

Editorial

Unmet need in the treatment of multiple myeloma in Thailand: early mortality predicted by older age and high β_2 -microglobulin

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Multiple myeloma (MM) is a clonal malignant plasma cell disorder encompassing a spectrum that ranges from asymptomatic monoclonal gammopathy of undetermined significance to fully symptomatic MM. Manifestations of symptomatic MM include the classic 'CRAB' criteria: hypercalcemia, renal impairment, anemia and bony lytic lesions.¹ MM is considered a disease of the aging population, with a median age of 65 years at diagnosis.² Recent advances in the treatment of MM have established new standard of care and significantly improved patient survival over time. Current prognostication in MM is based on the Revised international staging system (R-ISS)¹ or the International Staging System (ISS) in areas without access to fluorescent in situ hybridization (FISH) cytogenetic study.¹ Upfront treatment with proteasome inhibitors and/or immunomodulatory drugs, including autologous stem cell transplantation when appropriate, has demonstrated the best survival outcomes. With current therapies, long-term survivals in the range of 5-10 years is achievable.

Despite these advances, a major challenge in MM management remains early mortality, occurring before patients can fully benefit from treatment. Definitions of early mortality vary across studies, typically ranging from 6 to 24 months following MM diagnosis.³⁻⁶ Several studies have attempted to identify predictors of early mortality in newly diagnosed MM. A recent real-world analysis from a United States claims database including 7,512 patients treated in community-based oncology practices reported an early (6-month) mortality rate of 8.3%. Predictors of early mortality included Eastern

Cooperative Oncology Group (ECOG) performance status ≥ 2 , R-ISS stage III, age ≥ 70 , receipt of proteasome inhibitor doublet therapy, light-chain isotype and renal dysfunction (estimated glomerular filtration rate < 30 mL/min).⁵ Another study from the United Kingdom involving an earlier cohort of 3,107 patients enrolled in MM trials between 1980 and 2002 reported an early (60-day) mortality rate of 10%. Predictors of early mortality in this study included serum β_2 -microglobulin level, performance status and age, with a sensitivity of 61% and specificity of 73%. The leading cause of death was infectious complications (45%).⁶

In Thailand, access to novel treatments such as bortezomib and immunomodulatory drugs remains limited. Under the universal coverage scheme, bortezomib has only recently become reimbursable for transplant-eligible MM patients since 2023. Limited access to novel therapies likely contributes to higher mortality rates. A previous retrospective single-center study from Chiang Rai province involving 212 MM patients treated between 2010 and 2020 reported an early (12-month) mortality rate of 34%. Renal impairment was the primary predictor of early mortality, while receipt of chemotherapy was a protective factor. The leading causes of death were septicemia (38%), pneumonia (33%) and kidney failure (26%).⁷

To further explore predictors of early mortality in MM, Sirisanthiti P conducted a retrospective analysis of another single-center cohort comprising 153 MM patients in Nakhon Ratchasima province between 2018 and 2023. The reported early (12-month) mortality rate

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was 41%. Predictors of early mortality were older age (per 1-year increase) and serum β_2 -microglobulin ≥ 5.5 mg/L. Causes of deaths were mainly MM-related, with disease progression accounting for 58.6% and therapy-related infectious complications for 41.4%. When comparing patients who received novel agents with those who received conventional chemotherapy, early mortality occurred in 14.6% and 39.6% of patients, respectively. The odds ratio for early mortality with conventional chemotherapy was 3.31 (95% confidence interval, 1.26-8.70), highlighting the impact of novel agents in reducing early mortality.

Notably, both Thai studies demonstrated poorer survival outcomes in MM, particularly with a markedly high rate of early mortality. Early mortality in MM is known to result from disease-related immunoparesis as well as treatment-related complications. Access to frontline novel agent-based therapy in the two Thai studies was limited to 15% and 27% of patients, respectively, which may explain the disparity in outcomes compared with international studies where novel agents are routinely used upfront.

The higher early mortality rates observed in Thai cohorts compared with international studies underscore a critical unmet need to improve access to effective therapies in resource-limited settings. Early death in these studies appears to be driven primarily by disease burden and aggressiveness. Early and effective disease control would likely reduce early mortality and improve overall survival. Expanding reimbursement for proteasome inhibitors and/or immunomodulatory drugs beyond

transplant-eligible MM patients represents a crucial intervention to bridge this disparity. The Thai Myeloma Working Group and the Thai Society of Hematology are actively collaborating with the central government to address this issue for all Thai MM patients, with the goal of improving outcomes in this substantial patient population. Future studies involving larger cohorts treated with modern novel agent-based frontline regimens are expected to demonstrate reductions in early mortality and improved survival outcomes in Thailand.

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