OncoLink
Abramson Cancer Center of the University of Pennsylvania

A Phase III Comparison of Standard Radiation Therapy (RT) Versus RT Plus Concurrent Cisplatin (CDDP) Versus Split-Course RT Plus ConcurrentCDDPP and 5-Flourouracil (5-FU) in Patients with Unresectable Squamous Cell Head and Neck Cancer (SCHNC): An Intergroup Study

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Background:
Unresectable squamous cell carcinoma of the head and neck region conotates a very poor prognosis overall. Recent Phase II trials have suggested the addition of concurrent chemotherapy to radiation therapy may improve survival. This study was performed to compare standard radiation therapy to concurrent chemotherapy and radiation therapy for unresectable squamous cell carcinoma of the head and neck.

Materials and Methods:

- Head and neck Intergroup trial of patients with Stage III and IV unresectable squamous cell carcinoma of the head and neck (nasopharynx, paranasal sinus, and parotid primaries excluded.
- There were three treatment arms:
  - Arm A - Since daily fractionated RT (70 Gy/day @ 2 Gy/day)
  - Arm B - Identical Radiation with concurrent CDDP (100mg/m^2 x 3 q 3 wk
  - Arm C - Split course of RT and 3 cycle of concurrent chemotherapy, 30 Gy given with the first and 30-40 Gy given with the third cycle (chemo q 4 weeks 75 mg/m^2 DDP & 5-FU 1000 mg/m^2/day X 4)
- Due to declining accrual, the study was prematurely closed after 295 of planted 369 patients were enrolled. There were 273 patients eligible for evaluation. The median follow up was 25 months.

Results:

- Grade 3 toxicity of worse occurred in 54% Arm A patients versus 87% Arm B, and 77% Arm C ($p < 0.001$)
- 3 year projected survivals are 20% Arm A, 36% Arm B, and 28% Arm C
- Median survivals are 12.6 months Arm A, 18.8 months Arm B, and 14.0 months Arm C
- A significant improvement in survival was found only for Arm B ($p = 0.02$)

Authors' Conclusions

- In poor prognosis unresectable Squamous Cell Carcinoma of the head and neck:
  a. Concurrent chemotherapy and RT can be safely administered with acceptable toxicity
  b. The addition of concurrent high-dose single- agent DDP to conventional standard Rt significantly improved survival
  c. The use of multi-agent chemotherapy does not offset the loss of efficacy resulting from split- course RT

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Cyclophosphamide (Cytoxan®, Neosar®, Endoxan®)

Pronounced: SYE-kloe-FOS-fa-mide
Classification: Alkylating Agent

About Cyclophosphamide

Cyclophosphamide exerts its anti-cancer affect by a process called alkylation. Alkylation damages the DNA of cells, which prevents them from dividing, and causes them to die. Since cancer cells, in general, divide faster and with less error correcting than healthy cells, cancer cells are more sensitive to this damage.

How to Take Cyclophosphamide

Cyclophosphamide can be given through intravenous (into a vein) infusion or taken orally (by mouth) as a pill. Oral doses should be taken whole (not crushed or broken) and with food to decrease nausea. The dosage and schedule is determined by the person's size, type of cancer, and mode of administration.

Possible Side Effects of Cyclophosphamide

There are a number of things you can do to manage the side effects of Cyclophosphamide. Talk to your doctor or nurse about these recommendations. They can help you decide what will work best for you. These are some of the most common side effects:

Low White Blood Cell Count (Leukopenia or Neutropenia)

White blood cells (WBC) are important for fighting infection. While receiving treatment, your WBC count can drop, putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4 F), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- Washing hands, both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bath daily and perform frequent mouth care.
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your doctor or nurse before scheduling dental appointments or procedures.
- Ask your doctor or nurse before you, or someone you live with, has any vaccinations.

For more suggestions, read the Neutropenia Tip Sheet.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the red cell count is low, you may feel tired or weak. You should let your doctor or nurse know if you experience any shortness of breath, difficulty breathing or pain in your chest. If the count gets too low, you may receive a blood transfusion. Read the anemia tip sheet for more information.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the count is low you are at a higher risk of bleeding. Let your doctor or nurse know if you have any excess bruising or bleeding, including nosebleeds, bleeding gums or blood in your urine or stool. If your platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor to shave (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin®, Aleve®, Advil®, etc. as these can all increase the risk of bleeding. Unless your healthcare team tells you otherwise, you may take acetaminophen (Tylenol).
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Read the thrombocytopenia tip sheet for more information.

Nausea and/or Vomiting

Take anti-nausea medications as prescribed. If you continue to have nausea or vomiting, notify your doctor or nurse so they can help you manage this side effect. In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try antacids, (e.g. milk of magnesia, calcium tablets such as Tums), saltines, or ginger ale

to lessen symptoms. Read the Nausea & Vomiting Tip Sheet for more suggestions.

Call your doctor or nurse if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Mouth Ulcers (Sores)

Certain cancer treatments can cause sores or soreness in your mouth and/or throat. Notify your doctor or nurse if your mouth, tongue, inside of your cheek or throat becomes white, ulcerated or painful. Performing regular mouth care can help prevent or manage mouth sores. If mouth sores become painful, your doctor or nurse can recommend a pain reliever.

- Brush with a soft-bristle toothbrush or cotton swab twice a day.
- Avoid mouthwashes that contain alcohol. A baking soda and/or salt warm water mouth rinse (2 level teaspoons of baking soda or 1 level teaspoon salt in an eight ounce glass of warm water) is recommended 4 times daily.
- If your mouth becomes dry, eat moist foods, drink plenty of fluids (6-8 glasses), and suck on sugarless hard candy.
- Avoid smoking and chewing tobacco, drinking alcoholic beverages and citrus juices.

Read the mouth ulcer tip sheet for more information.

Decrease in Appetite

Visit OncoLink's section on Nutrition for tips on dealing with this side effect. Ask your nurse about nutritional counseling services.

- Try to eat five or six small meals or snacks throughout the day, instead of 3 larger meals.
- If you are not eating enough, nutritional supplements may help.
- You may experience a metallic taste or dislike foods or beverages that you liked before receiving chemotherapy. These symptoms can last up to several months.
- Avoid any food that you think smells or tastes bad. If red meat is a problem, eat chicken, turkey, eggs, dairy products and fish without a strong smell.
- Flavor meat or fish by marinating it in sweet juices, sweet and sour sauce or dressings. Use seasonings like basil, oregano or rosemary. Bacon, ham and onion can also add flavor to vegetables.

Heart Concerns

In rare cases, the heart muscle is weakened on this medication. It is important that you report immediately to your doctor or nurse any shortness of breath, cough, ankle swelling, chest pain, rapid or irregular heartbeats. Your doctor may order tests to check your heart function prior to receiving this drug or to evaluate your heart if symptoms develop.

Sexual and Reproductive Changes

This drug can affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may

experience menopausal effects including hot flashes and vaginal dryness – read more about coping with vaginal dryness. In addition, the desire for sex may decrease during treatment. See OncoLink's section on sexuality for helpful tips for dealing with these side effects.

Diarrhea

Your oncology team can recommend medications to relieve diarrhea. Also, try eating low-fiber, bland foods, such as white rice and boiled or baked chicken. Avoid raw fruits, vegetables, whole grain breads, cereals and seeds. Soluble fiber is found in some foods that absorbs fluid and can help relieve diarrhea. Foods high in soluble fiber include: applesauce, bananas (ripe), canned fruit, orange and grapefruit sections, boiled potatoes, white rice and products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses on non-alcoholic, un-caffeinated fluid a day to prevent dehydration. Read Low Fiber Diet for Diarrhea for more tips.

Taste and smell changes

You may experience a metallic taste or dislike foods or beverages that you liked before receiving chemotherapy. These symptoms can last up to several months. Avoid any food that you think smells or tastes bad. If red meat is a problem, eat chicken, turkey, eggs, dairy products and fish without a strong smell. Flavor meat or fish by marinating it in sweet juices, sweet and sour sauce or dressings. Use seasonings like basil, oregano or rosemary. Bacon, ham and onion can add flavor to vegetables. Ask your nurse about nutritional counseling services.

Loss or Thinning of Scalp and Body Hair (Alopecia)

Your hair may become thin, brittle, or may fall out. This typically begins two to three weeks after treatment starts. This hair loss can be all body hair, including pubic, underarm, legs/arms, eyelashes, and nose hairs. The use of scarves, wigs, hats and hairpieces may help. Hair generally starts to regrow soon after treatment is completed. Remember your hair helps keep you warm in cold weather, so a hat is particularly important in cold weather or to protect you from the sun. Read more on alopecia.

Bladder Irritation

Cyclophosphamide may irritate your bladder, cause blood in your urine or pain with urination. Drink at least 6 to 8 glasses of fluid/day to flush out your bladder. Let your doctor or nurse know if you have difficulty, pain, or bleeding during urination. When given in high doses, your doctor may give you a mediation to protect your bladder.

Other Concerns

Notify your healthcare team if you develop any of the following:

- Call your doctor or nurse if you have shortness of breath, cough or difficulty breathing.
- Call your doctor or nurse if you do not urinate for more than 12 hours, experience shortness of breath, unexpected weight gain or swelling in your hands, feet or legs.
- If during the infusion you develop a rash, itching, or difficulty breathing, call

your nurse.

- You may experience nasal congestion for several days after treatment. Call your doctor or nurse if you experience sinus pain.

Secondary Malignancies

There is a slight risk of developing leukemia or other type of cancer due to treatment with this medication. This is most often associated with repeated treatments or high doses.

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