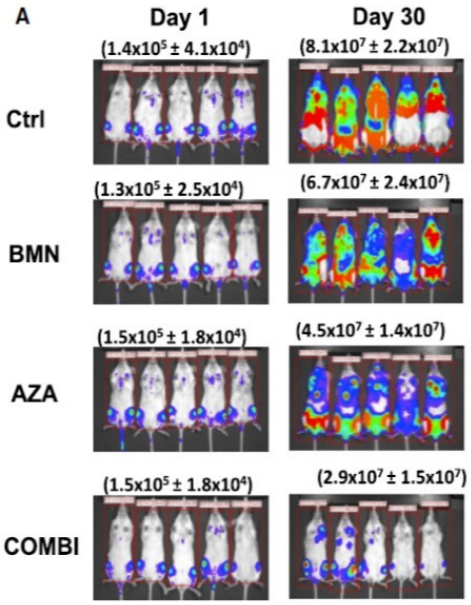
TECHNOLOGY

Therapy Regimen and Methods to Reprogram Cancer Cells and Sensitize Multiple Cancers to PARP Inhibitors

OVERVIEW

Epigenetics is the regulation of genomic functions including the reversible modification of gene expression through DNA methylation and histone modifications (acetylation, methylation, phosphorylation). Dysregulation of epigenetic modifications can lead to the development of diseases. However, due to the reversible nature of epigenetic changes, there is considerable interest in the development of therapeutic inhibitors. This technology is a method of using a combination treatment using a low dose of a DNA demethylating (DNMT) agent in conjunction with a PARP inhibitor to increase the cytotoxic effects for the treatment of cancers.

This technology has been demonstrated in multiple cancer types (leukemia, breast, ovarian, and lung) using low dose Dacogen (10nM) or Vidaza (50 nM) in combination with a PARP inhibitor (Veliparib or BMN673) to demonstrate enhanced efficacy in *in vitro* and *in vivo* studies. In particular, the drug combination of Vidaza and BMN673 strikingly decrease tumor burden when used *in vivo* to treat immuno-incompetent mice bearing human AML. These results suggest that DNMT agents can distinctly augment the cytotoxic effects of PARP inhibitors on tumor cells leading to the enhanced efficacy of these latter inhibitors to treat AML and other cancers.



APPLICATIONS

Recent studies have shown that epigenetics plays a central role in many types of diseases, including cardiovascular diseases, neurological diseases, metabolic disorders, and cancer. The epigenetic market is experiencing exponential growth due to the wide application of epigenetic modifiers, intense research interest, and the influx of investor support and strategic industry alliances. Currently, there are two FDA approved DNMT inhibitors, Dacogen (DAC, Eisai) and Vidaza (5-AZA, Celgene), and two HDAC inhibitors Zolinza (vorinostat, Merck) and Istodax (romidepsin, Celgene). Though current targets remain solid tumors and hematological cancers, there is growing evidence suggesting epigenetic mechanisms contribute to the pathogenesis of a wide range of diseases. Research suggests that environmental factors such as nutrition and the microbiome play a greater role than previously assumed. The three segments of the epigenetic market are research tools, therapeutics, and diagnostics, with the diagnostic sector growing the fastest due to demands for research tools and companion diagnostics for developing therapies.

ADVANTAGES

This combined low dose regimen offers a novel strategy to increase cytotoxic effects of both DNA demethylating agents and PARP inhibitors to reprogram cancer cells for a therapeutic effect.

STAGE OF DEVELOPMENT

Phase I Clinical Trials: AML

Additional *in vivo* studies

(RB- 9/2017)

LICENSING POTENTIAL

Available for licensing

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PATENT STATUS

US Patent CON 10,105,382, CON 10,105,383, issued 10/23/18, US patent 10,363,264 issued on 7/20/19, EU patent 15 740 207.4,

LICENSE STATUS

Available for licensing

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ATTACHMENTS

- Download FR-2013-075 market sheet final.pdf

EXTERNAL RESOURCES

- Enhancing the Cytotoxic Effects of PARP Inhibitors with DNA Demethylating Agents - A Potential Therapy for Cancer.

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