Trends in Utilization and Outcomes of Autologous Hematopoietic Cell Transplantation (AHCT) in the Upfront Management of Patients with Multiple Myeloma: A CIBMTR Analysis

CIBMTR Study MM12-01

There are no relevant conflicts of interest to disclose.
Writing Committee

- Luciano Costa, MD, PhD
- Mei-Jie Zhang, PhD
- Xiaobao Zhong, MS
- Angela Dispenzieri, MD
- Amrita Krishnan, MD
- Sagar Lonial, MD
- Parameswaran Hari, MD, MS

On behalf of the Plasma Cell Disorders Working Committee and the Center for International Blood and Marrow Transplantation Research
Introduction

- Population-based studies* have indicated improvement in survival for patients with MM over the last two decades.

- MM survival improvement coincides with increased use of AHCT in mid-1990s and early-2000s.

- The relative contribution of better supportive care, greater access to AHCT and availability of new drugs is mostly unknown.

Pulte et al. Oncologist. 2011;16:1600-1603
Purpose of the Study


- Compare survival between the 3 time cohorts with “era” used as a surrogate for the impact of novel therapies
Inclusion Criteria

- Recipients of first AHCT in US or Canada
- First autologous transplant 1995-2010
- First autologous transplant <1 year from diagnosis ("upfront")
- Registered at CIBMTR (TED dataset)
- Reported to CIBMTR (CRF dataset)
- At least 100 days of follow up
Utilization
Utilization (US data only)

- Estimated 32,151 AHCT performed in the period (23,725 registered)
- 26,960 (68.3%) procedures performed < 1 year from diagnosis
- Estimated 13.4% of the 238,235* MM new cases received AHCT, 9.2% within one year of diagnosis

* SEER database
Utilization (US data only)

50-64 years

- First transplant in 12 months
- First transplant at any time
- Number of newly diagnosed patients

1995-1999: 15000
2000-2004: 20000
2005-2009: 25000

CIBMTR
Utilization (US data only)

≥ 65 years

First transplant in 12 months
First transplant at any time
Number of newly diagnosed patients

CIBMTR
Characteristics of AHCT Recipients
<1 year from diagnosis (US and Canada)

- Two datasets:
  - Transplant essential data (TED N= 29,489)
  - Case report forms (CRF N= 4,373)

- Demographics

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Median age*</td>
<td>54</td>
<td>57</td>
<td>58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥65*</td>
<td>8%</td>
<td>19%</td>
<td>24%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female gender</td>
<td>41%</td>
<td>41%</td>
<td>41%</td>
<td>NS</td>
</tr>
<tr>
<td>African-American#</td>
<td>14%</td>
<td>13%</td>
<td>15%</td>
<td>NS</td>
</tr>
</tbody>
</table>

*TED dataset #CRF dataset
### Characteristics of AHCT Recipients
< 1 year from diagnosis (US and Canada)

- **Disease and Induction**

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Stage 3 (DSS or ISS)</td>
<td>64%</td>
<td>64%</td>
<td>44%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 line of therapy</td>
<td>70%</td>
<td>63%</td>
<td>63%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thalidomide use</td>
<td>&lt;1%</td>
<td>22%</td>
<td>52%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lenalidomide use</td>
<td>0%</td>
<td>&lt;1%</td>
<td>21%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bortezomib use</td>
<td>0%</td>
<td>2%</td>
<td>35%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CR/PR prior to AHCT</td>
<td>79%</td>
<td>87%</td>
<td>88%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

#CRF dataset

[Image: CIBMTR logo]
Evolution of Induction Approaches
## Characteristics of AHCT Recipients

### <1 year from diagnosis (US and Canada)

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Median time to AHCT</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>From diagnosis (mo)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemo mobilization</td>
<td>74%</td>
<td>74%</td>
<td>57%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Melphalan-only</td>
<td>54%</td>
<td>93%</td>
<td>99%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>conditioning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D100 TRM</td>
<td>2%</td>
<td>2%</td>
<td>1%</td>
<td>NS</td>
</tr>
<tr>
<td>Planned 2\textsuperscript{nd} transplant</td>
<td>14%</td>
<td>18%</td>
<td>28%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maintenance therapy</td>
<td>46%</td>
<td>31%</td>
<td>27%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

#CRF dataset
Outcomes
Probability of Overall Survival (OS) after Auto-HCT Stratified by Period of Transplant (CRF)

- 1995-99 (n=686):
  - 2 years: 72% (81%*)
  - 5 years: 47% (55%*)

- 2000-04 (n=1,464):
  - 2 years: 81%*
  - 5 years: 55%*

- 2005-10 (n=2,223):
  - 2 years: 86%**
  - 5 years: 57%*

* vs. 1995-1999, P<0.05
# vs. 2000-2004, P<0.05
Probability of Overall Survival (OS) after Auto-HCT Stratified by Period of Transplant (TED)

- 1995-1999 (n=2,226)
- 2000-2004 (n=6,408)
- 2005-2010 (n=11,644)

Years

Probability, %

0 1 2 3 4 5

CIBMTR
# Multivariate Analysis for Mortality (CRF)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period of transplant (Main effect)</td>
<td>2 D.F. Overall Test</td>
<td>P-value&lt;0.0001</td>
</tr>
<tr>
<td>2000-2004 vs. 1995-1999</td>
<td>0.77 (0.67-0.89)</td>
<td>0.0003</td>
</tr>
<tr>
<td>2005-2010 vs. 1995-1999</td>
<td>0.68 (0.59-0.79)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2005-2010 vs. 2000-2004</td>
<td>0.88 (0.78-0.99)</td>
<td>0.0340</td>
</tr>
<tr>
<td>Age at transplant</td>
<td>2 D.F. Overall Test</td>
<td>P-value&lt;0.0001</td>
</tr>
<tr>
<td>50-64 vs. &lt;50</td>
<td>1.29 (1.13-1.47)</td>
<td>0.0002</td>
</tr>
<tr>
<td>≥65 vs. &lt;50</td>
<td>1.45 (1.23-1.72)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Karnofsky Performance Score</td>
<td>2 D.F. Overall Test</td>
<td>P-value&lt;0.0001</td>
</tr>
<tr>
<td>80-100 vs. &lt;80</td>
<td>0.59 (0.51-0.70)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unknown vs. &lt;80</td>
<td>0.57 (0.43-0.76)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Durie-Salmon/ISS stage III</td>
<td>2 D.F. Overall Test</td>
<td>P-value&lt;0.0001</td>
</tr>
<tr>
<td>Yes vs. No</td>
<td>1.56 (1.39-1.76)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Unknown vs. No</td>
<td>1.59 (1.29-1.98)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lines of chemotherapy</td>
<td>2 D.F. Overall Test</td>
<td>P-value=0.0397</td>
</tr>
<tr>
<td>&gt;1 vs. 1</td>
<td>1.15 (1.03-1.28)</td>
<td>0.0116</td>
</tr>
<tr>
<td>Unknown vs. No</td>
<td>0.96 (0.51-1.80)</td>
<td>0.8992</td>
</tr>
<tr>
<td>Sensitivity to therapy</td>
<td>2 D.F. Overall Test</td>
<td>P-value=0.0004</td>
</tr>
<tr>
<td>Sensitive vs. resistant</td>
<td>0.76 (0.66-0.87)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Unknown vs. resistant</td>
<td>0.45 (0.10-2.05)</td>
<td>0.3003</td>
</tr>
</tbody>
</table>
Progression-free Survival (PFS) after Auto-HCT Stratified by Period of Transplant (CRF)

- 1995-1999 (n=686):
  - 1 year: 50%
  - 2 years: 55%
  - 3 years: 57%*
  - 5 years: 26%

- 2000-2004 (n=1,464):
  - 1 year: 55%*
  - 2 years: 57%*
  - 3 years: 27%
  - 5 years: 27%

- 2005-2010 (n=2,218):
  - 1 year: 57%*
  - 2 years: 23%
  - 3 years: 23%
  - 5 years: 23%

* vs. 1995-1999, P<0.05
Overall Survival (OS) after REL/PROG Stratified by Period of Transplant (CRF)

Years | 1995-99 | 2000-04 | 2005-10 |
--- | --- | --- | --- |
Survival Probability, % | 58% | 65%* | 72%** |

* vs. 1995-1999, P<0.05
# vs. 2000-2004, P<0.05
Conclusions I

- Increasing utilization of AHCT as initial therapy for MM in the US
- Stable proportion of first AHCT being performed in the first year after diagnosis.
- Expansion of use among older patients and patients with stage 1 or 2.
- Stable but lower than expected utilization among AA patients.
Conclusions II

- Increased use of novel drugs between the 3 cohorts ⇒ better disease response prior to AHCT

- AHCT practice changed towards less use of chemomobilization and near universal use of single agent melphalan conditioning

- AHCT remained safe, with low TRM

- There was improvement in OS post progression in later cohorts
Conclusions III

- There was progressively improved survival for MM patients managed with AHCT as initial therapy, independent of other patient and disease-related characteristics.

- Improvement in survival driven less by improvement in post transplant PFS and more by the success of post relapse/progression management.
High dose melphalan and novel biological agents are complementary, non-redundant therapies and should be combined in the management of suitable MM patients