Table 1. Overview on recent preclinical and clinical application of CDK inhibitors in hematological malignancies as well as potential combination partners showing boosted effects.

CDK inhibitor	Target structure	Entity	Main mechanism	Synergistic effects in combination with…	Study type pre-clinical	Study type clinical	Ref.
palbociclib	CDK4/6	AML, B-ALL, CML, CLL, MCL, DLBCL, BL, ALCL, MM	Rb dephosphorylation, G1 arrest/senescence, apoptosis, autophagy	AML: sequential low-dose cytarabine, danusertib, MK-2206 ALL: FGFR1 inhibitor PD-173074, imatinib MM: dexamethasone, bortezomid CML: ponatinib MCL: ibrutinib, PI3K inhibitors (re-sensitization) MM: dexamethasone, bortezomib	✓	✓	14, 17, 20-22, 25-30, 32, 33, 35-40, 42-45
ribociclib	CDK4/6	AML, ALL	G1 arrest/senescence/apoptosis	ALL: dexamethasone, everolimus	✓	✓	48, 49, 51
abemaciclib	CDK4/6	AML, MCL, DLBCL, MM	G1 arrest/senescence, autophagy, decreased MAPK and AKT pathway signaling				54-58
lerociclib	CDK4/6	AML, ALL, CML, BL	decreased Rb phosphorylation, G1 arrest		✓		59, 83
roniciclib	Pan-CDKs (CDK1/2/3/4/7/9)	CLL, HL			✓	✓	113
flavopiridol	Pan-CDKs (CDK1/2/4/6/7/9)	AML, ALL, CML, CLL, DLBCL	cell cycle arrest , MCL-1, BIM and NOXA reduction, ER stress-mediated death	AML/MM: venetoclax/obatoclax CML: pyrrolo-1,5-benzoxazepine compounds	✓	✓	79, 80, 82, 83, 86, 113
voruciclib	Pan-CDKs (CDK1/2/4/5/6/8/9)	AML, CLL, FL, MCL, DLBCL, AML	Mcl-1 and c-Myc downregulation, caspase-3 and PARP-dependent apoptosis, JNK and p38	AML: venetoclax	✓	✓	61, 107

			phosphorylation, NOXA induction				
THZ1	CDK7/12/13	AML	apoptosis	MM: venetoclax or carfilzomib	✓	✓	75, 76
SY-1365	CDK7	AML	apoptosis	AML: venetoclax	✓		77
YKL-06-101	CDK8, mTOR	AML, ALL	growth inhibition				73
SEL120-34A	CDK8/19	AML, MDS	growth inhibition		✓	✓	74
atuveciclib	CDK9, PTEFb, GSK3	AML, MCL, BL	apoptosis	AML: venetoclax MCL: metformin	✓		66, 67, 128
AZD4573	CDK9	AML, ALL, MCL, DLBCL, BL, MM	Caspase activation, PARP cleavage, MCL-1 suppression, XIAP down-regulation	AML/ALL/ DLBCL: venetoclax DLBCL: EZH2 inhibitors EPZ6438 and GSK126	✓	✓	62
CDKI-73	CDK1, 2, 9	AML, ALL, CLL, DLBCL	MCL-1 down-regulation, apoptosis induction	AML: venetoclax CLL: fludarabine	✓	✓	65
A-1592668	CDK9	AML, NHL	reduced RNA polymerase II activity, loss of MCL-1 protein, apoptosis	AML/NHL: venetoclax	✓	✓	70
LDC526	PTEFb/CDK9	CLL	Inhibited proliferation		✓		68
dinaciclib	CDK1/2/5/9	MLL-rearranged AML, B- and T-ALL, CLL, MCL, MM	Mcl-1 downregulation, senescence	CLL: ibrutinib, venetoclax, rituximab/ ofatumumab MCL: orlistat MM: doxorubicin, PARP inhibitor ABT-888	✓	✓	47, 89, 91-93, 95-98, 100-102, 106
AT7519 (alternative name: AT7519M)	CDK1/2/4/5/9, GSK3β	CLL, MCL, MM	apoptosis, inhibition of RNA polymerase II and GSK3b phosphorylation		✓	✓	103, 104, 106
P276-00	CDK1/4/9	AML, MM	cell cycle arrest, caspase activation, Rb dephosphorylation, cyclin downregulation	MM: bortezomib	✓	✓	109-112
TG02	CDK1/2/7/ 9, JAK2, FLT3	AML, MM	G1 arrest, ERK5 blockade, intrinsic and extrinsic apoptosis induction	MM: dexamethasone, melphalan, bortezomib lenalidomide	✓		119-123

AML – acute myeloid leukemia, ALCL - Anaplastic large cell lymphoma, B-ALL – B- acute lymphoblastic leukemia, BL – burkitt lymphoma, CLL - chronic lymphoblastic leukemia, CML – chronic myeloid leukemia, DLBCL - Diffuse large B cell lymphoma, FL – follicular lymphoma, MCL - Mantle cell lymphoma, MDS - Myelodysplastic syndrome, MM – multiple myeloma, NHL – non-Hodgkin lymphoma, Rb – retinoblastoma