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Tumor biomarkers related to the management of advanced neuroendocrine Tumors

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Québec

SUMMARY

Tumor biomarkers related to the management of advanced neuroendocrine Tumors

Introduction

Cancer represents a group of complex pathologies marked by profound heterogeneity. Beyond the different tumor sites and disease stages, each tumor displays a set of characteristics that distinguish it from others at the pathological/cellular/molecular levels. Tumor biomarkers come in a variety of forms (DNA, RNA, proteins) and lay the foundations for the concept of personalized (or precision) medicine. In oncology, personalized medicine makes it possible, based on the molecular profile of a given tumor, to refine diagnosis, evaluate prognosis and adapt therapeutic decisions to increase the likelihood of treatment efficacy and/or mitigate adverse events.

Laboratory techniques commonly used to reveal the presence of tumor biomarkers include polymerase chain reaction (PCR) amplification, first-generation sequencing (Sanger method), immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH).

Next-generation sequencing (NGS) is a more recent method that provides gene panel-based analysis of different combinations of target sequences in a variety of genes associated with several pathological conditions, including cancer. As such, NGS has the potential to replace several laboratory analyses, which are currently performed independently. The added value of introducing a given sequencing gene panel partly relies on the proportion of target sequences included in the gene panel that are useful for the management of individuals with a particular disease.

With the aim of promoting the judicious use of this type of analysis and to standardize patient care, INESSS has been mandated by the Direction de la cancérologie (DC) to compile a list of useful biomarkers to guide the management of people with various types of solid tumors, including advanced neuroendocrine tumors (NET).

Methodology

An exhaustive literature review (practice guidelines and expert consensus) was conducted to identify tumor biomarkers recommended for the management of advanced NET or solid tumors targeted by an agnostic therapeutic approach (indirectly including NET).

Evidence supporting recommendations from cited organizations was extracted from published primary studies to document the magnitude of benefit derived from the decision to personalize management according to the biomarker detected.

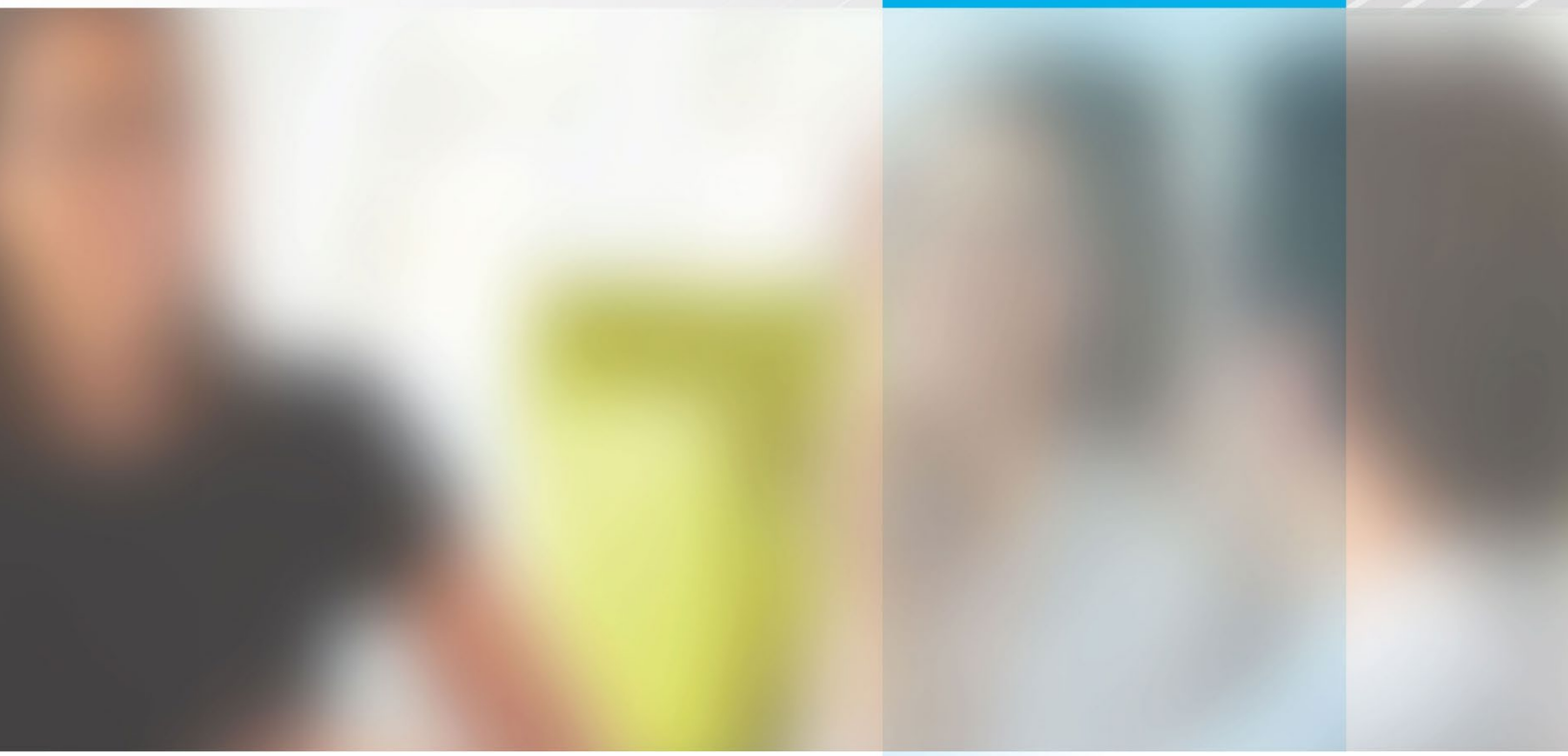
Information pertaining to approval and listing status of drugs associated with predictive biomarkers was collected to determine the value of testing for these biomarkers in the current context of Quebec practice.

Results

A total of 20 publications were selected regarding tumor biomarkers recommended for the management of advanced NET or solid tumors aimed by agnostic therapy (indirectly including NET). The biomarkers recommended in the selected publications are predictive and include various types of alterations in the *BRAF* genes (mainly V600E mutations), the *VHL gene*, fusions involving the *RET* and *NTRK genes*, high microsatellite instability (MSI-H), mismatch repair defects (dMMR), and high tumor mutational burden (TMB-H). The ability of these genes to predict treatment response is based on cohorts of various solid tumors, including a very limited number of NETs. In addition to their ability to predict treatment response, some of these biomarkers, as well as Ki-67, also have prognostic and/or diagnostic value, according to some organizations.

Conclusion

There are some tumor biomarkers associated with the management of individuals with advanced NET. Only treatment targeting the *VHL* gene mutation is currently available in Quebec, while others are associated wit drugs approved for other indications, not yet evaluated, or which have been refused listing for the indication under consideration. According to the experts consulted, information provided by biomarker testing would be useful for the management of people with advanced NET, as it contributes to a better characterization of the disease and enables a certain number of individuals to benefit from it. To find ongoing clinical trials in Quebec that have addressed NET, readers are invited to consult the Registre public des essais cliniques du Québec.



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