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What's New in the Treatment of Melanoma

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Melanoma is the most important cause of death from dermatological diseases and metastatic melanoma has a very poor prognosis. After decades of research, in 2011 new molecules have been approved for the treatment of advanced melanoma (1).

Ipilimumab is the first agent ever proven to improve survival in advanced melanoma. In 2011, ipilimumab has been approved for patients with advanced melanoma in first and second-line treatment by the Food and Drug Administration and in second line treatment by the European Medicines Agency. A significant survival benefit of combination of ipilimumab with dacarbazine compared with dacarbazine alone for first-line treatment was also reported (2).

Ipilimumab is an antibody that activates the body's immune system to fight melanoma by inhibiting the cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) molecule. The presence of CTLA-4 suppresses the immune system's response to disease, so blocking its activity stimulates the immune system to fight melanoma (3).

Early-phase (phase II) and advanced (phase III) clinical trials have shown that treatment with ipilimumab almost doubled the one-year survival rate for patients with stage III or IV melanoma; also treatment with ipilimumab alone and in combination with vaccines, immunotherapies (such as interleukin-2) and chemotherapies (such as dacarbazine) in patients with metastatic disease results in long term survival benefit, a rare success in the treatment of melanoma. Additionally, ipilimumab is undergoing clinical trials for the treatment of non-small cell lung carcinoma, small cell lung cancer and metastatic hormone-refractory prostate cancer (3).

Side effects of ipilimumab result from autoimmune responses associated with the drug use. Adverse effects include fatigue, diarrhea, skin rash, endocrine deficiencies and inflammation of the intestines. Severe to fatal autoimmune reactions were seen in 12.9% of patients treated with ipilimumab.

Vemurafenib (PLX4032), a BRAF enzyme inhibitor was also approved in august 2011 for the treatment of late stage melanoma with the BRAF V600E mutation. PB Chapman and all demonstrated that vemurafenib improved the rates of response, progression-free and overall survival as compared with dacarbazine in patients with untreated, unresectable stage IIIC or stage IV melanoma with the BRAF V600E mutation (4).

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