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Review onTheoretical study of capacitabine use in colon cancer

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Abstract

Chemotherapy is an important part of treatment for patients with gastric cancer. Although there is no single globally accepted standard of care for patients with advanced disease, regimens typically include a fluoropyrimidine and a platinum compound with or without a third drug (usually epirubicin or docetaxel). Oral fluoropyrimidines, such as capecitabine, offer clear advantages to patients in terms of convenience, but it is only recently that comprehensive data on their efficacy and safety in patients with gastric cancer have become available. The present article reviews capecitabine in the treatment of advanced and resectable gastric cancer. Ongoing Phase III trials involving capecitabine are also discussed. The data show that capecitabine is now established as an integral part of the multi-agent regimens used in the management of patients with gastric cancers.

Keywords:- chemotherapy, medication used in chemotherapy, medication of clone cancer…

Introduction

Capecitabine is used to help treat patients with Dukes' C colon cancer (colon cancer that has spread to lymph nodes in the area close to the colon), after having surgery. This medicine is also used to treat metastatic colorectal cancer (cancer of the colon or rectum that has spread to other parts of the body). Capecitabine is also used together with docetaxel to treat metastatic breast cancer (breast cancer that has spread to other parts of the body) in patients who have received other medicines (eg, paclitaxel) but did not worked well, or in patients who cannot receive cancer medicines anymore. Capecitabine belongs to the group of medicines called antineoplastics (cancer medicines). It interferes with the growth of cancer cells, which are eventually destroyed by the body. Since the growth of normal cells may also be affected by the medicine, other side effects may also occur. Some of these may be serious and must be reported to your doctor. This medicine is available only with your doctor's prescription.

Stomach Cancer Or Intestinal Cancer

The stomach :-

The stomach is a sac-like organ that's an important part of the digestive system. After the food is chewed and swallowed it can be enter the esophagus , a tube that carries food through the thought and chest to the stomach. The esophagus join stomach at the at the gastro esophageal (GE) junction ,Which is the just beneath the diaphragm (the thin sheet of breathing muscle under the lungs). The Stomach then starts to digest the food by secreting to digest juice. The food and gastric juice are mixed and then peptide into the first part of the small intestine called the duodenum.

Stomach Cancer can different from other cancer that can occur in the abdomen like cancer of the follows,

A) Colon or Rectum clarge intestine
B) Liver ,Pancreas
C) Small Intestine

Theses cancer can have different symptoms ,different out looks and Different Treatment

Development Of Stomach Cancer :-

Stomach cancer tend to develop slowly over many years before a true cancer develop , Pre – cancer occure in the lining of the stomach

Chemo Drug used to treat colorectay cancer (colon Cancer)

1. 5- Fluorouracil (5-fu)
2. Capecitubine
3. Irinotecan (Cumptosar)

A)

1] 5- Fluorouracil PH

A clear colorless solution with a PH in the range of 8.6 to 9.4 fluorouracil should be administered only under the supervision of a qualified physician with extensive experience in cytotoxic treatment patient must be cone fully and frequently monitored during the treatment.

2] 5- Fluorouracil mode of action

5-Fu can activate P53 by more than one mechanism incorporation of fluorouracil triphosphate (FUTP) into RNA and inhibition of thymidylate synthase (TS) by fluorodeoxyuridine monophosphate (FDUMP) with Resultant DNA damage.

3] C Dissolves

5- Fluorouracil is soluble in 1N NH4OH ,which yields a clear colorless to light yellow solution the product is also soluble in Danso (10/50mg/ml).

B)

1] Capecitabine PH:-

Assuming that capecitabine is weak acid 11,12 with a Pak of 8.8 theoretically it should be minimally ionized at the normal fasting gastric PH (1.3 to 1.7)

2] Capecitabine mode of action:-

Capecitabineis re3latively non-cytotoxic invitro .this drug is enzymatically converted to 5-Fluorouracil in vivo. Both normally and tumor cell metabolize 5–fu to 5fluro-2 deoxyuridine monophosphate (FDUMP) and 5- Fluorouridine triphosphate (FUTP).

3] Capecitabine Dissolve :-

They may suggest that you to dissolve the capecitabine tablet in water. In this case dissolve the tablet in a 200ml glass of warm water. Stir the water with a spoon the until the tablet completely dissolved and then drink it immediately

C)

1] Ironotecan – PH

Each milliliter of solution contain 20 mg of irinotecan hydrochloride (on The basis of) 45 gm of sorbitol NF powder and 0.9 gm of lactic acid, The PH of the solution has been adjusted to 3.5 with sodium hydroxide or hydrochloric acid.

2] Irinotecan mode of action

It is a derivative of camptothecin that inhibit the action of topoisomerase I. Irinotecan prevent relingation of the DNA strand by binding to topoisomerase I-DNA complex and causes double strand DNA breakage and cell death. It is derivative of comptothecin

3] Irinotecan Dissolve

For maximum solubility in acquiesce buffer irinotecan (hydrochloride hydrate) should first be dissolve in DMSO and then dilute with the the acquiesce buffer of choice Irinotecan has a solubility of approximately 0.5 mg/ml in a 1:1 solutions of DMSO: PBS (PH7.2) using these method [1]

- **Stomach Cancer / Intestinal Cancer**

Capecitabine :- (500mg)

- Pckaging Size 10 Tablet Strip
- Composition Capecitabine 500mg
- Manufacture Cipla
- Treatment Breast Cancer and Cancer of Colon and Rectum
- Prescription/Non Prescription
- Capegar d 500mg Tablets 10. Price 1200/-

Capegard and xeloda Capecitabine (500mg) (Xeloda ,Capegard),Prescription,Cipla [2]

 # Capecitabine :- (500mg) Film-Coated tablets:-

- Qualitative and Quantitative composition:- Each film coted tablet contain 500mg of Capecitabine .
- Excipient with known Effect:- Each film coated tablet contain 25.470mg anhydrous lactose.
- Film coated tablet dissolution time:- Soluble tablet are un coated or film be coated tablets that are intended to be dissolve in the water giving a clear or slightly opalescent solution. Soluble tablets disintegrate with in 3 minuets when Examined by 5.3 Disintegration test for tablets and capsuies , but using water R at 15-25 ^{o}c.
- Film Coated tablets dissolution time in Stomach :- In varies form 30 min upto 7 hr, with an average time of 6 hr. Although some studies indicate that large size dosage forms may required additional time for gastric emptying , other suggested that the size shape or volume of the tablet posses no significant effect instead. [3]

Technique use in film coated tablets:-

Film coating :- the process involves spraying of a solution of polymer, pigment and plasticizer onto a rotating tablets bed to form a thin uniform film on the tablet surface the choice of polymer mainly depends on the desired site of drug release (stomach / intestine) or on the desired release rate.[4]

solvent use in film coated tablet:-

The most commonly used organic solvents are IPA and methylene chloride film coating of the tablets is a multivariable process, with many different factors, such as coating equipment's.[5]

Ingredient use in film coated tablets:-

The most widely used polymers in non-functional film coating are cellulose derivative such as hypromellose (HPMC) plasticizer use to improve the flexibility of the film formed and prevent it form cracking or breaking. They work by weakening the attraction between the polymer molecule to make the film more malleable.[6]

PH of Film Coated Tablet:-

It is reaction product fo Phthalicanhydride , sodium acetate and a partiallyhydrolyzed polyvinyl alcohol. The onset of aqueous dissolution of PVAD beings at a PH of about 5.0 allowing for enteric release as well as the potential for fargeted drugs release to the proximal small intestine.[7]

PH Of Sugar Bigases:- (sugar solution) 7 to 7.4

Sugar when dissolved in water does not give or take any hydrogen ions form the water sugar in non ionic compound thus it does not release H+ or Oh Ions in the water solution. The PH values of the sugar solution will be as that of water is 7 to 7.4. This a sugar solution will asways be natural.[8]

Natural Polymer More than 7.8 PH

1) **Milk of magnesia PH=10.5:-**
   With a PH grater than 7 milk magnesia is basic. (milk of magnesia is largely mg $(OH)_2$.)
2) **Pure water with a PH 7**
   Pure water with a PH of 7 is natural
3) **Wine with PH 3.0**
   With a pH of less than 7 wine is Acidic
   Identify each substance as acidic basic or natural base only on the stated PH

- Human Blood PH = 7.4 (basic)
- Household ammonic, PH=11.0 (basic)

- Cherries , PH =3.6 (acidic) [9]

Film Coating Over Sugar Coating:-

Enhances the elegance and glossy appearance of coated tablets . 3 Minimal weight increase (typically 2 - 3% of tablet core weights) as opposed to more than 50% with sugarcoating.

How to Prepare sugar Bigasess:-

1) Harvesting sugar cane and sugar beets are typically harvested from fields mechanically.
2) Washing and Initial Prepration
3) Juice Extraction
4) Purification of Juice
5) Crystallization
6) Centrifugation
7) Drying and [10]

Sugar Bigasess Formulaton:-

- Chemical formula C_{12} H_{22} O_{11}
- Molecular Weight 342.30 g/mol
- Density 1.587 g/cm^3
- Melting Point Decomposes 186 ^{o}c [11]

Which Kind Of Drug Use of Sugar Bigasess:-

- **Flavor Balance:-** Sugar adds Sweetness and balance acidic and bitter flavors in tomato an vinegar based sauce's, dressing and brains.
- **Preservative:-** Sugar staps bacteria from growing and delays spoilage.
- **Texture and Mouthfeel:-**sugar helps provide the soft structure in backed good and smoothness in frozen dairy product.
- **Volume:-** Sugar adds volume to different product and that allows them to be tall, fluffy or soft
- **Colour:-** Sugar reats with heat carumelization) or with heat and proteins (maillard reaction) to creat a golden brown colour in based goods and sauces.
- **Taste**:- a little bit of sugar can mike high fiber food taste better [12]

 # Props Of Use :-

Medicines used to treat cancer are very strong and can have many side effects. Before using this medicine, make sure you understand all the risks and benefits. It is important for you to work closely with your doctor during your treatment. Take this medicine exactly as directed by your

doctor. Do not take more of it, do not take it more often, and do not take it for a longer time than your doctor ordered. To do so may increase the chance of side effects. This medicine should come with a patient information leaflet. Read and follow these instructions carefully. Ask your doctor if you have any questions. Take this medicine with food or within 30 minutes after you eat. Swallow the tablet whole with water. Do not cut, crush, break, or chew it. If the tablet must be cut or crushed, it should be done by a pharmacist.[13]

 # Dosing

The dose of this medicine will be different for different patients. Follow your doctor's orders or the directions on the label. The following information includes only the average doses of this medicine. If your dose is different, do not change it unless your doctor tells you to do so.

The amount of medicine that you take depends on the strength of the medicine. Also, the number of doses you take each day, the time allowed between doses, and the length of time you take the medicine depend on the medical problem for which you are using the medicine.

- For oral dosage form (tablets):
    - For metastatic breast and colorectal cancer:
        - For patients receiving this medicine alone:
            - Adults—Dose is based on body size and must be determined by your doctor. At first, 2500 milligrams (mg) per square meter (m(2)) of body size per day, divided in 2 doses and taken about 12 hours apart. These doses are taken for 2 weeks, followed by 1 week rest, given as 3 weeks cycle. Your doctor may adjust your dose if needed.
            - Children—Use and dose must be determined by your doctor.
        - For patients receiving this medicine with docetaxel:
            - Adults—Dose is based on body surface and must be determined by your doctor. At first, 2500 milligrams (mg) per square meter (m(2)) of body surface area per day, divided in 2 doses and taken about 12 hours apart. These are taken for 2 weeks, followed by 1 week rest, given as 3 weeks cycle Your doctor may adjust your dose if needed.
            - Children—Use and dose must be determined by your doctor.[14]

 # Side Effect

Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.[15]

Check with your doctor immediately if any of the following side effects occur:

More common

Abdominal or stomach pain

- diarrhea
- loss of fingerprints
- nausea
- numbness, pain, tingling, or other unusual sensations in the palms of the hands or bottoms of the feet
- pain, blistering, peeling, redness, or swelling of the palms of the hands or bottoms of the feet
- pain, redness, swelling, sores, or ulcers in your mouth or on your lips
- unusual tiredness or weakness
- vomiting

Less common or rare

- Abdominal or stomach cramping or pain (severe)
- agitation
- back pain
- bleeding and bruising
- bleeding gums
- blood in the urine or stools
- bloody nose
- bloody or black, tarry stools
- blurred vision
- burning, dry, or itching eyes
- chest pain
- chills
- clumsiness or unsteadiness
- cold
- collapse
- coma
- confusion
- constipation
- convulsions
- cough or hoarseness (accompanied by fever or chills)
- cough producing mucus
- coughing or spitting up blood
- dark urine
- decreased frequency or amount of urine
- difficulty with breathing
- difficulty with swallowing or pain in the back of throat or chest when swallowing
- discharge from the eyes
- drowsiness
- dry mouth
- excessive tearing
- extra heartbeats
- eye redness, irritation, or pain
- fainting
- fast or irregular heartbeat
- fever or chills
- flu-like symptoms
- hallucinations
- headache, sudden and severe
- heavier menstrual periods
- high fever
- hot, red skin on the feet or legs
- inability to speak
- increased menstrual flow or vaginal bleeding
- increased thirst
- irritability
- itching in the genital or other skin areas
- lightheadedness
- light-colored stools
- loss of consciousness
- lower back or side pain (accompanied by fever or chills)

  muscle aches or cramps

- muscle spasms
- nosebleeds
- numbness or tingling in the hands, feet, or lips
- painful or difficult urination (accompanied by fever or chills)
- painful, swollen feet or legs
- pain, tenderness, or swelling in the upper abdominal or stomach area
- pale skin
- paralysis
- pinpoint red spots on the skin
- problems with coordination
- prolonged bleeding from cuts
- rapid, shallow breathing
- red or dark brown urine

- redness, pain, or swelling of the eye, eyelid, or inner lining of the eyelid
- scaling
- seizures
- severe constipation
- skin rash or itching
- slow or irregular heartbeat
- slurred speech
- sneezing, sore throat, or stuffy nose
- sores, ulcers, or white spots on the lips or in the mouth
- stiff neck
- stomach bloating, burning, or cramping
- swelling of the face, fingers, feet, or lower legs
- swelling of the lymph nodes
- swollen glands
- temporary blindness
- tiredness or weakness
- trouble with speaking
- troubled breathing or tightness in the chest
- unexplained nosebleeds
- unusual bleeding or bruising
- unusual lump or swelling in the chest
- vomiting blood or material that looks like coffee grounds
- weakness in the arm or leg on one side of the body, sudden and severe
- weight gain or loss
- white patches in the mouth or throat or on the tongue
- white patches with diaper rash

Conclusion

Capecitabine-based chemotherapy regimens, especially XELOX, offer good efficacy following radical gastrectomy in Chinese patients with AGC, with a low incidence of adverse events, acceptable tolerance, greater patient convenience and a lower overall cost than other regimens. However, because of the limited data available, further clinical research with capecitabine is still necessary to establish the optimum strategy. The Committee concluded that capecitabine, in combination with a platinum-based regimen, should be recommended for the first-line treatment of inoperable advanced gastric cancer.

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