Longest follow-up of melanoma patients treated with ipilimumab shows some survive up to 10 years

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Patients with advanced melanoma, who have been treated with the monoclonal antibody, ipilimumab, can survive for up to ten years, according to the largest analysis of overall survival for these patients, presented at the 2013 European Cancer Congress (ECC2013) [1] today (Saturday).

Professor Stephen Hodi (MD), Assistant Professor of Medicine at the Dana-Farber Cancer Institute (Boston, USA), told the congress: "Our findings demonstrate that there is a plateau in overall survival, which begins around the third year and extends through to the tenth year.

"These results are important to healthcare providers and patients with advanced melanoma since they provide a perspective on long-term survival for ipilimumab patients who are alive after three years of treatment. Our data, which represent the longest follow-up of the largest numbers of patients on any globally approved melanoma therapy, will provide a benchmark for future medicines for advanced melanoma."

Ipilimumab is a human monoclonal antibody that activates the immune system to fight melanoma skin cancer by targeting a protein receptor called Cytotoxic T-Lymphocyte Antigen 4 (CTLA-4). In melanoma, CTLA-4 is inhibited from recognising and destroying cancer cells, but ipilimumab turns off the inhibitory mechanism, enabling CTLA-4 to continue killing the cancer cells.

It is already known that some patients treated with the drug survive for long periods, with one phase III clinical trial showing an overall survival rate of 18% after five years. Therefore, Prof Hodi and colleagues from Germany, France and the USA collected data on 1861 patients in 12 prospective and retrospective studies to provide a more precise estimate of ipilimumab's effect on long-term survival. In addition, they analysed data from a further 2985 patients who had been treated with the drug but were not part of any clinical trial, giving the researchers data on a total of 4846 patients.

The analysis of the 1861 patients showed that the median overall survival was 11.4 months (11.4 being the middle number separating the higher half of the patient survival time from the lower half). "Among these patients, 254 patients (22%) were still alive after three years. There were no deaths among patients who survived beyond seven years, at which time the overall survival rate was 17%. The longest overall survival follow-up in the database is 9.9 years," said Prof Hodi.

"The plateau, which started at three years and continued through to ten years, was observed regardless of dose (3 or 10 mg/kg), whether the patients had received previous treatment or not, and whether or not they had been kept on a maintenance dose of the drug. However, as this was not a randomised comparison, one cannot draw direct conclusions on differences between the doses or the populations."

When data from the total 4846 patients were analysed, the median overall survival was 9.5 months, with a plateau in overall survival starting around three years for 21% of the patients. "This slightly lower survival rate was because there were limited and incomplete data on overall survival, and patients given ipilimumab through the extended access programme tended to be more ill and with more advanced disease," explained Prof Hodi.

He concluded: "The limitation of this study is that it is a pooled analysis from phase II, phase III and observational data and not from a single randomised, controlled study. However, these results are consistent with our findings from randomised clinical trials and confirm the durability of the plateau in overall survival, previously shown to extend to at least five years but now shown to extend up to ten years."

Past President of ECCO, Professor Alexander Eggermont, Directeur Général of the Institut Gustave Roussy Comprehensive Cancer Center (France), who specialises in the treatment of melanoma, commented: "This pooled analysis clearly demonstrates that ipilimumab can lead to long-lasting tumour control in metastatic melanoma patients. With a response rate of only 10-15%, one can achieve more than 3-10 years survival in 17-25% of patients who have received only a few doses of ipilimumab. Thus, patients apparently can keep residual tumours under control for a long time when the immune system is properly 'reset', and the concept of 'clinical cures' becomes a reality. These survival results could even double or triple with anti-PD1/PDL1 monoclonal antibodies, and metastatic melanoma could become a curable disease for perhaps more than 50% of patients over the coming 5-10 years." [3]

More information: [1] The 2013 European Cancer Congress is the 17th congress of the European CanCer Organisation (ECCO), the 38th congress of the European Society for Medical Oncology (ESMO) and the 32nd congress of European Society for Therapeutic Radiology and Oncology (ESTRO).

[2] This pooled analysis received no funding. Three phase II studies were conducted by the US National Cancer Institute. The remaining studies were conducted by Bristol-Myers Squibb.

[3] The programmed death 1 protein PD-1 and its signalling molecule (or ligand) PD-L1 prevent the body's immune system from attacking and

killing cancer cells and this allows the cancer to spread. Anti-PD1/PDL1 monoclonal antibodies work by blocking the interaction between PD-L1 and the immune system, thereby boosting a patient's anti-cancer immune response. They are being investigated in a range of different cancers.

Abstract no: LBA 24, "Pooled analysis of long-term survival data from phase II and phase III trials of ipilimumab in metastatic or locally advanced, unresectable melanoma". Melanoma and skin cancer proffered papers session, 11.15 hrs CEST, Saturday 28 September, Elicium 1.

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