FDA approves ipilimumab for treatment of melanoma

The Food and Drug Administration (FDA) has approved ipilimumab (Yervoy) for the treatment of patients with newly diagnosed or previously treated unresectable or metastatic melanoma.

'The results of the 020 study on which the FDA based their decision represents the first time ever that a drug has been shown to increase overall survival in advanced melanoma,' said Dr Paul Lorigan, a consultant oncologist from the Christie Hospital NHS Foundation Trust, who has been involved in the trials. 'This is the first time in 40 years,' he added, 'that there is a new treatment option in melanoma.'

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) molecules found on T cells. CTLA-4 has been characterized as a 'brake' that binds to co-stimulatory molecules on antigen-presenting cells, preventing their interaction with CD28 on T cells, thereby generating a signal that prevents further T-cell activation.

In the 020 study, 676 patients with unresectable or metastatic melanoma (who had received at least one prior systemic treatment) were randomized 3:1:1 to one of three treatment arms consisting of ipilimumab 3 mg/kg intravenously in combination with the tumour vaccine (n=403); ipilimumab plus vaccine placebo (n=137); and tumour vaccine with placebo (n=136). Overall survival was 10 months for ipilimumab alone *vs* 6 months for vaccine alone (hazard ratio=0.66; 95% confidence interval=0.51–0.87, P=0.0026).

The most common adverse events were immune-related and occurred in around 60% of patients treated with ipilimumab and 32% treated with the comparator arm. Immune-related adverse events were treated with the use of supportive care and systemic steroids using established protocol specific treatment guidelines. 'There has been a suggestion that response to ipilimumab is correlated with toxicity, and that toxicity is a surrogate for immune stimulation,' said Dr Lorigan.

The approved dose for ipilimumab is 3 mg/kg administered intravenously over 90 minutes every 3 weeks for a total of four doses.

Bristol Myers Squibb have also announced that study 024, comparing ipilimumab 10 mg/kg in combination with dacarbazine to dacarbazine alone, has met its primary end point of improving overall survival in previously untreated patients with unresectable stage III or IV melanoma.

'The study was event driven, i.e. a certain number of deaths had to be reported to reach the primary end point. The fact that 024 reported 12 months later than expected offers an impressive indication that overall survival in the ipilimumab arm increased markedly,' said Dr Lorigan, cautioning that the extent of benefit will only be fully appreciated when the study reports. An abstract of the 024 data has been submitted to the American Society of Clinical Oncology for potential presentation in June.

Dr Lorigan said that the European Medicines Agency is expected to make their announcement on ipilimumab later this year. 'The National Institute for Health and Clinical Excellence have been horizon scanning on ipilimumab for a while, and already have a date scheduled in 2012 to consider the agent's cost effectiveness,' he added.

Janet Fricker

Survival benefit of cetuximab in metastatic colorectal cancer

An updated analysis of the phase III CRYSTAL study has included the evaluation of overall survival according to KRAS mutation status in patients with metastatic colorectal cancer.

The analysis found that the addition of Erbitux (cetuximab) to standard chemotherapy (FOLFIRI) in patients with KRAS wild-type disease resulted in a significant improvement in overall survival of 3.5 months compared with FOLFIRI alone (Van Cutsem et al, 2011).

CRYSTAL is the only trial to date to demonstrate a significant overall survival benefit of a targeted therapy in combination with current standard chemotherapy (FOLFIRI) in first-line treatment of metastatic colorectal cancer.

Van Cutsem E, Köhne CH, Láng I et al (2011) Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status. *J Clin Oncol* Apr 18 [Epub ahead of print]

First oral treatment provides choice for multiple sclerosis

The first oral treatment for multiple sclerosis, fingolimod 0.5 mg (Gilenya), has been authorised for people with highly active relapsing remitting multiple sclerosis who have failed to respond to treatment with an interferon, or for those with rapidly evolving severe disease.

Once-monthly injectable treatment for schizophrenia

Xeplion (paliperidone palmitate), a new once-monthly, long-acting injectable antipsychotic, provides sustained and consistent symptom control and a reduced risk of relapse compared to placebo for patients with schizophrenia. It also offers practical features, including the option of being delivered in the arm and simple, convenient administration.

New standards for cross-border reproductive care

The European Society of Human Reproduction and Embryology is setting the first ever standards in cross border reproductive care, which will focus on the safety of patients, gamete donors, surrogates and future children.