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**Association of increased microvessel density with skeletal extramedullary disease relapse in multiple myeloma patients who have skeletal extramedullary disease at diagnosis**

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**Running title : Microvessel density and skeletal EMD relapse**

**Declarations of interest: none**

**Abstract**

The aim of the study was to investigate whether microvessel density (MVD) could be associated with skeletal extramedullary disease relapse (skeletal-EMDR) in patients with multiple myeloma (MM) who have skeletal-EMD at diagnosis. Seventy-nine newly diagnosed MM patients who have skeletal-EMD were retrospectively enrolled in this study. The 4-year cumulative incidence of skeletal-EMDR was  $35.0\% \pm 8.3\%$ . The 4-year probability of overall survival (OS) was  $54.0\% \pm 7.6\%$ . Multivariate analysis showed that skeletal-EMDR (HR=4.144; 95% CI: 1.608-10.685; P=0.003) was independently associated with inferior OS for the MM patients who have skeletal-EMD at diagnosis. The factors associated with skeletal-EMDR were MVD (HR=3.990, 95% CI:1.136-14.018; P=0.031), white blood cell (WBC) (HR=0.262, 95% CI:0.090-0.769; P=0.015), and the EMD sites involved at onset (HR=0.263, 95% CI: 0.074-

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