FoundationOne Heme
manuscript outlining analytical validation and clinical experience published in *Blood*

In press (He J, et al, 2016)

FoundationOne® Heme has demonstrated highly accurate detection of genomic alterations known to impact diagnosis, therapy selection and prognosis in hematologic cancers. It is the only marketed test of its kind with a published analytical validation.

Analytical Validation Summary

- FoundationOne Heme demonstrated 99% cordance with CLIA-certified diagnostic assays, including Sequenom, RT-PCR, FISH, and PCR fragment analysis in 11 genes that are known and routinely tested in clinical practice in AML, ALL and MDS (FLT3, NPM1, CEBPA, BCR-ABL1, KIT, IDH2, IDH1, JAK2, MPL, PML-RARA, MLL)
- FoundationOne Heme demonstrated >99% concordance with FoundationOne. Compared to FoundationOne, FoundationOne Heme contains an additional 90 genes relevant to hematologic malignancies
- The combined DNA and RNA sequencing approach accurately detects a wide variety of genomic rearrangements and gene fusions with immediate clinical value in hematologic malignancies (sensitivity of 100% at 20-100% tumor fraction and 98% at 10% tumor fraction)

Clinical Summary

- Clinical experience described in 3,696 patients showcases diverse use of the platform across hematologic malignancies
- At least one driver alteration was identified in 3,246/3,433 (95%) tumor specimens, and 2,650 (77%) cases harbored at least one alteration linked to a commercially-available targeted therapy or one that is in clinical development. In addition, 61% of cases harbored at least one alteration with known prognostic relevance in that tumor type
- In a group of 16 of patients with high-risk "Philadelphia chromosome-like" ALL, FoundationOne Heme identified a spectrum of alterations in the kinase signaling pathway that can guide the use of molecularly targeted therapies

Conclusion

Current diagnostic assays, including FISH and real-time PCR, are designed ad hoc to identify specific genomic alterations, and in some cases there are no assays that can reliably identify specific rearrangements. In developing FoundationOne® Heme, an integrated DNA/RNA profiling platform using targeted next-generation sequencing, the comprehensive genomic profiling approach has proved effective in detecting all types of genomic alterations, single-nucleotide substitutions, insertions and deletions, copy number alterations and rearrangements, which increases the ability to identify clinically relevant genomic alterations with therapeutic relevance. Furthermore, these results indicate that the sequencing-based assay can robustly detect a wide range of alterations in driver genes that are not fully evaluated using conventional methods.

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