Clinical Impact of a Validated Myeloid-Targeted Next-Generation Sequencing Panel in Myeloid Malignancies

Grace Zhang, Christina Ferrone, and Michael Rauh

Background

Myeloid malignancies arise from aberrant clonal proliferation of hematopoietic stem cells that favour myeloid lineages, and include myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPN), and acute myeloid leukemia (AML). Diagnosis of myeloid malignancies is based on evidence of clonal proliferation in the peripheral blood and in the bone marrow. The diagnosis of MDS currently relies on the identification of dysplasia on a histological bone marrow sample, which is subjective and often non-specific.

Next-generation sequencing (NGS) has revealed novel somatic gene mutations that are associated with clonal hematopoiesis and may be implicated in the development of myeloid malignancies. While not currently widely available in Canada, this modality of testing has the potential to contribute to the diagnostic pathway, provide additional information about prognosis which may influence management and follow-up, as well as to offer potential targets for the development of new targeted drug therapies.
The goal of this study is to assess the clinical impact of the implementation of NGS testing in suspected or confirmed myeloid malignancies at the KHSC.

Methods

The Oncomine Myeloid NGS Panel (OMP) offered by Thermo Fisher, which targets 40 DNA genes and 29 RNA fusion driver genes recurrently mutated in myeloid malignancies, has recently been validated for use at KHSC. Patients with a new diagnosis of AML or with uncertain/complicated diagnoses of MDS or MPN received NGS testing.

We conducted a retrospective chart review on all Oncomine NGS testing conducted at KHSC between December 2017 and September 2019. Each NGS result was categorized as either being actionable or not actionable, with “actionability” defined as influencing the diagnosis, management, and/or prognostication of disease.

Results/Discussion

In total, 192 samples from 173 individual patients were included. Further results are pending analysis of the collected data. Based on abstract results of similar studies, we expect that 40-60% of mutations detected by NGS will be actionable. Further analysis will examine the incidence of each reason for actionability (i.e. diagnosis vs. management vs. prognosis), as well as understanding which genes are most frequently actionable and for which myeloid neoplasms they are highest yield. Potential future steps in this area of research include prospective data collection to assess whether NGS confers benefit in clinical and quality-related outcomes such as overall survival, disease-free survival, and hospital resource utilization.