National Cancer Institute

National Cancer Institute
Cairo University

February 2024

NEWSLETTER

IMPROVE YOUR KNOWLEDGE, IMPROVE PATIENT HEALTH

Volume 07

ISSUE 07

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FDA announcements:

Elranatamab-bcmm and Talquetamab-tgvs approval for multiple myeloma

The reason why The Food and Drug Administration granted accelerated approval to elranatamab-bcmm (Elrexfio, Pfizer, Inc.)On August 14, 2023, and talquetamab-tgvs (Talvey, Janssen Biotech, Inc.) On August 9, 2023.

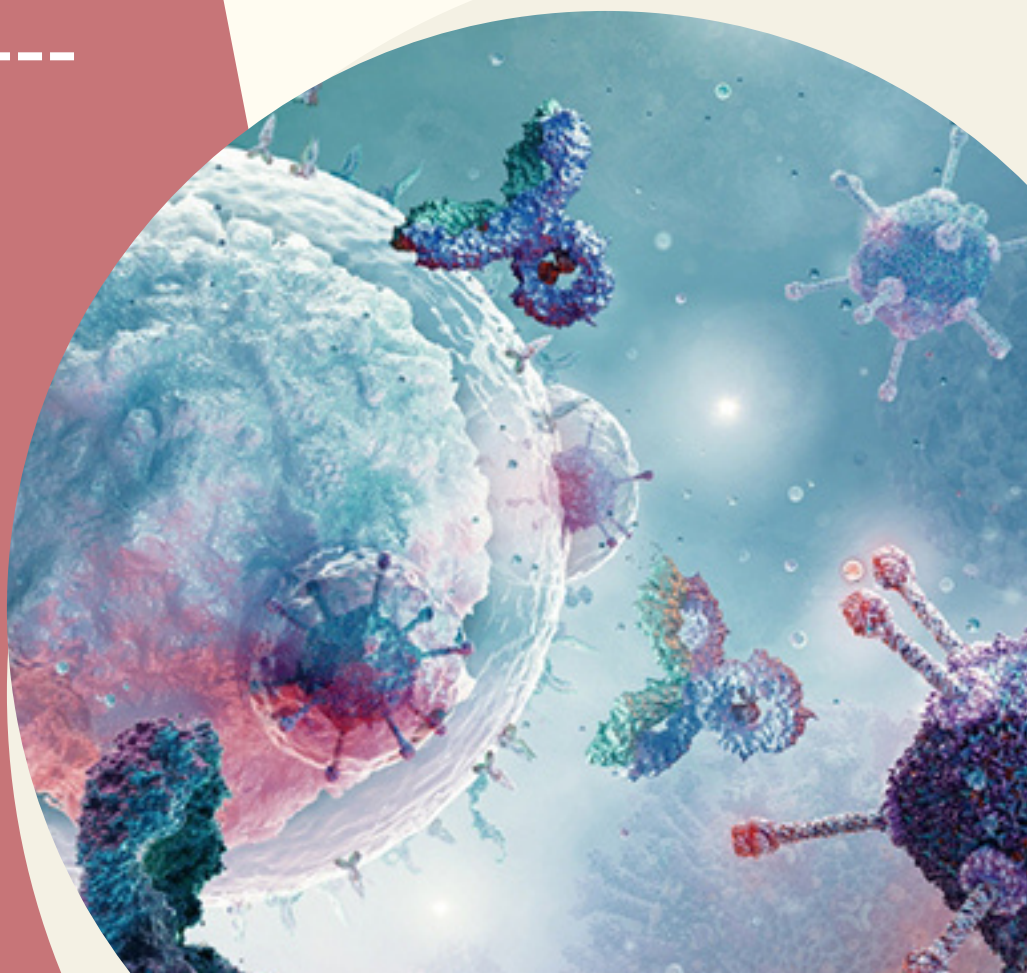
New in research

CAR-T Therapy future outlook and limitation

CAR T-cell therapy represents a ground breaking approach in cancer treatment, harnessing the power of the immune system to target and eliminate cancer cells.

Mission

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



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New FDA Announcement

Introduction:

The Food and Drug Administration granted accelerated approval to elranatamab-bcmm (Elrexfio, Pfizer, Inc.)On August 14, 2023, and talquetamab-tgvs (Talvey, Janssen Biotech, Inc.) On August 9, 2023. [1][2]

Bispecific drugs:

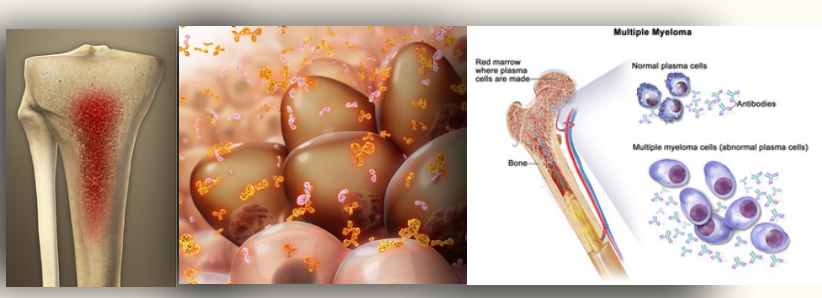
A bispecific monoclonal antibody (BsMAb, BsAb) is an artificial protein that can simultaneously bind to two different types of antigen or two different epitopes on the same antigen.[1][2]

Mechanisms of Action:

They are bispecific antibodies that target B-cell maturation antigen (BCMA) and engage T-cells. These antibodies bind to BCMA on plasma cells, plasmablasts, and multiple myeloma cells, while also binding to CD3 on T-cells. This dual binding leads to the lysis of BCMA-expressing cells. Additionally, they activate T-cells, triggering the release of proinflammatory cytokines and ultimately resulting in the lysis of multiple myeloma cells. [1][2]

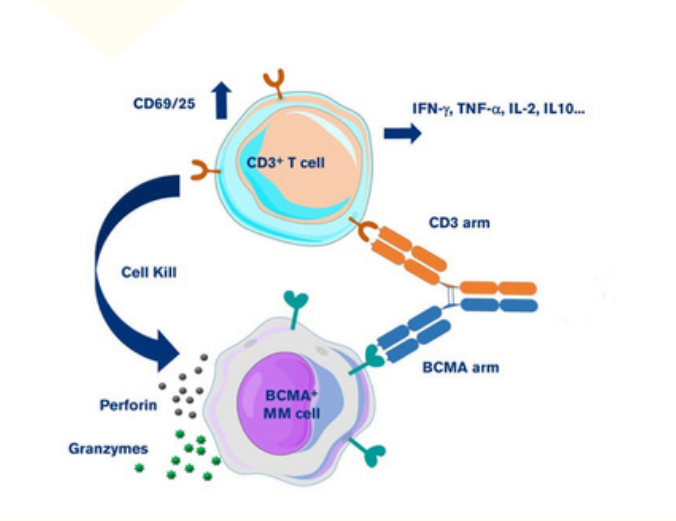
Indication and usage:

They are indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have undergone at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 Monoclonal antibody. [1][2]



Warnings and precautions:

• Oral Toxicity and Weight Loss: Monitor for oral toxicity and weight loss.
• Infections: Can cause serious, life-threatening, or fatal infection.
• Cytopenias: Monitor complete blood counts.
• Skin Toxicity: Monitor for skin toxicity, including rash progression.
• Hepatotoxicity: Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated.
• Embryo-Fetal Toxicity: May cause fetal harm.[1][2]



Adverse reactions:

The most common adverse reactions (≥20%) are pyrexia,Cytokinase release syndrome (CRS), dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight decreased, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache.[1][2]

Dosage: [2]

ELREXFIO™ (elranatamab-bcmm)
INJECTION FOR SUBCUTANEOUS USE | 44 mg/1.1 mL, 76 mg/1.9 mL

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

Indicated for the Treatment of Adults with relapsed or refractory multiple myeloma

	ELREXFIO Dosing Schedule		
Dosing Schedule	**Day**	**ELREXFIO Dose**	
Step-up Dosing Schedule	Day 1	Step-up dose 1	12 mg
	Day 4	Step-up dose 2	32 mg
	Day 8	First treatment dose	76 mg
Weekly Dosing Schedule	One week after first treatment dose and weekly thereafter through week 24	Subsequent treatment doses	76 mg

	ELREXFIO Dosing Schedule		
Dosing Schedule	**Day**	**ELREXFIO Dose**	
Biweekly (Every 2 Weeks) Dosing Schedule*	Week 25 and every 2 weeks thereafter	Subsequent treatment doses	76 mg

*Responders only week 25 onward.

TALVEY Weekly Dosing Schedule			
Dosing Schedule	**Day**	**Dose**	
Step- up dosing schedule	**Day 1**	**Step-up dose 1**	**0.01 mg/kg**
	Day 4	**Step-up dose 2**	**0.06 mg/kg**
	Day 7	**First treatment dose**	**0.4 mg/kg**
Weekly dosing schedule	**One week after first treatment dose and weekly thereafter through week 24**	**Subsequent treatment doses**	**0.4 mg/kg once weekly**

TALVEY Biweekly (Every 2 Weeks) Dosing Schedule			
Dosing schedule	**Day**	**Dose**	
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4	Step-up dose 2	0.06 mg/kg
	Day 7	Step-up dose 3	0.4 mg/kg
	Day 10	First treatment dose	0.8 mg/kg
Biweekly (every 2 weeks) dosing schedule	Two weeks after first treatment dose and every 2 weeks thereafter[d]	Subsequent treatment doses	0.8 mg/kg every 2 weeks

Refrances:
1- https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-elranatamab-bcmm-multiple-myeloma
2- https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-talquetamab-tgvs-re

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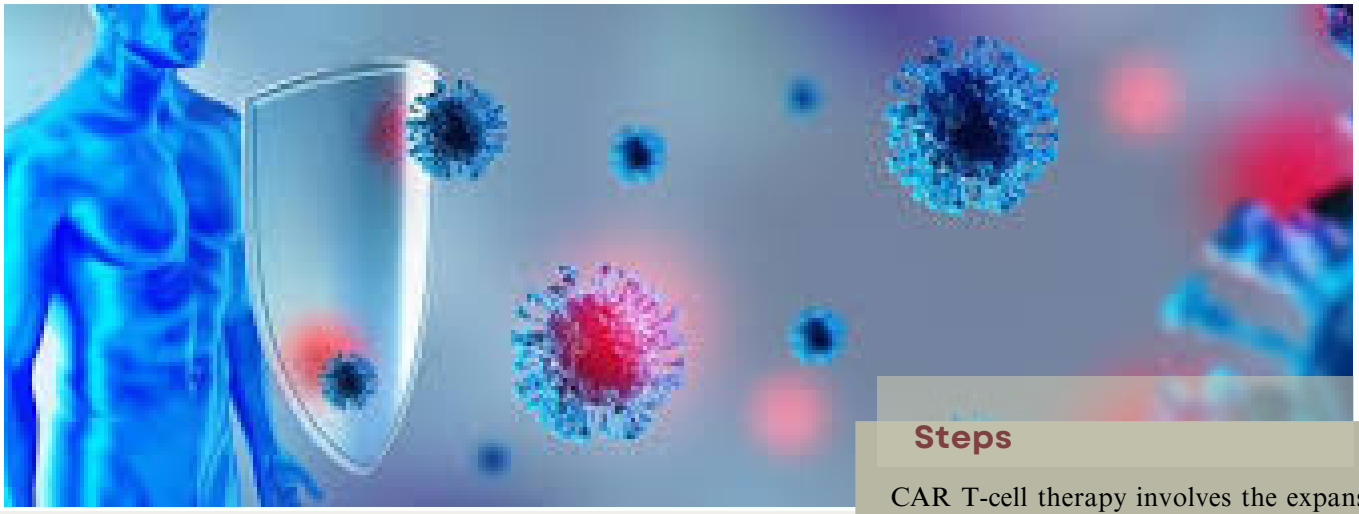
CAR-T THERAPY



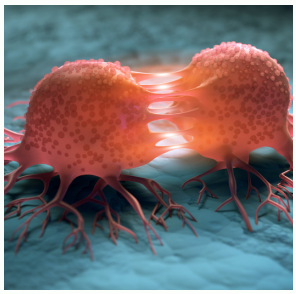
Introduction

Cancer immunotherapy is a treatment that utilizes the body's immune system to fight cancer by using immune cells or antibodies to recognize and kill cancer cells. T cells are effective in fighting infections but can have difficulty distinguishing between cancer cells and normal cells, allowing cancer cells to go unrecognized. [1]

CAR T-cell therapy is a promising form of cancer immunotherapy that aims to enhance the ability of T cells to recognize and attack cancer cells. By genetically modifying Tcells in the lab to express chimeric antigen receptors (CARs), which are designed to target specific proteins on cancer cells, researchers hope to improve the T cells' ability to distinguish between cancer cells and normal cells. *Apheresis* is the process by which a sample of T cells is taken from the patient's blood for use in CAR T-cell therapy. The collected T cells are then genetically engineered by introducing DNA into them, which leads to the production of CARs on their surface [1]

Components

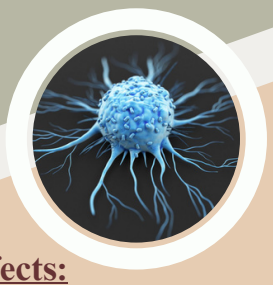
The CARs used in therapy typically consist of an antigen-binding domain, a hinge region, a transmembrane domain and one or more intracellular signaling domains. The antigen-binding domain is responsible for interacting with the target, and its affinity must be high enough to recognize the cancer cells but not trigger toxicities. The hinge region provides flexibility and length to allow the antigen-binding domain to access the targeted epitope. The transmembrane domain anchors the CAR to the T cell membrane. Intracellular signaling domains, such as CD28 or 4-1BB, play crucial roles in activating the T cells and enhancing their anti-tumor functions [1]



Steps

CAR T-cell therapy involves the expansion of the genetically modified T cells in the lab, allowing them to multiply into a large population. Once a sufficient number of CAR T cells are obtained, they are infused back into the patient's bloodstream through a drip. The goal is for the CAR T cells to recognize and attack the cancer cells that express the targeted protein.

Prior to CAR T-cell infusion, many patients receive a brief course of chemotherapy called lymphodepletion. This treatment reduces the number of existing T cells in the patient's body, creating space for the CAR T cells to expand and exert their anti-tumor effects more effectively. Monitoring and close observation are essential during and after CAR T-cell therapy to manage potential side effects. [1]

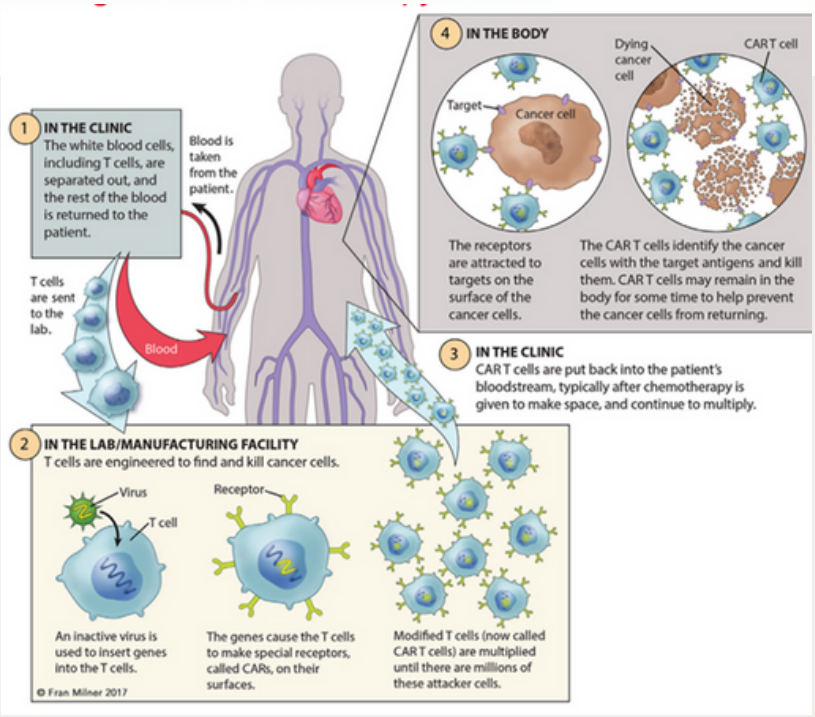


Side effects:

Common side effects include cytokine-release syndrome (CRS), which is characterized by flu-like symptoms and can be severe in some cases, and neurologic toxicities, which may cause confusion, seizures, or other neurological problems. Prompt intervention and appropriate management strategies are employed to address these side effects. [1][3]

Medical teams developed protocols to mitigate these side effects according to the grade such infusion of the monoclonal antibody tocilizumab and Corticosteroids [1][3]

CAR-T THERAPY



Approved drugs:

Several CAR T-cell therapies have been approved by the FDA for specific types of cancer, including Axicabtageneciloleucel, Brexucabtageneautoleucel, Ciltacabtageneautoleucel, Idecabtagenevicleucel, Lisocabtagenemaraleucel, and Tisagenlecleucel. These therapies have demonstrated effectiveness in treating relapsed or refractory forms of lymphomas and leukemias.[(1) (3)]

Challenges and solutions:

One of the challenges in CAR T-cell therapy is the potential for the development is antigen escape variants in which Cancer cells can undergo changes that result in the loss or down-regulation of the targeted protein, making them less susceptible to CAR T-cell recognition [(2)]

Researchers are actively investigating strategies to overcome this challenge, such as the use of dual-targeted CAR T cells, targeting multiple antigens simultaneously or using CAR T cells in combination with other therapies.[(2)]

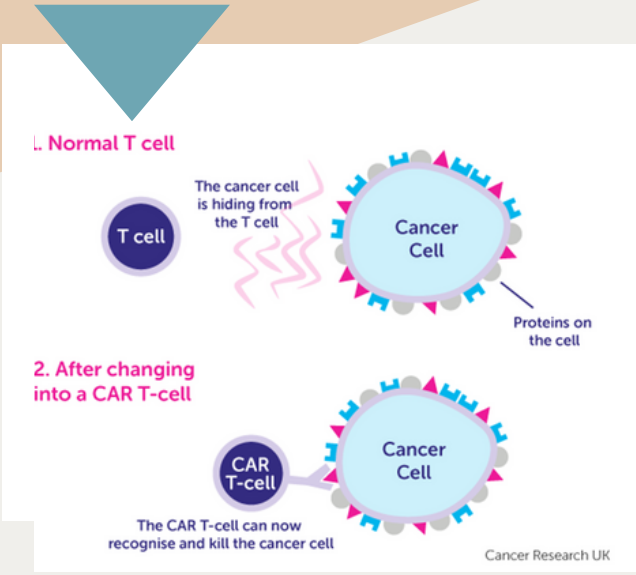
Another area of research focuses on improving the safety profile of CAR T-cell therapy. Strategies are being developed to control the activation and expansion of CAR T cells to minimize the risk of severe side effects. This includes the use of switchable CARs, which can be activated or deactivated using specific molecules, allowing greater control over T cell activity.[(2)]

Beyond hematological malignancies, efforts are underway to expand the application of CAR T-cell therapy to solid tumors. Solid tumors present unique challenges due to the complex tumor microenvironment, limited T cell infiltration, and the presence of inhibitory factors. Overcoming these barriers is an active area of research, and scientists are exploring approaches such as engineering CAR T cells with additional features to enhance infiltration and their functionality within the solid tumor environment.[(2)]

Future outlook

CAR T-cell therapy is a rapidly evolving field, with ongoing advancements and innovations. Researchers are investigating new targets for CAR T cells, exploring novel gene-editing techniques to enhance CAR T cell properties, limiting side effects and developing strategies to improve the manufacturing and delivery of CAR T cells. Ongoing research and clinical trials continue to explore the potential of this therapy and refine its application in different cancer settings.

The cost and accessibility of CAR T-cell therapy remain significant considerations. Currently, CAR T-cell therapies are complex and expensive to produce, limiting their availability to specialized centers and certain patient populations. However, ongoing efforts are being made to optimize manufacturing processes and reduce costs, with the aim of making CAR T-cell therapy more widely accessible in the future.[(2)(4)]



Summary

Overall, CAR T-cell therapy represents a groundbreaking approach in cancer treatment, harnessing the power of the immune system to target and eliminate cancer cells. Further research and advancements in this field hold great potential for expanding the applications of CAR T-cell therapy and improving outcomes for patients with various types of cancer.

References;

1- https://www.lls.org/treatment/types-treatment/immunotherapy/chimeric-antigen-receptor-car-t-cell-therapy

2- Sterner, R.C., Sterner, R.M. CAR-T cell therapy: current limitations and potential strategies. Blood Cancer J. 11, 69 (2021). https://doi.org/10.1038/s41408-021-00459-7.

3- https://online.lexi.com/lco/action/search?q=car%20t%20therapy&t=name&acs=true&acq=car%20t

4- https://www.mdanderson.org/cancerwise/what-s-new-in-car-t-cell-therapy--solid-tumor-advances.h00-159617856.html

PEG-ASPARAGINASE AND ASPARAGINASE

Today, we shed light on the remarkable potential of Pegaspargase, a modified version of the well-known L-asparaginase enzyme. Pegaspargase has shown promising results in targeting leukemia cells.

In terms of mechanism of action, Pegaspargase functions by hydrolyzing L-asparagine, an essential amino acid for leukemia cells, into ammonia and L-aspartic acid. By depleting asparagine levels in leukemic cells, Pegaspargase effectively inhibits protein synthesis and triggers apoptosis, leading to the depletion and elimination of these cancerous cells.

One of the key advantages of Pegaspargase is its ability to selectively target leukemia cells while sparing normal cells, which can synthesize asparagine independently. This targeted approach allows for more effective treatment while minimizing detrimental side effects on healthy cells.

Pegaspargase, offers several advantages over conventional asparaginase formulations. Unlike standard asparaginase, Pegaspargase is conjugated with monomethoxypolyethylene glycol (mPEG). This modification enhances its stability and prolongs its half-life, allowing for less frequent administrations and improved convenience for patients.

Let's delve into some essential details surrounding the administration and usage of Pegaspargase.

DOSAGE

In addition to the differences in formulation, Pegaspargase and asparaginase also differ in their recommended dosages.

For Pegaspargase, the recommended dosages are as follows:

- Patients aged 21 years and below:
  2,500 units/m2 every 14 days.

- Patients above 21 years:
  2,000 units/m2 every 14 days.

While, asparaginase may be administrated 3 times per week.

PREPARATION, ADMINISTRATION & STORAGE OF PEG-ASPARGASE:

1. Intravenous (IV) administration: Dilute in 100 mL of normal saline (NS) or D5W and infuse over 1-2 hours
2. Intramuscular (IM) administration: Inject deeply into a large muscle, limiting the injection volume to 2 mL per site. If the volume exceeds 2 mL, multiple injection sites should be used.

Pegaspargase should be used immediately after preparation.
Store intact vials and diluted solutions protected from light at temperatures between 2°C - 8°C or 15°C - 25°C for a maximum of 48 hours.

Discard if frozen, excessively shaken, stored at room temperature for over 48 hours, or if the solution becomes cloudy, discolored, or precipitated.

PREMEDICATION

To mitigate the risk and severity of infusion and hypersensitivity reactions, premedication is recommended 30 to 60 minutes before Pegaspargase administration. The premedication includes:

- Acetaminophen.
- H1 antagonist.
- H2 antagonist.
- Thromboprophylaxis with low molecular weight heparin (LMWH) may be considered for patients at high risk of venous thromboembolism, with LMWH withheld for platelet counts below 30,000/mm^3..

MONITORING AND ADVERSE REACTIONS

During and after administration, close monitoring of the patient is crucial. Common adverse reactions associated with Pegaspargase include hypersensitivity reactions, thromboembolic complications, hyperglycemia, pancreatitis, and febrile neutropenia, among others. Regular monitoring of blood parameters, liver function, renal function, glucose levels, and coagulation parameters is recommended.

CONTRAINDICATIONS AND PRECAUTION

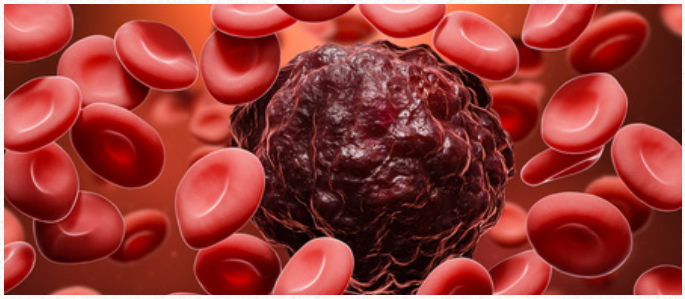
Pegaspargase should not be administered to patients with a history of serious hypersensitivity reactions, serious thrombosis with prior L-asparaginase therapy, pancreatitis, serious hemorrhagic events with prior L-asparaginase therapy, or severe hepatic impairment. Additionally, it is important not to interchange Pegaspargase with other types of asparaginase.

REPRODUCTION AND BREASTFEEDING CONSIDERATION

Due to potential adverse effects on fetal development, effective nonhormonal contraception should be used during Pegaspargase therapy and for three months after the last dose. Hormonal contraceptives are not recommended.

As for breastfeeding, the presence of Pegaspargase in breast milk is currently unknown, and breastfeeding is not recommended during therapy and for one month after the last dose.

Pegaspargase represents a significant breakthrough in leukemia treatment, offering hope to patients and healthcare professionals alike. Its targeted mechanism of action, combined with careful administration and monitoring, makes it a valuable asset in our fight against ALL.



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Inhaling Danger:

The smoking Gun Behind Cancer Menace

There are 69 different chemicals in one cigarette that can possibly cause cancer which are known as (carcinogens). Smoking tobacco causes the most common type of cancer which is lung cancer, But did you know the other 16 types of cancer that can be caused by smoking tobacco ?

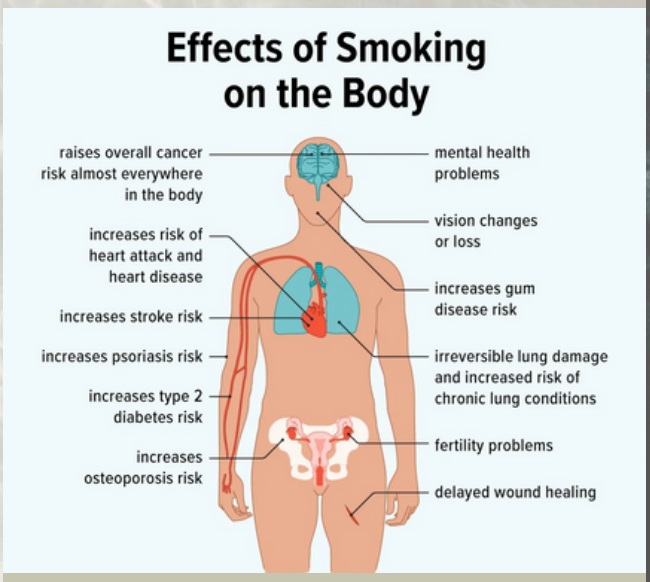
The 16 types of induced Cancers are : [1]

1. **Lung cancer.**
2. **Bladder cancer.**
3. **Liver cancer.**
4. **Esophagus cancer.**
5. **Larynx cancer.**
6. **Mouth cancer.**
7. **Pharyngeal cancer.**
8. **Stomach cancer.**
9. **Bowel cancer (colorectal cancer).**
10. **Acute myeloid leukemia.**
11. **Ovary cancer.**
12. **Cervix cancer.**
13. **Kidney cancer.**
14. **Nose cancer.**
15. **Sinus cancer.**
16. **Ureter cancer.**

Our bodies starts to repair every 6 hours , so you can control smoking and decrease the risk of cancer death.

Quitting smoking (active and passive smoking) lowers the risk of 15 type of cancers :-

- **Within 5-10 years of quitting smoking your chance of getting cancer of Esophagus , larynx and mouth decreases.**
- **Within 10 years of controlling smoking your chance of getting cancer of kidney and bladder decreases.**
- **Within 15 years of controlling smoking your chance of getting cancer of lung drops by half.** [2]



Terrie H.'s story

Terrie was diagnosed with oral cancer at first, and later , with throat cancer. Doctors informed her that they would need to remove her larynx. later , Terrie was diagnosed with cancer 10 times .

Recently, she diagnosed with all voice box cancer in her throat, Terrie died in September 2013 from smoking-related cancer. She was 53 years old.

How can cancers caused by smoking be prevented and controlled?

The first important thing to avoid smoking – related cancer is not to smoke cigarettes.
Second, avoiding passive smoking.

Some cancers respond well to single type of treatment and others respond to combination treatments .
Controlling smoking improves the the prognosis for people with cancer, People who continue to smoke after diagnosis raise their risk for future cancers and death. [3]

References;

1. https://www.cancercouncil.com.au/news/there-are-16-cancers-that-can-be-caused-by-smoking/
2. https://www.cdc.gov/tobacco/campaign/tips/diseases/cancer.html#:~:text=It%20is%20also%20important%20to,acute%20myeloid%20leukemia%20(AML).
3. https://www.cdc.gov/tobacco/campaign/tips/stories/terrie.html

Our Achievements

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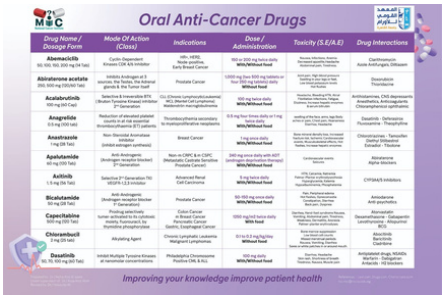
Booklet

Lectures

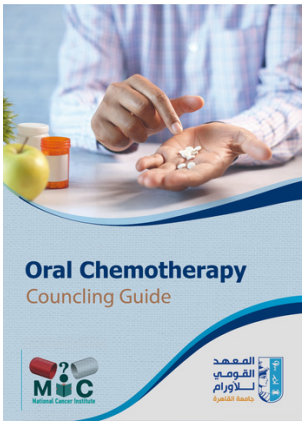
Posters

Lectures

Posters



Poster



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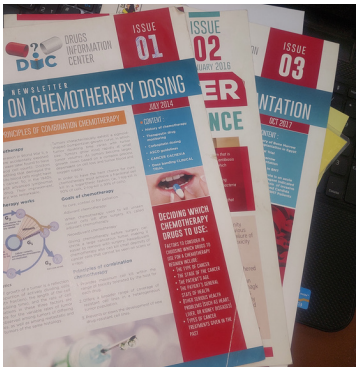

Newsletters

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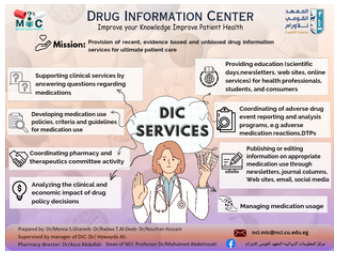

Posters

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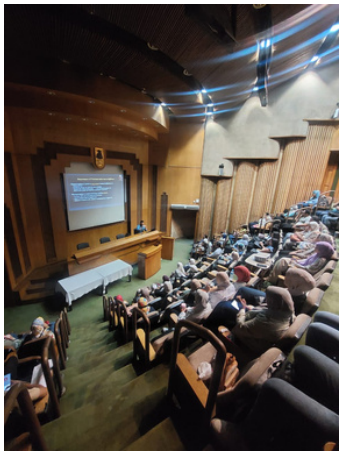

Lectures

Flyers

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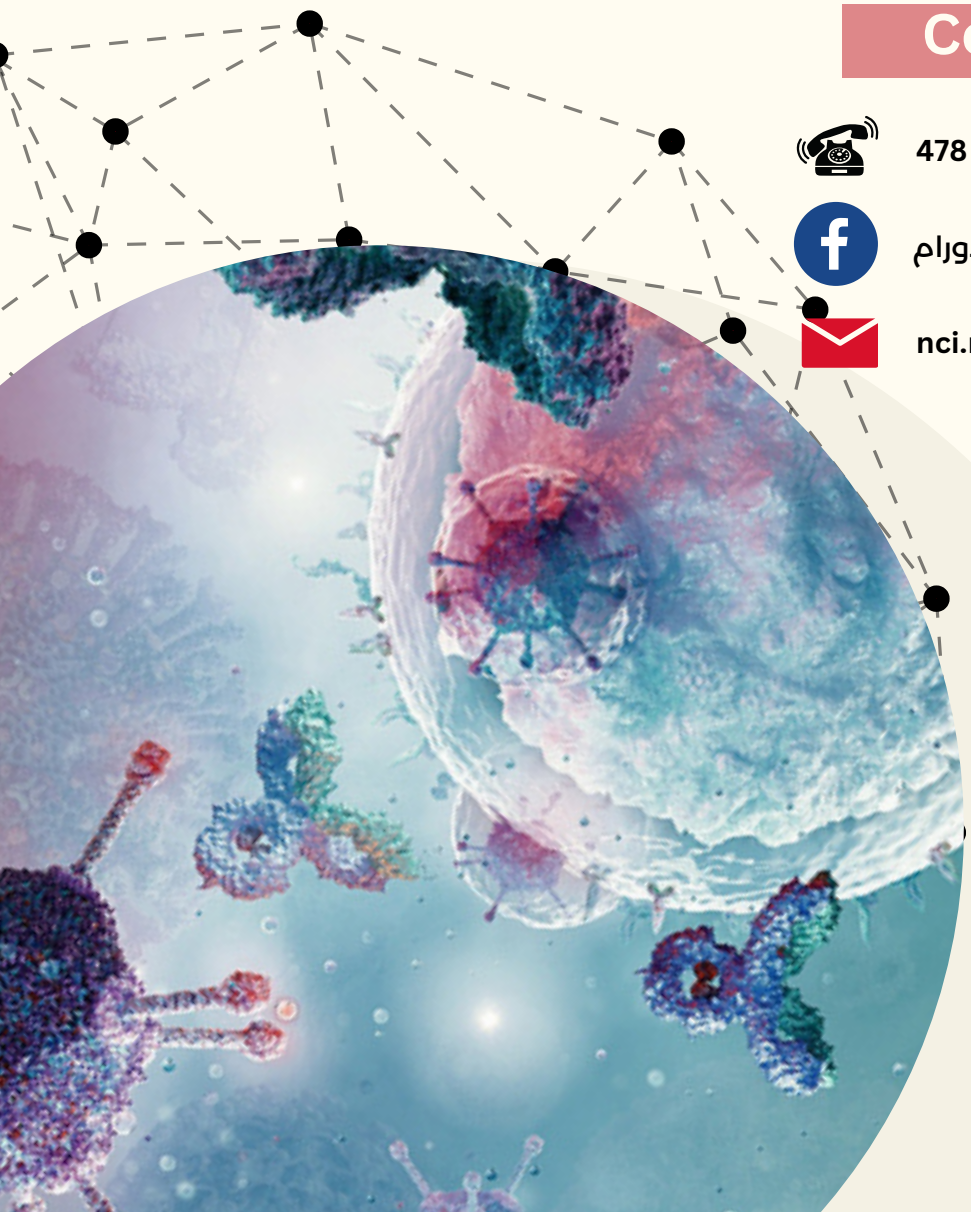

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مركز المعلومات الدوائيه-المعهد القومي للأورام

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IMPROVE YOUR KNOWLEDGE
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