**Immunotherapy Prolongs Long-Term Real-World Survival Compared to Chemotherapy for Metastatic Non-Small Cell Lung Cancer: A Propensity Score-Matched Analysis**

*Kun Kim1,2, Michael Sweeting3, Linus Jönsson1, Nils Wilking4*

- **Introduction**
  
  Clinical benefits demonstrated during trials may not be entirely translated into the real-world practice. This retrospective and observational study aimed to evaluate whether IO has improved the long-term real-world overall survival (rwOS) and real-world time to receive next line of therapy (rwTTNT) in mNSCLC.

- **Method**
  
  Patients who received either IO (IO mono or IO+CT) or CT in 1L and 2L from January 1, 2015 and onwards were extracted from Flatiron Health oncology database. Eligible patients were selected to match based on a developed propensity score to balance covariates that may confound the treatment effect. The effect of IO rwOS and rwTTNT was estimated using Cox regression. Subgroup analysis was performed to assess effect modification of known prognostic factors in mNSCLC. Finally, we developed a flexible parametric model that uses splines to model time-varying hazard ratios and used it to visualize long-term effects of treatment. A spline function with 3 internal knots was used to capture the shape of the log baseline cumulative hazard using the default knot locations at the centiles of the log of the event times. The effect of treatment was allowed to be time-dependent through a further spline function. All statistical analyses were conducted using RStudio.

- **Results**
  
  - A total of 16,856 1L patients and 6,570 2L patients were included in the analysis. Patient characteristics between IO and CT arms were balanced after 1:1 propensity score matching with replacement.
  - In the 1L matched cohort, the mean age was 68.7 years with a majority were male (55.3%), previous smokers (90.4%), and non-squamous cell carcinoma (73.2%). 32.6% were PD-L1 positive. The median follow-up was 7.3 months.
  - In the 2L matched cohort, the mean age was 68.3 years with a majority were male (53.1%), previous smokers (88.4%), and non-squamous cell carcinoma (66.9%). 26.3% were PD-L1 positive. The median follow-up was 6.9 months.
  - Among 1L IO patients, median rwOS was 10.8 months (95% CI: 10.5 – 11.2) (vs. 1L CT: 9.0 [95% CI: 8.7 – 9.3]) with hazard ratio (HR) 0.84 (95% CI: 0.80 – 0.89). The HR for rwTTNT was 0.54 (95% CI: 0.51 – 0.57).
  - Among 2L IO patients, median rwOS was 8.9 months (95% CI: 8.6 – 9.4) (vs. 2L CT: 8.3 [95% CI: 7.8 – 9.0]) with HR 0.91 (95% CI: 0.84 – 0.98). The HR for rwTTNT was 0.74 (95% CI: 0.69 – 0.79).
  - Median rwOS was shorter than the previous trials plausibly due to the inclusion of patients with poor prognostic factors.
  - Subgroup analyses among IO patients showed better survival outcomes for patients with younger age, low ECOG score, low comorbidity index, no history of smoking, PD-L1 positivity, and high PD-L1 expression level.
  - The flexible parametric model estimated considerable uncertainty in the HR estimate after year 2, although the HR remained highly statistically significant.

None of the authors have conflicts of interest to declare. License for accessing to Flatiron data was paid by AstraZeneca.