

Overweight or Obese Patients May Take Longer to Respond and Be Less Responsive to Immune Checkpoint Inhibitors in Non-Small cell Lung Cancer. A Retrospective Review.

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Background

- Immune checkpoint inhibitors (ICI) are now the standard of care in the treatment of non-small cell lung cancer (NSCLC) without any targeted mutation.
- ICIs may be used as monotherapy or in combination with chemotherapy.
- Increased recruitment of inflammatory cells in the tumor microenvironment is associated with a poor response to ICIs.
- Although obesity is a risk factor for many types of cancers, including lung cancer, it is associated with a low systemic inflammation state.
- This creates an effect known as the “obesity paradox,” resulting in better treatment-related outcomes in overweight and obese patients receiving ICIs.
- However, in obesity, the neutralizing interleukin (IL) - 1 β level is high, which can decrease the responsiveness to ICI.
- We aim to study the effect of increased weight on treatment-related outcomes in NSCLC patients receiving ICI.

Methods

- We conducted a retrospective analysis on 178 NSCLC patients treated with ICIs, such as pembrolizumab, nivolumab, ipilimumab/nivolumab or atezolizumab, alone or in combination with chemotherapy.
- Overweight was defined as having a BMI of 25 – 29.9 while obesity was defined as having BMI of ≥ 30 .
- Overall survival (OS), progression free survival (PFS), best radiographic response, and the time to achieve radiographic response were evaluated.
- Cox regression univariate and multivariate analyses were performed. Logistic regression and Chi-square tests were applied.

Results

| Features | BMI ≤ 24.9 N= 89 (51.5%) | BMI ≥ 25 N= 84 (48.5%) | P-value |
|--|----------------------------------|--------------------------------|---------|
| Sex | | | |
| Male | 32 (36%) | 44 (52.4%) | P=0.03 |
| Female | 57(64%) | 40 (47.6%) | |
| Median Age at Diagnosis (years) | 68 | 68 | |
| Immune Checkpoint Inhibitors | | | |
| Ipilimumab/Nivolumab | 1 (100%) | 0 (0%) | P=0.3 |
| Pembrolizumab, Nivolumab | 79 (50.6%) | 77 (49.4%) | P=0.5 |
| Atezolizumab | 9 (56.3%) | 7 (43.7%) | P=0.6 |
| ICI as Second Line Therapy | 32 (49.2) | 33 (50.8%) | P=0.6 |
| Radiation Therapy | 45 (52.3%) | 41 (47.7%) | P=0.8 |
| Metastatic Sites | | | |
| Skeletal | 25 (43.9%) | 32 (56.1%) | P=0.1 |
| Hepatic | 12 (37.5%) | 20 (62.5%) | P=0.08 |
| Brain | 30 (60%) | 20 (40%) | P=0.1 |
| Adrenal Gland | 16 (55.2%) | 13 (44.8%) | P=0.6 |
| Any Immune Related Adverse Events | 20 (51.3%) | 19 (49.7%) | P=0.9 |
| ECOG-PS | | | |
| 0 | 18 (21.2%) | 11 (13.6%) | |
| 1 | 45 (52.9%) | 59 (72.8%) | P=0.01 |
| 2 | 22 (25.9%) | 9 (11.1%) | |
| 3 | 0 (0%) | 2 (2.5%) | |
| Progressed | 61 (69.3%) | 67 (80.7%) | P=0.08 |
| Dead | 48 (54.5%) | 54 (65%) | P=0.1 |

Table 1: Demographics of the study

- The objective response rate (ORR) was 45.1% and the disease control rate (DCR) was 75.8%. The ORR was 37% in overweight/obese patients compared to 52% in patients with a normal weight (p=0.06).
- The DCR was 76% vs. 73.9%, (p= 0.7). The median time to achieve the best radiographic response was 3.7 months in overweight/obese patients compared to 2.5 months in those of normal weight (p=0.2).

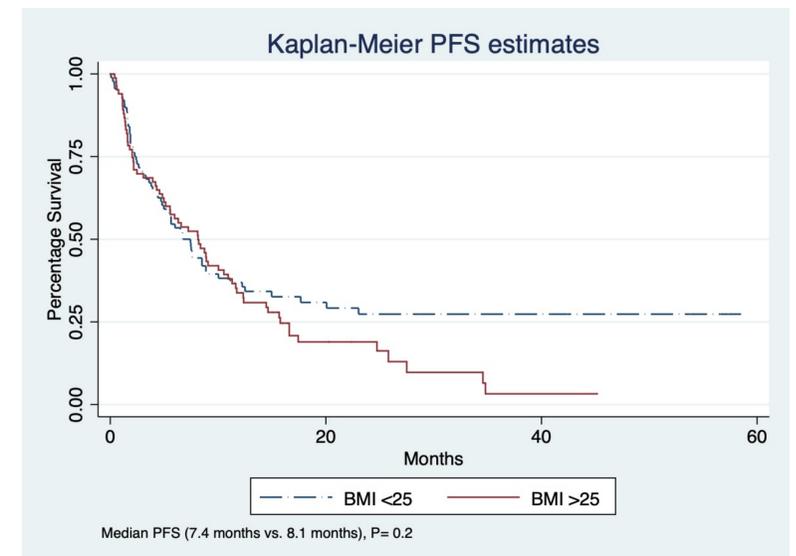


Figure 1: Progression-free Survival in normal weight vs. overweight/obese patients

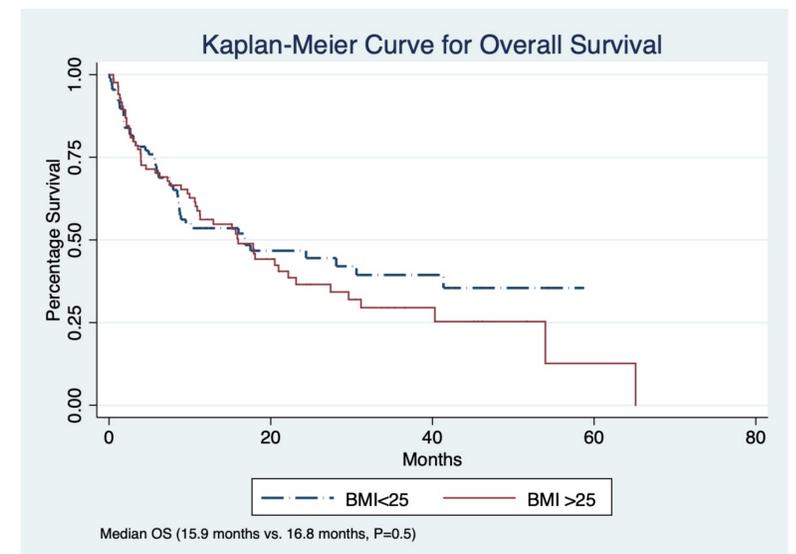


Figure 2: Overall Survival in normal weight vs. overweight/obese patients

Conclusion

- Our study suggests that obesity and overweight status can result in a low response rate to ICIs in NSCLC patients and can delay the time to achieve the best radiographic response per RECIST criteria.
- However, we did not observe any significant impact on the overall or progression free survival.
- A large population-based study will help to elucidate the impact of weight on the responsiveness to ICI.