

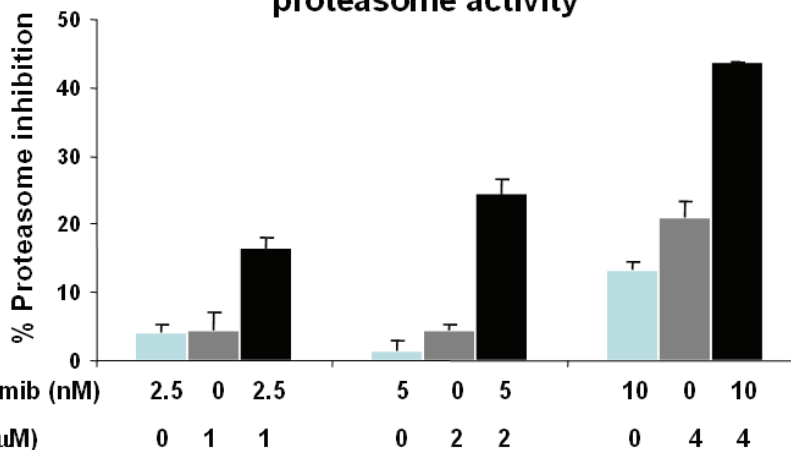
Combination Therapy using a Clioquinol Analogue and Bortezomib (Velcade) for Treatment of Lymphoid Malignancies

Overview of Technology:

Acute myeloid leukemia (AML) and multiple myeloma (MM) are malignant diseases resulting in the proliferation of abnormal cells of myeloid and lymphoid origin, respectively. Both diseases are characterized by poor responses to standard therapies. For example, elderly patients with either AML or myeloma and poor risk cytogenetics have a median survival of less than one year. Thus, for these patients and those with relapsed refractory disease novel therapies are needed. As many of these patients are frail, therapies that achieve an anti-myeloma or anti-leukemia effect without significant toxicity are highly desirable.

A high throughput screen identified the clioquinol analogue 5AHQ as an inhibitor of cyclin D2 transactivation, which is over-expressed in patients with high risk AML and MM. 5AHQ was subsequently shown to inhibit proteasome activity by binding to the same complex at a site independent from the active site. Inhibition of proteasome function has recently been demonstrated to be an effective treatment strategy for multiple myeloma. Subsequently, the researchers demonstrated that 5AHQ in combination with Velcade (bortezomib), the only existing licensed anti-cancer proteasome inhibitor, has synergistic effects for inducing cell death in hematological malignancies including multiple myeloma and leukemia cells.

5AHQ enhances Bortezomib inhibition of proteasome activity



Thus the use of 5AHQ in combination with Velcade provides the potential for a new approach to treat proliferative diseases involving increased expression of D-cyclins and/or hematological malignancies, such as leukemias including acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL), and multiple myeloma (MM).

Patent:

PCT/CA2010/000282 - Filed 2 March 2010

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UHN Reference # - 9009