High-quality diagnostic solutions

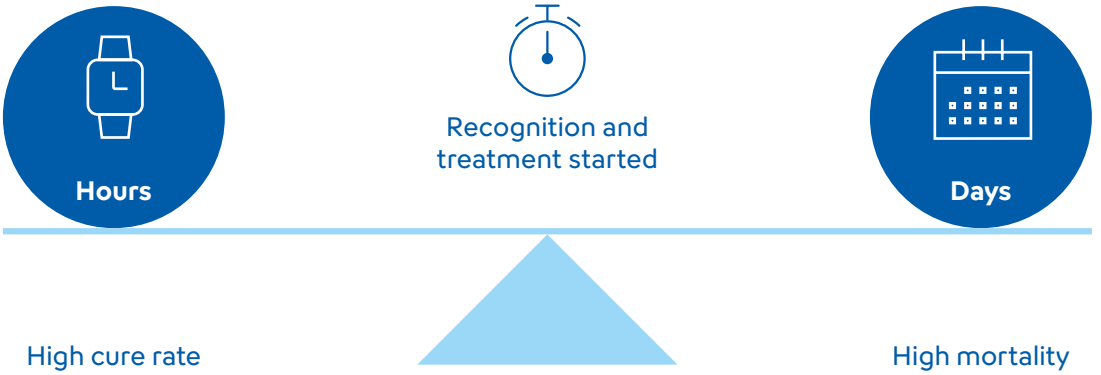
Smartly linked APL diagnostics

Together for a better
healthcare journey

A clinical challenge: acute promyelocytic leukaemia (APL) is a medical emergency, but it is rare, and symptoms are non-specific.

APL is a distinct form of acute myeloid leukaemia (AML), characterised in 95% of the cases by the presence of the PML-RARA fusion gene transcript, a result of the t(15;17) chromosomal translocation. Classic APL (75%) is characterised by hypergranular promyelocytes and cytopenia, whereas in variant or microgranular APL (25%) leucocytosis is common and promyelocyte appearance overlaps with the blast morphology of other AMLs. APL is strongly associated with dysregulated coagulation; consequently, haemostasis plays a critical role in the clinical presentation and treatment of this rare disease. The abnormal promyelocytes trigger hyperfibrinolysis and activation of the coagulation system, very frequently resulting in disseminated intravascular coagulopathy (DIC), which can cause life-threatening bleeding and thrombotic complications, especially in the early stages of the disease.

Close monitoring of coagulation activation, and effective management of these coagulation complications, are vital for successful treatment and improving the prognosis of patients with APL.



APL is highly curable if recognised early and promptly treated with all-trans retinoic acid (ATRA), an agent that induces differentiation of the malignant clone, thereby reducing the DIC trigger, but delay results in the rapid evolution of bleeding abnormalities with a high mortality rate. Improved linkage of diagnostic information from e.g. haematology, morphology and clinical flow cytometry allows for earlier diagnosis, followed by genetic confirmation, which is essential for the timely design of a targeted treatment plan. This contributes to a higher quality of care, especially for patients with such rare conditions, where rapid and accurate diagnosis is vital for improved outcomes.

Reference:
Yilmaz M, Kantarjian H, Ravandi F. Acute promyelocytic leukemia current treatment algorithms. Blood Cancer J. 2021 Jun 30;11(6):123. doi: 10.1038/s41408-021-00514-3. PMID: 34193815; PMCID: PMC8245494.
Hermsen J, Hambley B. The Coagulopathy of Acute Promyelocytic Leukemia: An Updated Review of Pathophysiology, Risk Stratification, and Clinical Management. Cancers (Basel). 2023 Jul 3;15(13):3477. doi: 10.3390/cancers15133477. PMID: 37444587; PMCID: PMC10340352.

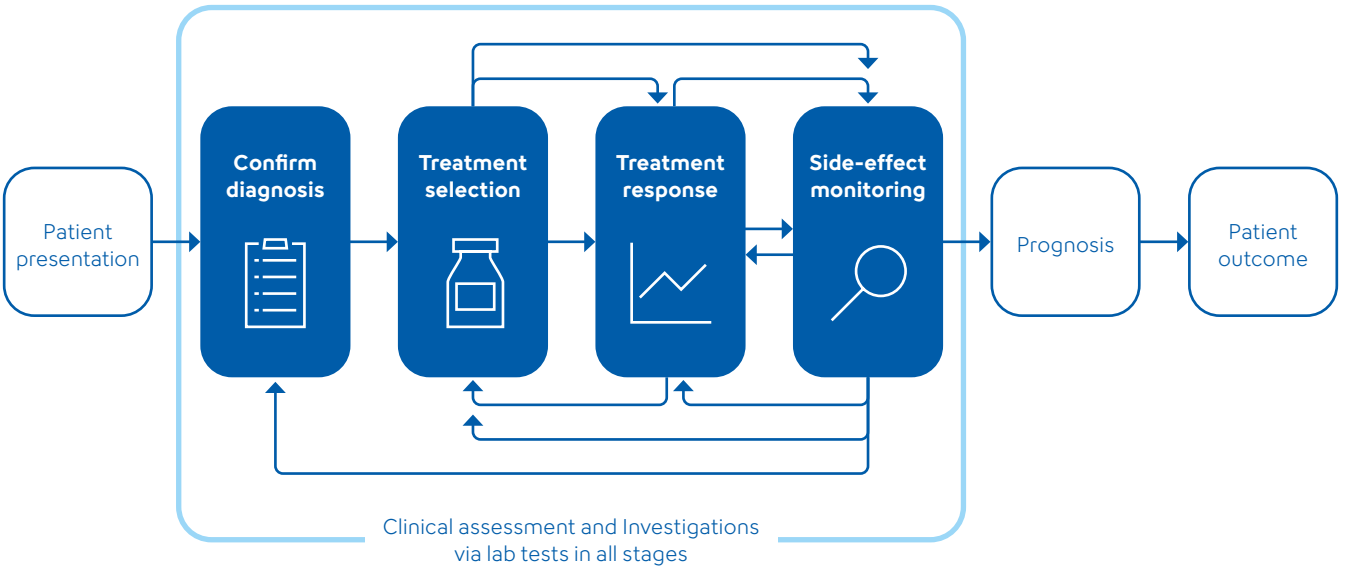
Comprehensive diagnostics and timely action are key: a clinical patient case

A 32-year-old female, previously well, attended her general practitioner (GP) because of fever and fatigue. Physical examination revealed some bruising but was otherwise normal. The GP suspected a seasonal acute viral illness and advised the patient to return if she did not feel better in a couple of days.

That evening, the patient was seen at the emergency department because of a severe nosebleed. A complete blood count and differential (CBC DIFF) and coagulation screen were requested. The blood count results were as follows: haemoglobin 8.7 g/dL, white blood cell count (WBC) 2.1 x 10^9/L (neutrophils 0.6 x 10^9/L), platelet count (PLT) 49 x 10^9/L. The peripheral blood smear examination revealed abnormal promyelocytes, many of which exhibited bilobed nuclei and an abundance of cytoplasmic granules, including Auer rods, in keeping with APL. The coagulation screen results were in keeping with a DIC: prothrombin time 14 seconds, activated partial thromboplastin time 29 seconds, fibrinogen 0.9 g/L, and D-dimer 15.7 mg/L (FEU).

The patient was admitted to hospital and ATRA therapy commenced immediately. Flow cytometry, performed on the peripheral blood, confirmed the presence of large numbers of primitive cells, with high FSC and SSC (due to size and granularity, respectively) and were CD117+, CD64+, CD33+ and CD13+ but HLA-DR and CD34 negative, highly suggestive of APL. FISH analysis confirmed a t(15;17)(q22;q12) translocation. Arsenic trioxide (ATO) was added to the ATRA therapy.

The role of diagnostics in the patient healthcare journey



The progression of this patient along her healthcare journey encompassed various stages, namely diagnosis, treatment selection, treatment monitoring and side-effect monitoring, all of which were determined by her clinician, whose judgment or decision on what to do next was heavily guided by investigations. What tests are ordered, and how these are interpreted, therefore have a major influence on clinical decision-making and thus patient outcomes.

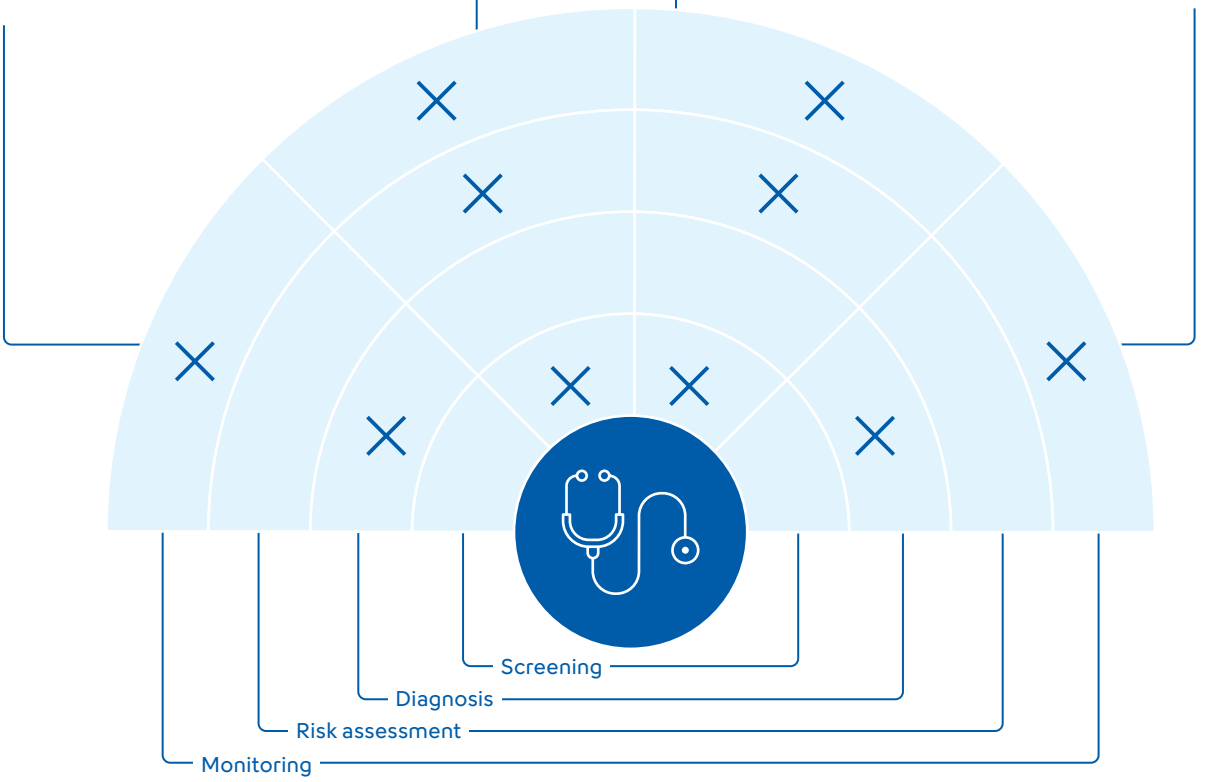
In this case the CBC revealed that the patient was low risk (WBC <10x10^9/L, PLT >40x10^9/L), hence no need for additional chemotherapy. She did, however, require a temporary dose reduction of ATO because of worsening neutropenia. Subsequent CBC DIFF and coagulation test monitoring revealed an excellent treatment response, with full resolution of the neutropenia and coagulopathy. Bone marrow immunophenotyping four weeks later confirmed that she had gone into complete remission. She continued with four cycles of consolidation therapy as an out-patient, during which no further side effects were observed. Molecular testing was negative on therapy completion and the patient was asked to return for a CBC DIFF test every three months.

Coagulation
Reliable screening for signs of DIC is vital for early detection and disease monitoring. Low fibrinogen and high fibrin degradation products are associated with bleeding risk severity.

Haematology
Reliable screening for cytopenias or leucocytosis, and abnormal cell populations (suspect flag-triggered smear review) is vital for early detection. Risk assessment is essential as older age, WBC >10 x10^9/L and PLT <40x10^9/L are considered high risk, as is APL variant, all of which need additional therapy.

Immunophenotyping
Rapid confirmation of abnormal promyelocytes by flow cytometry is critical so that lifesaving ATRA treatment can be started.

Molecular/cytogenetics
Detection of PML-RARA translocation confirming the diagnosis is critical so that ATRA therapy can be continued.



Empowering clinicians to attain better patient outcomes with Sysmex solutions

Doctors must be empowered to make swift decisions based on comprehensive, reliable information continuously available during the treatment process. This is particularly critical for the care of APL patients as their clinical condition can change rapidly. Serial testing is also essential to confirm treatment success. The availability of multiple diagnostic test results facilitates rapid clinical decision-making, giving each patient the best chance of a cure.

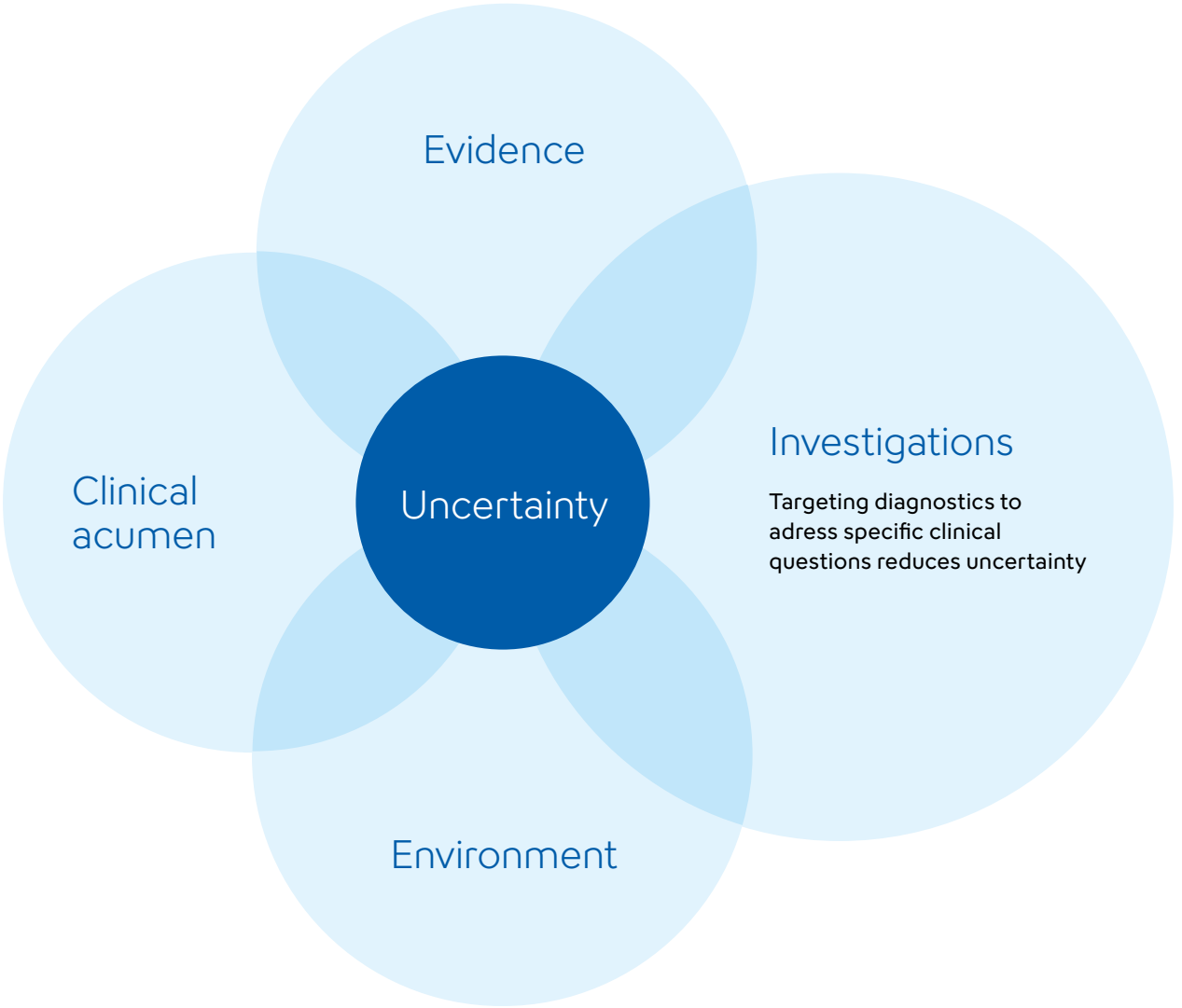
Sysmex's products can reduce uncertainty and assist clinicians in making timely decisions that prompt early interventions, ultimately improving patient outcomes and enhancing the quality of care.

“Together for a better healthcare journey”

Sysmex is committed to playing a leading role in the transformation of healthcare beyond delivering high-quality diagnostic solutions. Guided by the core values of patient-centricity, collaboration and innovation, working together, we strive to improve the healthcare journey of individuals from prevention to diagnosis and treatment, and aftercare.

To put our vision ‘Together for a better healthcare journey’ into practice, we have expanded our focus to the clinician’s perspective.
The patients’ progression along their healthcare journey is largely determined by their clinicians, whose decisions on next steps are heavily influenced by investigations.

By targeting diagnostic innovations to disease-specific challenges that clinicians face, we reduce clinical uncertainty, which improves patient outcomes, and with it their overall healthcare journey.



Factors influencing clinical decision-making

Discover more about smartly linked APL diagnostics:
www.sysmex-europe.com/apl