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Drugging the undruggable: a market readiness analysis for *KRAS*-G12C

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Background

KRAS G12C is a distinctively aggressive, poor survival tumor genotype conferring resistance to anti-EGFR therapies in lung, colorectal (CRC), and pancreatic cancers. Prospective therapies targeting G12C have demonstrated promising activity in Phase I trials. In the advent of potentially transformative novel inhibitor therapies, we assess the need for earlier and repeated tumor profiling between treatments to accurately guide further therapeutics and assess market readiness for specified testing.

Methods

Treatment-naïve patients and cell-lines were assessed for genomic change by consensus molecular classification in CRC pre/post treatment with standard chemotherapy. Assessing mutation occurrence, prevalence and testing rates, we aimed to identify areas of translational potential for testing within common cancers. A laboratory and prescriber mapping of the US across lung, CRC, and pancreatic cancer types was carried out using Diaceutics' proprietary Global Diagnostics Index (GDI), a real-world data diagnostic database, to determine market readiness for companion diagnostic (CDx) and follow-on testing in the dawn of transformative therapies. Potential barriers to test adoption were explored including reimbursement analysis.

Results

Genomic analysis shows CRC tumors change after treatment with first-line therapies rendering the primary tumor profile result less reliable. This highlights a distinct need for repeated testing post-treatment for continued efficacy in therapeutics. Patients with pancreatic cancer would benefit the most from increased testing for G12C, particularly earlier testing as *KRAS* mutants occur before neoplastic transformation. Although the market appears ready, reimbursement for *KRAS* G12C remains a challenge for pancreatic cancer compared to either lung or CRC.

Discussion

This study provides genomic evidence of the necessity for more frequent tumor testing post-treatment with chemotherapy, and earlier testing in pancreatic cancer to enhance efficacy of targeted therapies. The market is ready for increased testing volumes, yet problems surrounding reimbursement and stage of testing remain. Earlier testing may increase survival and decrease cost of patient care, suggesting more frequent testing is imperative across cancer types.