Prevalence of Fibroblast Growth Factor Receptor (FGFR) Alterations and Programmed Death-ligand 1 (PD-L1) Expression in Chinese Solid Tumor Patients

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INTRODUCTION

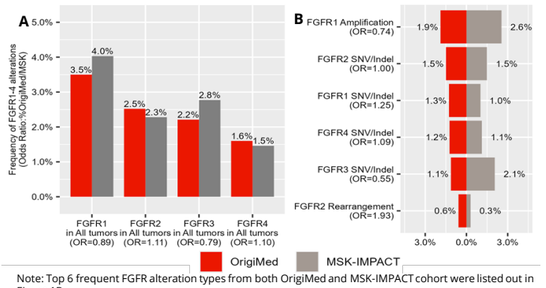
- PD-L1 expression drives anti-PD(L)-1 treatment decisions across many cancer indications.
- FGFR inhibitors have been approved for the treatment of advanced or metastatic urothelial neoplasms and cholangiocarcinoma with FGFR alterations[1]. Erdafitinib, a selective pan-FGFR1-4 kinase inhibitor, has shown clinical activity against FGFR altered solid tumors in patients who exhausted standard treatment options[2].
- It is important to understand the prevalence of FGFR alterations and relationship between FGFR alterations and PD-L1 expression levels in different cancer types.

METHODS

- In this real-world study, 9937 Chinese solid tumor cases with PD-L1 immunohistochemistry (22C3) and OrigiMed 450-gene next-generation sequencing (NGS) panel results were selected.
- Frequencies of FGFR somatic alterations from OrigiMed Chinese cohort were summarized and compared with MSK-IMPACT western cohort[3].
- Association between FGFR somatic alterations and PD-L1 expression was examined by non-parametric test.

RESULTS

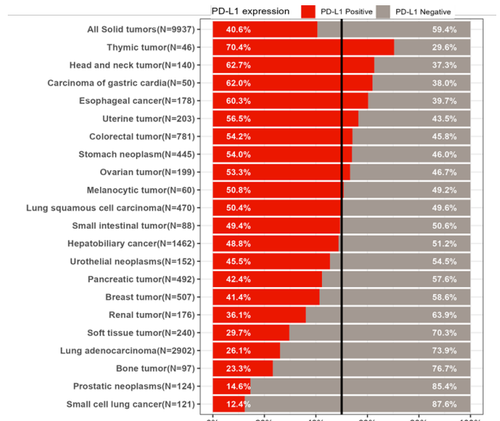
FIGURE 1: Frequency of FGFR1-4 somatic alterations in OrigiMed Chinese cohort and MSK-IMPACT western cohort



Note: Top 6 frequent FGFR alteration types from both OrigiMed and MSK-IMPACT cohort were listed out in Figure 1B.

- OrigiMed Chinese and MSK-IMPACT western cohort (n=10945) cover all major solid tumor types. Comparable frequency of FGFR 1-4 alterations was observed between the two databases(Figure 1A).
- FGFR1-4 somatic alterations were found in 9.0% of of evaluated OrigiMed Chinese tumor samples. FGFR1 alteration was most frequent (3.5%), followed by FGFR2 (2.5%), FGFR3 (2.2%), and FGFR4 (1.6%) (Figure 1A).
- FGFR1 amplification was the most prevalent alteration identified in both OrigiMed (1.9%) and MSK-IMPACT (2.6%) (Figure 1B).

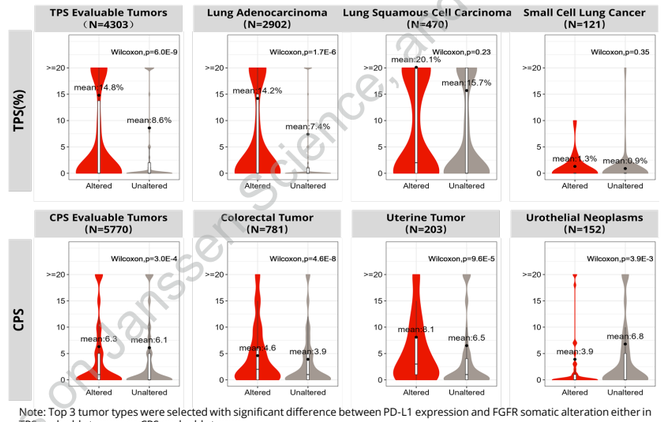
FIGURE 2: PD-L1 expression status in different tumor types



Note: PD-L1 positive: tumor cell proportion score (TPS) ≥1% (small cell lung cancer, lung squamous cell carcinoma and lung adenocarcinoma); Combined positive score (CPS) ≥1 (other tumors except TPS evaluable tumors)

- Total 40.6% of cases were PD-L1 positive (CPS ≥1 or TPS ≥1%) in all solid tumor samples from OrigiMed Chinese tumor cohort . The PD-L1 positive rate varies across tumor types, with the highest to be thymic tumor (CPS ≥1, 70.4%, n=46) and lowest to be small cell lung cancer (TPS ≥1%, 12.4%, n=121).

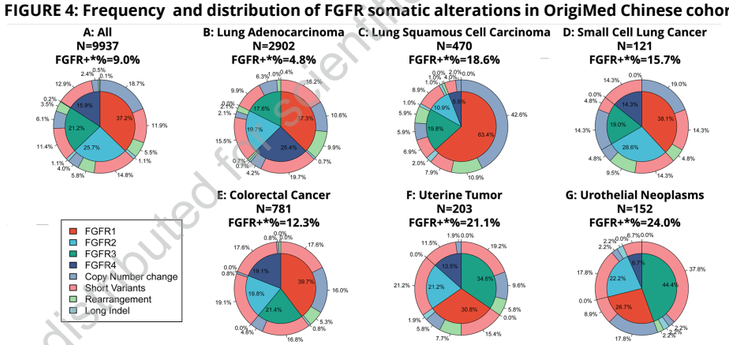
FIGURE 3: PD-L1 expression in tumor samples with/without FGFR somatic alteration



Note: Top 3 tumor types were selected with significant difference between PD-L1 expression and FGFR somatic alteration either in TPS evaluable tumors or CPS evaluable tumors

- Taking all the evaluable tumors together, higher expression of PD-L1 was observed in FGFR altered samples compared with FGFR unaltered samples (mean TPS 14.8% vs. 8.6%, P=6.0*E-9; mean CPS 6.3 vs. 6.1, P=3*E-4). Those includes lung adenocarcinoma (mean TPS 14.2% vs. 7.4%, P = 1.7*E-16), colorectal tumor (mean CPS 4.6 vs. 3.9, P = 4.6*E-8), and uterine tumor (mean CPS 8.1 vs. 6.5, P = 9.6*E-5). Whereas PD-L1 expression was lower in FGFR altered samples than FGFR unaltered samples in urothelial neoplasms (n=152; mean CPS 3.9 vs. 6.8, P = 0.004).

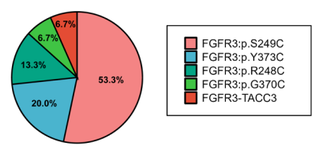
FIGURE 4: Frequency and distribution of FGFR somatic alterations in OrigiMed Chinese cohort



Note: *: the frequency of FGFR1-4 somatic alterations in different tumor types

- The FGFR somatic alteration spectrum varies among tumor types described in Figure 3.
- The inverse relationship between FGFR alterations and PD-L1 expression in urothelial neoplasms (Figure 3) may explain variable role of FGFRs since FGFR3 short variants was enriched in urothelial neoplasms but not such predominant in other types of tumor (Figure 4G vs Figure 4B-F).

FIGURE 5: Distribution of most prevalent FGFR alterations in urothelial neoplasms



- Specific FGFR alterations eligible for erdafitinib treatment were further investigated in urothelial neoplasms and observed with rate 9.9%, including FGFR3 short variants as main alterations .
- Specific FGFR altered tumors showed similar trend with lower PD-L1 expression than FGFR unaltered tumors in urothelial neoplasms as observed in Figure 3 (data not shown here).

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Solid Tumors

KEY TAKEAWAY

FGFR alteration prevalence observed in Chinese and Western population was comparable.

Differential relationship between FGFR alterations and PD-L1 expression across tumor types reflects the differential role of predominant FGFR types in each tumor types.

CONCLUSIONS

Comparable prevalence of FGFR 1-4 somatic alterations between OrigiMed Chinese cohort and MSK-IMPACT western cohort was observed.

In OrigiMed Chinese cohort, 40.6% of solid tumors evaluated were PD-L1 positive (CPS ≥1 or TPS ≥1%). FGFR somatic alteration frequency and distribution were varied in different tumor types.

Higher expression of PD-L1 was detected in FGFR altered samples compared with FGFR unaltered samples in some tumor types, including lung adenocarcinoma, colorectal tumor and uterine tumor; While an inverse relationship was observed in urothelial neoplasms.

DISCLOSURES

Min Qing, Fei Yang, Xiaowei Chen, Xuesong Lyu, Shibu Thomas and Longen Zhou are full employee of Janssen Research & Development.
Aodi Wang and Yanfei Yu are full employee of Origimed.

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