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NCCN Guideline® Panel: Non-Small Cell Lung Cancer (NSCLC)

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed clinical data for OPDIVO® (nivolumab) and YERVOY® (ipilimumab) from the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting for the Panel's consideration. This phase 1 study evaluated the use of nivolumab plus ipilimumab as first-line treatment of patients with advanced NSCLC.[1]

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

FDA Clearance (NSCLC indication): Currently, nivolumab is approved for the treatment of patients with metastatic NSCLC, who have progressed on or after platinum-based chemotherapy. Patients with EGFR or ALK aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving nivolumab.[2]

Rationale: We are providing a summary of the data presented at the ASCO 2016 Annual Meeting from a cohort in a phase 1 study (CA209-012), evaluating the safety and efficacy of nivolumab in combination with ipilimumab for the treatment of patients with stage IIIB/IV NSCLC who had no prior chemotherapy for advanced disease.

Study CA209-012, combination therapy cohort (N = 77): In this cohort, patients received nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg either every 12 weeks (n = 38) or every 6 weeks (n = 39) until unacceptable toxicity or disease progression.[1]

The primary endpoint of the study was safety. Secondary endpoints included objective response rate (ORR) and 24-week progression free survival (PFS) rate. Overall survival (OS) and efficacy by PD-L1 expression were exploratory endpoints.[1]

Baseline characteristics, highlights

Table 1. Selected Baseline Characteristics[1]

	Nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 12 weeks (n = 38)	Nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 6 weeks (n = 39)
Median age (range), years	68 (50-91)	62 (47-87)
Stage IV, %	89	97
Non-squamous histology, %	82	85
PD-L1 quantifiable, n (%) ▪ ≥ 1%, n/N (%) ▪ ≥ 5%, n/N (%)	31 (82) 21/31 (68) 16/31 (52)	30 (77) 23/30 (77) 19/30 (63)

Safety findings, highlights

A summary of safety findings is presented in Table 2. No treatment-related deaths were reported. The safety results from another cohort in this study which evaluated nivolumab monotherapy, is included for reference.[1]

Table 2. Safety Data[1]

	Nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 12 weeks* (n = 38)	Nivolumab 3 mg/kg every 2 weeks + iIpilimumab 1 mg/kg every 6 weeks* (n = 39)	Nivolumab 3 mg/kg every 2 weeks† (n = 52)
Treatment-related AEs ▪ Any grade, % ▪ Grade 3-4, %	 82 37	 72 33	 71 19
Any grade treatment-related AEs leading to discontinuation, %	11	13	10

*Based on a February 2016 database lock. †Based on a March 2015 database lock.

Efficacy findings, highlights

A summary of the efficacy results are presented in Tables 3 and 4. The results from another cohort in this study which evaluated nivolumab monotherapy, is included for reference.[1]

Table 3. Efficacy Data[1]

	Nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 12 weeks* (n = 38)	Nivolumab 3 mg/kg every 2 weeks + ipilimumab 1 mg/kg every 6 weeks* (n = 39)	Nivolumab 3 mg/kg every 2 weeks† (n = 52)
Confirmed ORR, % (95% CI)	47 (31, 64)	39 (23, 55)	23 (13,37)
Median duration of response, months (95% CI)	NR (11.3, NR)	NR (8.4, NR)	NR (5.7, NR)
Best overall response, %			
▪ Complete response	0	0	8
▪ Partial response	47	39	15
▪ Stable disease	32	18	27
▪ Progressive disease	13	28	38
▪ Unable to determine	8	15	12
Median PFS, months (95% CI)	8.1 (5.6, 13.6)	3.9 (2.6, 13.2)	3.6 (2.3, 6.6)
OS rate at 1 year, % (95% CI)	Not calculated	69 (52, 81)	73 (59, 83)
Median follow-up, months (range)	12.9 (0.9-18.0)	11.8 (1.1-18.2)	14.3 (0.2-30.1)
Efficacy by PD-L1 expression			
ORR by PD-L1 expression, %, n/N			
▪ < 1% PD-L1	30 (3/10)	0 (0/7)	14 (2/14)
▪ ≥ 1% PD-L1	57 (12/21)	57 (13/23)	28 (9/32)
▪ ≥ 50% PD-L1	100 (6/6)	86 (6/7)	50 (6/12)
Median PFS (95% CI), mo			
• <1% PD-L1	4.7 (0.9, NR)	2.4 (1.7, 2.9)	6.6 (2.0, 11.2)
• ≥1%PD-L1	8.1 (5.6, NR)	10.6 (3.6, NR)	3.5 (2.2, 6.6)
• ≥50%PD-L1	13.6 (6.4, NR)	NR (7.8, NR)	8.4 (2.2, NR)
1-year OS rate (95% CI), %			
• <1% PD-L1	NC	NC	79 (47, 93)
• ≥1%PD-L1	90 (66, 97)	83 (60, 93)	69 (50, 82)
• ≥50%PD-L1	NC	100 (100, 100)	83 (48, 96)

Abbreviations: NC, not calculated (when > 25% of patients are censored); NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.
*Based on a February 2016 database lock. †Based on a March 2015 database lock with the exception of OS data which are based on a August 2015 database lock.

The following resources are included for your reference. We would like to acknowledge the contributions of NCCN Panel members who are also co-authors or co-contributors of the presentation.

1. Hellmann MD, Gettinger SN, Goldman J, et al. CheckMate 012: Safety and Efficacy of First-line Nivolumab and Ipilimumab in Advanced NSCLC. Presented at: The 52nd American Society of Clinical Oncology (ASCO) Annual Meeting. June 3-7, 2016; Chicago, IL, USA.
2. OPDIVO Prescribing Information.

Sincerely,

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