

## PRE-TREATMENT INTERSTITIAL ABNORMALITIES IS A RISK FACTOR FOR IMMUNE CHECKPOINT INHIBITOR PNEUMONITIS IN PATIENTS WITH LUNG CANCER

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**Background** Immune checkpoint inhibitors (ICIs) are a first line and adjuvant treatment in advanced stage lung cancer. One of the main complications of ICI treatment is pneumonitis with an overall incidence of 2-5%; however, patient specific risk factors for developing ICI-pneumonitis (ICI-p) haven't been well elucidated.<sup>1,2</sup> We evaluated potential pre-treatment risk factors for ICI-p including pre-treatment interstitial abnormalities on computed tomography of the chest (CT chest).

**Methods** We conducted a retrospective cohort study of consecutive patients with lung cancer who received at least one dose of ICI between 2015-2020 at The Ohio State University. Potential risk factors for ICI-p were recorded and summarized between those with and without pneumonitis. Among patients who developed pneumonitis, these factors were compared between Grade <3 and Grade ≥3 severities as well as among patients with different cancer stage (3 vs 4). Multivariable survival analysis was used to examine the association of potential risk factors with pneumonitis. Pneumonitis cases were documented by the treating oncologist and retrospectively evaluated by an oncologist and pulmonologist.

**Results** 473 patients with lung cancer were included, 401 with Non-Small Cell Lung Cancer and 72 with Small Cell Lung Cancer. 38 developed ICI-p and 435 did not. Of the potential risk factors, the following were significantly associated with ICI-p: pre-existing interstitial abnormalities (30.8% vs 4.2%,  $p < 0.001$ ), prior concurrent chemoradiation (17.7% vs 4.2%,  $p < 0.001$ ), stage of cancer (19.8% for stage III vs 4.4% for stage IV,  $p < 0.001$ ), and type of immunotherapy (12.5% for PD1 vs 3.6% for chemo-IO,  $p < 0.001$ ) (table 1). Pre-existing interstitial abnormalities remained strongly correlated with development of pneumonitis on multivariable analysis including prior chemoradiation, pre-treatment interstitial abnormalities, and type of immunotherapy, (hazard ratio 8.54 [4.45-16.42],  $p < 0.001$ ) (table 2). Interstitial abnormalities also remained significant in subgroup analysis of both stage 3 and 4 lung cancer ( $p < 0.001$ ). Patients with grade 3/4 pneumonitis had decreased overall survival compared to those with grade 1/2 pneumonitis ( $p = 0.0342$ ) (figure 1).

**Conclusions** Pre-existing interstitial abnormalities on CT chest is strongly associated with development of ICI-p in patients with lung cancer. It remains an independent risk factor after accounting for common treatment-related risk factors such as prior chemoradiation and chest radiation. Pre-treatment interstitial abnormalities could be utilized as a risk stratification tool to identify patients at highest risk for developing ICI-p, a devastating complication associated with higher mortality in more severe cases.

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**Ethics Approval** Human data was utilized in this project; CIRB approval was obtained and all participants provided informed consent prior to taking part in the study (Study number 2021C0069).

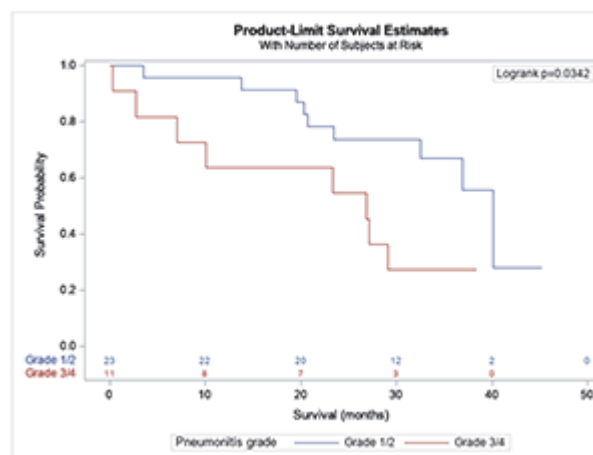
**Abstract 442 Table 1** Pre-treatment risk factors for pneumonitis

| Development of Pneumonitis                 | Yes | No  | % of Total | p value |
|--|-----|-----|------------|---------|
| Pre-existing Interstitial Abnormalities    | 21  | 47  | 30.8%      | <0.001  |
| No Pre-existing Interstitial Abnormalities | 16  | 362 | 4.2%       |         |
| Prior Chemoradiation                       | 24  | 112 | 17.6%      | <0.001  |
| No Prior Chemoradiation                    | 14  | 323 | 4.2%       |         |
| Type of Therapy: PD1                       | 30  | 210 | 12.5%      | <0.001  |
| Type of Therapy: Chemo-IO                  | 8   | 212 | 3.6%       |         |
| Stage 3 Lung Cancer                        | 23  | 93  | 19.8%      | <0.001  |
| Stage 4 Lung Cancer                        | 13  | 285 | 4.6%       |         |

**Abstract 442 Table 2** Multivariate analysis of risk factors

| Parameter                               | Hazard Ratio | 95% Hazard Ratio Confidence Limits | p-value |
|---|--------------|------------------------------------|---------|
| Pre-existing Interstitial Abnormalities | 8.548        | 4.450, 16.420                      | <.0001  |
| Prior Chemoradiation                    | 3.189        | 1.526, 6.663                       | 0.0020  |
| Type of Therapy: Chemo-IO               | 0.482        | 0.206, 1.131                       | 0.0935  |

**Figure 1: Overall Survival by Pneumonitis Grade (1/2 vs 3/4)**



**Abstract 442 Figure 1** Overall survival by pneumonitis grade

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