National Cancer Institute
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JUNE 2024

NEWSLETTER

IMPROVE YPUR KNOWLEDGE,
IMPROVE PATIENT HEALTH

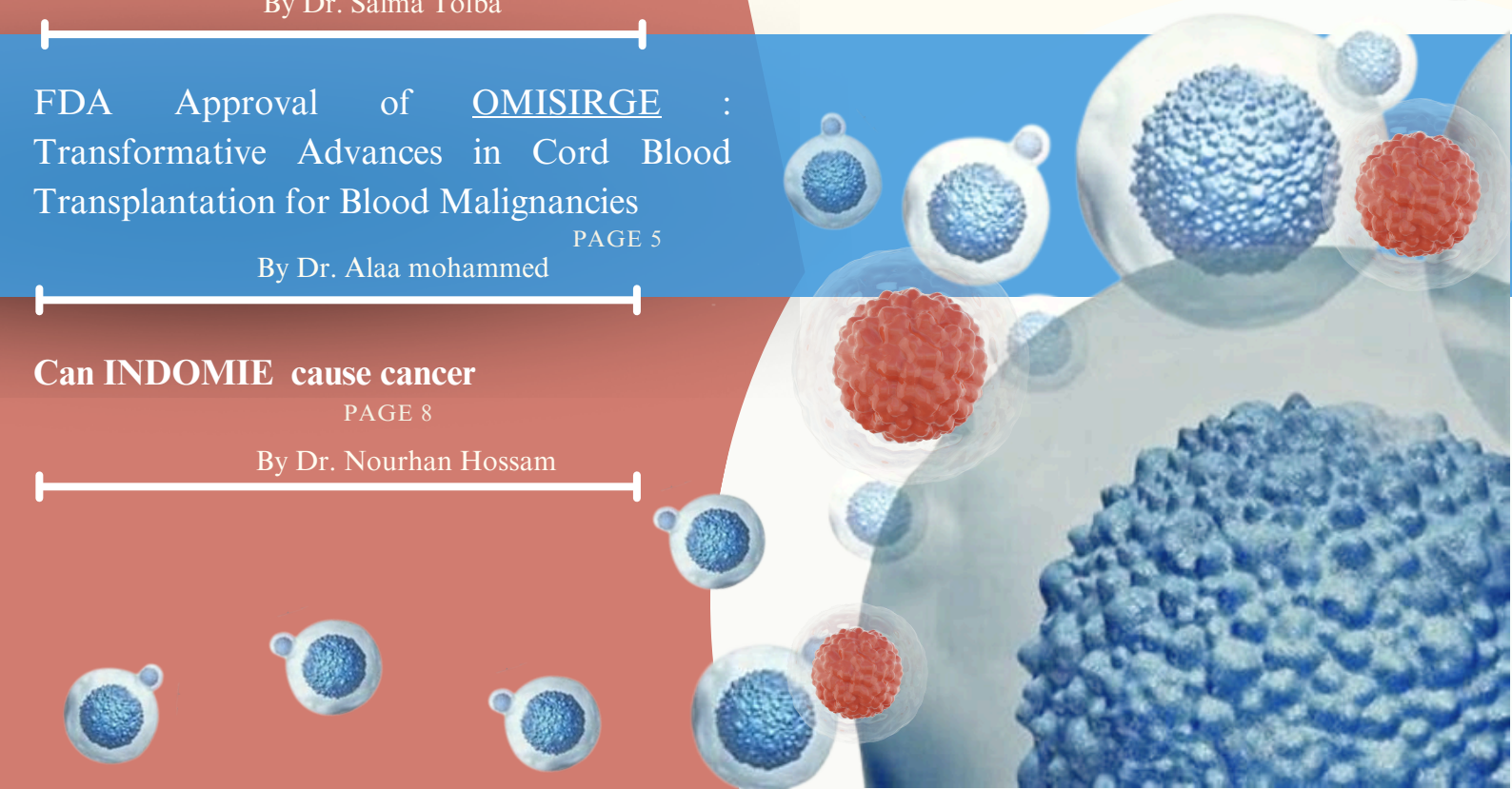
Volume 07

ISSUE 02

In This Issue

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

Fruzaqla™
(fruquintinib) capsules
5 mg • 1 mg

On 8 November 2023, Fruqunitinib (FruzaqlaTM, Takeda Pharmaceuticals, Inc.) has been approved by FDA for adult metastatic colorectal cancer (mCRC).[1]

Indications:

FRUZAQLA ™ is oral targeted therapy tailorated for patients who received specific chemotherapy such as fluoropyrimidine, oxaliplatin, and irinotecan-based chemotherapy, as well as antivascular endothelial growth factor (VEGF) therapy.

Furthermore, it could combined with anti-EGFR therapy for those with RAS wild-type who are medically appropriate.[1]

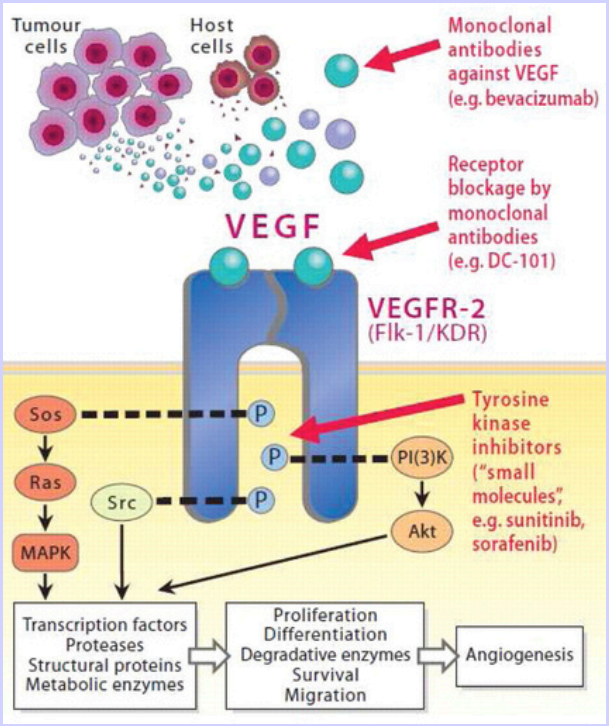
Dosage and administration : [2]

The recommended dose of FRUZAQLA is 5 mg orally once daily, with or without food for the first 21 days of each 28-day cycle.

Dosage form and strengths:
Capsules: 1 mg and 5 mg

Mechanism of Action:

Fruquintinib is a small molecule kinase inhibitor of vascular endothelial growth factor receptors (VEGFR)-1, -2, and -3 with IC50 values of 33, 35, and 0.5 nM, respectively. In vitro studies showed that Fruquintinib inhibited VEGF-mediated endothelial cell proliferation and tubular formation. In addition, In vivo studies revealed Fruquintinib inhibited tumor growth in a tumor xenograft mouse model of colon cancer. Both displayed that Fruquintinib inhibited VEGF-induced VEGFR-2 phosphorylation.[(2)]



References: V. Dempke, W. M.; Heinemann, V. Resistance to EGF-R (erbB-1) and VEGF-R modulating agents. 2009. Eur J Cancer., 45(7):1117-1128

Warnings and precautions:

Before administering Fruzaqla, physician should ask if patients:

- Have high blood pressure
- Have bleeding problems
- Have an infection
- Have liver or kidney problems
- Plan to have surgery or have had recent surgery
- Have recently had a blood clot, stroke, or heart attack
- Are allergic to FD&C Yellow No. 5 (tartrazine) or FD&C Yellow No. 6 (sunset yellow FCF)
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed (Embryo-Fetal Toxicity) [(2)]

Adverse reactions:

Most common adverse reactions (incidence ≥20%) are hypertension, palmar-plantar erythrodysesthesia, proteinuria, dysphonia, abdominal pain, diarrhea, and asthenia.

References;
1-https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-fruquintinib-refractory-metastatic-colorectal-cancer
2-https://www.fruzaqla.com

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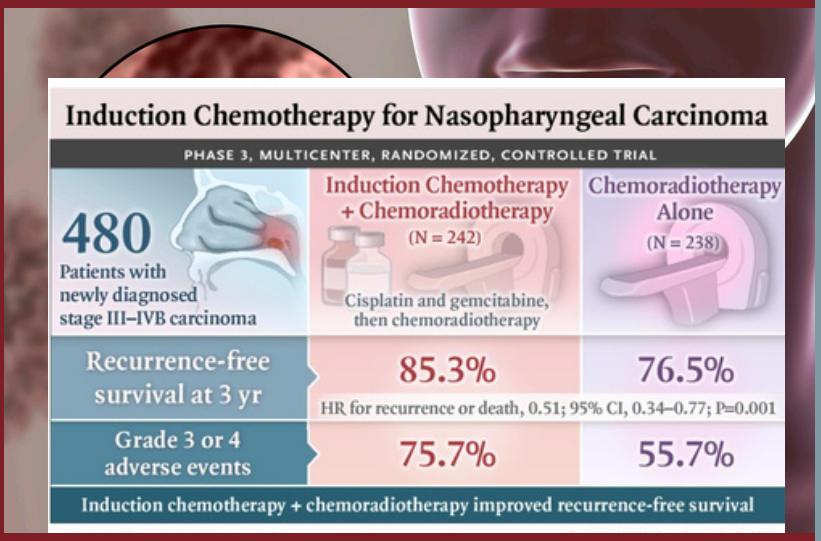
INDUCTION AND ADJUVANT THERAPY IN NASOPHARYNGEAL CANCER.



Nasopharyngeal carcinoma (NPC) is a metastasis-prone malignancy that arises in the nasopharynx epithelium. It is considered the most common malignancy originating in the nasopharynx. It is endemic to parts of Asia and Africa but it is found worldwide. (1)

Risk factors: Epstein-Barr virus, heavy alcohol consumption, smoking, regularly eating salt-cured foods, sex and race.

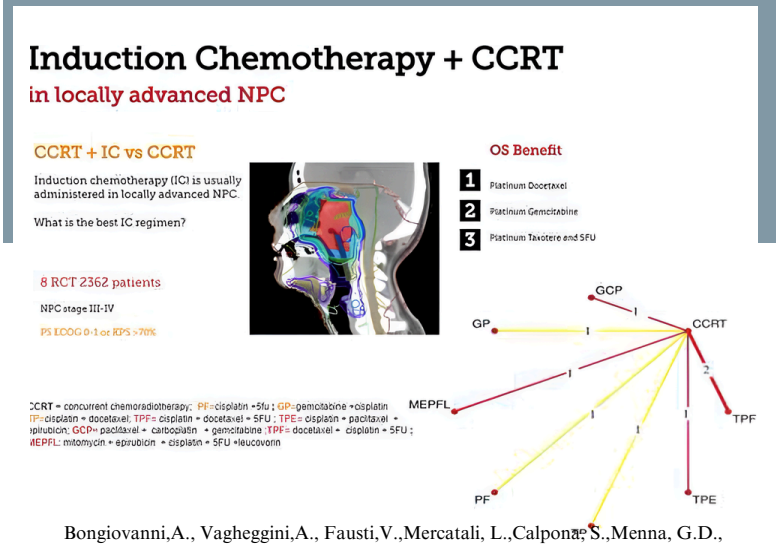
NPC has traditionally been treated with radiation therapy (RT) due to its sensitivity to radiation and its anatomic location that limits the surgical procedure. (1)

A combined-modality approach that includes concurrent chemoradiation is considered the basis of standard treatment for advanced, non-metastatic NPC patients. Other options involve using induction chemotherapy followed by concurrent chemoradiation or concurrent chemoradiation with or without adjuvant chemotherapy with the preferred regimen [Cisplatin + Radiotherapy followed by Cisplatin (or Carboplatin) /5-FU]. (2)

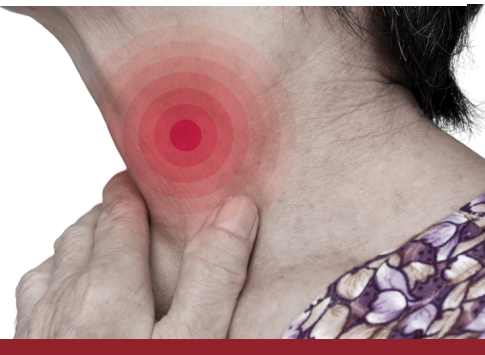
First line Chemotherapy regimens for NPC include combination regimens (ex. Cisplatin plus Gemcitabine) or single agents including (Cisplatin, Carboplatin, Paclitaxel, Gemcitabine, 5-FU).

For patients with more advanced stage III to IVA NPC, it is suggested to use induction chemotherapy followed by concurrent chemoradiation.This approach enhances the overall survival (OS) in randomized trials. It also reduces tumor burden and increases the control of both locoregional and systemic disease. In addition, it improves recurrence-free survival and allows for smaller high-dose radiation volumes. (3)

For patients who are candidates for induction chemotherapy, it's recommended to use three cycles of Gemcitabine plus Cisplatin (GP), as this regimen improves OS, has a manageable toxicity profile, and is easier to administer than other available regimens. (2)



Bongiovanni,A., Vagheggini,A., Fausti,V.,Mercatali, L.,Calpona, S.,Menna, G.D., Miserocchi, G., Ibrahim, T. Induction chemotherapy plus concomitant chemoradiotherapy in nasopharyngeal carcinoma: An updated network meta-analysis. 2021. Critical Reviews in Oncology/Hematology, 160, 103244



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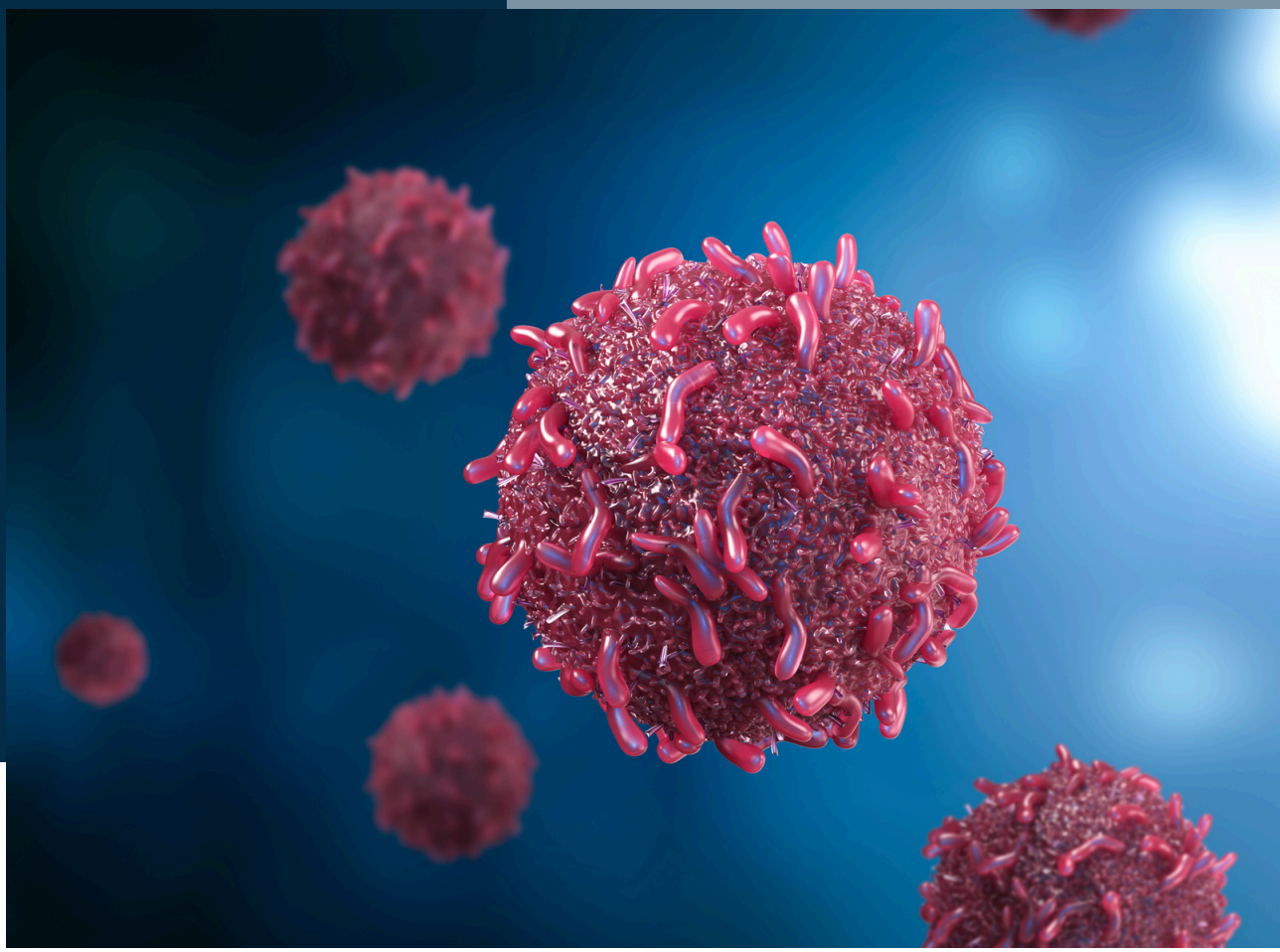
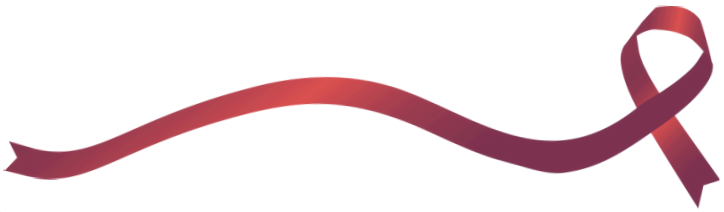


In a conducted meta-analysis for nasopharynx carcinoma chemotherapy (MAC-NPC) on 28 randomized controlled clinical trials at a median follow-up of 7.6 years; induction chemotherapy plus chemoradiation improved overall survival. [5] [6]

Adjuvant chemotherapy is also used for most patients with locoregionally advanced disease who are ineligible for or unable to tolerate Cisplatin-based induction chemotherapy, it is suggested to use concurrent chemoradiation followed by adjuvant chemotherapy.[4]

However, concurrent chemoradiation alone is also a reasonable alternative for patients who choose to forego or cannot tolerate adjuvant chemotherapy (ie, due to decreased performance status or comorbidities).

Further studies on the benefits of chemotherapy use as induction and adjuvant therapy in Nasopharyngeal cancer need to be carried out but the available studies show that the use of chemotherapy improves outcomes in patients with locally advanced nasopharyngeal cancer, especially when it is delivered as concomitant, concomitant+adjuvant, or induction in addition to concomitant therapy. [7]



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3) https://www.sciencedirect.com/science/article/abs/pii/S1470204523001638
4) https://www.uptodate.com/contents/treatment-of-early-and-locoregionally-advanced-nasopharyngealcarcinoma?search=nasopharyngeal%20carcinoma&source=search_result&selectedTitle=2~73&usage_type=default&display_rank=2#H2421983109
5) https://www.ctro.science/article/S2405-6308(21)00098-7/fulltext
6) https://www.nccn.org/patients/guidelines/content/PDF/hn-nasopharynx-patient.pdf
7) https://www.cancer.org/cancer/types/nasopharyngeal-cancer/treating/radiation-therapy.html

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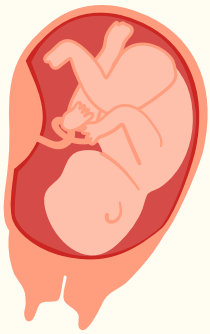
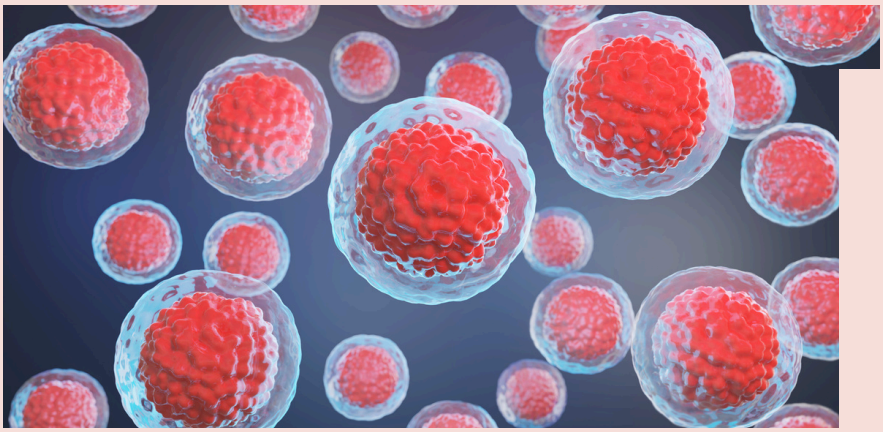
Omisirge®

Transformative Advances in Cord Blood Transplantation for Blood Malignancies





Allogeneic hematopoietic cell transplantation (HCT)

Hematopoietic Cell Transplantation (HCT) has long been a crucial treatment for cancer and blood system. Diseases, involving stem cell collection from related or unrelated donors.

The conditioning phase, utilizing high-dose chemotherapy, aims to eradicate diseases, followed by stem cell infusion to restore normal immune function. However, this technique presents challenges, including heightened risks for morbidity and mortality in specific cases. Stem cell transplants, with their preparative regimens, come with inherent toxicity, leading to common side effects like loss of appetite, alopecia, and nausea. Additionally, complications such as mucositis and pancytopenia increase infection risks, impacting physical and emotional tolerance. The quest is to decrease toxicity without compromising efficacy, recognizing the need for advancements in this critical medical procedure. [1]

Myeloablative therapy

It means that the treatment kills (ablates) the stem cells in the bone marrow; the cells that produce new blood cells. Myeloablative conditioning (MAC) is a regimen that consists of a single agent or combination of agents that are anticipated to destroy the hematopoietic cells in the bone marrow. Extensive pancytopenia occurs within one to three weeks after administration of a MAC regimen and is typically irreversible.[2]

Types of Stem Cell and Bone Marrow Transplants [2]

Stem cell transplants are used to put blood stem cells back into the body after the bone marrow has been destroyed by disease, chemotherapy (chemo), or radiation. Depending on where the stem cells come from, the transplant procedure may go by different names:

- Bone marrow transplant (BMT)
- Peripheral blood stem cell transplant (PBSCT)
- Umbilical cord blood (UCB) transplant

In cancer stem cell transplants, a person undergoes intense chemotherapy, possibly with radiation, to eliminate cancer cells and also destroy bone marrow stem cells, termed myeloablation. Subsequently, blood stem cells are transplanted to replace the depleted ones. This engraftment process involves introducing replacement cells into a vein, akin to a blood transfusion, with the aim that they settle in the bone marrow, regenerating healthy blood cells. Two primary transplant types exist: autologous, where the patient serves as their own stem cell donor, and allogeneic, where stem cells come from another person, either a matched related or unrelated donor.

Allogeneic stem cell transplants involve using donor stem cells, commonly sourced from a closely matched family member, such as a brother or sister. If no suitable family match exists, donors can be found in the general public through a national registry, termed a Matched Unrelated Donor (MUD) transplant. While MUD transplants pose higher risks than those with close relatives, the procedure is akin to autologous transplants. Stem cells are collected from the donor, stored or frozen, and then infused into the patient after undergoing intensive chemotherapy and/or radiation for myeloablative therapy. Allogeneic transplants are frequently employed to treat specific cancers like leukemia, lymphomas, multiple myeloma, myelodysplastic syndromes, and bone marrow disorders like aplastic anemia.[3]

Umbilical Cord Blood Transplant

Involves using blood from the placenta and umbilical cord of a newborn for an allogeneic transplant. Despite the small volume, cord blood is rich in stem cells, providing certain advantages.

Cord blood banks already contain numerous donated units, facilitating easier donor matches without the need for collection upon identification. Additionally, cord blood transplants have a lower risk of rejection compared to adult donor transplants. However, they come with downsides, such as a lower quantity of stem cells, making them more suitable for children.[3]

Adults may require multiple cord blood units for an adequate stem cell supply. Cord blood transplants also have a longer time frame for initiating blood cell production, making recipients vulnerable to infections. A newer product, omidubicel (Omisirge), undergoes lab treatment to expedite the process of bone marrow integration and hasten the production of new blood cells in the body.[3]

April 2023,

The U.S. Food and Drug Administration (FDA) granted approval for **Omisirge,** a nicotinamide-modified allogeneic hematopoietic progenitor cell therapy derived from cord blood. Specifically designed for patients aged 12 and older with blood malignancies planning umbilical cord blood transplantation post-myeloablative conditioning, Omisirge accelerates neutrophil recovery and reduces infection risks. A randomized, multicenter study involving 125 participants demonstrated Omisirge's safety and effectiveness.

DOSAGE FORMS

OMISIRGE is a cell suspension for intravenous infusion.

PREMEDICATION

Premedicate with diphenhydramine 50 mg IV (or 0.5 mg/kg up to a maximum of 50 mg) or dexchlorpheniramine 10 mg IV, hydrocortisone 50 mg IV (or 0.5 mg/kg up to a maximum of 50 mg) and acetaminophen 650 mg PO (or 10 mg/kg up to a maximum of 650 mg).

•Avoid prophylactic use of methylprednisolone in conjunction with OMISIRGE.

• Ensure the patient is adequately hydrated.[2]

The study revealed that 87% of Omisirge recipients achieved neutrophil recovery within an average of 12 days, compared to 83% of those who received traditional umbilical cord blood transplantation (average recovery time of 22 days). Notably, Omisirge recipients experienced fewer bacterial or fungal infections than the umbilical cord blood transplantation group, further supporting the product's favorable outcomes. [5]

Administered as a single intravenous dose, is composed of human allogeneic stem cells from umbilical cord blood that are processed and cultured with nicotinamide (a form of vitamin B3). Each dose is patient-specific, containing healthy stem cells from an allogeneic pre-screened donor [5]

CONTRAINDICATIONS

OMISIRGE is contraindicated in patients with known hypersensitivity to dimethyl sulfoxide (DMSO), Dextran 40, gentamicin, human serum albumin, or bovine products.[6]

ADVERSE REACTIONS

- Hypersensitivity reactions
- Infusion reactions
- Graft versus Host Disease
- Engraftment Syndrome
- Graft failure
- Malignancies of donor origin [6]

Refrences

1. FDA Approves Cell Therapy for Patients with Blood Cancers to Reduce Risk of Infection Following Stem Cell Transplantation | FDA
2. HIGHLIGHTS OF PRESCRIBING INFORMATION of OMISIRGE® (omidubicel)
3. Lee JY, Hong SH. Hematopoietic Stem Cells and Their Roles in Tissue Regeneration. Int J Stem Cells. 2020 Mar 30;13(1):1-12. doi: 10.15283/ijsc19127. PMID: 31887851; PMCID: PMC7119209.
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5. Socié G, Mary JY, Esperou H, et al. Health and functional status of adult recipients 1 year after allogeneic haematopoietic stem cell transplantation. Br J Haematol 2001; 113:194.
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CAN Indomie ? CAUSE CANCER

Knowing the causes of cancer provides a basis for understanding the potential for preventing cancer. If a cause is known, it is much easier to know whether it can or cannot be avoided easily. (2)

The Egyptian Food Safety Authority (FSA) conducted safety tests on Indomie instant noodles, revealing concerning findings:

- Aflatoxins and pesticide residues were found in the chili and flavor packets, exceeding safe limits. Other Indomie products were generally safe.
- Immediate actions included removing non-compliant packets from the supply chain and instructing Indomie Egypt to withdraw these products and remove certain health claims from packaging. (1)

Indomie Egypt complied by withdrawing affected products and offering noodles without chili packs.

The FSA ordered Indomie Egypt to sever ties with the chili powder supplier until safety measures are taken.

Indomie, a famous Indonesian brand, raised concerns after reports of illness in children in April. (2)

Evidence showed that in Ah Lai White Curry Noodles, a total of 0.149mg/kg of ethylene oxide was found whilst Indomie: Special Chicken Flavour contained 0.187mg/kg of the compound in its seasoning and the carcinogenic ethylene oxide level is 50mg/kg (4)

While these recalls occurred, Indofood's products are exported to over 90 countries, including the Middle East, and Indonesia's food and drugs agency, BPOM, declared the product safe in its domestic market.

Indofood, renowned for its diverse flavors and affordability, beloved instant noodle brand both in Indonesia and globally, originating in 1972 with its chicken flavor.

Conclusion: The agency said that INDOMIE doesn't contain Ethylene glycol, but some investigation said that the spices contain traces of aflatoxins and pesticide , so the FSA ordered to remove the spices until more data and investigation on this claim These findings emphasize the need for stringent food safety measures and regulatory actions to protect consumers. Further investigations and corrective actions are needed. (3)

References;

1. https://indomie.com.eg/
2. https://www.safefood.net/food-safety/news/ethylene-oxide#:~:text=The%20EU%20set%20out%20its,of%20the%20product%20.
3. https://english.ahram.org.eg/NewsContentP/1/465284/Egypt/Indomie-flavoured-instant-noodles-to-be-pulled-fro.aspx
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Special thanks to

Prof.Dr. Mohamed AbdElmoaty
(Dean of National Cancer Institute)

Under supervision

Dr. Azza Abdullah
(Director of NCI pharmacy units)

Chief editor

Dr. Howayda Ali
(Manager of Drug Information Center)

In Participation with

Dr. Noha Anis
Manager of Oncology Pharmacy Unit
Egyptian Drug Authority

Prepared by

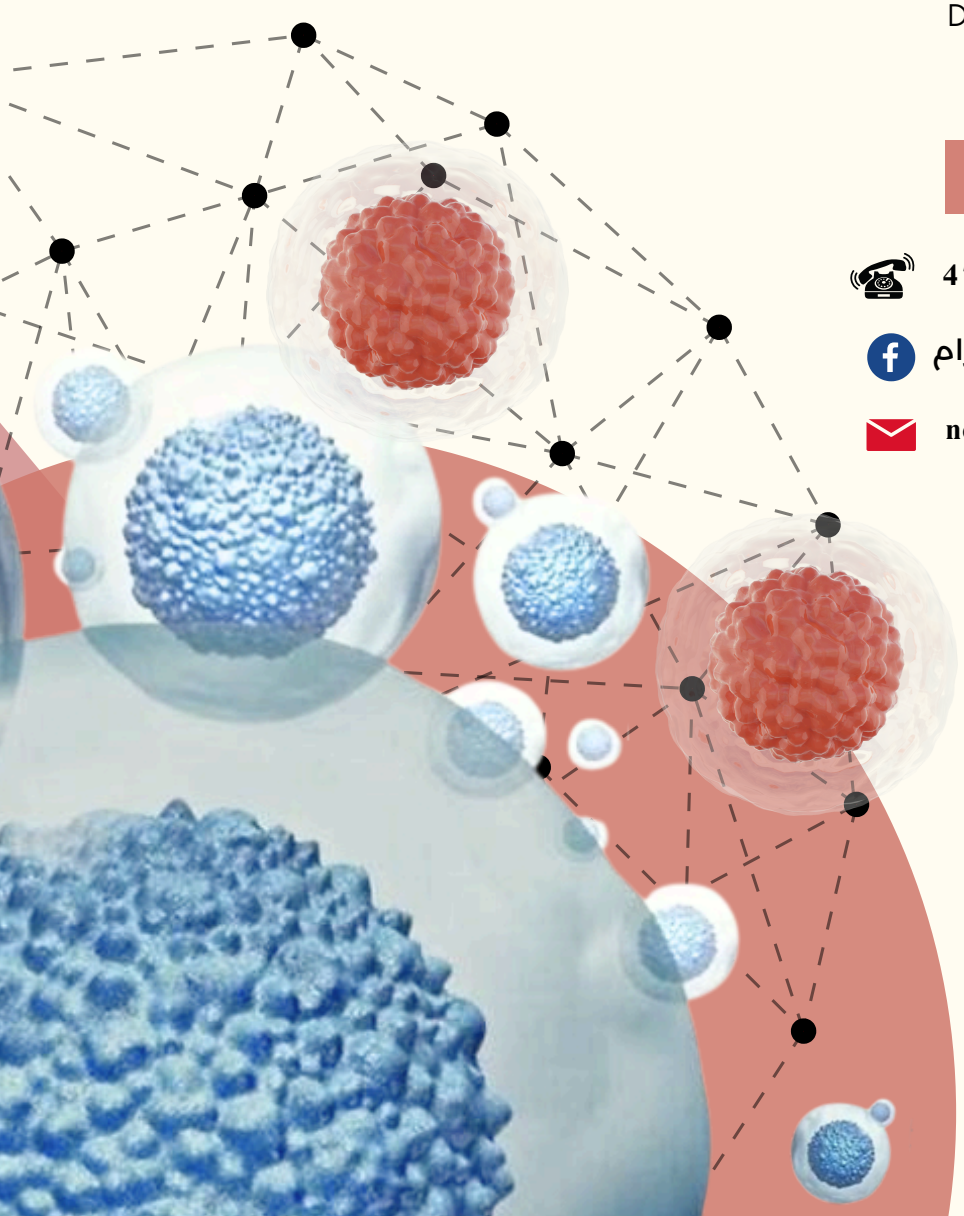
Dr. Ahmed Mohamed
Dr. Salma Tolba
Dr. Alaa Mohammed
Dr. Nourhan Hossam

Revised by

Dr. Abdel Moneim M. Osman
Prof. Of clinical pharmacology NCI

Dr. Ahmed Serag
Senior specialist at Drug Information Center

Dr. Esraa Abdelmonem
Senior specialist at Drug Information Center



Contact us:

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nci.mic@nci.cu.edu.eg

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