

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

Presenter: DJ Adelstein

Affiliation: ECOG & SWOG

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/m² 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/m² DDP & 5-FU 1000 mg/m²/day X 4)

- Due to declining accrual, the study was prematurely closed after 295 of planned 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

ASCO Abstract 1624

Cyclophosphamide Oral Formulation (Cytoxan®, Neosar®, Endoxan®)

Pronounced: SYE-kloe-FOS-fa-mide

Classification: Alkylating Agent

About Cyclophosphamide

Cyclophosphamide exerts its anti-cancer effect 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 by intravenous (IV, into a vein) infusion or taken orally



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(by mouth) in a pill form. This information is about the oral (by mouth) formulation.

Oral doses should be taken whole (not crushed, chewed, or broken) and with food in order to decrease nausea. The dosage and schedule are determined by the person's size and type of cancer.

Storage and Handling of Oral Cyclophosphamide

Store your medication in the original, labeled container, at room temperature, and in a dry location (unless otherwise directed by your healthcare provider or pharmacist). This medication should not be stored in a pillbox. Keep containers out of reach of children and pets.

If a caregiver prepares your dose for you, they should wear gloves or pour the pills directly from their container into the cap, a small cup, or directly into your hand. They should not touch the pills. They should always wash their hands before and after giving you the medication. Pregnant or nursing women should not prepare the dose for you. Ask your oncology team where to return any unused medication for disposal. Do not flush down the toilet or throw in the trash.

Where do I get this medication?

Depending on your insurance coverage, oral cyclophosphamide is available through retail/mail order and some specialty pharmacies. Your oncology team will work with your prescription drug plan to identify an in-network retail/mail order pharmacy or specialty pharmacy for medication distribution.

Insurance Information for Oral Formulation

Oral cyclophosphamide may be covered under your prescription drug plan. Co-pay assistance from third party independent foundations may be available depending on your income and diagnosis. Your care team can help you find these resources, if they are available.

If you have Medicare, the oral formulation of this medication is covered under Medicare part B for Medicare recipients. Make sure your pharmacist knows to process this prescription through your Medicare part B and NOT part D.

Possible Side Effects

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

Nausea and/or Vomiting

Talk to your doctor or nurse so they can prescribe medications to help you manage



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nausea and vomiting. 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.

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.

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 and absorbs fluid, which can help relieve diarrhea. Foods high in soluble fiber include: applesauce, bananas (ripe), canned fruit, orange sections, boiled potatoes, white rice, products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses of non-alcoholic, un-caffeinated fluid a day to prevent dehydration.

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), 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.

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



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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.

Decrease in Appetite

Nutrition is an important part of your care. Cancer treatment can affect your appetite and, in some cases, the side effects of treatment can make eating difficult. Ask your nurse about nutritional counseling services at your treatment center to help with food choices.

- 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 find that food has no taste at all. You may dislike foods or beverages that you liked before receiving cancer treatment. These symptoms can last for several months or longer after treatment ends.
- 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. Sometimes cold food has less of an odor.
- Add extra flavor to meat or fish by marinating it in sweet juices, sweet and sour sauce or dressings. Use seasonings like basil, oregano or rosemary to add flavor. Bacon, ham and onion can add flavor to vegetables.

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 urinating, pain, notice pink or red urine, or bleeding during urination. When given in high doses, your doctor may give you a medication to protect your bladder.

Nail and Skin Changes

Your fingernails/toenails may become dark, brittle or fall off. You may notice dry skin or changes in the color or tone of your skin. Your skin may be more sensitive to the sun, which can result in severe sunburn or rash. Sun sensitivity can last even after chemotherapy is completed. Avoid the sun between 10-2pm, when it is strongest. Wear sunscreen (at least SPF 15) everyday, wear sunglasses and long sleeves/pants to protect your skin. Keep your fingernails and toenails clean and dry. You may use nail polish, but do not wear fake nails. If any nails fall off, clean the nail bed well with soap and water and cover with a band aid.

Secondary Malignancies

There is a very low risk of developing leukemia or other type of cancer due to treatment



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with this medication, which can occur many years after treatment. This is most often associated with repeated treatments or high doses.

Lung Changes

In rare cases, this medication may cause lung changes, including pneumonitis (irritation of the lung tissue) and pulmonary fibrosis (a scarring and stiffening of the lung tissue). These problems can develop during treatment, or months to years after treatment is completed. Call your physician right away if you have new or worsening shortness of breath, cough, wheezing or difficulty breathing.

Heart Problems

In rare cases, this medication can affect your heart function, cause abnormal heartbeats (afib or aflutter), or an abnormal heart rhythm called QT prolongation. Notify your healthcare provider right away if you develop swelling of the feet or ankles, shortness of breath, have a rapid weight gain, feel abnormal heartbeats or if you feel dizzy or faint.

Wound Healing

This medication can lead to slower or incomplete wound healing, such as a surgical wound not healing or staying closed. Therefore, it is recommended that the medication be discontinued prior to any surgery. In addition, any surgical incision should be fully healed prior to starting or restarting the medication. If you have a surgical wound that has not healed or begins to have signs of infection (redness, swelling, warmth), report this to your healthcare team.

Reproductive Concerns

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Effective birth control is necessary during treatment and for women for at least 1 year after treatment, and for 4 months after treatment for men. Even if your menstrual cycle stops or you believe you are not producing sperm, you could still be fertile and conceive. You should consult with your healthcare team before breastfeeding while receiving this medication.



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