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NCCN Guidelines® Panel: Gastric Cancer

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit to the Gastric Cancer Panel the enclosed Opdivo clinical data that has been presented at the 2016 American Society of Clinical Oncology (ASCO) conference, for the Panel's consideration. The phase 1/2 study evaluated the use of nivolumab as monotherapy or in combination with ipilimumab for the treatment of patients with advanced or metastatic gastric cancer.[1]

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

Rationale: We are providing recently presented data from a cohort in a phase 1/2 trial (CA209-032) that evaluated the safety and efficacy of nivolumab as monotherapy or in combination with ipilimumab for the treatment of patients with advanced gastric cancer who had progressed on at least one prior chemotherapy.[1]

Study CA209-032, Gastric Cancer cohort[1]: In this open-label phase 1/2 study, patients with stage IV gastric, esophageal, or gastroesophageal junction adenocarcinoma who had progressive disease after ≥ 1 prior chemotherapy, were eligible to receive intravenous nivolumab 3 mg/kg every 2 weeks (n = 59), or the combination of nivolumab 1 mg/kg plus ipilimumab 3 mg/kg (n = 49) every 3 weeks for 4 cycles followed by nivolumab 3 mg/kg every 2 weeks, or nivolumab 3 mg/kg plus ipilimumab 1 mg/kg (n = 52) every 3 weeks for 4 cycles followed by nivolumab 3 mg/kg every 2 weeks. Patients were treated until disease progression or unacceptable toxicity.

The primary endpoint was objective response rate (ORR) by RECIST 1.1. Secondary endpoints were treatment-related adverse events, overall survival, progression-free survival, and duration of response.

Baseline characteristics, highlights:

Table 1. Selected Baseline Characteristics

	Nivolumab 3 mg/kg (n = 59)	**Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg (n = 49)**	**Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg (n = 52)**
Age, mean (SD), years	57 (11)	53 (13)	56 (13)
Number of prior treatment regimens, %			
▪ 0	0	2	0
▪ 1	17	12	31
▪ 2-3	71	65	56
▪ > 3	12	20	13
PD-L1 quantifiable, %			
▪ < 1% expression	42	59	52
▪ ≥ 1% expression	25	18	21
▪ < 5% expression	58	76	65
▪ ≥ 5% expression	10	2	8

Abbreviation: SD - standard deviation

Efficacy findings, highlights:

Table 2. Efficacy Data in Evaluable Patients

	Nivolumab 3 mg/kg (n= 59)	**Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg (n=46)**	**Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg (n=49)**
ORR, %	14	26	10
▪ Complete response	2	2	0
▪ Partial response	12	24	10
▪ Stable disease	19	17	31
▪ Progressive disease	58	50	47
▪ Unable to determine	10	7	12
Median time to response, months (range)	1.6 (1.2, 4.0)	2.6 (1.2, 4.1)	2.6 (1.2, 4.1)
Median duration of response, months (95% CI)	7.1 (3.0, 13.2)	5.6 (2.8, NE)	NA (2.5, NE)
Disease control rate, %	32	43	41
	Nivolumab 3 mg/kg (n= 59)	**Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg (n=49)**	**Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg (n=52)**
ORR by PD-L1 expression, % (95% CI)			
▪ PD-L1 < 1%	12 (3, 31)	21 (8, 40)	0 (0, 13)
▪ PD-L1 ≥ 1%	27 (8, 55)	44 (14, 79)	27 (6, 61)
▪ PD-L1 < 5%	15 (5, 31)	27 (14, 44)	6 (1, 20)
▪ PD-L1 ≥ 5%	33 (4, 78)	0 (0, 98)	25 (1, 81)
Median PFS, months (95% CI)	1.36 (1.25, 1.51)	1.45 (1.25, 3.94)	1.58 (1.38, 2.60)
Median OS, months (95% CI)	5.03 (3.35, 12.42)	6.87 (3.61, NA)	4.83 (3.02, 9.07)

Abbreviations: NA, not available; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival

Safety findings, highlights:

A summary of safety findings is presented in Table 3. Grade 5 treatment-related tumor lysis syndrome was reported in one patient in the nivolumab 3 mg/kg plus ipilimumab 1 mg/kg arm.

Table 3. Safety Data

	Nivolumab 3 mg/kg (n = 59)	**Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg (n = 49)**	**Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg (n = 52)**
Treatment-related AEs occurring in ≥ 10% of patients, %			
▪ Any grade	70	84	75
▪ Grade 3-4	17	45	27
Therapy discontinued, %	93	88	90

Abbreviations: AE, adverse event

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 of this presentation.

1. Janjigian YY, Bendell J, Calvo E, et al. Phase 1/2, open-label study of safety and activity of nivolumab alone or with ipilimumab in advanced and metastatic gastric cancer: CheckMate 032. Poster presentation presented at: The 52nd American Society of Clinical Oncology (ASCO) Annual Meeting; June 3-7, 2016; Chicago, Illinois, USA.
2. OPDIVO Prescribing Information.

Thank you for your consideration of this request.

Sincerely,

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Vice President, Head US Medical Oncology
Bristol-Myers Squibb Company