard did not meet inclusion criteria
Marchant, Julie, Mange, Alain, Larrieux, Marion et al. (2014) Comparative evaluation of the new FDA approved THxID TM-BRAF test with High Resolution Melting and Sanger sequencing. <i>BMC cancer</i> 14: 519	- Did not look at immunohistochemistry
Marin, Cristi, Beauchet, Alain, Capper, David et al. (2014) Detection of BRAF p.V600E Mutations in Melanoma by Immunohistochemistry Has a Good Interobserver	- Reference standard did not meet inclusion criteria

Study reference	Reason for exclusion
Reproducibility. Archives of pathology & laboratory medicine 138(1): 71-5	
Massi, Daniela, Simi, Lisa, Sensi, Elisa et al. (2015) Immunohistochemistry is highly sensitive and specific for the detection of NRASQ61R mutation in melanoma. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc 28(4): 487-97	- Could not create 2 x 2 table for relevant study population
McEvoy, Ashleigh C, Wood, Benjamin A, Ardakani, Nima M et al. (2018) Droplet Digital PCR for Mutation Detection in Formalin-Fixed, Paraffin-Embedded Melanoma Tissues: A Comparison with Sanger Sequencing and Pyrosequencing. The Journal of molecular diagnostics : JMD 20(2): 240-252	- Did not look at immunohistochemistry
Melchior, Linea, Grauslund, Morten, Bellosillo, Beatriz et al. (2015) Multi-center evaluation of the novel fully-automated PCR-based Idylla TM BRAF Mutation Test on formalin-fixed paraffin-embedded tissue of malignant melanoma. Experimental and molecular pathology 99(3): 485-91	- Reference standard did not meet inclusion criteria
Mourah, Samia, Denis, Marc G, Narducci, Fabienne Escande et al. (2015) Detection of BRAF V600 mutations in melanoma: evaluation of concordance between the Cobas R 4800 BRAF V600 mutation test and the methods used in French National Cancer Institute (INCa) platforms in a real-life setting. PloS one 10(3): e0120232	- Did not look at immunohistochemistry
Orchard, G E, Wojcik, K, Rickaby, W et al. (2019) Immunohistochemical detection of V600E BRAF mutation is a useful primary screening tool for malignant melanoma. British journal of biomedical science 76(2): 77-82	- Reference standard did not meet inclusion criteria
Panka, David J, Buchbinder, Elizabeth, Giobbie-Hurder, Anita et al. (2014) Clinical utility of a blood-based BRAF(V600E) mutation assay in melanoma. Molecular cancer therapeutics 13(12): 3210-8	- Did not look at immunohistochemistry
Pearlstein, Michelle V, Zedek, Daniel C, Ollila, David W et al. (2014) Validation of the VE1 immunostain for the BRAF V600E mutation in melanoma. Journal of cutaneous pathology 41(9): 724-32	- Reference standard did not meet inclusion criteria
Pellegrini, Cristina, Di Nardo, Lucia, Cipolloni, Gianluca et al. (2018) Heterogeneity of BRAF, NRAS, and TERT Promoter Mutational Status in Multiple Melanomas and Association with MC1R Genotype: Findings from Molecular and Immunohistochemical Analysis. The Journal of molecular diagnostics : JMD 20(1): 110-122	- Reference standard did not meet inclusion criteria
Petty, D.R., Hassan, O.A., Barker, C.S. et al. (2020) Rapid BRAF Mutation Testing in Pigmented Melanomas. The American Journal of dermatopathology 42(5): 343-348	- Did not look at immunohistochemistry
Pisareva, Ekaterina, Gutkina, Nadezhda, Kovalenko, Sergei et al. (2014) Sensitive allele-specific real-time PCR test for mutations in BRAF codon V600 in skin melanoma. Melanoma research 24(4): 322-31	- Did not look at immunohistochemistry
Ponti, Giovanni, Tomasi, Aldo, Maiorana, Antonio et al. (2016) BRAFp.V600E, p.V600K, and p.V600R Mutations in Malignant Melanoma: Do They Also Differ in Immunohistochemical Assessment and Clinical Features?. Applied immunohistochemistry & molecular morphology : AIMM 24(1): 30-4	- Reference standard did not meet inclusion criteria

Study reference	Reason for exclusion
Qiu, T., Lu, H., Guo, L., Huang, W., Ling, Y., Shan, L., ... & Lv, N. (2015). Detection of BRAF mutation in Chinese tumor patients using a highly sensitive antibody immunohistochemistry assay. <i>Scientific reports</i> , 5, 9211.	- Reference standard did not meet inclusion criteria
Qu, Kevin, Pan, Qiulu, Zhang, Xi et al. (2013) Detection of BRAF V600 mutations in metastatic melanoma: comparison of the Cobas 4800 and Sanger sequencing assays. <i>The Journal of molecular diagnostics : JMD</i> 15(6): 790-5	- Did not look at immunohistochemistry
Reid, Anna L, Freeman, James B, Millward, Michael et al. (2015) Detection of BRAF-V600E and V600K in melanoma circulating tumour cells by droplet digital PCR. <i>Clinical biochemistry</i> 48(15): 999-1002	- Did not look at immunohistochemistry
Richter, Anna, Grieu, Fabienne, Carrello, Amerigo et al. (2013) A multisite blinded study for the detection of BRAF mutations in formalin-fixed, paraffin-embedded malignant melanoma. <i>Scientific reports</i> 3: 1659	- Did not look at immunohistochemistry
Routhier, Caitlin Ann, Mochel, Mark C, Lynch, Kerry et al. (2013) Comparison of 2 monoclonal antibodies for immunohistochemical detection of BRAF V600E mutation in malignant melanoma, pulmonary carcinoma, gastrointestinal carcinoma, thyroid carcinoma, and gliomas. <i>Human pathology</i> 44(11): 2563-70	- Reference standard did not meet inclusion criteria
Salvianti, Francesca, Massi, Daniela, De Giorgi, Vincenzo et al. (2019) Evaluation of the liquid biopsy for the detection of BRAFV600E mutation in metastatic melanoma patients. <i>Cancer biomarkers : section A of Disease markers</i> 26(3): 271-279	- Did not look at immunohistochemistry
Schafroth, Christian, Galvan, Jose A, Centeno, Irene et al. (2015) VE1 immunohistochemistry predicts BRAF V600E mutation status and clinical outcome in colorectal cancer. <i>Oncotarget</i> 6(39): 41453-63	- Could not separate out melanoma population from overall cohort
Schiefer, Ana-Iris, Parlow, Laura, Gabler, Lisa et al. (2016) Multicenter Evaluation of a Novel Automated Rapid Detection System of BRAF Status in Formalin-Fixed, Paraffin-Embedded Tissues. <i>The Journal of molecular diagnostics : JMD</i> 18(3): 370-377	- Did not look at immunohistochemistry
Serre, D., Salleron, J., Husson, M. et al. (2018) Accelerated BRAF mutation analysis using a fully automated PCR platform improves the management of patients with metastatic melanoma. <i>Oncotarget</i> 9(63): 32232-32237	- Did not look at immunohistochemistry
Seto, K., Haneda, M., Masago, K. et al. (2020) Negative reactions of BRAF mutation-specific immunohistochemistry to non-V600E mutations of BRAF. <i>Pathology International</i> 70(5): 253-261	- Included all melanomas without information on tumour stage or timing of tests
Shapochka, D, Shapochka, T, Seleznyov, O et al. (2018) USE OF CIRCULATING TUMOR DNA FOR DETECTION OF BRAF V600E MUTATION AND TREATMENT MONITORING IN MELANOMA PATIENTS. <i>Georgian medical news</i> : 76-81	- Did not look at immunohistochemistry
Shofty, B., Artzi, M., Shtrozberg, S. et al. (2020) Virtual biopsy using MRI radiomics for prediction of BRAF status in melanoma brain metastasis. <i>Scientific reports</i> 10(1): 6623	- Did not look at immunohistochemistry
Skorokhod, Alexander (2015) Universal BRAF State Detection by the Pyrosequencing R-Based U-BRAF(V600) Assay. <i>Methods in molecular biology (Clifton, N.J.)</i> 1315: 63-82	- Did not look at immunohistochemistry

Study reference	Reason for exclusion
Thiel, Alexandra, Moza, Monica, Kytola, Soili et al. (2015) Prospective immunohistochemical analysis of BRAF V600E mutation in melanoma. <i>Human pathology</i> 46(2): 169-75	- Reference standard did not meet inclusion criteria
Tzanikou, E., Haselmann, V., Markou, A. et al. (2020) Direct comparison study between droplet digital PCR and a combination of allele-specific PCR, asymmetric rapid PCR and melting curve analysis for the detection of BRAF V600E mutation in plasma from melanoma patients. <i>Clinical Chemistry and Laboratory Medicine</i>	- Could not create 2 x 2 table for relevant study population
Uguen, Arnaud, Talagas, Matthieu, Costa, Sebastian et al. (2015) NRAS (Q61R), BRAF (V600E) immunohistochemistry: a concomitant tool for mutation screening in melanomas. <i>Diagnostic pathology</i> 10: 121	- Reference standard did not meet inclusion criteria
Vallee, Audrey, Denis-Musquer, Marie, Herbreteau, Guillaume et al. (2019) Prospective evaluation of two screening methods for molecular testing of metastatic melanoma: Diagnostic performance of BRAF V600E immunohistochemistry and of a NRAS-BRAF fully automated real-time PCR-based assay. <i>PLoS one</i> 14(8): e0221123	- Reference standard did not meet inclusion criteria
Van Haele, Matthias, Vander Borght, Sara, Ceulemans, An et al. (2020) Rapid clinical mutational testing of KRAS, BRAF and EGFR: a prospective comparative analysis of the Idylla technique with high-throughput next-generation sequencing. <i>Journal of clinical pathology</i> 73(1): 35-41	- Did not look at immunohistochemistry
Yaman, Banu; Kandiloglu, Gulsen; Akalin, Taner (2016) BRAF-V600 Mutation Heterogeneity in Primary and Metastatic Melanoma: A Study With Pyrosequencing and Immunohistochemistry. <i>The American Journal of dermatopathology</i> 38(2): 113-20	- Reference standard did not meet inclusion criteria
Zhang, W., Song, G., Han, X. et al. (2017) A validation study for the use VE1 immunohistochemical staining in screening for BRAF mutation in cutaneous malignant melanoma. <i>Biomedical Research (India)</i> 28(11): 4886-4890	- Reference standard did not meet inclusion criteria
Zhu, Meng-Lei; Zhou, Lan; Sadri, Navid (2018) Comparison of targeted next generation sequencing (NGS) versus isolated BRAF V600E analysis in patients with metastatic melanoma. <i>Virchows Archiv : an international journal of pathology</i> 473(3): 371-377	- Did not look at immunohistochemistry