# Defining High-Risk Multiple Myeloma

## Cytogenetic Abnormalities

- Not all chromosomal abnormalities are viewed as portending equally poor prognosis
- Having > 1 abnormality is associated with poorer prognosis

- **IgH Translocations**
  - t(4;14)
  - t(14;16)
  - t(14;20)

- **Genomic Imbalance**
  - del 17p
  - Gain 1q

## Clinical/Disease Features

- R-ISS (stage II/III)
- High serum β2-microglobulin (≥ 5.5 mg/L)
- Renal insufficiency
- Low serum albumin
- Elevated LDH: (LDH > Upper Limit of Normal)
- Presence of EMD or plasma cell leukemia

## Quality of Response

- Primary resistant MM/inadequate response to frontline therapy
- Early relapse after first line of therapy is associated with poor prognosis
- Relapse occurring within ≤ 12 months of autologous stem cell transplantation and/or primary therapy

## Unmet Need & Challenges

- Lack of upfront testing in NDMM
- Lack of common ways to categorize high-risk disease
- Lack of consensus or standardized treatment

---

Investigational therapies aim to overcome high-risk status and produce outcomes that more closely match those of standard-risk patients

---

**Graphic**: Hypothetical Kaplan-Meier curve

- **Survival**
- **Time**

---

**Key**

- **Standard risk, investigational therapy**
- **High risk, investigational therapy**
- **Standard risk, conventional therapy**
- **High risk, conventional therapy**

---

**References**