BCMA-DIRECTED BISPECIFIC ANTIBODIES:

An emerging immunotherapeutic approach in multiple myeloma (MM)[1-3]

MM is considered an incurable disease and relapse is inevitable, leading to the development of relapsed and refractory multiple myeloma (RRMM)[4,5]

New treatments are needed for RRMM patients that explore novel therapeutic targets and counter mechanisms that lead to treatment resistance, including immune evasion[3,4]

BCMA is a promising therapeutic target in MM[2]

Selectively expressed on plasma cells:

BCMA is expressed on B-lineage cells, particularly plasmablasts and differentiated plasma cells, with minimal expression on hematopoietic stem cells or nonhematopoietic tissue[4,6]

Overexpressed in MM:

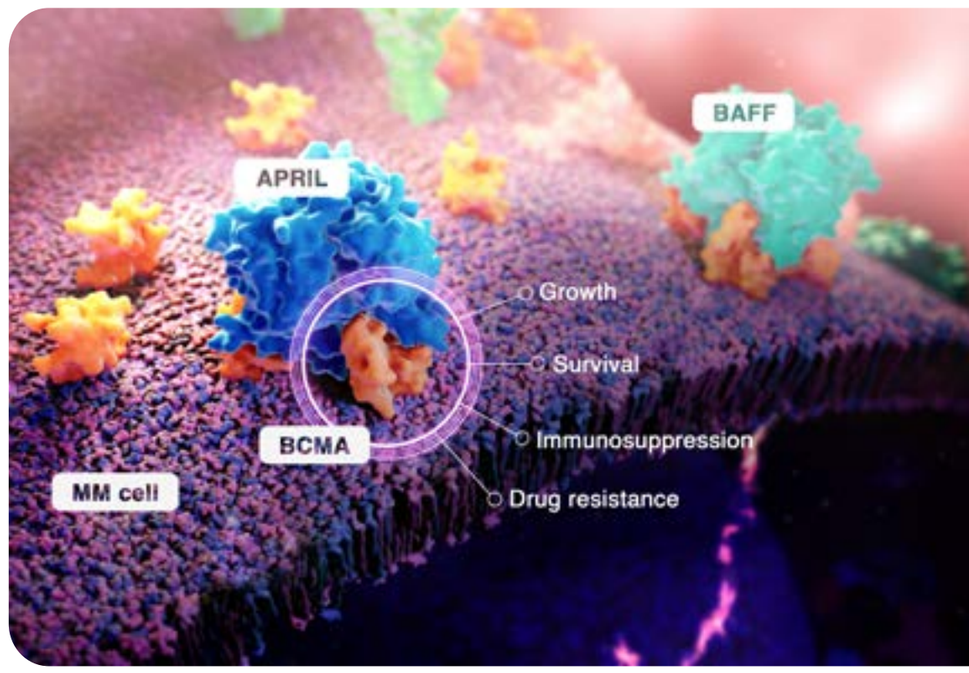
BCMA is expressed at higher levels on malignant plasma cells compared with nonmalignant cells[4,7]

Associated with disease progression:

BCMA overexpression and activation can upregulate various pathways and enhance expression of genes critical for survival, growth, metastasis, and immunosuppression[4,8]

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. In addition, pDCs promote survival and development of drug resistance in MM cells[4,6,8]



BCMA-directed therapies currently under investigation[1,2,4]

Bispecific antibodies (BsAbs)

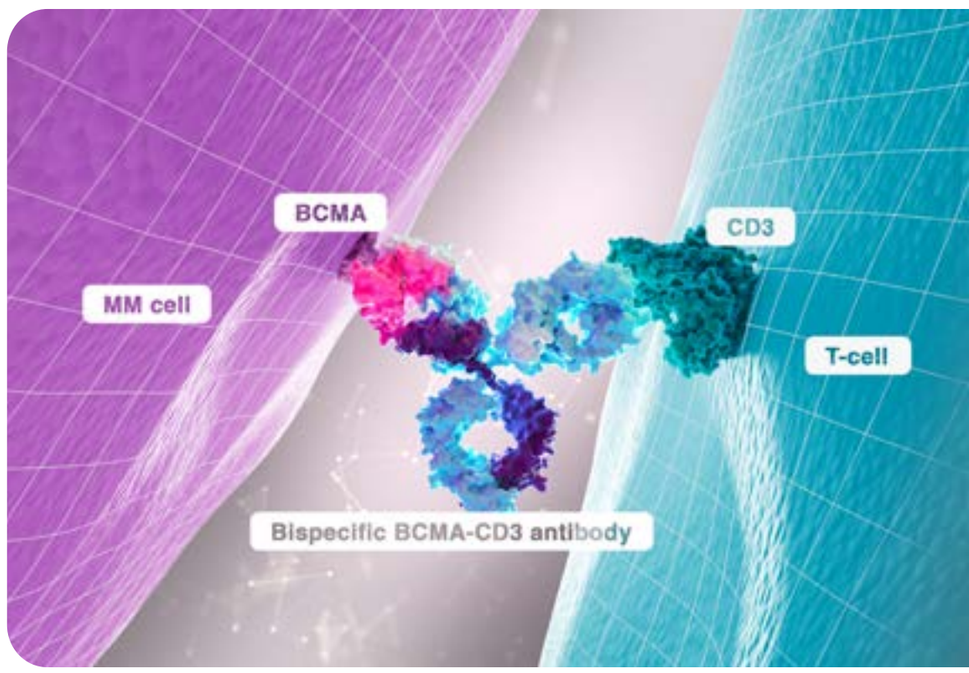
Antibody-drug conjugates (ADCs)

Chimeric antigen receptor (CAR) T-cells

BCMA-directed BsAbs are an immunotherapeutic approach currently being studied in clinical trials for the treatment of MM[9,10]

Engineered to have dual antigen specificity to facilitate cell-to-cell interactions between T-cells and malignant cells expressing tumor-specific antigens[4,11]

BsAbs can engage BCMA and CD3 simultaneously to bring T-cells in close proximity to myeloma cells, leading to potent activation and antitumor response[3,7]



APRIL=a proliferation-inducing ligand; BAFF=B-cell activating factor; BCMA=B-cell maturation antigen; CD=cluster of differentiation; IL-10=interleukin 10; PD-L1=programmed death-ligand 1; pDCs=plasmacytoid dendritic cells.

Tap for References

This document contains medical information concerning a mechanism of action under investigation for treatment of MM.

Pfizer Oncology

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References: 1. Cho SF, Lin L, Xing L, et al. BCMA-targeting therapy: driving a new era of immunotherapy in multiple myeloma. *Cancers.* 2020;12:1473. doi:10.3390/cancers12061473 **2.** 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 **3.** Nadeem O, Tai YT, Anderson KC. Immunotherapeutic and targeted approaches in multiple myeloma. *Immunotargets Ther.* 2020;9:201-215. doi:10.2147/ITT.S240886 **4.** 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.org/10.1038/s41375-020-0734-z **5.** 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 **6.** Tai YT, Anderson KC. Targeting B-cell maturation antigen on multiple myeloma. *Immunotherapy.* 2015;7(11):1187-1199. doi:10.2217/imt.15.77 **7.** 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 **8.** 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 **9.** PF-06863135 as a single agent and in combination with immunomodulatory agents in relapse/refractory multiple myeloma. ClinicalTrials.gov. Published August 31, 2017. Updated June 2, 2021. Accessed June 25, 2021. Clinicaltrials.gov/ct2/show/NCT03269136 **10.** Study of PF 06863135 in Japanese participants with multiple myeloma. ClinicalTrials.gov. Published March 15, 2021. Updated June 2, 2021. Accessed June 25, 2021. Clinicaltrials.gov/ct2/show/NCT04798586 **11.** Huehls AM, Coupet TA, Sentman CL. Bispecific T-cell engagers for cancer immunotherapy. *Immunol Cell Biol.* 2015;93:290-296. doi:10.1038/icb.2014.93

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Tap to Close

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