Molecular profiling in myeloproliferative neoplasms (MPNs): conventional testing vs. innovative use of rapid NGS

Next-generation sequencing (NGS) at initial MPN workup offers a simple, rapid, and comprehensive biomarker assessment, reducing the need for time-consuming and costly sequential single-gene testing (SGT) [1].

Initial diagnostic workup

The initial workup for MPNs includes peripheral blood findings, bone marrow morphology, cytogenetics, and molecular testing for ***JAK2***, ***CALR***, or ***MPL*** mutations. ***BCR::ABL1*** fusion and ***CSF3R*** mutations are also assessed for suspected chronic myeloid leukemia (CML) and chronic neutrophilic leukemia (CNL), respectively, among other MPN subtypes [2].

Assessing clonality

Assessing clonality, especially in triple-negative MPNs (i.e., negative for ***JAK2***, ***CALR***, and ***MPL*** mutations), includes identifying mutations in genes such as ***ASXL1***, ***EZH2***, ***TET2***, ***IDH1***, ***IDH2***, ***SRSF2***, and ***SF3B1*** [3,4], which are frequently implicated in primary myelofibrosis (PMF).

Prognosis and therapy selection

Evaluating prognosis involves identifying mutations in genes such as ***ASXL1***, ***CBL***, ***CSF3R***, ***DNM3TA***, ***EZH2***, ***IDH1***, ***IDH2***, ***SF3B1***, ***SRSF2***, ***TET2***, ***TP53***, and ***U2AF1***. Additionally, mutations in genes such as ***JAK2***, ***IDH1***, and ***IDH2*** can aid in therapy selection [2].

Conventional testing approach

Many laboratories initially screen for ***JAK2***, ***CALR***, and ***MPL*** mutations in suspected MPN cases by sequential SGT using technologies such as PCR and Sanger sequencing. NGS is then utilized to refine diagnosis, assess clonality, and guide prognosis and therapy selection (Figure 1). This conventional approach can be time-consuming, often taking weeks to provide a complete genomic profiling for MPN cases, potentially delaying patient management.

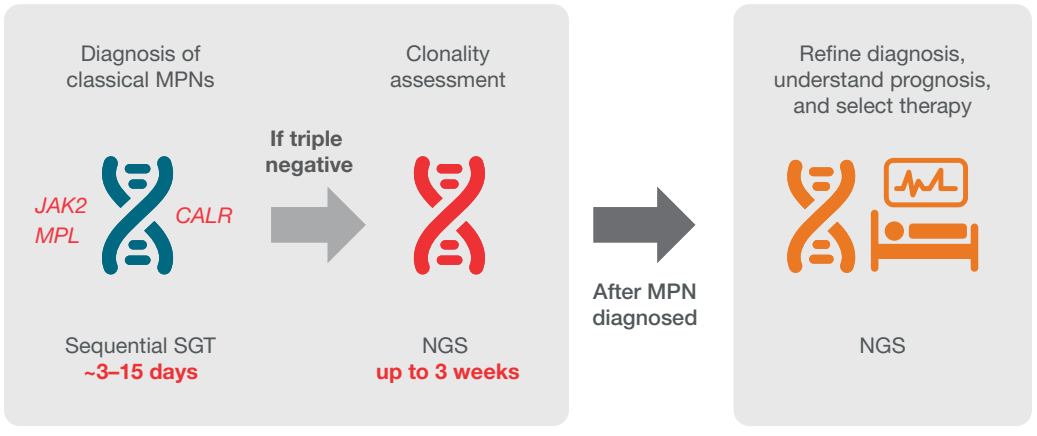

Figure 1. Sequential SGT with reflex to traditional NGS testing.

Innovative use of rapid NGS at initial workup

Using a single rapid NGS panel that interrogates ***JAK2***, ***CALR***, ***MPL***, and other key genes implicated in MPN at initial workup can help establish diagnosis (including subtype classification), assess clonality, and guide prognosis and therapy selection (Figure 2). This innovative approach can deliver fast and more complete genomic profiling for MPNs, enabling more timely patient management.

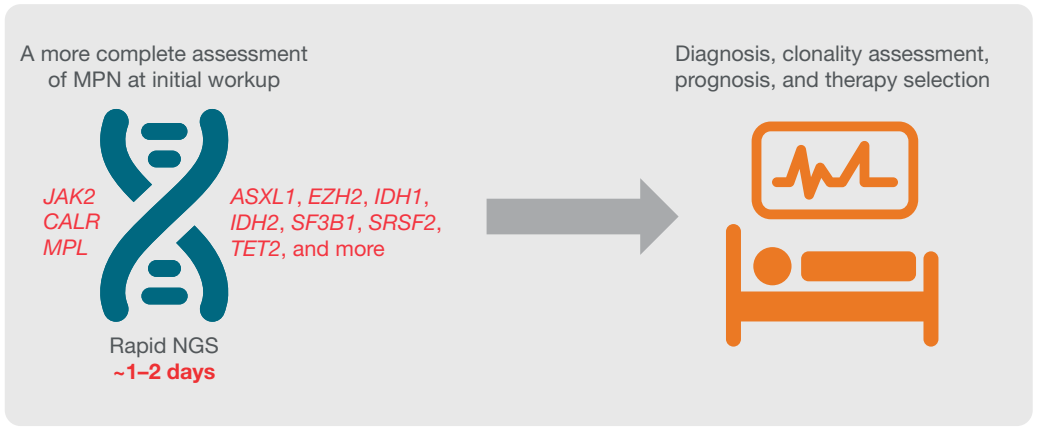

Figure 2. A rapid NGS panel at initial workup.

References

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