HOSPITAL SERI MANJUNG

FARMASI BULETIN BIL. 1/2021

TOPICS

EDITORIAL BOARD

ALL - TRANS RETINOIC ACID 10MG CAPSULE (VESANOID) FOR ACUTE PROMYELOCYTIC LEUKEMIA

By: Norzulaikha bt Norahzan

WHAT IS VESANOID?

- Vesanoid is also known as tretinoin which is a retinoid and an acid form of vitamin A that used to treat a certain type of cancer of the white blood cells known as acute promyelocytic leukemia (APL).
- It specifically binds to 1 or more nuclear retinoic acid receptors (RAR), induces cellular differentiation, and decreases proliferation of acute promyelocytic leukaemia (APL) cells.
- Tretinoin works by promoting the growth of normal, mature cells in the bone marrow and blood.
- This medication helps to reverse symptoms of APL such as infections, tiredness, and bleeding.
- Synonym: All-trans retinoic acid (ATRA).

Pharmacodynamics and Pharmacokinetics	
Absorption	Well absorbed from the gastrointestinal tract (oral). Enhanced absorption with food (oral). Bioavailability: Approx 50% (oral). Time to peak plasma concentration: 1-2 hours (oral).
Distribution	Plasma protein binding: >95%, mainly to albumin.
Metabolism	Metabolised in the liver by CYP450 enzymes to form 4-oxo-trans-retinoic acid (primary metabolite); displays auto-metabolism.
Half-life, elimination	0.5-2 hour
Excretion	Via urine (63%); faeces (30%)

Dose and duration	Adult	Induction of remission in previously untreated patients and those who have relapsed from or refractory to standard chemotherapy: • 45 mg/m^2 daily in 2 equally divided doses, continued until complete remission. • Max treatment duration: 90 days. • Dose reduction, dosing interruption or re-initiation may be required according to individual safety and tolerability
	Children	Induction treatment of APL with tretinoin should be initiated early • 25 mg/m^2/ day in 2 divided doses day 1 to 30
Dose adjustment		Renal impairment and hepatic impairment: • Reduce dose to 25mg/m2 daily

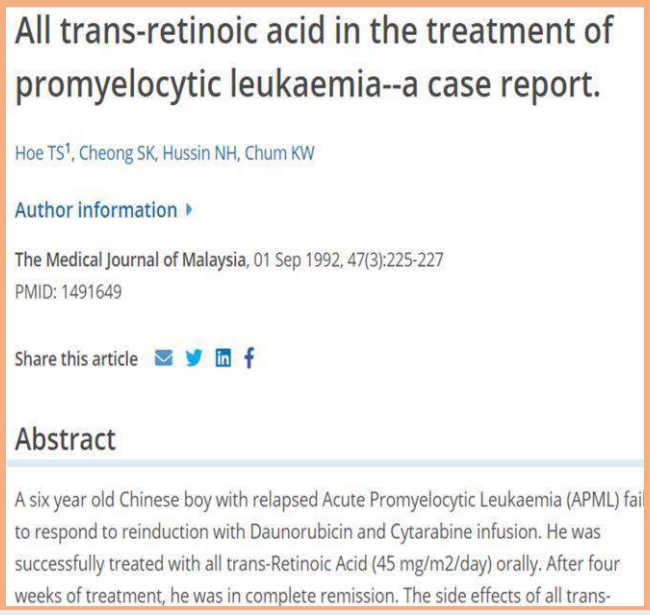
ACUTE PROMYELOCYTIC LEUKEMIA

Acute promyelocytic leukemia is a form of acute myeloid leukemia, a cancer of the blood-forming tissue (bone marrow). In normal bone marrow, hematopoietic stem cells produce red blood cells (erythrocytes) that carry oxygen, white blood cells (leukocytes) that protect the body from infection, and platelets (thrombocytes) that are involved in blood clotting. In acute promyelocytic leukemia, immature white blood cells called promyelocytes accumulate in the bone marrow. The overgrowth of promyelocytes leads to a shortage of normal white and red blood cells and platelets in the body, which causes many of the signs and symptoms of the condition.

People with acute promyelocytic leukemia are especially susceptible to developing bruises, small red dots under the skin (petechiae), nosebleeds, bleeding from the gums, blood in the urine (hematuria), or excessive menstrual bleeding. The abnormal bleeding and bruising occur in part because of the low number of platelets in the blood (thrombocytopenia) and also because the cancerous cells release substances that cause excessive bleeding.

The low number of red blood cells (anemia) can cause people with acute promyelocytic leukemia to have pale skin (pallor) or excessive tiredness (fatigue). In addition, affected individuals may heal slowly from injuries or have frequent infections due to the loss of normal white blood cells that fight infection. Furthermore, the leukemic cells can spread to the bones and joints, which may cause pain in those areas. Other general signs and symptoms may occur as well, such as fever, loss of appetite, and weight loss.

Acute promyelocytic leukemia is most often diagnosed around age 40, although it can be diagnosed at any age.



All trans-retinoic acid in the treatment of promyelocytic leukaemia--a case report.

Hoe TS[1], Cheong SK, Hussin NH, Chum KW

Author information

The Medical Journal of Malaysia, 01 Sep 1992, 47(3):225-227

PMID: 1491649

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Abstract

A six year old Chinese boy with relapsed Acute Promyelocytic Leukaemia (APML) fai to respond to reinduction with Daunorubicin and Cytarabine infusion. He was successfully treated with all trans-Retinoic Acid (45 mg/m2/day) orally. After four weeks of treatment, he was in complete remission. The side effects of all trans-

Dose and Administration??

Administration to Patients who have difficulty swallowing solids
ORAL
For patient who is unable to swallow capsules: • Poke a small hole in the capsule and patient may chew the capsule • Soften the capsule in water then chewed, swallowed or mix with jam/fatty food then consumed • Puncture the capsule and squeeze content onto a fatty food, mix and consume
NASOGASTRIC
• Cut open, with partial aspiration of the content into a glass syringe and administered • Also can mix with sterile water (20ml) and heated in water bath (37˚C) to melt the capsules and create an oily suspension for NG tube administration • Administered sublingually by squeezing the capsule contents beneath the tongue.

Common side effect:
Headache
Dizziness
Fever
Weakness
Dry mouth
Dry skin or other skin changes
Nausea and vomiting
Itching
Increased sweating

Contraindicated:
Pregnant women
Breastfeeding mother
Concomitant use with tetracyclines, vitamin A, retinoids and anti-fibrinolytic agents (e.g. tranexamic acid, aminocaproic acid, aprotinin).

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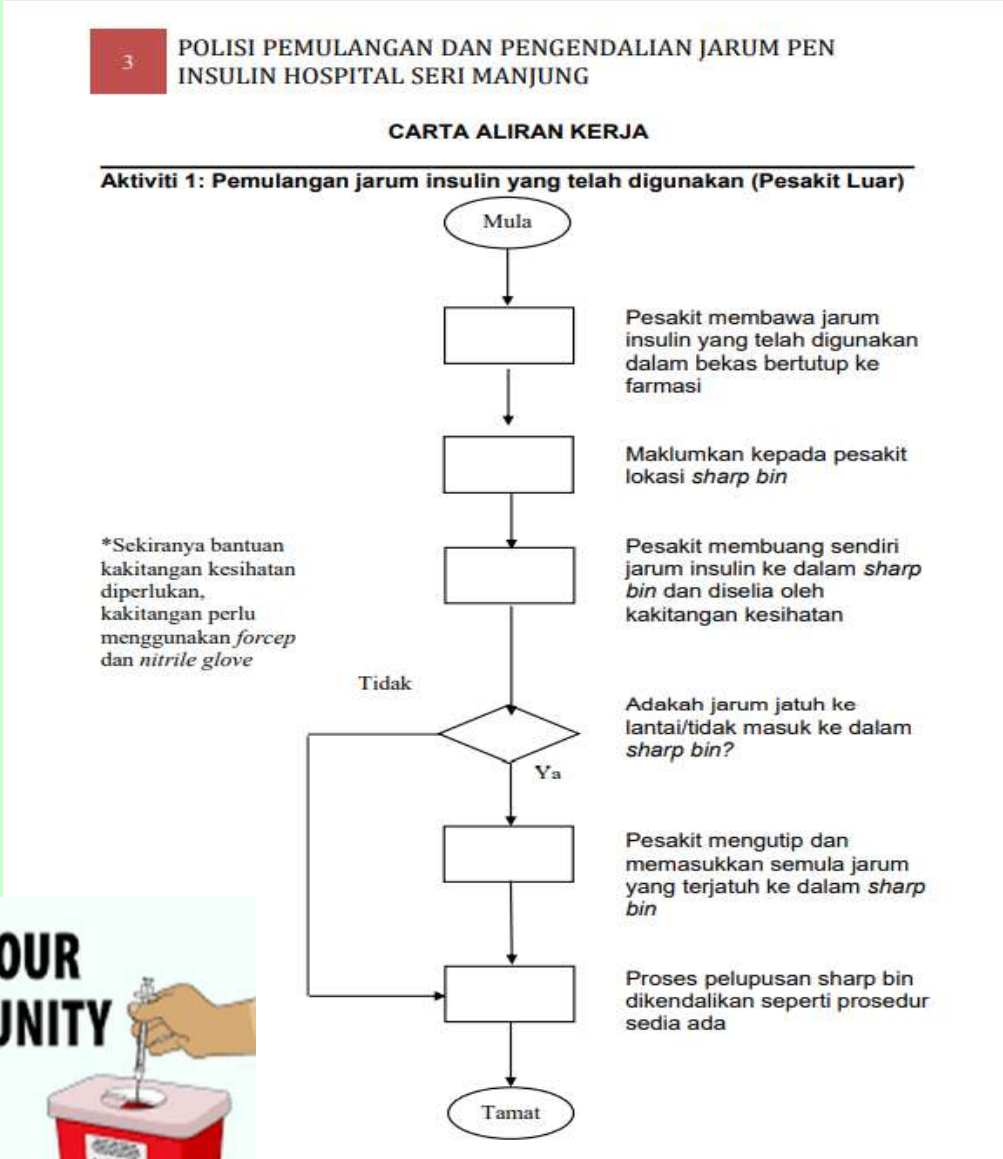
3. https://www.rxlist.com/vesanoid-drug.htm#indications
4. https://medlineplus.gov/genetics/condition/acute-promyelocytic-leukemia/
5. http://chemocare.com/chemotherapy/drug-info/Vesanoid.aspx

POLISI PEMULANGAN DAN PENGENDALIAN JARUM PEN INSULIN HOSPITAL SERI MANJUNG

By: Norzulaikha bt Norahzan

1: Pemulangan jarum insulin yang telah digunakan **(Pesakit Luar)**



3 POLISI PEMULANGAN DAN PENGENDALIAN JARUM PEN INSULIN HOSPITAL SERI MANJUNG

CARTA ALIRAN KERJA

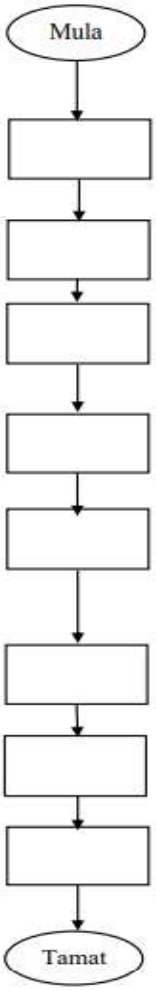
Aktiviti 1: Pemulangan jarum insulin yang telah digunakan (Pesakit Luar)

2: Mengendalikan dan melaksanakan pemeriksaan fungsi pen insulin **(pesakit luar)**

5 POLISI PEMULANGAN DAN PENGENDALIAN JARUM PEN INSULIN HOSPITAL SERI MANJUNG

CARTA ALIRAN KERJA

Aktiviti 2: Mengendalikan dan melaksanakan pemeriksaan fungsi pen insulin (Pesakit Luar)



Panggil pesakit ke bilik kaunseling

Temuramah pesakit/penjaga untuk pemeriksaan fungsi pen insulin

Pastikan pesakit buka penutup pen insulin. Sekiranya terdapat jarum, minta pesakit/penjaga untuk mengeluarkan jarum tersebut.

Buat demonstrasi dengan demo set atau menggunakan pen insulin pesakit sekiranya perlu

Sekiranya pen insulin pesakit perlu dikendalikan oleh Pegawai Farmasi, gunakan *nitrile glove* dan *forcep* semasa proses pemeriksaan pen insulin

Tentukan masalah pen insulin. Gantikan pen insulin sekiranya perlu.

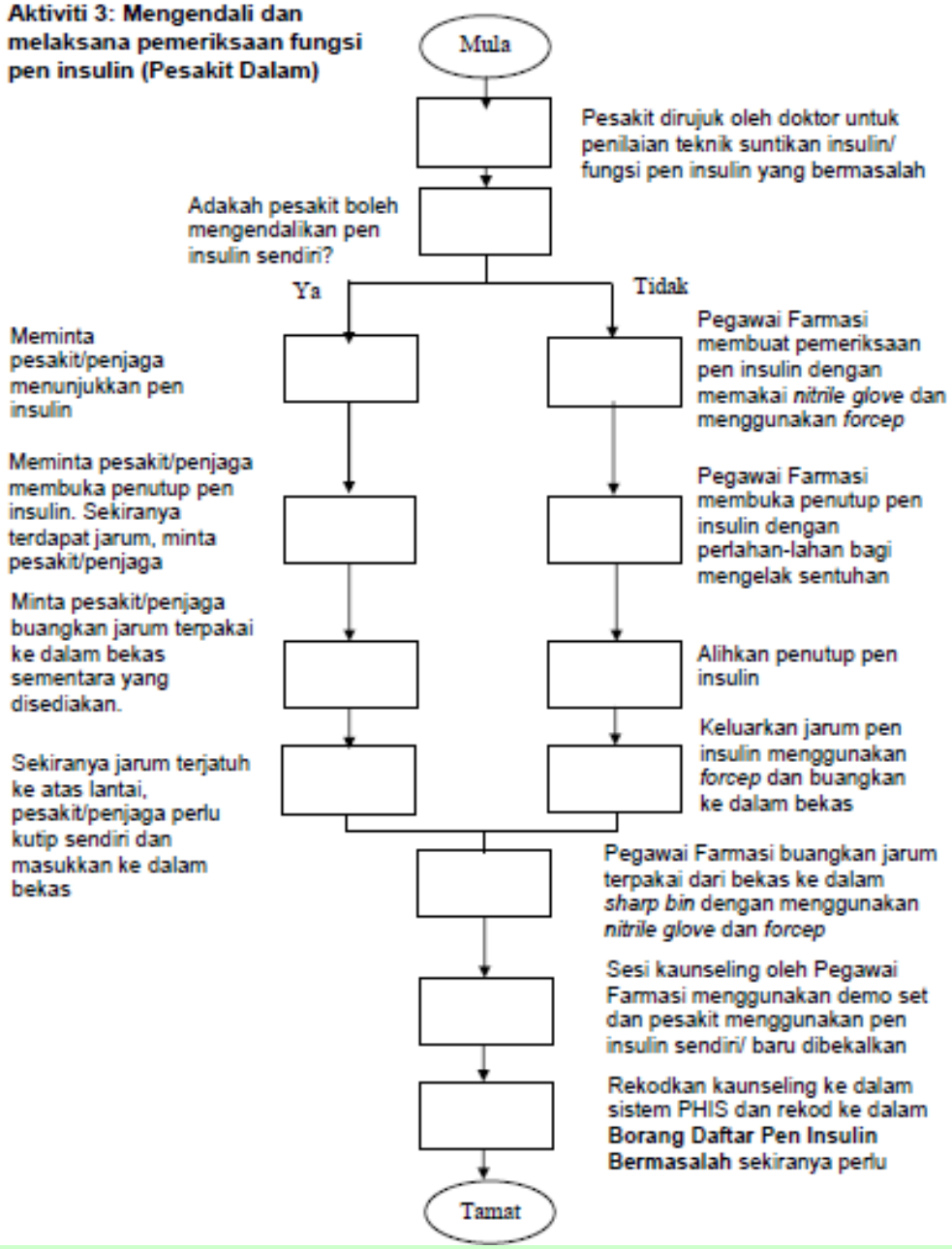
Nilai semula teknik pen insulin

Rekod data pesakit di dalam **Borang Daftar Pen Insulin Bermasalah** dan masukkan rekod ke dalam sistem PHIS sekiranya sesi kaunseling dilakukan.

3: Mengendalikan dan melaksanakan pemeriksaan fungsi pen insulin **(Pesakit Dalam)**

8 POLISI PEMULANGAN DAN PENGENDALIAN JARUM PEN INSULIN HOSPITAL SERI MANJUNG

CARTA ALIRAN KERJA



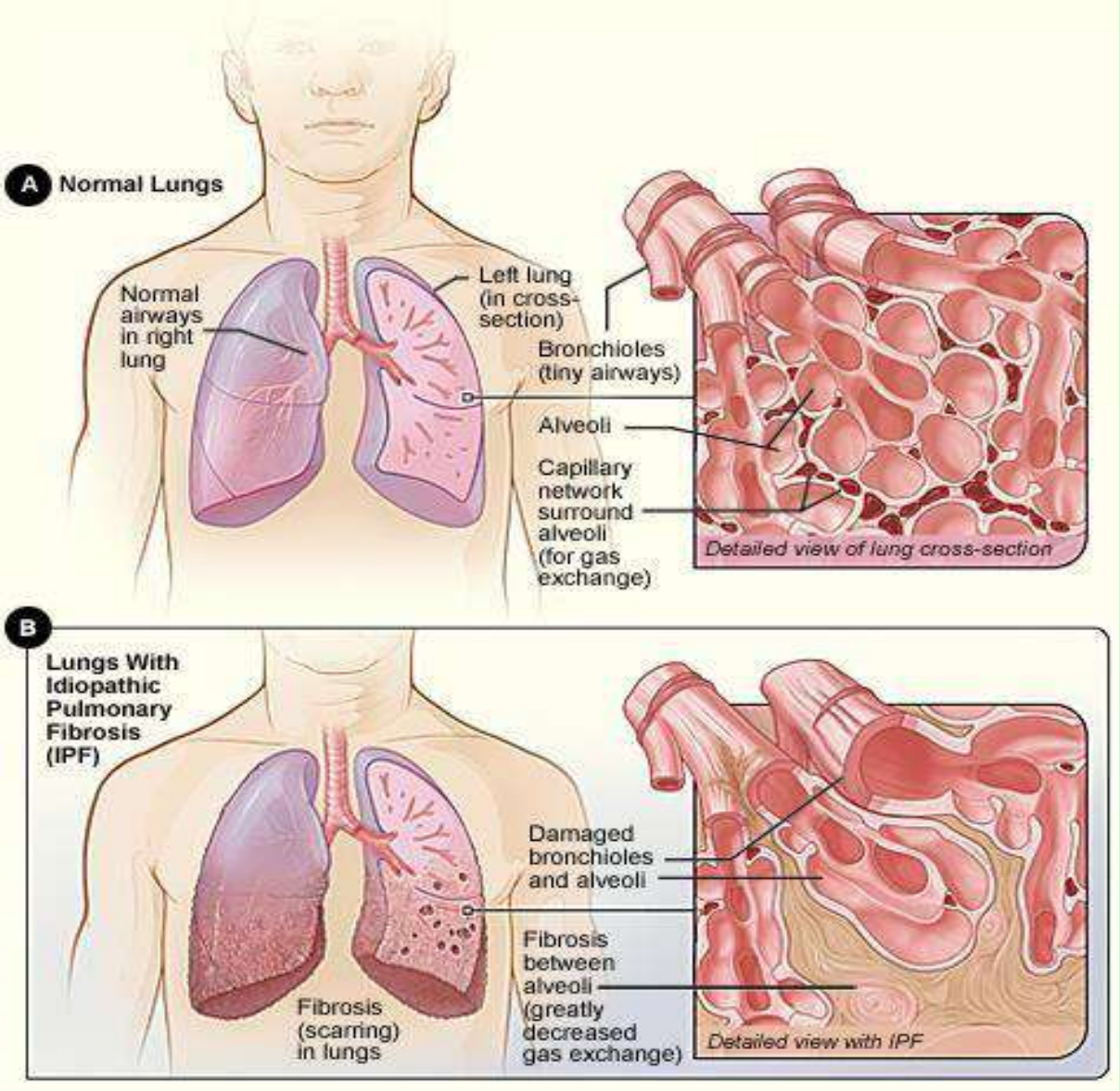
Rujukan: *Polisi Pemulangan dan Pengendalian Jarum Pen Insulin Hospital Seri Manjung.*

PIRFENIDONE (ESBRIET) VS NINTEDANIB (OFEV)

By: Tan Swee Li

Idiopathic pulmonary fibrosis is a specific form of chronic, progressive fibrosing interstitial pneumonia that primarily involve the tissue and space around air sacs of lungs but does not directly affect the blood vessels or airway. It causes scar tissues to grow inside the lungs and eventually scarring gets worse, making it harder to breathe as lungs can't take in enough oxygen. Most cases are sporadic, but familial causes have been described. There is **no cure**, but medication and other therapies may help with the symptoms. (1,2,3)

Pirfenidone and Nintedanib may help to slow the disease progression.(4)



Source: https://www.physio-pedia.com/Pulmonary_Fibrosis

Capsule PIRFENIDONE 267mg (ESBRIET) **KPK ITEM!!**	**Differences**	Capsule NINTEDANIB 150mg (OFEV)
		
Shown in slowing the progression of IPF when administered to patient with mild-to-moderate disease Possible mortality benefit as it can inhibit the decline of forced vital capacity (FVC)/ vital capacity (VC)	**Efficacy**	Shown reduction in the rate of decline in lung function and a longer time to first exacerbation
Role in more advanced disease Studies are limited. Subsequent data suggest similar efficacy in slowing decline of disease across the range of disease severity. However, further studies on improving daily activity, adverse effects and benefit in term of survival rate are needed.		
Transforming Growth factor inhibitors Exert antifibrotic properties by inhibiting transforming growth factor-beta. Exert anti-inflammatory properties by inhibiting synthesis of TNF- alpha.	**Drug class**	Pulmonary, Tyrosine Kinase Inhibitors Inhibit multiple receptor tyrosine kinase and nonreceptor tyrosine kinase. Bind competitively to the adenosine triphosphate binding pocket of receptors.

Day **1 to 7**: 267 mg three times a day Day **8 to 14**: 534 mg three times a day Day **15 and thereafter**: 801 mg three times a day Should always be taken with food at the same time each day Limit and avoid grapefruit juice	**Dose and administration**	150 mg two times a day (MAX:300mg/day Administer with food. Swallow whole with liquid, do not chew or crush
RM 4177.50 per pack of **270**'s Total cost/patient/year : RM 49,851.50	**Pricing**	RM 3441.50 per pack of **60**'s Total cost/patient/year : RM 41,871.58
Rash, photosensitivity, nausea, diarrhea, abdominal discomfort, dyspepsia, anorexia, fatigue	**Adverse effects**	Diarrhea, nausea, vomiting, elevation in liver function test
Current data are insufficient to direct a firm choice between both medications. Suggest initiating with the available agent for the patient with mild or moderate IPF based on pulmonary function test who do not have underlying liver disease. However, if both medications are available, need to take in account patient **preference** and **tolerances** regarding the potential adverse effects.(4,5,6)		

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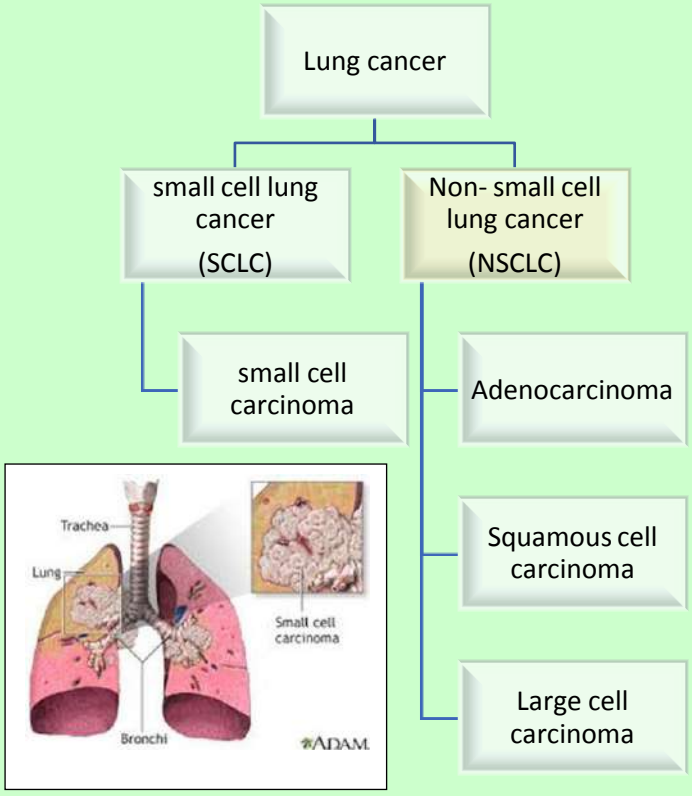
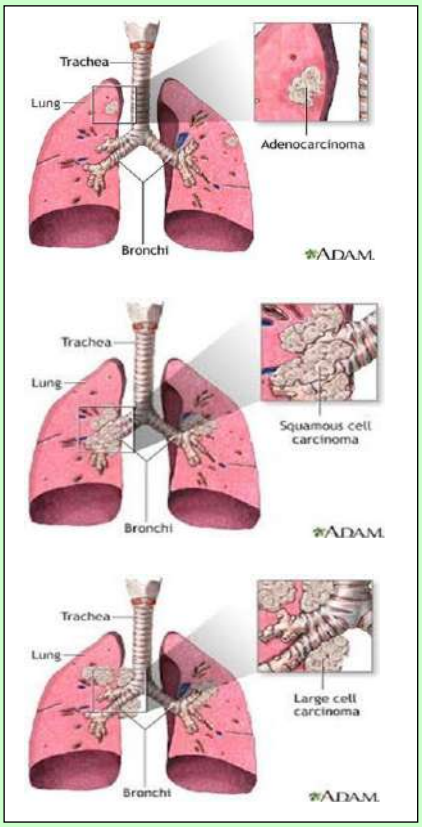
OSIMERTINIB

80mg film-coated tablet (TAGRISSO)
IN THE TREATMENT OF **NON-SMALL CELL LUNG CARCINOMA** (NSCLC) associated with **T790M MUTATION**

By: Tan Swee Li





OSIMERTINIB belongs to selective 3rd generation, irreversible Epidermal Growth Factor Receptor (EGFR) tyrosine kinase inhibitors (TKI). It binds to select mutant forms of EGFR including L858R/ T790M, and exon 19 deletion at lower concentrations than wild- type. It has a nearly 200-fold potency against L858R/T790M as compared with wild-type EGFR. It also demonstrated minimal off-target kinase activity, thus confirm the overall selectivity of this drug.

Initially, **OSIMERTINIB** was approved as the 2nd line treatment for T790-mutant NSCLC. However, FLAURA study has proved significant benefit on progression-free survival, prolongation of all post-progression outcome endpoints, acceptable toxicity, outcome on better quality of life. Eventually, those data favor **OSIMERTINIB** as first line treatment of T790-mutant NSCLC.

OSIMERTINIB

80mg film- coated tablet

Indication and dose of administration	Treatment of metastatic EGFR T790M mutation associated with NSCLC	**80mg** orally once daily, with or without food, until disease progression or unacceptable toxicity.
	as adjuvant therapy after tumor resection in adult patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations	**80mg** orally once daily, with or without food, until disease recurrence, or unacceptable toxicity, or for up to **3 years**.
	the first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations	
Administration to patients who have difficulty swallowing solids	Oral	Disperse tablet in **60 mL** of non-carbonated water. Stir until tablet is dispersed into small pieces and swallow immediately. Rinse the container with **120 mL to 240 mL** of water and immediately administer.
	Nasogastric	Disperse tablet in **15 mL** of non-carbonated water, and then use an **additional 15 mL** of water to transfer any residues to the syringe. The **resulting 30 mL** liquid should be administered with appropriate water flushes (approximately 30 mL).

Side effect	Most common	 Rash  diarrhoea
	Severe	 Interstitial pneumonia
Pricing	Pack of 30's	RM 12,180
	Patient/year	RM 146,160

Reference

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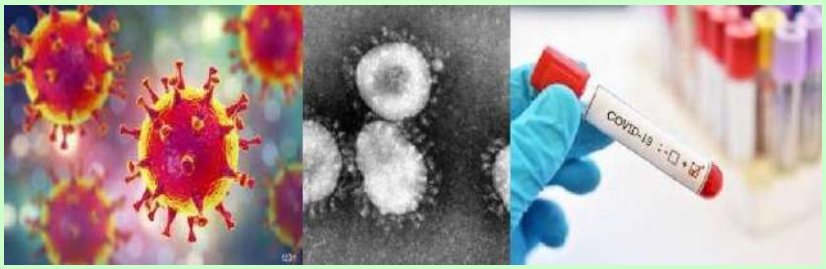
Favipiravir to treat Coronavirus disease (COVID-19)

By: Norzulaikha bt Norahzan

What is COVID-19?



Coronavirus disease or commonly known as COVID-19, is an infectious disease caused by a type of virus, namely SARS-CoV-2.

This virus itself belongs to a family of viruses called coronavirus. Coronavirus disease (COVID-19) is a new strain that was discovered in 2019 and has not been previously identified in humans.

Coronaviruses comprise an entire branch of the virus family tree that includes the disease-causing pathogens behind SARS, MERS and several variants of the common cold.

The fact that this new virus belongs to the coronavirus group, however, is telling that humans have encountered plenty of these pathogens before.

Named for the spiky, crown-like fringe that shrouds each viral particle—giving them a "coronated" appearance — coronaviruses tend to target the respiratory systems of bats and other mammals, as well as birds.

More often than not, the viruses remain restricted to their wild hosts. But occasionally, they make the hop into humans, as occurred with the 2003 SARS and 2012 MERS outbreaks, both of which likely originated in bats.

Coronaviruses are zoonotic, meaning they are transmitted between animals and people.

Detailed investigations found that SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans.

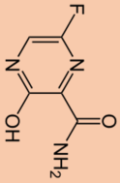
Several known Coronaviruses are circulating in animals that have not yet infected humans.

The first case of COVID-19 was on 31 Dec 2019, reported as a case of pneumonia of unknown cause, detected in the city of Wuhan in Hubei province, China.

According to the authorities, some patients were operating dealers or vendors in the Huanan Seafood market.

Later on, on 12 Jan 2020, the new found virus was named 2019-nCoV. Its genome sequencing was publicly announced by China to WHO.

What is Favipiravir?

Drug	Pharmacology	
Favipiravir 	• RNA-dependent RNA polymerase (RdRp) inhibitor. • Converted to the ribofuranosyl triphosphate derivative by host enzymes and is a promising antiviral drug targeting the influenza viral RNA-dependent RNA polymerase (RdRP). • Has been **approved for treatment of novel influenza on February 15, 2020** in China. This drug is currently undergoing clinical trials in treating COVID-19.	

Management of Covid-19 with Favipiravir

Drug	Favipiravir
Dose and duration	➢ **1800mg BD for 1 day then 800mg BD 5 days** ➢ Optimal duration of antiviral treatment is unknown. ➢ Antivirals have not shown to be effective when initiated in hyper inflammatory phase of disease ➢ Consider stopping or not initiating the drug in hyperinflammatory phase of disease.
Side effect	➢ Hyperuricemia ➢ Diarrhea ➢ Decrease appetite ➢ Vomiting ➢ Elevated transaminase ➢ Neutropenia
Drug adjustment	➢ **Avoid if GFR <30ml/min** ➢ Avoid if have hepatic impairment
Drug interaction	➢ Paracetamol – maximum 3gm per day ➢ Theophylline – increases Favipiravir levels ➢ Pyrazinamide – both cause hyperuricemia ➢ Repaglinide – may increase serum concentration of Repaglinide
Contraindication	➢ Contraindicated for **women of childbearing potential (teratogenic effects)** ➢ Contraindicated in en whose **partner is of childbearing potential (distributed in sperm).** ➢ **Breastfeeding women** (distributed in breast milk). Instruct to stop lactating. ➢ **Avoid in children**

Clinical stage	
1	Asymptomatic
2	Symptomatic, No Pneumonia
3	Symptomatic, Pneumonia
4	Symptomatic, Pneumonia, Requiring supplemental oxygen
5	Critically ill with multi-organ involvement

Category	Treatment
1	No treatment required
2	No treatment required • Close observation of vital signs and oxygen saturation as stated in monitoring guidelines. Look for warning signs at each review.
3	Generally, no treatment required • Close observation of vital signs and oxygen saturation as stated in monitoring guidelines. • Treat with Favipiravir as category 4 if patient has any of the following risk factors: ○ Age ≥ 50years with co-morbid ○ ESRF (consult ID physician on the choice of treatment) ○ In the presence of any warning signs

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5. Clinical Management in Confirmed Covid-19 case in adults and peadiatrics 3.11.2020. Annex 2e

PHARMACY STAFF MOVEMENT

NOVEMBER 2020- FEBRUARY 2021

NEW STAFF	
1. CIK LING WEN WEN	PRP UF41 (KONTRAK)
2. CIK YOU XI LIN	PRP UF41 (KONTRAK)
3. EN MUHAMMAD AMAR BIN MOHAMAD AFFENDI	PA H11
TRANSFERRED IN	
1. PN NG LI MENG	PF UF52
2. EN TAN YI JING	PF UF44
3. PN NUR SYAWALINA BINTI ABDUL MAJID	PF UF41
4. EN HAFIZUDDIN BIN ABDUL A'TAS	PPF U29
TRANSFERRED OUT	
1. PN ERIN BINTI AZMEE	PF UF52
2. CIK LIM CHIEW YEE	PF UF44
3. EN RUBANANTHAN A/L RAMASAMY	PF UF44
4. CIK AIN ZUBAIDAH BINTI PAHAT	PF UF41 (KONTRAK)
5. EN MUHAMMAD HAIQAL BIN MOHAMAD KHAIR	PF UF41 (KONTRAK)
6. PN MARIATIE BINTI MOHD NOOR	PPF U29
7. EN MEOR MUHAMAD HAZWAN BINTI HASHIM	PA H11