Best of ASH: What are the takeaways?
Thursday, January 10, 2019
Los Angeles, CA
• 939 myeloma abstracts at ASH 2018!

• Massive number of orals and posters on CAR T and related immunotherapy

• Many important novel therapy updates

• Interesting abstracts on molecular and biology topics
Today’s Topics

- **B**ispecific **T**-cell **E**ngangers (BiTEs)
- CAR T Cells
- Frontline Therapy
- Maintenance
- Blood Monitoring
- MRD in Relapse
Impact of a Bispecific Antibody (BiTE)

Abstract #1010

Secretions attacking myeloma
Something New: BiTEs!

- BCMA BiTE: Abstract #1010 AMG 420 BiTE: Phase 1 dose escalation

Impact of higher doses

Abstract #1010

*MTD = maximum tolerated dose
AMG 420, an Anti-BCMA BiTE®, Induces MRD-Negative CRs in Relapsed/Refractory MM Patients: Results of a Dose Escalation FIH Phase 1 Study

Max S Topp,1 Johannes Duell,1 Gerhard Zugmaier,2 Michel Attal,3 Philippe Moreau,4 Christian Langer,5 Jan Krönke,6 Thierry Facon,7 Hermann Einsele,1* Gerd Munzert8*

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7Regional University Hospital of Lille, Lille, France, 8Boehringer Ingelheim, Ingelheim am Rhein, Germany

*Contributed equally
Preliminary Conclusions

This is encouraging!

What is the future for BiTEs versus CAR T therapies?

Resources to help understand BiTEs:

Ask Dr. Durie video explaining What are Bispecific Antibodies (BiTES)
Draw to Science Animation on Bispecific Antibodies
More Detail on CAR T Therapies

- So many abstracts!
  - **Abstract #955:** follow up Legend (China) trial results
  - **Abstract #1011:** a fully humanized CAR T therapy
  - **Abstract #591:** an allo CAR T therapy (“off the shelf”)
  - **Abstract #1014:** a multi-antigen approach
  - **Abstract #589:** novel GPRC5D target
  - **Abstract #488:** bb21217, a next generation anti-BCMA CAR T (longer-lived “memory” T cells)
  - ... And many, many more, such as with an EGFR safety switch to reduce/eliminate CRS!!
Abstract #955: Legend-2 Anti-BCMA CAR T

Updated Analysis of a Phase 1, Open-Label Study of LCAR-B38M, a Chimeric Antigen Receptor T Cell Therapy Directed Against B-Cell Maturation Antigen, in Patients with Relapsed/Refractory Multiple Myeloma

Wan-Hong Zhao,1 Jie Liu,1 Bai-Yan Wang,1 Yin-Xia Chen,1 Xing-Mei Cao,1 Yun Yang,1 Yi-Lin Zhang,1 Fang-Xia Wang,1 Peng-Yu Zhang,1 Bo Lei,1 Liu-Fang Gu,1 Jian-Li Wang,1 Nan Yang,1 Ru Zhang,1 Hui Zhang,1 Ying Shen,1 Ju Bai,1 Yan Xu,1 Xu-Geng Wang,1 Rui-Li Zhang,1 Li-Li Wei,1 Zong-Fang Li,2 Zhen-Zhen Li,2 Yan Geng,3 Qian He,3 Qiu-Chuan Zhuang,4 Xiao-Hu Fan,4 Ai-Li He,1,2 Wang-Gang Zhang1

1Department of Hematology, The Second Affiliated Hospital of Xi’an Jiaotong University, Xi’an, ShaanXi, China; 2National-Local Joint Engineering Research Center of Biodiagnostics & Biotherapy, The Second Affiliated Hospital of Xi’an Jiaotong University, Xi’an, ShaanXi, China; 3Department of Clinical Laboratory, The Second Affiliated Hospital of Xi’an Jiaotong University, Xi’an, ShaanXi, China; 4Nanjing Legend Biotech Inc., Nanjing, Jiangsu, China
LCAR-B38M is a chimeric antigen receptor (CAR) T cell therapy with 2 BCMA targeting domains.
- Confers high avidity binding and distinguishes LCAR-B38M from other BCMA-targeted CAR T cell therapies.

**LEGEND-2: Phase 1 investigator-initiated study in R/R multiple myeloma (MM) conducted at 4 sites in China**
- Variable preconditioning regimens (Cy-Flu vs. Cy)
- Variable CAR T infusion methods (split vs. single infusion)

**LEGEND-2 results previously presented**
- First 35 patients at the Xi’an site at ASCO and EHA 2017
- First 11 patients at the 3 other sites at ASH 2017

**57-patient experience at Xi’an site as of 25 June 2018 is presented here, with a 12-month (0.7–25.1) follow-up**
**Best Responses**

**Best Overall Response (N=57)**

- CR: 42 (74%) ORR = 88%
- VGPR: 2 (3%)
- PR: 6 (11%)
- SD: 4 (7%)
- PD: 1 (2%)
- NE: 2 (3%)

- mDOR = 16 mo (95% CI, 12–NR)
- mDOR for MRD-neg CR = 22 mo (95% CI, 14–NR)
- Median time to initial response = 1 mo (0.4–3.6)

**Best Overall Response by Dose**

<table>
<thead>
<tr>
<th>Dose</th>
<th>CR</th>
<th>VGPR</th>
<th>PR</th>
<th>SD</th>
<th>PD</th>
<th>NE</th>
<th>All Doses</th>
<th>&lt;0.5x10^6 cells/kg</th>
<th>≥0.5x10^6 cells/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=57</td>
<td>39 (68%)</td>
<td>2 (3%)</td>
<td>6 (11%)</td>
<td>4 (7%)</td>
<td>1 (2%)</td>
<td>2 (3%)</td>
<td>100%</td>
<td>90%</td>
<td>70%</td>
</tr>
<tr>
<td>n=25</td>
<td>2 (3%)</td>
<td>4 (7%)</td>
<td>2 (3%)</td>
<td>1 (2%)</td>
<td>4 (7%)</td>
<td>1 (2%)</td>
<td>100%</td>
<td>90%</td>
<td>80%</td>
</tr>
<tr>
<td>n=32</td>
<td>2 (3%)</td>
<td>4 (7%)</td>
<td>1 (2%)</td>
<td>2 (3%)</td>
<td>3 (5%)</td>
<td>2 (3%)</td>
<td>100%</td>
<td>90%</td>
<td>80%</td>
</tr>
</tbody>
</table>

- ORR: Overall Response Rate
- CR: Complete Response
- VGPR: Very Good Partial Response
- PR: Partial Response
- SD: Stable Disease
- PD: Progressive Disease
- NE: Not Evaluable

- BCMA <40% (n=26/53)b = 92% ORR
- BCMA ≥40% (n=27/53)b = 82% ORR

a8-color flow cytometry with cell count up to 500,000 cells; bBCMA expression data available for 53 patients

**Abstract #955**
Progression Free Survival

Patients at risk:

- All Patients: 57, 53, 48, 37, 21, 11, 7, 4, 1, 0
- Patients Achieving MRD-neg CR: 39, 39, 38, 33, 20, 10, 7, 4, 1, 0
- Patients Not Achieving MRD-neg CR: 18, 14, 10, 4, 1, 1, 0, 0, 0, 0

Patients Achieving MRD-neg CR
- mPFS: 24 mo (95% CI, 15–NR)
- 12-mo PFS: 87%

Patients Not Achieving MRD-neg CR
- mPFS: 6 mo (95% CI, 3–8)
- 12-mo PFS: 6%

All Patients
- mPFS: 15 mo (95% CI, 11–NR)
- 12-mo PFS: 61%

*30/39 patients still in remission
Overall Survival

Overall Survival (%)

0 3 6 9 12 15 18 21 24 27
Months

Patients Achieving MRD-neg CR
mOS: not reached
12-mo survival: 94%

Patients Not Achieving MRD-neg CR
mOS: 8 mo (95% CI, 4–14)
12-mo survival: 29%

All Patients
mOS: not reached
12-mo survival: 75%

Patients at risk:

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>15</th>
<th>18</th>
<th>21</th>
<th>24</th>
<th>27</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>57</td>
<td>55</td>
<td>51</td>
<td>40</td>
<td>25</td>
<td>15</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Patients Achieving MRD-neg CR</td>
<td>39</td>
<td>39</td>
<td>39</td>
<td>34</td>
<td>21</td>
<td>13</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Patients Not Achieving MRD-neg CR</td>
<td>18</td>
<td>16</td>
<td>12</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

Abstract #955
PFS with BCMA (bb2121) CAR T: ASCO 2018

PFS at Inactive ($50 \times 10^6$) and Active ($150–800 \times 10^6$) Dose Levels

- mPFS for $50 \times 10^6$ (n=3): 2.7 months (95% CI: 1.0–2.9 months)
- mPFS for $150–800 \times 10^6$ (n=18): 11.8 months (95% CI: 8.8–NE months)

mPFS = 11.8 mo

Patients at risk, n
- $50 \times 10^6$: 3 3 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
- $\geq 150 \times 10^6$: 18 18 17 17 17 14 14 11 11 10 6 5 5 4 3 3 2 2 2 0
Lead candidates
• bb2121 ASCO 2018
• Legend ASH 2018

+ multiple new alternatives

• What does the future hold?
• Will there be approvals?
• SWOG 0777 Updates: Abstract #1992
• DRd versus Rd: Late Breaking Abstract #2

... + impact of t(11;14) in frontline setting: Abstract #3282
### Updated Response Results*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>VRd (n=215)</th>
<th>Rd (n=207)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response (CR)</td>
<td>24.2% (52)</td>
<td>12.1% (25)</td>
</tr>
<tr>
<td>Very good partial response (VGPR)</td>
<td>50.7% (109)</td>
<td>41.1% (85)</td>
</tr>
<tr>
<td><strong>VGPR or better</strong></td>
<td><strong>74.9%</strong></td>
<td><strong>53.2%</strong></td>
</tr>
<tr>
<td>Partial response (PR)</td>
<td>15.3% (33)</td>
<td>25.6% (53)</td>
</tr>
<tr>
<td><strong>Overall Response Rate (ORR)</strong></td>
<td><strong>90.2% (194)</strong></td>
<td><strong>78.8% (163)</strong></td>
</tr>
<tr>
<td>Stable disease (SD)</td>
<td>7.0% (15)</td>
<td>16.4% (34)</td>
</tr>
<tr>
<td>PD or death</td>
<td>2.8% (6)</td>
<td>4.8% (10)</td>
</tr>
</tbody>
</table>

*Both SWOG and IRC stratified Cochran-Mantel-Haenszel analyses indicated improved responses with VRd (odds ratio = 0.528: P=0.006 [ITT] odds ratio= 0.38: P=0.001 [sensitivity analysis])
SWOG 0777: Progression-Free Survival

- **PFS**
- Events / N: Rd 185 / 225, VRd 167 / 235
- Median in Months: Rd 29 (24, 37), VRd 41 (33, 51)
- *P-value = 0.003*
SWOG 0777: Overall Survival

- VRd: 55% OS at 7 years

*P-value = 0.0114

Deaths / N  | Median in Months
Rd  125 / 225  | 69 (59, 88)
VRd  102 / 235  | NR
**Impact of Age in SWOG 0777 Trial**

**Median PFS (months)**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>VRd</th>
<th>Rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65</td>
<td>48</td>
<td>34</td>
</tr>
<tr>
<td>≥65</td>
<td>34</td>
<td>24</td>
</tr>
<tr>
<td>&gt;75</td>
<td>34</td>
<td>17</td>
</tr>
</tbody>
</table>

*For all analyses, both SWOG and IRC assessments have been conducted using the fully updated datasets with current datalock in May 2018*
Late Breaking Abstract #2

Phase 3 Randomized Study of Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Patients With Newly Diagnosed Multiple Myeloma (NDMM) Ineligible for Transplant (MAIA)*

Thierry Facon,1 Shaji Kumar,2 Torben Plesner,3 Robert Z. Orlowski,4 Philippe Moreau,5 Nizar Bahlis,6 Supratik Basu,7 Hareth Nahi,8 Cyrille Hulin,9 Hang Quach,10 Hartmut GoldeSchmidt,11 Michael O’Dwyer,12 Aurore Perrot,13 Christopher P. Venner,14 Katja Weisel,15 Joseph R. Mace,16 Tahamtan Ahmadi,17 Christopher Chiu,18 Jianping Wang,19 Rian Van Ramplebergh,20 Clarissa M. Uhlar,18 Rachel Kobos,19 Ming Qi,18 Saad Z. Usmani21

1Service des Maladies du Sang, Hôpital Claude Huriez, Lille, France; 2Department of Hematology, Mayo Clinic Rochester, Rochester, MN, USA; 3Vejle Hospital and University of Southern Denmark, Vejle, Denmark; 4Department of Lymphoma-Myeloma, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; 5Hematology, University Hospital Hôtel-Dieu, Nantes, France; 6University of Calgary, Arnie Charbonneau Cancer Institute, Calgary, AB, Canada; 7Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, United Kingdom; 8Karolinska Institute, Department of Medicine, Division of Hematology, Karolinska University Hospital at Huddinge, Stockholm, Sweden; 9Department of Hematology, Hospital Haut Leveque, University Hospital, Pessac, France; 10St. Vincent’s Hospital, University of Melbourne, Melbourne, Australia; 11University Hospital Heidelberg and National Center of Tumor Diseases (NCT), Heidelberg, Germany; 12Dept. of Medicine/Haematology, NUI, Galway, Republic of Ireland; 13Hematology Department, University Hospital, Vandoeuvre Les Nancy, France; 14Division of Medical Oncology University of Alberta, Edmonton, AB, Canada; 15Universitaetsklinikum Tuebingen der Eberhard-Karls-Universitaet, Abteilung fuer Innere Medizin II, Tuebingen, Germany; 16Florida Cancer Specialists & Research Institute, St. Petersburg, FL, USA; 17Genmab US, Inc., Princeton, NJ, USA; 18Janssen Research & Development, Spring House, PA, USA; 19Janssen Research & Development, Raritan, NJ, USA; 20Janssen Research & Development, Beerse, Belgium; 21Levine Cancer Institute/Atrium Health, Charlotte, NC, USA.

*ClinicalTrials.gov Identifier: NCT02252172
Abstract LBA-2: MAIA Overview: Primary Endpoint

- Median follow-up: 28 months
- PFS hazard ratio: 0.56 (95% CI, 0.43 to 0.73; $P < 0.0001$)
- 44% reduction in the risk of progression or death in patients treated with D-Rd
- The median PFS for the Rd arm was 31.9 months and not reached for the D-Rd arm
A total of 19% of patients have died and the HR for OS was 0.78 (95% CI, 0.56 to 1.1).

Higher rates (5% or more difference) of grade 3/4 pneumonia, neutropenia, and leukopenia were observed in the D-Rd arm.

The safety profile is consistent with previously reported DARA studies.

The addition of DARA to Rd in patients with transplant-ineligible NDMM significantly reduced the risk of progression or death by 44%.

There are no new safety signals using DARA plus Rd in NDMM.

These data together with the phase 3 ALCYONE study (D-VMP vs VMP) support the addition of DARA to standard-of-care combinations in patients with NDMM ineligible for transplant.

<table>
<thead>
<tr>
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<th>D-Rd</th>
<th>Rd</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR or better</td>
<td>47.6%</td>
<td>24.9%</td>
</tr>
<tr>
<td></td>
<td>(P &lt; 0.0001)</td>
<td>(P &lt; 0.0001)</td>
</tr>
<tr>
<td>VGPR or better</td>
<td>79.3%</td>
<td>53.1%</td>
</tr>
</tbody>
</table>

Impact of t(11;14) in Frontline Setting

Abstract #3282: Outcomes in 1,000 patients receiving frontline bortezomib/lenalidomide/dexamethasone (VRd)

Figure 2.
What Is the Future for Frontline Therapy?

4 Drug-combinations: Daratumumab added to VRd, KRd (or alternatives VTd/VCd)

3 Drug-combinations: Use of Dara-Rd or Dara-Vd versus VRd?

Or perhaps

• Introduction of venetoclax early for t(11;14)?

• Early introduction of CAR T cells or BiTEs?

• Other?
New Information on Maintenance

• Ixazomib maintenance
• R versus Rd for maintenance
Maintenance Therapy With the Oral Proteasome Inhibitor (PI) Ixazomib Significantly Prolongs Progression-Free Survival (PFS) Following Autologous Stem Cell Transplantation (ASCT) in Patients With Newly Diagnosed Multiple Myeloma (NDMM): Phase 3 TOURMALINE-MM3 Trial

Meletios A. Dimopoulos,¹ Francesca Gay,² Fredrik Schjesvold,³ Meral Bekas,⁴ Roman Hajek,⁵ Katja C. Weisel,⁶ Hartmut Goldschmidt,⁷ Vladimir Maisnar,⁸ Philippe Moreau,⁹ Chang Ki Min,¹⁰ Agnieszka Pluta,¹¹ Wee-Joo Chng,¹²,¹³ Martin Kaiser,¹⁴,¹⁵ Sonja Zweegman,¹⁶ Maria-Victoria Mateos,¹⁷ Andrew Spencer,¹⁸ Shinsuke Iida,¹⁹ Gareth Morgan,²⁰ Zhaoyang Teng,²¹ Kaveri Suryanarayan,²¹ Tomas Skacel,²¹ Antonio Palumbo,²¹,²² Ajeeta B. Dash,²¹ Richard Labotka,²¹ S. Vincent Rajkumar,²³ on behalf of the TOURMALINE-MM3 study group
• There was a significant 39% improvement in overall PFS from time of randomization for patients receiving ixazomib vs. placebo maintenance:
  • HR: 0.72; 95% CI: 0.582–0.890
  • p=0.002
  • Median 26.5 months vs. 21.3 months

• With only 14% of deaths reported, at a median follow-up of 31 months, median OS has not been reached in either treatment arm and follow up continues.

Abstract #355

CI, confidence interval; HR, hazard ratio; OS, overall survival.
Efficacy and Feasibility of Dose/Schedule-Adjusted Rd-R Vs. Continuous Rd in Elderly and Intermediate-Fit Newly Diagnosed Multiple Myeloma (NDMM) Patients: RV-MM-PI-0752 Phase III Randomized Study

Benevolo, 1 Monica Galli, 1 Vittorio Montefusco, 1 Tommaso Caravita di Toritto, 1 Anna Baraldi, 1 Stefano Spada, 1 Nicola Giuliani, 1 Chiara Pautasso, 1 Stefano Pulini, 1 Sonia Ronconi, 1 Norbert Pescosta, 1 Anna Marina Liberati, 1 Francesca Patriarca, 1 Claudia Cellini, 1 Patrizia Tosi, 1 Massimo Offidani, 1 Michele Cavo, 1 Antonio Palumbo, 2 Mario Boccadoro, 1 Sara Bringhen. 1

1 GIMEMA / European Myeloma Network, Italy; 2 University of Torino - Currently Takeda Pharmaceuticals Co.
Clinical trials usually have stringent eligibility criteria and *myeloma patients 75 years or older are an understudied population*. Older patients are susceptible to AEs that may negatively affect duration of treatment and outcome due to increased comorbidities and altered pharmacodynamics.

We designed a trial for elderly INTERMEDIATE-FIT patients (IMWG Frailty SCORE=1) and compared standard continuous Rd vs Rd induction followed by R maintenance.
Rd-R vs Rd: Event-free Survival

**Primary endpoint: Event-free Survival (EFS)**

*Definition of the event*: hematologic grade 4 AEs
- non-hematologic grade 3-4 AEs including SPM
- discontinuation of lenalidomide therapy
- disease progression
- death for any cause

**Median follow-up**: 25 months

**Rd-R vs Rd: HR 0.72; CI 0.52-0.99; p=0.044**

<table>
<thead>
<tr>
<th></th>
<th>Median EFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rd-R</td>
<td>9.3 months</td>
</tr>
<tr>
<td>Rd</td>
<td>6.6 months</td>
</tr>
</tbody>
</table>

Rd-R vs Rd: HR 0.72; CI 0.52-0.99; p=0.044

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**Abstract #355**

R, Lenalidomide; d, dexamethasone; EFS, event-free survival; AEs, adverse events; SPM, second primary malignancy

*related to study drugs*
How do we select maintenance in 2018?
The role of circulating myeloma cells
Transcriptomic Profiling of Circulating Tumor Cells (CTCs) in Multiple Myeloma (MM): A New Model to Understand Disease Dissemination

Circulating myeloma cells can be key drivers to myeloma progression

Plasmacytoma | Circulation | New lesion | Multiple lytic lesions

Abstract #245

Gene expression of CTCs is almost identical to that of patient-matched bone marrow clonal plasma cells... except for a few genes that are involved in interferon and inflammatory response, hypoxia, cell cycle and migration (CD44).

Some of these genes are related to more aggressive disease and modulating their expression may impact migration and adhesion of clonal PCs.
New Options for Blood Monitoring

- Clonal plasma cells using NGF with molecular/immune testing of cells
- M-component using Mass Spec
- DNA/RNA using ctDNA/RNA
Abstract #1912: Mayo Clinic follow up of 2,125 patients at ≥ 10 years
“Cure Fraction” from IMWG Analyses*

Cured fraction: 14.37%
### Key highlights: Characteristics of long survivors

<table>
<thead>
<tr>
<th>Factor</th>
<th>PFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>1.15 (1.04;1.28)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Year of ASCT (1 year increase)</strong></td>
<td>1.01 (0.99;1.03)</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>MM type (reference: IgG)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgA</td>
<td>1.06 (0.84;1.34)</td>
<td>0.61</td>
</tr>
<tr>
<td>IgD</td>
<td>0.70 (0.28;1.72)</td>
<td>0.44</td>
</tr>
<tr>
<td>Bence-Jones</td>
<td>1.05 (0.83;1.33)</td>
<td>0.67</td>
</tr>
<tr>
<td><strong>ISS stage (reference: 1)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.05 (0.84;1.30)</td>
<td>0.69</td>
</tr>
<tr>
<td>3</td>
<td>1.30 (0.98;1.73)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Laboratory values at diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin &lt; 10g/dL</td>
<td>1.09 (0.87;1.37)</td>
<td>0.48</td>
</tr>
<tr>
<td>Thrombocytes &lt; 150,000/µL</td>
<td>1.48 (1.07;2.04)</td>
<td>0.02</td>
</tr>
<tr>
<td>Creatinine ≥ 2mg/dL</td>
<td>0.99 (0.72;1.38)</td>
<td>0.97</td>
</tr>
<tr>
<td>LDH &gt; upper limit of normal</td>
<td>1.11 (0.87;1.43)</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>CR after ASCT (ref. non-CR)</strong></td>
<td>0.69 (0.52;0.93)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Novel agent based induction</strong></td>
<td>0.58 (0.45;0.74)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Tandem ASCT (ref. single)</strong></td>
<td>0.93 (0.75;1.14)</td>
<td>0.46</td>
</tr>
<tr>
<td><strong>Maintenance therapy (time dep.)</strong></td>
<td>0.53 (0.42;0.65)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Achievement of MRD undetected (negative) in the relapse setting

CASTOR and POLLUX follow up
Abstract #3272: MRD in POLLUX and CASTOR trials

DRd vs Rd: MRD negative sustained at 6 months
Importance of MRD Undetected in Relapse

Abstract #3272: MRD in POLLUX and CASTOR trials

DVd vs Vd: MRD negative sustained at 12 months
Should achievement of MRD negative (undetected) status be the goal of therapy in early relapse setting?
Other “Hot Topics”

- venetoclax
- selinexor
- melflufen
Melflufen

- Melflufen is a highly lipophilic alkylating peptide, belonging to the novel class of Peptidase Enhanced Compounds.

- Intracellular amino-peptidases that are overexpressed in most malignant cells, will rapidly cleave melflufen releasing the hydrophilic, active alkylating metabolite.

- In vitro, treatment of tumor cells with melflufen results in 50-fold higher intracellular concentration of alkylating metabolite than those treated with equimolar melphalan alone. In vivo, human xenograft mouse models treated with equimolar melflufen showed prolonged survival.

**Melflufen 40 mg iv every 28 days + Dex 40 mg weekly**

**Phase II O-12-M1 trial**

RRMM pts ≥ 2 lines and refr. to last line.

n=45 4 (2-14) lines; 64% double refr.; 53% Alkylator refr.

ORR 31% .......... 5 VGPR & 9 PR patients
PFS: 5.7m; DOR 8.4m; OS: 20.7m

G3/4 AEs: Thromboc. (58%), Neutrop. (51%), Anemia: 42%

**Blood 2017, 130: 3150**

**Phase II Horizon trial**

RRMM pts ≥ 2 lines and 86% double Ref
n=83 5 (2-13) lines; Alkylator refr. 55%; Pom & Dara Refr: 60%

ORR 33% .......... 1 sCR, 9 VGPR & 17 PR patients
PFS: 4.0m

G3/4 rel. TEAEs: Thromboc. (59%), Neutropenia (61%), Anemia: 25%

**Richardson P. ASH 2018 (Abst 600)**
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