Survival and Therapy Analysis of small-scale NSCLC-driver ROS1 mutations

Introduction

- ROS1 Fusions

**Methods**

- Next-generation sequencing (NGS) was performed on tissue samples from NSCLC patients within the Network Genomic Medicine (NGM).

- Patients with activating ROS1 fusions detected by fluorescence in situ hybridization (FISH) were excluded.

- We analyzed the mutations' frequencies and clinical characteristics as well as co-occurring mutations, survival of Stage IV patients and treatment where data was retrospectively available.

**Results**

- 79% male patients (~60% female with ROS1 Fusions [Shaw et al.])
- 10% ROS1 mutant patients of 12,998 in total (~100%)
- Median age of 67 years older than fusions median (~50 years)

**Discussion and Next Steps**

- Small-scale ROS1 are not drivers in general, but relevant predictors of treatment efficacy at least.

**Conclusion**

- Pro relevancy of small-scale ROS1 Mutations:
  - distinct clinical characteristics (e.g. co-occurring drivers but < 10% without potential driver)
  - unique KRAS mutational landscape (60% G12V)
  - striking benefit from immunotherapy (HR 0.14, p=0.009)

- Con relevancy of small-scale ROS1 Mutations:
  - no ROS1 protein expression in 14 tumors
  - co-occurrence of driver mutations

**Contact**

- @MoritzGlS
- @tmatni

---

**Goal of this study**

- Exploratively analyse the patient characteristics (e.g. co-mutational pattern), survival and treatment
- Inquire the role of small-scale ROS1 mutations in NSCLC (inconsequential, predictive factor or driver?)

---

**Figure 1** Cohort Building

**Figure 2** Survival Comparison: ICB Treatment

**Figure 3** - Stage IV patients with survival data available.

**Figure 4** - Survival Comparison: KRAS

**Figure 5** - Survival Comparison: KRAS

---

**Figure 4** - Survival Comparison: KRAS

---

**Results**

- Clinical Characteristics:
  - 79% male patients (~60% female with ROS1 Fusions [Shaw et al.])
  - 10% ROS1 mutant patients of 12,998 in total (~100%)
  - Median age of 67 years older than fusions median (~50 years)

- Small-scale ROS1 Fusions:
  - Median survival of 10.5 months (~5.5 with KRAS mutation only)
  - Most common KRAS mutation (93%; G12V)

- Patients treated with ICB (n=20/29) lived significantly (p=0.003) longer than patients without ICB treatment.

- Immunohistochemical analysis of ROS1/ALK treated group (90.4; HR 0.74; 95% CI 0.49 to 0.99) vs non-ICB treated group (41.4 months; HR 0.59; 95% CI 0.40 to 0.86; p=0.036)

- Mutations besides TP53 did not affect ICB efficacy (p=0.56)

- Unimpaired survival of EGFR & MET mutant patients receiving targeted therapy.