Observed overall survival benefit with limited exposure of durvalumab in unresectable stage III non-small cell lung cancer

Christopher R. Pallas MD, Deepak Vadehra DO, Donald Moore PharmD, Jeryl Villadolid PharmD, Myra M. Robinson MSPH, Kathryn F. Mileham MD FACP, and Daniel R. Carrizosa MD MS

Department of Solid Tumor Oncology, Levine Cancer Institute, Atrium Health, Charlotte, NC

LEVINE CANCER INSTITUTE

Atrium Health

LEVINE CANCER INSTITUTE

Atrium Health

Background

- Before 2017 patients with unresectable stage III non-small cell lung cancer (NSCLC) received definitive chemoradiation without maintenance therapy.
- Immunotherapy, including immune checkpoint inhibition with durvalumab, represents a major therapeutic breakthrough in cancer and has changed clinical practice in the treatment of NSCLC.
- The PACIFIC trial ushered in a paradigm shift in the management of unresectable, non-metastatic NSCLC with the comparison of durvalumab versus placebo as consolidative therapy following chemoradiotherapy.[1]
- At four-year follow-up, data from PACIFIC has demonstrated improvement in 12, 24, 36, and 48-month overall survival (OS) leading to the 2018 FDA approval for durvalumab in unresectable or locally advanced stage III NSCLC.[2]
- With almost 3 years of follow-up since FDA approval, we performed a retrospective analysis of patient experiences and outcomes at Levine Cancer Institute analyzing patient data to assess survival and relevant patient characteristics affecting outcomes.

Methods

- Patients over the age of 18, who met criteria similar to the PACIFIC trial (i.e., unresectable or locally advanced stage III NSCLC) from February 2018 through September 2020 were analyzed. Those who were receiving active treatment at the data cutoff were excluded.
- Patient characteristics, prior treatment, durvalumab doses administered, immune-related adverse events (irAEs), and efficacy data were summarized and evaluated.
- OS and progression free survival (PFS) were evaluated with Kaplan Meier methods.

Table 1: Trial Profile

Characteristics	N	%
Gender		
Female	65	40.9%
Male	94	59.1%
Race		
White	138	86.8%
Non-White	21	13.2%
Age		
Median (range)	67	38 – 83
Histology		
Squamous	85	53.5%
Non-squamous	74	46.5%
Smoking History		
Y (any hx)	152	95.6%
N	7	4.4%

Characteristics	N	%
Post-Chemo Pneumonitis		
Y	24	15.1%
N	133	83.6%
Unknown	2	1.3%
PD-L1 Expression		
<1%	49	30.8%
≥1%	51	32.1%
Unknown	59	37.1%

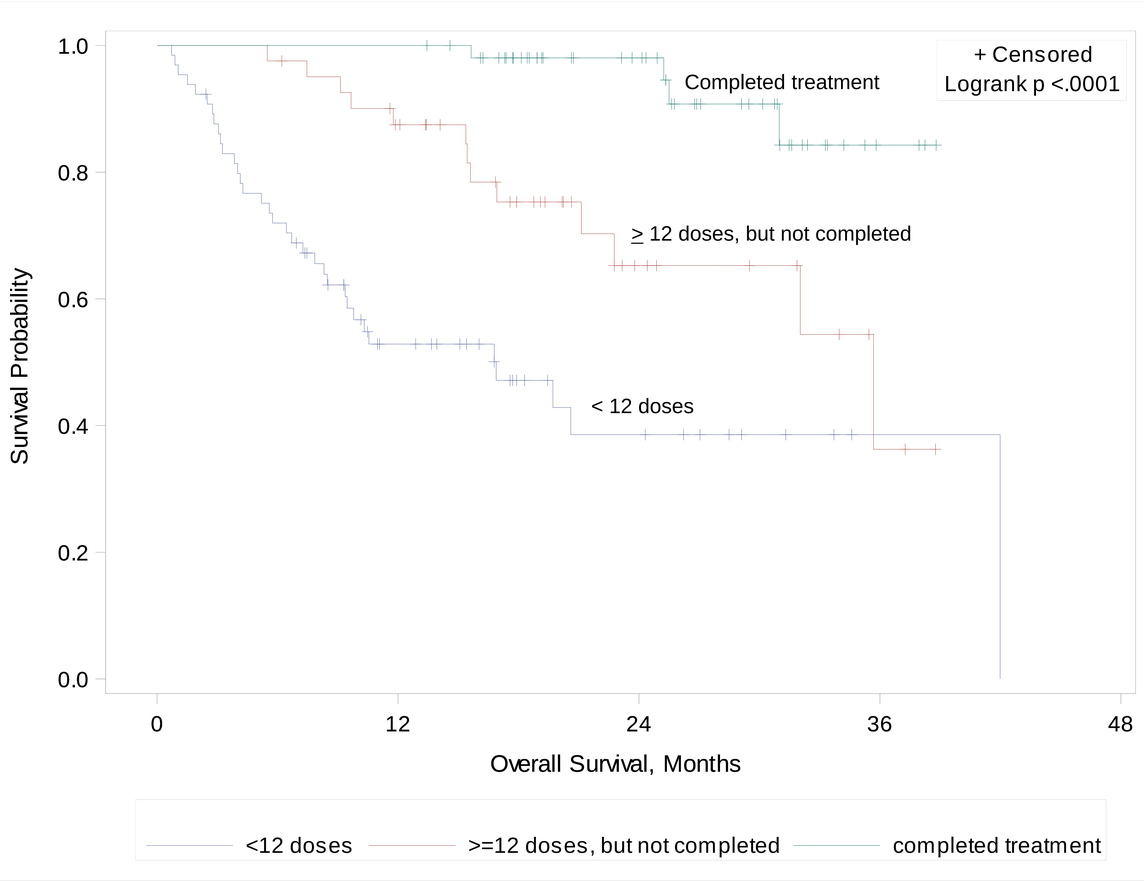
Table 2: Overall Survival by Exposure to Durvalumab

Durvalumab doses received*	Patients	Median OS (months)	12-Month OS	24-Month OS
< 12 doses (Approx. < 6 months)	65	16.9	52.9%	38.6%
≥ 12 doses, but not completed	41	35.7	87.5%	65.3%
Completed treatment	53	NA	100.0%	98.0%

*1 dose = every 2 weeks. The median number of doses of durvalumab received was 14 (range 1-26).
For every additional dose of durvalumab received, the risk of death decreased by approximately 10%.

HR (for 1 unit increase in durvalumab doses) = 0.90 (95% CI: 0.87 – 0.93, p<.001)
HR (<12 doses vs ≥12 doses, not complete) = 2.66 (95% CI: 1.39– 5.10)
HR (<12 doses vs completed treatment) = 14.03 (95% CI: 4.92 – 40.01)
HR (≥12 doses not complete vs completed treatment) = 5.27 (95% CI: 1.71 – 16.19)

Figure 1: Overall Survival in Months by Exposure to Durvalumab



Results

- A total of 159 patients were evaluated. 40.9% were female and 59.1% were male. The median age was 67. Of note, 86.8% of patients were white, whereas 13.2% were nonwhite.
- 50.3% patients experienced irAEs with 29.6% requiring steroid use.
- The most common reasons for discontinuation of durvalumab were completion (at least 24 doses), progressive disease, or toxicity (33.3%, 30.8%, 26.4%, respectively).
- Predictor of irAEs included elevated BMI (p<0.05).
- The median PFS was 15.3 months with a 12-month PFS of 54% and 24-month PFS of 41.1%..
- Predictor of PFS included baseline ANC/ALC ratio with HR = 1.10 (95% CI: 1.04-1.16, p<0.001).
- Median OS was 42 months with a 12-month OS of 78.1% and 24-month OS of 67.8%.
- PD-L1 expression (≥1% compared to <1%) did not predict PFS or OS benefit. However, PD-L1 expression was unknown in a significant proportion of patients.
- Our analysis compared outcomes in those who completed adjuvant durvalumab versus those who did not complete adjuvant therapy (Table 2 and Figure 1).
- The risk of death in those with < 12 doses of durvalumab is 2.7 times the risk of death in those with ≥ 12 doses. For every additional dose of durvalumab received, this risk of death was decreased by approximately 10% (p<0.001).

Conclusion

- Data shows the best survival in those who completed durvalumab (comparable to historic values) and novel data shows a perceived survival benefit in those completing a minimum of 12 doses compared to those who did not.
- Partial treatment may provide a survival advantage and suggests a need to better understand the mechanisms responsible for response and resistance to immunotherapy.
- Further investigation will also delve into this cohort's small proportion of non-white patients, evaluating for possible barriers to care that may lead to more patients being diagnosed with stage IV NSCLC.

Resources

1. Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer. *N Engl J Med*. 2017;377(20):1919-1929.
2. Faivre-Finn C, Vicente D, Kurata T, et al. Four-Year Survival With Durvalumab After Chemoradiotherapy in Stage III NSCLC-an Update From the PACIFIC Trial. *J Thorac Oncol*. 2021;16(5):860-867.