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What is the rationale for targeting BCL-2 in AML?

B-cell lymphoma-2 (BCL-2) is anti-apoptotic or pro-survival protein that is localized to the mitochondria. It is a member of the BCL-2 family of proteins, several other proteins including BCL-XL and MCL-1 can function in a similar fashion. Expression levels of BCL-2 are generally high in AML in comparison to normal bone marrow progenitor cells. This offers the rationale for targeting BCL-2 in AML, and additionally, there's a concept of addiction or dependence of AML cells toward certain BCL-2 family members. Acute myeloid leukemia (AML) is thought to be a BCL-2 driven disease, meaning that the survival of AML blasts depends on BCL-2, while in normal cells this may not be the case. So BCL-2 is thought to be critical for survival of AML blasts, and preclinical data have indicated that use of BCL-2 inhibitors can induce cell death in the majority of primary AML cells.[1]

For more information on intensive therapy, please view the full newsletter by clicking here.
(https://managingaml.com/ce-education/39-apoptosis-and-selective-bcl-inhibition-changing-treatment-paradigms-in-aml)

Reference:
1. Konopleva M, Contractor R, Tsao T, et al. Mechanisms of apoptosis sensitivity and resistance to the BH3 mimetic ABT-737 in acute myeloid leukemia. *Cancer Cell.* 2006;10(5):375-388. doi:10.1016/j.ccr.2006.10.006