Table SI. Classification of chemotherapeutic drugs, including their mechanism of action, targets and running clinical trials.

First author/s, year	Types of drugs	Names	Mechanism of action	Targets	Running clinical trials	(Refs.)
Lee, 1995	Alkylating agents	Altretamine	Unknown, it is considered to induce DNA damage by producing intermediate compounds, which interact covalently with DNA strand.	Most cancer types, such as ovarian cancer, Kaposi sarcoma, prostate cancer, head and neck cancer, lymphoma, pancreatic cancer, bladder cancer, colorectal cancer, small cell lung carcinoma and others.	38	(1)
Bendamustine, 2006		Bendamustine		Most solid and hematopoietic cancers, such as breast, ovarian and lung cancer, Hodgkin and non-Hodgkin lymphomas, multiple myeloma, and others.	311	(2)
Dechant KL, 1991		Ifosfamide		Testicular and germ cell cancers, breast, pancreatic, lung, kidney, bladder, ovarian, cervical and brain cancer, and unspecific solid cancers.	469	(3)
O'Marcaigh, 1996		Busulfan	Upon hydrolysis, the produced carbonium ions induce DNA alkylation, which results in adenine-guanine crosslinking. Disturbing DNA replication and RNA transcription processes.	Vast majority of hematological cancers, multiple myeloma, brain cancers, sarcoma, breast, liver and renal cancer, and other solid cancers.	493	(4)

Fox, 2000		Carboplatin	In general, they induce DNA damage in three different mechanisms: i) Induce mispairing of DNA nucleotides; ii) induce DNA fragmentation upon alkylation. This action is a consequence of DNA repair mechanisms attempting to replace the alkyl group; and iii) interatomic-crosslinking of DNA strand, thus preventing the separation of the double strand. Overall, preventing DNA synthesis and replication.	Variety of solid cancers, mainly ovarian, breast, lung, endometrial, prostate, head and neck, and cervical cancer.	2,645	(5)
Vidal L, 2016		Chlorambucil		Mainly leukemia and lymphoma, also gastric and bladder cancer.	65	(6)
Dasari S, 2014		Cisplatin		Majority of solid and epithelial cancers, such as ovarian, breast, gastric, lung, bladder, esophageal, head and neck, gallbladder, cervical and pancreatic cancer, and others.	3,589	(7)
Emadi A, 2009		Cyclophosphamide		Breast, prostate, ovarian, lung, pancreatic, endometrial, colorectal, and head and neck cancer, and hematopoietic malignancies.	3,400	(8)
Nichols, 2006		Mechlorethamine		Advanced solid cancers, prostate, ovarian, brain, breast, colon, esophageal and lung cancer, neuroblastoma, multiple myeloma, and hematological cancer.	232	(9)
Thirumaran R, 2007		Melphalan		Liver, prostate, pancreatic, colorectal, breast and ovarian cancer, central nervous system cancers, sarcomas, multiple myeloma, leukemia and lymphoma.	813	(10)
Koprowska K, 2011		Dacarbazine	Unknown, it may inhibit DNA synthesis by acting as an analog for purines and/or interacting with SH (thiol) group on DNA strands. It is	Melanoma, sarcomas, neuroendocrine cancers, thyroid and lung cancer, and Hodgkin lymphomas.	218	(11)

			also considered to induce DNA alkylation preventing nucleic acid synthesis.			
Riddell, 2018		Oxaliplatin	Non-enzymatic lysis of oxaliplatin produces diaquo cyclohexanediamine platinum reactive derivatives, which bind to the guanine and cytosine and thus enhance DNA crosslinking. Eventually, inhibiting nucleic acid function.	Breast, head and neck, colorectal, liver, gastric, esophageal, pancreatic, ovarian, prostate, lung, endometrial and thyroid cancer, cholangiocarcinoma, and B cell lymphoma.	2,033	(12)
Thomas, 2017		Temozolomide	Activated upon the conversion to 3-methyl-(triazen-1-yl) imidazole-4-carboxamide, which induces DNA alkylation at specific positions of guanine and adenosine. The specific guanine methylation leads to DNA strand breaks and thus induces cell death (apoptosis). It is also suggested that the active derivatives interfere with the DNA mismatch repair system, leading to failure in finding a complementary base for methylated guanine. This induces DNA nicking, which inhibits the replication process and sequesters	Colorectal, breast, ovarian, prostate, lung and gastrointestinal cancer, glioblastoma, astrocytoma and glioma neuroblastoma.	928	(13)

			the cell at G_2-M phase, thus blocking the cell cycle.			
Beilke LD, 2014		Thiotepa	Unspecific drug, it crosslinks the DNA strand at guanine residue upon alkylation. Preventing DNA unwinding and replication, thus inhibiting the cell division process.	Brain, ovarian and testicular, breast, and hematologic cancer, and sarcomas.	233	(14)
Carter NJ, 2007		Trabectedin	It may affect the transcription-coupled nucleotide excision repair system by alkylating guanine residues upon the interaction with the DNA minor groove. It inhibits G_2 phase and cell division, as well as the expression of multi-drug resistance gene, which is responsible for developing resistance to treatment in cancer cells.	Sarcomas, prostate, ovarian, breast, pancreatic and peritoneal cancer, and unspecified childhood cancer.	93	(15)
Pai VB, 2000	Nitrosoureas alkylating agents sub group	Carmustine	Induces DNA alkylation that results in adenine-guanine crosslinking. Disturbing DNA replication and RNA transcription processes. It also interferes and modifies glutathione reductase.	Multiple myeloma, glioblastoma and brain cancers, and Hodgkin and non-Hodgkin lymphomas.	238	(16)
Krug S, 2015		Streptozocin	Upon activation produces methyl-carbonium ions, which induces DNA alkylation and crosslinking,	Pancreatic, neuroendocrine and brain cancers.	15	(17)

			and thus inhibits nucleic acid synthesis. Manipulates different biochemical reactions, such as NAD and NADH, and inhibits essential enzymes for gluconeogenesis.			
Nikolova T, 2017		Lomustine and semustine	Upon hydrolysis, produces reactive metabolites that induce DNA alkylation and crosslinking. Inhibits nucleic acid synthesis and the cell cycle, while it induces cytotoxicity.	Glioblastoma and brain cancers, and relapsed Hodgkin lymphoma, melanoma and neuroectodermal cancers.	116	(18)
Lombardi G, 2014		Fotemustine	Interferes with actin and tubulin polarization by inhibiting thioredoxin reductase 1.	Melanoma, relapsed glioma, brain metastasis and central nervous system lymphomas.	13	(19)
Endo T, 2020		Nimustine	Interferes with DNA to induce its fragmentation and inhibits protein synthesis.	High grade glioma.	1	(20)
Kameoka Y, 2018		Ranimustine	Crosslinks DNA strands and inhibits DNA synthesis.	Leukemia and lymphoma.	1	(21)
Kennedy BJ, 1961		Uracil mustard	Crosslinks DNA strands and inhibits DNA synthesis.	Lymphoma.	n/a	(22)
El Fakih R, 2018	Antimetabolites	Azacitidine	At low doses, binds covalently to DNA methyltransferase by inducing hypomethylation and preventing nucleic acid synthesis. At high doses, induces cytotoxicity upon incorporation with RNA and DNA.	Myeloid and lymphoid malignancies. It can be used with solid cancers, such as head and neck, pancreatic, prostate, colorectal, esophageal, and non-small cell lung cancer.	523	(23)

			It has higher affinity toward RNA, preventing the assembly of polyribosomes and inhibiting protein synthesis, thus causing cell death.			
Longley DB, 2003		5-fluorouracil	Binds covalently to thymidylate synthase with methylenetetrahydrofolate, thus inhibiting thymidylate synthesis from uracil. It blocks DNA and RNA synthesis and promotes cell death. Additionally, it interacts with uridine triphosphate of RNA, leading to the disfunction of RNA processing and the inhibition of protein synthesis.	Esophageal, gastric, colorectal, breast, biliary tract, stomach, colorectal, head and neck, nasopharyngeal, cervical, endometrial pancreatic, and renal cancer. Basal, squamous cell and hepatocellular carcinoma.	2,125	(24)
Bostrom, 1993		6-mercaptopurine	Is converted to TIMP via the action of the enzyme hypoxanthine guanine phospho-ribosyltransferase. TIMP prevents the conversion of inosinic acid to xanthylic acid and adenylic acid, respectively. Therefore, it interferes with purine metabolism and blocks purine synthesis. Additionally, TIMP undergoes methylation to form MTIMP, which inhibits glutamine-	A range of hematological cancers, mostly for acute myeloid and lymphatic leukemia.	201	(25)

			5-phosphoribosylpyrophosphate amidotransferase. The latter is the most important enzyme for purine ribonucleotide synthesis.			
Walko, 2005		Capecitabine (Xeloda)	Requires activation to its cytotoxic derivative fluorouracil. The fluorouracil and methylenetetrahydrofolate bind covalently to thymidylate synthase, thus inhibiting thymidylate synthesis from uracil. They block DNA and RNA synthesis and promote cell death. Additionally, fluorouracil interacts with uridine triphosphate of RNA, leading to the disfunction of RNA processing and the inhibition of protein synthesis.	Breast, gastric, colorectal, pancreatic, biliary tract, thyroid and metastatic solid cancer. Hepatocellular and nasopharyngeal carcinomas.	1,688	(26)
Spurgeon, 2009		Cladribine	May undergo phosphorylation by deoxycytidine kinase and form intermediate metabolites, such as nucleotide cladribine triphosphate. The intermediate metabolites accumulate in specific cells (such as lymphocytes) that are saturated with deoxycytidine kinase, while they have less deoxynucleotidase. This reduces DNA synthesis, induces	Hematological cancers, such as acute myeloid leukemia and other myeloid neoplasms, and lymphomas.	82	(27)

			DNA strand breaks and blocks repair mechanisms. Additionally, high levels of the intermediate metabolites inhibit ribonucleotide reductase, which in turn leads to the inconsistency in dNTP pools, and induces DNA breaks, while reducing DNA repair and synthesis. It also leads to the depletion in ATP and NAD, and eventually causes cell death. Cladribine leads to the accumulation of cells at G_1 phase of the cell cycle, preventing them from entering into S phase.			
Pui, 2005		Clofarabine	Is activated and converted to 5-monophosphate and 5-triphosphate via enzymatic actions of deoxycytidine kinase and mono/di phospho-kinases, respectively. These intermediate metabolites inhibit ribonucleotide reductase, thus depleting dNTP levels, and block DNA synthesis. They also compete with DNA polymerases leading to the termination of DNA elongation. Disrupting DNA repair mechanisms as the triphosphate	Relapsed pediatric cancers, acute myeloid and lymphatic leukemia, and Hodgkin and non-Hodgkin lymphomas.	159	(28)

			metabolite incorporates into DNA strands during repairing process. It also affects mitochondrial membrane integrity, inducing the apoptotic pathway via the enhancement of releasing cytochrome C and pro-apoptotic factors.			
Murphy, 2017		Cytarabine	Unknown specificity. It can inhibit DNA polymerase and may incorporate into RNA and DNA. Cytarabine has a specificity to kill cells in S phase of the cell cycle (DNA synthesis phase).	A range of hematological cancers, such as acute and chronic myeloid leukemia, and lymphoblastic leukemia. At lower level for prostate, breast and brain cancers.	1,302	(29)
Dhillon, 2020		Decitabine	Upon activation, it is converted to decitabine triphosphate, which inhibits DNA methyltransferase upon direct integration into DNA strands. Therefore, it induces DNA hypomethylation (the methyltransferase leads to the methylation of newly synthesized DNA), and eventually drives the cells into apoptosis or cellular differentiation. The inhibition of DNA methylation but not DNA synthesis in cancer cells might be	Solid and hematological cancer, such as liver, ovarian, prostate, lung, breast, colorectal, head and neck, and pancreatic cancer, and acute and chronic myeloid leukemia.	370	(30)

			crucial to restore normal gene function to control cellular proliferation and differentiation. Decitabine has a specificity to kill cells in the S phase of the cell cycle (DNA synthesis phase).			
Floxuridine, 2012; Power, 2009		Floxuridine	It is catabolized into an intermediate metabolite called 5-fluorouracil. The fluorouracil and methylenetetrahydrofolate bind covalently to thymidylate synthase, thus inhibiting thymidylate synthesis from uracil. They block DNA and RNA synthesis and promote cell death. Additionally, fluorouracil interacts with uridine triphosphate of RNA, leading to the disfunction of RNA processing and the inhibition of protein synthesis.	Metastatic cancer and gastrointestinal, colorectal, ovarian, liver, esophageal, nasopharyngeal and appendix cancer.	59	(31,32)
Anderson, 2007		Fludarabine	It enters phosphorylation/dephosphorylation cycles, and produces several intermediate metabolites ending with an active intracellular form called triphosphate, 2-fluoro-ara-ATP. This active metabolite inhibits several enzymes, such as	Hematologic malignancies.	1,385	(33)

			ribonucleotide reductase, DNA polymerase α and primase, leading to the inhibition of DNA synthesis.			
Mini, 2006		Gemcitabine	It is activated and converted into two reactive metabolites gemcitabine diphosphate and triphosphate. The diphosphate metabolite inhibits ribonucleotide reductase, whereas the triphosphate integrates into DNA upon competing with endogenous deoxy nucleoside triphosphates. The metabolites can also induce thymidylate synthetase inhibition. Altogether, the drug inhibits DNA synthesis and induces cell death.	Advanced and metastatic solid cancer, such as pancreatic, ovarian, lung, bladder, breast, urethral and testicular, endometrial, biliary tract, colorectal, esophageal, and head and neck cancer. Squamous cell carcinoma and lymphoma.	2,521	(34)
Madaan K, 2012		Hydroxyurea	It is converted into free radical NO, which in turn inactivates ribonucleotide reductase upon quenching tyrosyl free radicals. Therefore, it depletes dNTP levels and blocks DNA synthesis. Hydroxyurea also inhibits DNA repair mechanisms.	Myeloid leukemias, such as chronic and acute myeloid leukemia. Head and neck, brain, squamous cell, esophageal and cervical cancer.	123	(35)
Gervasini G, 2019		Methotrexate	Upon the action of folylpolyglutamate, methotrexate is	Pediatric cancers, gestational choriocarcinoma, and head and neck,	953	(36)

			activated and converted to methotrexate polyglutamate. This active metabolite inhibits several enzymes essential for nucleotide synthesis, such as thymidylate synthase, dihydrofolate reductase, amido phosphoribosyltransferase and AICART. Therefore, it blocks nucleic acid synthesis, prevents cell division and induces cell death. Additionally, inhibition of AICART has been shown to have an anti-inflammatory effect in rheumatoid arthritis. This may suggest an additional effect of methotrexate in modulation of the cancer microenvironment and anticancer immunity; however, this requires more studies and validation.	breast, lung, colorectal, ovarian, bladder, and brain cancer. Hematological cancer, such as advanced non-Hodgkin's lymphoma, acute lymphatic leukemia and others.		
Kadia, 2017		Nelarabine	Upon activation, produces intermediate metabolites (ara-GTP), which integrates into DNA competing with endogenous deoxyGTP. This will stop DNA elongation and induce cellular destruction and apoptosis. The	Hematological cancers, especially T cell lymphoblastic leukemia and lymphoma in children and adults.	27	(37)

			cytotoxicity of nelarabine has cell cycle S-phase specificity.			
Rossi G, 2018 Seitz JF, 2004		Pemetrexed	Upon activation it produces intermediate metabolites (polyglutamate forms) via folylpolyglutamate synthetase activity. This active metabolite inhibits several enzymes, such as glycinamide ribonucleotide formyltransferase, thymidylate synthase and dihydrofolate reductase, which have essential roles in purine and thymidine biosynthesis. Therefore, it prevents DNA synthesis, and cell division, while it induces cell death.	Lung (mostly, non-small cell, pleural mesothelioma), pancreatic, head and neck, esophageal, breast, colorectal, ovarian, and gastric cancer.	845	(38,39)
Spiers, 1996		Pentostatin	It inhibits adenosine deaminase enzymatic activity, leading to the accumulation of adenosine and deoxyadenosine, and the inhibition of ribonucleotide reductase, thus blocking DNA synthesis. Additionally, it may incorporate into DNA and RNA by competing with purine base, thus exerting cytotoxic activity. The drug has cell cycle-S-phase specificity.	Leukemias, lymphomas, bladder and urothelial cancer, and multiple myeloma.	46	(40)

Dondi A, 2014		Pralatrexate	It is highly effective against cells that are actively dividing and express high levels of reduced folate carrier protein-1, which permits the entrance of the drug into the cell. Upon activation (via catalytic activity of folypolyglutamate synthase), it inhibits thymidylate synthase and dihydrofolate reductase. This will lead to reduced thymidine monophosphate levels, thus blocking DNA and RNA synthesis. It prevents cell proliferation and induces apoptosis.	Relapsed lymphomas, in particular peripheral T cell and NK cell lymphomas, relapsed leukemias, and solid cancer, such as head and neck, lung, and breast cancer.	37	(41)
Munshi, 2014		Thioguanine	It represents a favorable substrate for hypoxanthine-guanine phosphoribosyltransferase (competing with guanine and hypoxanthine). Upon enzymatic activity, it is converted to 6-thioguanilyic monophosphate, which inhibits purine synthesis by preventing the enzymatic action of glutamine-5-phosphoribosylpyrophosphate amidotransferase. The reactive metabolite competes with IMP	Leukemias, such as acute myeloid leukemia, Hodgkin and non-Hodgkin lymphomas, and brain and urothelial cancer.	88	(42)

			dehydrogenase and inhibits the conversion of IMP to XMP. It also integrates into both the DNA and the RNA via phosphodiester bonds. Altogether, it prevents purine synthesis and cell division, while it induces cell death.			
Burness, 2016		Trifluridine	It is converted to active intermediate metabolites (trifluridine monophosphate then triphosphate forms) upon phosphorylation via thymidine kinase. The triphosphate form incorporates into DNA, disturbs DNA function and synthesis, and inhibits cell division. The monophosphate metabolite, in turn, inhibits thymidylate synthetase, which is crucial for DNA synthesis as its expression is upregulated in a number of cancer cell lines.	Metastatic colorectal, rectal, metastatic breast, advanced bile duct and gallbladder, gastrointestinal, and esophageal cancer.	39	(43)
Kim, 2018	Anticancer antibiotics	Daunorubicin	They intercalate the base pairs and thus form complexes with DNA. They also reduce the activity of topoisomerase II by stabilizing the complex of topoisomerase II-DNA.	Hematological cancer, such as acute myeloid leukemia, acute monocytic, chronic myeloid and acute lymphocytic leukemia. To a lesser extent, liver cancer and sarcoma.	380	(44)

Rivankar S, 2014 Speth PA, 1988		Doxorubicin	As a result, they disturb DNA unwinding and prevent DNA replication and transcription (they may inhibit DNA helicase activity, too). Therefore, they inhibit mitotic cell division and have cytotoxic activity.	Acute lymphoblastic and myeloid leukemia, Hodgkin lymphoma, Wilms' cancer, neuroblastoma, sarcomas, and breast, ovarian, bladder, thyroid, liver, gastric, and primary and metastatic breast cancer.	2,127	(45,46)
Conte, 2000 Petrioli R, 2008		Epirubicin		Mainly for breast cancer. Also, prostate, lung, gastric, esophageal, liver, pancreatic, gallbladder and urinary bladder cancer.	504	(47,48)
Hollingshead LM, 1991		Idarubicin		Leukemia, multiple myeloma and hepatocellular carcinoma.	257	(49)
Onrust SV, 1999		Valrubicin	It intercalates with DNA and disturbs nucleic acid metabolism, preventing the nucleosides integration into nucleic acid. It induces chromosomal destruction and inhibits cell division in the G_2 phase of the cell cycle.	Mainly bladder cancer.	9	(50)
Froudarakis, 2013		Bleomycin	It chelates iron and other metal ions, assimilating an enzyme that produces free radicals (hydroxide and superoxide) upon reacting with oxygen. As a result, it damages and	Lung and trachea cancer, squamous cell carcinoma, Hodgkin and non-Hodgkin lymphoma, cervical, head and neck, ovarian, and testicular cancer, germ cell cancers, and early Kaposi sarcoma.	186	(51)

			cleaves DNA and prevents its synthesis.			
Veal, 2005		Dactinomycin	It incorporates with DNA, preventing RNA synthesis by blocking the RNA polymerase.	Wilms' cancers, childhood rhabdomyosarcoma, gestational trophoblastic cancers, Ewing's sarcoma, testicular, germ cell and kidney cancer, and melanoma.	54	(52)
Volpe, 2010 Guadagni S, 2017		Mitomycin-C	Upon activation, it crosslinks DNA strands, thus inhibiting DNA function and synthesis.	Bladder, lip, oral cavity, pharynx and esophagus cancer. Gastric, peritoneum, breast, pancreatic, biliary tract, colorectal, liver and lung cancer.	214	(53,54)
Fox EJ, 2004		Mitoxantrone (also considered as topoisomerase inhibitor)	Interferes with RNA, binds and intercalates crosslinked DNA strands, and breaks them. It is also a potent topoisomerase II inhibitor, preventing DNA unwinding and replication. It can affect both proliferating and non-proliferating cells.	Prostate, breast, ovarian and lung cancer, acute myeloid leukemia and follicular lymphoma.	298	(55)
Bailly, 2019	Topoisomerase I inhibitors	Irinotecan	It binds to the complex of topoisomerase I and DNA, preventing DNA relegation. Prevents DNA unwinding via interference with the replication fork and induces lethal DNA strand	Metastatic colorectal and pancreatic, small cell lung, cervical, breast, and gastric cancer.	1,485	(56)

			breaks. Such non-repairable defects will induce cell death (apoptosis).			
Lihua P, 2008 Nicum SJ, 2007		Topotecan	It is an uncompetitive inhibitor that binds to the enzyme-substrate complex and induces DNA base pairing. It prevents DNA ligation at the cleavage site. Such non-repairable defects will induce cell death (apoptosis).	Advanced carcinoma, ovarian, lung (small cell lung), cervical and endometrial cancer, neuroblastoma, relapsed brain cancer in children and leukemia.	400	(57,58)
Baldwin EL, 2005	Topoisomerase II inhibitors	Etoposide	It inhibits topoisomerase II by preventing DNA ligation, thus inducing apoptosis. This drug can inhibit both α and β isoforms of the enzyme, thus it has therapeutic and anticarcinogenic effects, respectively. It has cell cycle specificity, targeting cells at the S and G_2 phase of the cell cycle.	Testicular cancers, small cell and non-small cell lung, childhood kidney, gastrointestinal, breast, prostate, and ovarian cancer, germ cell cancers, brain metastasis, lymphoma, non-lymphocytic leukemia, and glioblastoma.	1,482	(59)
Sonnevel d, 1992		Teniposide	Directly binds to topoisomerase II, inhibiting its enzymatic activity and inducing DNA double strand breaks. It also exerts cytotoxic activity (cell death).	Acute lymphoblastic leukemia, lymphomas, pediatric leukemia and lymphoma. Lung and brain cancer.	21	(60)
Di Nunno V, 2020	Mitotic inhibitors (taxanes)	Cabazitaxel	It inhibits microtubule disassembly while inducing its assembly, which leads to microtubule stabilization. It	Metastatic prostate cancer. Also, breast, gastric, colorectal, esophageal, head and neck, lung, urothelial, and ovarian cancer.	119	(61)

			sequesters the cell at the metaphase preventing its progression within the cell cycle, and thus initiates apoptotic activity.			
Varnai, 2019		Docetaxel	By attaching to the tubulin subunit, it stabilizes and arrests dynamic instability of microtubules. Therefore, it blocks a number of cellular activities such as mitosis where the microtubules are vital for chromosomal alignments and the formation of the mitotic spindle. It also induces apoptosis by inhibiting Bcl-2 protein function.	Breast, ovarian, non-small cell lung and prostate cancer. Also, gastric, head and neck, pancreatic, esophageal, and bladder cancer.	2,449	(62)
Weaver, 2014		Paclitaxel		Platinum-resistant ovarian cancer, Kaposi's sarcoma, lung, breast and gastric cancer.	3,424	(63)
Yardley, 2013		Nab-paclitaxel		Advanced pancreatic cancer. Also, other advanced cancers, such as gastric, breast, and lung cancer.		(64)
Chong, 1988	Mitotic inhibitors (Vinca alkaloids)	Vinblastine	It interacts with tubulin and binds to the mitotic spindle, leading to microtubule crystallization, and induces cell death or growth arrest.	Solid cancers, such as bladder, urethral, testicular, kidney, breast, non-small cell lung, and head and neck cancer, and melanomas. Lymphomas, neuro-blastoma, Hodgkin and non-Hodgkin lymphomas, childhood cancer, and Kaposi's sarcoma.	198	(65)
Moore AS, 2011		Vincristine	It inhibits mitosis at metaphase by interacting with tubulin. Vincristine can interfere with lipid and nucleic acid synthesis, and affects cyclic AMP, glutathione and amino acid	Childhood cancer, acute lymphocytic leukemia, Hodgkin and non-Hodgkin lymphomas, Wilms' cancers, neuroblastoma, and rhabdomyosarcoma.	1,108	(66)

			metabolism. It may also interfere with $Ca^{+}2$-transport ATPase activity as well as with cellular respiration.			
Capasso, 2012		Vinorelbine	It inhibits mitosis at metaphase by interacting with tubulin. It stops cells at the G_2-M phase at concentrations close to the IC_{50}. It also induces apoptosis by inhibiting Bcl-2 protein function by reducing the formation of heterodimers between Bcl-2 and the pro-apoptotic protein BAX.	Advanced breast and non-small cell lung cancer, relapsed Hodgkin lymphoma, relapsed ovarian, and head and neck cancer. Prostate and brain cancer, Wilms' cancers, sarcoma, and esophageal and cervical cancer.	459	(67)
Frey, 1990	Corticosteroids	Prednisone	They bind to glucocorticoid receptor inducing downstream gene expression and signaling effects. For example, inhibiting phospholipase A2 reduces the synthesis of arachidonic acid and its derivatives. They inhibit the expression of inflammatory transcription factors, such as NF-kB, while they may promote anti-inflammatory genes, such as interleukin-10. They can also bind to the estrogen receptor	Mostly prostate cancer and multiple myeloma. Also, cancers of the kidney, breast, lung, head and neck, and leukemia and lymphoma.	1,076	(68)
Bruera, 1985		Methyl-prednisolone		Hodgkin and non-Hodgkin lymphoma. Leukemia, such as chronic and acute lymphatic leukemia, and multiple myeloma. Prostate, breast, lung, ovarian, and head and neck cancer.	432	(69)
Burki, 2018; Bertoli, 2018		Dexamethasone		Mostly multiple myeloma and lymphomas. Chronic and acute lymphatic leukemia, and acute myeloid leukemia. Prostate, breast, lung and ovarian cancers.	1,762	(70,71)

Kantoff, 1999 Nazer L, 2015		Hydrocortisone	preventing estrogen from inducing cell proliferation.	Breast, prostate and colorectal cancer, multiple myeloma, acute myeloid and lymphoblastic leukemia, and lymphomas.	408	(72,73)
Siddikuzzaman,, 2011	Others	All-trans-retinoic acid (tretinoin)	The exact mechanism of action is unknown. It has been demonstrated that it binds to three retinoic acid receptors (α, β and γ) and induces cellular differentiation, while it reduces the proliferation rate.	Acute promyelocytic leukemia. Breast, lung, skin cancer and leukemia.	138	(74)
Hoonjan, 2018		Arsenic trioxide	The exact mechanism of action is unknown. It may induce apoptosis by enhancing DNA fragmentation and terminal differentiation by degrading the fusion of promyelotic leukemia/retinoic acid receptor α protein.	Mainly acute promyelocytic leukemia. Also, prostate, cervical, liver, germ cell, kidney and breast cancer.	124	(75)
Asselin, 2015		Asparaginase	Converts asparagine to aspartic acid and ammonia. This reduces the level of asparagine in the plasma and specifically harms the cancer cells. Unlike normal cells, some types of cancer cells lack the asparagine synthetase enzymatic activity and thus are incapable of converting aspartic acid to asparagine, thus they	Leukemia, mainly acute lymphoblastic leukemia. Less likely, pancreatic, breast and ovarian cancer.	259	(76)

			rely on exogenous asparagine. Asparaginase eliminates exogenous asparagine, which is crucial for protein, DNA and RNA synthesis. This will lead to cell proliferation inhibition and cell death activation.			
Swami, 2015		Eribulin	It sequesters and produces nonproductive aggregates of tubulin, thus inhibiting the microtubule growth phase, while the shortening phase remains unaffected. Blocks the G_2/M cell-cycle and disrupts the mitotic spindle, which leads to apoptotic cell death.	Mostly relapsed metastatic breast cancer. Also lung, and head and neck cancer.	168	(77)
De Luca, 2015		Ixabepilone	It binds to β-tubulin and stabilizes microtubules. This prevents and stops the cells from ordinary cell division. It also binds to the αβ-tubulin heterodimer decreasing the dissociation rate and stabilizing microtubules.	Breast, head and neck, prostate and lung cancer, melanoma, non-Hodgkin lymphoma, and renal cell carcinoma.	120	(78)
Waszut, 2017		Mitotane	Unknown. It may suppress the adrenal cortex and modify steroid metabolism.	Adrenocortical cancers. Less likely, bladder and urothelial cancer.	18	(79)

Winer, 2018		Omacetaxine	It prevents protein synthesis by binding to the A-site cleft of the large ribosomal subunit.	Leukemia, specifically chronic myeloid leukemia.	18	(80)
Heo YA, 2019		Pegaspargase	Prevents the cancer cells from utilizing the exogenous source of asparagine by converting it to aspartic acid and ammonia. This may lead to cancer cell death especially if cell has no endogenous asparagine synthesis capability.	Leukemia and lymphomas, specifically acute lymphoblastic leukemia.	166	(81)
Goerne, 2008		Procarbazine	It may inhibit t-RNA synthesis and function by preventing the transmethylation of methyl groups of methionine. This leads to the inhibition of RNA and protein synthesis. It may also produce hydrogen peroxide, which can damage DNA directly.	Mostly lymphomas and brain cancers.	81	(82)
Smolewski, 2017		Romidepsin	The drug gets activated only when it enters the cell. It has a specific action against cancer cells that have high histone deacetylase activity. Upon conversion to the active metabolite, it binds to the zinc ions of the active site on histone deacetylases and eventually inhibits	Mainly T cell lymphoma, leukemia, and advanced breast, lung, pancreas, colorectal and ovary cancer.	90	(83)

			its activity. Such inhibition may lead to growth arrest and apoptosis as it restores the normal gene expression phenotype in cancer cells.			
Richon, 2010		Vorinostat	The exact mechanism is unknown. It has a specific action against cancer cells that have high histone deacetylase activity. It can inhibit the histone deacetylase activity, which may lead to growth arrest and apoptosis as it restores the normal gene expression phenotype in cancer cells.	Mostly lymphoma and leukemia. Lung, breast, kidney, bladder, pancreatic, gastric, and head and neck cancer.	257	(84)

AICART, aminoimidazole caboxamide ribonucleotide transformylase; IMP, inosinic acid; n/a, not applicable; TIMP, thioinosine monophosphate; XMP, xanthylic acid.

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