Title

P-135: Time to event surrogate endpoints in multiple myeloma randomized trials from 2005-2019: a systematic review and surrogacy analysis

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Introduction: POEMS syndrome is a rare paraneoplastic syndrome caused by an abnormal plasma cell clone. Prospective data regarding therapy outcomes are scarce and treatment is based on small case series and single institution experiences. We report herein our institution's experience over a 10-year time period. **Methods:** We conducted a retrospective analysis of the clinical features and therapy outcomes of 29 patients (pts) with POEMS syndrome treated at our institution from 2010 to 2020. Kaplan-Meier method was used to estimate the progression free (PFS) and overall survival (OS). **Results:** The median age of our pts was 67 years; 72% were male. 16 (55%) and 10 (34.5%) pts had IgG and IgA heavy chain isotypes respectively, with 25 (86%) pts having involved lambda light chain. Median % of bone marrow plasma cells was 5 (range 0-20). At diagnosis, 18 (62%) pts had peripheral edema, 8 (28%) organomegaly, 11 (38%) endocrinopathy, 18 (62%) skin changes, 8 (28%) thrombocytosis, 6 (21%) deep venous thrombosis and 2 (7%) papilledema. Elevated VEGF level was noted in 55% of our cohort, with a median of 216 pg/ml. The median number of treatment (Tx) lines was 1 (range 1-5). Frontline Tx included immunomodulatory drug (IMiD)-based, proteasome inhibitor (PI)-based and Cyclophosphamide (Cy)-only therapies at 23 (80%), 2 (6.6%), and 2 (6.6%) pts respectively, whereas 2 (6.6%) pts received only radiation (RT) therapy. Eleven (38%) pts were non-evaluable (NE) for hematologic response, whereas 12 (41%) achieved ≥VGPR (of these 9, 1 and 2 pts were treated with IMid, PI, and RT-only regimens, respectively). In terms of VEGF response, 14 (48%) pts were NE, 12 (42%) achieved CR (11 received IMiD-based Tx, 1 RT-only) and 3 (10%) improvement. Clinically, 27 (93%) pts demonstrated improvement. Consolidation with autologous hematopoietic cell transplant (AHCT) after 1 line of Tx was used in 5 (17%) pts; of those 4 achieved ≥VGPR. Daratumumab was used as monotherapy in 7 (24%) pts with relapsed disease as 3rd or 4th line. Of them, 1 achieved VGPR, 2 Partial response, and 3 were NE; clinically 71% had improvement. VEGF response was NE in 5/7 pts, 1 had improvement and 1 no response. The median PFS of 1st line Tx for the entire cohort and the subset of pts who received IMiD-based therapy was 63 (95% CI, 32, not reached [NR]) and 63 (95% CI, 31, NR) months respectively. The median OS for the entire cohort was NR. Only 4 pts died; cause of death was unrelated to POEMS. All pts who underwent AHCT are alive. **Conclusions:** Our cohort treatment outcomes are similar to what has been published. IMiD-based therapy is very effective in the upfront setting. AHCT also leads to excellent response rates translating into long survival. Daratumumab appears to be increasingly utilized, mainly in the relapsed setting and has shown marked activity. A prospective study is currently enrolling to assess the latter's safety and efficacy in combination with lenalidomide in POEMS syndrome.

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Time to event surrogate endpoints in multiple myeloma randomized trials from 2005-2019: a systematic review and surrogacy analysis

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