

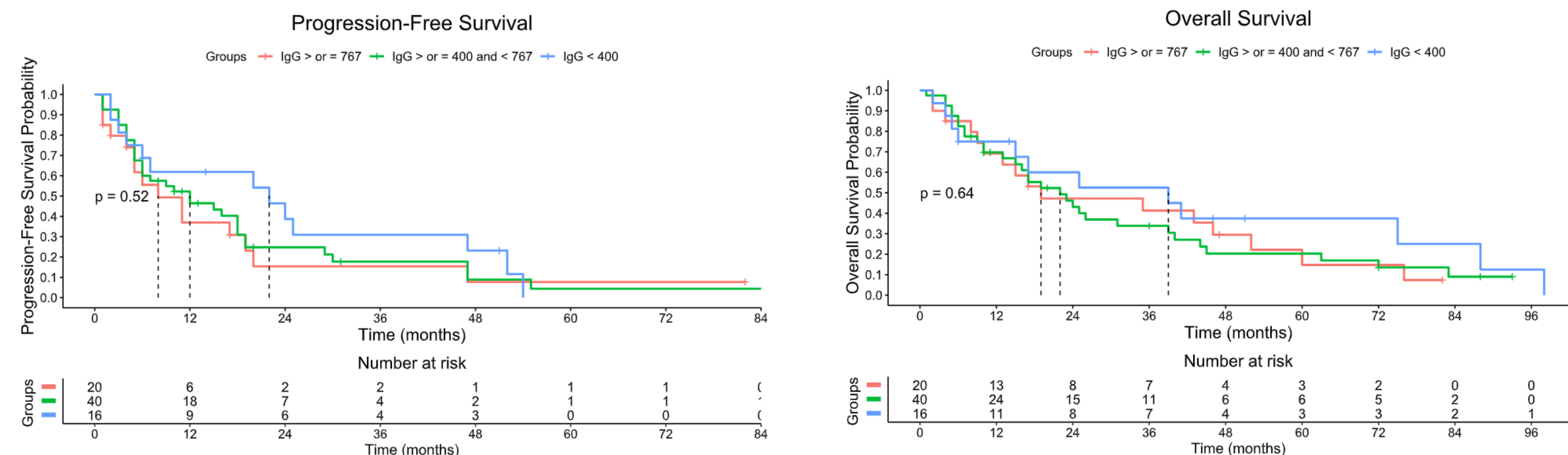
INTRODUCTION

In addition to their prominent impact on T cells, immune checkpoint inhibitors (ICIs) exert effects on a wide array of immune effectors, including B cells. Emerging evidence suggests immunoglobulin levels or changes in serum IgG could correlate with survival, but remain very limited in number and scope. Almost no data has been published examining serum IgG nadir or IgG changes during ICI therapy and their association with survival in patients with non-small cell lung cancer (NSCLC).

METHODS

We identified 76 patients with NSCLC (primarily metastatic) who had received pembrolizumab alone or in combination with chemotherapy at Mayo Clinic sites. We collected clinical parameters (e.g. age, performance status, PD-L1 tumor proportion score, stage, etc.), mutation status, treatment regimens, immunoglobulin levels, and survival outcomes, and categorized patients based on lowest recorded (nadir) IgG, IgM, and IgA levels. Survival was evaluated by the Kaplan-Meier method and analyzed using univariate Cox regression models. The primary endpoint was progression-free survival (PFS), with secondary endpoints of overall survival (OS) and treatment discontinuation.

RESULTS



Figures 1, 2. Kaplan-Meier survival curves of patients with normal/high IgG (≥ 767 mg/dL), mildly low IgG ($400 \leq \text{IgG} < 767$ mg/dL), or very low IgG ($\text{IgG} < 400$). Patients were divided into groups based on overall nadir IgG (before or after ICI initiation), and Kaplan-Meier analysis was used to compare progression-free survival (left) or overall survival (right) from initiation of ICI.

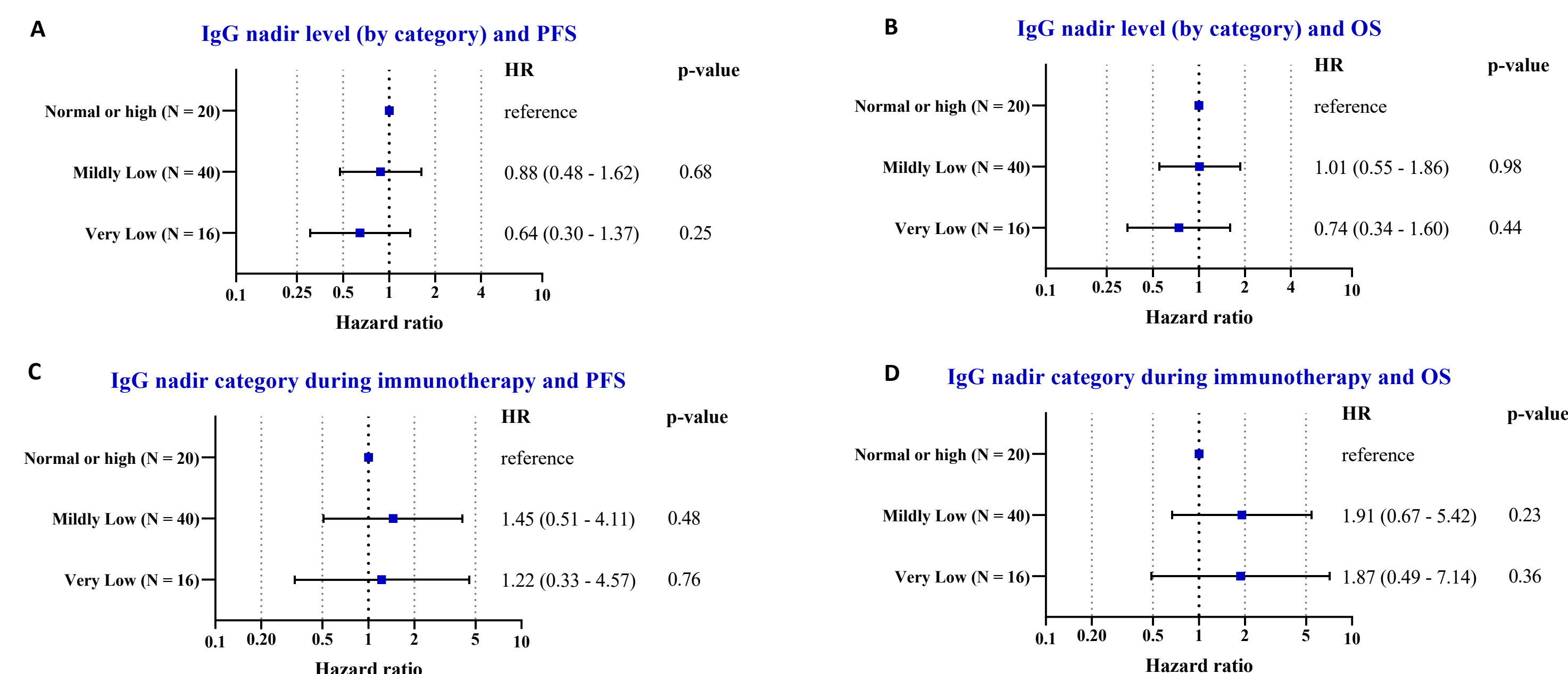


Figure 3. Cox regression and corresponding forest plots comparing IgG nadir levels and survival. Progression-free survival and overall survival were compared between patients with higher or lower overall IgG nadirs (A, B) or IgG nadirs specifically during ICI therapy (C, D). No consistent or statistically significant associations were observed. There was a trend toward longer survival in patients with lower overall IgG nadir (lower hazard ratio of progression or death) and shorter survival in patients with lower IgG nadir during ICI therapy.

Table 1. Change in IgG after ICI initiation and survival			
	HR	Confidence interval	p-value
% change IgG and PFS	0.9926	(0.9830, 1.0022)	0.131
% change IgG and OS	0.9964	(0.9883, 1.0045)	0.3808

Table 1. Change in IgG from baseline to after ICI initiation and survival. Only patients with baseline IgG recorded prior to ICI initiation and repeat IgG level after ICI initiation were included. No significant associations between the change in IgG and either PFS or OS were found.

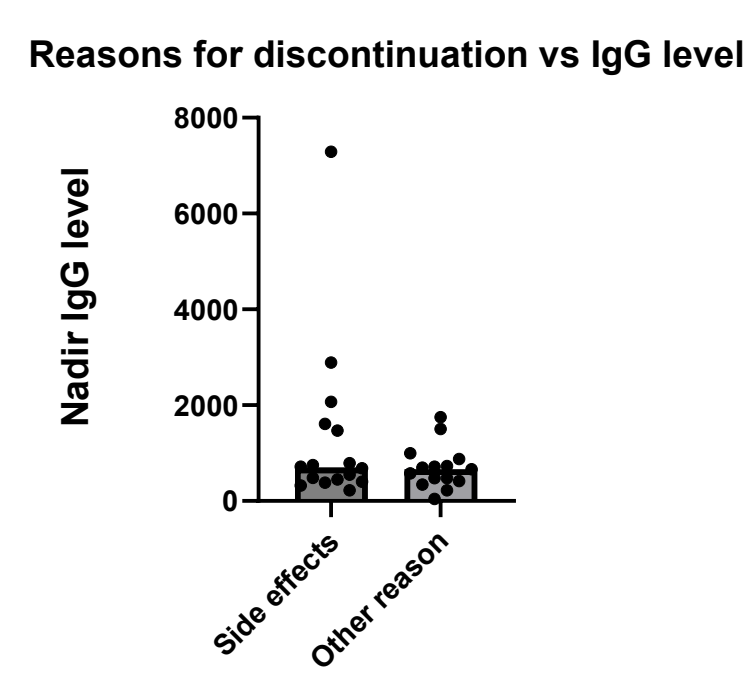


Figure 4. Reasons for discontinuation of ICI therapy in patients with various IgG nadir levels. IgG nadir level was not associated with discontinuation of ICI therapy due to side effects versus other reasons (e.g. progression, functional decline, patient choice) ($p = 0.19$)

Table 2. Baseline characteristics (continuous)				
Continuous variable	Normal or high (N=20)	Mildly Low (N=40)	Very Low (N=16)	p-value
Age				0.424
- Mean (SD)	73.25 (8.03)	71.60 (9.20)	72.94 (8.36)	
- Median (Q1, Q3)	74.50 (67.75, 80.25)	70.50 (65.75, 79.25)	71.50 (68.75, 77.50)	
PD-L1%				0.948
- Mean (SD)	8.90 (7.56)	8.38 (6.37)	8.06 (6.54)	
- Median (Q1, Q3)	4.50 (2.00, 16.75)	8.50 (2.00, 15.00)	5.00 (2.75, 15.00)	
TMB (mut/Mb)				0.269
- Mean (SD)	20.55 (7.42)	20.05 (6.95)	17.38 (7.86)	
- Median (Q1, Q3)	25.00 (16.00, 25.00)	25.00 (16.00, 25.00)	19.00 (11.25, 25.00)	
IgG nadir (reference: 767-1590)				< 0.001
- Mean (SD)	2285.75 (1442.66)	585.42 (105.64)	249.81 (91.06)	
- Median (Q1, Q3)	1710.00 (1607.50, 2370.00)	581.50 (495.50, 669.50)	270.00 (207.00, 319.25)	
Baseline IgG				< 0.001
- No data	10	25	9	
- Mean (SD)	1951.50 (843.30)	661.13 (258.73)	246.00 (143.66)	
- Median (Q1, Q3)	1795.00 (1505.00, 2527.50)	584.00 (520.00, 646.00)	257.00 (169.00, 305.00)	
IgG nadir during immunotherapy				< 0.001
- No data	12	21	9	
- Mean (SD)	2358.00 (1444.82)	576.53 (109.14)	275.86 (122.17)	
- Median (Q1, Q3)	1895.00 (1607.50, 2447.50)	576.00 (487.50, 656.00)	301.00 (244.00, 352.50)	
PFS				0.174
- Mean (SD)	13.20 (19.50)	15.60 (17.53)	21.19 (19.46)	
- Median (Q1, Q3)	5.50 (2.00, 17.00)	10.00 (5.00, 18.25)	17.00 (5.50, 30.50)	
OS				0.901
- Mean (SD)	28.05 (35.22)	26.40 (25.26)	33.25 (31.26)	
- Median (Q1, Q3)	17.00 (8.75, 46.25)	17.00 (8.75, 36.75)	21.00 (6.00, 47.25)	

Tables 2, 3. Baseline characteristics of patients included in this study. No significant differences were found among the three groups except race ($p = 0.042$) and IgG levels which are included here for reference.

Table 3. Baseline characteristics (categorical)				
Categorical variables	Normal or high (N=20)	Mildly Low (N=40)	Very Low (N=16)	p-value
Sex				0.783
- Male	13 (65.0%)	22 (55.0%)	9 (56.2%)	
- Female	7 (35.0%)	18 (45.0%)	7 (43.8%)	
Race				0.042
- White	20 (100.0%)	40 (100.0%)	14 (87.5%)	
- Black	0 (0.0%)	0 (0.0%)	1 (6.2%)	
- American Indian/Alaskan Native	0 (0.0%)	0 (0.0%)	1 (6.2%)	
Stage just prior to getting ICI				0.494
- I	1 (5.0%)	0 (0.0%)	0 (0.0%)	
- II	0 (0.0%)	4 (10.0%)	1 (6.2%)	
- III	4 (20.0%)	4 (10.0%)	2 (12.5%)	
- IV	14 (70.0%)	31 (77.5%)	13 (81.2%)	
- Relapsed/recurrent/relapsed	1 (5.0%)	1 (2.5%)	0 (0.0%)	
ECOG just prior to getting ICI				0.602
- 0	6 (30.0%)	12 (30.0%)	7 (43.8%)	
- 1	8 (40.0%)	18 (45.0%)	6 (37.5%)	
- 2	4 (20.0%)	9 (22.5%)	2 (12.5%)	
- 3	2 (10.0%)	0 (0.0%)	1 (6.2%)	
- Unknown	0 (0.0%)	1 (2.5%)	0 (0.0%)	
Tumor histology				0.827
- Adenocarcinoma or adenocarcinoma spectrum	13 (65.0%)	30 (75.0%)	12 (75.0%)	
- Squamous Cell Carcinoma or SCC spectrum	6 (30.0%)	8 (20.0%)	3 (18.7%)	
- Other NSCLC	1 (5.0%)	2 (5.0%)	1 (6.2%)	
Tumor grade				0.587
- Unknown	7 (35.0%)	19 (47.5%)	9 (56.2%)	
- well differentiated	2 (10.0%)	1 (2.5%)	0 (0.0%)	
- moderately differentiated	4 (20.0%)	8 (20.5%)	1 (6.2%)	
- poorly differentiated	7 (35.0%)	12 (30.8%)	6 (37.5%)	
ICI regimen				0.728
- Pembrolizumab/nab-paclitaxel	1 (5.0%)	1 (2.5%)	0 (0.0%)	
- Pembrolizumab/carboplatin/pemetrexed	8 (40.0%)	20 (50.0%)	7 (43.8%)	
- Pembrolizumab monotherapy	10 (50.0%)	9 (22.5%)	7 (43.8%)	
- Pembrolizumab/carboplatin/paclitaxel	0 (0.0%)	3 (7.5%)	2 (12.5%)	
- Pembrolizumab/carboplatin/nab-paclitaxel	1 (5.0%)	2 (5.0%)	0 (0.0%)	
- Pembrolizumab/paclitaxel	0 (0.0%)	1 (2.5%)	0 (0.0%)	
- Pembrolizumab/gemcitabine	0 (0.0%)	1 (2.5%)	0 (0.0%)	
- Clinical trial including pembrolizumab	0 (0.0%)	1 (2.5%)	0 (0.0%)	
Best response to this line				0.271
- Complete response	2 (10.0%)	4 (10.0%)	4 (25.0%)	
- Partial response	10 (50.0%)	19 (47.5%)	6 (37.5%)	
- Stable disease	5 (25.0%)	12 (30.0%)	1 (6.2%)	
- Progression	3 (15.0%)	5 (12.5%)	5 (31.2%)	

RESULTS, CONTINUED

Among the cohort of 76 patients, 20 had IgG ≥ 767 mg/dL (lower limit of our lab reference range) and 56 had IgG < 767 mg/dL.

- Baseline characteristics (demographic, tumor, and treatment) were similar.
- Median follow up was 51 months.
- No difference in PFS or OS by either overall nadir IgG or nadir IgG specifically during ICI course was observed between patients with normal/high (≥ 767 mg/dL), mildly low ($400 \leq \text{IgG} < 767$ mg/dL), or very low (IgG < 400) IgG groups.
- Changes in IgG from baseline to after ICI initiation were not associated with survival.
- Nadir IgG level was similar between patients who discontinued ICI due to side effects or other reasons.

Similarly, no associations between nadir IgM or IgA and survival were seen (data not shown).

DISCUSSION AND CONCLUSION

- In this study, nadir immunoglobulin levels and their longitudinal changes were not associated with survival outcomes, suggesting a limited role for immunoglobulins as a predictor or biomarker for response to pembrolizumab in NSCLC.

- Larger, prospective studies are needed to confirm these findings.

ACKNOWLEDGEMENTS

Artificial Intelligence (AI) Use Disclaimer

AI was used in the preliminary literature search for background information related to this project. AI was not used in data acquisition or analysis and was not used in the creation of this poster.