Multiple Myeloma: The Past, the Present and the Future

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Multiple myeloma (MM) arises from neoplastic proliferation of plasma cells, and presents with hypercalcemia (C), renal failure (R), anaemia (A) and bone pain (B) or fractures (CRAB), hence a miserable disease. MM may be preceded by an asymptomatic stage, monoclonal gammopathy of unknown origin (MGUS). However, apart from MM, differential diagnoses of MGUS include solitary plasmacytoma, chronic lymphocytic leukaemia, lymphoproliferative disease and light chain amyloidosis, all of which carries different prognosis and requires different treatments.

The incidence of MM in Hong Kong is rising with >300 new cases/100,000/year. Transplant-eligible myeloma patients will receive induction, followed by autologous stem cell transplantation (ASCT), and then maintenance therapy. A decade ago, MM patients received induction with conventional chemotherapy, followed by ASCT with complete remission (CR) rate of 5% after chemotherapy induction, and 20% after ASCT. In the recent decade, major advances emerged with the advent of novel agents including proteasome inhibitor (PI) and immunomodulatory agent (IMiD). Induction with novel agent-based regimen generally comprises a triplet with a proteasome inhibitor (PI), an immunomodulatory agent (IMiD), and dexamethasone that results in a much higher CR rate of about 25% after induction, and up to 60-70% after ASCT. Moreover, the increase in CR rates translates into improvement of survival with median survival of about 10 years, compared with two to three years using conventional chemotherapy. However, despite a high CR rate, most patients eventually relapse. Active salvage therapy includes triplets composed of next generation PIs (carfilzomib or ixazomib), IMiD (lenalidomide or pomalidomide) and dexamethasone. On the other hand, monoclonal antibodies including daratumumab and elotuzumab are important breakthroughs in the treatment of relapsed MM. Besides, BCL2 inhibitors and exportin-1 inhibitor are promising new drugs. Furthermore, antibody conjugate (ADC) and bispecific antigen engager (BiTE) are also undergoing clinical trials. In addition, CAR-T cell has also been shown effective in advanced, refractory MM. Finally, minimal residual disease (MRD), a low level of cancer cells that escapes detection by conventional serological techniques, is being extensively studied for informing treatment strategies, or as a prognostic factor for survival. Therefore, with the advent of novel agents, antibodies, and cell therapy, MM is making great strides and the future is promising.