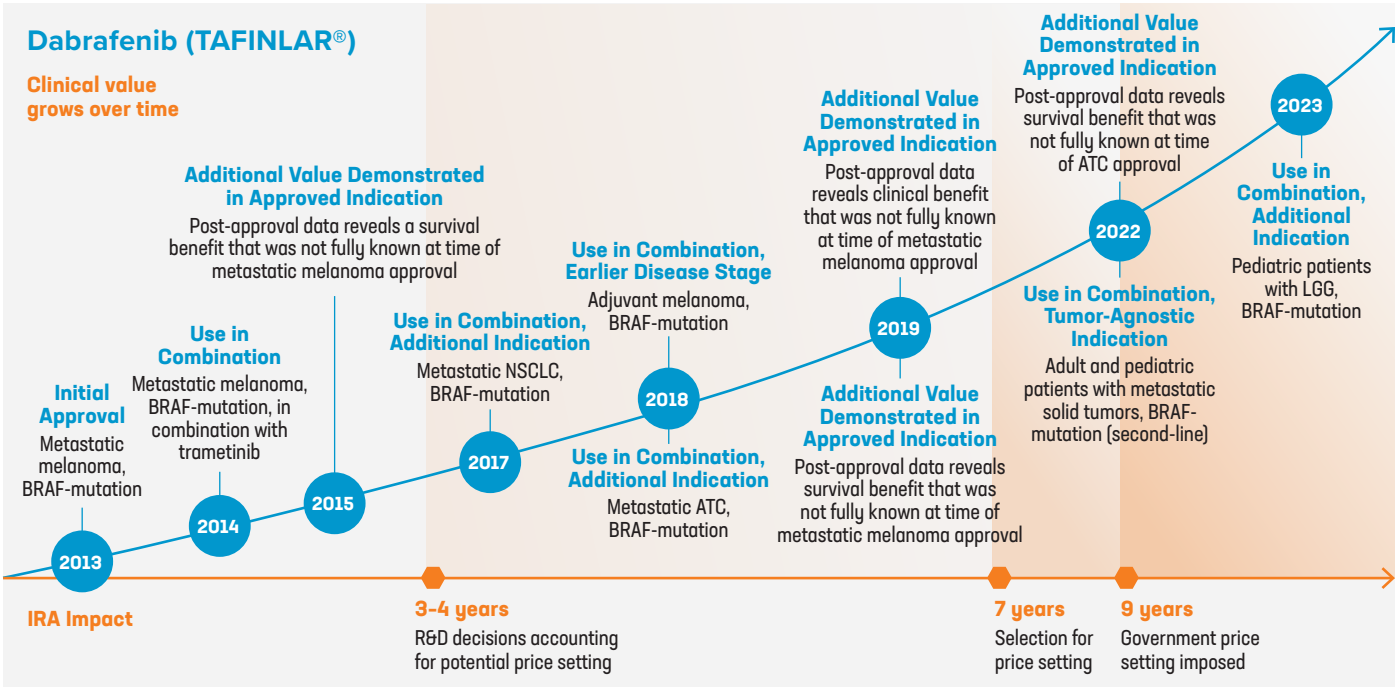
Dabrafenib | TAFINLAR®

In 2013, FDA granted approval of dabrafenib, a targeted oral cancer medicine, for the treatment of patients with metastatic melanoma whose tumors express the BRAF mutation, a genetic change that can cause some melanoma tumors to grow and spread.[1] About half of all metastatic melanoma cases involve changes in the BRAF gene, which has been identified as a driver of cancer growth across a wide range of other solid tumors.[2,3] Dabrafenib was approved as a single agent. It is a BRAF inhibitor designed to block activity of the BRAF protein directly.[4]

Since its initial approval, dabrafenib has demonstrated clinical benefit in numerous cancers that have the BRAF mutation, specifically when taken in combination with trametinib, another targeted oral cancer medicine known as a MEK inhibitor. The MEK gene and BRAF gene work together in the same pathway leading to cancer cell growth.[4] The combination of these therapies, targeting cancer cell growth at multiple points along the pathway, has been studied extensively across many indications, including pediatric patients and rare cancer types that often have limited treatment options, revealing a wide range of benefits that were not known at the time of initial approval.[3]



Use in Combination (January 2014): Granted accelerated approval in combination with trametinib for patients whose melanomas have spread or cannot be removed completely by surgery (metastatic or unresectable melanoma) and express the BRAF mutation. In initial clinical trials, 76% of patients treated with dabrafenib and trametinib responded to the combination, compared to 54% for those on dabrafenib alone.[5] This indication was later converted to traditional approval because of a superior survival benefit of the combination.[6]

Additional Value Demonstrated in Approved Indication (November 2015): Granted traditional approval in combination with trametinib to treat patients with unresectable or metastatic melanoma whose tumors express the BRAF mutation. Two Phase III clinical trials demonstrated a survival benefit confirming the superiority of the dabrafenib and trametinib combination vs one BRAF-targeted treatment alone.[6]

Use in Combination, Additional Indication (June 2017): Approved in combination with trametinib for the treatment of patients with metastatic NSCLC whose tumors express the BRAF mutation, the first approved treatment to specifically target this type of lung cancer. In the clinical trial supporting this approval, the response rate to the combination was over 60%.[7]

Use in Combination, Earlier Disease Stage (April 2018): Approved in combination with trametinib for the adjuvant treatment of patients with melanoma whose tumors express the BRAF mutation and have lymph node involvement. Adjuvant therapy is an additional treatment after surgical resection to help reduce the risk of melanoma returning.[8] In the Phase III study supporting this approval, the risk of disease recurrence or death for patients treated with the combination of dabrafenib and trametinib was reduced by over 50% compared to patients who were not prescribed treatment after surgery.[9]

Use in Combination, Additional Indication (May 2018): Approved in combination with trametinib for the treatment of patients with metastatic anaplastic thyroid cancer (ATC) whose tumors express the BRAF mutation. This is the first treatment approved specifically for ATC, a rare and aggressive type of thyroid cancer accounting for approximately one to two percent of all thyroid cancers.[10,11]

Additional Value Demonstrated in Approved Indication (October 2019): Clinical trial results in patients with metastatic melanoma whose tumors express the BRAF mutation and whose tumors have metastasized to the brain, demonstrated an intracranial response for 50% of patients treated with the dabrafenib and trametinib combination.[12,13] Brain metastases are one of the most common and difficult-to-treat complications in melanoma. Given more than 60% of patients with metastatic melanoma will develop brain metastases, research on this specific type of metastases remains critical to advance improved treatment outcomes for patients.[14]

Additional Value Demonstrated in Approved Indication (June 2019): Long-term clinical data demonstrated that the dabrafenib and trametinib combination led to a 5-year survival rate of one-third among patients with BRAF-mutated metastatic melanoma, an aggressive skin cancer with a historically poor prognosis. These results represented the largest collection of data and the longest follow-up among patients with this type of melanoma who were treated with these targeted therapies.[15]

Additional Value Demonstrated in Approved Indication (January 2022): Clinical data with four years of additional follow-up confirmed the substantial clinical benefit of the dabrafenib and trametinib combination in BRAF-mutated ATC. Study results showed a median survival of 15 months and a 12-month survival rate of 52%. These findings are notable given a historic median survival of less than six months.[16]

Use in Combination, Tumor-Agnostic Indication (June 2022): Granted accelerated approval in combination with trametinib for the treatment of adult and pediatric patients with metastatic solid tumors that express the BRAF mutation who have progressed on previous treatment and have no alternative treatment options. As the first approved tumor-agnostic treatment targeting the BRAF mutation, which drives cancer growth in more than 20 different tumor types, this new indication marked a significant advance for patients. It also marked the first combination approved to target the BRAF mutation in pediatric patients.[3]

Use in Combination, Additional Indication (March 2023): Approved, in combination with trametinib, for the treatment of pediatric patients with BRAF-mutated low-grade glioma (LGG). LGG is the most common pediatric brain cancer. BRAF-mutated tumors account for 15–20% of LGGs and are associated with poor patient outcomes and limited response to available treatments. In a clinical study, 47% of patients responded to the combination, compared to only 11% of patients taking chemotherapy. The FDA also approved a liquid formulation suitable for children who cannot swallow pills, demonstrating how additional research can advance treatment options that can improve administration for specific patient groups, including pediatric populations.[17]

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