Daratumumab, Bortezomib and dexamethasone (DVd) at first relapse for patients with Relapsed/ Refractory Multiple Myeloma (RRMM): a UK Myeloma Research Alliance (UK-MRA) real-world multicentre analysis

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Disclosures

Nil

Introduction

- Daratumumab, bortezomib and dexamethasone (DVd) demonstrated superior overall response rates (ORR) and progression free survival (PFS) compared to Vd in the CASTOR phase 3 trial for patients with relapsed refractory multiple myeloma (RRMM)[1,2]

- In patients treated after 1 prior line of therapy (1PL) the ORR was 92% and with a median follow up of 40m the median PFS was 27m[3]

- Since March 2019 it has been available on the CDF in the UK for patients with RRMM after 1 prior line of therapy (1PL)

- Discrepancies in outcomes between patients treated in clinical trials compared to routine practice are well-recognised[4]

- The real-world outcomes of patients treated with DVd at first relapse is yet to be determined

1. Palumbo A et al. NEJM 2016; 375: 754-766
2. Spencer et al. Haematologica 2018; 103: 2079-2087
3. Richardson et al. Blood Cancer Journal 2018; 109
4. Mateos et al. CLML 2020; 20: 509-18

Aims

- To assess DVd use after 1PL for patients with RRMM in UK routine clinical practice
  - Primary aims
    - Overall response rate (ORR)
    - Progression free survival (PFS)
  - Secondary aims
    - Overall survival (OS)
    - Time to next treatment (TTNT)
    - Efficacy in different subgroups
      - Cytogenetics
      - Treatment free interval (TFI)
      - Weekly vs biweekly velcade

Methods

- Retrospective analysis
- 296 consecutive patients included
- 14 centres (academic and community hospitals)

  - Data was analysed for patients treated between March 2019 and August 2021

  - Patients received daratumumab (IV and then SC from June 2020) as per CASTOR protocol[1]

  - SC bortezomib was given as per standard institutional practice

  - Adverse events were graded as per CTCAE criteria (Version 5)

Patient demographics

- 92% (273/296) had received 1PL (8% (23) 2PL due to COVID measures)
- 67% received weekly velcade (197/296)

	CASTOR ITT DVd arm [1,2] (n=251)	CASTOR DVd arm 1PL[1,2] (n=122)	UK real world (n=296)	
Median age (range)	64 (30-88)	63 (30-84)	69 (20-88)	
Age >75 years (%)	23 (9)	**8 (7)**	**81 (27)**	***P*=<0.0001**
ISS				
n	251	122	212	
I	98 (39)	57 (47)	84 (39)	
II	94 (37.5)	42 (34)	63 (30)	
III	59 (23.5)	**23 (19)**	**65 (31)**	***P*=0.0203**
Cytogenetics				
n	167		103	
Standard risk	123 (74)		82 (80)	
High risk[#]	44 (26)		21 (20)	
Prior therapy				
n	251	122	296	
ASCT	157 (62.5)		144 (49)	
Bortezomib	162 (64.5)	**62 (51)**	**211 (71)**	***P*=0.0003**

#High risk= 17p del, t(4;14), t(14;16)

- **The real world population differed from CASTOR in being older, more patients who were ISS 3, and more with prior bortezomib exposure**
- **Additionally 4% were PI refractory, and 9% had a GFR <30ml/min**

1. Palumbo A et al. NEJM 2016; 375: 754-766
2. Spencer et al. Haematologica 2018; 103: 2079-2087

Results

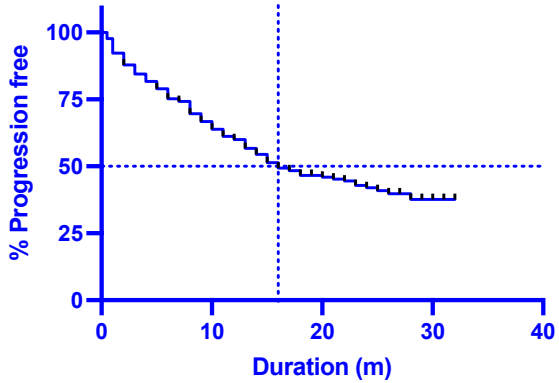
- ORR was 82% with >=VGPR in 57%
- Median time to response 35 days

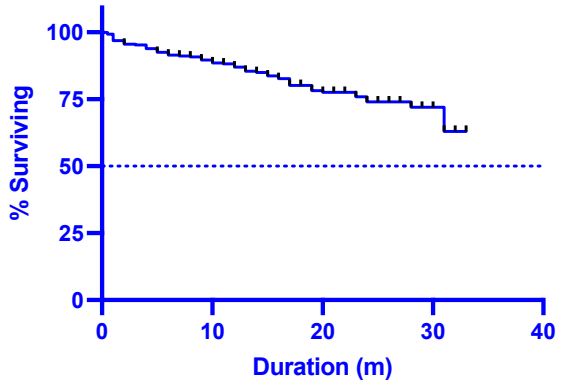
Response	CASTOR DVd arm ITT[1,2] (n=240)	CASTOR DVd arm 1PL [1,2] (n=199)	UK real world (n=296)
ORR (%)	203 (85)	109 (92)	244 (82)
VGPR or better (%)	151 (63)	91 (77)	168 (57)
PR (%)	53 (22)	18 (15)	76 (26)
MR (%)	9 (4)		14 (5)
SD (%)	5 (2)		19 (6)
PD (%)	2 (2)		19 (6)

1. Palumbo A et al. NEJM 2016; 375: 754-766
2. Spencer et al. Haematologica 2018; 103: 2079-2087

Results

- With a median follow up of 20m
  - The median PFS is 16m *(95% CI 11.5- 20)*
  - Median OS has not been reached with an estimated 2-year OS of 74%
  - Median TNTT is 20m *(95% CI 15-25)*





- In CASTOR, with median follow up 40m, the median PFS for DVd was 16.7m in the ITT population, and 27m in the 1PL group[1]

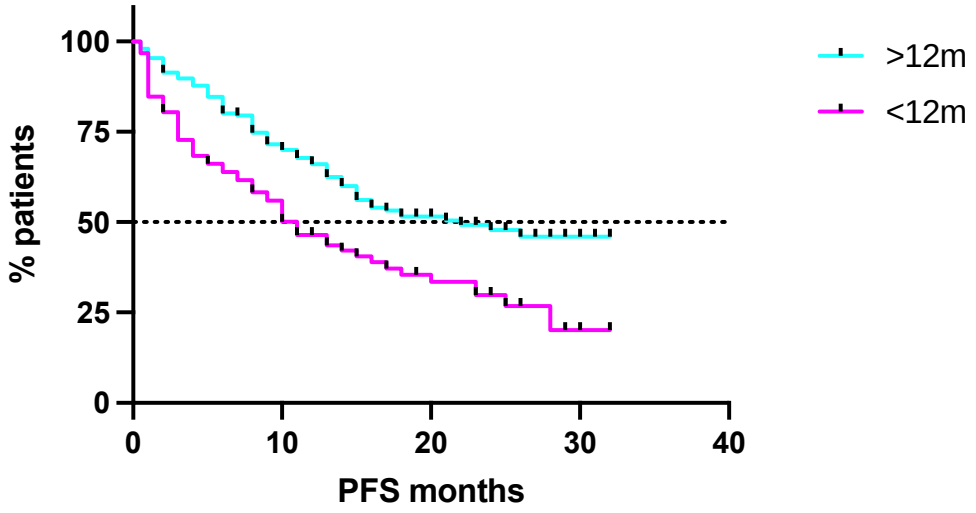
1. Mateos VM et al. CLM&L 2020; 20: 509-518

Subgroups

- No difference between weekly vs biweekly velcade
  - ORR 81% weekly vs 85% biweekly (p= 0.5)
  - No difference in PFS (18 vs 14m; p= 0.17) or OS (not reached for either; p=0.4)
- Cytogenetics
  - There was no differences in ORR between high and standard risk patients (81% vs 83%; p= 0.78), and a nonsignificant difference in PFS (15m vs 28m; p= 0.15)
  - However, OS was significantly worse for high-risk patients (19m vs not reached; p=0.002)

Subgroups

- Prior treatment free interval
  - ORR 75% vs 86% for patients with TFI <12m vs >12m (p=0.03)
  - PFS 11m vs 22m (p=0.0002)
  - OS not reached for either group



Toxicity

- DVd was generally well tolerated
  - 6% stopped due to adverse events (CASTOR 9.5%[1])
  - Grade 3 or 4 toxicity occurred in 62 (22%) most commonly neutropenia and thrombocytopenia
  - Any grade infusion reactions were reported in 27 (9%) of which the majority were grade 1 or 2 (78%)

1. Spencer et al. Haematologica 2018; 103: 2079-2087

Conclusions

- DVd at first relapse has demonstrated high response rates in real-world population

- PFS in this cohort appeared lower than CASTOR; however, the population was more heterogenous (older, more ISS 3, some PI refractory cases and poor renal function)

- High risk cytogenetics, and those treated within 12 months of first line therapy had inferior outcome

- There was no significant difference in efficacy between weekly and bi-weekly bortezomib

- Tolerability appeared to be good with a low discontinuation rate

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