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Clinical efficacy of a next-generation sequencing (NGS) and immunohistochemistry (IHC) panel in patients with advanced cancer in Argentina.

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Background: The analysis of somatic genomic alterations, evaluation of DNA mismatch repair (MMR) proteins, and examination of PD-L1 expression in tumor biopsies are crucial for prognosis and informed therapeutic decisions. However, their clinical implementation in Argentina faces challenges due to economic costs and lack of evidence. To address this, we conducted a retrospective study to assess the impact of this molecular panel testing on treatment decisions and clinical management of cancer patients in Argentina. Additionally, we evaluated its ability to detect clinically relevant alterations and analyzed the frequency and co-occurrence of mutations in our cohort. **Methods:** Tumor tissue samples from 266 patients with primary tumors, representing 26 different anatomical sites (53% lung cancer), underwent molecular testing using the Optimus panel developed by Biomakers. The assay integrates somatic sequencing of 52 genes through NGS with IHC assessment of MMR and PD-L1 proteins. A retrospective evaluation of the clinical effectiveness of the test was conducted on 133 patients. Genomic and clinical data were analyzed using R with the pairwise Fisher's exact test applied for statistical analysis. **Results:** This panel facilitates molecular characterization, identifying clinically relevant genetic alterations in 65% of patients and detecting deficiency in MMR proteins in 3%. Findings align with global clinical trial availability for identified alterations in 97% of cases. KRAS is the most frequently mutated gene (38%), followed by EGFR (19%), PIK3CA (12%), BRAF (9%), CDK4, and CTNNB1 (5% each), correlating with lung cancer overrepresentation. Simultaneous alterations in EGFR, PIK3CA, CTNNB1, and KIT genes were observed. Pan-tumoral interaction analysis revealed mutual exclusivity between KRAS mutations and those in EGFR, BRAF, CDK4, and CTNNB1. CTNNB1 mutations co-occurred with EGFR mutations, akin to KIT and PDGFRA ($p<0.05$). The retrospective analysis indicated that the Optimus panel contributed to clinical management of patients in 56% of cases, with 85% detecting clinically relevant variants, aiding treatment definition in 74% of these cases. **Conclusions:** The Biomakers-developed Optimus panel empowers the molecular characterization of genomic and proteomic biomarkers across tumor types. Its significance in clinical practice lies in contribution to vital decision-making processes, particularly in treatment selection. Research Sponsor: None.