Study on Anticancer Drugs Approved by the FDA from 2014 to 2023

By

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A thesis submitted to the Department of School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons)

School of Pharmacy

Brac University

April, 2024

Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The thesis titled “Study on anticancer drugs approved by the FDA from 2014 to 2023” submitted by Faria Rahman Rattry (20146013) of Spring, 2020 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on [Date-of-Defense].

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Ethics Statement

This study doesn’t involve any human and animal trial.

Abstract

Cancer is a condition of uncontrolled growth and spread of cells in the body. Cancer is the second leading cause of death in the world. Cancer is basically classified according to the resemblance of tumor cell to a specific type of cell, which is believed to be the origin of the tumor. Most common type of cancers are lung cancer, liver cancer, breast cancer, colorectal cancer, prostate cancer, thyroid cancer, leukemia, lymphoma, melanoma, bladder cancer etc. Various types of cancer treatment are available like chemotherapeutic drugs, radiation therapy, surgery etc. One of the most used cancer treatments is chemotherapy. But it developed chemotherapy resistance. Particularly in progressive disease, resistance to chemotherapy is frequently observed. Thus, researchers are now focusing on targeted therapies based on the tumor-specific factors. In this research, chemotherapeutic drug is the main focus among the different types of cancer treatment. A detailed analysis is done by compiling all the approved chemotherapeutic drugs by the FDA from 2014 to 2023. This study highlights the approved anticancer drugs with their indication and dosage forms.

Keywords: Cancer, FDA, Chemotherapeutic drugs, Chemotherapy resistance, Radiation therapy, Tumors.

Dedication

I would like to dedicate my thesis to my parents for their immense support and motivation.

Thank you.

Acknowledgement

I am deeply grateful for the invaluable opportunity that the School of Pharmacy at Brac University in Bangladesh has bestowed upon me. I would like to extend my deepest gratitude to the Almighty for providing assistance throughout my entire life.

I would like to extend my heartfelt thanks to Dr. Muhammad Asaduzzaman, Professor at the School of Pharmacy and my project supervisor, for his precious time and support during the course of my project work.

I would also like to express my sincere appreciation to Professor Dr. Eva Rahman Kabir, Dean, School of Pharmacy, and Professor Dr. Hasina Yasmin, Program Director and Assistant Dean, School of Pharmacy, for their exceptional guidance and assistance throughout my Bachelor of Pharmacy (Hons) journey.

Moreover, I would also like to express my gratefulness to my family for their unwavering support and selfless sacrifices.

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List of Acronyms

FDA	Food and Drug Administration
KIs	Kinase inhibitors
mAbs	Monoclonal antibodies
ICIs	Immune checkpoint inhibitors
PARPIs	Poly ADP-ribose polymerase inhibitors
ADP	Adenosine diphosphate
ADCs	Antibody-drug conjugates
HPV	Human papillomavirus
HER2+	Human epidermal growth factor receptor 2 positive
NSCLC	Non-small cell lung cancer

Chapter 1

Introduction

1.1 Overview of Cancer

Cancer can originate in various organs or tissues following the uncontrolled growth of abnormal cells that infiltrate neighboring areas, and potentially metastasize to other regions of the body. Cancer can originate in any organ or tissue of the body when abnormal cells proliferate without restraint, beyond their normal limitations to infiltrate neighboring areas and/or metastasize to other organs (Alberts et al., 2013). Cancer is often referred to as a neoplasm or malignant tumor.

Cell division is a fundamental process for meeting the body's requirements and generating new cells as needed. When cells become damaged or aged, they undergo apoptosis, enabling the creation of fresh cells. While this cycle is typically regulated, instances of dysregulation may result in the uncontrolled proliferation of abnormal or impaired cells. These cells have the potential to form tumors, abnormal clusters of tissue. Tumors are categorized as either benign or malignant. Malignant tumors have the ability to spread to distant body parts, invade nearby tissues, and accelerate cancer growth. (Lee, 2014). Malignant tumors are an alternative term for cancerous tumors. Benign tumors lack the ability to metastasize or infiltrate adjacent organs. Benign tumors often do not regenerate after removal, although malignant tumors may occasionally reoccur. Benign tumors can occasionally attain significant size. Certain conditions can lead to severe symptoms or pose a risk to life, such as noncancerous brain tumors (National Cancer Institute, 2019).

1.2 Types of cancer

Cancers are classified according to the resemblance of tumor cells to a particular type of cell, which is believed to be the origin of the tumor. Tumors are clusters of abnormal cells that develop into masses or lumps. A malignant tumor refers to the formation of a mass or growth composed of cancer cells (Lee, 2014). A general classification of cancer can be broken down into two distinct categories: Solid cancer and Liquid cancer.

i. **Solid cancer:** Tumors that develop into solid masses in particular organs or tissues (e.g., breast or lung cancer) are the cause of solid cancer. These tumors are composed of abnormal and diverse cells that aggregate. Tumors of solid nature are categorized according to their anatomical source within the body (National Cancer Institute, 2011). Tumors can arise from bone, muscle, or organs such as the liver and lungs. Common forms of cancers include carcinomas, sarcomas, lymphomas, and gliomas.

ii. **Liquid cancer:** Liquid cancer, also known as hematological malignancy, refers to the development of cancerous tumors in the blood, bone marrow, or lymphatic system. Leukemia, lymphoma, and myeloma are all examples of liquid tumors (MassiveBio, 2022).

Below are several classifications of malignancies that originate from distinct cell types:

1. **Carcinoma:** Carcinoma refers to cancers that originate from epithelial cells. There are different names for cancers that start in different types of epithelium cells:

- **Adenocarcinoma:** Adenocarcinoma refers to a category of malignancies that encompasses a majority of the prevalent types, such as those affecting the breast, prostate, lung, pancreas, and colon (National Cancer Institute, 2019).
- **Basal cell Carcinoma:** Cancer that originates in the outermost layer of the epidermis, is referred to as basal cell carcinoma (National Cancer Institute, 2019).

- **Squamous cell carcinoma:** Squamous cell carcinoma is a malignancy that develops in squamous cells, which are epithelial cells located just beneath the skin's epidermis. Squamous cells can also be found in organs such as the stomach, intestines, lungs, bladder, and kidneys (National Cancer Institute, 2019).
- **Urothelium carcinoma:** Cancer that develops in a type of epithelial tissue known as transitional epithelium, also known as urothelium carcinoma, is referred to as transitional cell carcinoma. This tissue is capable of expanding and contracting, which can be found in the linings of the bladder, ureters, and a portion of the kidneys (renal pelvis), in addition to a few other organs (National Cancer Institute, 2019).

2. **Sarcoma:** Cancers known as sarcomas include those that develop in bone and soft tissues, such as muscle, fat, blood vessels, lymph vessels, and fibrous tissue like tendons and ligaments. Leiomyosarcoma, Kaposi sarcoma, malignant fibrous histiocytoma, and liposarcoma are the most prevalent forms of soft tissue sarcoma (National Cancer Institute, 2019).
3. **Leukemia:** Leukemia refers to cancers that originate in the bone marrow's blood-forming tissue. Tumors of this type do not develop into solid lumps. Conversely, a significant quantity of abnormal WBCs accumulates in the bloodstream and bone marrow, displacing healthy blood cells. Leukemia can be categorized into four distinct groups, based on the rate of disease progression (acute or chronic) and the specific blood cell from which the cancer originates (lymphoblastic or myeloid) (Lee, 2014).
4. **Lymphoma:** Lymphoma is a type of cancer that arises in lymphocytes, which can be either T cells or B cells. Lymphoma is characterized by the accumulation of atypical lymphocytes in lymph nodes, lymph arteries, and various organs (National Cancer Institute, 2019).

   The two most common forms of lymphoma are:

i. *Hodgkin lymphoma* is characterized by the presence of Reed-Sternberg cells, which are aberrant lymphocytes. These cells typically originate from B cells (National Cancer Institute, 2019).

ii. *Non-Hodgkin lymphoma* is an extensive category of malignancies that originate from lymphocytes. Cancers can exhibit varying rates of growth, either rapid or gradual, and can originate from either B cells or T cells (National Cancer Institute, 2019).

5. **Multiple myeloma:** Multiple myeloma is a malignancy originating from plasma cells, which are a distinct type of immune cell. Myeloma cells, which are aberrant plasma cells, accumulate in the bone marrow and develop tumors in various bones across the body (National Cancer Institute, 2019).
6. **Melanoma:** Melanoma is a type of cancer that originates from melanocytes, specialized cells responsible for producing melanin (National Cancer Institute, 2019).
7. **Germ cell cancer:** Tumors that originate from pluripotent stem cells, commonly seen in the testicles and ovaries, are known as germ cell tumors (National Cancer Institute, 2019).

1.3 Epidemiology of Cancer

The list of common cancers was compiled using data from the National Cancer Institute, which provided information about cancer incidence and mortality. A cancer has to have an anticipated annual incidence of 40,000 cases or higher in 2023 in order to be included in the list. The table below (Table 1.1) provides the projected figures for the incidence and mortality rates of various prevalent cancer types in the year 2023.

Table 1.1: Estimated new cases and deaths based on cancer type (National Cancer Institute, 2018)

Cancer type	Estimated new cases	Estimated deaths
Bladder	82290	16710
Breast (Female-Male)	297790-2800	43170-530
Colorectal	153020	52550
Endometrial	66200	13030
Kidney	81800	14890
Leukemia	59610	23710
Liver and intrahepatic bile duct	41210	29380
Lung	238340	127070
Melanoma	97610	7990
Non-Hodgkin lymphoma	80550	20180
Pancreatic	64050	50550
Prostate	288300	34700
Thyroid	43720	2120

It can be seen that Breast cancer is the most prevalent type of cancer on the list, with an expected 300,590 new cases in the United States in 2023 (National Cancer Institute, 2018).

Following breast cancer, next most common types of cancers are prostate cancer and lung cancer. Given that rectal and colon cancers are frequently combined in the list under the general heading "colorectal cancers," the two terms have been merged. An estimated 106,970 new cases of colon cancer and 46,050 new cases of rectal cancer are anticipated to be diagnosed in 2023, for a cumulative total of 153,020 new cases of colorectal cancer.

In 2023, according to the research from the National Cancer Institute; nearly fifty percent of newly diagnosed cancer cases in the United States are colorectal, lung and bronchus, prostate, and breast cancers and nearly half of all deaths are caused by cancers of the breast, colorectal, lung, and bronchus (Figure 1.1).

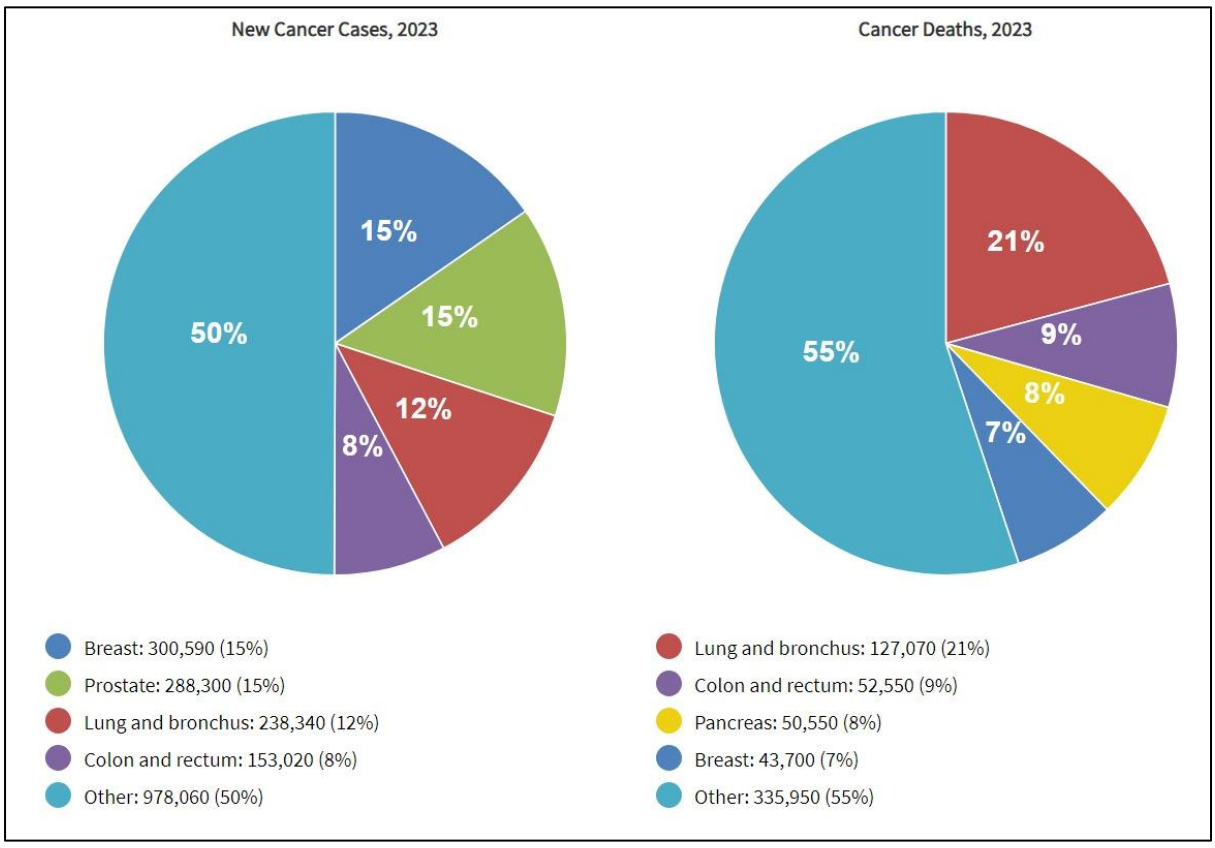


Figure 1.1: Cancer incidence and death (National Cancer Institute, 2023)

1.4 Risk factors for Cancer

Identifying and comprehending the diverse risk factors associated with cancer is essential for both prevention and early detection. According to World Health Organization (WHO, 2022), several crucial elements that are linked to cancer are:

- **Age:** The likelihood of having cancer rises as we age. This occurs due to the gradual accumulation of genetic mutations, which increases the vulnerability of cells to develop cancer.
- **Tobacco Use:** The act of smoking or utilizing tobacco products greatly increases the likelihood of developing many types of cancer, such as lung, oral, pharyngeal, and bladder cancer.
- **Alcohol Consumption:** Consuming an excessive amount of alcohol is associated with a heightened chance of developing liver, breast, and other types of cancer.
- **Unhealthy Eating Habits:** Cancer risk can be increased by eating a diet high in processed foods and sweets and low in fruits and vegetables.
- **Lack of regular physical activity:** Not getting enough exercise is linked to a higher chance of some cancers.
- **Carcinogen Exposure:** Chemicals, radiation, and environmental contaminants can increase the risk of cancer when exposed to them in the workplace.
- **Chronic inflammation**, which refers to long-lasting inflammation in the body, can contribute to the development of cancer.
- **Insufficiencies in hormones**, such as estrogen exposure (for example, through hormone replacement therapy), can have an effect on the likelihood of developing cancer.
- **Infectious Agents:** Individuals who have persistent infections, such as human papillomavirus (HPV), hepatitis B and C, and Helicobacter pylori, are at an increased risk for developing certain malignancies.

Chapter 2

Cancer Chemotherapy

Given the diversity of cancers and the fact that each subtype requires a specialized approach, oncology offers a vast array of therapies. Surgical procedures, radiation treatments, hormone treatments, hormonal replacement, PARP inhibitors, small-molecule medications, and targeted therapy are all possible methods of treatment. The use of stem cells, immunotherapy, photodynamic therapy, and hyperthermia are some of the additional treatments that are available (National Cancer Institute, 2020). Typically, cancer treatment consists of a sequence of distinct therapies, such as chemotherapy administered prior to surgery. A number of factors, including the location and grade of the tumor, the stage of the disease, and the overall condition of the patient, all play a role in determining the treatment that is most appropriate. The main objective of cancer treatment is to either achieve a complete eradication of the cancer or significantly extend the lifespan of the individual (WHO, 2022). This research will provide a comprehensive analysis of chemotherapy and chemotherapeutic medications that are used in the treatment of cancer.

Chemotherapy is the treatment that involves the use of chemical substances to kill cancer cells. This particular method of treating cancer is effective because it prevents cancer cells from expanding, proliferating, and producing other cells. Chemotherapy is an administration of drug that affects the entire body. This implies that it circulates inside the bloodstream and disseminates to all regions of the body (Lee, 2016). Chemotherapy medications are potent chemicals that fight against cancer by targeting cells at specific stages of the cell cycle. In order to produce new cells, every cell must go through the process known as the cell cycle. Cancer cells undergo this process at an accelerated rate compared to normal cells, rendering chemotherapy more impactful on these rapidly proliferating cells (Cancer.Net, 2019).

2.1 Delivery route of Chemotherapy

Chemotherapy can be administered by several ways (Cancer.Net, 2022), including intravenous infusion, oral ingestion, injection, arterial delivery, abdominal administration, and topical application.

- **Intravenous route:** Administration of chemotherapy into a vein (IV). There are numerous medications that must be administered by injecting them straight into a vein. This treatment is referred to as intravenous or IV chemotherapy. The duration of treatment can range from a few minutes to a few hours. Certain intravenous medications have enhanced efficacy when administered over an extended period of many days or weeks. This type of treatment is known as continuous infusion chemotherapy.

- **Oral:** It is administered by the mouth. It can be administered as a pill, capsule, or liquid. The use of oral cancer treatments has become increasingly prevalent.

- **Injection:** This refers to the administration of chemotherapy through a direct injection. These injections can be administered in the arm, leg, or abdomen. The administration of the shot can be either intramuscularly or subcutaneously.

- **Intra-arterial:** An artery is a vascular conduit responsible for transporting oxygenated blood from the heart to various tissues and organs throughout the body. Occasionally, chemotherapy is administered via arterial injection, targeting the cancerous area directly.

- **Intra-peritoneal:** Administering chemotherapy directly into the peritoneum or abdominal cavity. This type of treatment approach is effective for malignancies that affect the peritoneum. The peritoneum envelops the inner surface of the abdomen and encircles the intestines, liver, and stomach. Ovarian cancer is a common malignancy that often metastasizes to the peritoneum.

- **Topical:** Application of chemotherapeutic drugs directly to the affected area. Certain chemotherapy treatments are developed as a topical cream that is applied directly to the skin.

2.2 Types of chemotherapeutic drugs available in the market

Chemotherapy for cancer involves the use of various pharmaceutical agents. While it is true that all chemotherapeutic drugs cause cell damage, they specifically target particular cell components at various stages of the cell cycle (Cancer.Net, 2022).

The following table (Table 2.1) represents the primary categories of chemotherapeutic agents:

Table 2.1: Primary type of chemotherapeutic agents with example

Chemotherapeutic agents	Examples
Alkylating agents	Trabectedin
Antimetabolites	Hydroxyurea
Kinase inhibitors	Ibrutinib, Dasatenib, etc.
Mitotic inhibitors	Paclitaxel, Vinblastine, etc.
Monoclonal antibodies	Pembrolizumab, Atezolizumab, etc.
PARP inhibitors	Olaparib, Niraparib, etc.

Chapter 3

Objective of the study

The objective of this research was to compile the approved chemotherapeutic drugs by the FDA for various types of cancer from 2014 to 2023. This study aimed to provide a detailed overview of the current landscape of FDA-approved anticancer drugs, including their mechanisms of action, their dosage forms and their therapeutic indication. This research also aimed to list down the chemotherapeutic drugs that were developed based on the tumor-specific factors, to deliver targeted chemotherapy.

Chapter 4

Methodology

This research work is done by compiling the list of FDA approved drugs which were used for cancer therapy from 2014 to 2023. It is mainly done to analyze which types of drug were approved and among them which cancer has the highest number of drugs approved for.

This research was done by data mining by using the Food and Drug Administration (FDA) website to list down the approved anticancer drugs from the year of 2014 to 2023.

In order to compile the information of anticancer drugs approval, FDA's '*Drug Approval and Databases*' section was used. Then, the contents uploaded by the FDA in the section of "Oncology (Cancer) / Hematologic Malignancies Approval Notifications" were used.

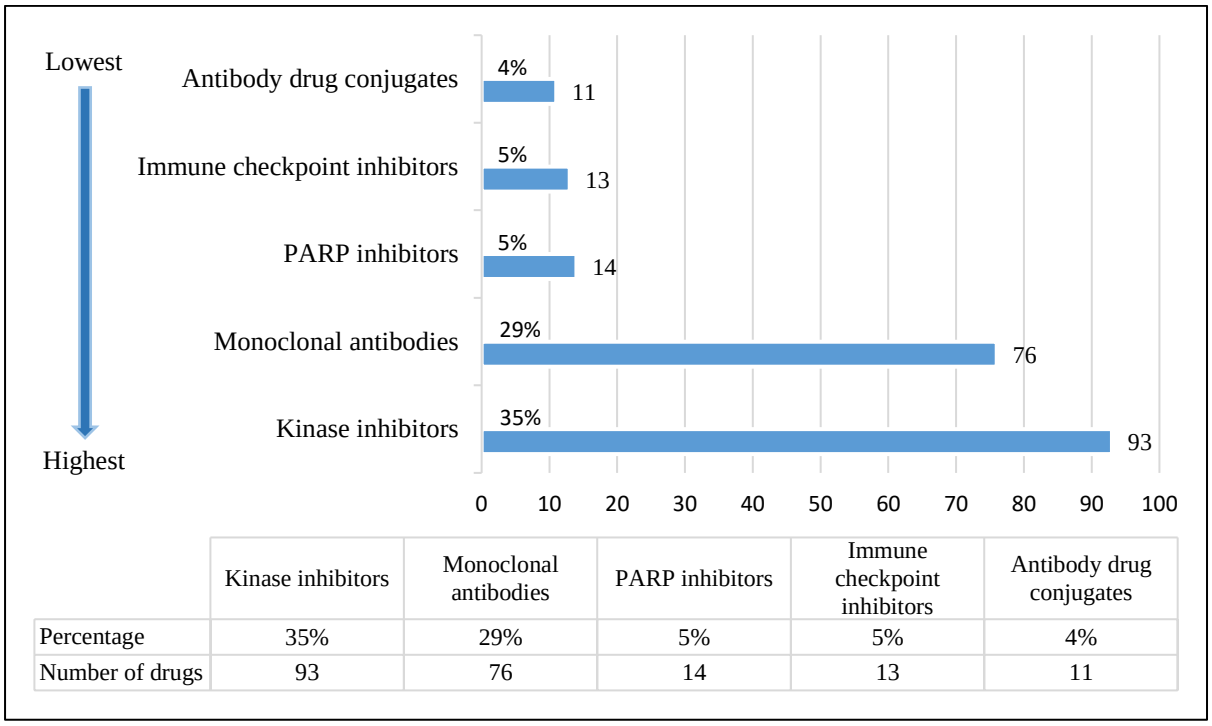
First of all, drugs approved in a particular year was identified year-wise, and data regarding approval date, approval indication and cancer type, dose, dosage form and dosage regimen were investigated. All the data were enlisted using MS Excel Spreadsheet and the analyses were done based on that raw data.

Chapter 5

Result and Discussion

5.1 Chemotherapeutic drug approved by FDA from 2014 to 2023

Over the years the FDA approved a lot of chemotherapeutic drugs like alkylating agents, anti-androgen anti-neoplastic agents etc. with a total of 260 drugs. Among them, top 5 chemotherapeutic drugs which were the most approved for anticancer treatment are shown in figure 5.1 as follows:



	Kinase inhibitors	Monoclonal antibodies	PARP inhibitors	Immune checkpoint inhibitors	Antibody drug conjugates
Percentage	35%	29%	5%	5%	4%
Number of drugs	93	76	14	13	11

Figure 5.1: Top 5 chemotherapeutic drug approved based on pharmacological classification

The detailed number of drugs approved by FDA for the top 5 pharmacological class with the indication is given below:

5.1.1 <u>Kinase Inhibitors (KIs):</u> Protein kinases are essential for cell growth, proliferation, and differentiation. Mutations affecting these kinases can lead to uncontrolled growth and proliferation, a characteristic feature of cancer cells. In the fight against cancer, kinase inhibitors are potent antineoplastic agents that target the specific protein kinases altered in cancer cells, impeding their abnormal progression. Kinase inhibitors approved by the FDA from 2014-2023 are listed below in table 5.1:

Table 5.1: FDA approved kinase inhibitors (2014-2023)

Sl.	Indication	Name of drugs (Approval year)	
1.	Lymphoma	Idealisib (2014)	Crizotinib (2021)
		Ceritinib (2014)	Lorlatinib (2021)
		Acalabrutinib (2019)	Zanubrutinib (2023)
2.	Leukemia	Ibrutinib (2014)	Gemtuzumab (2020)
		Dasatinib (2017)	Onureg (2020)
		Bosutinib (2017)	Asciminib (2021)
		Nilotinib (2018)	Azacitidine (2022)
		Duvelisib (2018)	Zanubrutinib (2023)
		Gilteritinib (2018)	Quizartinib (2023)
		Acalabrutinib (2019)	Bosutinib (2023)
3.	HER2+ Breast cancer	Palbociclib (2015)	Sacituzumab govitecan (2020)
		Abemaciclib (2017)	Tucatinib (2020)
		Neratinib (2018)	Traztuzumab (2020)
		Ribociclib (2018)	Capivasertib (2023)

Table 5.1: contd.

Sl.	Indication	Name of drugs (Approval year)	
		Alpelicib (2019) Mergetuximab-cmkb (2020) Capecitabine (2020)	
4.	Renal cancer	Cabozantinib (2016) Lenvatinib (2016) Sunitinib malate (2017)	Everolimus (2018) Tivozanib (2021) Belzutifan (2023)
5.	Non-small cell lung cancer (NSCLC)	Idelalisib (2014) Gefitinib (2015) Osimertinib (2015) Alectinib (2015) Everolimus (2016) Crizotinib (2016) Ceritinib (2017) Dabrafenib+Trametinib (2017)	Afatinib (2018) Dacotinib (2018) Lorlatinib (2018) Capmatinib (2020) Selpercatinib (2022) Pralsetinib (2023) Encorafenib + Binimetinib (2023) Repotrectinib (2023)
6.	Gastrointestinal stromal cancer	Everolimus (2016) Trifluridine + Tipiracil (2019)	Avapritinib (2020)
7.	Melanoma	Trametinib (2014) Cobimetinib (2015) Dabrafenib (2015)	Encorafenib + Binimetinib (2018) Tebentafusp-tebn (2022)
8.	Thyroid cancer	Lenvatinib (2015) Selprecatinib (2020)	Pralsetinib (2020) Cabozantinib (2021)

5.1.2 <u>Monoclonal antibodies (mAbs):</u> Monoclonal antibodies are synthetic proteins designed to specifically bind to particular targets in the body, including antigens found on cancer cells. Monoclonal antibodies approved by the FDA from 2014-2023 are listed below in table 5.2:

Table 5.2: FDA approved monoclonal antibodies (2014-2023)

Sl.	Indication	Name of drugs (Approval year)	
1.	Non-small cell lung cancer (NSCLC)	Ramucirumab (2014) Pembrolizumab (2015) Necitumumab (2015) Atezolizumab (2016)	Durvalumab (2018) Pembrolizumab + Paclitaxel (2018) Cemiplimab-rwlc (2022)
2.	Large B-cell lymphoma	Obinutuzumab (2016) Rituximab (2017)	Pembrolizumab (2018)
3.	Melanoma	Pembrolizumab (2014) Ipilimumab (2015)	Atezolizumab (2020) Cobimentinib (2020)
4.	HER2+ breast cancer	Pertuzumab (2017) Trastuzumab (2019)	Atezolizumab (2019)
5.	Multiple myeloma	Daratumumab (2015) Elotuzumab (2019) Daratumuab + lenalidomide and dexamethasone (2020)	Daratumumab + hyaluronidase (2021)
6.	Endometrial cancer	Pembrolizumab (2019) Pembrolizumab + Lenvatinib (2019)	Dostarlimab (2023)
7.	Renal cancer	Pembrolizumab (2019) Axitinib (2019)	Avelumab (2019)

Monoclonal antibodies are utilized for diagnosing and treating many disorders, including certain forms of cancer.

5.1.3 <u>PARP inhibitors (PARPIs):</u> PARP, an enzyme found in cells, is short for poly-ADP ribose polymerase. It plays a role in the self-repair process of damaged cells. By inhibiting the repair function of PARP in cancer cells, PARP inhibitors induce cell death, making them a valuable treatment for cancer. PARP inhibitors approved by the FDA from 2014-2023 are listed below in table 5.3:

Table 5.3: FDA approved PARP inhibitors (2014-2023)

Sl.	Indication	Name of drugs (Approval year)	
1.	Ovarian cancer	Olaparib (2014)	Niraparib (2019)
		Rucaparib (2018)	Bevacizumab (2020)
2.	Breast cancer	Olaparib (2018)	Talazoparib (2018)
3.	Prostate cancer	Rucaparib (2020)	Talazoparib (2023)
		Olaparib + Prednisone (2023)	Olaparib (2023)
4.	Peritoneal cancer	Olaparib (2017)	Olaparib + Bevacizumab
		Rucaparib (2018)	(2020)

5.1.4 <u>Immune checkpoint inhibitors (ICIs):</u> Checkpoint inhibitors are medications that block proteins produced by certain immune system cells, like T cells and certain cancer cells. These checkpoints control immune responses to avoid overstimulation and can stop T cells from targeting cancer cells. By obstructing these checkpoints, T lymphocytes are empowered to eradicate cancer cells. Immune checkpoint inhibitors approved by the FDA from 2014-2023 are listed below in table 5.4:

Table 5.4: FDA approved immune checkpoint inhibitors (2014-2023)

Sl.	Indication	Name of drugs (Approval year)	
1.	Endometrial Cancer	Pembrolizumab (2014)	Dostarlimab (2021)
2.	Urothelial Cancer	Nivolumab (2014) Pembrolizumab (2014)	Avelumab (2017)
3.	Colorectal Cancer	Nivolumab (2014)	Pembrolizumab (2014)
4.	Classical Hodgkin Lymphoma	Pembrolizumab (2014)	Nivolumab (2016)
5.	Squamous Cell Cancer	Pembrolizumab (2014) Nivolumab (2014)	Cemiplimab (2019)
6.	Renal Cancer	Ipilimumab (2014) Nivolumab (2014)	Pembrolizumab (2014) Avelumab (2017)
7.	Hepatocellular carcinoma	Nivolumab (2014) Pembrolizumab (2014)	Atezolizumab (2016) Durvalumab (2017)
8.	Lung Cancer (Non-Small Cell)	Nivolumab (2014) Pembrolizumab (2014) Atezolizumab (2016)	Durvalumab (2017) Cemiplimab (2019)
9.	Melanoma	Nivolumab (2014) Pembrolizumab (2014)	Atezolizumab (2016) Relatlimab (2022)
10.	Gastric Cancer	Pembrolizumab (2014) Nivolumab (2021)	

5.1.5 <u>Antibody drug conjugates (ADCs):</u> Antibody drug conjugates (ADCs) are medications created to selectively target particular cancer cells and deliver a cytotoxic chemical directly into the cancerous cell. Antibody-drug conjugates approved by the FDA from 2014-2023 are listed below in table 5.5:

Table 5.5: FDA approved antibody-drug conjugates (2014-2023)

Sl.	Indication	Name of drugs (Approval year)
1.	Classical Hodgkin lymphoma	Brentuximab vedotin (2015)
2.	Anaplastic large cell lymphoma	Brentuximab vedotin (2017)
3.	HER2+ breast cancer	Ado trastuzumab emtansine (2019) Fam-trastuzumab deruxtecan-nxki (2022)
4.	Acute lymphoblastic leukemia	Brexucabtagene autoleucel (2021)
5.	Large B-cell lymphoma	Polatuzumab vedotin (2019) Brexucabtagene autoleucel (2021)

Apart from these major 5 class of chemotherapeutic drugs shown in Figure 5.1, some other minor categories of drugs approved by the FDA from 2014 to 2023 are listed below in the table 5.6.

Table 5.6: Minor categories of chemotherapeutic drugs approved by FDA (2014-2023)

Sl.	Indication	Pharmacological class	Name of drugs (Approval year)		Number of drugs
1.	Prostate cancer	Anti-androgen	Abiraterone acetate Prednisone	Apulutamide Darolutamide Enzalutamide	5

Table 5.6: contd.

Sl.	Indication	Pharmacological class	Name of drugs (Approval year)	Number of drugs
2.	Cervical cancer	Anti-angiogenic agents	Bevacizumab	1
3.	Autologous cellular immunotherapy	Leukemia	Tisagenlecleucel	1
4.	B-cell lymphoma-2 inhibitor	Chronic lymphocytic leukemia	Venetoclax	1
5.	Chimeric antigen receptor t-cell immunotherapy	Large B-cell lymphoma	Axicabtagene ciloleucel	1
6.	Estrogen receptor antagonist	HER2- breast cancer	Elacestrant	1
7.	Hedgehog signaling pathway inhibitor	Basal cell carcinoma Leukemia	Sonidegib Glasdegib	2
8.	IDH1 inhibitors	Myeloid leukemia	Ivosidenib Olutasidenib	2
9.	Purine antagonists	Leukemia	Mercaptopurine	1
10.	T-cell engager antibody	Leukemia	Blinatumomab	1

5.2 Year-wise Chemotherapeutic drugs approved from 2014 to 2023

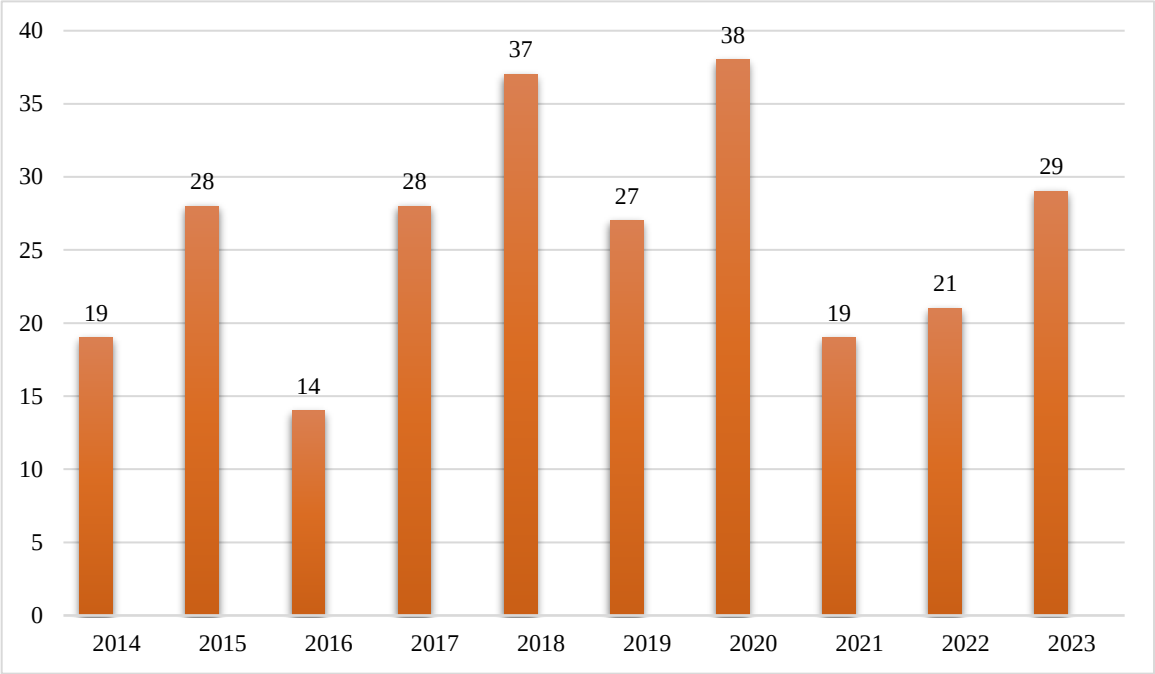


Figure 5.2: Number of drugs approved per year, 2014 - 2023

Above figure 5.2 illastrates the number of drugs approved by the FDA per year for anticancer treatment. It can be seen that there is a huge drop in approval of drugs in year 2021 compared to 2020, due to the Corona virus pandemic. Afterwards, we can see a steady growth in number of drug approvals in year 2022 and 2023. In conclusion, the number of chemotherapeutic drugs approved by FDA (from 2014 to 2023) is 260.

5.3 Chemotherapeutic drugs approved for major type of cancer from 2014 to 2023

There are many types of chemotherapeutic drugs that have been approved by FDA over the years. Among them, the drugs approved for major types of cancer from 2014 to 2023 are listed in the table 5.7:

Table 5.7: Drugs approved by FDA for major types of cancers

Types of cancer	Name of drugs		Number of drugs
Bladder Cancer (solid cancer)	Adstiladrin	Sacituzumab govitecan	13
	Avelumab	Pembrolizumab	
	Erdafitinib	Mitomycin	
	Avelumab	Nivolumab	
	Cisplatin	Valrubicin	
	Doxorubicin Hydrochloride	Erdafitinib	
	Enfortumab Vedotin		
Breast Cancer (solid cancer)	Abemaciclib	Capecitabine	19
	Fulvestrant	Olaparib	
	Ado-trastuzumab emtansine	Palbociclib	
	Alpelisib	Partuzumab	
	Atezolizumab	Ribociclib	
	Capivasertib	Sacituzumab govitecan	
	Fam-trastuzumab deruxtecan	Talazoparib	
	Margetuximab-cmkb	Trastuzumab	
	Neratinib	Tucatinib	

Table 5.7: contd.

Types of cancer	Name of drugs			Number of drugs
Colorectal cancer (solid cancer)	Trifluridine Tipiracil Encorafenib	Cetuximab Pembrolizumab Fruquintinib		6
Endometrial Cancer (solid cancer)	Lanreotide Everolimus Pembrolizumab	Lenvatinib Palbociclib Dostarlimab-gxly		6
Renal Cancer (solid cancer)	Avelumab Axitinib Belzutifan Cabozantinib Everolimus Lenvatinib	Nivolumab Ipilumumab Pembrolizumab Sunitinib malate Tivozanib		11
Leukemia (liquid cancer)	Acalabrutinib Asciminib Azacitidine Blinatumomab Bosutinib Brexucabtagene autoleucel Dasatinib Duvelisib	Enasidenib Gemtuzumab ozogamicin Gilteritinib Inotuzumab ozogamicin Ivosidenib Mercaptopurine Nilotinib	Ofatumumab Olutasidenib Onureg Quizartinib Rituximab Tisagenlecleucel Venetoclax Zanubrutinib Ibrutinib	24

Table 5.7: contd.

Types of cancer	Name of drugs		Number of drugs
Lymphoma (liquid cancer)	Acalabrutinib	Lorlatinib	23
	Alectinib	Nivolumab	
	Axicabtagene ciloleucel	Obinutuzumab	
	Belinostat	Olaparib	
	Brentuximab vedotin	Pembrolizumab	
	Ceritinib	Polatuzumab vedotin	
	Crizotinib	Rituximab	
	Duvelisib	Selinexor	
	Ibrutinib	Tisagenlecleucel	
	Idelalisib	Venetoclax	
	Lenalidomide	Zanubrutinib	
	Lisocabtagene maraleucel		
Liver cancer (solid cancer)	Lenvatinib	Ramucirumab	9
	Bevacizumab	Nivolumab	
	Cabozantinib	Atezolizumab	
	Durvalumab	Tremelimumab	
	Ipilimumab		
Non-small cell Lung Cancer (solid cancer)	Afatinib	Lorlatinib	27
	Alectinib	Necitumumab	
	Atezolizumab	Nivolumab	
	Cemiplimab-rwlc	Olaparib	

Table 5.7: contd.

Types of cancer	Name of drugs		Number of drugs
	Ceritinib	Osimertinib	
	Crizotinib	Pembrolizumab	
	Dabrafenib	Paclitaxel or	
	Trametinib	nab-paclitaxel	
	Dacotinib	Pralsetinib	
	Durvalumab	Ramucirumab	
	Encorafenib	Erlotinib	
	Binimetinib	Repotrectinib	
	Everolimus	Selpercatinib	
	Gefitinib	Tremelimumab	
Melanoma (solid cancer)	Atezolizumab	Ipilimumab	13
	Cobimetinib	Nivolumab	
	Dabrafenib	Pembrolizumab	
	Trametinib	Talimogene	
	Encorafenib	Laherparepvec	
	Binimetinib	Tebentafusp-tebn	
		Vemurafenib	
Non-Hodgkin Lymphoma (liquid cancer)	Brentuximab vedotin	Nivolumab	3
	Idelalisib		

Table 5.7: contd.

Types of cancer	Name of drugs		Number of drugs
Pancreatic Cancer (solid cancer)	Lanreotide Irinotecan	Fluorouracil Leucovorin	4
Prostate Cancer (solid cancer)	Abiraterone acetate Prednisone Apulutamide Darolutamide Enzalutamide	Niraparib Olaparib Pluvicto Rucaparib Talazoparib	10
Thyroid Cancer (solid cancer)	Cabozantinib Lenvatinib	Pralsetinib Selpercatinib	4

The data collected from the table is presented in the figure 5.3 in percentage that indicates the prevalent types of cancers for which the most number of drugs were approved.

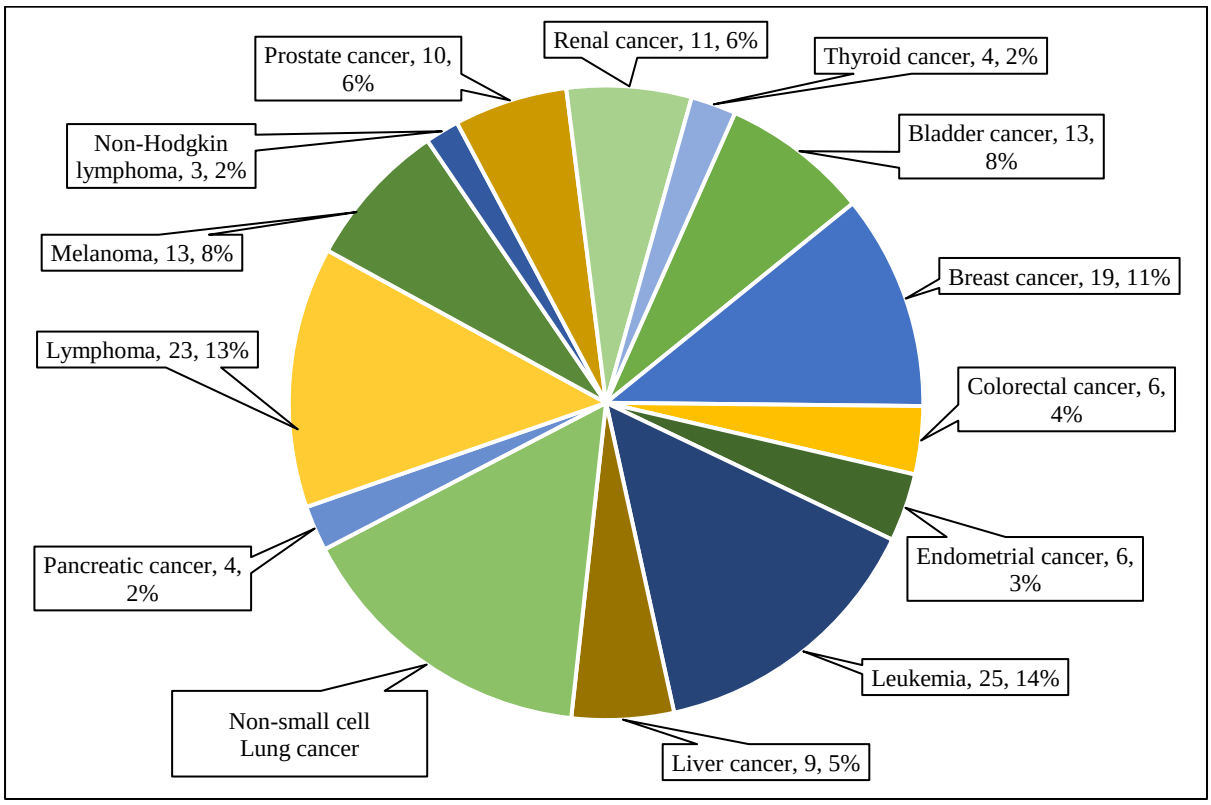


Figure 5.3: Percentage of chemotherapeutic drugs approved for major types of cancer

5.4 Chemotherapeutic drugs approved based on the dosage forms

There are varieties of dosage form for anticancer drugs, like oral suspension, tablets, capsules injectable solutions. Among the 260 chemotherapeutic drugs approved by FDA from 2014-2023; most common dosage form of drugs approved were injectable solution (133), tablets (81) and capsules (43).

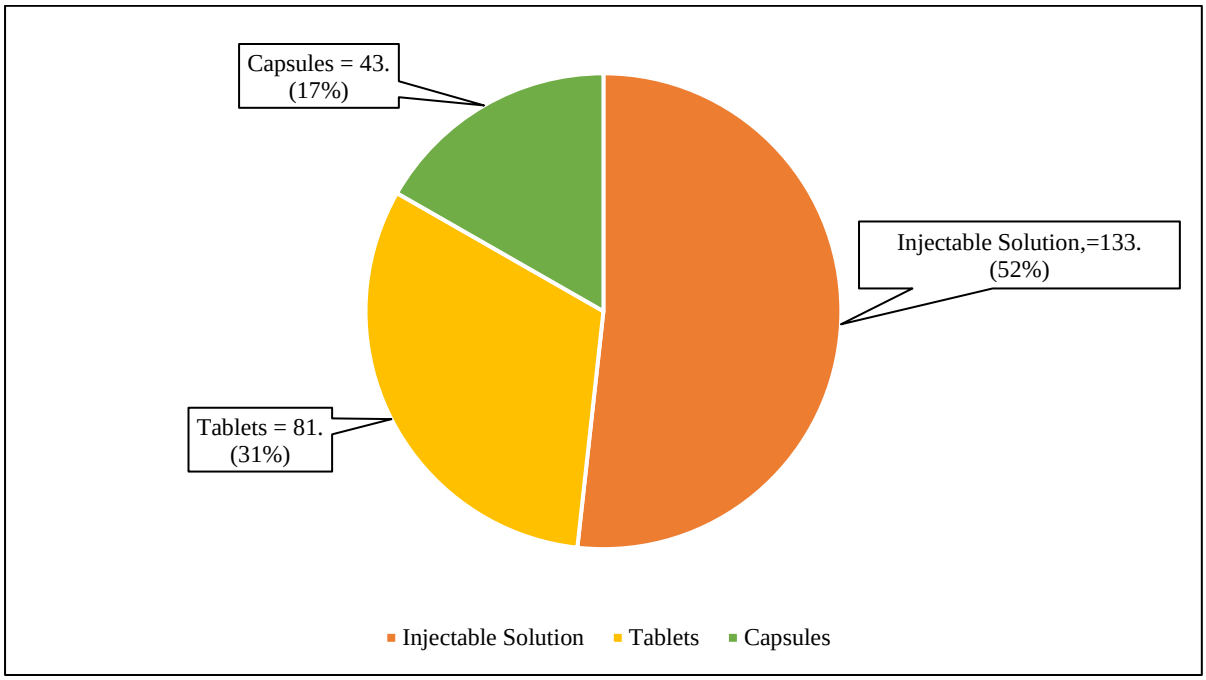


Figure 5.4: Chemotherapeutic drugs approved based on the dosage forms

5.5 Oral chemotherapeutic drugs

The use of oral chemotherapy appears to hold great potential for the advancement of oncology in the years to come. Traditionally, the majority of anticancer medications were administered intravenously, providing the most direct method for immediate and full absorption of the medicines. Nevertheless, this method of administration may lead to various adverse effects and necessitates a visit to a clinic or hospital, in addition to nursing care and palliative care. Because of these later factors, oral administration of anticancer medications is becoming an increasingly popular option in today's world. Oral chemotherapy allows for administration without the need for injections and can be done in the comfort of one's home (Halfdanarson & Jatoi, 2010). This method can improve patient compliance and their overall well-being, making it a crucial aspect that should be a priority in any medical intervention. Tablets and capsules are the most common oral dosage form, but oral chemotherapeutic drugs also come in oral suspension, powder and oral granules.

Table 5.8: Oral chemotherapeutic drugs approved by FDA

Types of cancer	Drugs approved		Number of drugs
Breast cancer	Abemaciclib	Capecitabine	13
	Alpelisib	Olaparib	
	Fulvestrant	Palbociclib	
	Capivasertib	Ribociclib	
	Elacestrant	Talazoparib	
	Neratinib	Tucatinib	
	Trastuzumab		

Table 5.8: contd.

Types of cancer	Drugs approved		Number of drugs
Leukemia	Acalabrutinib	Rituximab	16
	Asciminib	Ivosidenib	
	Bosutinib	Olutasidenib	
	Dasatinib	Onureg	
	Duvelisib	Quizartinib	
	Enasidenib	Venetoclax	
	Gilteritinib	Zanubrutinib	
	Ibrutinib	Glasdegib	
Non-small cell lung cancer (NSCLC)	Afatinib	Everolimus	18
	Alectinib	Gefitinib	
	Capmatinib	Lorlatinib	
	Ceritinib	Olaparib	
	Crizotinib	Osimertinib	
	Dabrafenib	Pralsetinib	
	Trametinib	Repotrectinib	
	Dacotinib	Selpercatinib	
	Encorafenib	Binimetinib	
Colorectal cancer	Trifluridine	Cetuximab	5
	Tipiracil	Fruquintinib	
	Encorafenib		

Table 5.8: contd.

Types of cancer	Drugs approved		Number of drugs
Prostate cancer	Apulutamide	Abiraterone acetate	9
	Darolutamide	Prednisone	
	Olaparib	Enzalutamide	
	Rucaparib	Talazoparib	
	Niraparib		
Ovarian cancer	Niraparib	Bevacizumab	4
	Olaparib	Rucaparib	
Thyroid cancer	Cabozantinib	Lenvatinib	4
	Selpercatinib	Pralsetinib	
Renal cancer	Belzutifan	Tivozanib	7
	Cabozantinib	Sunitinib malate	
	Lenvatinib	Cabozantinib	
	Everolimus		

Chapter 6

Conclusion

In the present study, the approval of these medications was determined by the frequency of various types of cancer. Between 2014 and 2023, the most prevalent cancer types were breast cancer, leukemia, lymphoma, and lung cancer. The FDA predominantly approves kinase inhibitors and monoclonal antibodies as the most effective category for the targeted cancer therapies. Moreover, FDA approved overall 260 chemotherapeutic drugs, among them 133 drugs are in injectable solutions and total 127 drugs are in oral dosage forms. The latest addition to the chemotherapy treatment for cancer from 2024 to 2023 thus shows that there is a huge potential to deliver targeted cancer treatment.

Chapter 7

References

1. National Cancer Institute. (2018). *Common Cancer Sites - Cancer Stat Facts*. SEER. https://seer.cancer.gov/statfacts/html/common.html
2. *SEER Cancer Stat Facts*. (2018). SEER. https://seer.cancer.gov/statfacts/
3. *What Are the Differences Between Solid and Liquid Tumors?* (2022, February 16). Massive Bio. https://massivebio.com/what-are-the-differences-between-solid-and-liquid-tumors/
4. Lee, S. (2014). *Types of tumours*. Canadian Cancer Society. https://cancer.ca/en/cancer-information/what-is-cancer/types-of-tumours#:~:text=Tumours%20are%20groups%20of%20abnormal
5. Mattiuzzi, C., & Lippi, G. (2019). Current Cancer Epidemiology. *Journal of Epidemiology and Global Health*, *9*(4), 217–222. https://doi.org/10.2991/jegh.k.191008.001
6. National Cancer Institute. (2019). *About Cancer*. National Cancer Institute; Cancer.gov. https://www.cancer.gov/about-cancer
7. Research, C. for D. E. and. (n.d.). *Approved Drugs - Hematology/Oncology (Cancer) Approvals & Safety Notifications*. Wayback.archive-It.org. Retrieved February 24, 2024, from https://wayback.archive-it.org/7993/20170111064250/http:/www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm
8. Research, C. for D. E. and. (2021). Oncology (Cancer) / Hematologic Malignancies Approval Notifications. *FDA*. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

9. World Health Organization. (2022). *Cancer*. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/cancer

10. Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., & Walter, P. (2013). Cancer as a Microevolutionary Process. Nih.gov; Garland Science. https://www.ncbi.nlm.nih.gov/books/NBK26891/

11. National Cancer Institute. (2011, February 2). NCI Dictionary of Cancer Terms. National Cancer Institute. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/solid-tumor

12. Lee, S. (2016). Chemotherapy. Canadian Cancer Society. https://cancer.ca/en/treatments/treatment-types/chemotherapy

13. Types of Cancer Treatment. (2020). National Cancer Institute; Cancer.gov. https://www.cancer.gov/about-cancer/treatment/types

14. Cancer.net. (2019). Cancer.net. https://www.cancer.net/

15. Halfdanarson, T. R., & Jatoi, A. (2010). Oral Cancer Chemotherapy: The Critical Interplay Between Patient Education and Patient Safety. Current Oncology Reports, 12(4), 247–252. https://doi.org/10.1007/s11912-010-0103-6

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