2015 Updates in Multiple Myeloma

Siddhartha Ganguly, MD, FACP
Professor of Medicine
Director, Lymphoma and Myeloma
Blood and Marrow Transplantation Program
The University of Kansas Medical Center

Earliest Evidence of Myeloma

Myeloma in Mummies: Ancient affliction. A high-resolution CT scan of the lumbar spine region of a 2150-year-old Egyptian mummy revealed small, round lesions.

Ancient affliction, A high-resolution CT scan of the lumbar spine region of a 2150-year-old Egyptian mummy revealed small, round lesions.
Sarah Newbury, the first reported patient with multiple myeloma

“The bones had a red grumous matter
(Thick and lumpy, as clotting blood) 

Kyle R A, Rajkumar S V Blood 2008;111:2962-2972
### Premalignant condition

**MGUS**

(Monoclonal Gamopathy of Undetermined Significance)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Asymptomatic</th>
<th>Asymptomatic</th>
<th>Symptomatic (~89%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active treatment</td>
<td>No</td>
<td>No or clinical trial</td>
<td>Yes</td>
</tr>
<tr>
<td>M-protein (per dL)</td>
<td>&lt;3 g</td>
<td>≥3 g</td>
<td>M-spike or plasmacytoma</td>
</tr>
<tr>
<td>Clonal plasma cells in bone marrow</td>
<td>&lt;10%</td>
<td>≥10%</td>
<td>&gt;10%</td>
</tr>
<tr>
<td>End-organ damage</td>
<td>None</td>
<td>None</td>
<td>1 or more CRAB criteria</td>
</tr>
</tbody>
</table>

| Likelihood of progression | 1% per year | 10% per year for first 5 years; 73% by 15 years | Not Applicable |

### Plasma cell malignancy

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Asymptomatic</th>
<th>Asymptomatic</th>
<th>Symptomatic (~89%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active treatment</td>
<td>No</td>
<td>No or clinical trial</td>
<td>Yes</td>
</tr>
<tr>
<td>M-protein (per dL)</td>
<td>&lt;3 g</td>
<td>≥3 g</td>
<td>M-spike or plasmacytoma</td>
</tr>
<tr>
<td>Clonal plasma cells in bone marrow</td>
<td>&lt;10%</td>
<td>≥10%</td>
<td>&gt;10%</td>
</tr>
<tr>
<td>End-organ damage</td>
<td>None</td>
<td>None</td>
<td>1 or more CRAB criteria</td>
</tr>
</tbody>
</table>

| Likelihood of progression | 1% per year | 10% per year for first 5 years; 73% by 15 years | Not Applicable |

---

High Risk Smoldering Myeloma
Now Considered as Myeloma

Any one or more of the following biomarkers of malignancy:
- Clonal bone marrow plasma cell percentage $\geq 60$
- Involved/uninvolved serum free light chain ratio $\leq 100$
- $> 1$ focal lesions on MRI studies

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>2-year probability of progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>High levels of circulating plasma cells</td>
<td>80% $^{10}$</td>
</tr>
<tr>
<td>Abnormal plasma cell immunophenotype $\geq 95%$ plus immunopa resized</td>
<td>50% $^{10,13,14,15}$</td>
</tr>
<tr>
<td>Evolution of smouldering multiple myeloma $^*$</td>
<td>65% $^8$</td>
</tr>
<tr>
<td>Cytogenetic subtypes: t (4;14), 1q amp, or del 17p</td>
<td>50% $^{3,15}$</td>
</tr>
<tr>
<td>High bone marrow plasma cell proliferative rate</td>
<td>80% $^{9}$</td>
</tr>
<tr>
<td>Unexplained decrease in creatinine clearance by $\geq 25%$ accompanied by rise in urinary monoclonal protein or serum free light-chain concentrations</td>
<td>Not known</td>
</tr>
</tbody>
</table>

$^*$ Increase in serum monoclonal protein by $\geq 10\%$ on each of two successive evaluations within a 6-month period.

Table 2: Potential future biomarkers for diagnosis of multiple myeloma

Case I

- 65 year old female, IgG Lambda; ISS Stage III myeloma with T12, L1 vertebral collapse and an M-spike of 3.2 g/dl; Beta 2 Microglobulin 6.2 ng/ml; Fair performance status, Marrow clonal plasmacytosis 60%. Translocation (4:14)
- Treated with triplet therapy with an imid, a proteasome inhibitor and dexamethasone for 2 cycles.
- M-spike was 0.2 g/dl, Serum Immunofixation IgG lambda, Marrow 5% clonal plasma cells
### What is her Disease Status?

- CR
- sCR
- VGPR
- iCR
- mCR

<table>
<thead>
<tr>
<th>Response</th>
<th>IMWG criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCR</td>
<td>CR as defined below plus normal FLC ratio and absence of clonal cells in bone marrow(^3) by immunohistochemistry or immunofluorescence(^4)</td>
</tr>
<tr>
<td>CR</td>
<td>Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and (&lt; 5%) plasma cells in bone marrow(^3)</td>
</tr>
<tr>
<td>VGPR</td>
<td>Serum and urine M-protein detectable by immunofixation but not on electrophoresis or (\geq 90%) reduction in serum M-protein plus urine M-protein level (&lt; 100 \text{ mg/24 h})</td>
</tr>
<tr>
<td>PR</td>
<td>(\geq 50%) reduction of serum M-protein and reduction in 24 hours urinary M-protein by (\geq 90%) or to (&lt; 200 \text{ mg/24 h})</td>
</tr>
</tbody>
</table>

If the serum and urine M-protein are unmeasurable,\(^5\) a \(\geq 50\%\) decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria.

If serum and urine M-protein are not measurable, and serum free light assay is also not measurable, \(\geq 50\%\) reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was \(\geq 50\%\).

In addition to the above listed criteria, if present at baseline, a \(\geq 50\%\) reduction in the size of soft tissue plasmacytomas is also required.
Case 1

- After 4 cycles:
  - M-spike not detectable
  - Serum Immunofixation no paraprotein seen
  - Free Light chain Ratio- kappa/lambda= 0.8 (normal: 0.26-1.65)
  - Marrow no clonal plasma cells

<table>
<thead>
<tr>
<th>Response</th>
<th>IMWG criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCR</td>
<td>CR as defined below plus normal FLC ratio and absence of clonal cells in bone marrow(^3) by immunohistochemistry or immunofluorescence(^4)</td>
</tr>
<tr>
<td>CR</td>
<td>Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and &lt; 5% plasma cells in bone marrow(^1)</td>
</tr>
</tbody>
</table>
| VGPR     | Serum and urine M-protein detectable by immunofixation but not on electrophoresis or  
|          | ≥ 90% reduction in serum M-protein plus urine M-protein level < 100 mg/24 h |  
| PR       | ≥ 50% reduction of serum M-protein and reduction in 24 hours urinary M-protein by ≥90% or to ≤ 200 mg/24 h  
|          | If the serum and urine M-protein are unmeasurable,\(^5\) a ≥ 50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria  
|          | If serum and urine M-protein are not measurable, and serum free light assay is also not measurable, ≥ 50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was ≥ 30%  
|          | In addition to the above listed criteria, if present at baseline, a ≥ 50% reduction in the size of soft tissue plasmacytomas is also required |
Myeloma: Is There a Cure?

Prognostic value of deep sequencing method for minimal residual disease detection in multiple myeloma

MRD Negativity Cure in Myeloma?
But How Do We Get There?

Stages of myeloma treatment

- Induction
- Consolidation
- Maintenance

SCT eligible

SCT ineligible

Diagnosis & Risk Stratification

Induction followed by continuous therapy

Tumor Burden
Curing Multiple Myeloma (MM) with Total Therapy (TT)

Bart Barlogie, Alan Mitchell, Frits van Rhee, Joshua Epstein, Shmuel Yaccoby, Maurizio Zangari, Christoph Heuck, Antje Hoering, Gareth Morgan and John Crowley

Myeloma Institute for Research and Therapy, University of Arkansas for Medical Sciences, Little Rock, AR; Cancer Research And Biostatistics, Seattle, WA

Beyond Perspectives article:
Curing myeloma at last: defining criteria and providing the evidence. Blood 2014; 124:3043-3051

Abstract 195; Sunday, December 7, 2014: 4:30 PM-6:00 PM

TT3 : VTD – tandem ASCT – VTD – VTD/TD

Usmani et al; Leukemia 2013
Usmani et al; Leukemia 2013

Relative Survival ratio

Usmani et al; Leukemia 2013
So How About Our Patient?

65 year old female with IgG Kappa Myeloma, ISS Stage III, High cytogenetic risk in sCR after 4 cycles of Triplet therapy

Does she need transplant now or later?

Early Myeloablative Therapy in Autologous BM Transplant Patients

IFM 901

MRC72

1. Adapted with permission from Alcal M et al. N Engl J Med. 1996;335:91
Autologous Transplantation and Maintenance Therapy in Multiple Myeloma


Treatment schedule

- 402 patients (younger than 65 years) randomized from 62 centers
- Patients: Symptomatic disease, organ damage, measurable disease

*Randomisation (2x2 design)

Rd
four 28-day courses

MPR
six 28-day courses

MPR
six 28-day courses

MEL 200
Two courses*

MEL 200
Two courses*

R MAINTENANCE
28-day courses until PD

NO MAINTENANCE

R MAINTENANCE
28-day courses until PD

NO MAINTENANCE

* MPR vs MEL 200; R maintenance vs no maintenance; Anti-thrombotic substudy: Aspirin vs Low molecular weight heparin
Rd (R: 25 mg, days 1-21; d: 40 mg, days 1, 8, 15, 22); MPR (M: 0.18 mg/kg/d, days 1-4; P: 2 mg/kg/d, days 1-4; R: 25 mg, d 1-21); MEL 200 (M: 200 mg/m², days 2-21; R: maint (R: 10 mg/day, days 1-21); # One course MEL 200 if patients achieves VSPR after cycle 1
R: lenalidomide; MEL200: melphalan 200 mg/m² and autologous stem cell transplant; MPR: melphalan-prednisone-lenalidomide; NDMM: newly diagnosed multiple myeloma.
From start of consolidation (Mel 200 or MPR)

Probability of 4-Y. Overall Survival

Hazard ratio for death with high-dose melphalan, 0.55 (95% CI, 0.32–0.93); P=0.02

Early-vs-Late SCT Study?

Optimal induction regimen

COLLECT HD THERAPY + SCT

Maintenance

HARVEST AND HOLD SCT UPON RELAPSE

Risk profile
MAG 90
High dose therapy (HDT): front-line or as rescue treatment?

Early versus delayed autologous transplantation after immunomodulatory agents-based induction therapy in patients with newly diagnosed multiple myeloma

Cancer Volume 118, issue 6; pages 1585-1592, 25 AUG 2011 DOI: 10.1002/cncr.26422

Preliminary (randomized) data favor early ASCT plus novel agents over novel agents alone.

**Lenalidomide + Low- or High-Dose Dex ECOG E4A03**

- **Newly Diagnosed Multiple Myeloma**
  - N = 445

- **Lenalidomide**
  - High-Dose Dexamethasone (LD)
  - Low-Dose Dexamethasone (Ld)

- **Primary Endpoint**
  - Response at 4 months

ECOG E4A03

Progression Free Survival

Overall Survival

Courtesy Dr Siegel (ASH 2010)

Early ASCT: risk of death TRM < 2%
Delaying ASCT: Feasibility?

- Risk of resistant relapse
- Renal impairment
- PS
- Comorbidity

→ Early ASCT: feasible 90%
→ Delayed ASCT: <70%!!

Cost-effectiveness analysis of early vs. late autologous stem cell transplantation in multiple myeloma


Results: The Consumer Price Index adjusted 2012 costs of eASCT and dASCT were $249 236 and $262 610, respectively. eASCT cohort had a benefit of 1.96 quality-adjusted life years (QALYs), 0.23 QALYs more than dASCT, implying that eASCT is preferred (dominant) over dASCT. The most critical variables in one-way sensitivity analysis were treatment-related mortality and OS associated with eASCT strategy.
Ongoing Studies

• EMN
• BMT-CTN 1304 (IFMDFCI Study)

Blood and Marrow Transplant Clinical Trials Network State of the Science Symposium
All Transplant-Eligible Patients With Myeloma Should Receive Autologous Stem Cell Transplant in First Response?

**YES**
Our Patient...
What if?

• Initial M spike 3.2 g/dl; Bone Marrow Plasma Cells 60%; IgG Kappa

• After 4 cycles of Triplet therapy: M spike 2.8 g/dl; Marrow plasma cells 50%; IgG Kappa

<PR

< PR or Minimal Response after Induction

• Different Triplet:
  – Cy,Bor, Dex
  – Carfilzomib, Pom, Dex
  – Carfilzomib, Rev, Dex
  – Carfilzomib, Cy, Dex
  – VDR-pace

Or, Proceed with Transplant?
Impact of Depth of Disease Response Before Autologous Stem Cell Transplantation

- CIBMTR 1995-2010
- ASCT within 12 months of Dx & suboptimal response (≤PR)
- N=539 (324 Salvage Rx)
- Response to Salvage: 60% PR 8% CR

Vij et al. BBMT 2014

Outcomes with/without Pre-AHCT Salvage

(Source: Txz12_23 & _24) MM06-04-12_15.ppt

P = 0.3470

P = 0.2622
Impact of Pre-transplant Therapy and Depth of Disease Response before Autologous Transplantation for Multiple Myeloma

- No difference in OS between salvage and no salvage groups even when OS limited to patients who got Bz or Len as first line therapy (39%)
- CONCLUSION: PATIENTS WITH LESS THAN PR AFTER one line of induction have an inferior survival to those with CR/PR but can still move on to SCT and derive comparable benefit to those who undergo salvage


How About Tandem Transplant?
**Single vs Double ASCT for Newly Diagnosed MM**

<table>
<thead>
<tr>
<th>Study</th>
<th>ASCT</th>
<th>n</th>
<th>CR (%) / CR (%)*</th>
<th>Median EFS (mo)</th>
<th>Median OS (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attal et al1</td>
<td>Single</td>
<td>199</td>
<td>42†</td>
<td>25</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>Double</td>
<td>200</td>
<td>50†</td>
<td>30</td>
<td>58</td>
</tr>
<tr>
<td>Fermand et al2</td>
<td>Single</td>
<td>94</td>
<td>42‡</td>
<td>No difference</td>
<td>No difference</td>
</tr>
<tr>
<td></td>
<td>Double</td>
<td>99</td>
<td>37‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sonneveld et al3</td>
<td>Single</td>
<td>148</td>
<td>13</td>
<td>21</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>Double</td>
<td>155</td>
<td>32</td>
<td>22</td>
<td>50</td>
</tr>
<tr>
<td>Cavo et al4</td>
<td>Single</td>
<td>163</td>
<td>33§</td>
<td>23</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Double</td>
<td>158</td>
<td>47§</td>
<td>35</td>
<td>25</td>
</tr>
</tbody>
</table>

Prognostic indicators: β2M; del 13; 1 p/q del

*ITT analysis
†CR + VGPR; NS by ITT
‡CR + minimum residual disease; NS
§CR + nCR


**OS According to Presence/Absence of VGPR at First ASCT**

A. Very Good Partial Response After First Transplantation

B. Absence of Very Good Partial Response After First Transplantation

BMT CTN 0702: 750 patients in record time

Register and Randomize → MEL 200mg/m² → Lenalidomide Maintenance

VRD x 4* → MEL 200mg/m² → Lenalidomide Maintenance**

* Bortezomib 1.3mg/m² days 1, 4, 8, 11
Lenalidomide 15mg days 1-15
Dexamethasone 40mg days 1, 8, 15

**Lenalidomide 15 mg daily x 3 years

Role of maintenance therapy in myeloma
Stages of myeloma treatment

SCT eligible
Diagnosis & Risk Stratification
Induction → Consolidation → Maintenance

SCT ineligible
Induction followed by continuous therapy

Tumor Burden

Phase 3 IFM 2005-02: Lenalidomide as Consolidation/Maintenance Post-ASCT

N=614
First-line ASCT <65 years
≤6 months No PD

Consolidation
Lenalidomide: 25 mg/d Days 1–21/month 2 months
Lenalidomide: 25 mg/d Days 1–21/month 2 months
Lenalidomide: 10–15 mg/d until relapse
Placebo until relapse

Primary end point: PFS

### PFS According to Response Preconsolidation

**PR or SD**
- HR = 0.37 - CI 95% [0.25–0.58]
- P<10^-5

**VGPR or CR**
- HR = 0.54 - CI 95% [0.37–0.78]
- P=0.001


### CALGB 100104 Schema

**Registration**
- D-S Stage 1-3, ≤ 70 years ≥ 2 cycles of induction
- Attained SD or better ≤ 1 year from start of therapy
- ≥ 2 x 10^6 CD34 cells/kg

**Restaging**
- Days 90–100

**Randomization**
- CR
- PR
- SD
- Placebo

- Mel 200 ASCT
- Lenalidomide* 10 mg/d with ↑↓ (5–15 mg)

[NCI-CC University of Kansas Cancer Center]
R maintenance vs No maintenance

Progression-free survival
48% reduced risk of progression

Median PFS
R maint. 37 months
No maint. 26 months

Overall survival
38% reduced risk of death

5-year OS
R maint. 75%
No maint. 58%

HR 0.52, 95% CI 0.40-0.67, P < .0001

HR 0.62, 95% CI 0.42-0.93, P = .02

Future Maintenance Trials
with or without Transplantation
**EMN 02 Treatment Schedule**

- **1570** patients (younger than 65 years) randomized from 12 countries
- Patients: Symptomatic disease, organ damage, measurable disease

### 1st Randomization

**VMP**
- Four 42-day courses
  - V: 1.3g/sqm, d 1,4,8,11
  - M: 9 mg/sqm, d 1-4
  - P: 90 mg/sqm, d 1-4

**MEL 200**
- One course
  - M: 200 mg/m² day -2
  - Stem cell support day 0

**MEL 200**
- Two courses
  - M: 200 mg/m² day -2
  - Stem cell support day 0

### 2nd Randomization

**MAINTENANCE**
- 28-day courses until relapse
  - R: 10 mg/day, days 1-21

**CONSOLIDATION**
- Two 28-day courses
  - V: 1.3 mg/sqm d 1,4,8,11
  - R: 25 mg/day, d 1-21
  - D: 40 mg, d 1,4,8,11

**MAINTENANCE**
- 28-day course until relapse
  - R: 10 mg/day, days 1-21

**VCD**
- Three 21-day courses
  - V: 1.3g/sqm, d 1,4,8,11
  - C: 500 mg/sqm, d 1,8
  - D: 40 mg, d 1,4,8,11

### Myeloma XI – Trial Design

http://www.controlled-trials.com/ISRCTN49457852/myeloma+XI

**Intensive**

**Randomise**

- **CTD**
  - Assess response
    - PD + NC
  - CR + VGPR
  - PR + MR

- **CRD**

**Assess response**

- **CVD**
  - Randomise
    - Nothing
  - CVD
  - Assess response
  - High dose Melphalan + ASCT
  - Lenalidomide versus Placebo

Slide courtesy F Davies

Abbreviations: CTD Cyclophosphamide (500mg p.o. D 1-8,15) Thalidomide (100-200mg p.o. daily) Dexamethasone (40mg p.o. D1-4, 12-15), CTDx Cyclophosphamide (500mg p.o. D1,8,15, 22) Thalidomide (100-200mg p.o. daily) Dexamethasone (40mg p.o. D1-4, 12-15), CRD Cyclophosphamide (500mg p.o. D1-8) Lenalidomide (25mg p.o. daily) Dexamethasone (40mg p.o. D1-4, 12-15), CRDx Cyclophosphamide (500mg p.o. D1,8) Lenalidomide (25mg p.o. daily) Dexamethasone (20mg p.o. D1-4, 12-15), CVD Cyclophosphamide (500mg p.o. D1,8,15) Bortezomib (1.3mg/m² i.v. D 1,4,8,11) Dexamethasone (20mg p.o. D1-2, 4-5, 6-9, 11-12) Melphalan (200mg/m²) ASCT Autologous stem cell transplant.
Patients with positive MRD will continue with LEN/DEX for 3 more years.

* Induction:
  - VRDx6

* Consolidation:
  - VRDcon x 2

* Maintenance:
  - LEN/DEX x 2 yrs*.
  - LEN/DEX + MLN9708 x 2 yrs*

* Patients with positive MRD will continue with LEN/DEX for 3 more years.

** Daratumumab trial in transplant eligible NDMM Hovon/IFM **

- **Induction**: 4 cycles
  - VTD + Dara

- **Consolidation**: 2 cycles
  - VTD + Dara

- **Maintenance Until progression**
  - Dara
  - Observation

Endpoints:
- sCR
- PFS, OS

**Courtesy P Sonneveld**
Alliance Len +/- Daratumumab post ASCT for NDMM

Pre-registration
Mel 200 + ASCT

Restaging
Days 90–100

CR, PR or SD
Registration/Randomization

Lenalidomide

Daratumumab + Lenalidomide

Progression
Off Study

Progression

Daratumumab + Lenalidomide

Extended Follow-up

Progression

Extended Follow-up

When Do We Consider Allogeneic Transplantation In Multiple Myeloma?
Tandem AutHCT with or without Maintenance Therapy (auto-auto) versus Single AuHCT Followed by HLA Matched Sibling Non-Myeloablative Allogeneic HCT (auto-allo) for Patients with Multiple Myeloma: Results from the BMT-CTN 0102 Trial


On behalf of the Blood and Marrow Transplant Clinical Trials Network

Diagram:
1st Autologous Transplant N=710
- No Sibling Donor
  - Auto-Auto N=484
  - Standard Risk N=436
  - High Risk N=48
- Sibling Donor
  - Auto-Allo N=226
  - Standard Risk N=189
  - High Risk N=37

Groups being compared
BMT-CTN 0102 Trial: Outcomes of Patients With Standard-Risk and High-Risk Multiple Myeloma

<table>
<thead>
<tr>
<th>3-Year Outcomes After First Transplantation</th>
<th>Standard Risk</th>
<th>High Risk</th>
<th>P Value</th>
<th>Standard Risk</th>
<th>High Risk</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tandem ASCT (n = 436)</td>
<td>ASCT→AlloHSCT (n = 189)</td>
<td></td>
<td></td>
<td>Tandem ASCT (n = 48)</td>
<td>ASCT→AlloHSCT (n = 37)</td>
<td></td>
</tr>
<tr>
<td>Progression-Free Survival</td>
<td>46%</td>
<td>43%</td>
<td>.67</td>
<td>33%</td>
<td>40%</td>
<td>NS</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>80%</td>
<td>77%</td>
<td>.19</td>
<td>67%</td>
<td>59%</td>
<td>NS</td>
</tr>
<tr>
<td>Treatment-Related Mortality</td>
<td>4%</td>
<td>12%</td>
<td>&lt;.001</td>
<td>11%</td>
<td>24%</td>
<td>NS</td>
</tr>
</tbody>
</table>

- Maintenance therapy with thalidomide/dexamethasone following tandem ASCT in patients with standard-risk and high-risk MM yielded no benefit in PFS or OS.
- Discontinuation rate of thalidomide/dexamethasone by day 365:
  - Standard risk: 84%
  - High risk: 75%

Survival Outcomes of Auto-Auto vs. Auto-Allo after the First Autologous Transplant: Combined Standard and High Risk Cohorts (710 pts)

- **Progression-Free Survival**
  - Auto/Auto (n=484), 45% @ 3yr
  - Auto/Allo (n=226), 42% @ 3yr
  - P-value = NS

- **Overall Survival**
  - Auto/Allo (n=226), 75% @ 3yr
  - Auto/Auto (n=484), 79% @ 3yr
  - P-value = NS

Krishnan et al. ASH 2010; abstract 41; Stadtmauer et al. ASH 2010; abstract 526.
What is Coming Next?

High Risk or Relapsing MM Patients
Investigational Allografting

FLUMELVEL Conditioning
Allo SCT

Placebo X 12 months
Maintenance Ixazomib x 12 months
CTN 1401 Randomized Trial of Post-transplant Vaccination with DC/Myeloma Fusions + Lenalidomide Maintenance vs. Lenalidomide Maintenance Alone

David Avigan, MD, PI
Nina Shah, Co-PI
Study Schema

- Accrual targets 188 patients to be enrolled with a target of 132 patients to be randomized
- Assuming about 30% of patients are unable to proceed with post-transplant immunotherapy.
  - Arm A: Maintenance lenalidomide + vaccine + GM-CSF (n=66)
  - Arm B: Maintenance lenalidomide + GM CSF (n=33)
  - Arm C: Maintenance lenalidomide alone (n=33)
- Patients will be stratified according to disease status at time of randomization between CR and sCR and VGPR/PR/Stable disease.
Multiple Myeloma: Treatment History

**History**

- **1950's**: First documented case of multiple myeloma.
- **1955**: Abnormal urine protein, later termed Bence Jones protein.
- **1960's**: First large case series of myeloma.
- **1965**: Serum protein spike identified.
- **1968**: Light chain types (kappa and lambda) recognized.
- **1975**: Durie-Salmon staging system.
- **1980's to Today**: Cytogenetic classification.
- **2012**: Carfilzomib.
- **2013**: Pomalidomide.
- **2015**: Panobinostat.

**Treatment**

- **1950's**: Urethane (N. Alwell).
- **1960's**: Melphalan (N. Bickham).
- **2000's**: Thalidomide (S. Singhal and B. Barlogie).
- **2002**: Bortezomib (R. Z. Offit).
- **2005**: Lenalidomide (P. G. Richardson and K. C. Anderson).

**Chromosome 4**

- **1950's**: Huntington disease.
- **1960's**: Widespread studies.
- **1980's to Today**: The Future?
Acknowledgement

• BMT CTN Group
• Amrita Krishnan, City of Hope, CA
• David Avigan, BIDMC, Harvard, Boston
• Phil McCarthy, Buffalo, NY, CALGB
• David Vesole, MD-Hackensack Univ, NJ
• P. Hari, MD- CIBMTR, Medical College of Wisconsin
• Shaji Kumar, Mayo Clinic, Rochester, MN