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Novel Anticancer Drugs Approved in 2020

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ABSTRACT

Cancer is one disease that carries the burden of increased death rate and in the last 50 years, the disease has progressed through various stages from understanding the pathophysiological mechanism of the disease to identification of newer drugs. Cancer is one of the leading causes of death is treated by three major modes of treatment like chemotherapy, radiotherapy, and surgery. The chemotherapeutic drugs include non-cell cycle-specific drugs, cell cycle-specific drugs, and hormonal drugs. In addition to the conventional treatment, the current treatment approach is more towards specific therapies that target the molecular genetics involved in the tumor progression. The greatest challenges in cancer drug discovery that it includes various processes like genome sequencing, high throughput screening, identification of lead molecules, testing of drugs in complex multicentric trials. Despite all the steps and efforts involved in cancer drug discovery, the drugs the proportion of newly discovered highly efficacious drugs is still less. There is a great demand to follow up and identify the newer anticancer drugs that can combat the challenges imposed by cancer. The recently approved drugs in 2020 are mostly specific target drugs like monoclonal antibodies, antibody-drug conjugates, tyrosine kinase inhibitors and some of these drugs are accelerated approvals by FDA, used in the resistance cases who doesn't respond to previous treatments, add on therapies.

INTRODUCTION

As per WHO cancer is the second leading cause of death worldwide. It is estimated that there were 9.8 million deaths in 2018 and around 1 in every 6-person died due to cancer. The mortality, morbidity, and the economic cost spent on healthcare; research was also increasing. The leading number of cancers are cancers of the lung, breast and colon [1]. The pathogenesis of cancer is complex which demands innovative discoveries in drug research. The first drug for cancer was discovered in 1949 and the life expectancy was around 47 years at that time. Now with the introduction of more than 150 drugs in the market, though the life expectancy has increased the clinical benefit to the patients with the chemotherapy treatment is still at a modest level. Cancer pharmacology also has been modified drastically which involves the understanding of cancer biology, discovery & development of newer drugs that are more specific, targeted like immune checkpoint inhibitors, PARP inhibitors, monoclonal antibodies. The current review summarizes the novel anticancer drugs approved in 2020, their efficacy, and adverse effects.

HALLMARKS OF CANCER

Cancer and cancerous cells have special characteristics compared to normal cells. These special characteristics or hallmarks of cancer include higher proliferative signaling stimulated by overproduction of growth factors, resistance to apoptosis/cell death, immortalized nature of cells mediated by lengthening of telomeres, induction of angiogenesis, high resistance to the conventional drug therapy, increased metastatic spread, genetic/epigenetic modifications, disrupted energy metabolism of the cancer cells, increased resistance to destruction by the immune system [2].The mechanisms by which the cancer cells develop resistance include inactivation of the chemotherapeutic drug, alteration of the drug target, increased DNA repair mechanisms, and inhibition of apoptotic mechanisms [3].

NEWER DRUGS APPROVED IN 2020

Relugloix

A phase III randomized clinical trial comparing Relugolix, a luteinizing hormone-releasing hormone (LHRH) antagonist, and injectable leuprolide acetate for advanced prostate cancer is highly significant in approval of the drug. The trial included 934 patients who were newly diagnosed with advanced prostate cancer or relapse were randomized to receive either Relugolix in oral tablet (120 mg daily single dose after a loading dose of 360 mg. The primary endpoint

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was assessed at weeks 29 to 48 by the rate of castration. The castration rate was higher in men who were prescribed Relugolix with a percentage of 96.7% compared to 88.8% in leuprolide acetate group. [4]. The drug was approved by FDA on December 18 2020 for the treatment of advanced prostate cancer. The drug is a GnRH antagonist. A loading dose of 360 mg is given on the first day followed by a daily oral dose of 120 mg. The major outcome is achieving testosterone suppression. The lab abnormalities include increased glucose levels, increased triglycerides, decreased hemoglobin, and increased liver enzymes [5].

Margetuximab (anti-HER2 mAb)

It is an antiHER2 monoclonal antibody approved for the treatment of HER2-positive breast cancer. A phase I trial in which the patients were randomized to receive either treatment A and treatment B which include Margetuximab infusion at a dose of 0.1-6.0 mg/kg and Margetuximab at a dose of 10-18 mg/kg respectively. The drug was well tolerated with grade 1 and grade 2 toxicities [6]. A phase III randomized multicenter open-label trial includes 536 patients who were randomized to receive Margetuximab plus chemotherapy or transtuzumab plus chemotherapy. The major outcome measures were progression-free survival and overall survival. The median progression-free survival in patients who received the Margetuximab plus chemotherapy arm was 5.8 months when compared with 4.9 months in the control arm. The drug is given as an IV infusion at a dose of 15 mg/kg over 120 min. The adverse effects include left ventricular dysfunction and embryofetal toxicity [7,8].

Naxitamab

It is a humanized antiGD2 monoclonal antibody that was granted accelerated approval to treat high-risk refractory or relapsed neuroblastoma. The drug is given as an IV infusion at a dose of 3 mg/kg/day on days 1, 3, and 5. The drug approval was granted accelerated approval and recommended in combination with granulocyte macrophage colony-stimulating factor for the patients in the pediatric age group [9,10].

Pralsetinib

Pralsetinib is a tyrosine kinase inhibitor that targets the RET gene to treat medullary carcinoma. RET gene is a protooncogene that will be overexpressed in cancers like papillary thyroid cancer, medullary carcinoma thyroid, A diagnostic test to confirm the expression of RET gene includes gene sequencing, fluorescence in situ hybridization test. The drug is used in a dose of 400 mg orally once daily on an empty stomach with no food intake for at least 2 hours. The adverse effects include increased liver enzymes, electrolyte abnormalities [11,12].

Belantamab mafodotin

'It is an antibody-drug conjugate i.e., a monoclonal antibody is attached to a cytotoxic agent with the linker molecule. The monoclonal antibody specifically targets the cells with a particular antigen and the cytotoxic drug is delivered to the target cell. B cell maturation antigen is highly expressed in mature B cells and plasma cells. It is a humanized antibody targeted against B cell maturation antigen which is used to treat multiple myeloma. It is given as an IV drug at a dose of 2.5 mg/kg once every three weeks [13]. The drug was approved in August 2020 for the patients with refractory multiple myeloma A multicentric trial in which the patients were randomized to receive at a dose of 2.5 mg/kg and 3.5 mg/kg intravenously. The adverse effects are keratopathy, thrombocytopenia and infusion-related reactions [14].

Capmatinib

Capmatinib is a tyrosine kinase inhibitor approved for the management of non-small cell lung cancer. The tumor cells exhibit a mutation called (MET) mesenchymal-epithelial transition exon 14 skipping and it is diagnosed by FDA-approved test. A phase 2 trial demonstrated the efficacy of the Capmatinib drug in which 364 patients were divided into various cohorts based on the MET gene amplification gene copy number and it was identified that the drug was effective in 41% of 69 patients who received previous treatment and 68% of 28 patients who had not received previous treatment [15].The drug was evaluated in a non-randomized multicentric open-label study in which 97 patients with a confirmed diagnosis and diagnostic test received the drug at a dose of 400 mg orally twice daily. The major efficacy outcome is the overall response rate and the adverse effects are hepatotoxicity, interstitial lung disease, photosensitivity, embryo fetal toxicity. The drug was declared an orphan drug and breakthrough therapy by FDA [16].

Sacituzumab

The drug is an antibody-drug conjugate. It is a Trop-2-directed antibody and topoisomerase inhibitor drug conjugate approved for the treatment of patients with triple-negative breast cancer. The protein Trophoblast cell surface antigen (Trop-2) is highly expressed in epithelial cell cancers. A phase I/II single-arm multicentric study involving 108 patients identified that the overall response rate with the drug was 33.3% and the median duration of response was 7.7 months [17]. It is given as an IV drug 10 mg/kg iv on days 1 and 8 every 21 days. The adverse effects are severe neutropenia and diarrhea [18].

Tucatinib

It is a tyrosine kinase inhibitor that targets the human epidermal growth factor receptor 2 used for advanced unresectable or metastatic HER 2 positive breast cancer and it is preferred in combination with transtuzumab and capecitabine. A trial (HER2CLIMB) recruited 612 patients with HER2 positive metastatic breast cancer, who also had undergone treatments with drugs like transtuzumab, pertuzumab, and ado transtuzumab ematansine. In the test

arm, the total number of patients who received Tucatinib along with transtuzumab, capecitabine is 412 and in the control arm, around 202 patients received placebo, transtuzumab, and capecitabine. The progression-free survival in the Tucatinib group was 7.8 months and 5 months in the control group. It is taken as an oral drug at a dose of 300 mg [19,20].

Isatuximab

It is an IgG monoclonal antibody that targets the glycoprotein CD38 and it is used to treat multiple myeloma. It is given as an iv infusion at a dose of 10 mg/kg every week for 4 weeks. The adverse effects are neutropenia, infusion-related reactions, pneumonia, upper respiratory infections, and diarrhea [21]. The drug was approved as a combination of pomalidomide and dexamethasone in those patients who had been treated with at least two prior treatments [22].

Tazemetostat

It is an epizyme (EZH2-histone methyl transferase) inhibitor introduced first in this class approved for the treatment of patients with follicular lymphoma. The phase 2 trial is an open-label, single-arm trial that recruited 99 patients at 38 clinics for four years from the year 2015 to 2019. The patients are categorized into EZH2 mutant and EZH2 wild type and the objective response rate was 69% in the mutant category whereas the rate was 35% in the wild type. A diagnostic test is also approved as a companion diagnostic test for the drug [23,24]. It is given at a dose of 800 mg orally twice daily. The adverse effects are upper respiratory infection, musculoskeletal pain, nausea, and abdominal pain [25].

Avapritinib

A drug that targets the platelet-derived growth factor-alpha and it is indicated for the adults with unresectable metastatic stromal tumor at a dose of 300 mg orally once daily [26]. The efficacy of the drug was evaluated in a multicentric single-arm trial involving 43 patients diagnosed with gastrointestinal stromal tumor in which the cells are harbored with platelet-derived growth factor receptor alpha mutation exon 18 mutation (GIST). It is a highly protein-bound drug and the adverse effects are cognitive impairment, diarrhea, hair color changes, and increased lacrimation [27].

Tafasitamab

It is a monoclonal antibody targeted against CD19 and it is approved for the treatment of relapsed or refractory B cell lymphoma in combination with the drug lenalidomide. The approval is an accelerated approval based on the results of the phase II trial in refractory diffuse large B cell lymphoma patients [28]. It is given as an IV infusion at a dose of 12 mg/kg. The adverse effects are neutropenia, fatigue, anemia, diarrhea, thrombocytopenia, cough, pyrexia, and peripheral edema [29].

Lurbinectedin

A drug that causes cell cycle arrest in the G2/M phase and cell death to treat metastatic small cell lung cancer after platinum-based chemotherapy. The efficacy was evaluated in 105 patients diagnosed with small cell lung cancer. The primary outcome was the overall response rate evaluated by RECIST and response duration. It is given at a dose of 3.2 mg/m^2 every 21 days. The adverse effects are Increased liver enzymes electrolyte imbalance [30,31].

Ripretinib

The major molecular pathway involved in gastrointestinal stromal tumors include KIT, PDGFRA, GIST involved in tumor progression. The major tyrosine kinase inhibitors approved for the management of gastrointestinal stromal tumor include imatinib, sunitinib, regorafenib, avapritinib, ripretinib [32]. A multicentric double-blinded placebo-controlled trial was conducted in 129 patients diagnosed with gastrointestinal stromal tumor who had already undergone treatment with kinase inhibitors. The primary outcome was progression-free survival. Ripretinib was better compared to placebo which had progression-free survival of 6.3 months compared to 1 month for placebo. A dose of 150 mg orally was recommended once daily. The adverse effects are GI disturbances, erythrodysesthesia, cardiac abnormalities, and cutaneous malignancies [33].

Selpercatinib

Selpercatinib is a tyrosine kinase inhibitor that targets the RET mutation (rearranged during transfection and this oncogene is abnormally activated in certain cancers like papillary thyroid cancer and non-small cell lung cancer. The drug got accelerated approval for the treatment of RET positive non-small cell lung cancer in adult patients and RET positive medullary thyroid cancer in adult, pediatric more than or equal to 12 years of age. The dose recommended is 120 mg (in patients weighing <50 kg) and 160 mg (in patients weighing >50 kg) till the progression of cancer [34,35].

DIAGNOSTIC AGENTS

Gallium

It is a radioactive diagnostic imaging agent used in PET scans to detect the prostate-specific membrane antigen-positive areas while diagnosing prostate cancer in men [36].

Copper Cu64dotatate Injection

An investigational agent used to diagnose the certain type of somatostatin receptor-positive neuroendocrine tumors [37].

CONCLUSION

The cancer drug therapy is now directed towards the targeted therapies, immunotherapy, hormonal therapy which is good at attacking the cancerous cells compared to the normal cells. This is completely different from cytotoxic drugs which affect both cancerous and normal cells. Carugo [38] describe the three ages of cancer drug discovery which include bronze, silver, and gold age. The bronze age is the era of the discovery of the cytotoxic drugs by a team of academicians, the silver age is the period in which the discoveries in the cancer field were led by profit organizations and the golden age in which there are well-defined biomarkers that predict and performed by academic institutions. The efforts of the academicians, researchers, organization helps identify drugs with newer targets, good efficacy and still many drugs are under clinical trials. The other treatment options like surgery, radiotherapy along with targeted drugs can reduce the morbidity depending on the stage of the cancer.

REFERENCES

1. WHO (2020) Cancer. Accessed on: March 15, 2021. Available online at: https://www.who.int/westernpacific/health-topics/cancer
2. Dembic Z (2020) Antitumor Drugs and Their Targets. Mol Basel Switz 25(23): 5776.
3. Mansoori B, Mohammadi A, Davudian S, Shirjang S, Baradaran B (2017) The Different Mechanisms of Cancer Drug Resistance: A Brief Review Adv Pharm Bull 7(3): 339-348.
4. Jena R. Relugolix (2020) The novel oral androgen deprivation therapy for prostate cancer. Indian J Urol IJU J Urol Soc India 36(4): 327-328.
5. USFDA (2020) FDA approves Relugolix for advanced prostate cancer. Accessed on: February 20, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-Relugolix-advanced-prostate-cancer
6. Bang YJ, Giaccone G, Im SA, Oh DY, Bauer TM, et al. (2017) First-in-human phase 1 study of Margetuximab (MGAH22), an Fc-modified chimeric monoclonal antibody, in patients with HER2-positive advanced solid tumors. Ann Oncol 28(4): 855-861.
7. USFDA (2020) FDA approves Margetuximab for metastatic HER2-positive breast cancer. Accessed on: March 13, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-margetuximab-metastatic-her2-positive-breast-cancer
8. Tarantino P, Morganti S, Uliano J, Giugliano F, Crimini E, et al. (2021) Margetuximab for the treatment of HER2-positive metastatic breast cancer. Expert Opin Biol Ther 21(2): 127-133.
9. Markham A (2021) Naxitamab: First Approval. Drugs 81(2): 291-296.
10. USFDA (2020) FDA grants accelerated approval to naxitamab for high-risk neuroblastoma in bone or bone marrow. Accessed on: March 3, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-naxitamab-high-risk-neuroblastoma-bone-or-bone-marrow
11. Markham A (2020) Pralsetinib: First Approval. Drugs 80(17): 1865-1870.
12. USFDA (2020) FDA approves pralsetinib for lung cancer with RET gene fusions. Accessed on: March 5, 2021. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pralsetinib-lung-cancer-ret-gene-fusions
13. Lassiter G, Bergeron C, Guedry R, Cucarola J, Kaye AM, et al. (2021) Belantamab Mafodotin to Treat Multiple Myeloma: A Comprehensive Review of Disease, Drug Efficacy and Side Effects. Curr Oncol Tor Ont 28(1): 640-660.
14. USFDA (2020) FDA granted accelerated approval to belantamab mafodotin-blmf for multiple myeloma. Accessed on: March 13, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-granted-accelerated-approval-belantamab-mafodotin-blmf-multiple-myeloma
15. Wolf J, Seto T, Han J-Y, Reguart N, Garon EB, et al. (2020) Capmatinib in MET Exon 14–Mutated or MET-Amplified Non–Small-Cell Lung Cancer. N Engl J Med 383(10): 944-957.
16. USFDA (2020) FDA grants accelerated approval to capmatinib for metastatic non-small cell lung cancer. Accessed on: March 15, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-capmatinib-metastatic-non-small-cell-lung-cancer
17. Seligson JM, Patron AM, Berger MJ, Harvey RD, Seligson ND (2021) Sacituzumab Govitecan-hziy: An Antibody-Drug Conjugate for the Treatment of Refractory, Metastatic, Triple-Negative Breast Cancer. Ann Pharmacother 55(7): 921-931
18. USFDA (2020) FDA grants accelerated approval to sacituzumab govitecan-hziy for metastatic triple negative breast cancer. Accessed on: March 15, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-sacituzumab-govitecan-hziy-metastatic-triple-negative-breast-cancer

19. USFDA (2020) FDA approves tucatinib for patients with HER2-positive metastatic breast cancer. Accessed on: March 17, 2021. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tucatinib-patients-her2-positive-metastatic-breast-cancer

20. Bartsch R (2021) ASCO 2020: highlights in breast cancer. Memo 14: 58-61.

21. Dhillon S (2020) Isatuximab: First Approval. Drugs 80(9): 905-912.

22. USFDA (2020) FDA approves isatuximab-irfc for multiple myeloma. Accessed on: March 18, 2021. Available online at: https://www.fda.gov/drugs/development-approval-process-drugs/fda-approves-isatuximab-irfc-multiple-myeloma

23. PubChem (2020) Tazemetostat. Accessed on: March 20, 2021. Available online at: https://pubchem.ncbi.nlm.nih.gov/compound/66558664

24. Morschhauser F, Tilly H, Chaidos A, McKay P, Phillips T, et al. (2020) Tazemetostat for patients with relapsed or refractory follicular lymphoma: An open-label, single-arm, multicenter, phase 2 trial. Lancet Oncol 21(11): 1433-1442.

25. USFDA (2020) FDA granted accelerated approval to tazemetostat for follicular lymphoma Accessed on: March 20, 2021. Available online at: https://www.fda.gov/drugs/fda-granted-accelerated-approval-tazemetostat-follicular-lymphoma

26. Dhillon S (2020) Avapritinib: First Approval. Drugs 80(4): 433-439.

27. USFDA (2020) FDA approves avapritinib for gastrointestinal stromal tumor with a rare mutation. Accessed on: March 20, 2021. Available online at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-avapritinib-gastrointestinal-stromal-tumor-rare-mutation

28. Hoy SM (2020) Tafasitamab: First Approval. Drugs 80(16): 1731-1737.

29. USFDA (2020) FDA grants accelerated approval to tafasitamab-cxix for diffuse large B-cell lymphoma. Accessed on: March 22, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-tafasitamab-cxix-diffuse-large-b-cell-lymphoma

30. USFDA (2020) FDA grants accelerated approval to lurbinectedin for metastatic small cell lung cancer. Accessed on: March 22, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-lurbinectedin-metastatic-small-cell-lung-cancer

31. Subbiah V, Paz-Ares L, Besse B, Moreno V, Peters S, et al. (2020) Antitumor activity of lurbinectedin in second-line small cell lung cancer patients who are candidates for re-challenge with the first-line treatment. Lung Cancer 150: 90-96.

32. Lostes-Bardaji MJ, García-Illescas D, Valverde C, Serrano C (2021) Ripretinib in gastrointestinal stromal tumor: The long-awaited step forward. Ther Adv Med Oncol 13: 1758835920986498.

33. USFDA (2020) FDA approves ripretinib for advanced gastrointestinal stromal tumor. Accessed on: March 9, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-ripretinib-advanced-gastrointestinal-stromal-tumor

34. Markham A (2020) Selpercatinib: First Approval. Drugs 80(11): 1119-1124.

35. USFDA (2020) FDA approves selpercatinib for lung and thyroid cancers with RET gene mutations or fusions. Accessed on: March 9, 2021. Available online at: https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-selpercatinib-lung-and-thyroid-cancers-ret-gene-mutations-or-fusions

36. NEWS (2020) FDA Approves Radioactive Diagnostic Agent for Prostate Cancer. J Clin Pathw Accessed on: March 23, 2021. Available online at: https://www.journalofclinicalpathways.com/news/fda-approves-radioactive-diagnostic-agent-prostate-cancer

37. Slater H (2020) FDA Approves Copper Cu 64 Dotatate Injection for Somatostatin Receptor-Positive NETs. Cancer Netw Accessed on: March 23, 2021. Available online at: https://www.cancernetwork.com/view/fda-approves-copper-cu-64-dotatate-injection-for-somatostatin-receptor-positive-nets

38. Carugo A, Draetta GF (2019) Academic Discovery of Anticancer Drugs: Historic and Future Perspectives. Ann Rev Cancer Biol 3: 385-408.