SUPPLEMENT TO CARE™ GUIDANCE ON
MULTIPLE MYELOMA

SUPPORTING TRIAL UPDATES FROM ASH 2020

MARCH 2021
CARE™ Recommendation: Dara-RD for transplant ineligible patients

Supporting Trial Highlights from ASH 2020:

- Updated efficacy and safety findings from MAIA after approximately 4 years of follow-up
- D-Rd demonstrated a significant benefit in PFS, with a 46% reduction in the risk of progression or death
- PFS benefit was generally consistent across subgroups, including patients with high cytogenetic risk (figure 1)
- Longer follow-up demonstrated a significant benefit in PFS2 favoring D-Rd versus Rd alone (figure 2)
- The MRD-negativity rate was significantly higher in the D-Rd group (31% vs 10%; p < 0.0001)
  - D-Rd also achieved sustained MRD-negativity rates of 20% (vs. 5% with Rd) at the data cutoff point of ≥ 12 months

Figure 1. Subgroup Analysis of PFS

Figure 2. PFS2 for D-Rd versus Rd
The CARE™ Multiple Myeloma Guidance draws upon insight from both Canadian and international leaders who have participated in recent CARE™ programs.

To hear more on MAIA from a global perspective access the recent presentation given by Dr. María Victoria Mateos, MD, PhD (University of Salamanca, Spain) during the CARE™ WHU 2021 live stream!

Access More On-Demand Content:

Refer to the end of this report for additional CARE™ Hematology Resources
**CARE™ Recommendation**: Oral and sub-cutaneous drugs reduce time and frequency of potential exposure so should be prioritized (During COVID-19)

*Click on the CARE™ Recommendations to view the full MM Guidance*

**Supporting Trial Highlights from ASH 2020:**

Interim* Results of a Time and Motion Survey Regarding Subcutaneous Versus Intravenous Administration of Daratumumab in Patients with Relapsed or Refractory Multiple Myeloma. Mary Slavcev et al.

- This time and motion survey was undertaken to elicit HCPs’ understanding of workflow and time estimates for administration of DARA IV and SC (beyond injection time alone)
- Results suggest that DARA SC is associated with less active HCP involvement in drug preparation and administration/patient care (figure 3) and less patient chair usage as compared to DARA IV

Figure 3. Median HCP Active Time for First and Subsequent Treatment

- When extrapolated for the anticipated number of treatments per year, estimated savings in HCP time per patient for DARA SC vs. IV was 50% in years 1 and 2
- Shorter administration time could lead to reduced burden on patients and their caregivers, and efficiencies for HCPs and healthcare institutions allowing for more patients to be treated

*Data collection was halted due to the COVID-19 pandemic so was presented as interim results*
CARE™ Recommendation: Novel Regimens to watch for on the horizon

Click on the CARE™ Recommendations to view the full MM Guidance

Supporting Trial Highlights from ASH 2020: Early Phase approaches with novel immune targets

Updated Phase 1 Results of Teclistamab, a B-Cell Maturation Antigen (BCMA) x CD3 Bispecific Antibody, in Relapsed and/or Refractory Multiple Myeloma (RRMM). Alfred L. Garfall et al.

- Results indicate response is durable and can deepen over time, and that teclistamab has a manageable safety profile, which includes low-grade CRS (with no gr ≥3 events) and low severe infection and neurotoxicity rates with both IV and SC administration
- The primary objective was to identify a recommended phase 2 dose(s) (RP2D)
  - Pharmacodynamics support RP2D of 1500 µg/kg SC (figure 4)
  - Of 11 evaluable patients across all IV and SC doses, 8 had MRD- negative CR at 10^-6 and 1 at 10^-5 sensitivity

Figure 4. PK Profile Following Selected IV and SC Doses

CARTITUDE-1: Phase 1b/2 Study of Ciltacabtagene Autoleucel (Cilta-cel), a B-Cell Maturation Antigen-Directed Chimeric Antigen Receptor T Cell Therapy, in Relapsed/Refractory Multiple Myeloma. Deepu Madduri et al.

- Cilta-cel has a manageable safety profile and yielded early, deep, and durable responses in heavily pre-treated patients (96.9% ORR, with sCR 67.0%)
- Median PFS not reached; 12-month PFS rate was 76.6%, OS rate was 88.5%
- Further investigation of cilta-cel in other MM populations is underway, including in earlier-line settings and with outpatient administration (CARTITUDE-2, and CARTITUDE-4)
- Of evaluable patients, 93% achieved MRD 10^-5 negativity, with a median time of 1 month (0.8-7.7)
Table 1. Summary of efficacy data and corneal toxicity per dosing cohort

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Median number for treatment cycles (range)</th>
<th>≥ G3 Keratopathy/MECN (%)</th>
<th>≥ G3 decreased VA n (%)</th>
<th>PR n</th>
<th>VGPR n</th>
<th>sCR n</th>
<th>ORR n/N (%)</th>
<th>PD</th>
</tr>
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<tbody>
<tr>
<td>1.92 SINGLE N=12</td>
<td>6.5 (2-15)</td>
<td>2 (16.7%)</td>
<td>2 (16.7%)</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>9/11 (81.8%)</td>
<td>2</td>
</tr>
<tr>
<td>2.5 SINGLE N=7</td>
<td>16 (13-20)</td>
<td>7 (100%)</td>
<td>2 (28.6%)</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>7/7 (100%)</td>
<td>2</td>
</tr>
<tr>
<td>2.5 LOADING N=5</td>
<td>4 (2-5)</td>
<td>1 (20%)</td>
<td>1 (20%)</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>4/4 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>2.5 SPLIT N=6</td>
<td>3.5 (2-10)</td>
<td>2 (33.3%)</td>
<td>1 (16.7%)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3/4 (75%)</td>
<td>0</td>
</tr>
<tr>
<td>3.4 SPLIT N=5</td>
<td>5.0 (1-8)</td>
<td>2 (40%)</td>
<td>2 (40%)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2/3 (66.7%)</td>
<td>2</td>
</tr>
<tr>
<td>All cohorts N=35</td>
<td>6.0 (1-20)</td>
<td>14 (40%)</td>
<td>7 (22.9%)</td>
<td>6</td>
<td>14</td>
<td>5</td>
<td>25/29 (86.2%)</td>
<td>6</td>
</tr>
</tbody>
</table>

Supporting Trial Highlights from ASH 2020: Carfilzomib, Daratumumab, Dex (KDa)

Carfilzomib, Dexamethasone, and Daratumumab Versus Carfilzomib and Dexamethasone in Relapsed or Refractory Multiple Myeloma: Updated Efficacy and Safety Results of the Phase 3 Candor Study. Meletios A Dimopoulos et al.

Evaluation of Minimal Residual Disease (MRD) Negativity in Patients with Relapsed or Refractory Multiple Myeloma Treated in the Candor Study. Ola Landgren et al.

- After a median follow-up of 28 months, median PFS for KDa of 28.6m continues being significantly longer than Kd (15.2m)
- At the 12-month landmark, the MRD-negativity CR rate was 12.5% vs 1.3% in the Kd arm (OR, 11.3; P<0.0001) and the MRD-negativity rate was 17.6% vs 3.9% (OR, 5.76; P<0.0001)

Carfilzomib 56mg/m2 Twice-Weekly in Combination with Dexamethasone and Daratumumab (KDa) Versus Daratumumab in Combination with 8 Cycles of Bortezomib and Dexamethasone (Dvd): A Matching-Adjusted Indirect Treatment Comparison. Katja Weisel et al.

- After adjusting for cross-trial differences, KDa was associated with a substantial reduction in the risk of progression or death compared with Dvd (risk reduction was 39% overall and 64% after 8 cycles)
- PFS favourability was consistent in the Len-exposed and Len-refractory patient subgroups.

Supporting Trial Highlights from ASH 2020: Selinexor, pomalidomide, dex (Spd)

Selinexor in Combination with Carfilzomib and Dexamethasone, All Once Weekly (Skd), for Patients with Relapsed/Refractory Multiple Myeloma. Cristina Gasparetto et al.

- This combination is active with an ORR of 75.0% and deep responses (CR 16.7%, VGPR 29.2%)
- ORR of 57.1% in patients previously treated with daratumumab warrants further investigation
Other CARE™ Hematology Resources

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  - Click Here to Participate

- **Immune thrombocytopenic purpura (ITP)**
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  - Conférence Canadienne sur l’hématoLOGIE PRINTEMPS 2021
  - Conférence virtuelle

- **CARE™ AT ASCO/EHA**
  - JUNE 2021

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06 SUPPLEMENT TO CARE™ GUIDANCE ON MULTIPLE MYELOMA