Key Summary of Conference Abstract

Analytical Validation of a 47-gene NGS Panel for Molecular Profiling of Myeloid Neoplasms

Background

- Myeloid neoplasms are cancers that originate in the bone marrow. The types of myeloid neoplasms include acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), and myeloproliferative neoplasms (MPN).
- Mutations in many genes are associated with the diagnosis, prognosis, and treatment of the different types of myeloid neoplasms.
- Next-generation sequencing (NGS) in the clinical laboratory allows assessment of many genes simultaneously, which may facilitate clinical management of myeloid neoplasms.[1]
- **Objective:** The investigators developed and validated an NGS panel for 47 genes related to the diagnosis, prognosis, and/or therapy of myeloid neoplasms.

Methods

- The study included 154 unique de-identified specimens.
- Forty-seven gene targets for the NGS panel were selected based on their association with diagnosis, prognosis, or treatment of myeloid neoplasms: 42 were associated with AML, 36 with MDS, and 26 with MPN.
- The panel targeted the entire coding regions of 23 genes and targeted exons of 24 genes. Single-nucleotide variations, insertions/deletions, and FLT3 partial tandem duplications were assessed.
- Sequencing was performed using an Illumina NextSeq500 instrument, and results were analyzed using a bioinformatics pipeline developed in-house.
  - For quality coverage, ≥500 unique reads with base quality (Q) ≥20 (99% confidence) were required; 250 unique reads were required for targets on the X chromosome of male specimens.
- Intra-assay (7 specimens) and inter-assay (21 specimens) analyses were conducted according to standard laboratory protocols. An accuracy study compared this NGS method to other molecular methods including Sanger sequencing.

Results

- An average of 13.2 million reads per specimen were generated with a mean coverage of 1,952 (SD=873). All target regions met coverage requirements.
- Intra-assay and inter-assay analyses demonstrated 100% concordance among replicates.
- The accuracy study of 131 specimens demonstrated 99.6% (755/758 variants, 95% CI: 99.4%-100%) concordance for variants with allele frequencies ≥5%.
- Reportable variants were not identified in any normal specimens (n=17).

Conclusions

- The investigators developed and validated an NGS panel with 47 genes related to diagnosis, prognosis, and treatment of myeloid neoplasms.
- It performed with high accuracy, thereby demonstrating potential utility for clinical management of myeloid neoplasms.

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Webpage

https://meetinglibrary.asco.org/record/173724/abstract

References

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