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A MODEL FOR ACUTE MYELOID LEUKEMIA (AML)

Fabio A. Milner* and
Jana van den Berg

School of Mathematical and Statistical Sciences,
Arizona State University, USA

fmilner@asu.edu (*corresponding author),
jevanden@asu.edu

Idasanutlin (RG7388) is a potent and selective MDM2 antagonist showing promising responses in phase I studies in relapsed/refractory AML. The drug is presently undergoing Phase I and II clinical trials. RG7388 was generally well tolerated with GI toxicity being the most commonly reported adverse event. In laboratory cultures of MOLM-13 wild type cells it was observed that using increasing dosages of RG7388 led, within 96 days, to a complete replacement of wild type (drug-sensitive) cells by mutant (drug-resistant) cells. We propose a model for the growth of the two strains of cells in such cultures that is designed to elucidate whether the replacement is due to the natural mutation of the wild type cells or rather to the use of RG7388 for AML treatment.