A Comparative Analysis of Cancer NGS Reporting Practices between Europe and North America

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Results of Next Generation Sequencing (NGS) are increasingly incorporated in routine clinical oncology. Multiple guidelines and standards have been issued globally to support clinical NGS variant interpretation and are currently integrated in different ways into cancer NGS reports around the world. However, a thorough capture of how these guidelines are being translated in real-world laboratory reporting has not yet been clearly studied. To this end, the Variant Interpretation for Cancer Consortium Virtual Molecular Tumor Board (VICC-VMTB), in collaboration with the Cancer Genomics Consortium (CGC) and the ClinGen Somatic Clinical Domain Working Group (CDWG), distributed a comprehensive survey regarding reporting practices for cancer NGS testing worldwide to identify essential elements and their actual occurrence in NGS reports.

Preparing a comprehensive survey regarding reporting practices

Similar assays are performed at different institutions around the world in which the reporting elements vary. We addressed two questions:

- Which elements are currently included in NGS cancer reports?
- Which elements are perceived as critical to the understanding of the report?

The survey is based on report examples seen in the VICC-VMTB working group and asks about general information on the tumor entity, the reported variants and their functional assessments, and treatment recommendations. Furthermore, the survey covers more complex information, such as the reporting of mutational signatures. Participants could also provide more context in free form.

Overview of survey responses across the globe. Most respondents represented laboratories in North America (n=34) and Europe (n=33), giving us the unique opportunity to evaluate the respective use of reporting elements.

Defining a score of essentiality to summarize results

Each element of an NGS report can be defined as a) essential (E), b) preferred, but not essential (P) or c) not recommended (N). The responses are summarized as a score of essentiality (SE), which is normalized between the range of -1 (contra-productive) and 1 (essential).

This score allows the comparison of responses from different continents, independent of the number of participants.

Only variant allele frequency is asked for more often in European countries.

Functional annotation of variants using additional guidelines is discouraged in North America

The description, how a variant functions and whether it has a pathogenic effect is highly relevant to aid potential treatment recommendations. However, the use of guidelines differs profoundly between participants from Europe and North America.

Summarizing free form results

The survey allowed for free form answers, which were meant to drive further conversations about the survey as well as NGS reporting practices. In summary:

- In both North America and Europe, the vast majority of institutions summarize any specific interactions between variants.
- Assay limitations are more relevant in Northern America,
- whereas the inability to distinguish between germline and somatic variants seems to be more of concern in Europe.

Clinical trials can provide a great opportunity for precision oncology, but they are not deemed essential for an NGS cancer report. If clinical trials are reported, they should provide information on trial ID, recruitment status and contact information.

More complex variants and profiles are part of NGS reports with increasing frequencies

Molecular profiles are being reported in different ways across all tumors or only specified tumor and qualitative or quantitative values. Most molecular profiles are reported across all tumor types, in particular, tumor mutational burden (TMB) is reported more frequently in reports from Northern America (dark blue). Qualitative values are used to describe the presence of most molecular profiles except for TMB in general, which is typically reported as a quantitative value.

As these type of information are still not very common, our survey did not ask participants to decide, whether molecular profiles are essential.

Conclusion

This global survey provides a snapshot of current reporting practices and can support guidance refinement on reporting structure and necessary components of cancer NGS reporting. Comparison between geographic regions advances the discussion about differentially utilized report elements and clarifies the context of their use globally.

We are writing a manuscript based on our cumulative findings.