Blood Cancer Sample to Insight® Series: Real-Life Experience

Quest Diagnostics uses QCI® Precision Insights for rapid interpretation of novel LeukoVantage® assay

Frederick K. Racke, MD, PhD, Medical Director of Hematology/Oncology and Coagulation at Quest Diagnostics Nichols Institute

This flyer describes the experiences of a clinical laboratory in North America using QCI Precision Insights.

About the Laboratory

Quest Diagnostics is the world's leading provider of diagnostic information services. Serving about half of the physicians and hospitals in the United States, Quest Diagnostics has more than 6600 patient access points and offers an industry-leading test menu, ranging from routine biological tests to complex and specialized molecular and gene-based testing (1).

Customer Profile

Dr. Frederick K. Racke is the Medical Director of Hematology/Oncology and Coagulation at the Quest Diagnostics Nichols Institute in San Juan Capistrano, California. He earned his MD and PhD from the Medical Scientist Training Program at Case Western Reserve University in Cleveland, Ohio. He completed postdoctoral training in Clinical Pathology followed by training in Hematopathology at University Hospitals of Cleveland. Dr. Racke is board certified in Clinical Pathology and Hematology. He was a faculty member in the Department of Pathology at Johns Hopkins University in Baltimore, Maryland, where he served for 5 years as the co-director of the residency program in charge of the Clinical Pathology curriculum. Following his time at Johns Hopkins, Dr. Racke joined the faculty at Ohio State University and served as director of the division of Hematopathology and director of the Hematopathology fellowship program. In addition, he served as the leukemia cadre pathology leader for CALGB clinical trial cooperative group. In addition to his clinical activities, Dr. Racke ran a research laboratory that investigated mechanisms involved in platelet production.

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Medical Director

The Challenge

Given the vast phenotypic and genetic heterogeneity of myeloid malignancies, hematologists have eagerly awaited the introduction of next-generation sequencing (NGS) into routine clinical diagnostics to enable a more differentiated disease classification, risk stratification and improved therapeutic decisions. At present, an increasing number of hematologic laboratories are in the process of integrating NGS procedures into the diagnostic algorithms of patients with acute myeloid leukemia (AML), myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPNs).

In 2015, Quest Diagnostics launched the next iteration of the innovative LeukoVantage assay, a selection of three NGS panels offering physicians testing solutions for AML, MPN and MDS. The new solution replaced an earlier version of the LeukoVantage assay, which was a single 30-gene panel, with three tests covering 48 unique genes (Figure 1).

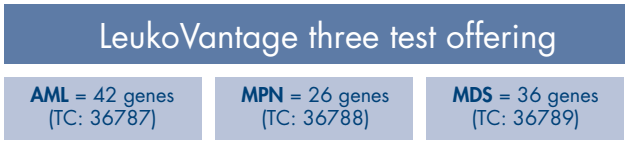

Figure 1. The LeukoVantage solution. **TC:** Test code.

"All the genes present within each panel have known documented relevance, including all the genes cited in both the National Comprehensive Cancer Network© (NCCN) guidelines and World Health Organization (WHO) classifications," says Racke. "This enables us to define a patient's diagnosis, provide a prognosis and aid in the therapeutic determinations."

However, while the new LeukoVantage offering increases the diagnostic scope and affords greater insight into potential treatment options for myeloid malignancies, the larger panels require much more time and effort for down-stream variant analysis and interpretation. As panels grow in size, so too does the number of variants detected.

When it comes to diagnosing and treating myeloid malignancies, time is of the essence. Multiple studies indicate that the faster a patient can be diagnosed and started on a treatment regimen, the better the survival outcomes (2-4). Therefore, to deliver on the promise of precision medicine, Quest Diagnostics needed to accelerate the variant annotation and interpretation steps of the LeukoVantage workflow to ensure the physicians they served received timely test results to better care for their patients.

The challenge for Quest Diagnostics became how to grow test volume and scale-up their variant interpretation without requiring more lab personnel.

The Solution

After considering several variant interpretation solutions, Quest Diagnostics decided to partner with QCI Precision Insights, a professional variant interpretation service for clinical NGS oncology testing powered by N-of-One, a QIAGEN company.

"Molecular profiling has become standard of care in the evaluation of myeloid neoplasms. Mutational analysis benefits greatly from having comprehensive expert annotation," says Racke.

Supporting clinical laboratories that already have an in-house bioinformatics solution to prioritize and report variants, QCI Precision Insights helps labs grow caseload volume without requiring extra personnel. The professional service is composed of a team of molecular biologists, variant scientists and oncologist who annotate and interpret clinically relevant variants according to WHO, NCCN and European LeukemiaNet (ELN) guidelines, providing multivariant analysis, pathway treatment matching and variant-level molecular impact assessments.

Leveraging a proprietary knowledge base of over 200,000 de-identified patient cases across 1000 cancer types covering over 1900 genes, QCI Precision Insights returns oncologist-reviewed, variant-specific expert interpretation summaries for every single variant submitted.

This enables Quest Diagnostics to quickly build patient-specific reports with the latest biological, diagnostic, prognostic and therapeutic evidence, as well as provide a list of approved targeted therapies and regional clinical trials.

"The LeukoVantage report includes an overall summary, as well as a mutation summary and therapeutic interaction summary," says Racke. "This is followed by more detailed information around the clinical relevance of each mutation, such as whether the mutation has prognostic or diagnostic significance, whether there are specific therapies for that mutation, as well as the alterations that make patients eligible for clinical trials. It also includes variants of unknown significance and which genes showed normal sequencing."

Through the partnership, Quest Diagnostics would submit variant files to QCI Precision Insights that contain only the clinically relevant alterations that were detected by the LeukoVantage. QCI Precision Insights' team runs the variants through the proprietary knowledge base to determine which of the variants have been seen and reported before. For recognized variants, biologically and clinically relevant information, including FDA-approved drugs, professional guidelines, clinical trials, prognostic and diagnostic information, is quickly compiled, reviewed by an oncologist and uploaded to the Quest Diagnostics' case review and sign-out portal. For rare or novel variants, the QCI Precision Insights team conducts in-depth research, manual curation and interpretation and submits the results in the same manner.

A pathologist from Quest Diagnostics reviews the clinical annotation and treatment recommendations, edits information if needed, generates a report and signs the case out.

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The Benefit

"The clinical annotation provided by QCI Precision Insights is critical. The rapid insights allow for rapid turnaround time. This is because there is a comprehensive database that has been accumulated at N-of-One," says Racke.

On average, 70% of the cases submitted to QCI Precision Insights are returned within minutes with full annotation. For the remaining 30%, Quest Diagnostics usually receives results back within 2 to 3 working days.

Another benefit of partnering with QCI Precision Insights is the control that Quest Diagnostics retains over the variant classification process even though they are not the ones completing the annotations and assessments. Unlike other variant interpretation solutions, such as informatics platforms that use artificial intelligence, QCI Precision Insights shows the reasoning behind each variant classification with actual links to the supporting evidence. This allows the pathologists at Quest Diagnostics to easily review the literature and decide for themselves if they agree with QCI Precision Insights' interpretation.

"Sometimes the significance of alterations is uncertain and there can also be legitimate differences in opinion regarding the pathogenicity of an alteration," says Racke. "The QCI Precision Insights annotation team has been very responsive to the inquiries by our pathologists regarding questions around annotation."

Each month, Quest Diagnostics and the QCI Precision Insights team meet to discuss any issues or updates. This ensures that Quest Diagnostics receives services tailored to their expectations.

"In summary," Racke says, "The Quest/QIAGEN partnership has allowed us to provide rapid and insightful information to our clinical colleagues, allowing us to better take care of their patients."

Learnings

- QCI Precision Insights significantly accelerates the turnaround time of the LeukoVantage assay, returning 70% of the cases within minutes.
- QCI Precision Insights shows the reasoning behind each variant classification with actual links to supporting evidence, giving Quest Diagnostics full control over final assessments and interpretations.
- The expert-curated, oncologist-reviewed content from QCI Precision Insights helped enable Quest Diagnostics to quickly build patient-specific reports with the latest diagnostic, prognostic and therapeutic information.

"The clinical annotation provided by QCI Precision Insights is critical. The rapid insights allow for rapid turnaround time."

Go to **www.qiagen.com/blood-cancer-awareness** to learn about our oncohematology solutions

References

1. Quest Diagnostics Fact Sheet, 2020. https://newsroom.questdiagnostics.com/index.php?s=30664. Accessed: September 11, 2020.
2. Jabbour, E. and Kantarjian, H. (2016) Chronic myeloid leukemia: 2016 update on diagnosis, therapy, and monitoring. Am. J. Hematol. 91, 252-265.
3. Mauro, M.J., Davis, C., Zyczynski, T., Khoury, H.J. (2015). The role of observational studies in optimizing the clinical management of chronic myeloid leukemia. Ther. Adv. Hematol. 6, 3-14.
4. Bower, H., Bjorkholm, M., Dickman, P.W., Hoglund, M., Lambert, P.C., Andersson, T.M. (2016). Life expectancy of patients with chronic myeloid leukemia approaches the life expectancy of the general population. J. Clin. Oncol. 34, 2851-2857.

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