



## Glimpses of FDA Approved Anti - Neoplastic Drugs 2016

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### Abstract

The article is all about the anti – cancer drugs approved by the FDA for treating different forms of cancers. Article gives complete idea about each drug which was approved by FDA, which includes the use, route of administration, the dosing & the side effects. The article also gives brief about the pharmacokinetics & pharmacodynamics of the drugs.

## 1 Introduction

In 2016, the FDA has approved new drugs for different cancer types. Chemotherapy is one of the commonest tools which are used to treat cancer, and research continues in finding newer drugs and to find newer uses of existing drugs. The drugs aim precisely in identifying the cancerous cells and to reduce the effect on normal cells.

45 new molecular entities and biologic license applications were introduced in 2016, among these 16 were novel therapies for cancer. Newer oncology drugs concentrated in development of immunotherapies, adoptive cell therapies and new vaccines. Anti cancer drugs are used to control the growth of the unwanted cells. Cancer is commonly defined as multiplication of unwanted cells, which could be benign or malignant. There are several anti cancer drugs but FDA has approved only certain drugs, where several drugs are under an accelerated approval category, that is the drugs which need to undergo phase 4 confirmatory trials<sup>1</sup>.

## 2 Anticancer drugs

### 2.1 Cabometyx

Cabometyx or otherwise called as cabozantinib (generic name) is used for treating renal cell carcinoma in the patients who have already received a prior anti- angiogenic therapy<sup>2,3</sup>. This drug is manufactured by Exelixis Inc. The usual recommended

dose is 60mg once daily through oral route. Regarding the administration of the drug, the patient should be instructed, of not consuming food before or after 2 hours after taking the cabometyx. Missed dose should not be compensated by the patient with the next dose. Apart from this, ingestion of grape fruit or grape juice along with cabometyx is contraindicated as it inhibits the cytochrome p450. In case of adverse drug reactions based on the grade of severity either reduce the dose to two fold or completely discontinue the usage of drug. The severe drug interaction where the usage of drug is discontinued includes conditions like severe haemorrhage, development of GI perforation, arterial thromboembolic events and leukoencephalopathy syndrome etc<sup>4</sup>.

The usage of drug in case of special population needs to be restricted. In case of pregnant women cabometyx leads to foetal toxicity, in case of nursing mothers or lactating women there is a chance of potential toxicity to the infant through breast feeding, so the drug need to be completely avoided during the lactation period. Cabometyx usage is restricted in patients suffering from renal & hepatic diseases with high degree of severity, but not with respect to moderate & low severity. Cabometyx is a tyrosine kinase inhibitor which acts by inhibiting tyrosine kinase activity of VEGFR-1, -2,-3, MET, AXL, RET, ROS1, TYRO3, MER, KIT, TRKB, FLT-3and TIE-2<sup>5</sup>. These receptors act by modifying normal cellular and pathologic functions and thereby maintaining tumor microenvironment. The adverse reactions

include hemorrhage, fistula, thrombotic events, hypertension, diarrhoea, embryo-fetal toxicity, palmar – plantar erythrodysesthesia syndrome. The drug should be stored at 20-25°C.

### 2.1.1 Clinical assessments

A randomized study was carried out in patients with advanced renal cell carcinoma, who have undergone a prior anti-angiogenic therapy. 330 patients have received cabometyx 60 mg orally once daily & 328 patients have received everolimus 10mg orally daily. Confirmed response rate was found to be 17% in the cabometyx treated patient & 3% in the everolimus treated patients. The overall survival in the intent to treat population was 21.4 and 16.5 months in both cabometyx and everolimus treated patients.

Safety of cabometyx for the human use was evaluated in 331 patients. The most common adverse reactions included diarrhoea, fatigue, nausea, decreased appetite, vomiting, constipation and decrease in weight etc in 25% of the patients. Where in 60% of the patients who have received cabometyx required atleast reduction in one dose. 40% of the patients showed serious adverse reactions, which included abdominal pain, nausea, and diarrhoea<sup>6,7</sup>.

### 2.2 Darzalex

Darzalex otherwise called as daratumumab (generic name) is used for treating multiple myeloma. Drug is manufactured by Janssen biotech<sup>11</sup>. This drug is administered as such and as well as in two combinations; one is along with lenalidomide & dexamethasone & the other is bortezomib & dexamethasone. If the drug is given along with lenalidomide and dexamethasone combination, the optimum dose to be given is 16 mg/kg. The drug is administered weekly for 1-8 weeks followed by a dosing frequency of 2 weeks for a period of 9-24 weeks, and then 4weeks for a period of 25<sup>th</sup> week, until the patient shows progression<sup>8, 9</sup>. The route of administration is an intravenous infusion on dilution. If the drug is given along with bortezomib and dexamethasone combination the dose to be administered is 16 mg/kg.

The frequency of administration is weekly for 1- 9 weeks, followed by weekly thrice for 10-24 weeks, then 4weeks for 25<sup>th</sup> week until progression. The rate of infusion is in range of 50-200 ml/ hour for a dilution volume of 500 and 1000 ml. Increment in rate of infusion is 50 ml per every hour. During the increment in the infusion rates, two factors need to be taken into count that is the infusion reaction and severity of infusion reaction. If there are no infusion reactions, then increment is recommended, where in if it is of 3<sup>rd</sup> or the 4<sup>th</sup> grade of severity administration of the drug should be stopped or dilution is recommended. The accompanying or medications associated for pre and post infusion therapy for darzalex as such and for combination therapy include long-acting or intermediate acting

corticosteroids, antipyretics, and antihistamines. In case of special populations, darzalex may cause foetal myeloid or lymphoid depletion and decrease in bone density specially with respect to pregnant women. No dosage adjustments are required in case of renal and hepatic impairment conditions, but in case of females with reproductive potential use of contraception are recommended<sup>10</sup>. Darzalex is an IgG1k human monoclonal antibody which acts by binding to transmembrane glycoprotein CD38 there by inhibiting the growth of tumour cells expressing CD38.<sup>11</sup> The most commonly occurring adverse reactions include neutropenia, thrombocytopenia, lymphopenia, fatigue, anaemia, nausea etc. The drug need to be stored away from light and should not be freezeed.

### 2.2.1 Clinical assessments

An open- label, single -arm study was carried out in 106 patients, who have already undergone 3 prior therapies. The response rate reported was 29.2 .Combination therapy using lenalidomide and dexamethasone in the form of open – label, randomized, active- controlled phase 3 trial was carried out in 569 patients. Where patients (1:1) were randomly given lenalidomide and dexamethasone combination with darzalex. Among this progression free survival was not shown in 286 patients, where in 283 patients (randomized) took 18.3 months. The response rate was 91.3% in (286) patients and the response rate were 74.6% in (283) patients. In case of combination therapy with bortezomib and dexamethasone the trial was conducted in 498 patients. Where in patients were randomly given (1: 1) bortezomib and dexamethasone with darzalex. Among this progression free survival was not reported in 251 patients, whereas 247 patients (randomized) took 7.2 months. The response rate was reported to be 79.3% in 251 patients and 59.9% in 247 patients<sup>12</sup>.

### 2.3 Gazyva

Gazyva otherwise called as Obinutuzumab (generic name). This is used for treating the patients with follicular lymphoma who have shown refractory response to rituximab regimen. This drug is given in the form of injection. This is used as monotherapy and as well as in combination along with bendamustine. This is manufactured by Genentech. This was previously used in combination along with chlorambucil for treating patients who are left untreated for chronic lymphocytic leukemia<sup>13</sup>. The patients are administered with drug for 2 to 6 cycles. The recommended dose is 1000 mg on day 1, 8 and 15 for the first cycle and for 2-6 cycles it is 1000mg on day 1and in case of monotherapy it is given every 2 months for a period of 2 years<sup>14</sup>. The drug should be administered as an intravenous infusion. Adverse reactions includes tumor lysis syndrome, neutropenia, & thrombocytopenia<sup>15</sup>.

Administration of infusion need to be adjusted, in case of life threatening situation or higher severity the administration should

be completely stopped. The medications which are recommended to be given to reduce the risk of infusion reactions include anti-histamine on day one of cycle 1. In case of pregnant women especially pregnancy category C use of contraception is recommended during the treatment and as well as 12 months after the treatment. Data is not established in case of geriatric and paediatric patients. Hepatitis B virus reactivation and progressive multifocal leukoencephalopathy are major conditions which tend to occur on administration of gazyva. Obinutuzumab is CD-20 directed cytolytic antibody, which acts by causing lysis of B-cell through different mechanisms<sup>16</sup>. It is stored at a temperature of 2-8°C. It should not be frozen and should be stored away from light.

### 2.3.1 Clinical assessments

A randomized, open-label, multicenter trial was used to analyse the efficacy of the drug taking 321 patients. In a randomized study 155 patients were given combination of obinutuzumab & bendamustine and 166 patients were given only bendamustine. Trial is carried out in patients who have already received two prior therapies. Progression free survival was reported to be 13.8 months in bendamustine group and progression free survival has not reached in case of bendamustine and obinutuzumab group<sup>17</sup>.

### 2.4 Opdivo

Opdivo injection otherwise called as Nivolumab (Generic name). Nivolumab is used to treat recurrent or metastatic head and neck squamous cell carcinoma with platinum based therapy<sup>18,19</sup>. This drug is manufactured by Bristol-Myers Squibb Company. The ideal dose to be administered is 3mg per kg for every 2 weeks over a time period of 60 minutes. Major kind of adverse reactions were immune mediated reactions, which included immune mediated; colitis, hepatitis, pneumonitis, nephritis, encephalitis etc. The frequently occurring adverse reactions include rashes, fatigue, nausea, diarrhoea, cough and back pain etc. Infusion reactions were reported to be less common in case of nivolumab, but 6.4% of patients who were on monotherapy of OPDIVO showed infusion reactions and 2.5% of patients who received a combination of OPDIVO and ipilimumab showed infusion reactions. In case of special populations, foetal toxicity is reported in case of pregnant women and well established data is not available in case of pediatric patients and dosage adjustment is required in case of both hepatic and renal impairment category. Effective contraception is insisted in case male and female reproductive potential. Nivolumab being a monoclonal antibody acts by inhibiting the interaction between PD-1 and its ligands. It does not require any special storage conditions; it is stored at room temperature.

### 2.4.1 Clinical assessments

A randomized, active-controlled, open-label multicenter trial was carried out in 361 patients. Where 240 patients received

3mg/kg of nivolumab every 2 weeks and based on investigators choice among 121 patients 13 patients were given cetuximab with a loading dose of 400mg/m<sup>2</sup> followed by a weekly dose of 250mg/m<sup>2</sup>, or 46 patients were given methotrexate of 40 – 60 mg/ m<sup>2</sup> weekly or 52 patients were given 30-40mg/m<sup>2</sup> of docetaxel weekly. The overall survival was reported to be 7.5 months in nivolumab and 5.1 months for investigators choice<sup>20, 21</sup>.

### 2.5 Keytruda

Keytruda otherwise called as pembrolizumab (Generic name). This is used for treating the patients suffering from metastatic non-small lung cancer whose tumors expressed high PD-L1 that is tumour proportion score is more than 50%. This is also recommended for treating the patients suffering from metastatic head and neck squamous cell carcinoma. This drug is manufactured by Merck<sup>22</sup>. A dose of 200 mg for 3 weeks for 30 mins in the form intravenous infusion is recommended for patients. In case of adverse reactions like pneumonitis, colitis, endocrinopathies and in case of increased bilirubin levels completely stop keytruda. If the adverse reactions are of 0-1 grade resume keytruda. In case of pregnant women risk of foetal toxicity is reported and keytruda need to be stopped. In case of lactating women they need to be instructed of not to breast feed and use of contraceptive is recommended in case of reproductive potential while administering keytruda. Pembrolizumab is a monoclonal antibody which acts by inhibiting the interaction between PD-L1 and PD-L2 by bind to PD-1 receptor. The patient need to be warned about immune mediated adverse reactions, the most commonly occurring adverse reactions include hyponatremia, increased alkaline phosphatase, decreased appetite, dyspnea etc. The drug is stored in vials in refrigerating temperature of 2-8 °C.<sup>23</sup>

### 2.5.1 Clinical assessments

A randomized phase 3 trial was carried out involving 305 patients who either received 200 mg for 3 weeks or platinum-based chemotherapy on investigators choice. Where 154 patients who have received keytruda took 10.3 months for progression free survival and in case of patients, who have received platinum based chemotherapy, took 6 months for progression free survival. The response rate was found to be 45% in patients who received keytruda and 28% in patients who received platinum based chemotherapy<sup>24</sup>.

### 2.6 Venclexta

Venclexta otherwise called as Venetoclax (Generic name). This drug is manufactured by Abbvie Company. This is used for treating patients suffering from chronic lymphocytic leukemia, who have undergone at least one anti-angiogenic therapy<sup>25</sup>. The dose is administered on weekly basis, for first week the recommended dose is 20mg daily, followed by for the second week it is 50 mg daily then 100mg daily for third week and for

the fourth week it is 200 mg daily. After this for the following weeks it is 400mg daily until progression is shown in the patient. Oral route is used to administer the drug. Dose need to be adjusted in case severe toxicological or adverse reactions. 3 or 4 and grade 3 or 4 neutropenia. In case the patient have missed a dose of venclexta in such case the individual can take the missed dose within next 8 hours, if it is more than 8 hours in such case patient should not take the missed dose and should resume the scheduled dose. In case of special populations; pregnant women need to stop taking venclexta as it causes foetal toxicity, in case of lactating mother there is a chance of toxicity through breastfed milk to the infants so nursing mothers are advised to discontinue breast feeding. Well established data is not available for toxicity studies for the paediatrics and gediatics. In case of individuals with hepatic impairment dosage adjustment is not required, but in case of renal impairment dosage adjustment is required only in severe condition. Venclexta acts by inhibiting an antiapoptotic protein BCL-2<sup>28</sup>. Precautions need to be taken while administering venclexta in conditions like tumour lysis syndrome, neutropenia, during immunization and foetal toxicity. The drug should be stored below 30°C. The most commonly reported adverse reactions were neutropenia, nausea, diarrhoea and thrombocytopenia<sup>26,27</sup>.

#### 2.6.1 Clinical assessments

An open- label, single -arm, multicenter clinical trial was carried out in 106 patients, who have received venclexta on weekly basis. The starting dose was 20mg and the dose is ramped up to 50mg, followed by 100mg, 200mg and the end dose of 400mg once daily. The overall response rate was 80.2%<sup>25</sup>.

#### 2.7 Lenvima

Lenvima also called as Lenvatinib (Generic name). This drug is manufactured by Eisai Company. Lenvima is used to treat renal cell carcinoma. This was previously used for treating the patients suffering from thyroid cancer particularly with metastatic radioactive iodine-refractory differentiated cancer. The optimum dose to be given for the patients is 18 mg lenvatinib plus 5mg of everolimus once daily through oral route<sup>29,30</sup>. No premedication is insisted for the patients and the drug can be administered with or without consumption of food. Dosage adjustments are recommended in case of hypertension, cardiac dysfunction, arterial thrombotic events, renal failure, proteinuria, GI perforations. In all conditions dosage adjustment is required in case grade 3 and 4 kind of severity only or lenvima is completely stopped. In case of pregnant women lenvima is completely avoided, in case of lactating mother's breastfeeding should be stopped. A well established data is not available in pediatric patients and in case of severe renal and hepatic impairment 14mg once daily is recommended. lenvatinib is an tyrosine kinase inhibitor which acts by inhibiting kinase activities of vascular endothelial growth factor receptors.

The drug is stored at 25°C. Adverse reactions include hypertension, diarrhoea, fatigue, decreased appetite, decrease in weight nausea, stomatitis and headache, myalgia etc. Warnings and precautions include hypertension, cardiac failure, hepatotoxicity, protenuria, embryo-foetal toxicity, QT interval prolongation etc.<sup>31</sup>

#### 2.7.1 Clinical safety and efficacy

A randomized multicenter study was carried out involving 153 patients, where 51 patients received 18mg lenvatinib plus 5mg everolimus, 52 patients received 24 mg of lenvatinib or 10mg everolimus as monotherapy<sup>32,33</sup>.

#### 2.8 Xalkori

Xalkori otherwise called as Crizotinib (Generic name). The drug was manufactured by Pfizer.<sup>34</sup> This drug is used for treating patients suffering from metastatic non-small lung cancer with ROS1-positive tumours. This drug was first approved for treating the patients with anaplastic lymphoma kinase tumours. The optimum dose to be administered for the patients is 250mg twice daily through oral route. The drug is available as capsule. In case of pregnant women administration of crizotinib causes foetal toxicity, particularly in case of category D pregnant women. Toxicity data is not established in case of lactating women, paediatrics and geriatrics. Dose adjustment is required in case of renal and hepatic impairment cases. Crizotinib is a tyrosine kinase inhibitor which acts by inhibiting hepatocyte growth factor receptor. The drug is stored at 20-25°C. The adverse reactions include vision disorders, nausea, diarrhoea, vomiting, edema etc.<sup>35,36</sup>.

#### 2.8.1 Clinical assessments

A multi-center, single-arm study was carried out in 136 patients who were given 250mg twice daily for a period of two weeks. The response rate was reported to be 10n the basis of evaluation made by independent radiology review and by the investigators as well. Another trial was carried out involving 50 patients whose tumours were ROS1-positive by fluorescence using in situ hybridization or by reverse transcription polymerase chain reaction. The response was reported to be 66% as per independent radiology review and 72% as per investigators<sup>36</sup>.

#### 2.9 Atezolizumab

Atezolizumab otherwise called as tecentriq is manufactured by Genentech. This drug is used for treating patients suffering from metastatic non-small cell lung cancer, even after receiving the platinum containing chemotherapy.<sup>37,38</sup> The optimum dose recommended for the patients is 1200mg which is administered as intravenous infusion over a time period of 60 minutes for three weeks. Atezolizumab is a monoclonal antibody which acts by binding to PD-L1 and thereby inhibiting it from binding to B7.1 receptors. The most commonly reported adverse reactions

include fatigue, decreased appetite, dyspnea, cough, nausea, pyrexia urinary tract infection and constipation. Warnings and precautions include about immune related reactions like immune related: colitis, pneumonitis, hepatitis etc. In case of pregnant women it cause foetal toxicity and in case of lactating mothers the drug need to be discontinued as it may be present in breastfed milk which leads to toxicity in case of infants. The drug is stored in vials under refrigerating conditions but should not be freeze<sup>39,40</sup>.

### 2.9.1 Clinical assessments

Two multicenter, international, randomized open-label trials were carried out in patients who suffered from metastatic non-small cell lung cancer even after receiving platinum-chemotherapy. Study one was carried out in 1225 patients among which 850 patients were randomized. Where 450 patients received atezolizumab and remaining 450 received docetaxel, whereas study 2 was carried out involving 287 patients in whom 144 patients received atezolizumab and 143 patients received docetaxel. The overall survival in study one was 13.8 months for atezolizumab and 9.6 months in docetaxel received patients. In study 2 it is 12.6 months and 9.7 months for atezolizumab and docetaxel received patients<sup>41</sup>.

### 2.10 Afinitor

Afinitor otherwise called as everolimus (generic name). This drug is manufactured by Novartis.<sup>42</sup> This is used for treating patients suffering from progressive, metastatic neuroendocrine tumours of GI and lung origin. The optimum dose to be given to the patients is 10mg once daily. This drug is available in two different dosage forms, that is Afinitor tablets and Afinitor Disperz tablets for oral suspension. In case of special populations; in pregnant women use of everolimus causes foetal toxicity and lactating mothers need to completely stop taking everolimus as it may cause toxicity to infants, through breastfed milk. Use of everolimus is recommended in case of one year old children in case of paediatric patients. In case of renal and hepatic impairment conditions dosage adjustment is required<sup>43,44</sup>. The most commonly occurring adverse reactions reported were stomatitis, and respiratory infections. Warnings and precautions include embryo-foetal toxicity, increased risk for infections, oral ulceration, angioedema and vaccination should be prevented<sup>45</sup>. Everolimus is a kinase inhibitor.

#### 2.10.1 Clinical assessments

A multicenter, randomized, placebo- controlled clinical trial was carried out involving 302 patients suffering from neuroendocrine tumours of lung or GI origin. In this randomized trial 204 patients were made to receive everolimus and 203 patients received placebo along with supportive care in both the cases. The progression free survival was reported to be 3.9months in case of everolimus received patients and 11months in placebo individuals<sup>46</sup>.

### 2.11 Halaven injection

Halaven otherwise called as Eribulin (generic name). Eisai and co manufactures Eribulin.<sup>47</sup> This is used to treat metastatic liposarcoma in anthracycline-containing regimen received patients. The optimum dose to be administered for patients include 1.4mg/m<sup>2</sup> on days 1 and 8 of 21 days cycle. Eribulin is a microtubule inhibitor. Adverse reactions include fatigue, nausea, alopecia, constipation, nausea and pyrexia. In case of renal and hepatic impairment lower dosing is recommended based on the grade of severity. Warnings and precaution include neutropenia, peripheral neuropathy, embryo-foetal toxicity and QT-prolongation etc<sup>48,49</sup>.

#### 2.11.1 Clinical assessments

An open-label, randomized, multicenter, active controlled trial was carried out in 446 patients who were randomized in which 225 patients received eribulin and 225 patients received dacarbazine. The overall survival was reported to be 13.5 months in eribulin and 11.3 months in dacarbazine<sup>50</sup>.

### 2.12 Arzerra injection

Arzerra injection otherwise called as ofatumumab (generic name). This drug is manufactured by Galaxosmithekline. This drug is used for treating patients suffering from chronic lymphocytic leukemia. The optimum dose to be given to the patients is 300 mg on day 1 followed by 1000mg on day 8 after one week and 1000mg after 7 weeks and after that every 8<sup>th</sup> week for a period of 2 years. The warnings and precautions include infusion reactions. The most commonly reported adverse reactions include neutropenia, infusion reactions, upper respiratory tract infections etc. In case of special populations like pregnant women it causes depletion of beta cells in foetus.<sup>51, 52</sup> Ofatumumab is a CD20-directed cytolytic monoclonal antibody<sup>53</sup>.

#### 2.12.1 Clinical assessments

An open-label parallel arm randomized study was carried out in 474 patients who were administered with regular scheduled dose of ofatumumab and the adverse reactions were reported<sup>54</sup> (Table 1).

## 3 Conclusion

For the past several years, FDA has been approving numerous anti cancer drugs and has been giving modifications for several drugs. Modifications are made in order to reduce the toxicity and increase the therapeutic efficacy in the patients. This article provides an overview about the 2016 approvals with an objective of helping the physicians for betterments in treating the cancer patients.

## 4 Conflict of interest

The authors declare that there are no conflicts of interest.

## 5 Author's contributions

KC- Assistance in sending the article for plagiarism check.

CV – guidance in selecting the topic for review article.

Table 1: FDA Approved Anti Neoplastic Drugs for the year 2016 at a Glance

Name of the Drug	Use	Dose	Warnings & Precautions	Adverse Reactions
Cabozantinib (Cometriq)	To treat advanced renal cell carcinoma in patients who have already undergone anti-angiogenic therapy.	60mg once daily orally.	Hemorrhage, GI perforations, Thrombotic events, Hypertension, Reversible posterior, leukoencephalopathy syndrome. Embryo-foetal toxicity.	Decrease in weight, Diarrhoea, Fatigue, Constipation, Palmar-plantar, erythrodysesthesia.
Daratumumab (Darzalex )	To treat multiple myeloma.	16mg/kg intravenously	Infusion reactions, Neutropenia, Thrombocytopenia	Fatigue, Nausea, Diarrhoea, Pyrexia, Muscle spasm, Upper respiratory tract infections
Obinutuzumab (Gazyva)	Used in combination with bendamustine to treat follicular lymphoma.	1000mg intravenously on day 1,8&15 of cycle1 & on day 1 of cycles 2-6 & then every 2 months for 2 years. Then bendamustine 90mg/m <sup>2</sup> by IV on days 1&2 of cycles 1-6.	Infusion reactions, Tumour-lysis, syndrome, Neutropenia, Thrombocytopenia	Pyrexia,Cough,Nause, Diarrhoea, Anaemia
Nivolumab (OPDIVO)	To treat metastatic squamous cell carcinoma of head &neck.	240mg every 2 weeks.	Immune mediated reactions, Infusion reactions, Embryo-foetal toxicity	Fatigue, Rashes, Dyspnea, Arthralgia, Asthenia, Cough
Pembrolizumab (Keytruda)	To treat metastatic non-small cell lung cancer in patients with PDL -1 expressing tumours.	200mg intravenously every3 weeks.	Immune mediated reactions, Infusion reactions, Embryo-foetal toxicity	Rashes, Dyspnea, Nausea, Decreased appetite, Constipation, Fatigue, Pruritis
Venetoclax (Venclexta)	To treat chronic lymphocytic leukemia.	Initial dose is 20mg for 1 week, which is ramped up each week to 50mg, 100mg then to 200mg. Then the recommended dose is 400mg.	Tumour lysis syndrome, Neutropenia, Embryo-foetal toxicity.	Anemia, Upper respiratory tract infections, Thrombocytopenia, Fatigue.
Lenvatinib (Lenvima)	Used in combination with everolimus to treat renal cell carcinoma.	18mg plus 5mg of everolimus orally once daily.	Hepatotoxicity, Hypertension, Cardiac failure, Arterial thromboembolic events, Renal	Fatigue, Myalgia, Decreased, appetite, Cough, Abdominal pain, Vomiting, Oral inflammation, Hypertension,

				impairment, Protenuria, Hemorrhage, GI perforations	
Crizotinib (Xalkori)	To treat patients with metastatic non-small cell lung cancer with ROS-1 positive tumours.	250 mg twice daily orally.		Embryo-foetal toxicity,	Dizziness, Edema, Constipation, Vomiting, Neuropathy, Diarrhoea,
Atezolizumab (Tecentriq)	To treat metastatic non-small cell lung cancer in patients who have undergone platinum-chemotherapy.	1200mg as IV infusion every three weeks.		Infections, Ocular inflammatory toxicity, Infusion reactions, Myasthenia gravis, Immune related reactions	Fatigue, Decreased appetite, Dyspnea, Cough, Nausea, Musculoskeletal pain, Constipation
Everolimus (Afinitor)	Used to treat progressive, metastatic neuro endocrine tumours.	10mg once daily orally.		Embryo-foetal toxicity.	Stomatitis, Respiratory infections, Oral ulceration, Angioedema, Increased risk of infections
Eribulin (Halaven)	To treat metastatic liposarcoma who have already received anthracycline – containing regimen.	1.4mg/m <sup>2</sup> on days 1&8 of 21 day cycle.		Peripheral neuropathy, Embryo-foetal toxicity, QT-prolongation.	Pyrexia, Febrile, neutropenia, Fatal neutropenic sepsis
Ofatumumab (Arzerra)	To treat chronic lymphocytic leukemia.	300 mg one day 1 followed by 1000mg 1 week later on day 8 , followed by 1000mg 7 weeks later and every 2 weeks up to 2 years.		Cytopenia, Tumour lysis syndrome, Infusion reactions.	Neutropenia, Upper-respiratory tract infections, Infusion reactions

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