The KRAS gene is mutated in approximately 22% of all tumors, predominantly in pancreatic, colorectal and lung cancer [1,2]. Apart from G12C selective inhibitors there are presently no effective KRAS targeted therapies available. Drug resistance to upstream and downstream inhibitors [3], such as anti-EGFR or anti-Her2 therapy [4-6], means few gain-of-function co-mutations can be targeted.

**Background**

To investigate the clinical impact of performing extensive genomic analysis in patients with KRAS mutated solid tumors by

- examining the distribution and frequency of concurrent genomic alterations found in different KRAS mutation subtypes across histological cancer diagnoses and in different cancer diagnoses across KRAS subtypes,
- identifying potentially actionable targets and patients who received targeted therapy matched to their genomic profile.

**Methods**

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**Results**

The majority of patients had colorectal cancer (CRC, 60.1%), non-small cell lung cancer (NSCLC, 11.2%) or pancreatic cancer (10.6%). Most tumors were KRAS mutated in exon 2 (12 or 13 (83.7%) including G12D (27%), G12V (27%), G12C (12%), and G13D (11%). 175 different cancer related co-occurring genomic alterations were recorded with a median of 4 co-alterations per tumor.

**Conclusion**

- Although many tumors had potentially actionable targets, few patients received therapy matched to their genomic profile.
- Concurrent genomic alterations may provide prognostic and treatment-predictive information (e.g., EGFR co-mutations).
- The co-occurring targets at DNA or chromosomal level were mainly characterized by being loss-of-function alterations (e.g., ATM and HRD) constituting a potential target for synthetic lethality drugs (PARP and ATR inhibitors) or TRB-high status constituting a potential target for checkpoint inhibitors.
- New potential combination treatment strategies may be derived from extensive genomic profiling of KRAS mutated solid tumors. These benefits appear most marked in KRAS G12C mutated tumors where KRAS G12C selective inhibitors are available.

**REFERENCES**


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