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NCCN Guidelines® Panel: Bladder Cancer

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit to the Bladder Cancer Panel the enclosed Opdivo clinical data that has been presented at the 2016 American Society of Clinical Oncology (ASCO), for the Panel's consideration. The phase I/II study evaluated the use of nivolumab monotherapy for the treatment of patients with locally advanced or metastatic urothelial carcinoma.[1]

These data are being submitted in response to a standing request from the NCCN for new data.

Rationale: We are providing data from a cohort of an open-label phase I/II clinical trial (CA209-032) that evaluated the safety and efficacy of nivolumab monotherapy for the treatment of patients with locally advanced or metastatic urothelial carcinoma who had received at least one prior platinum-containing regimen.[1]

Study CA209-032, Urothelial Carcinoma cohort: This cohort enrolled patients with locally advanced or metastatic urothelial carcinoma who progressed after ≥ 1 prior platinum based therapy for metastatic disease, or had recurrence within 1 year of completing prior platinum-based neo-adjuvant or adjuvant therapy. Patients received nivolumab 3 mg/kg every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study end.

The primary endpoint was investigator-assessed objective response rate (ORR). Secondary endpoints were safety, duration of response, progression-free survival (PFS), and overall survival (OS).

Results: The cohort enrolled 78 patients. Patients had a minimum follow-up of 9 months and received a median of 8.5 doses (range 1-46). Baseline characteristics, efficacy and safety findings are described below:

Table 1. Baseline Characteristics, highlights:

	Nivolumab 3 mg/kg (n = 78)
Age, years, median (min, max)	65.5 (31, 85)
Number of prior treatment regimens, %	
▪ 1	33.3
▪ 2-3	53.8
▪ >3	12.8
Number of Bellmunt risk factors, %	
0	34.6
1	50.0
2	10.3
3	5.1
Patients with quantifiable tumor PD-L1 expression	n = 67
PD-L1 expression, %	
▪ < 1%	62.7
▪ ≥ 1%	37.3

Table 2. Efficacy findings, highlights:

	Nivolumab 3 mg/kg (N = 78)
ORR, % (95% CI)	24.4 (15.3-35.4)
Best overall response, %	
▪ Complete response	6.4
▪ Partial response	17.9
▪ Stable disease	28.2
▪ Progressive disease	38.5
ORR by PD-L1 expression, % (95% CI)	
▪ PD-L1 < 1%	26.2 (13.9-42.0)
▪ PD-L1 ≥ 1%	24.0 (9.4-45.1)
Median time to response, months (SD)	1.48 (2.14)
Median duration of response, months (95% CI)	NR (9.92-NE)
Median PFS, months (95% CI)	2.78 (1.45-5.85)
Median OS, months (95% CI)	9.72 (7.26-16.16)

Abbreviations: ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SD, standard deviation.

Safety findings, highlights:

A summary of safety findings is presented in Table 3. Grade 5 treatment-related adverse events were reported in 2 patients, thrombocytopenia (n = 1) and pneumonitis (n = 1). A total of 2.6% of patients discontinued treatment due to study drug toxicity. Treatment related adverse events (TRAEs) of any grade were reported in 83% of patients; 22% experienced a Grade 3-4 TRAE. Select TRAEs, which are events of interest based on the mechanism of action of nivolumab, are described below.

Table 3. Select TRAEs.

	Nivolumab 3 mg/kg (N = 78)	
	Any Grade	**Grade 3-4**
Select TRAEs, %		
▪ Gastrointestinal	10	1
▪ Hepatic	5	1
▪ Pulmonary	3	0
▪ Renal	9	1
▪ Skin	42	3

The following resources are submitted for your review. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors on this publication.

1. Sharma P, Bono P, Kim J, et al. Efficacy and safety of nivolumab monotherapy in metastatic urothelial cancer: results from the phase I/II CheckMate 032 study. Oral presentation presented at The American Society of Clinical Oncology (ASCO) 2016 Annual Meeting; June 3-7, 2016; Chicago, Illinois.
2. Opdivo Prescribing Information.

Thank you for your consideration of this request.

Sincerely,

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Bristol-Myers Squibb Company