



Minimal Residual Disease (MRD) as a Surrogate Endpoint in Acute Myeloid Leukemia (AML) Workshop

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Objectives

- Review and discuss available data on the prognostic significance of MRD in genetic/ biologic subtypes of AML and the relative strengths of specific markers for MRD assessment and technology platforms utilized
- Discuss the regulatory context in the consideration of biomarker qualification and the use of a surrogate endpoint which can adequately predict clinical benefit (OS, EFS, Transplant eligibility, other)
- Consider potential indications and corresponding clinical trial designs of new drugs which might incorporate MRD as a surrogate endpoint
- Discussion to help inform OHOP and DHP with respect to next steps required for future regulatory decisions re MRD as a surrogate endpoint.

Agenda

- Regulatory Considerations
- Clinical Context
- Technical Considerations
- Clinical experience within genetic subtypes
- Study design
- Discussion points.

Discussion Points

- Do current data on the prognostic significance of post-Induction MRD in AML warrant consideration of its potential as a surrogate for OS or EFS in the evaluation of new drugs and regulatory decision-making?
- Given the biologic heterogeneity of AML and the sub-type-specific molecular markers used in MRD assessment, for which genetic subtype(s) of AML would MRD be an appropriate surrogate? Is there a rationale for the exclusion of a certain subtype from such consideration?

Discussion Points (cont'd)

- Please discuss the need for designation of a target threshold value, the timing of assessment, and the potential limitations of MRD as a surrogate endpoint for EFS if alternative therapeutic interventions are instituted in clinical trials based on the results of early MRD assessment.
- Please discuss the preferred optimal technology platform for MRD assessment within the context of specific disease sub-types and the need for assay performance characterization, standardization, and centralization.
- Please discuss the feasibility of emerging technologies, eg. NextGen sequencing as a potential method for MRD assessment.