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MRD Implications for High risk Disease

Scottsdale, Arizona
Rochester, Minnesota
Jacksonville, Florida
Biomarker

- The disease with best biomarkers ever!
- Personalized medicine is now based on understanding biology and genetics
- MRD is the ultimate frontier to adjust and personalize management of MM
Imatinib mesylate versus allogeneic hematopoietic stem cell transplantation for patients with chronic myelogenous leukemia in the accelerated phase

Qian Jiang, Lan-Ping Xu, Dai-Hong Liu, Kai-Yan Liu, Shan-Shan Chen, Bin Jiang, Hao Jiang, Huan Chen, Yu-Hong Chen, Wei Han, Xiao-Hui Zhang, Yu Wang, Ya-Zhen Qin, Yan-Rong Liu, Yue-Yun Lai, and Xiao-Jun Huang

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The relative merits of allogeneic hematopoietic stem cell transplantation (allo-HSCT) and imatinib for chronic myelogenous leukemia in the accelerated phase (AP-CML) have not previously been evaluated. This cohort study was designed to compare the outcomes of imatinib (n = 87) versus allo-HSCT (n = 45) for AP-CML. A multivariate analysis of the total population revealed that a CML duration ≥12 months, hemoglobin < 100 g/L, and peripheral blood blasts ≥5% were independent adverse prognostic factors for both overall survival (OS) and progression-free survival (PFS). Both treatments resulted in similar survival in low-risk (no factor) patients, with 6-year event-free survival (EFS), OS, and PFS rates of more than 80.0%. Intermediate-risk (any factor) patients showed no difference in EFS and OS, but 6-year PFS rates were 55.7% versus 92.9% (P = .047) with imatinib versus allo-HSCT, respectively. Among high-risk (at least 2 factors) patients, imatinib was by far inferior to allo-HSCT, with 5-year EFS, OS, and PFS rates of 9.3% versus 66.7% (P = .034), 17.7% versus 100% (P = .008), and 18.8% versus 100% (P = .006), respectively. We conclude that allo-HSCT confers significant survival advantages for high- and intermediate-risk patients with AP-CML compared with imatinib treatment; however, the outcomes of the 2 therapies are equally good in low-risk patients. All trials were registered with the Chinese Clinical Trial Registry (www.chictr.org) as CHICTR-TNC-10000955. (Blood. 2011;117(11):3032-3040)
Figure 2. OS difference among different inter-quartile groups by (a) CINGEC, (b) GII of Mayo patient aCGH data and (c) CINGEC, (d) GII of UAMS patient.

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0066361
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del 17 p, sCR prior to ASCT

Diagram:
- Diagnosis: 17p deleted, renal failure, dialysis
- ASCT
- CyBorD x 5
- Myeloma molecules per 1M leukocytes
- Bone marrow

Graph:
- Date (Month/Year):
  - 2/14
  - 4/14
  - 6/14
  - 8/14
  - 10/14
  - 12/14
- Myeloma molecules per 1M leukocytes scale:
  - $10^{-1}$
  - $10^{0}$
  - $10^{1}$
  - $10^{2}$
  - $10^{3}$
  - $10^{4}$
  - $10^{5}$
  - $10^{6}$
Clinical Scenarios

Myeloma is always preceded by MGUS
Will not address subclone principles

MM
- Persistent disease
- Clonal enrichment
- Quiescent MM cells
- Low proliferation

CR/sCR
- Persistent disease
- Clonal enrichment

MM
- Quiescent MM cells
- Low proliferation

MGUS
- Clonal
- non malignant

Observed

MYC

Treat?

Observe?

Back off!
Clinical Scenarios

When to test for MRD?

Diagnosis
KRD

Relapse (e.g. ASPIRE)

SCT
Maintenance

CR
sCR

Prognosis
Decide
Monitor

Value
Sagar’s iceberg
Better Icerberg Than Sagar’s?

MAYO CLINIC

Diagnosis

1x10^{12}

1x10^{8}

CR

Flow

NGS

1x10^{4}

Std. Cells

High Risk Cells?

Cure 0

MGUS Clones?