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653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

Daratumumab, Bortezomib, and Dexamethasone (D-Vd) Versus Bortezomib and Dexamethasone (Vd) Alone in Chinese Patients with Relapsed/Refractory Multiple Myeloma: Final Analysis of the Phase 3 Lepus Study

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Introduction: Daratumumab is a human IgGκ monoclonal antibody targeting CD38 with a direct on-tumor and immunomodulatory mechanism of action. D-Vd prolonged progression-free survival (PFS) and induced deeper and more durable responses versus Vd alone in patients with relapsed/refractory multiple myeloma (RRMM) in the global phase 3 CASTOR study. A prior updated analysis of the phase 3 LEPUS study (median follow-up, 25.1 months) showed significant clinical benefit for D-Vd versus Vd in Chinese patients who have RRMM, and a safety profile generally consistent with that observed in CASTOR. Here, we report results from the final analysis of LEPUS with an extended median follow-up of >3 years.

Methods: In the randomized, multicenter, phase 3 LEPUS study (ClinicalTrials.gov Identifier: NCT03234972), Chinese patients with RRMM who had received ≥1 prior line of therapy were randomized 2:1 to 8 cycles (21 days/cycle) of Vd (bortezomib 1.3 mg/m ^{2} SC on Days 1, 4, 8, and 11; dexamethasone 20 mg PO/IV on Days 1, 2, 4, 5, 8, 9, 11, and 12) ± daratumumab (16 mg/kg IV weekly in Cycles 1-3, every 3 weeks in Cycles 4-8, and every 4 weeks thereafter until disease progression). Per a protocol amendment, on Day 1 of any cycle patients receiving daratumumab IV were permitted to switch to daratumumab SC 1800 mg (same schedule as IV). The primary endpoint was PFS.

Results: A total of 211 patients were randomized to D-Vd (n = 141) or Vd (n = 70). At a median follow-up of 37.1 months, D-Vd continued to prolong PFS versus Vd alone (median, 14.9 vs 6.3 months; hazard ratio [HR], 0.36; 95% confidence interval [CI], 0.25-0.52; P <0.00001; *Figure 1*). Time to progression (median, 15.7 vs 6.8 months; HR, 0.34; 95% CI, 0.23-0.51; P <0.00001) and overall survival (median, not reached vs 40.7 months; HR, 0.76; 95% CI, 0.50-1.17; P = 0.21; *Figure 2*) were longer with D-Vd versus Vd. The duration of response among patients who achieved a partial response or better was also longer with D-Vd versus Vd (median, 16.8 vs 9.0 months). The measurable residual disease-negativity rate (10 $^{-5}$) was higher with D-Vd versus Vd (32.6% vs 4.3%; odds ratio, 10.81; 95% CI, 3.23-36.23; P <0.0001). The safety profile of D-Vd observed at the final analysis was generally consistent with that observed for the prior updated analysis. Grade 3/4 treatment-emergent adverse events (TEAEs) were primarily hematologic events. Grade 3/4 infections were reported for 77 (55.0%) patients who received D-Vd and 28 (41.2%) patients who received Vd; lung infection (30.7% vs 22.1%, respectively) was the only nonhematologic grade 3/4 TEAE reported in ≥20% of patients. For patients who received D-Vd and Vd, respectively, TEAEs were classified as serious for 76 (54.3%) and 27 (39.7%) patients, led to treatment discontinuation in 7 (5.0%) and 2 (2.9%) patients, and led to death in 6 (4.3%) and 7 (10.3%) patients. None of the 123 patients in the D-Vd group who had appropriate immunogenicity samples were positive for antibodies to daratumumab.

A total of 31 patients in the D-Vd group switched from daratumumab IV to daratumumab SC during the study (after completion of bortezomib and dexamethasone); among these patients, 24 (77.4%) preferred SC administration, 2 (6.5%) preferred IV administration, and 5 (16.1%) had no preference. For the 24 patients who indicated they preferred daratumumab SC administration, key reasons for their preference included treatment administration time (83.3%), more comfortable administration process (70.8%), fewer administration-related reactions (45.8%), and less caregiver burden (25.0%). Among the 31 patients who switched to daratumumab SC, 6 (19.4%) patients experienced grade 3 TEAEs (most commonly hyperglycemia and hypokalemia, n = 2 each) and 2 (6.5%) patients experienced serious AEs (pyrexia and hyperglycemia, n = 1 each).

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Conclusions: In this final analysis of LEPUS with a median follow-up of >3 years, D-Vd continued to demonstrate substantial efficacy benefits versus Vd and the safety profile of D-Vd remained stable, with no new safety concerns identified. In addition, several patients switched their daratumumab administration from IV to SC, which was preferred by most patients who switched. These results further support the feasibility of daratumumab SC administration and the use of D-Vd as a standard of care in Chinese patients with RRMM who have received ≥1 prior line of therapy.

Disclosures Fu: *Takeda Pharmaceutical Company Limited.:* Research Funding; *Shanghai Changzheng Hospital:* Other: WJF is a former staff of Shanghai Changzheng Hospital and now is a staff of Shanghai Fourth People's Hospital affiliated to Tongji University. . **Gai:** *Janssen:* Current Employment, Current holder of *stock options* in a privately-held company. **Liu:** *Janssen:* Current Employment, Current holder of *stock options* in a privately-held company. **Chen:** *Xian Janssen Pharmaceutical Ltd.:* Current Employment, Current holder of *stock options* in a privately-held company. **Cui:** *Xian Janssen Pharmaceutical Ltd.:* Current Employment, Current holder of *stock options* in a privately-held company. **Lu:** *Jassen Pharmaceutical Ltd:* Consultancy, Speakers Bureau.

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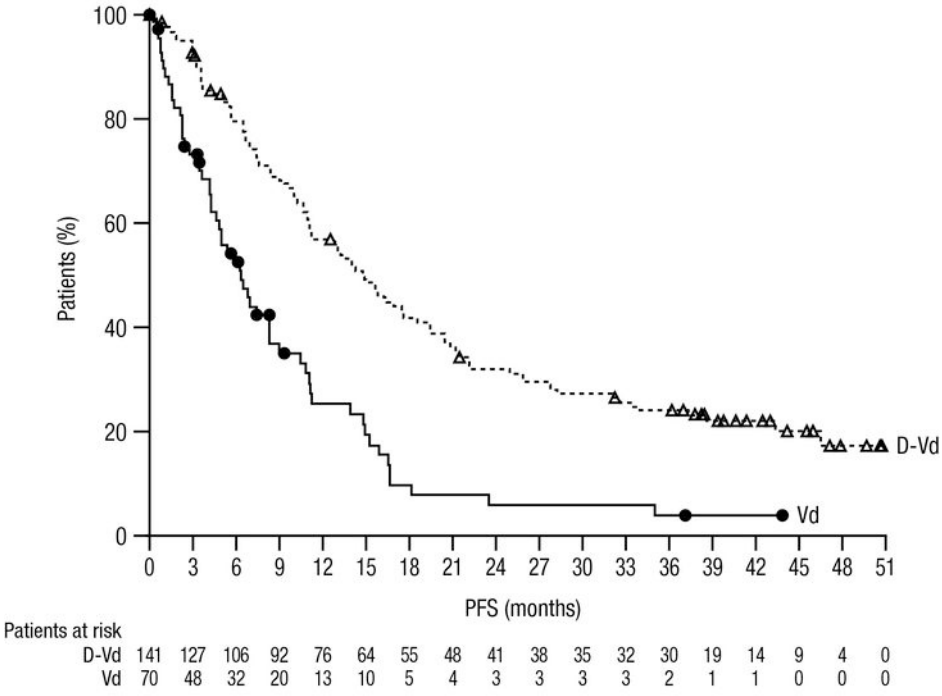
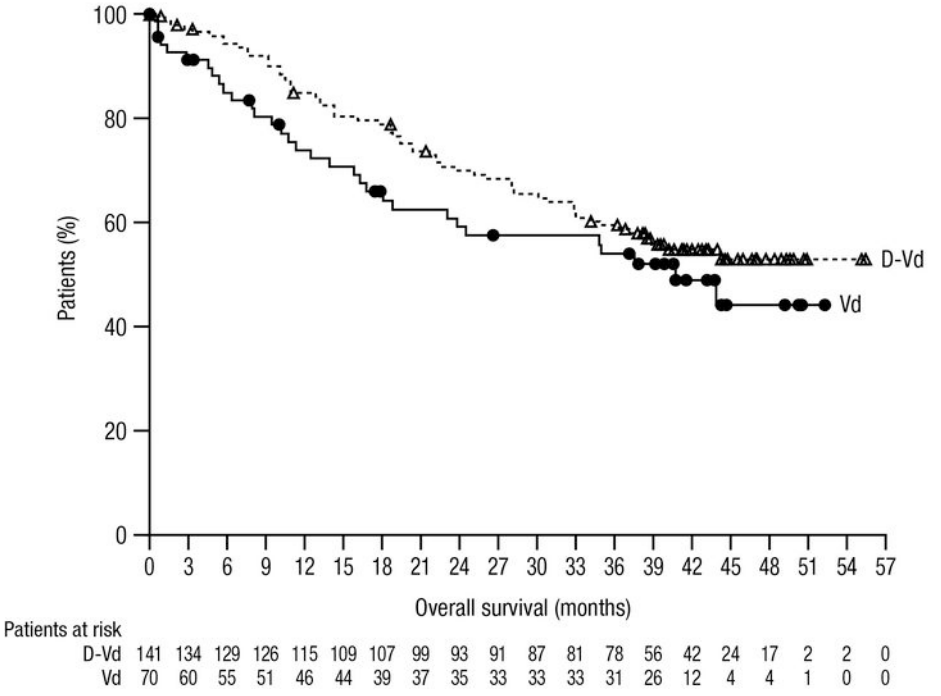
Figure 1. Kaplan-Meier plot of PFS.



Patients at risk

D-Vd	141	127	106	92	76	64	55	48	41	38	35	32	30	19	14	9	4	0
Vd	70	48	32	20	13	10	5	4	3	3	3	3	2	1	1	0	0	0

Figure 2. Kaplan-Meier plot of overall survival.



Patients at risk

D-Vd	141	134	129	126	115	109	107	99	93	91	87	81	78	56	42	24	17	2	2	0
Vd	70	60	55	51	46	44	39	37	35	33	33	33	31	26	12	4	4	1	0	0

Figure 1

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