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UN TRAITEMENT GUIDÉ PAR LE PROFIL MOLÉCULAIRE DANS LES TUMEURS SOLIDES RÉFRACTAIRES: IMPACT PRATIQUE ET RÉPONSE CLINIQUE EXPÉRIENCE D'UN CENTRE UNIQUE AU LIBAN

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Introduction • Une étude pilote avait montré qu'un profil moléculaire compréhensif tumoral pourrait être utilisé pour retrouver des cibles moléculaires chez des patients ayant un cancer métastatique réfractaires à plusieurs lignes de chimiothérapie. Chez 18 de 66 patients ayant reçu un traitement guidé par le profil moléculaire, cette approche avait prouvé son efficacité en augmentant la durée de survie sans progression. Une étude récente sur le cancer du sein réfractaire avait montré un bénéfice clinique chez 52% des sujets.
Le but de cette étude est de décrire l'impact de l'utilisation d'une thérapie guidée par le profil moléculaire chez des patients ayant des tumeurs réfractaires suivis dans un centre hospitalier universitaire libanais.
Méthodes • Tous les patients ayant eu une analyse moléculaire de leur tumeur par le laboratoire Caris Life Science entre août 2011 et juin 2015, ont été inclus. Nous avons revu rétrospectivement les informations cliniques en se basant sur les dossiers médicaux intra- et extrahospitaliers.
Résultats • ***Résultats démographiques:*** 101 patients au total (52 femmes, 49 hommes), 1 ayant un matériel insuffisant. Âge moyen : 59,8 (médiane 61, intervalle 21-81). La majorité des patients ont un état de performance ECOG 0 à 1. Nombre médian de lignes de traitement est de 2 (intervalle entre 0-10). 70% des biopsies ont été réalisées des sites métastatiques.
Sélection du traitement • 57 patients ont été traités selon le profil moléculaire tumoral et ont eu au moins une évaluation clinique ou radiologique après. 52 (76%) patients ont reçu seulement des traitements considérés bénéfiques par le profil moléculaire. 4 (6%) patients ont reçu un traitement non mentionné dans le rapport. 22 (39%) patients ont reçu une monothérapie parmi lesquelles 8 (36%) étaient per os.
Réponse clinique • Parmi 68 patients, 57 ont été évaluables et 11 non évaluables. Taux de réponse complète (CR): 12%; réponse partielle (PR): 21%; maladie stable (SD): 35% ; maladie Progressive (PD): 32%. Le taux de contrôle de la maladie tumorale est égal à 68% avec une moyenne de durée de réponse de 4,7 mois.
Conclusions • Une base de données tumorale moléculaire est faisable avec des cibles ayant des médicaments commercialisés. Son utilisation pourrait aider les oncologues dans leur choix chez des patients ayant une maladie réfractaire.

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MOLECULAR PROFILING GUIDED TREATMENT IN REFRACTORY SOLID TUMORS: PRACTICAL IMPACT AND CLINICAL RESPONSES EXPERIENCE OF A SINGLE CENTER

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Introduction • A pilot study has shown that comprehensive molecular profiling can be used to find molecular targets in patients with refractory metastatic cancer. In 18 of 66 patients treated with a molecularly guided therapy, the approach resulted in a longer PFS on an MP-suggested regimen than on the prior regimen on which the patient had just experienced progression. Exploratory analysis demonstrated that this PFS ratio correlated with the clinical parameter of overall survival. A recent study in patients with refractory breast cancer showed that tumor profiling resulted in a revision of the original treatment decision for all patients and tumor profiling-based therapy resulted in a clinical benefit in 52% of heavily pretreated patients. Similar outcomes were recently reported in pancreatobiliary cancer (clinical benefit in 37.5%) and adenoid cystic carcinoma (response in 4/11) patients treated in line with tumor profiling results in Israel. A review of all patients treated in a single center in Australia resulted in clinical and survival benefits in over half of the patients and confirmed the role of molecular profiling in a clinical practice setting.

The aim of this study was to retrospectively assess the impact of using molecular profiling to guide treatment choice in patients with rare or refractory cancer in routine clinical practice at a single center in Lebanon.

Methods • One hundred one patients with rare or refractory cancer being treated at Hôtel-Dieu de France – Saint Joseph University were referred to Caris Life Science for comprehensive tumor profiling between August 2011 and February 2015. Specific testing was performed on tumor biopsy samples from all patients per physician request and included a combination of sequencing (Sanger, NGS or pyrosequencing), protein expression (IHC), gene amplification (CISH or FISH), and/or RNA fragment analysis. IHC analysis was performed on formalin-fixed paraffin-embedded tumor samples using commercially available detection kits, automated staining techniques (Benchmark XT, Ventana, and AutostainerLink 48, Dako), and commercially available antibodies. Fluorescent in-situ hybridization (FISH) was used for evaluation of the HER-2/neu [HER-2/CEP17 probe], EGFR [EGFR/CEP7 probe], and cMET [cMET/CEP7 probe] (Abbott Molecular/Vysis). HER-2/neu and cMET status were evaluated by chromogenic in-situ hybridization (INFORM HER-2 Dual ISH DNA Probe Cocktail; commercially available cMET and chromosome 7 DIG probe; Ventana). The same scoring system was applied as for FISH. Direct sequence analysis was performed on genomic DNA isolated from formalin-fixed paraffin-embedded tumor samples using the Illumina MiSeq platform. Specific regions of 45 genes of the genome were amplified using the Illumina TruSeq Amplicon Cancer Hotspot panel.

Results • Demographic results: 101 patients in total (52 females, 49 males), 1 with insufficient material. Average age : 59.8 (median 61, range 21-81). The majority of patients had an ECOG performance status of 0 or 1. Median prior lines of therapy : 2 (range 0 -10). Average time to testing from biopsy: 172 days (median 18 days, range 7-2551). 70% of biopsies assessed were taken from a metastatic site.

Treatments associated with potential benefit and potential lack of benefit: The drug classes most commonly associated with benefit were commercially available and approved in at least one cancer type. Targeted therapies were associated with benefit in less than a quarter of patients overall and could be avoided in the majority of patients.

Treatment Selection • 57 patients were treated according after tumor profiling was performed and had at least one study evaluation afterwards; 52 (76%) received drugs associated with potential benefit only; 4 (6%) received treatments not mentioned in the report; 22 (39%) received monotherapy of which 8 (36%) were per os.

Clinical Outcomes • Among 68 patients, 57 were evaluable and 11 non evaluable. Complete response (CR): 12%; partial response (PR): 21%; stable disease (SD): 35% ; progressive disease (PD) : 32%. Disease control rate: 68% with an average duration of response of 4.7 months.

Conclusions • Comprehensive multiplatform tumor profiling is feasible, with turnaround time amenable to routine clinical practice. The most common mutations identified were not direct candidates for targeted therapies. The majority of treatments associated with benefit are commercially available cytotoxic agents which allow high clinical utility of the approach. Clinical outcomes are very promising with the use of tumor-profiling guided treatment.