Transplant for every NDMM transplant eligible?

Immediate Transplant No Longer Required

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18th International Myeloma Workshop
Sept 2021 Vienna
Disclosures

• BMS
• AbbVie
• Prothena
• Janssen
• Takeda
• Ionis
OS according to treatment group
At 48 months, OS 66% (range, 56% to 76%) and 61% (range, 51% to 71%), respectively

Even prior to novel agents
Early SCT did not provide OS benefit and time without symptoms and treatment toxicity (TWISTT) inferior with early HDT

https://doi.org/10.1182/blood.V92.9.3131
Early harvest and late transplantation in MM

**Figure 1** Kaplan-Meier actuarial survival from diagnosis for all 118 patients.

**Figure 2** Kaplan-Meier actuarial time from diagnosis to day 0 of bone marrow transplant.
Delayed stem cell transplantation for the management of relapsed or refractory multiple myeloma

Overall survival after stem cell transplantation based on disease status at the time of transplantation. Rx, treatment.

Overall survival from original diagnosis of multiple myeloma.
Early versus Delayed Autologous Transplantation Following IMiD-based Induction Therapy in Patients with Newly Diagnosed Multiple Myeloma

Early versus delayed autologous stem cell transplantation in patients receiving novel therapies for Multiple Myeloma

early or late ASCT is a viable option for MM patients receiving induction treatment with novel targeted therapies

<table>
<thead>
<tr>
<th>Therapy</th>
<th>SCT &lt;1 yr N=102</th>
<th>SCT &gt;1 yr N=65</th>
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</thead>
<tbody>
<tr>
<td>Thalidomide</td>
<td>39 N=38 %</td>
<td>43 N=66 %</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>64 N=63 %</td>
<td>32 N=49 %</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>34 N=33 %</td>
<td>18 N=28 %</td>
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Overall Survival comparing early vs. delayed first ASCT in multiple myeloma patients (p=0.45).
• With a FU of almost 8 years, median OS was NR and there was no difference between the 2 strategies with respect to PFS2 and OS.

MRD appears to predict outcome and might be used after induction to identify those pts who probably do not require a transplant.

As MRD- rates rise with novel agents need for SCT will continue to decline.
EMN02/HO95 MM study design

**Intensification**
- **VMP x 4 cycles**
  - Bortezomib 1.3 mg/m²
  - d 1,4,8,11,22,25,29,32/42
- **Melphalan 9 mg/m²**
  - d 1-4/42
- **Prednisone 60 mg/m²**
  - d 1-4/42
  - (495 pts)

**Induction**
- **VCD x 3-4 cycles**
  - + PBSC collection (1493 pts)

**Consolidation**
- **VRD x 2 cycles**
  - (449 pts)

**Maintenance**
- **Lenalidomide**
  - (977 pts)

**Primary endpoints:**
- PFS from R1: ASCT vs VMP
- PFS from R2: VRD consolidation vs no consolidation

**Secondary endpoints:**
- PFS from R1: HDM-1 vs HDM-2
- Rates of response to ASCT or VMP
- OS from R1: ASCT vs VMP
- Toxicities with ASCT and VMP
EMN02/HO95

![Graph showing overall survival over time with number at risk for each group listed.](image)

**Table:**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number at Risk (Number Censored)</th>
</tr>
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<tbody>
<tr>
<td>Autologous HSCT</td>
<td>702 (0) 658 (16) 614 (24) 569 (36) 487 (78) 276 (268)</td>
</tr>
<tr>
<td>VMP</td>
<td>495 (0) 463 (12) 430 (20) 391 (31) 331 (62) 174 (198)</td>
</tr>
</tbody>
</table>

**Figure 2:**

HR 0.90 (95% CI, 0.71–1.13); adjusted p=0.35
ASCT + R maintenance vs MPR-R

3-year overall survival was not significantly prolonged (88.0% vs. 79.2%; hazard ratio for death, 0.64; 95% CI, 0.36 to 1.15; P=0.14).
Interpretation

• the lack of overall survival benefit suggests that deferred stem cell transplant until relapse is feasible without compromising outcome
Conclusions

• The goal of therapy is MRD-
  • No matter how this goal is achieved outcomes are identical
  • As combinations of non cross resistant agents are used in induction, consolidation and maintenance the need/role for SCT will continue to decline
  • In Castor Pollux Alcyone and Maia median MRD- 28%

https://doi.org/10.1182/blood.2021011101
MRD negativity with non transplant regimens

- carfilzomib with lenalidomide and dexamethasone followed by lenalidomide to patients with NDMM N=45

- near-complete response or better (n = 28), minimal residual disease negativity was 100% by multiparametric flow cytometry and 67% by next-generation sequencing.

MRD negativity in the bone marrow; $10^{-5}$ sensitivity) was achieved in 29 of 41 patients (71%; the 1-year PFS rate and the OS rate were 98% and 100%, respectively.
Timing of Autologous Stem Cell Transplantation for Multiple Myeloma in the Era of Current Therapies

consecutive patients with newly diagnosed myeloma who had undergone stem cell harvest (SCH) from 2005 to 2014 and separated them into early (SCT within 12 months of diagnosis) and delayed.

Delaying SCT did not affect OS or even PFS to second relapse
Autologous Transplantation for Newly Diagnosed Multiple Myeloma in the Era of Novel Agent Induction

3171 patients in these trials
The role of high-dose melphalan with autologous stem-cell transplant in multiple myeloma: is it time for a paradigm shift?
Summary

• We need to stop thinking of SCT as the platform on which all myeloma therapy is built (transplant eligible is no longer question 1)

• Sct is a regimen and selection, and sequencing depends on availability of other regimens, reimbursement, trial access and availability of novel agents
Questions & Discussion
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