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NEWSLETTER

*IMPROVE YOUR KNOWLEDGE,
IMPROVE PATIENT HEALTH*

Volume 07

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NEW FDA ANNOUNCEMENT

New Targeted Therapy drug approved by FDA on August 2024 announcement

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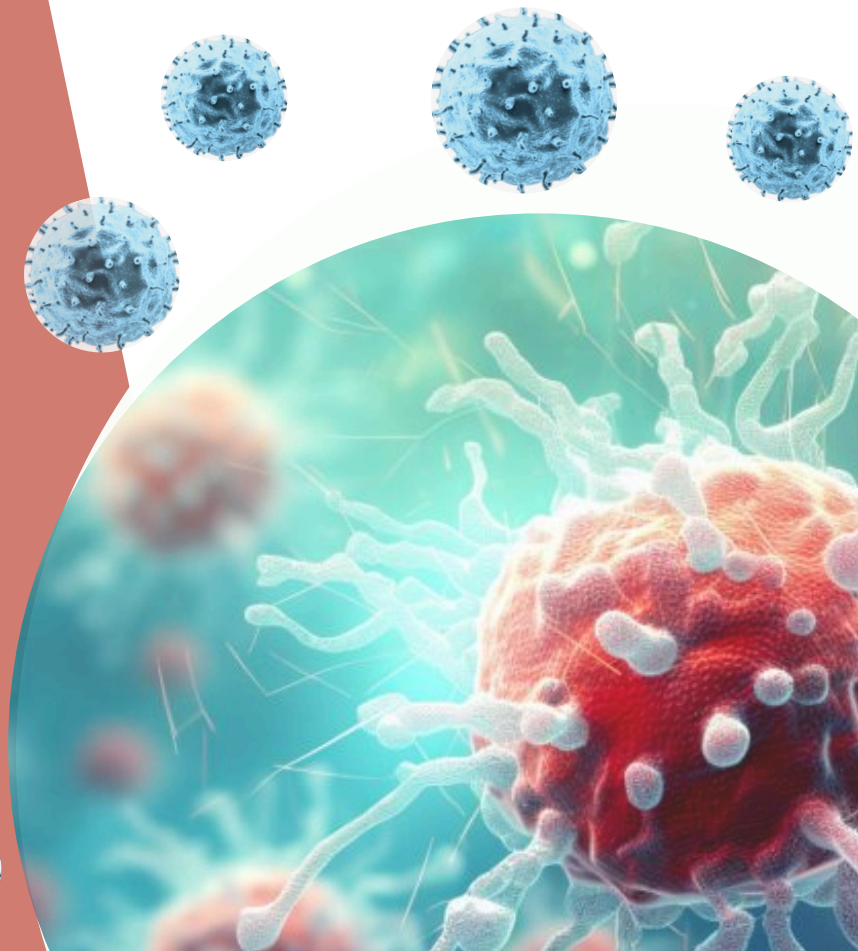
Patient Counselling

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By Dr. Marina Maged

Mission

Providing trusted evidence based medication information for all health care givers and patients to ensure best use of medications, that leads to better outcome.



NEW FDA ANNOUNCEMENT (AUG 2024)

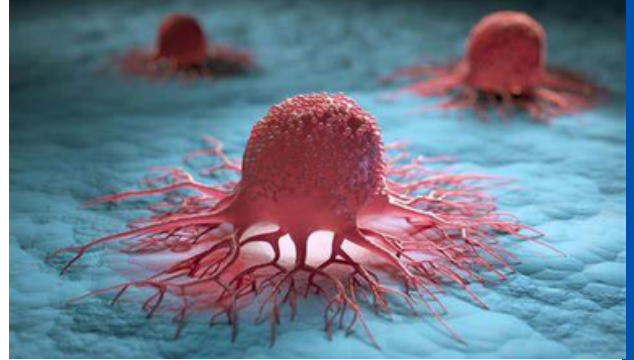
FDA APPROVES FIRST GENE THERAPY TO TREAT ADULTS WITH METASTATIC SYNOVIAL SARCOMA

SYNOVIAL SARCOMA:

It is a rare cancer type in where malignant cancer cells grow at body's soft tissue usually affects young adults

It mainly tends to occur near large joints such as knees, as well in tissue deep within the arms, legs and feet

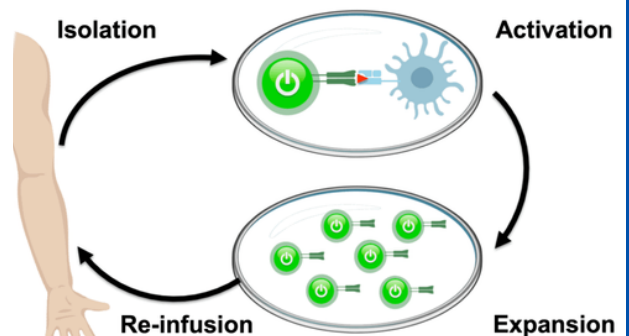
Swelling or lump under the skin is commonly the 1st signs of this cancer type



CELLULAR IMMUNOTHERAPY DRUGS:

Is an adoptive immunotherapy drug or method based on the immune system cells to eliminate the cancer cells.

This medication prepared using cells from the patient's blood. It works by causing the body's immune system (a group of cells, tissues, and organs) to fight the cancer cells.



Tecelra®

(Afamitresgene autoleucel).

Tecelra is the first FDA-approved T cell receptor (TCR) gene therapy, which is an autologous T cell immunotherapy composed of a patient's own T cells for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy.

Mechanism of Action:

patient's own T cells, modified to express a TCR that targets MAGE-A4, an antigen (substance that normally triggers your immune system) expressed by cancer cells in synovial sarcoma.

Dosing and Administration

IV: Target dose: 2.68×10^9 to 10×10^9 MAGE-A4 T cell receptor-positive T cells.

Ensure patients are euvolemic prior to initiating afamitresgene autoleucel infusion. Premedicate with acetaminophen and an H1 antihistamine 30 to 60 minutes prior to infusion.



Avoid prophylactic systemic corticosteroids, as they may interfere with afamitresgene autoleucel activity.

Do not administer afamitresgene autoleucel in patients with active infections and/or inflammatory conditions.

Warnings & Precautions:

- Monitoring full CBC before dosing
- Check the chest and lungs if there is any pain (Symptoms of Cytokine Release Syndrome)
- check if there are any seizures, strokes, confusion and any active infection
- Avoid Prophylactic systemic corticosteroids.

**Contraindications:**

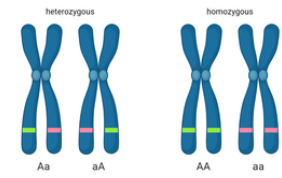
- Heterozygous or Homozygous for HLA-A*02:05P.
- Breast feeding
- Cytokine Release Syndrome (CRS) related symptoms

BOXED WARNING:

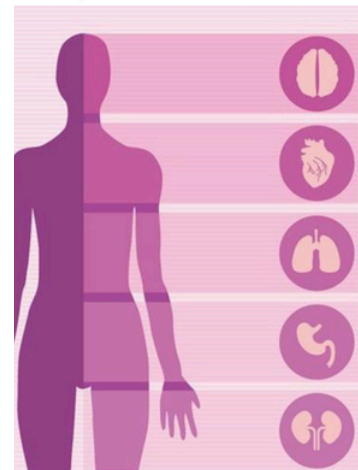
Severe Life threatening Cytokine Release Syndrome (CRS) may occur, in this case the patient should be hospitalized and start symptoms treatment (respiratory distress and cardiac dysfunction).

Premedication:

- 1 gm Paracetamol and normal dose of H1-antagonist antihistaminic. (30-60 mins before infusion).
- 4 days of chemotherapy (fludarabine and cyclophosphamide) before administration.



Fevers
Malaise
Fatigue
Anorexia

CRS SYMPTOMS

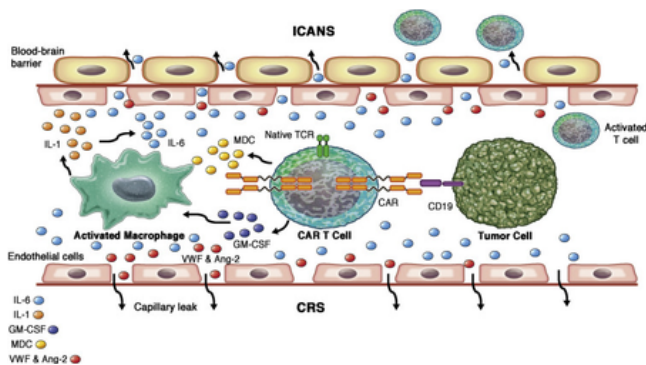
Headaches
Change in level of consciousness
Delirium
Aphasia
Apraxia
Ataxia
Agraphia
Facial nerve palsy
Seizures

Tachycardia
Hypotension
Arrhythmias
QT prolongation
Ventricular dysfunction

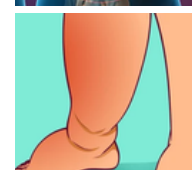
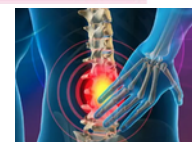
Tachypnea
Hypoxia
Lung infiltrates

Emesis
Diarrhea
Transaminitis
Hyperbilirubinemia

Acute kidney injury
Hyponatremia
Hypokalemia

**Tecelra side effects :**

- Alopecia
- Weight loss
- Back pain, limb pain
- Increased serum alanine aminotransferase
- Edema
- Low blood pressure
- Infection
- Thrombopenia
- Nausea/Vomiting

**References:**

<https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapy-treat-adults-metastatic-synovial-sarcoma>

<https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-soft-tissue-tumors/synovial-sarcoma>

CHEMOTHERAPY AND ERLOTINIB REGIMEN FOR NON SMALL CELL LUNG CANCER

INTRODUCTION:

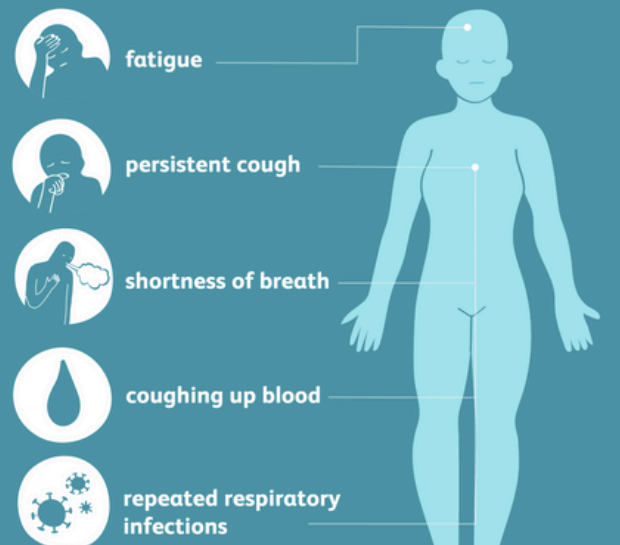
Lung Cancer is the most Common Cause of Cancer –Related death worldwide. 85 to 90 % of all Lung Cancer cases are NSCLC , where 70% of all NSCLC are diagnosed with Advanced stage. The displayed Clinical trial study compares the effect of Chemotherapy alone against the combination regimen of Erlotinib and Chemotherapy. Erlotinib is an oral Epidermal Growth Factor Receptor tyrosine kinase inhibitor which is considered as the Standard treatment for patients with EGFR mutant tumors.

CHEMOTHERAPY AND TARGETED THERAPY

Chemotherapy:

- Kills normal cells when eliminating the cancer cells (Lack of specificity)
- Chemotherapy drugs effectively target vital processes during cancer cell proliferation such as DNA replication
- They also destroy fast growing normal cells such as hair cells.
- Severe side effects of chemotherapeutic drugs prevent administering doses to eradicate cancer cell effect.

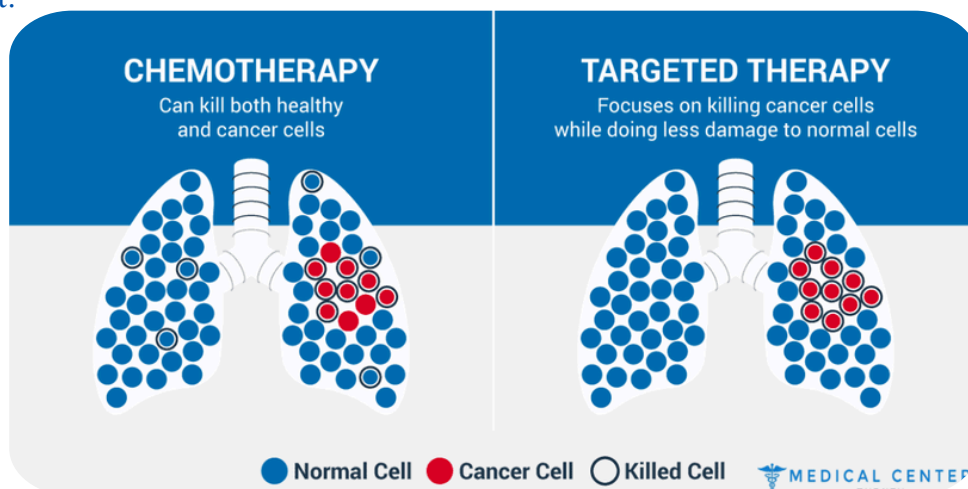
Symptoms



ELDRIDGE, L. (2019). SYMPTOMS OF NON-SMALL CELL LUNG CANCER. [ONLINE] VERYWELL HEALTH. AVAILABLE AT: [HTTPS://WWW.VERYWELLHEALTH.COM/NON-SMALL-CELL-LUNG-CANCER-SYMPTOMS-4588803](https://www.verywellhealth.com/non-small-cell-lung-cancer-symptoms-4588803).

Targeted Therapy

- Normal cells can survive during targeted therapy administration.
- The crucial fundamental in cancer cells is presence of oncogenes mutation in proto-Oncogenes which have important role in cell division
- Targeted Therapy blocks only the mutant form of the protein without interfering with the ability of normal cell to divide.





ERLOTINIB MECHANISM OF ACTION

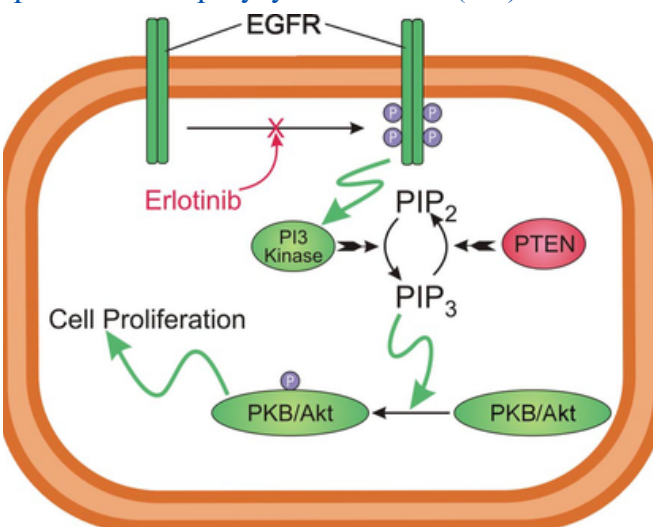
Erlotinib is an inhibitor of the epidermal growth factor receptor (EGFR) tyrosine kinase.

Indications:

- Non-small cell lung cancer
- Advanced pancreatic cancer

Erlotinib binds to the epidermal growth factor receptor (EGFR) tyrosine kinase in a reversible fashion at the receptor's adenosine triphosphate (ATP) binding site.

Erlotinib inhibits JAK2V617F, which is a mutant form of tyrosine kinase JAK2 found in most patients with polycythemia vera (PV).



ER KRUEGER, K. (2006). POSTTRANSLATIONAL PROTEIN MODIFICATIONS CURRENT IMPLICATIONS FOR CANCER DETECTION, PREVENTION, AND THERAPEUTICS. [ONLINE] RESEARCH GATE. AVAILABLE AT: https://www.researchgate.net/publication/6940513_POSTTRANSLATIONAL_PROTEIN_MODIFICATIONS_CURRENT_IMPLICATIONS_FOR_CANCER_DETECTION_PREVENTION_AND_THERAPEUTICS.

ADVERSE EFFECTS:

- Grade 3 or 4 Anemia, rash & Diarrhea in Erlotinib plus chemotherapy than chemotherapy alone.
- Grade 3 or 4 Neutropenia, Leucopenia or thrombocytopenia

References:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4493135/>.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9128600/>



STEPS OF CLINICAL STUDY:

The clinical trials were performed on 3599 patients divided into:

- Four trials were placebo-controlled double blinded trials
- Five trials were intercalated Erlotinib plus Chemotherapy as drug delivery method.
- Four trials used continuous Erlotinib plus chemotherapy treatment.
- One trial patients who never smoked
- Five trials were for the patients who use Gemzar arm against Gemzar plus Erlotinib
- Two trials for patients who use Erlotinib plus Pemetrexed or Erlotinib plus Gemzar against either Gemzar or Pemetrexed alone
- One trial for patients who use Erlotinib plus Docetaxel against Docetaxel alone or Erlotinib alone
- One trial for patients who use the combination regimen of Paclitaxel plus Erlotinib against the use of Paclitaxel based chemotherapy.

RESULTS OF STUDY:

- The combination regimen of Erlotinib plus Chemotherapy has a longer Patient free survival than chemotherapy alone.
- It demonstrated an improvement in patient free survival in non smoking patients and patients with EGFR mutant tumors.
- The results of patients with EGFR wild type tumors displayed no Significant difference between both regimens.

SUMMARY:

Combination of chemotherapy and Erlotinib is a viable treatment option for patients with NSCLC, especially for patients who never smoked and patients with EGFR mutation – positive disease in addition intercalated Administration is an effective combination strategy

ORAL CONTRACEPTIVES

>>> CAN CAUSE CANCER ?



INTRODUCTION:

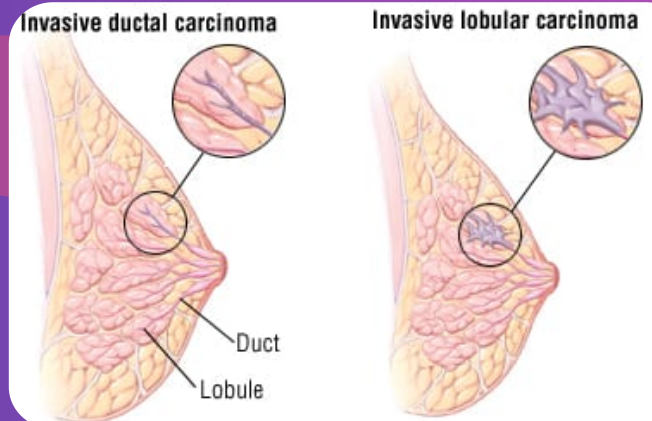
- Oral contraceptives are known as birth control pills
- It is an oral dosage form of either combination of estrogen and progesterone or progesterone alone.
- It also used to treat other medical conditions such as: menstrual cramps, polycystic ovary syndrome (PCOS), endometriosis, amenorrhea, acne and lower risk ovarian & uterine cancer
- Its the most widely used Hormonal Contraceptive method by women of reproductive age worldwide, In the United States, an estimated 26% of women aged 15 to 44 Years were current Oral Contraceptive users in 2011 to 2013



WARNING ALARM !!

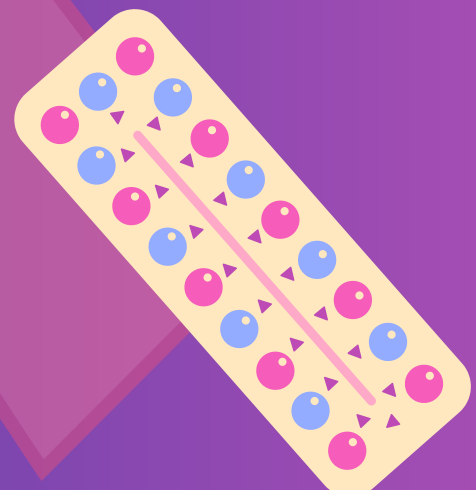
- Oral contraceptive use has been associated with a higher breast cancer risk levels 7-8% when compared with never used.
- Report from Danish sex hormone shown (20-33%) Breast Cancer Risk with these pills.

INVESTIGATION:



<https://my.clevelandclinic.org/health/diseases/3986-breast-cancer>

- There is an association between the different types & doses of the Estrogen and Progestin Components of more contemporary oral contraceptive and Breast Cancer risk.
- They provide a prospective investigation with 28 years of follow-up on the association between oral contraceptive with updated data through the premenopausal period & detailed consideration of formulation & Breast Cancer Risk overall.
- **The aim of this study** is to evaluate the associations between oral contraceptive use by formulation & Breast Cancer risk by the Disease Subtype.

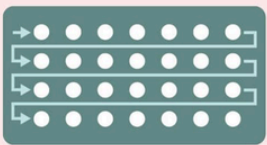


STEPS OF CLINICAL STUDY :

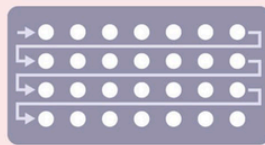
Randomly selected women (n= 215) were Contacted Via Telephone Call 6 to 14 months after they completed the baseline questionnaire agreement between the baseline questionnaire and telephonic interview was 99% for ever Oral Contraceptive use & 76% for the duration of use. Self –reported data were also compared with prescription records (n=150) agreement for the exact brands was 42%, however when considering brands with the same formulation (Estrogen, Progestin type & doses together, agreement increased to 75%

Birth control options**Combination Pill**

Estrogen & Progestin

**Minipill**

Progestin Only

**RESULTS :**

- Compared with never users current, oral contraceptive users had a higher risk for invasive, but not in situ breast cancer.
- For invasive disease, a stronger association was observed among women reporting a longer duration of current use.
- Past oral contraceptive use was associated with a higher risk of breast cancer up to 5 years after cessation.
- Former use was not associated with invasive breast cancer risk overall and there was no observation of any association in the Analysis of cross-classified duration of use & time since last use.

SUMMARY :

- .No significant heterogeneity was observed by ER or PR Status.
- .Significant heterogeneity was observed in the association for duration of oral contraceptive use for former users.
- .Higher risk for HER-2 enriched and Triple negative carcinoma was observed among past oral contraceptive users with ≥ 5 years of oral contraceptive use who stopped using oral contraceptive.
- .A lower risk for ER + ve/ PR +ve/HER2 –ve tumor was observed in women who used oral contraceptive for ≥ 5 years with ≥ 10 years after cessation of use when compared with never Oral Contraceptive users.
- In Analysis by Progestin generation, no significant heterogeneity in the associations was observed by disease subtypes.
- Current oral contraceptive use was associated with a higher risk for invasive breast cancer regardless of disease subtype, however, the risk in former users was comparable with never users 5 years after cessation. In analyses by progestin type, associations were observed for select formulations containing levonorgestrel and norgestrel. Assessment of the associations for newer progestin types (desogestrel, norgestimate, drospirenone) was limited by sample size, and further research on more recently introduced progestins is warranted



Refrences:

<https://pubmed.ncbi.nlm.nih.gov/34921803/>



PATIENT COUNSELLING



It's the process of providing patients, orally or written information, advice and assistance on the direction of use, precaution, storage, side effects, diet, and lifestyle modification to improve their health and treatment adherence, and quality of life.

Steps of Counselling:

1 - Welcome: Quickly observe asses counselee's mood

2 - Ask: Identify Counselee's Problems

3 - Provide: Accurate, appropriate and necessary information for counselee's

- **Aims** to enhance patients' understanding of their medication, Promoting treatment adherence, preventing potential side effects, and interactions ...etc.,
- Guiding patients on how to store their medications correctly,
- Promoting patients' self-monitoring by recognizing signs and warnings of medications,
- The most important one is to encourage patients to open a dialogue with healthcare providers to discuss their concerns, and challenges they face during therapy.

4 - Help: Understand the exact nature of the problem and how to choose the suitable solution independently

5 - Explain: Clear and adequate information on solutions that counselees has chosen

6 - Follow Up: Make an appointment with Counselee's to assess the outcome and counsel further



Data collected from patient counseling documented by the pharmacist and harmonized with patient care plans, health system's policies and procedures, patient details, disease counseled, date and time, and patient follow-up.

PATIENT COUNSELLING TIPS FOR DRUGS: 1- ETOPOUL 100 MG IV (ETOPOSIDE)

•The patient has to elevate his legs.
•Proper hydration.

Hypotension,
Dizziness, nausea,
blurred vision,
fainting, and trouble
concentrating.

Mouth ulcers and
sores which is
painful

Patient should take
proper oral products
(Mycostatin and
mouthwash drugs)

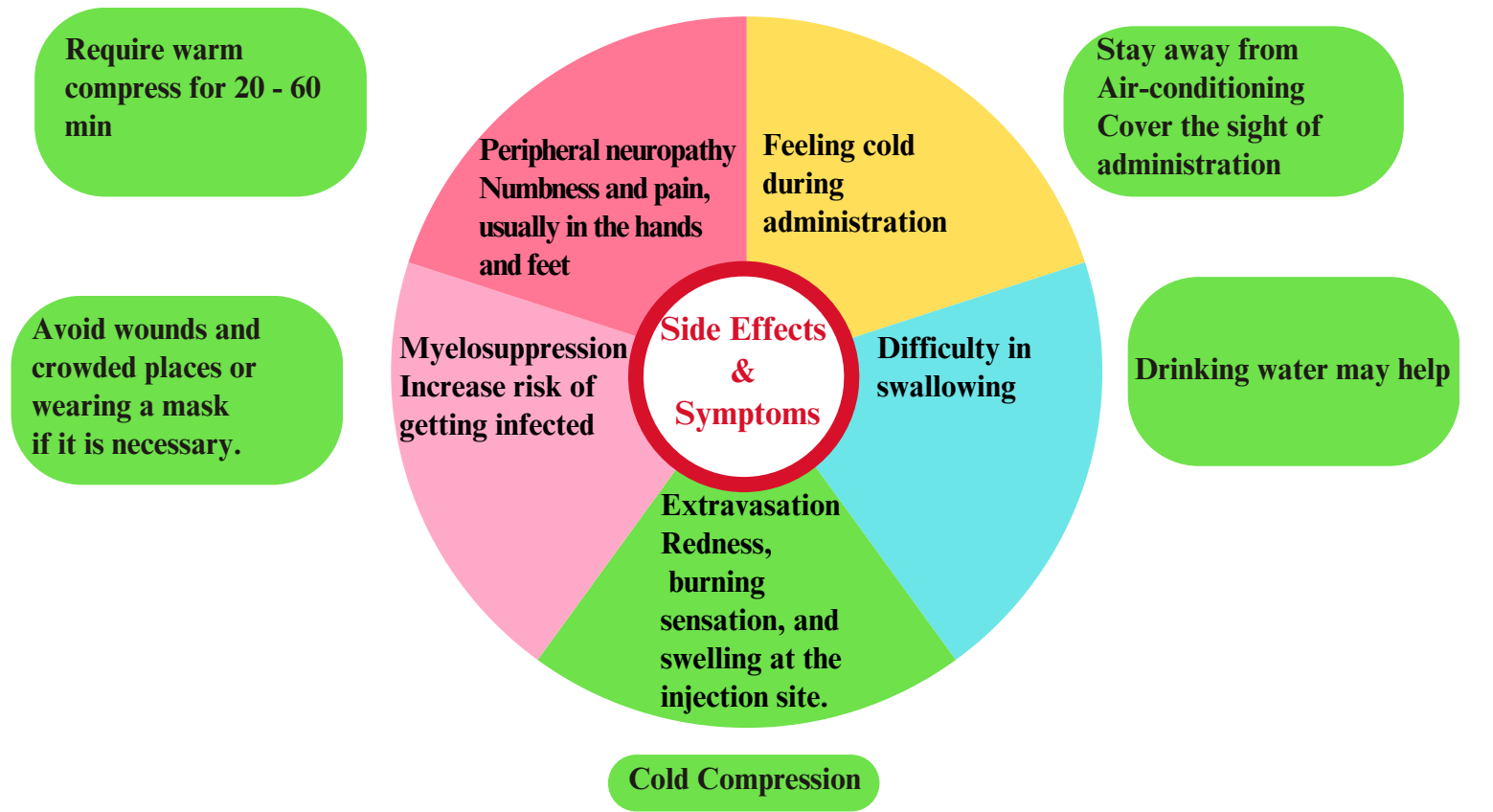
May relief after finishing
the therapy

May cause skin
pigmentation
appears as changing
in skin color or
spotting.

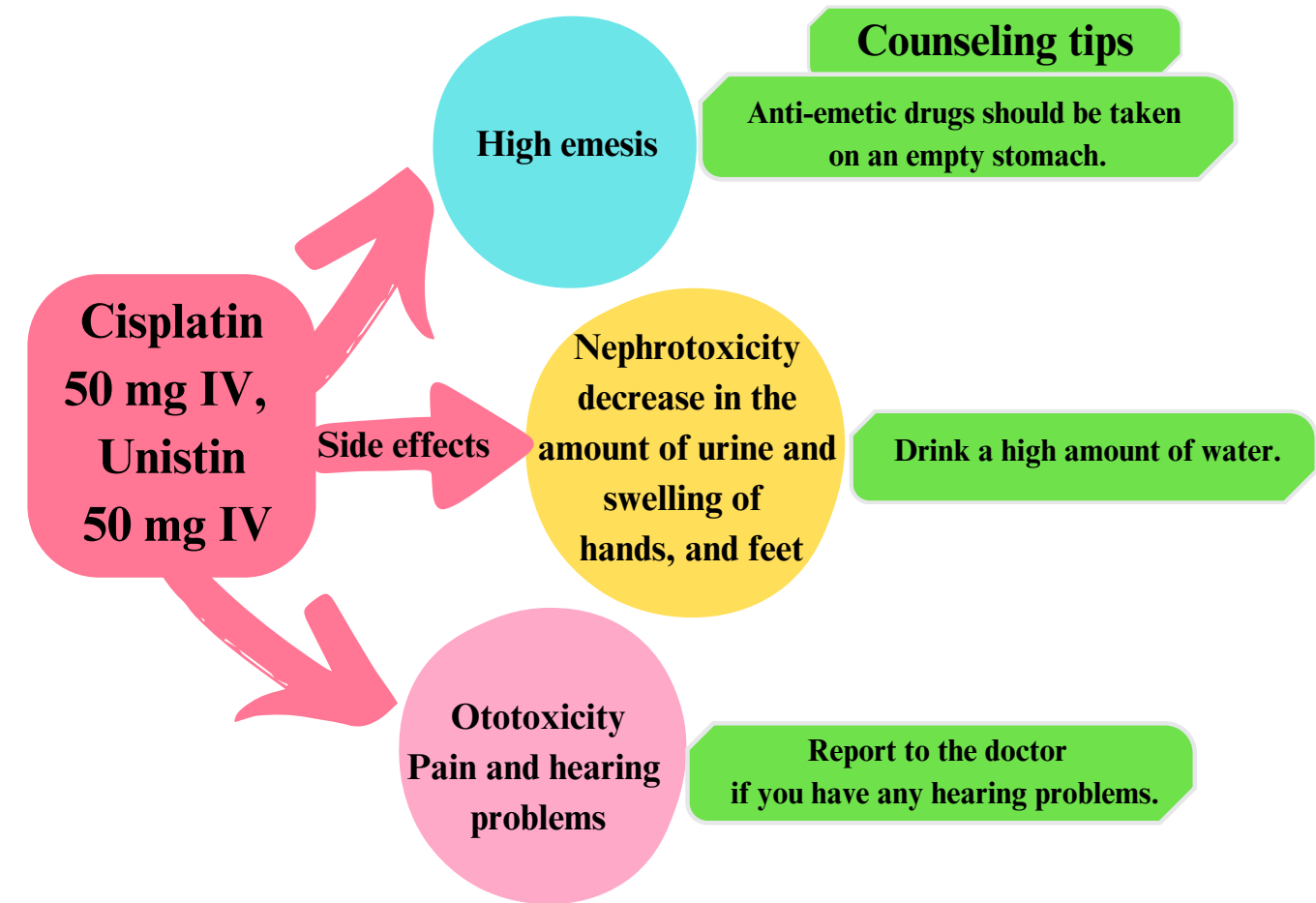
Side Effects
&
Symptoms

Allergic
reaction as:
rash, itching, swelling
of the face, lips,
tongue, or throat.

Patient should report
to the doctor to take
anti-hypersensitivity
drugs.



PATIENT COUNSELLING TIPS FOR DRUGS: 2 - CISPLATIN



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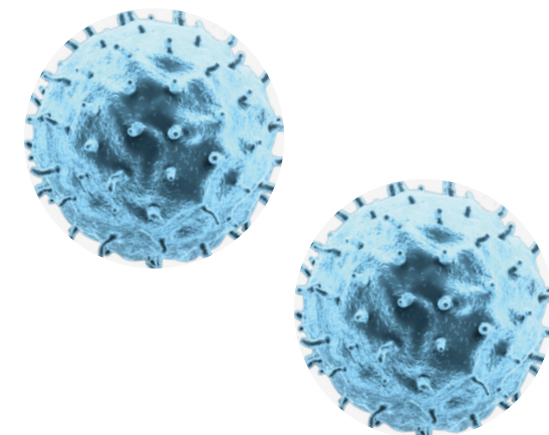
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