SAPACITABINE

Orally available 2’-deoxyribosyl analogue, converted to CNDAC in vivo

Incorporated into DNA during replication or repair, resulting in siDNA breaks via a covalent rearrangement

During further rounds of replication, siDNA breaks converted to dSNA breaks, resulting in cell death

Active in solid tumors (BRCA mutated breast, ovarian, and pancreatic cancers) and hematological malignancies (AML, MDS)

Synergy between venetoclax and cytotoxic therapy in AML models is mediated by combined targeting of hypomethylating agents (HMA)

CNDAC treatment increases p53, Puma and Noxa protein levels and combines synergistically with BCL2 inhibitors

CNDAC (2’-cyano-2’-deoxy-arabino-furanosylcytosine, the active metabolite of sapacitabine), was synergistic with BCL2 inhibitor ABT737 in inducing apoptosis in AML cell line M4a-11 (Frame et al., 14th EHA, 2009, Abs 0761)

CNDAC (Green S et al., Leukemia, 2018)

DOSING SCHEDULE

Cohort 1: Sapacitabine bid x 5 days every 4 weeks

Cohort 2: Sapacitabine bid x 3 days/week for 2 weeks every 4 weeks

ENROLLMENT

Cohort 1 Sapacitabine 250 mg b.i.d. x 5 days/venetoclax q.d. x 14 days

1. 5 patients dosed

2. Prior therapies included eposmal ara-C/daunorubicin, cladribine, dacarbazine, melphalan, cytarabine

Cohort 2 Sapacitabine 300 mg b.i.d. x 3 days/week x 2 weeks/venetoclax q.d. x 14 days

1. 2 patients dosed

2. Prior therapies included ara-C/daunorubicin, cladribine, dacarbazine, melphalan, cytarabine