Nivolumab Benefits Durable in Three Tumor Types

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Nivolumab, the most advanced agent in the rapidly developing field of PD-1-targeting cancer immunotherapy, delivered durable clinical benefits across multiple solid tumor types, according to long-term data from a phase I trial.

Benefits in overall response rates and survival were evident in patients with advanced, treatment-refractory melanoma, non-small cell lung cancer (NSCLC), or renal cell carcinoma (RCC), with the most dramatic results seen in melanoma, according to Suzanne L. Topalian, MD, who presented the findings during the 2013 American Society of Clinical Oncology Annual Meeting in Chicago in June.[1]

The overall response rates (ORRs), defined as complete or partial responses by standard RECIST criteria, were 31% for patients with melanoma, 29% for those with RCC, and 17% for participants with NSCLC.

The results represent long-term efficacy data involving 306 patients who received nivolumab from 2008-2012, with at least 14 months' follow-up. The participants had a median age of 63 years and good performance status scores, and nearly half had received three or more prior therapies.

Topalian, a professor of Surgery and Oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University in Baltimore, Maryland, said overall survival results (**Table**) "compare favorably to published results in similar heavily pretreated patient groups with advanced metastatic disease."

Table. Nivolumab Phase I Long-Term Results[1]

Tumor Type	ORR (%; no patients)	Response Duration (median; mo)	OS (median; mo)	Survival (%)	
				1 yr	2 yr
Melanoma	31 (33/107)	24.0	16.8	62	43
NSCLC	17 (22/129)	17.0	9.6	42	14
RCC	29 (10/34)	12.9	>22	70	50

NSCLC indicates non-small cell lung cancer; ORR, overall response rate; OS, overall survival; RCC, renal cell carcinoma.

Earlier data from the trial, presented last year at ASCO's annual meeting, have generated much excitement. The ongoing positive findings have prompted Bristol-Myers Squibb to advance development of the drug; there are now six ongoing phase III trials in the three tumor types.

Nivolumab, also known as BMS-936558, targets the PD pathway. "This is a normal turnoff mechanism that's used by the immune system to terminate immune responses at the appropriate time," said Topalian. "It's a pathway that can be co-opted by cancer cells to fly below the radar of the immune system."

A fully human monoclonal antibody, nivolumab blocks the PD-1 receptor from binding to both of its known ligands, PD-L1 (B7-H1) and PD-L2 (B7-DC), thus "rejuvenating antitumor immunity," Topalian said.

Topalian said the results suggest that "nivolumab can reset the balance between the immune system and cancer." Of the 65 patients who responded to the drug, 65% (42 patients) had a response lasting more than a year and 54% (35 patients) had ongoing responses at the time of data analysis. "Responses are persisting in some cases for a fairly long time after the drug is stopped," said Topalian.

The treatment consisted of four-dose cycles of intravenously administered nivolumab (0.1-10 mg/kg) every two weeks for eight-week cycles, with a maximum duration of treatment for up to two years. Among 27 responding patients who had discontinued treatment for reasons other than disease progression, 70% (19 patients) maintained responses off-drug for 16-59 weeks, including 14 patients whose response was ongoing at time of analysis, Topalian said.

In terms of adverse events (AEs), Topalian said most of the toxicities occurred within the first six months of treatment, with skin and gastrointestinal reactions most frequently reported. Drug-related AEs of all grades occurred among 75% of the patients, including 17% of patients who experienced grades 3/4 AEs. Immune-related AEs of all grades occurred in 46% of patients, including grades 3/4 AEs in 6% of participants.

There were three deaths associated with pneumonitis early in the trial, resulting in the development of treatment algorithms for early detection and management, said Topalian.

Reference

1. Topalian SL, Sznol M, Brahmer JR, et al. Nivolumab (anti- PD-1; BMS-936558; ONO-4538) in patients with advanced solid tumors: survival and long-term safety in a phase I trial. Presented at: 2013 American Society of Clinical Oncology Annual Meeting; May 31-June 4, 2013; Chicago, IL. Abstract 3002.

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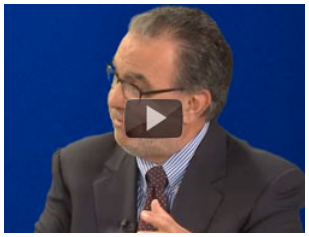

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