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Letter to the Editor

Real-World Experience of Patients with Inoperable, Stage III Non-small-Cell Lung Cancer Treated with Durvalumab after Chemoradiotherapy: Indian Experience

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Approximately 30% of patients with non-small-cell lung cancer (NSCLC) are diagnosed with Stage III disease, which is often unresectable. Historically, the standard of care has been platinum-based chemoradiotherapy (CRT), but outcomes have been poor. Durvalumab is a selective high-affinity, human immunoglobulin G1 monoclonal antibody that blocks programmed death-ligand 1 (PD-L1) binding to PD-1 and CD80. In the phase 3, PACIFIC trial of durvalumab versus placebo in patients with unresectable NSCLC without progressive disease after chemoradiation CRT, both primary end points progression-free survival (PFS) and overall survival (OS) were met and significantly improved with durvalumab (hazard ratio [HR] for PFS, 0.52; 95% confidence interval [CI]: 0.42–0.65; $p < 0.001$; HR for OS, 0.68; 99.73% CI: 0.47–0.997; $p = 0.0025$) with similar safety profiles between treatments.[1] There are limited data from India for durvalumab use in NSCLC. We present initial experience for its use in our patients.

The details of these patients were obtained from the prospective lung cancer audit database that is maintained in the department of medical oncology. It included 15 NSCLC patients who have received durvalumab between March 2018 and March 2019. All eligible patients were adults with histologically or cytologically documented unresectable, Stage III NSCLC, regardless of tumor PD-L1 expression, which have not progressed after definitive CRT. Patients received durvalumab (l0 mg/kg intravenously) every 2 weeks. We collected the demographic data, date of starting durvalumab, date of disease progression, date and reason for stopping or interrupting durvalumab, date of death, response to previous treatment and durvalumab, and side effects. Data were collected with grading as per the Common Terminology Criteria for Adverse Events (version 4.03). Descriptive statistics were performed for analyzing demographic data, while PFS and OS were analyzed by plotting Kaplan–Meier curve and compared by log-rank test appropriately.[2] ►Tables 1 and 2 tabulate baseline characteristics and side effects of durvalumab, respectively. The mean PFS in our study was 8.5 months (range: 5.5–11.6 months) (►Fig. 1). Of these 15 patients, six has progressive disease and none of the patients have died

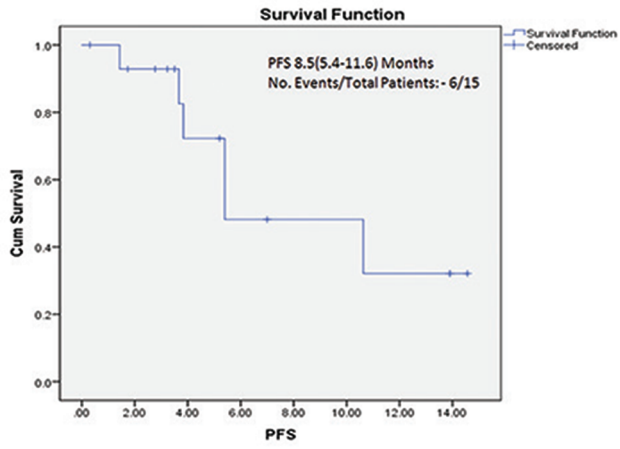

Fig. 1 Progression-free survival in patients on durvalumab.

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Table 1 Baseline characteristics of patients treated with durvalumab (n = 15)

Demographic	*n* (%)
Median age (y) (range)	61 (36–75)
Gender	
Female	5 (33.3)
Male	10 (66.7)
History of smoking/tobacco use	
Yes	10 (66.7)
No	5 (33.3)
Histopathology	
Adenocarcinoma	8 (53.3)
Squamous carcinoma	4 (26.7)
Poorly differentiated	3 (20)
EGFR status	
Wild	12 (80)
Exon 19 del	1 (6.7)
Exon 21 L858R mutation	2 (13.3)
Other mutations	
ALK	1 (6.7)
ROS	1 (6.7)
Stage of lung cancer (TNM 8th)[3]	
IIIA	5 (33.3)
IIIB	5 (33.3)
IIIC	5 (33.3)
Best responses post-CRT (PET-CT)	
CMR	1 (6.7)
PR	7 (46.7)
SD	7 (46.7)
Baseline CEA levels (ng/ml)	54 (4–242)
Nodes (N stage)	
NO	1 (6.7)
N2	13 (86.7)
N3	1 (6.7)
Regimen used during CRT	
Cisplatin–etoposide	1 (6.7)
Carboplatin–paclitaxel	12 (80)
Carboplatin–pemetrexed	1 (6.7)
Best overall response to durvalumab	
CR	1 (6.7)
PR	3 (20)
SD	7 (46.7)
PD	2 (13.3)
NE	2 (13.3)
PD-L1 status (%)	
<1	2 (13.3)
1–50	9 (60)
>50	4 (26.7)

Table 1 (*continued*)

Demographic	*n* (%)
Sites of new lesions	
Lung	2 (13.3)
Lymph node	1 (6.7)
Liver	1 (6.7)
Skeletal	2 (13.3)

Abbreviations: ALK, anaplastic lymphoma kinase; CEA, carcinoembryonic antigen; CMR, complete metabolic response; CR, complete response; CRT, chemoradiotherapy; EGFR, epidermal growth factor receptor; NE, not evaluable; PD, progressive disease; PD-Ll, Programmed death-ligand 1; PET-CT, positron emission computed tomography; PR, partial response; ROS, v-ros UR2 sarcoma virus oncogene homolog 1 (avian); SD, stable disease; TNM, tumor node metastasis.

Table 2 Adverse effects of durvalumab

Adverse event	Any grade, *n* (%)	Grade 3/4, *n* (%)
Any	12 (80)	3 (20)
Arthritis	2 (13.3)	1 (6.7)
Dermatitis	2 (13.3)	1 (6.7)
Nephritis	1 (6.7)	1 (6.7)
Pneumonitis	1 (6.7)	0
Hypophysitis	1 (6.7)	0
Hypothyroidism	2 (13.3)	0
Cough	2 (13.3)	0
Anemia	1 (6.7)	0

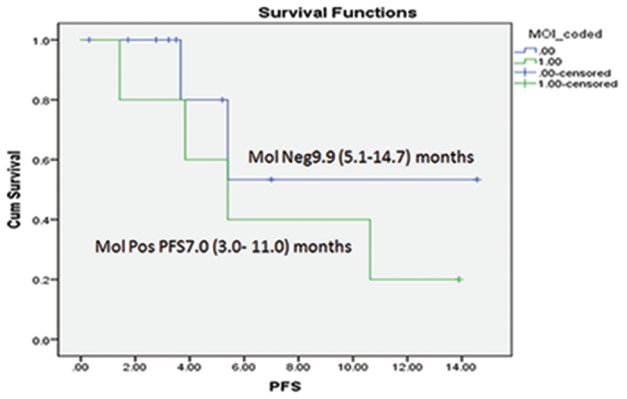

Fig. 2 Progression-free survival as per molecular status.

with a median follow-up of 9 months (1.4–14.5 months). All grade adverse effects were seen in 12 patients, wherein temporarily dosing was withheld in three patients due to nephritis (n = 1), arthritis (n = 1), and dermatitis (n = 1) (►Table 2). Of 15 evaluable patients, five patients were positive for any activating mutation and ten patients were mutation negative. Among those five mutation-positive patients, four had progressed (epidermal growth factor receptor-2, anaplastic lymphoma kinase-1, c-ros oncogene-1), while among 10 mutation-negative patients, two had progressed (►Fig. 2). None of the patients with PD-L1 >50% (n = 4) have

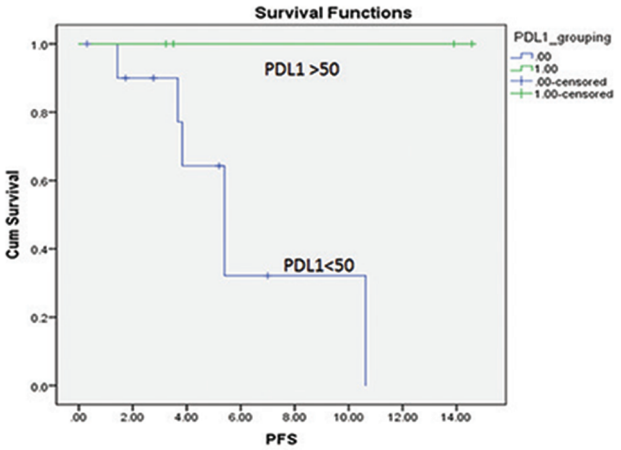

Fig. 3 Progression-free survival as per programmed death-ligand 1 status.

progressed at the last follow-up (►**Fig. 3**). This suggests that we need to develop these biomarkers further.

Durvalumab after chemoradiation can be safely administered in our population with efficacy similar to reported in the literature.

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Conflicts of Interest

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