

increased from 44% in 2011 to 77% in 2020. Of all patients, 44,926 (66.8%) were tested: 50.8% female; 3.3% Asian; 16.0% never-smokers. Of all patients, 22,355 (33.2%) were not tested: 41.4% female; 1.2% Asian; 7.5% never-smokers. Of those tested, 6,245 (13.9%) patients had EGFR mutations: 65.9% female; 11.8% Asian; 48.4% never-smokers.

EGFRex20ins detection rates changed from 0.6% in 2011 to 1.0% in 2019 and 0.7% in 2020. Of those tested, 304 patients had EGFRex20ins: 58.2% female; 8.2% Asian; 50.3% never-smokers. EGFR testing was higher in females (71.2%) than males (62.8%), never-smokers (84.5%) than those with a smoking history (64.6%), and Asian patients (84.2%) than White (66.6%), Black (65.4%), or other patients (69.5%). Of those tested, EGFRex20ins mutations were detected in 0.8% of females (males: 0.6%), 2.2% of never-smokers (with smoking history: 0.4%), and 1.7% of Asians (White: 0.6%, Black: 0.6%, other patients: 0.7%) had EGFRex20ins. A similar trend was observed for EGFR mutations with higher proportions of females, never-smokers, and Asian patients affected.

Conclusion: EGFR testing and EGFRex20ins detection rates have increased. However, not all patient subgroups were tested at the same rate and undertesting occurred in all subgroups. Further education of specialists diagnosing NSCLC is warranted to ensure all patients receive biomarker testing and benefit from emerging EGFRex20ins-targeted therapies.

Complete response of a colonic high-grade neuroendocrine carcinoma to platinum-based therapy: Insights from comprehensive genomic profiling

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Introduction/Objective: Comprehensive genomic profiling (CGP) is an essential tool in precision medicine, providing diagnostic, prognostic, and predictive (therapeutic) information to enable personalized and optimized care for cancer patients. We present the case of a patient with a metastatic high-grade tumor of the colon who showed an impressive response to systemic therapy and discuss the role of CGP in cancer management.

Methods/Case Report: A 54-year-old woman with was diagnosed with stage IV large-cell neuroendocrine carcinoma (LCNEC) of the colon with large volume liver and nodal metastases with imminent hepatic failure. CGP was performed on the resected tumor (TSO500

panel, 523 cancer-related genes, Illumina), showing pathogenic mutations in multiple oncogenes and tumor suppressor genes, including BRCA1, BAP1, and BRAF. Additionally, global parameters revealed a very high tumor mutation burden (TMB, 351 / Mb), and high-degree microsatellite instability (MSI-H). Treatment of the patient's metastases with platinum-based systemic therapy resulted in a complete radiographic response, with no evidence of disease recurrence after 6.5 years. This type of complete response to therapy is rarely reported in colonic LCNEC. Assessment by Medical Genetics did not identify a germline mutation suggestive of hereditary breast/ovarian cancer or Lynch syndrome.

Results (if a Case Study enter NA): NA

Conclusion: The patient's extraordinary response to therapy is likely due to loss of BRCA1 and/or BAP1 function, as deleterious mutations in both genes predict sensitivity to platinum-based therapy through exploitation of deficient homologous recombination repair (HRR). The high TMB and MSI-H status suggest the immune system may have contributed to tumor clearance through neoantigen activation of T-cells. The information provided by CGP also suggested potential tumor sensitivity to poly(ADP-Ribose) polymerase inhibitors (PARPi), immunotherapy (IT), and BRAF/MEK inhibitor therapy, should the tumor recur. This case highlights the value of CGP in guiding management of rare and aggressive tumors.

A case of NTRK-rearranged Spindle cell tumor in a Pediatric patient

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Introduction/Objective: Recent studies continue to demonstrate that NTRK fusions occur more frequently in pediatric than in adult patients involving a broader panel of fusion partners as well as a wider range of pediatric tumors than previously recognized. The identification of these NTRK fusions has facilitated precision cancer diagnosis and TRK inhibitor targeted therapy. With the recent FDA approval of larotrectinib and entrectinib for the treatment of adult and pediatric NTRK-positive, unresectable solid tumors, identification of these fusions directly impacts patient care.

Methods/Case Report: Our patient, a 10 year old female presented with a large right sided buttock mass and pressure effects from the tumor. An incisional biopsy showed a moderately cellular tumor with a collagenous and partially myxoid stroma. The atypical cells had ovoid nuclei with vesicular chromatin, minimal to no atypia, and rare mitotic activity (<2/30 high-power

fields), as well as fibrous tissue that appeared as ropy collagen. Some of the blood vessels were rimmed by a hyalinized cuff. A mild inflammatory component, namely scattered lymphocytes and fewer plasma cells were noted. Immunohistochemistry showed: SMA(faint+), S100(+), CD34(+), CD31(+), FLI1(+), NTRK(+). Negative for ALK1, desmin, SOX10, EMA, keratin AE1/3, CAM5.2, D2-40, myogenin, MUC4, TLE1, STAT6, BCOR, ERG. Both INI1 and H3K27me3 were retained. Proliferative rate by Ki-67 was low, showing <2% positivity.

Next generation sequencing revealed the following: LMNA-NTRK1 fusion; CD36 N53fs*24 and CDKN2A/B CDKN2A loss exon 1. Thus, the histologic, immunophenotypic, and molecular findings together supported a diagnosis of NTRK-rearranged spindle cell tumor. This entity has alternately been termed lipofibromatosis-like tumor. Following confirmation of NTRK fusion, she was treated with oral TRK inhibitor with near total response. With this NTRK-rearranged spindle cell tumor's minimal mitotic activity, absence of necrosis, and low cellularity, the behavior of this tumor was expected to be indolent rather than aggressive. However, the patient was presented for assessment and management at a recent tumor board about 8 months after her initial diagnosis as she had residual/recurrent tumor.

Results (if a Case Study enter NA): NA

Conclusion: Our case highlights the clinical utility of screening for NTRK fusions in all pediatric tumors.

Identifiable Mutations in Pancreatic Adenocarcinoma in the Veteran Population: Molecular Testing Guidelines by NCCN 2020

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Introduction/Objective: In 2019 and 2020, the National Comprehensive Cancer Network (NCCN) advanced a recommendation that all patients with metastatic, recurrent, or locally advanced pancreatic adenocarcinoma should undergo tumor gene profiling (TGP). Prior to these recommendations, TGP in targeted patients have demonstrated a high frequency of KRAS (>90%), TP53 (60-70%), CDKN2A (>50%), SMAD4, TGF- β R1, and TGF- β R2 mutations or alterations. Even less frequent mutations such as the homologous recombination repair (HRR) genes impact treatment by predicting tumor response to platinum-based therapies. However, the literature is sparse for the frequency of these mutations in patients with pancreatic adenocarcinoma undergoing generalized testing as part of the standard of care per NCCN guidance, particularly for veterans.

Methods/Case Report: For a quality assurance study, a retrospective review was performed to identify patients with pancreatic adenocarcinoma at a tertiary medical center serving veterans from January 2019 to February 2021 with TGP performed as part of their care. All of the TGP had been sent to Foundation Medicine (Cambridge MA), and the identifiable tumor mutations from the test reports were recorded to document the frequency of KRAS, TP53, CDKN2A, SMAD4, TGF- β R1, TGF- β R2 and HRR mutations or alterations.

Results (if a Case Study enter NA): There were a total of 11 patients with pancreatic adenocarcinoma who had a tumor specimen for TGP during the study period. All 11 patient tumors had KRAS mutation. 10 out of 11 had a mutation or alteration in TP53. 8 of 11 patients had a CDKN2A mutation or alteration. 7 of 11 patients had a mutation or alteration of SMAD4 though none had TGF- β R1 or TGF- β R2. 2 of 11 patients had HRR mutations (1 with FANCA and 1 with ATM).

Conclusion: Tumor mutations on generalized gene profiling per NCCN guidelines continue to identify important mutations in pancreatic adenocarcinoma for veteran patients.

Assessment of Comprehensive Mutational Profiling in T-lymphoblastic leukemia/lymphoma (T-ALL/LBL): A Single Center Experience

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Introduction/Objective: T-lymphoblastic leukemia/lymphoma (T-ALL/LBL) is a malignancy arising from immature precursor T cells with T-ALL involving bone marrow/blood and T-LBL occurring in the thymus and nodal/extranodal sites. Studies have now revealed >100 recurrently altered genes that are not necessarily disease initiating but can provide diagnostic, prognostic, and predictive information which can then be utilized in personalized therapy.

Methods/Case Report: Next-generation sequencing was performed on DNA and/or RNA extracted from blood/marrow aspirates or tissue at an external CLIA-certified, CAP-accredited laboratory. The hematology panel sequenced DNA of 406 genes, introns of 31 gene rearrangements, and RNA of 265 genes.

This retrospective single-center study highlights salient findings noted in genomic profiles of 15 T-ALL/LBL cases out of 83 total patients with ALL from 2018-2021. While the majority were B-ALL cases, T-ALL accounted for 18%, and all but 1 case were pediatric patients (ages 9-21 years).

Results (if a Case Study enter NA): In our pediatric cohort (14 patients; 9 males, 5 females), as in literature, NOTCH

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