

Expression of kappa myeloma antigen (KMA) and lambda myeloma antigen (LMA) on bone marrow plasma cells in patients with multiple myeloma: implications for antibody and cellular therapy

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Introduction

Kappa myeloma antigen (KMA) and lambda myeloma antigen (LMA) are found on the surface of malignant plasma cells (PCs) in the bone marrow (BM) of patients with multiple myeloma (MM) and other plasma cell diseases¹⁻⁴. Both antigens derive from specific conformational epitopes in the constant regions of cell surface-bound light chains that are not associated with heavy chain. KMA and LMA are not present on normal B cells but they are present on occasional mononuclear cells in tonsillar and some secondary mucosal lymphoid tissue^{1,2}. Targeting tumour specific KMA and LMA may reduce the risk of post-treatment hypogammaglobulinaemia and serious infection observed when broadly expressed antigens such as CD38, SLAM-F7 and B cell maturation antigen (BCMA) are targeted.

Methods

Patient BM samples were analysed using multiparametric FCM immunophenotyping with APC labelled LambdaMab (10B3) and KappaMab Fab'2 fragments, CD38, CD138, CD269 (BCMA), CD319 (SLAM-F7), CD56 and CD45 monoclonal antibodies. PCs were identified as previously described by initial gating using CD38 and CD138. LMA and KMA expression was determined and compared with the other cell markers.

Results

Patients (N=51) with confirmed MM (36 kappa isotype, 15 lambda isotype) that was either untreated (NDMM) or previously treated (RRMM) underwent BM biopsy. Of the 36 κMM cases, 21 were NDMM and 19 (90%) expressed BCMA whereas 15 (79%) expressed CD56. KMA was expressed in 14 (67%) cases, in all but one with co-expression of BCMA. Of the 15 RRMM patients, 11 (73%) expressed BCMA and 10 (67%) expressed CD56. KMA was expressed in 12 (80%) of the cases. Ten cases (67%) co-expressed KMA and BCMA with 2 cases positive for KMA but not for BCMA. The density of BCMA on PCs decreased in RRMM (mean 2232 v 1426 molecules PE/cell) whereas the density of KMA increased (mean 1503 v 1899).

Of the 15 λMM cases, 11 were NDMM and 10 (91%) expressed BCMA whereas 4 (36%) expressed CD56. LMA was expressed in 6 (55%) cases and all co-expressed BCMA. Of the 4 patients with RRMM all expressed BCMA, 2 (50%) expressed CD56 and LMA was expressed in 2 (50%) cases. The density of BCMA on PCs decreased in RRMM (mean 1874 v 817 molecules PE/cell) while the density of LMA increased (mean 1056 v 2439). All

Conclusions

In patients with diagnosed MM, KMA and LMA are expressed on malignant PCs in over half of all cases. In κ MM, the percentage of cases expressing KMA increases in RRMM however a larger cohort of λ MM patients is required to determine whether the same is true. In κ MM and λ MM, the density of KMA and LMA increases in RRMM while the antigen density of BCMA decreases. KMA and LMA represent valuable therapeutic targets in RRMM with the combination of high antigen density and target restriction to the malignant PCs. Early studies of immunotherapy with KappaMab, a monoclonal antibody targeting KMA, have shown encouraging results^{5,6}. A CAR T-cell targeting KMA is under development and may offer a useful option to patients with MM who have failed BCMA directed therapy.

References

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