A current view on new cancer drugs (2014-USFDA approved) drugs

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Abstract
Cancer is also known as a malignant tumor, is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Not all tumors are cancerous, benign tumors do not spread to other parts of the body. Treatment options depend on the stage and type of cancer. As compare to previous drugs the newly 2014 USFDA approved drugs work effectively in treating the cancer. The number of patients treated with new drugs such as Bevacizumab, Crizotinib, Pembrolizumab, Idelalisib was effectively against chronic lymphocytic leukemia patients without the need of chemotherapy and the treatment of pediatric osteosarcoma etc.

Keywords: Proliferation, Tumorigenic, Procarcinogens.

INTRODUCTION
Cancer refers to a group of illnesses that result from cells in the body growing abnormally. These cells divide and produce new cells in an uncontrolled way that can spread throughout the body and cause damage to essential organs. When cancer spreads to other parts of the body, this is called metastasis. Metastases can occur when cancer cells enter the bloodstream or lymph system. These systems circulate all over the body and allow the cells to travel [1]. Cancer is also known as a malignant tumor, is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. Not all tumors are cancerous, benign tumors do not spread to other parts of the body. The signs and symptoms of cancer are a new lump, abnormal bleeding, a prolonged cough, unexplained weight loss, and a change in bowel movements. There are over 100 different known cancers that affect humans. Tobacco use is the cause of about 22% of cancer deaths. Another 10% is due to obesity, a poor diet, lack of physical activity, drinking alcohol, radiation and environmental pollutants. Typically many such genetic changes are required before cancer develops. Approximately 5–10% of cancers are due to genetic defects inherited from a person’s parents. Cancer can be detected by certain signs and symptoms or screening tests. It is then typically further investigated by medical imaging and confirmed by biopsy. Many cancers can be prevented by stop smoking, eating more vegetables, fruits and whole grains, eating less meat and refined carbohydrates, maintaining a healthy weight, exercising, minimizing sunlight exposure, and being vaccinated against certain infectious diseases. Early detection through screening is useful for cervical and colorectal cancer. The benefits of screening in breast cancer are controversial. Cancer is often treated with some combination of radiation therapy, surgery, chemotherapy and targeted therapy. Pain and symptom management are an important part of care. The most common types of cancer in males are lung cancer, prostate cancer, colorectal cancer, and stomach cancer, and in females, the most common types are breast cancer, colorectal cancer, lung cancer, and cervical cancer. Skin cancer is not included in these statistics and if it were it would account for at least 40% of cases [2].

Pathophysiology
Chemical carcinogenesis is multistep process they are Initiation, Mutation, Proliferation.

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**Initiators**

1. Direct acting compounds: Direct acting carcinogens are bind covalently to cellular macromolecules. E.g. nitrogen mustard, bis(chloral-methyl) ether, benzyl chloride, Epoxides

2. Indirect acting carcinogen (Procarcinogens). Require metabolic conversion to form ultimate active carcinogen.

**Fig 1. Cellular proliferation**

![Diagram of cellular proliferation]

**Promoters**

A. Can cause cellular proliferation & induce tumors in initiated cells, e.g. estrogen but they are non tumorigenic by themselves.

B. Proliferation of a mutated cell may lead to accumulation of additional mutations shown in Figure 1 [3-6].

**TYPES OF TUMORS**

**Benign Tumors**

Benign tumors are not cancer. They usually can be removed and, in most cases, they do not come back. Most important, cells from benign tumors do not spread to other parts of the body. Cells from benign tumors stay together and often they are surrounded by a containing membrane. Benign tumors are not usually a threat to life [7]. The examples of Benign Tumors are

- **Papilloma** A projecting mass on the skin (eg - a wart)
- **Adenoma** A tumor that grows in and around the glands
- **Lipoma** A tumor in fatty tissue
- **Osteoma** A tumor originating in the bones
- **Myoma** A tumor of muscle tissue
- **Angioma** A tumor usually composed of small blood or lymph vessels (eg - a birthmark)
- **Nevus** A small skin tumor of one variety of tissues (eg - a mole).

**Malignant tumors**

Malignant tumors are cancer. Cancer cells can invade and damage tissues and organs near the tumor. Cancer cells also can break away from a malignant tumor and enter the lymphatic system or the bloodstream, which is how cancer can spread to other parts of the body. The characteristic feature of cancer is the cell’s ability to grow rapidly, uncontrollably, and independently from the tissue where it started. The spread of cancer to other sites or organs in the body through the blood stream or lymphatic system is called metastasis. Malignant tumors generally can be classified in two categories.

**Carcinomas** - These cancers originate in the epithelium. The epithelium is the lining cells of an organ. Carcinomas are the most common type of cancer. Common sites of carcinomas are the skin, mouth, lung, breast, stomach, colon and uterus [8].

**Sarcomas** - Sarcomas are cancers of connective and supportive tissue of all kinds. Sarcomas can be found anywhere in the body, and they often form secondary growths in the lungs [9, 10].
Table 1. Important Types of Cancer

<table>
<thead>
<tr>
<th>S.No</th>
<th>Different types of cancer</th>
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<tbody>
<tr>
<td>1</td>
<td>Adrenal Cancer</td>
<td>27</td>
<td>Leukemia - Chronic Myelomonocytic</td>
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<td>2</td>
<td>Anal Cancer</td>
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<td>Liver Cancer</td>
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<td>3</td>
<td>Bile Duct Cancer</td>
<td>29</td>
<td>Lung Cancer</td>
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<td>4</td>
<td>Bladder Cancer</td>
<td>30</td>
<td>Lung Cancer - Non-Small Cell</td>
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<td>Bone Cancer</td>
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<td>Lung Cancer - Small Cell</td>
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<tr>
<td>6</td>
<td>Brain/CNS Tumors</td>
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<td>Lung Carcinoid Tumor</td>
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<tr>
<td>7</td>
<td>Breast Cancer</td>
<td>33</td>
<td>Lymphoma</td>
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<tr>
<td>8</td>
<td>Breast Cancer</td>
<td>34</td>
<td>Lymphoma of the Skin</td>
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<td>9</td>
<td>Cervical Cancer</td>
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<td>Malignant Mesothelioma</td>
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<td>10</td>
<td>Colon/Rectum Cancer</td>
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<td>Myelodysplastic Syndrome</td>
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<td>Esophagus Cancer</td>
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<td>Nasal Cavity and Paranasal Sinus Cancer</td>
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<td>Eye Cancer</td>
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<td>Nasopharyngeal Cancer</td>
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<td>Gallbladder Cancer</td>
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<td>Gastrointestinal Carcinoid Tumors</td>
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<td>Oral Cavity and Oropharyngeal Cancer</td>
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<td>Gastrointestinal Stromal Tumor</td>
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<td>Kidney Cancer</td>
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<td>Pancreatic Cancer</td>
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<td>Laryngeal and pharyngeal Cancer</td>
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<td>Penile Cancer</td>
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<td>Leukemia</td>
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<td>Pituitary Tumors</td>
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<td>Salivary Gland Cancer</td>
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<td>Sarcoma - Adult Soft Tissue Cancer</td>
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<td>Skin Cancer - Squamous Cell</td>
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<td>Uterine Sarcoma</td>
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<td>25</td>
<td>Small Intestine Cancer</td>
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<td>Vaginal Cancer</td>
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<td>26</td>
<td>Stomach Cancer</td>
<td>52</td>
<td>Vulvar Cancer</td>
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</tbody>
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Fig 3. Outline on different types of cancer
Pancreatic cancer
Pancreatic cancer occurs when cancer cells develop in the pancreas, a glandular organ located behind the stomach. There are a number of different types of pancreatic cancer, but pancreatic adenocarcinoma represents about 85% of all cases. Signs and symptoms of pancreatic cancer may include abdominal or back pain, yellow skin, unexplained weight loss, light colored stools, dark urine and loss of appetite. Early on there are usually no symptoms. Symptoms that are specific enough to suspect pancreatic cancer often do not appear until the disease is already in an advanced stage [11]. By the time of diagnosis the cancer has usually spread to other parts of the body shown in Figure 4 [12].

![Fig 4. Pancreatic cancer](image)

Stomach cancer
Stomach cancer or gastric cancer, is when cancer develops from the lining of the stomach [13].

The most common cause is infection by the bacteria Helicobacter pylori, which accounts for more than 60% of cases [14, 15]. Certain type of H. pylori has greater risks than others. Other common causes include eating pickled vegetables and smoking was shown in Figure 5.

Leukemia
Leukemia is a group of cancers that usually begins in the bone marrow and results in high numbers of abnormal white blood cells [16]. These white blood cells are not fully developed and are called blasts or leukemia cells. Symptoms may include bleeding and bruising problems, feeling very tired, and an increased risk of infections. These symptoms occur due to a lack of normal blood cells [17]. It is shown in Figure 6.

![Fig 6. Leukemia](image)

Cervical and uterus cancer
Cervical cancer is a cancer arising from the cervix [18]. It is due to the abnormal growth of cells that have the ability to invade or spread to other parts of the body [19]. Early on there are typically no symptoms. Later symptoms may include: abnormal vaginal bleeding, pelvic pain or pain during sexual intercourse [20]. Human papillomavirus (HPV) infection appears to be involved in the development of more than 90% of cases [21, 22]. Most people who have had HPV infections, however, do not develop cervical cancer [23]. Other risk factors include: smoking, a weak immune system, birth control pills, starting sex at a young age and having many sexual partners, but these are less important shown in Figure 7.
Breast Cancer
Breast cancer is the development of cancer from breast tissue [24]. Signs of breast cancer may include a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, or a red scaly patch of skin [25]. In those with distant spread of the disease, there may be bone pain, swollen lymph nodes, shortness of breath, or yellow skin. Risk factors for developing breast cancer include obesity, lack of physical exercise, drinking alcohol, hormone replacement therapy during menopause, ionizing radiation, early age at first menstruation, and having children late or not at all mentioned in Figure 8 [26].

Genetics of Cancer
Only a small number of the approximately 35,000 genes in the human genome have been associated with cancer. Alterations in the same gene often are associated with different forms of cancer. These malfunctioning genes can be broadly classified into three groups. The first group, called proto-oncogenes, produces protein products that normally enhance cell division or inhibit normal cell death [29]. The mutated forms of these genes are called oncogenes. The second group, called tumor suppressors, makes proteins that normally prevent cell division or cause cell death. The third group contains DNA repair genes, which help prevent mutations that lead to cancer. Proto-oncogenes and tumor suppressor genes work much like the accelerator and brakes of a car, respectively. The normal speed of a car can be maintained by controlled use of both the accelerator and the brake. Similarly, controlled cell growth is maintained by regulation of proto-oncogenes, which accelerate growth, and tumor suppressor genes, which slow cell growth. Mutations that produce oncogenes accelerate growth while those that affect tumor suppressors prevent the normal inhibition of growth. In either case, uncontrolled cell growth occurs [30, 31].

Stages of Cancer
Cancer cells vary in how fast they grow and how they spread in the body. Most cancers are defined...
by stage of growth using a system developed by
the American Joint Committee on Cancer for solid
tumors (like cancer of the lung, breast or colon).
The stage is based on the size of the tumor and on
how much the cancer has spread.
Stage I – Primary tumor only
Stage II – Primary tumor, but larger than in Stage I
Stage III – Primary tumor and metastasis to lymph
nodes
Stage IV – Primary tumor and distant metastasis. It
is shown in Fig.no.10

Fig 10. Stages of Cancer

Risk factors
- Tobacco use
- High fat diet and being overweight
- Excessive exposure to sunlight
- Drinking too much alcohol
- X-rays and other sources of radioactivity
- Geographic area
- Chemicals and other substances in the
  environment (carcinogens)
- Unsafe sexual practices (through acquiring
  certain infections)
- Family members who have cancer

Cancer symptoms
- Thickening or lump in the body
- Cough or hoarseness that does not go
  away
- Obvious change in a wart or moles
- Changes in bowel or bladder habits
- Unexplained bleeding or discharge
- Any sore that does not heal
- Unusual upset stomach or difficulty

Diagnosing cancer
- Physical examination

- Laboratory tests – such as blood and
- Urine tests
- Imaging – X-ray, CT scan, and MRI
- Biopsy

Treatment of cancer
Most of the cancers diagnosed are now curable.
Even with cancers that cannot be cured, symptoms
are often greatly diminished by treatment.
Treatment options, which depend on the stage and
type of cancer, include:
- Surgery
- Radiation therapy
- Chemotherapy
- Biological therapy
- Hormone therapy [32]

2014 USFDA APPROVED CANCER DRUGS
Bevacizumab
Crizotinib
Pembrolizumab
Idelalisib

Bevacizumab
Chemistry: Typically, Bevacizumab is a monomer
with molecular weight of 149KDa. The heavy chains
show C-terminal heterogeneity (lysine variants) and
also contain one N-linked glycosylation on
asparagine at position 303. Two inter-chain covalent
disulfide bonds couple the two heavy chains. Each
light chain is covalently joined through a disulfide
bond at cysteine 214 to a heavy chain at cysteine
226 [33].

Structure

Fig 11. Bevacizumab

Introduction
It is an angiogenesis inhibitor, as a drug that
slows the growth of new blood vessels. It is licensed
to treat various cancers, including colorectal, lung,
breast, glioblastoma, kidney and ovarian.
Bevacizumab is a recombinant humanized monoclonal antibody that produces angiogenesis inhibition by inhibiting vascular endothelial growth factor A (VEGF-A). VEGF-A is a chemical signal that stimulates angiogenesis in a variety of diseases, especially in cancer. Bevacizumab was the first clinically available, angiogenesis inhibitor in the United States. Bevacizumab was approved by the U.S. Food and Drug Administration (FDA) for certain metastatic cancers. It received its first approval in 2004, for combination use with standard chemotherapy for metastatic colon cancer. It has since been approved for use in certain lung cancers, renal cancers, ovarian cancers, breast cancers and glioblastoma multiforme of the brain.

**Mechanism of Action**
Bevacizumab contains human framework regions with antigen binding regions of a humanised murine antibody that binds to VEGF. Bevacizumab is produced by recombinant DNA technology in a Chinese hamster ovary mammalian cell expression system in a nutrient medium containing the antibiotic gentamicin and is purified by a process that includes specific viral inactivation and removal steps. Gentamicin is detectable in the final product at 0.35 ppm.

AVASTIN inhibits the binding of VEGF to its receptors, on the surface of endothelial cells. Neutralising the biologic activity of VEGF reduces tumour angiogenesis, thereby inhibiting tumour growth. Administration of bevacizumab or its parental murine antibody to xenotransplant models of cancer in nude mice resulted in extensive anti-tumour activity in human cancers, including colon, breast, pancreas and prostate. Metastatic disease progression was inhibited and microvascular permeability was reduced.

**Pharmacokinetics**
The pharmacokinetics of bevacizumab were characterised in patients with various types of solid tumours. The doses tested were 0.1-10 mg/kg weekly in phase I; 3-20 mg/kg every two weeks or every three weeks in phase II; 5 mg/kg or 15 mg/kg q3w in phase III. In all clinical trials, bevacizumab was administered as an IV infusion. As observed with other antibodies, the pharmacokinetics of bevacizumab is well described by a two compartment model. Overall, in all clinical trials, bevacizumab disposition was characterized by a low clearance, a limited volume of the central compartment (Vc), and a long elimination half-life. This enables target therapeutic bevacizumab plasma levels to be maintained with a range of administration schedules. Low albumin and high tumour burden are generally indicative of disease severity. Bevacizumab clearance was approximately 30 % faster in patients with low levels of serum albumin and 7 % faster in subjects with higher tumour burden when compared with the typical patient with median values of albumin and tumour burden.

The Food and Drug Administration (FDA) approved bevacizumab for Metastatic Colorectal Cancer in Combination with Fluoropyrimidine-based Chemotherapy, Metastatic Renal Cell Carcinoma, Second-Line Treatment of Glioblastoma, First-Line Treatment of Non-Small Cell Lung Cancer (NSCLC), First-Line and Second-Line Treatment of Metastatic Colorectal Cancer

**Dose**
The recommended dose of bevacizumab is 15 mg/kg every 3 weeks as an intravenous infusion (IV) administered in combination with paclitaxel and cisplatin or paclitaxel and topotecan. The dosing regimens used in the clinical trial were as follows and repeated every 21 days [35].

**Crizotinib**

**Chemistry**
Crizotinib is an oral receptor tyrosine kinase inhibitor. The molecular formula for crizotinib is C21H22Cl2FN5O. The molecular weight is 450.34 Daltons. Crizotinib is described chemically as (R)-3-[(l-(2,6-Dichloro-3-fluorophenyl)ethoxy]-5-[1-(piperidin-4-yl)-1H-pyrazol-4-yl]pyridin-2-amine [Figure 12]. Crizotinib is a white- to pale-yellow powder with a pKa of 9.4 (piperidinium cation) and 5.6 (pyridinium cation).
The solubility of crizotinib in aqueous media decreases over the range of pH 1.6 to pH 8.2 from greater than 10 mg/mL to less than 0.1 mg/mL. The log of the distribution coefficient (octanol/water) at pH 7.4 is 1.65 [36, 37].

**History**
ALK (anaplastic lymphoma kinase) was first identified as a potential drug target in cancer over 15 years ago when it was discovered as a fusion kinase with nucleophosmin in anaplastic large cell lymphoma. However, in the field of lung cancer, ALK was only first recognized as a molecular target four years ago when Dr. Mano and colleagues reported that 6.7% of Japanese patients with NSCLC harbor a fusion of EML4 (echinoderm microtubule associated protein like 4) with the intracellular kinase domain of ALK. Based on in vitro studies with an ALK inhibitor WHI-P154 and a Ba/F3 cell line model, Dr. Mano's team suggested that ALK might represent a therapeutic target in patients with ALK-positive NSCLC [38].

**Mechanism of action**
Crizotinib is an inhibitor of receptor tyrosine kinases including ALK, Hepatocyte Growth Factor Receptor (HGFR, c-Met). Translocations can affect the ALK gene resulting in the expression of oncogenic fusion proteins. The formation of ALK fusion proteins results in the activation and dysregulation of the gene's expression and signaling, which can contribute to increased cell proliferation and survival in tumors expressing these proteins. Crizotinib demonstrates concentration-dependent inhibition of ALK and c-Met phosphorylation in cell-based assays using tumor cell lines, and also demonstrates antitumor activity in mice bearing tumor xenografts that express EML4 fusion proteins or c-Met [15,16]. Crizotinib is a multi targeted small molecule tyrosine kinase inhibitor, which had been originally developed as an inhibitor of the mesenchymal epithelial transition growth factor (c-MET); it is also a potent inhibitor of ALK phosphorylation and signal transduction. This inhibition is associated with G1-S phase cell cycle arrest and induction of apoptosis in positive cells in vitro and in vivo. Crizotinib also inhibits the related ROS1 receptor tyrosine kinase.

**Indications**

**Dose**
ALK-positive NSCLC, Oral: 250 mg twice daily, continue treatment until no longer clinically beneficial. It can be administered with or without food. If a dose is missed, take as soon as remembered, unless it is <6 hours prior to the next scheduled dose (skip the dose if <6 hours before the next dose); do not take two doses at the same time to make up for a missed dose [37].

**Pembrolizumab**
**Chemistry**
Pembrolizumab is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2. Pembrolizumab is an IgG4 kappa immunoglobulin with an approximate molecular weight of 149 kDa [39]. The Molecular formula of Pembrolizumab MC6504-H10004-N1716-O2036-S46 [40] Pembrolizumab (Trade name Keytruda formerly lambrolizumab also known as MK3475) [41, 42] in Figure 13.

**Structure**
Fig 13. Pembrolizumab

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**Introduction**
Pembrolizumab is a drug marketed by Merck that targets the programmed cell death 1 (PD-1) receptor. The drug is intended for use in treating metastatic melanoma. Pembrolizumab was invented by Gregory Carven, Hans van Eenennaam and John Dulos at Organon Biosciences which later became Schering Plough Research Institute and then Merck & Co.
On September 4, 2014 the US Food and Drug Administration (FDA) approved Pembrolizumab as a breakthrough therapy. It is approved for use following treatment with ipilimumab, or after treatment with ipilimumab and a BRAF inhibitor in patients who carry aBRAF mutation.

Mechanism
Pembrolizumab is a humanized monoclonal antibody which binds to the PD-1 receptor on T-cells. In some cancers, the PD-1 ligands are upregulated, which results in inhibition of T-cell immune surveillance of tumors. By blocking the interaction between the PD-1 receptor and its ligands PD-L1 and PD-L2, pembrolizumab decreases this immune system inhibition and facilitates anti-tumor immune response [44].

Indications
KEYTRUDA (Pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. This indication is approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Recommended Dosing
The recommended dose of KEYTRUDA is 2 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity [45].

Idelalisib
Chemistry
Idelalisib inhibits the production of the second messenger phosphatidylinositol-3,4,5-trisphosphate (PIP3), preventing the activation of the PI3K signaling pathway and inhibiting tumor cell proliferation, motility, and survival. The chemical structure of Idelalisib 5-fluoro-3-phenyl-2-[(S)-1-[(9H-purin-6-ylamino)-propyl]-3H-quinazolin-4-yl]-propyl]-3H-quinazolin-4-one [47]. The Molecular Formula of Idelalisib is C_{22}H_{18}FN_{7}O. The Molecular Weight of Idelalisib 415.42. Idelalisib solubilizes in water, ethanol. It is also called phosphoinositide-3 kinase delta inhibitor CAL-101 PI3K delta inhibitor CAL-101[48, 49]

Introduction
Idelalisib is a highly specific small-molecule phosphatidylinositol-3-kinase (PI3Kδ) inhibitor that has been developed as an oral treatment for B cell haematological cancers. It has received its first approval in the US in July 2014 for the treatment of relapsed chronic lymphocytic leukaemia (CLL), relapsed follicular B-cell non-Hodgkin lymphoma (NHL) and relapsed small lymphocytic leukaemia (SLL). Idelalisib is under regulatory review in the EU where it has received a positive opinion from the European Medicines Agency Committee for Medicinal Products for Human use and in clinical development for CLL in Australia and Canada. This article summarizes the milestones in the development of Idelalisib leading to this first approval for relapsed CLL, NHL and SLL [46].

FDA approved for the treatment of
- Chronic lymphocytic leukemia (CLL) and Small lymphocytic lymphoma (SLL)
- Follicular lymphoma
- Marginal zone lymphoma
- Waldenstrom macroglobulinemia

Approval by the FDA on 23 July 2014, the FDA granted Idelalisib approval to treat different types of leukemia [50].

Mechanism of action
Idelalisib inhibits modulation of integrin-mediated CLL-cell adhesion and integrin signaling events, according to Italian and US researchers. The study was set up to observe the effects of idelalisib on CLL-cell adhesion to endothelial and bone marrow stromal cells (EC and BMSC). Researchers collected
peripheral blood samples from untreated CLL-patients who met the clinical and immuno phenotypic criteria for CLL and analyzed EC and BMSC under static and shear flow conditions. Based on the results of this in vitro analysis, idelalisib has the potential to interfere with integrin-mediated adhesion, especially with VLA-4 on CLL-cells and vascular cell adhesion molecule-1 (VCAM-1), causing lymph node shrinkage with a redistribution of CLL into the blood. These results prove that idelalisib has an effect on survival by inhibiting the pro-survival pathways activated during CLL-cell adhesion. The authors of the study concluded: “Idelalisib interferes with integrin-mediated CLL-cell adhesion to EC and BMSC, providing a novel mechanism to explain idelalisib-induced redistribution of CLL-cells from tissues into the blood [51].

Dose
The recommended maximum starting dose of Zydelig is 150 mg administered orally twice daily. Zydelig can be taken with or without food. Tablets should be swallowed whole. Continue treatment until disease progression or unacceptable toxicity. The optimal and safe dosing regimen for patients who receive treatment longer than several months is unknown.

Indications
Idelalisib is a second line drug for patients whose chronic lymphocytic leukemia (CLL) has relapsed. Used in combination with Rituximab, Idelalisib is to be used in patients for whom Rituximab alone would be considered appropriate therapy due to other existing medical conditions. The FDA is also granted Idelalisib approval to treat patients with relapsed follicular B-cell non-Hodgkin lymphoma (FL) and relapsed small lymphocytic lymphoma (SLL). Idelalisib is intended to be used in patients who have received at least two prior systemic therapies.

CONCLUSION
1. As compare to previous drugs the newly approved drugs may work effectively in treating the cancer. Bevacizumab is not cost-effective compared with Ranibizumab. The drug is also undergoing initial trials as an addition to established chemotherapy protocols and surgery in the treatment of pediatric osteosarcoma and other sarcomas, such as leiomyosarcoma.
2. The effects of crizotinib on ID1 expression and cancer cell migration were associated with the presence of activated MET, rather than ALK fusion. The number of patients treated with crizotinib who experienced tumor responses was more to what was seen in the early-phase trials.
3. Pembrolizumab is tolerable and provides antitumour activity in treatment previously treated advanced NSCLC, regardless of dose/schedule. Patients with strong PD-L1 tumour expression may derive particular benefit from pembrolizumab. Validation of the prospective PD-L1 cutpoint will be performed in an additional 300 patients enrolled in KEYNOTE-001. Ongoing studies with pembrolizumab in NSCLC are KEYNOTE-010, 024, and 042.
4. A study of Idelalisib finds that this experimental targeted therapy drug may effectively treat chronic lymphocytic leukemia patients without the need for chemotherapy. CLL starts from white blood cells called lymphocytes in the bone marrow.

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