REVIEW ARTICLE

Chemotherapeutic Agents used to treat Malignant Tumors-an Essential Review

Nikolaos Andreas Chrysanthakopoulos PhD[1], Eleftheria Vryzaki MD, PhD[2]

[1]PhD in Oncology (Cand), Dental Surgeon (DDSc), Oncologist (MSc), Specialized in Clinical Oncology, Cytology and Histopathology, Dept.of Pathological Anatomy, Medical School, University of Athens, Athens, Greece. Resident in Maxillofacial and Oral Surgery, 401 General Military, Hospital of Athens, Athens, Greece.
[2]Department of Dermatology, Rio University Hospital of Patras, Greece

ABSTRACT

Every year, cancer is responsible for millions of deaths worldwide and, despite the progress that has been observed in medicine, there are still many issues that must be addressed in order to improve cancer treatment. For this reason, oncological research has been focused on finding new and efficient treatments which can relieve crucial side effects caused by conventional treatments. Different technologies are currently under assessment in clinical trials or have been already introduced into clinical practice. Cancer treatment has been characterized by the ineffectiveness of treatments and side effects, but also by hope of complete remission and treatment in many cases. Within the therapeutic choices except the choice of surgery in the case of solid tumors, antitumor drugs and radiation have been used as the treatment of choice in some cancer cases. Recently, immunotherapy has become a significant therapeutic alternative, and is now the first choice in many cases. These therapies can be applied either alone or in combination with other components. The current review presents the evolution of cancer treatments, giving emphasis to the most common chemotherapeutic agents.

Key words: Cancer, Medication, Chemotherapy, Targeted therapy, Cell therapy

INTRODUCTION

Cancer is one of the main causes of death worldwide, and many researches have focused on developing new treatments to be more efficient and to reduce the side effects caused by conventional therapies. In general, tumors become highly heterogeneous, during cancer progression, developing a mixed population of cells characterized by different molecular elements and diverse responsivity to treatments. This heterogeneity is responsible for the development of resistant phenotypes promoted by a selective pressure upon treatment management. [1]Consequently, a deep understanding of these complex processes is of vital importance in order to design precise and efficient treatments. Surgery, chemotherapy, and radiotherapy are the most common types of cancer treatments available nowadays. In 1950 monotherapy drugs only resulted in short responses in some types of cancers [2], where as the application of poly-chemotherapy in hematopoietic cancer showed that different agents act against cancer cells in different phases of their cell cycle (Table 1). Chemotherapy, in general, is therapeutic in some types of advanced cancer, such as small cell lungcancer (SCLC), ovarian cancer, etc.[3] Although chemotherapy regimens are notal ways therapeutic for various types of cancer, significant improvement in progression-free and overall Survival has been recorded. The advances in modern chemotherapy and in genetics and molecular biology resulted in the continuing reduction in death rates. Studies on the genome sequence suggested that

Address for correspondence:
Nikolaos Andreas Chrysanthakopoulos, Specialized in Clinical Oncology, 35, Zaimi Street, PC 26 223, Patra, Greece. Tel. /Fax: 0030-2610-225288

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many dysfunctions associated with cancercould be attributed to the abnormal function of some protein kinases. Targeted chemotherapy by screening for specific crucial molecular targets was introduced in 1990.[4] Targeted therapy attacks against a specific location, such as tumor vascular systemor intracellular organelles, without affecting the adjacent tissues, observation that increases to a large extent the treatment specificity, eliminating its disadvantages.[5] The current pharmacological management focused on developing kinase inhibitors.[6,7] Recently, many specific tumors have been investigated with various tyrosine kinase inhibitors (TKIs) and introduced a trend towards combining the conventional chemotherapy with these new targeted therapies.

Liposomal treatment was the next step in cancer treatment, that places agents inside liposomes, Vesicles constructed from lipid bilayers, in an effort to decrease some of the side effects of chemotherapy such as cardiotoxicity. Nano-medicine provides conventional chemotherapeutic drugs *in vivo*, increasing their bioavailability and concentration around tumor tissues, and improving their release profile.[8] Natural antioxidants and other phytochemical agents have been recently considered as anti-cancer adjuvant treatments due to their anti-proliferative and pro-apoptotic properties. [9]

The current article reviews a general and essential overview of the most applied medication used to treat malignancies focusing on conventional and modern chemotherapeutic agents and their combination that are indicated for a large spectrum of malignancy tumors.

Chemotherapeutic Agents Used in the Treatment of Cancer

Basic anticancer medication is classified into the following categories: Cytotoxic drugs with different mechanisms of action, such as Alkylating drugs and their associated agents, that act by forming covalent bonds with DNA, thereby inhibiting its replication, Antimetabolites, that inhibit or alter one or more of the metabolic reactions involved in DNA synthesis, Cytotoxic antibiotics, agents produced by microorganisms that prevent cell division in mammals, Plant derivatives that have a specific action in the formation of microtubules and therefore in the formation of the mitotic spindle, Hormones and drugs that suppress the secretion of hormones or compete with their action, and various agents that are not included in any of the previous categories and include drugs that aim at specific targets.[10](Table 1)

Alkylating agents and related substances

The main action of Alkylating agents occurs during replication, when certain parts of DNA are in the form of a single strandand are therefore more susceptible to alkylation. The effects are presented in the S phase of cell cycle causing inhibition of the G2 phase, and leading to apoptosis and cell death.[11,12]The following drugs belong to this category:Nitrogen mustards[10], Nitrosoureas[13], Alkylsulfonates[10], Triazines[14],Ethylenimines.[9](Table 1)

Antimetabolites

Antimetabolites affect the growth of cancer cells' DNA and RNA and include Folicacid antagonists[9,15], Pyrimidine analogues[16], Purine analogues.[9](Table 1).

Cytotoxic Antibiotics

These agents have a direct effect on DNA, as affect enzymes that are responsible for the reproduction of cancer cells. This category contains Anthracyclines, and other anti-cancer antibiotics such as actinomycin-D, bleomycin, mithramycin and mitomycin-C.[9,17-19](Table 1).

Mitosis Inhibitors Agents

This category contains agents thatare often plant derivatives. They stop mitosis or inhibit the action of certain enzymes, that produce proteins necessary for the proliferation of cancer cells. The agents of this category are shown in Table 1.[9,20,21]

Topoisomerase Inhibitors

These agents affect a group of enzymes called topoisomerases that participate in the overwinding orunderwinding of DNA. Topoisomerase Inhibitors are presented in Table 1.[9,22,23]

Hormones

Tumors derived from hormone-sensitive cells may be hormone-dependent. In this case, their development can be inhibited by hormones with opposite action, by hormone antagonists, or by drugs that inhibit hormones synthesis and secretion. Hormones and hormone analogues that have an inhibitoryeffect on some tissues can be used totreattumors that originate in these tissues.[9,24,25](Table 1).

Molecularly Targeted Treatment

The main categories of targeted therapy are currently monoclonal antibodies and small molecules. These agents target specific genes and proteins that are implicated in cancer cells survival and development. [24,26,27]Monoclonal antibodies are shown in antibodies (Table 1). Small molecules contain tyrosine-kinase inhibitors (TKIs). Tyrosine-kinases are enzymes involved inthe transmission of the signal from the cell membrane receptors to the cell nucleus.[28]

This category contains molecules that are able to target EGFR, Janus kinase inhibitors, ALK inhibitors, Bcl-2 inhibitors, PARP inhibitors, PI3K inhibitors, Braf inhibitors, MEK inhibitors, CDK inhibitors, act asanapoptosis-inducing proteasome inhibitor, etc.[29-33]In this category belong agents presented in Table 1.

Various Chemotherapeutic Agents

This category includes agents such as Crisantaspase, Mitotane, Amsacrine.[33-35](Table 1)

Table 1: Chemotherapeutic agents used to treat malignancies

Medication	Category	Indication(s)
Lenvatinib	TKI (Tyrosine Kinase Inhibitor)	Advanced hepatocellular carcinoma, advanced renal cancer, certain types of thyroid cancer
Neratinib	TKI	Early stage breast cancer
Nilotinib	TKI	Chronic myeloid leukemia
Nintedanib	TKI	Lung adenocarcinoma, recurrence or metastatic
Niraparib	PARP inhibitor	Some types of ovarian cancer, peritoneal cancer
Nivolumab	Monoclonal antibody	Different types of cancer
Obinutuzumab	Monoclonal antibody	Chronic lymphocytic leukemia, follicular lymphoma
Olaparib	PARP inhibitor	Ovarian, metastatic breast cancer
Palbociclib	CDK4 and CDK6 inhibitor	Advanced or metastatic, and locally advanced breast cancer
Panitumumab	Monoclonal antibody	Advanced colorectal cancer
Pazopanib	TKI	Advanced renal cell cancer, some types of advanced soft tissue sarcomas
Pembrolizumab	Monoclonal antibody	NSCLC, skin melanoma, breast cancer, stomach, cervical cancer, Hodgkin lymphoma
Pemigatinib	TKI	Cholangiocarcinoma, bile duct cancer, relapsed or metastatic
Pertuzumab	Monoclonal antibody	Breast cancer (neoadjuvant treatment, adjuvant treatment, secondary breast cancer, recurrent)
Ponatinib	TKI	Chronic myeloid leukemia, acute lymphoblastic leukemia
Regorafenib	Multi-KI	Advanced gastro intestinal stromal cancer (GIST), advanced HCC, metastatic colorectal cancer
Ribociclib	Cyclin D1/CDK4 and CDK6-inhibitor	Locally advanced, advanced or metastatic breast cancer
Rituximab	Monoclonal antibody	Chronic lymphocytic leukemia, some types of non-Hodgkin lymphoma
Rucaparib	PARP inhibitor	Relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer
Ruxolitinib	Janus kinase inhibitor	Myelofibrosis, polycythaemiavera
Sorafenib	Multi-KI	Advanced renal cell carcinoma, advanced primary HCC, FLT3-ITD positive AML and radioactive iodine resistant advanced thyroid carcinoma
Sunitinib	Multi-KI	Advanced renal cancer, gastrointestinal stromal tumor (GIST), pancreatic neuroendocrine tumors
Temsirolimus	mTOR inhibitor	Advanced renal cancer
Trastuzumab	Monoclonal antibody	Early and advanced breast cancer, advanced stomach cancer and gastro oesophageal junction cancer
Tivozanib	TKI	Relapsed or refractory advanced renal cell carcinoma
Vandetanib	TKI	Advanced medullary thyroid cancer

Vemurafenib	B-Raf enzyme inhibitor	Skin melanoma, unresectable and advanced
Venetoclax	BCL-2 inhibitors	Chronic lymphocytic leukemia, small lymphocytic lymphoma , acute myeloid leukemia
Melphalan	Alkylating agent	Multiple myeloma, ovarian cancer, melanoma
Busulfan	Alkylating agent	Chronic myeloid leukemia, myelodysplastic syndromes (MDS),other types of cancer that need treatment with a stem cell or bone marrow transplant
Chlorambucil	Alkylating agent	Chronic lymphocytic leukemia, Hodgkin lymphoma, Non-Hodgkin lymphoma
Cyclophosphamide	Alkylating agent	Lymphoma, multiple myeloma, leukemia, ovarian cancer, breast cancer, small cell lung cancer, neuroblastoma, and sarcoma
Bendamustine	Alkylating agent	Chronic lymphocytic leukemia, Multiple myeloma, Non-Hodgkin lymphoma
Carmustine	Alkylating agent	Glioma, glioblastomamultiforme, medulloblastoma and astrocytoma), multiple myeloma, and lymphoma (Hodgkin's and non-Hodgkin)
Cisplatin	Alkylating agent	Various types of cancers, including sarcomas, small cell lung cancer, squamous cell carcinoma of the head and neck and ovarian cancer, lymphomas, bladder cancer, cervical cancer, and germ cell tumors
Lomustine	Alkylating agent	Brain tumors, Hodgkin lymphoma
Ifosfamide	Alkylating agent	Testicular cancer, breast cancer, lymphoma (Hodgkin and non-Hodgkin), soft tissue sarcoma, osteosarcoma or bone tumor, lung cancer, cervical cancer, ovarian cancer
Procarbazine	Alkylating agent	Hodgkin's lymphoma and brain cancers
Streptozocin	Alkylating agent	Metastatic cancer of the pancreatic islet cells
Temozolomide	Alkylating agent	Glioblastoma multiforme (GBM), anaplasticastrocytoma
Thiotepa	Alkylating agent	Hodgkin's disease, leukemia
Trabectedin	Alkylating agent	Advanced soft-tissue sarcoma, ovarian cancer
Treosulfan	Alkylating agent	Ovarian cancer, other types of cancer
Capecitabine	Anti metabolite	Breast cancer, gastric cancer,colorectal cancer
Cladribine	Anti metabolite	Hairy cell leukemia, B-cell chronic lymphocytic leukemia
Clofarabine	Anti metabolite	Relapsed or refractory acute lymphoblastic leukemia
Fludarabine	Anti metabolite	Chronic lymphocytic leukemia, non-Hodgkin's lymphoma, acute myeloid leukemia, acute lymphocytic leukemia
Cytarabine	Anti metabolite	Acute myeloid leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, and non-Hodgkin's lymphoma
Fluorouracil	Anti metabolite	Colorectal cancer, oesophageal cancer, stomach cancer, pancreatic cancer, breast cancer, cervical cancer
Gemcitabine	Anti metabolite	Testicular cancer, breast cancer, ovarian cancer, non-small cell lung cancer, pancreatic cancer, and bladder cancer
Hydroxycarbamide	Anti metabolite	Chronic myeloid leukemia, policythaemiavera, essential thrombocythemia, acute myeloid leukemia, cervical cancer
Methotrexate	Anti metabolite	Breast cancer, leukemia, lung cancer, lymphoma, gestatio-nal trophoblastic disease, and osteosarcoma
Mercaptopurine	Anti metabolite	Acute lymphocytic leukemia, chronic myeloid leukemia
Nelarabine	Anti metabolite	T-cell acute lymphoblastic leukemia, T-cell lymphoblastic lymphoma

Pemetrexed	Anti metabolite	Pleural mesothelioma, NSCLC
Pentostatin	Anti metabolite	Hairy cell leukemia, relapsed chronic lymphocytic leukemia
Raltitrexed	Anti metabolite	Colorectal cancer, malignant mesothelioma
Tioguanine	Anti metabolite	Acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia
Liposomal doxorubicin	Anthracycline	Kaposi's sarcoma, breast cancer, ovarian cancer, other solid tumors
Daunorubicin	Anthracycline	Acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia, Kaposi's sarcoma
Epirubicin	Anthracycline	Breast, different types of cancer
Idarubicin	Anthracycline	Acute lymphoblastic leukemia, chronic myeloid leukemia
Triptorelin	Hormone therapy (HT)	Prostate cancer, locally advanced, metastatic
Anastrozole, Exemestane, Fulvestrant, Letrozole, Tamoxifen	HT	Breast cancer
Abiraterone, Bicalutamide, Buserelin, Cyproterone, Degarelix, Flutamide, Enzalutamide	HT	Prostate cancer
Goserelin, Leuprorelin	HT	Breast cancer, prostate cancer
Lanreotide	HT	Carcinoid syndrome, VIPomas
Megestrol acetate	HT	Breast cancer, endometrial cancer
Octreotide	HT	Carcinoid syndrome and advanced neuroendocrine tumors (NETs)
Raloxifene	HT	Reduce the risk of breast cancer
Docetaxel	Taxane	Breast cancer, head and neck cancer, stomach cancer, prostate cancer, NSCLC
Cabazitaxel	Taxane	Advanced prostate cancer
Paclitaxel	Taxane	Ovarian cancer, esophageal cancer, breast cancer, lung cancer, Kaposi's sarcoma, cervical cancer, pancreatic cancer
Amsacrine	Topoisomerase inhibitor (TI)	Acute lymphoblastic leukemia
Irinotecan	TI	Colon cancer, SCLC
Mitoxantrone	TI	Acute myeloid leukemia, children suffering from acute lymphoblastic leukemia relapse
Topotecan	TI	Ovarian , lung cancer, cervical cancer and other cancer types
Vindesine	Vinca alkaloids	Leukemia, lymphoma, melanoma, breast cancer, lung cancer
Vinblastine	Vinca alkaloids	Hodgkin's lymphoma, non-small cell lung cancer, bladder cancer, brain cancer, melanoma, testicular cancer
Vinorelbine	Vinca alkaloids	NSCLC, metastatic breast cancer and rhabdomyosarcoma
Eribulin	Non-taxane microtubule dynamics inhibitor	Breast cancer, Leiomyosarcoma, liposarcoma
Azacitidine	Hypomethylating agent	Myelodysplastic syndrome, acute myeloid leukemia, chronic myelomonocytic leukemia
Dactinomycin	Anti-cancer antibiotic	Wilms tumor, rhabdomyosarcoma, Ewing's sarcoma, trophoblastic neoplasm, testicular cancer, certain types of ovarian cancer

Asparaginase	Enzyme	Acute lymphoblastic leukemia
Bexarotene	Retinoid	Advanced skin lymphomas called cutaneous T cell lymphomas
Bleomycin	Anti-cancer antibiotic	Hodgkin's lymphoma, non-Hodgkin's lymphoma, testicular cancer, ovarian cancer, cervical cancer
Oxaliplatin	Alkylating agent	Colorectal cancer
Aldesleukin	Immunotherapy	Melanoma, renal cell cancer
Imiquimod cream		Superficial basal cell carcinoma
Lenalidomide	Immunomodulatory agent	Multiple myeloma, myelodysplastic syndromes
Interferon alpha	Immunotherapy	Metastaticrenal cell carcinoma, melanoma, non-Hodgkin lymphoma, some types of leukemia
Olaparib	PARP blocker	Ovarian, breast, prostate cancer
Mitotane	Steroidogenesis inhibitor	Adrenocortical carcinoma
Mitomycin C	Anti-cancer antibiotic	Esophageal carcinoma, anal cancers, breast cancers
Talimogene laherparepvec	Immunotherapy	Skin melanoma
Arsenic trioxide	Natural product	Acute promyelocytic leukemia
Zoledronic acid	Bisphosphonate	Breast cancer and bone metastases

CONCLUSION

It is clear that medication used to treat cancer is constantly evolving. The last decades there has been an increase in thenumber of therapies and drugs available for the treatment of all solid and hematological tumors that have contributed to the significant reduction in cancer mortality rates. Moreover, thanks to the primary and secondary prevention policies the reduction of incidence rates was recorded for many malignancy tumors, particularly for those of predominantly environmental etiology. Progress must also be focused on reducing the side effects of new medication established.

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The authors declare that they have no conflict of interest

REFERENCES

1. Dagogo-Jack I, Shaw AT. Tumour heterogeneity and resistance to cancer therapies. Nat Rev ClinOncol 2018;15(2):81-94.
2. Pearson OH, Eliel LP, Rawson RW, Dobriner K, Rhoads CP. ACTH- and cortisone-induced regression of lymphoid tumors in man: A preliminary report. Cancer 1949;2, 943-5.
3. Savage P. Clinical observations on chemotherapy curable malignancies: unique genetic events, frozen development and enduring apoptotic potential. BMC Cancer 2015; 15: 11.
4. Bhullar KS, Lagarón NO, McGowan EM, Parmar I, Jha A, Hubbard BP, et al.Kinase-targeted cancer therapies: progress, challenges and future directions. MolCancer2018; 17: 48.
5. Bazak R, Houri M, El Achy S,Kamel S, Refaat T.Cancer active targeting by nanoparticles: a comprehensive review of literature. J Cancer Res ClinOncol 2015;141(5):769-84.
6. Manning G, Whyte DB, Martinez R, Hunter T, Sudarsanam S. The protein kinase complement of the human genome. Science2002;298: 1912-34.
7. Krause DS, VanEtten RA. Tyrosine kinases as targets for cancer therapy. N Engl JMed 2005;353: 172-87.
8. Martinelli C, Pucci C, Ciofani G. Nanostructured carriers as innovative tools for cancer diagnosis and therapy. APL Bioeng 2019;3(1):011502.
9. De Vita VT, Chu EA. History of Cancer Chemotherapy. Cancer Res2008;68: 8643-53.
10. Falzone L, Salomone S, Libra M. Evolution of Cancer Pharmacological Treatments at the turn of the Third Millennium. Front Pharmacol 2018;9:1300.
11. Oronsky BT, Reid T, Knox SJ, Scicinski JJ. The Scarlet Letter of Alkylation: A Mini Review of Selective Alkylating Agents Transl Oncol 2012 ; 5(4): 226-9.
12. Editors: Donald W Kufe, Raphael E Pollock, Ralph R Weichselbaum, Robert C Bast, Jr, Ted S Gansler, James F Holland, Emil Frei, III.Holland-Frei Cancer Medicine, 6th edition Hamilton (ON): BC Decker; 2003.ISBN-10: 1-55009-213-8
13. Nitrosoureas Current Status and New Developments1st Edition - January 1, 1981Editors: Archie W. Prestayko, Laurence H. Baker, Stanley T. Crooke pp. 1-49, eBook ISBN: 978148 3219448

14. Serrone L, Zeuli M, Sega FM, Cognetti F. Dacarbazine-based chemotherapy for metastatic melanoma: thirty-year experience overview. J Experim Clin Cancer Res2000;19 (1): 21-34.
15. Fernández-Villa D, Aguilar MR, Rojo L . Folic Acid Antagonists: Antimicrobial and Immunomodulating Mechanisms and Applications. Int J Mol Sci. 2019;20: 4996.
16. vanKuilenburg AB, Maring JG. Evaluation of 5-fluorouracil pharmacokinetic models and therapeutic drug monitoring in cancer patients. Pharmacogenom 2013;14(7): 799-811.
17. Minotti G, Menna P, Salvatorelli E, Cairo G, Gianni L. Anthracyclines: molecular advances and pharmacologic developments in antitumor activity andcardiotoxicity. Pharmacol Rev 2004; 56 (2): 185-229.
18. Dorr RT. Bleomycin pharmacology: mechanism of action and resistance, and clinical pharmacokinetics. Semin Oncol1992; 19 (2 Suppl 5): 3-8.
19. Verweij J, Pinedo HM. Mitomycin C: mechanism of action, usefulness and limitations. Anti Cancer Drugs 1990;1 (1): 5-13.
20. Sears Justin E,Boger Dale L.Total Synthesis of Vinblastine, Related Natural Products, and Key Analogues and Development of Inspired Methodology Suitable for the Systematic Study of Their Structure-Function Properties. Account Chem Res2015; 48 (3): 653-62.
21. Weaver BA, Bement W. HowTaxol/paclitaxel kills cancer cells. MolBiol Cell. 2014; 25 (18): 2677-81.
22. Delgado JL, Hsieh CM, Chan N-L, Hiasa H.Topoisomerases as anticancer targets.Biochem J 2018; 475 (2): 373-98.
23. Wall ME. Camptothecin and taxol: Discovery to clinic. Med Res Rev1998;18 (5): 299-314.
24. DeVita VT, Hellman S, Rosenberg SA.,eds. (2005). Cancer: principles and practice of oncology. Philadelphia: Lippincott. ISBN 0-7817-4865-8.
25. Jordan VC. Tamoxifen (ICI46,474) as a targeted therapy to treat and prevent breast cancer. Brit J Pharmacol2006;147 Suppl 1 (Suppl 1): S269-76.
26. Carter P. Improving the efficacy of antibody-based cancer therapies. Nat Rev Cancer 2001;1: 118-29.
27. Stern M, Herrmann R. Overview of monoclonal antibodies in cancer therapy: present and promise. CritRev Oncol/Hematol 2005;54 (1): 11-29.
28. JännePasi A, Gray N, Settleman J. Factors underlying sensitivity of cancers to small-molecule kinase inhibitors. Nat Rev Drug Discov2 009; 8 (9): 709-23.
29. Gross S, Rahal R,Stransky N, Lengauer C, Hoeflich KP. Targeting cancer with kinase inhibitors. J ClinInvestig2015; 125(5): 1780-9.
30. Yaish P, Gazit A, Gilon C, Levitzki A. Blocking of EGF-dependent cell proliferation by EGF receptor kinase inhibitors. Science1988; 242 (4880): 933-5.
31. Meydan N, Grunberger T, Dadi H, Shahar M, Arpaia E, Lapidot Z, et al. Inhibition of acute lymphoblasticleukaemia by a Jak-2 inhibitor. Nature1996; 379 (6566): 645-8.
32. Rivera-Torres J, José ES. Src Tyrosine Kinase Inhibitors: New Perspectives on Their Immune, Antiviral, and Senotherapeutic Potential. Front Pharmacol 2019;10: 1011.
33. Broome JD. L-Asparaginase: discovery and development as a tumor-inhibitory agent. Cancer Treat Rep 1981; 65 Suppl 4: 111-4.
34. Hahner S, Fassnacht M. Mitotanefor adrenocortical carcinoma treatment. Curr Opin Investig Drugs. 2005; 6 (4): 386-94.
35. Horstmann MA, Hassenpflug WA, zur Stadt U, Escherich G, Janka G, Kabisch H. Amsacrine combined with etoposideand high-dose methylprednisolone as salvage therapy in acute lymphoblastic leukemia in children. Haematol 2005; 90 (12): 1701-3

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