Ipilimumab | YERVOY®

In 2011, the FDA approved ipilimumab for the treatment of unresectable or metastatic melanoma, a late-stage skin cancer and one of the deadliest cancers at the time, with a historic average survival of just six months.¹ Ipilimumab stems from a class of immunotherapies known as immune checkpoint inhibitors, a treatment class that helps activate a patient’s own immune system to fight cancer cells and has fundamentally changed outcomes for certain groups of patients with cancer.²,³ Ipilimumab was the first checkpoint inhibitor to be approved and targets a specific protein involved in regulating the immune system, called CTLA-4.² Since the initial approval, clinical studies have shown that ipilimumab has improved survival in melanoma and several other cancers, specifically when taken in combination with nivolumab, a checkpoint inhibitor that targets a different protein on immune cells, called PD-1.⁴ The combination, which targets two different checkpoints of the immune system, potentially works synergistically to increase the body’s ability to fight cancer and has been studied extensively for over a decade, revealing clinical benefits that were not known at the time of initial approval. These benefits highlight not only the tremendous progress that has been made with this class of treatments but underscore how critically important combination treatment approaches are to advancing the treatment paradigm for many forms of cancer.

Use in Combination (October 2015): Approved, in combination with nivolumab, for the treatment of patients with unresectable or metastatic melanoma whose tumors did not express the BRAF V600 mutation. In a clinical trial, 60% of patients treated with ipilimumab and nivolumab responded to the combination. This was the first FDA-approved combination of two immune checkpoint inhibitors in oncology, demonstrating the potential of targeting distinct and complementary immune system pathways involved in this type of cancer.⁵

Additional Indication (October 2015): Approved for the adjuvant treatment of certain patients with stage III melanoma who are at high risk of the cancer returning following surgery. Among these patients, the cancer returns in almost six out of every 10 patients, and patients have a historically low survival rate once the disease returns. Clinical data shows that patients treated with ipilimumab had a 25% reduction in the risk of recurrence or death than patients who received no treatment.⁶,⁷

Use in Combination, Indication Expansion (January 2016): Granted label expansion, based on accelerated approval, in combination with nivolumab for the treatment of patients with unresectable or metastatic melanoma, regardless of BRAF mutation. Clinical data showed that patients on the combination were significantly less likely to have their disease progress than ipilimumab alone.⁸

Indication Expansion (July 2017): Approved for the treatment of pediatric patients 12 years and older with unresectable or metastatic melanoma.³ Pediatric melanoma is rare, accounting for less than 1% of all new cases of melanoma, which makes it particularly difficult to investigate in clinical trials.³ This approval marked a critical new treatment option for this patient population.¹²

Use in Combination, Additional Indication (April 2018): Approved, in combination with nivolumab, as the first immune checkpoint combination therapy for patients with intermediate- and poor-risk advanced renal cell carcinoma (RCC) which affects 75%–80% of those with advanced RCC. These patients historically have had particularly poor prognosis and limited options to improve survival. Clinical data showed that patients treated with the combination had a 37% reduced risk of death versus a standard of care treatment.¹²
Use in Combination, Additional Indication (July 2018): Granted accelerated approval, in combination with nivolumab, for the treatment of patients 12 years of age and older with microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) metastatic colorectal cancer (mCRC) whose disease has progressed following treatment with chemotherapy. MSI-H and dMMR are biomarkers that may indicate likelihood of clinical benefit. Clinical data showed 46% of patients treated with this combination saw their tumor size or amount of cancer in their body decrease.\(^{13}\)

Use in Combination, Additional Indication (March 2020): Granted accelerated approval, in combination with nivolumab, for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib. Clinical data showed that one out of every three patients with this aggressive disease saw their tumor size or amount of cancer in their body decrease when treated with the combination therapy.\(^{14}\)

Use in Combination, Additional Indication (May 2020): Approved, in combination with nivolumab, for patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1. Clinical data showed that patients had a 21% reduction in the risk of death with the combination versus chemotherapy alone.\(^{15}\)

Use in Combination, Additional Indication (May 2020): Approved, in combination with nivolumab and two cycles of limited chemotherapy, in patients with metastatic or recurrent NSCLC, regardless of PD-L1 expression. At one year, more patients treated with the combination and limited chemotherapy were still alive versus those treated with chemotherapy alone.\(^{16}\)

Use in Combination, Additional Indication (October 2020): Approved, in combination with nivolumab, for the treatment of adults with unresectable malignant pleural mesothelioma (MPM). MPM is a rare cancer type, that is often aggressive and associated with poor patient outcomes. The combination, demonstrating superior survival to standard of care chemotherapy, was the first new systemic therapy in over 15 years to be approved by the FDA for MPM.\(^{17}\)

Additional Indication (May 2022): Approved, in combination with nivolumab, for the treatment of patients with advanced or metastatic esophageal squamous cell carcinoma (ESCC). Clinical data showed patients treated with the combination had a 26% reduction in the risk of death compared to patients on chemotherapy.\(^{18}\)

Additional Value Demonstrated in Approved Indication (July 2022): Follow-up data at 7.5 years showed a durable response for patients with metastatic melanoma treated with ipilimumab in combination with nivolumab, demonstrating a long-term survival rate of 48%, which was higher than either therapy taken alone. Prior to more recent novel therapies in melanoma, only about 5% of patients with metastatic melanoma survived for greater than five years.\(^{19,20,21}\)

Use in Combination, Indication Expansion (February 2023): Approved, in combination with nivolumab, for the treatment of pediatric patients 12 years and older with unresectable or metastatic melanoma.\(^{22}\) This approval occurred over a decade after initial approval, highlighting the critical importance of ongoing research for rare childhood cancers like melanoma.\(^{11}\)


