LUNG IMMUNE PROGNOSTIC INDEX (LIPI) CAN IDENTIFY THE FAST-PROGRESSOR TO IMMUNE CHECKPOINT INHIBITORS (ICI) IN MICROSATellite INSTABILITY (MSI) OR misMATCH REPAIR DEFICIENT (dMMR) TUMOURS

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INTRODUCTION

- Microsatellite instability (MSI) is a well-described carcinogenic pathway.
- MSI is associated with a deficiency of DNA repair system: Mismatch Repair (dMMR).
- This phenotype is observed in 1 to 3% of patients according to tumour type and can be related to Lynch syndrome.
- MSI-H/dMMR is considered the first predictive marker of efficacy for ICIs with tissue/site-agnostic approval. However, around 39% of cases are refractory and no additional biomarker has been identified.

OBJECTIVE

- We explored the prognostic value of pretreatment LIPI in MSI-H/dMMR patients (pts) treated with ICIs, particularly to identify the fast-progressors (FP).

METHODS

- Primary endpoints: OS and fast progression rate (fast-PD).
- Secondary endpoints: PS and objective response rate (ORR).
- We defined fast-PD as the occurrence of death in the 12 weeks following ICi start.
- LIPI calculation: LIPI was calculated based on LIPI = MSImut/SLI + MSSsat/SSL + 3 + LDL/LDNL + 0.5 LIPI, LIPI groups were [0, 4.34] (good), [4.34, 9.88] (intermediate), and [9.88, +∞] (poor).
- Statistical analysis: the association of demographic, clinical, and biological factors with survival was assessed with multivariate Cox proportional-hazards model. The association between LIPI and fast-PD ORR and LCR was evaluated with a logistic regression. Median OS and PFS were assessed with the Kaplan-Meier method, and rates were calculated at 1 year.

RESULTS

STUDY POPULATION

- We included a total of 151 patients between April 2014 and May 2019.
- The median follow-up of 32.1 months (95%CI: 24.8-46.83).
- Baseline characteristics are summarized in Table. 1. Immune checkpoint inhibitors were administered in monotherapy in 87% of the patients.

LIPi groups

- LIPI groups were distributed as follows:
  - good (n=67, 46.8%)
  - Intermediate (n=67, 43.4%)
  - poor (n=14, 9.8%)

LIPI, independent prognostic factor

In multivariate analysis, after adjustment on tumour site, number of metastatic sites, ECOG-PS, platelet count and albumin, LIPI score was an independent prognostic factor for OS.

STUDY DESIGN

- We performed a retrospective multicentre study (7 centers).
- Study population: Patients, aged ≥ 18 years, treated with immune checkpoint inhibitors (ICI) for a MSI-H tumour between April 2014 and May 2019.
- Data collection: Clinical, biological data were collected at baseline.
- Primary endpoints: OS and fast progression rate (fast-PD).
- Secondary endpoints: PS and objective response rate (ORR).

CONCLUSION

- LIPI was associated with immunotherapy outcomes in patients with MSI-H or dMMR tumours.
- LIPI score can identify a subgroup of patients that will not benefit from ICi for a MSI high tumour.
- It is a simple and accessible worldwide biomarker related to the host that should be prospectively investigated.

CLINICAL OUTCOMES by LIPI groups

- Overall, the 12-weeks death rate (Fast-PD) was significantly higher in the LIPI poor group (36%) (p = 0.03).
- The ORR was significantly lower in the LIPI poor group (6%) (p = 0.03).
- LIPI score was a significant predictor of overall survival (OS).

Table 1: LIPI score calculation, as reported by Mequetal et al., JAMA Oncol 2018.

Table 2: Patient characteristics according to LIPI group.

Table 3: LIPI LIPI Good LIPI Intermediate LIPI Poor

- Overall, median OS was not reached (95%CI: 23.4 to NR).
- Progression-Free Survival was 10.1 months (95%CI: 7.1 to 13.1)

Figure 1: LIPI score calculation, as reported by Mequetal et al., JAMA Oncol 2018.

Table 3: LIPI LIPI Good LIPI Intermediate LIPI Poor

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