Questions For Panel: Workshop on Endpoints in Acute Leukemia

Heterogeneity

- If the benefit of a targeted therapy is likely to be restricted to a subset of subjects with acute leukemia, should the achievement of a prospectively defined endpoint be assessed in all subjects enrolled in a pivotal trial or only in subjects in the targeted subset?

Clinical response

- Could a response less than a complete remission be acceptable as a clinical benefit?
  - What additional evidence is needed?
  - What metrics should be used to support its use?
  - Should "qualified" CRs (CRp or CRi) always require validation or are some qualified CRs clinical benefits? If so, under what conditions?

Clinical response

- Is CRp an endpoint that could be applied to all studies with all products without further validation?
- Is it reasonably likely to predict a benefit?
- What duration is needed?

Clinical response

- Is reversion to status (e.g. MDS) prior to Acute Leukemia an acceptable response? Is it a clinical benefit or a surrogate?
- Is duration needed?

Clinical response

- Could the persistence of non-proliferating malignant cells be acceptable?
  - What duration would be needed?

Clinical response

- Could the delayed appearance of complete remission be considered a clinical benefit?
  - If an agent only produced CRs after a delay of several months could the CR still be considered a benefit?

Minimal residual disease

- Does the presence or absence of MRD ever establish an additional benefit beyond CR?
  - If so, under what circumstances? Is a measure of survival still required?
  - What is the evidence?

Minimal residual disease

- Could the elimination of MRD in subjects in CR with MRD be considered a clinical benefit?
  - What evidence should be used to support a claim that it is a clinical benefit?

Bridge to Transplant

- Which, if either, should be considered the clinical benefit:
  - Response to the treatment?
  - Performance of a subsequent transplant?

Quality of Life

- What safety related ((i.e. "reduced" quality of life) endpoints should be considered in the selection of safety endpoints in support of licensing a product?