The emperor is naked:

The quality of response to first-line therapy is not related to survival in multiple myeloma (MM) patients.

CR rates of long term survivors are predictable by their ISS staging at diagnosis, rather than being a predictor of their survival.
The relation between overall survival time (OS) and response level was analyzed in 432 MM patients from 4 prospective Finnish Leukaemia group trials, treated with conventional chemotherapy. The primary regimen was either melphalan and prednisolone or combination chemotherapy with melphalan as a main component. The 324 patients aged up to 70 yr and the 10(8) older patients were dealt with as separate groups.

Irrespective of the primary chemotherapy regimen, the level of response was not significantly influencing in the OS time, and this was true in both age categories. The pretreatment prognosticators for the patients with minimal responses were not more favorable than for patients with responses at higher levels.

Accordingly, the primary goal of conventional chemotherapy for multiple myeloma is stabilization of disease, not the level of response.
Conclusion The depth of the response in myeloma does not necessarily lead to an improvement in TTP and OS. Tumor dynamics considerations show that the yield from sequential cycles of chemotherapy is minimal.

(A) time to progression
(B) overall survival for patients with complete response:

Before (continuous line)
After (dotted line)

High-dose therapy with autologous stem-cell transplantation.

There was no statistical difference between the two groups for either end point.
In newly diagnosed MM patients: a prospective, multicenter phase 3 study

Kumar A¹, Kharfan-Dabaja MA, Glasmacher A, Djulbegovic B. Moffitt Cancer Center, Tampa, FL, USA

Conclusion
In previously untreated MM patients, use of tandem AHCT did not result in improved OS or EFS.
P = .19

We conclude that tandem AHCT is associated with improved response rates but at risk of clinically significant increase in TRM.
Results from two phase III studies of bortezomib (BTZ) consolidation vs observation (OBS) post-transplant in patients (pts) with newly diagnosed multiple myeloma (NDMM)

Christian Straka, Martin Vogel, Hermann Einsele; Schön Klinik Starnberger See, Berg, Germany

Asco 2015 Abstract

**Methods:** 60-120 days after ASCT, Pts were randomized 1:1 to receive BTZ consolidation (1.6 mg/m² days 1, 8, 15, 22; 4 x 35-day cycles) for 7 month, or OBS.

**Conclusions:** A higher proportion of pts had a response of ≥ VGPR after BTZ consolidation than OBS. PFS was significantly improved by ~6 mos, but there was no improvement in OS.

* The name of the game: Is the depth of response related with survival


S Lonial and K C Anderson

* Quality of response alone is not a validated surrogate marker of overall survival (OS).

* There are currently no definitive data to validate the association between quality of response and survival outcomes.

Moreover, the association of depth of response with outcomes is not universal across studies. Biologically, MM is a spectrum of diseases and its course and response to therapy can be highly variable.
Cause Effect Relationship between the depth of response, and survival:

In Hematological malignancies

* **CML** - Quantitative Molecular Response predicts survival
* **AML** - Molecular Genetics predicts.
* **NHL** - CR All or None

Significance in MM

Clinical

* Intensity, Duration, Generation an combination of therapy: Burden.
* QOL and Anxiety.
* Exhaustion of lines of therapy, “The Sand Watch” Phenomenon.

Resources

* Cost of Specific, Palliative and Complication therapy.
* Cost of the investigation and application of MRD studies.
Observation:
40%-60% of Long Term MM Survivors, achieves CR on the way, compared with 20% in the whole MM population

Is the achievement of CR related with the Long Term Survival?

AS AML
**Materials and Methods**

**Long Term OS by ISS (b2MG + albumin)**

**Actual No. Of Remissions**

**Expected No. Of Remissions**

**ISS**

A $< 65 \text{ y.o}$  B $> 65 \text{ y.o}$

**Graphs**

- A: Median duration of remission
  - A stage I: 34 months
  - A stage II: 24 months
  - A stage III: 12 months

- B: Median survival time
  - B stage I: 14 months
  - B stage II: 18 months
  - B stage III: 24 months

**Table**

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<thead>
<tr>
<th>Stage</th>
<th>Expected No.</th>
<th>Actual No.</th>
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<tbody>
<tr>
<td>I</td>
<td>RR</td>
<td>RR</td>
</tr>
<tr>
<td>II</td>
<td>RR</td>
<td>RR</td>
</tr>
<tr>
<td>III</td>
<td>RR</td>
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Prediction of CR rates according to ISS

VISTA - (337 pt’s) and IMF 99-02 + 99-04 (761 pt’s)

<table>
<thead>
<tr>
<th>ISS</th>
<th>Expected No. of Remissions</th>
<th>Actual No. of Remissions</th>
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<tbody>
<tr>
<td>I</td>
<td>28%</td>
<td>N = 61</td>
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<tr>
<td>II</td>
<td>44%</td>
<td></td>
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<tr>
<td>III</td>
<td>30%</td>
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Demographics and clinical data

n = 61

Age (median) - 64y

Survival time from diagnosis
73 m (61-156)

ISS:
I - 16  II - 27  III - 18

Expected No. of Remissions

Actual No. of Remissions
Conclusions

• The CR rate of long term MM survivors is similar to the CR rate that was predicted for the group based upon ISS risk stratification.

• This suggests that the high CR rate observed in long term survivors is due to their favorable nature of disease, rather than being the cause of prolonged survival.

• This data strengthens the observation that there is no cause/effect relationship between the depth of response and survival, in newly diagnosed MM patients.

• Identification of novel targets for therapy, rather than the achievement of CR, is required.
הטיפול בחולי המיאלומה

372 שנות טיפול במשך 13 שנים

קומנדו חילוץ והצלה
שיקום טראומה ופוסט טראומה

צביקה אילה
שרית יהודה
פרופ' לישנר עפרה
לובנה רוזה ד"ר אליס

תודה מחולי המיאלומה

יעל אינבינדר ד"ר לייטנר
פרופ' גריטון
נסים יפרח
מירה מרם
רמי דוד
دورון נצר
טטיאנה ברלין
יורם נוימן
רינה שראלי
בעז ליברמן
פרופ' ארד