IMPACT OF AGE ON EFFICACY AND SAFETY OF DARATUMUMAB IN COMBINATION WITH LENALIDOMIDE AND DEXAMETHASONE (D-RD) IN PATIENTS WITH TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): MAIA

Author(s): Cyrille Hulin , Thierry Facon , Shaji Kumar , Torben Plesner , Robert Z. Orlowski , Cyrille Touzeau , Nizar Bahlis , Supratik Basu , Hareth Nahi , Hang Quach , Hartmut Goldschmidt , Michael O'Dwyer , Gordon Cook , Laurent Garderet , Christopher P. Venner , Katja Weisel , Noopur Raje , Benjamin Hebraud , Karim Belhadj-Merzoug , Lotfi Benboubker , Olivier Decaux , Salomon Manier , Denis Caillot , Christopher Chiu , Maria Krevvata , Jianping Wang , Rian Van Rampelbergh , Clarissa Uhlar , Rachel Kobos , Ming Qi , Saad Z. Usmani
EHA Library. Hulin C.

Jun 14, 2019; 266391

Abstract: PF592

Type: Poster Presentation

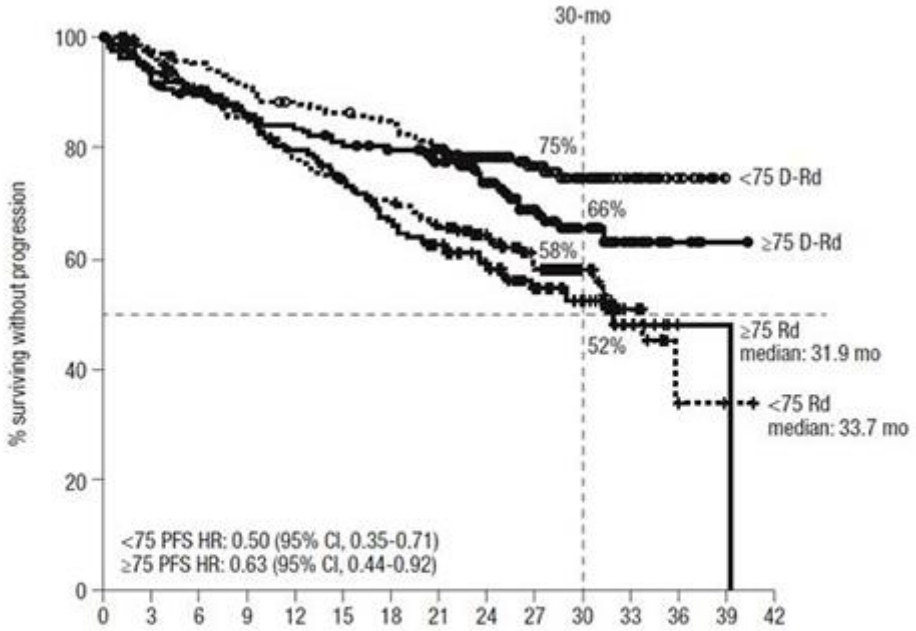
Presentation during EHA24: On Friday, June 14, 2019 from 17:30 - 19:00

Background
Elderly patients with MM often have low performance status, reduced organ function, and increased comorbidities, all of which affect their ability to tolerate MM treatment and may result in lower efficacy. In the recently reported phase 3 MAIA study, D-Rd significantly reduced the risk of progression or death by 44% vs lenalidomide and dexamethasone (Rd) alone in transplant-ineligible NDMM patients, and demonstrated tolerability consistent with previously reported studies of daratumumab and Rd alone.

Aims
To examine the impact of age on efficacy and safety of D-Rd vs Rd in this population, a subgroup analysis was conducted in patients <75 and ≥75 years of age.

Methods
Transplant-ineligible NDMM patients were randomized 1:1 to Rd with or without daratumumab; stratification was based on age (<75 vs ≥75 y), ISS (I, II, III), and region (North America vs Other). Patients received 28-day cycles of either lenalidomide 25 or 10 mg (based on renal function) PO QD on Days 1-21 and either dexamethasone 40 or 20 mg (based on age or BMI) PO/IV weekly until progression. In the D-Rd arm, patients received daratumumab 16 mg/kg IV QW for Cycles 1-2, Q2W for Cycles 3-6, and Q4W thereafter until progression. PFS was the primary endpoint.

Results
Among 737 randomized patients (D-Rd, n=368; Rd, n=369), 321 (44%) were ≥75 y of age. A higher proportion of patients in the D-Rd arm received a lower starting dose of lenalidomide (10 mg) compared with the Rd arm (30.8% vs 22.7%), and a lower relative median dose intensity for lenalidomide (<75 y: 79% vs 93%; ≥75 y: 66% vs 89%). After median follow-up of 28 mo, significant PFS benefit of D-Rd vs Rd was maintained in both <75 and ≥75 y subgroups (<75: median not reached [NR] vs 33.7 mo; HR 0.50; 95% CI 0.35-0.71; ≥75 y: median NR vs 31.9 mo; HR 0.63; 95% CI 0.44-0.92; **Figure**). Overall response rate (<75: 95% vs 82%; ≥75 y: 90% vs 81%), rate of complete response or better (<75: 52% vs 25%; ≥75 y: 41% vs 25%), rate of very good partial response or better (<75: 81% vs 53%; ≥75 y: 77% vs 53%), and minimal residual disease-negative rate (10^{-5} threshold; <75: 28% vs 7%; ≥75 y: 19% vs 8%) remained higher with D-Rd vs Rd in both age subgroups. Most common (≥10%; D-Rd/Rd) grade 3/4 TEAEs in <75 y patients were neutropenia (43%/31%), pneumonia (13%/6%), lymphopenia (12%/10%), leukopenia (10%/4%), and anemia (9%/18%). Most common (≥10%; D-Rd/Rd) grade 3/4 TEAEs in ≥75 y patients were neutropenia (60%/41%), lymphopenia (19%/12%), anemia (16%/22%), pneumonia (15%/10%), leukopenia (12%/6%), and thrombocytopenia (8%/11%). Fewer patients receiving D-Rd vs Rd discontinued treatment due to TEAEs (<75 y: 5% vs 12%; ≥75 y: 10% vs 21%); discontinuation rates due to infections for D-Rd vs Rd were low in both age groups (<75 y: 1% vs 1%; ≥75 y: 0% vs 2%). A higher proportion of ≥75 y patients discontinued lenalidomide due to TEAEs compared with <75 y patients (≥75 y: 29% vs 22%; <75 y: 15% vs 13%).



Patients at risk														
<75 Rd	208	191	175	158	141	132	126	116	86	56	31	11	2	1	0
<75 D-Rd	208	201	195	186	179	175	170	159	116	83	47	23	7	0	0
≥75 Rd	161	141	132	122	113	104	93	84	63	38	19	7	1	1	0
≥75 D-Rd	160	146	140	134	130	125	120	112	87	63	39	12	4	1	0

Conclusion

D-Rd patients received less lenalidomide compared with the Rd group regardless of age. Efficacy of D-Rd in <75 and ≥75 y patients was consistent with the ITT population, and D-Rd demonstrated a manageable safety profile regardless of age. Together with the phase 3 ALCYONE study, these studies confirm the clinical benefit of daratumumab plus standard-of-care in transplant-ineligible NDMM patients ≥75 y of age.