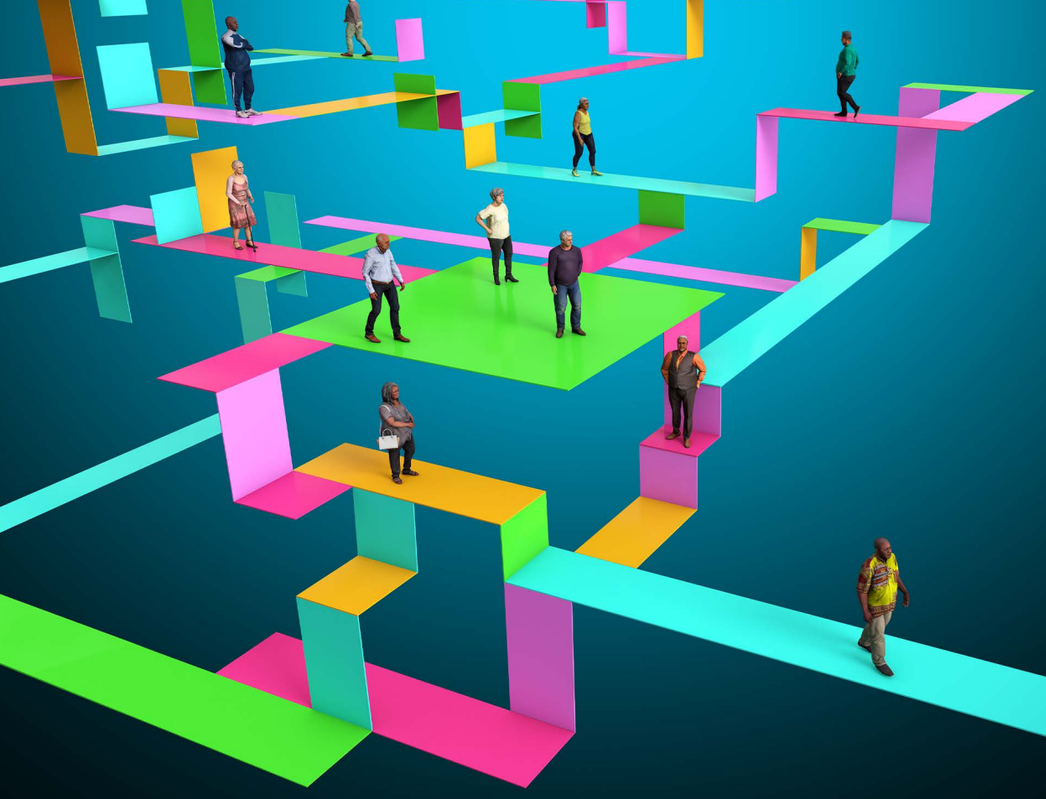


IN THE MAZE OF MULTIPLE MYELOMA,

BCMA-DIRECTED BsAbs MAY PROVIDE A NEW WAY FORWARD[1,2]

A COMPLEX DISEASE

Multiple myeloma (MM) is considered an incurable disease with inevitable relapse and ongoing unmet needs, leaving no clear way forward. Innovative approaches that enhance tumor-specific immune activity with the potential to provide deep and durable responses and improve QOL are urgently needed for all patients, including those with varying clinical risk factors, performance status, and prior therapies.[1,3-6]

BCMA IS A PROMISING THERAPEUTIC TARGET IN MM[7]

BCMA is a universally present and overexpressed antigen in MM that may offer a new path:

BCMA is a tumor-associated antigen that is universally present and expressed at higher levels on malignant plasma cells compared with nonmalignant cells.[1-3]

Selectively expressed on plasma cells:

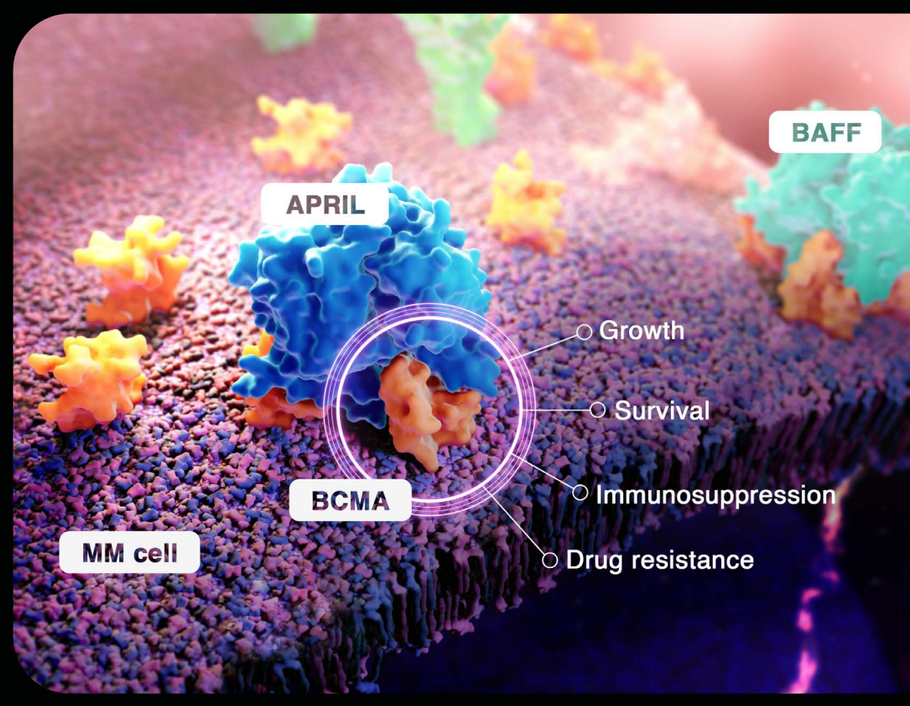
BCMA is a transmembrane glycoprotein of the TNFR superfamily. It is expressed on late-stage B-cells and on the surface of plasmablasts and differentiated plasma cells, and has minimal expression on hematopoietic stem cells or nonhematopoietic tissue.[1,3,8]

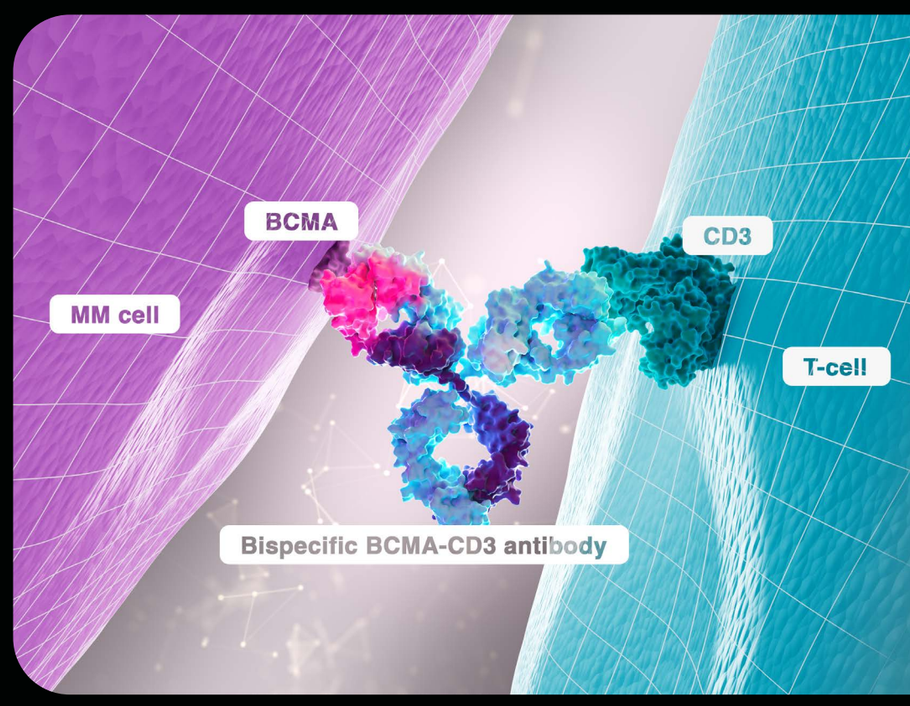
Associated with disease progression:

BCMA overexpression and activation can upregulate various pathways and enhance expression of genes critical for survival, growth, metastasis, and immunosuppression.[3,9]

Associated with drug resistance:

BCMA overexpression leads to enhanced expression of IL-10, PD-L1, and other immune-regulatory genes that are thought to suppress the immune response in the bone marrow microenvironment. BCMA is also detectable on pDCs, which protect MM cells in the bone marrow microenvironment and play a role in drug resistance.[7-9]





Current immunotherapeutic approaches targeting BCMA in MM include[3,7,10]:

- Bispecific antibodies (BsAbs)
- Antibody-drug conjugates (ADCs)
- Chimeric antigen receptor (CAR) T-cells

BCMA-directed BsAbs have the potential to function as tumor-recognizing immune enhancers[1,2,11-13]

BsAbs designed to target BCMA and CD3 on T-cells simultaneously have the potential to function as tumor-recognizing immune enhancers—they can bring T-cells into close proximity to MM cells, leading to T-cell activation and antitumor response.[1-3,12,13]

BCMA=B-cell maturation antigen; CD=cluster of differentiation; IL-10=interleukin 10; pDCs=plasmacytoid dendritic cells; PD-L1=programmed death-ligand 1; QOL=quality of life; TNFR=tumor necrosis factor receptor.

Tap for References

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References: 1. Caraccio C, Krishna S, Phillips DJ, Schürch CM. Bispecific antibodies for multiple myeloma: a review of targets, drugs, clinical trials, and future directions. *Front Immunol*. 2020;11:501. doi:10.3389/fimmu.2020.00501 **2.** Nadeem O, Tai YT, Anderson KC. Immunotherapeutic and targeted approaches in multiple myeloma. *Immunotargets Ther*. 2020;9:201-215. doi:10.2147/ITT.S240886 **3.** Shah N, Chari A, Scott E, Mezzi K, Usmani SZ. B-cell maturation antigen (BCMA) in multiple myeloma: rationale for targeting and current therapeutic approaches. *Leukemia*. 2020;34:985-1005. doi:10.1038/s41375-020-0734-z **4.** Chim CS, Kumar SK, Orlowski RZ, et al. Management of relapsed and refractory multiple myeloma: novel agents, antibodies, immunotherapies and beyond. *Leukemia*. 2018;32:252-262. doi:10.1038/leu.2017.329 **5.** Ramsenthaler C, Osborne TR, Gao W, et al. The impact of disease-related symptoms and palliative care concerns on health-related quality of life in multiple myeloma: a multi-centre study. *BMC Cancer*. 2016;16:427. doi:10.1186/s12885-016-2410-2 **6.** Mikhael J. Treatment options for triple-class refractory multiple myeloma. *Clin Lymphoma Myeloma Leuk*. 2020;20:1-7. doi:10.1016/j.clml.2019.09.621 **7.** Cho SF, Anderson KC, Tai YT. Targeting B cell maturation antigen (BCMA) in multiple myeloma: potential uses of BCMA-based immunotherapy. *Front Immunol*. 2018;9:1821. doi:10.3389/fimmu.2018.01821 **8.** Tai YT, Anderson KC. Targeting B-cell maturation antigen on multiple myeloma. *Immunotherapy*. 2015;7:1187-1199. doi:10.2217/imt.15.77 **9.** Tai YT, Acharya C, An G, et al. APRIL and BCMA promote human multiple myeloma growth and immunosuppression in the bone marrow microenvironment. *Blood*. 2016;127:3225-3236. doi:10.1182/blood-2016-01-691162 **10.** Cho SF, Lin L, Xing L, et al. BCMA-targeting therapy: driving a new era of immunotherapy in multiple myeloma. *Cancers (Basel)*. 2020;12:1473. doi:10.3390/cancers12061473 **11.** Zhou X, Einsele H, Danhof S. Bispecific antibodies: a new era of treatment for multiple myeloma. *J Clin Med*. 2020;9:2166. doi:10.3390/jcm9072166 **12.** Swann JB, Smyth MJ. Immune surveillance of tumors. *J Clin Invest*. 2007;117:1137-1146. doi:10.1172/JCI31405 **13.** Pratt G, Goodyear O, Moss P. Immunodeficiency and immunotherapy in multiple myeloma. *Br J Haematol*. 2007;138:563-579. doi:10.1111/j.1365-2141.2007.06705.x

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Tap to close

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