

**Title:**

**Changing trend in mortality rate of multiple myeloma after introduction of novel agents: a population-based study**

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**Short title:**

Trends in mortality rate and incidence rate of multiple myeloma

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**Key words:** mortality rate, incidence rate, multiple myeloma, Japan, SEER

**List of Abbreviations:**

AAPC, average annual percent change; APC, annual percent change; ASCT, autologous stem-cell transplantation; ASR, age-standardized rate; CI, confidence interval; ICD, International Classification of Diseases; MCIJ, Monitoring of Cancer Incidence in Japan; MM, multiple myeloma; OS, overall survival; SEER, Surveillance Epidemiology and End Results.

**Article category:** Research Article

**Brief description:**

Cancer mortality rate is an important public health measure of progress against cancer.

The authors assessed trends in mortality rates of multiple myeloma (MM) in parallel with incidence rates of MM in Japan and the U.S. Mortality rates of MM significantly decreased after introduction of novel agents despite increasing trends in incidence rates in both countries. Moreover, the improvements of mortality rates were particularly large in patients aged 70-79 years, who cannot receive stem-cell transplantation.

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## **Abstract**

Previously, the main treatment for multiple myeloma (MM) was cytotoxic chemotherapies, including autologous stem-cell transplantation (ASCT), but survival benefit in the elderly was limited. More recently, clinical trials and practical experience with novel agents with superior efficacy have shown improved survival, including in the elderly. However, this improvement cannot be simply interpreted as a decline of mortality rate that is an important public health measure of progress against cancer. Here, we assessed the trends in mortality rates of MM in parallel with incidence rates in Japan and the U.S. We used national mortality data and population-based cancer registry data in both countries from 1995 to 2015, during which 74,972 patients in Japan and 229,290 patients in the U.S. died of MM. Trends in mortality and incidence rates were characterized using joinpoint regression analysis. Despite upward trends in incidence, mortality rates showed a significant decrement after 2005 in Japan, with an annual percent change [APC (95% confidence interval)] of -2.5% (-2.9% to -2.1%), and after 2002 in the U.S., with an APC of -2.0% (-2.6% to -1.5%). In both countries, the change in mortality trend coincided with the introduction of the novel agents. Moreover, improvements in mortality were particularly large in patients aged 70-79 years, who cannot receive ASCT. Our results indicate that the benefits of novel agents for MM are

appreciable at the population level and may encourage further development of novel agents for malignancies that can be widely applied to the patients.