

Nordic AML Meeting 2026

The Nordic AML Meeting 2026 brought together leading researchers and clinicians to discuss recent advances in acute myeloid leukemia (AML), with a particular focus on **TP53-mutated myeloid malignancies, FLT3 biology and targeted therapy, novel therapeutic approaches, and emerging diagnostic technologies**. Across the meeting, several key themes emerged:

- TP53-mutated AML remains one of the highest-risk AML subgroups, with poor outcomes despite intensive therapy.
- Novel treatment strategies targeting mutant p53, exploiting synthetic lethality, and overcoming venetoclax resistance are showing promise.
- FLT3 inhibitors continue to improve outcomes in FLT3-mutated AML and may have broader applications beyond conventionally detected FLT3-ITD-positive disease.
- Measurable residual disease (MRD) is increasingly important for treatment decisions, particularly regarding transplantation and maintenance therapy.
- Advanced molecular profiling, multi-omics approaches, and computational modeling are expanding opportunities for personalized medicine in AML.

The meeting highlighted how integrating molecular biology, innovative therapeutics, and precision diagnostics is shaping the future management of AML.

TP53-Focused Sessions

TP53 Biology and Epidemiology

The meeting opened with a keynote lecture by **Jean-Christophe Bourdon**, who presented data demonstrating that the tumor-suppressive functions encoded by TP53 extend beyond the full-length p53 protein. Multiple p53 isoforms exist and can influence cell-cycle regulation, differentiation, treatment response, and survival outcomes. The presentation emphasized that TP53 mutation status alone may not adequately capture disease biology, and that p53 isoform profiling may provide additional prognostic and predictive information.

Christer Nilsson presented epidemiological data from the Swedish AML Registry involving approximately 2,740 patients. TP53 mutations were identified in roughly 14% of AML cases and were associated with advanced age, poorer performance status, inferior responses to treatment, and markedly reduced survival. The presentation further explored interactions between TP53 mutations and other genetic lesions, highlighting the complexity of risk stratification within this patient group.

Klas Wiman discussed therapeutic strategies targeting mutant p53, including restoration of normal p53 function, degradation of mutant protein, and mutation-specific approaches such as Y220C-targeted therapies. Agents including APR-246, arsenic trioxide, and MDM2 inhibitors

were highlighted, with particular emphasis on combination approaches to improve therapeutic efficacy.

Amos Tuval presented preclinical work demonstrating synergistic anti-leukemic activity when APR-246 is combined with novobiocin and related aminocoumarins. The combination appeared to enhance DNA damage and induce p53-dependent ferroptosis, suggesting a potential strategy to improve outcomes in TP53-mutated AML.

Shah Mithun examined TP53-mutated precursor states and leukemic transformation. The talk highlighted ongoing challenges in defining biologically meaningful disease categories and discussed the potential role of variant allele frequency, allelic status, mutation burden, and cytogenetic abnormalities in refining classification and risk assessment.

Diagnostic and therapeutic strategies

In another *SKG/CMYC* Keynote Lecture, **Marina Konopleva** discussed mechanisms of venetoclax resistance in AML and described the "Montefiore approach" for TP53-mutated AML and MDS. This treatment strategy utilizes metronomic weekly dosing of decitabine and venetoclax and has demonstrated encouraging clinical results in this difficult-to-treat patient population.

Kim Theilgaard-Mønch presented work investigating DNA-dependent protein kinase inhibitors (DNA-PKi) as a means of overcoming chemotherapy resistance. Experimental studies showed that DNA-PKi improved chemotherapy responses in AML models and enhanced chemosensitivity irrespective of TP53 status, supporting further evaluation of synthetic lethal therapeutic combinations.

Experimental Diagnostics and Multi-Omics

Anders Eivind Leren Myhre presented outcomes from a Scandinavian cohort of 180 patients with TP53-mutated AML or MDS who underwent allogeneic stem cell transplantation. Despite the high-risk nature of the cohort, a three-year overall survival of 36.6% was observed. However, graft-versus-host disease remained a significant complication, affecting more than half of long-term survivors.

Hussain Abbas explored the biological mechanisms underlying treatment resistance in TP53-mutated AML using advanced single-cell and multi-omic approaches. His findings suggested that relapsed TP53-mutated AML frequently exhibits an erythroid differentiation signature. Additionally, novel methods were presented for simultaneously evaluating spatial architecture and stromal interactions within the bone marrow microenvironment.

Industry Sessions

The industry-sponsored session focused on evolving treatment approaches for both unfit and fit AML patients.

Bjørn Tore Gjertsen reviewed current AML treatment standards and discussed emerging combination therapies designed to balance efficacy and tolerability in older unfit patients.

Gail Roboz provided a comprehensive overview of the rapidly evolving AML treatment landscape. She emphasized the importance of molecular diagnostics to guide individualized treatment selection and monitoring, highlighting personalized treatment decisions as a cornerstone of optimal patient management.

Pau Montesinos reviewed clinical development of FLT3 inhibitors including sorafenib and quizartinib across multiple studies such as SORAML, QUIWI, QuANTUM-Wild, and VEN-A-QUI. Evidence suggested that FLT3 inhibition may provide meaningful anti-leukemic activity not only in patients with detectable FLT3-ITD mutations but also in selected patients classified as FLT3 wild-type.

Mark J. Levis discussed contemporary management of FLT3-ITD AML, emphasizing the major advances achieved through FLT3 inhibitors including midostaurin and quizartinib. Data from pivotal trials such as RATIFY and QuANTUM-First have established FLT3 inhibition as an integral component of frontline therapy. He highlighted the increasing importance of MRD monitoring to inform both transplantation and maintenance treatment decisions.

FLT3-Focused Sessions

A major component of the meeting addressed advances in understanding FLT3 biology and the growing role of FLT3-targeted therapies.

FLT3 Biology and Epidemiology

Lars Rönnstrand reviewed the molecular biology of FLT3 signaling and receptor activation mechanisms. Particular attention was given to the role of juxtamembrane autoinhibition and its disruption in leukemogenesis.

Gunnar Juliusson analyzed real-world outcomes from the Swedish AML Registry. His data demonstrated the poor prognosis associated with high-risk FLT3-ITD AML, particularly among patients not undergoing transplantation. Elevated white blood cell count emerged as an additional adverse prognostic feature.

Novel FLT3-Targeted Approaches

Jing Tang presented computational and systems-biology approaches for identifying rational drug combinations in AML. These included digital-twin modeling, integration of CRISPR-derived gene-essentiality datasets, and predictive models combining molecular and drug-sensitivity profiling to support individualized treatment selection.

Ton Falques discussed clonal evolution during treatment of FLT3-N676K-positive KMT2A-rearranged leukemia, demonstrating how therapy shapes subclonal dynamics and contributes to resistance development. The work may inform future strategies to overcome acquired treatment resistance.

Yngvar Fløysand focused on FLT3 inhibitor maintenance therapy, addressing the ongoing challenge of identifying which patients derive greatest benefit from prolonged post-remission treatment.

Marc Raaijmakers presented results from studies evaluating upfront FLT3 inhibition in patients eligible for intensive chemotherapy. Although gilteritinib was generally well tolerated, the primary endpoint in a phase III comparison with midostaurin was not achieved.

FLT3 and Measurable Residual Disease

The final session examined important biological nuances of FLT3-mutated AML.

Francesca Sacco demonstrated how the location and length of FLT3-ITD insertions influence both prognosis and treatment response. Multi-omic and systems-biology approaches were proposed as tools to better understand this biological heterogeneity.

Further discussion by **Pau Montesinos** highlighted the possibility that undetected FLT3-positive subclones may explain activity of FLT3 inhibitors in apparently FLT3-wild-type AML, reinforcing the need for increasingly sensitive molecular diagnostics.

Mark J. Levis concluded by reviewing FLT3-based MRD monitoring. FLT3-ITD characteristics can serve as unique molecular fingerprints for tracking disease burden over time, with bone marrow assessment providing superior sensitivity compared with peripheral blood.

Key Conclusions

1. **TP53-mutated AML remains a major unmet clinical need**, requiring innovative therapeutic approaches beyond conventional chemotherapy.
2. **FLT3 inhibitors have transformed management of FLT3-mutated AML** and may have broader utility than previously recognized.
3. **MRD-guided treatment decisions are becoming increasingly important**, particularly for transplantation and maintenance therapy.

4. **Multi-omics, single-cell technologies, and computational modeling** are providing deeper insights into disease biology and treatment resistance, supporting the development of precision medicine strategies.
5. The future of AML treatment will likely depend on the integration of **molecular diagnostics, targeted therapies, and individualized treatment strategies** to improve outcomes across genetically diverse patient populations.