Pharmacotherapeutic report on ipilimumab (Yervoy®) for the indication 'treatment of advanced (unresectable or metastatic) melanoma in adults who have received prior therapy'.

Medicine. Ipilimumab 5 mg/ml concentrate for solution for infusion. Available vials: 10 ml and 40 ml (with resp. 50 mg and 200 mg ipilimumab).

Summary of the therapeutic value

Intended effects. In a single phase-3 study in patients with advanced (stage III or IV) melanoma who had been treated previously, and had a positive status for HLA-A2*0201, ipilimumab significantly improved the median overall survival in comparison with the GP100 vaccine. The effect of ipilimumab could be extrapolated to patients with a negative status for HLA-A2*0201. Estimating the one-year survival rates of patients with melanoma remains difficult, so it is not clear if the one-year survival rates found in the phase-3 study correspond to daily practice.

Unintended effects. Ipilimumab is associated with serious or life-threatening immune-related gastrointestinal reactions, hepatotoxicity, skin reactions, neurological reactions and endocrinopathy.

In the phase-3 study with ipilimumab, treatment-related grade 3 or 4 adverse events were very common, leading to discontinuation in 10% of the patients and to death in 3.1% of the patients treated with ipilimumab. Most of these adverse events resolved following initiation of appropriate medical therapy or withdrawal of ipilimumab.

Experience. Experience with ipilimumab is limited.

Applicability. In patients treated with ipilimumab early diagnosis and appropriate management of adverse events is essential in order to minimise life-threatening complications. Systemic high-dose corticosteroids with or without additional immunosuppressive therapy may be required for management of severe immune-related adverse reactions.

Ease of use. Ipilimumab is administered intravenously over a 90-minute period every 3 weeks for a total of 4 doses.

Final conclusion. Because of a significant improvement in median overall survival and in the absence of approved second line therapy, the conclusion that, despite the very common serious or life-threatening immune-related adverse events involved, ipilimumab has a therapeutic added value in comparison with the GP100 vaccine for the treatment of patients with unresectable or metastatic melanoma who have received prior therapy.

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