Immunotherapy: Promising results in first and second line treatment of metastatic bladder cancer

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Immunotherapy has shown promising results in first and second line treatment of metastatic bladder cancer in two phase II trials presented at the ESMO 2016 Congress in Copenhagen.

Up to half of patients with metastatic bladder cancer are not eligible for survival prolonging first line treatment with cisplatin-based chemotherapy. Survival in these patients is just nine to ten months with currently available alternative chemotherapy.

The phase II KEYNOTE-052 trial1 evaluated the efficacy and safety of PD-1 blockade with pembrolizumab as first line therapy in cisplatin ineligible patients with metastatic or locally advanced bladder cancer. Today researchers presented the preliminary analysis of the first 100 patients enrolled in the trial. The primary endpoint of objective response rate was 24%. The biomarker cut point to identify patients who are most likely to respond to the drug was determined to be 10% or greater total PD-L1 expression in immune cells or tumour cells. Thirty patients had this level of expression of whom 11 (37%) responded to treatment. The median duration of response has not yet been reached and treatment was well tolerated.

Lead author Dr Arjun Balar, Assistant Professor, NYU Langone Medical Centre, New York, US, said: "Pembrolizumab has substantial activity with a favourable safety profile as first line therapy in cisplatin

ineligible patients with metastatic bladder cancer. The biomarker cut point will need to be validated in the larger study population, but seems to identify patients most likely to respond to pembrolizumab well. Immunotherapy is rapidly redefining our treatment approach for patients facing this dreadful disease."

For several decades, there had been no global standard of care for second line treatment of patients with metastatic bladder cancer who progress despite platinum-based chemotherapy until the recent development of immune checkpoint blockade. In another study presented today, the phase II CheckMate 275 trial2 assessed the activity and safety of the PD-1 inhibitor nivolumab in 270 patients with metastatic bladder cancer who have progressed despite first line platinum-based chemotherapy. CheckMate 275 is the largest study of a PD-1 inhibitor in bladder cancer reported to date.

In the 265 patients who could be evaluated for efficacy, the primary endpoint of objective response rate was 19.6%. The median duration of response has not yet been reached, with a median follow-up of seven months. In both patients with tumours expressing higher and lower levels of PD-L1 (including those with less than 1% PD-L1), the objective response rate was above that achieved historically with chemotherapy.

"This data is being submitted to support registration of nivolumab for patients with metastatic urothelial cancer that has progressed despite platinum-based chemotherapy, an indication for which the US Food and Drug Administration has granted breakthrough therapy designation to nivolumab," said lead author Professor Matthew Galsky, Professor of Medicine, Mount Sinai School of Medicine, New York, US. "Immune checkpoint blockade has become the most promising approach for these patients."

Commenting on the current management of bladder cancer, Dr Maria

De Santis, Associate Clinical Professor for Oncology, Cancer Research Centre, University of Warwick, UK, said: "There are insufficient treatment options for patients ineligible for cisplatin and for those progressing on cisplatin-based chemotherapy."

She continued: "This year the first immune check point inhibitor, atezolizumab, was approved for patients with bladder cancer and CheckMate 275 provides similar results with nivolumab in the second line setting."

"KEYNOTE-052 confirms that immunotherapy is also active as first line therapy in cisplatin ineligible patients, with a slightly lower response rate than chemotherapy," said De Santis. "However, the duration of response with pembrolizumab seems to exceed that of chemotherapy in historical controls. The protocol included a new biomarker definition and cut-off which needs further evaluation."

She concluded: "Immune check point inhibitors have started to alter the therapeutic landscape for bladder cancer. We expect even more dramatic changes in the coming years with the use of immunotherapy in other clinical stages and as combination therapy."

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