Table 26 - Summary of Radiographic Time to Progression*

Arm	5-FU/LV (N=151)	ELOXATIN (N=156)	ELOXATIN + 5-FU/LV (N=152)
No. of Progressors	74	101	50
No. of patients with no radiological evaluation beyond baseline	22 (15%)	16 (10%)	17 (11%)
Median TTP (months)	2.7	1.6	4.6
95% CI	1.8-3.0	1.4-2.7	4.2-6.1

*This is not an ITT analysis. Events were limited to radiographic disease progression documented by independent review of radiographs. Clinical progression was not included in this analysis, and 18% of patients were excluded from the analysis based on unavailability of the radiographs for independent review.

At the time of the interim analysis 49% of the radiographic progression events had occurred. In this interim analysis an estimated 2-month increase in median time to radiographic progression was observed compared to 5-fluorouracil/leucovorin alone.

Of the 13 patients who had tumor response to the combination of ELOXATIN and 5-fluorouracil/leucovorin, 5 were female and 8 were male, and responders included patients <65 years old and ≥65 years old. The small number of non-Caucasian participants made efficacy analyses in these populations uninterpretable.

15 REFERENCES

1. NIOSH Alert: Preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings. 2004. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165.

2. OSHA Technical Manual, TED 1-0.15A, Section VI: Chapter 2. Controlling Occupational Exposure to Hazardous Drugs. OSHA, 1999. http://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html

3. American Society of Health-System Pharmacists. (2006) ASHP Guidelines on Handling Hazardous Drugs.

4. Polovich, M., White, J. M., & Kelleher, L.O. (eds.) 2005. Chemotherapy and biotherapy guidelines and recommendations for practice (2nd. ed.) Pittsburgh, PA: Oncology Nursing Society.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Powder for solution for infusion:
ELOXATIN is supplied in clear, glass, single-use vials with gray elastomeric stoppers and aluminum flip-off seals containing 50 mg or 100 mg of oxaliplatin as a sterile, preservative-free lyophilized powder for reconstitution. Lactose monohydrate is also present as an inactive ingredient.

NDC 0024-0596-02: 50 mg single-use vial with green flip-off seal individually packaged in a carton.

NDC 0024-0597-04: 100 mg single-use vial with dark blue flip-off seal individually packaged in a carton.

Concentrate for solution for infusion:
ELOXATIN is supplied in clear, glass, single-use vials with gray elastomeric stoppers and aluminum flip-off seals containing 50 mg, 100 mg or 200 mg of oxaliplatin as a sterile, preservative-free, aqueous solution at a concentration of 5 mg/ml. Water for Injection, USP is present as an inactive ingredient.

NDC 0024-0590-10: 50 mg single-use vial with green flip-off seal individually packaged in a carton.

NDC 0024-0591-20: 100 mg single-use vial with dark blue flip-off seal individually packaged in a carton.

NDC 0024-0592-40: 200 mg single-use vial with orange flip-off seal individually packaged in a carton.

16.2 Storage

Powder for solution for infusion:
Store under normal lighting conditions at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP controlled room temperature].

Concentrate for solution for infusion:
Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). Do not freeze and protect from light (keep in original outer carton).

16.3 Handling and Disposal

As with other potentially toxic anticancer agents, care should be exercised in the handling and preparation of infusion solutions prepared from ELOXATIN. The use of gloves is recommended.

If a solution of ELOXATIN contacts the skin, wash the skin immediately and thoroughly with soap and water. If ELOXATIN contacts the mucous membranes, flush thoroughly with water.

Procedures for the handling and disposal of anticancer drugs should be considered. Several guidelines on the subject have been published *[see References (15)]*. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate.

17 PATIENT COUNSELING INFORMATION

17.1 Information for Patients

Patients and patients' caregivers should be informed of the expected side effects of ELOXATIN, particularly its neurologic effects, both the acute, reversible effects and the persistent neurosensory toxicity. Patients should be informed that the acute neurosensory toxicity may be precipitated or exacerbated by exposure to cold or cold objects. Patients should be instructed to avoid cold drinks, use of ice, and should cover exposed skin prior to exposure to cold temperature or cold objects.

Patients must be adequately informed of the risk of low blood cell counts and instructed to contact their physician immediately should fever, particularly if associated with persistent diarrhea, or evidence of infection develop.

Patients should be instructed to contact their physician if persistent vomiting, diarrhea, signs of dehydration, cough or breathing difficulties occur, or signs of allergic reaction appear.

No studies on the effects on the ability to drive and use machines have been performed. However oxaliplatin treatment resulting in an increase risk of dizziness, nausea and vomiting, and other neurologic symptoms that affect gait and balance may lead to a minor or moderate influence on the ability to drive and use machines.

Vision abnormalities, in particular transient vision loss (reversible following therapy discontinuation), may affect patients' ability to drive and use machines. Therefore, patients should be warned of the potential effect of these events on the ability to drive or use machines.

17.2 FDA-Approved Patient Labeling

Patient Information

ELOXATIN® (eh-LOX-ah-tin)
(OXALIplatin)
powder, for solution for intravenous use
and
ELOXATIN® (eh-LOX-ah-tin)
(OXALIplatin)
concentrate, for solution for intravenous use

Read this Patient Information leaflet carefully before you start receiving ELOXATIN. There may be new information. It will help you learn more about ELOXATIN. This leaflet does not take the place of talking to your doctor about your medical condition or your treatment. Ask your doctor about any questions you have.

What is the most important information I should know about ELOXATIN?

Serious side effects can happen in people taking ELOXATION, including:

- **Serious allergic reactions. ELOXATIN can cause serious allergic reactions, including allergic reactions that may cause death**. ELOXATIN is a platinum base medicine. Serious allergic reactions including death can occur in people who take Eloxatin and who have had previous allergic reactions to platinum medicines. Serious allergic reactions can happen within a few minutes of your infusion or any time during your treatment with ELOXATIN.

Get emergency help right away if you:

- **have trouble breathing.**
- **feel like your throat is closing up.**

Call your doctor right away if you have any of the following signs or symptoms of an allergic reaction:

- rash
- flushed face
- hives
- itching
- swelling of your lips or tongue
- sudden cough
- dizziness or feel faint
- sweating
- chest pain

See "What are the possible side effects of ELOXATIN?" for information about other serious side effects.

What is ELOXATIN?

ELOXATIN is an anti-cancer (chemotherapy) medicine that is used with other anti-cancer medicines called 5-fluorouracil and leucovorin to treat people with:

- stage III colon cancer after surgery to remove the tumor
- advanced colon or rectal cancer (colo-rectal cancer).

ELOXATIN with infusional 5-fluorouracil and leucovorin was shown to lower the chance of colon cancer returning when given to patients with stage III colon cancer after surgery to remove the tumor. ELOXATIN also increases survival in patients with stage III colon cancer. ELOXATIN with infusional 5-fluorouracil and leucovorin was also shown to increase survival, shrink tumors and delay growth of tumors in some patients with advanced colorectal cancer.

It is not known if ELOXATIN works in children.

Who should not use ELOXATIN?

- Do not use ELOXATIN if you are allergic to any of the ingredients in ELOXATIN or other medicines that contain platinum. Cisplatin and carboplatin are other chemotherapy medicines that also contain platinum. See the end of this leaflet for a complete list of the ingredients ELOXATIN.

Ask your doctor if you are not sure if you take a medicine that contains platinum.

What should I tell my doctor before treatment with ELOXATIN?

Before receiving ELOXATIN, tell your doctor if you:

- have kidney problems
- have any other medical conditions
- have had any allergic reactions to any medicines
- are pregnant or plan to become pregnant. ELOXATIN may harm your unborn child. You should avoid becoming pregnant while taking ELOXATIN. Talk with your doctor about how to avoid pregnancy.
- are breastfeeding or plan to breastfeed. It is not known if ELOXATIN passes into your breast milk. You and your doctor should decide whether you will stop breastfeeding or not take ELOXATIN.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

How is ELOXATIN given to me?

ELOXATIN is given to you through your veins (blood vessels).

- Your doctor will prescribe ELOXATIN in an amount that is right for you.
- Your doctor will treat you with several medicines for your cancer.
- It is very important that you do exactly what your doctor and nurse have taught you to do.
- Some medicines may be given to you before ELOXATIN to help prevent nausea and vomiting.
- ELOXATIN is given with 2 other chemotherapy medicines, leucovorin and 5-fluorouracil.
- Each treatment course is given to you over 2 days. You will receive ELOXATIN on the first day only.
- There are usually 14 days between each chemotherapy treatment course.

Treatment Day 1:

ELOXATIN and leucovorin are given through a thin plastic tube put into a vein (intravenous infusion or I.V.) and given for 2 hours. You will be watched by a healthcare provider during this time.

Right after the ELOXATIN and leucovorin are finished, 2 doses of 5-fluorouracil will be given. The first dose is given right away into your I.V. tube. The second dose will be given into your I.V. tube over the next 22 hours, using a pump device.

Treatment Day 2:

You will not get ELOXATIN on Day 2. Leucovorin and 5-fluorouracil will be given the same way as on Day 1.

During your treatment with ELOXATIN:

- It is important for you to keep all appointments. Call your doctor if you must miss an appointment. There may be special instructions for you.
- Your doctor may change how often you get ELOXATIN, how much you get, or how long the infusion will take.
- You and your doctor will discuss how many times you will get ELOXATIN.

The 5-fluorouracil will be given through your I.V. with a pump. If you have any problems with the pump or the tube, call your doctor, your nurse, or the person who is responsible for your pump. Do not let anyone other than a healthcare provider touch your infusion pump or tubing.

What activities should I avoid while on treatment with ELOXATIN?

- Avoid cold temperatures and cold objects. Cover your skin if you must go outside in cold temperatures.
- Do not drink cold drinks or use ice cubes in drinks.
- Do not put ice or ice packs on your body.

See "How can I reduce the side effects caused by cold temperatures?" for more information.

Talk with your doctor and nurse about your level of activity during treatment with ELOXATIN. Follow their instructions.

What are the possible side effects of ELOXATIN?

ELOXATIN can cause serious side effects, including:

- **Serious allergic reactions.** See "What is the most important information I should know about ELOXATIN?"
- **Nerve problems.** ELOXATIN can affect how your nerves work and make you feel. Tell your doctor right away if you get any signs of nerve problems listed below:
    - very sensitive to cold temperatures and cold objects
    - trouble breathing, swallowing, or saying words, jaw tightness, odd feelings in your tongue, or chest pressure
    - pain, tingling, burning (pins and needles, numb feeling) in your hands, feet, or around your mouth or throat, which may cause problems walking or performing activities of daily living.

- **Reversible Posterior Leukoencephalopathy (RPLS).** RPLS is a rare condition that affects the brain. Tell your doctor right away if you have any of the following signs and symptoms of RPLS:
    - headache
    - confusion or a change in the way you think
    - seizures
    - vision problems, such as blurriness or vision loss. You should not drive, operate heavy machines, or engage in dangerous activities if you have vision problems while receiving ELOXATIN.

  The first signs of nerve problems may happen with the first treatment. The nerve problems can also start up to 2 days after treatment. If you develop nerve problems, the amount of ELOXATIN in your next treatment may be changed or ELOXATIN treatment may be stopped.

  For information on ways to lessen or help with the nerve problems, see the end of this leaflet, "How can I reduce the side effects caused by cold temperatures?"

- **Lung problems (interstitial fibrosis).** Tell your doctor right away if you

get a dry cough and have trouble breathing (shortness of breath) before your next treatment. These may be signs of a serious lung disease.

- **Liver problems (hepatotoxicity).** Your doctor will do blood tests to check your liver.

- **Harm to an unborn baby. ELOXATIN may cause harm to your unborn baby.** See "What should I tell my doctor before treatment with ELOXATIN?"

The most common side effects of ELOXATIN include:

- Decreased blood counts: ELOXATIN can cause a decrease in neutrophils (a type of white blood cells important in fighting in bacterial infections), red blood cells (blood cells that carry oxygen to the tissues), and platelets (important for clotting and to control bleeding).
- High blood pressure (hypertension)
- Infection Call your doctor right away if you get any of the following signs of infection:
    - fever (temperature of 100.5 F or greater)
    - chills or shivering
    - pain on swallowing
    - sore throat
    - cough that brings up mucus
    - burning or pain on urination
    - redness or swelling at intravenous site
- Bleeding or bruising. Tell your doctor about any signs or symptoms of bleeding or bruising.
- Diarrhea
- Nausea
- Vomiting
- Constipation
- Mouth sores
- Stomach pain
- Decreased appetite
- Tiredness
- Injection site reactions. Reactions may include redness, swelling, pain, tissue damage at the site of injection.
- Hair loss (alopecia)
- Dehydration (too much water loss). Call you doctor if you have signs of dehydration including:
    - tiredness
    - thirst
    - dry mouth
    - lightheadedness (dizziness)
    - decreased urination

Tell your doctor if you have any side effect that bothers your or that does not go

away. These are not all the possible side effects of ELOXATIN. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How can I reduce the side effects caused by cold temperatures?

- Cover yourself with a blanket while you are getting your ELOXATIN infusion.
- Do not breathe deeply when exposed to cold air.
- Wear warm clothing in cold weather at all times. Cover your mouth and nose with a scarf or a pull-down cap (ski cap) to warm the air that goes to your lungs.
- Wear gloves when taking things from the freezer or refrigerator.
- Drink fluids warm or at room temperature.
- Always drink through a straw.
- **Do not** use ice chips if you have nausea or mouth sores. Ask your healthcare provider or doctor about what you can use.
- Be aware that most metals are cold to touch, especially in the winter. These include your car door and mailbox. Wear gloves to touch cold objects.
- Do not run the air-conditioning at high levels in the house or in the car in hot weather.
- If your body gets cold, warm-up the affected part. If your hands get cold, wash them with warm water.
- Always let your healthcare provider or doctor know **before** your next treatment how well you did since your last visit.

This list is not complete and your healthcare provider or doctor may have other useful tips for helping you with these side effects.

General information about the safe and effective use of ELOXATIN

Medicines are sometimes prescribed for purposes other than those listed in the Patient Information leaflet.

This Patient Information leaflet summarizes the most important information about ELOXATIN. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about ELOXATIN that is written for health professionals.

What are the ingredients in ELOXATIN?
Active ingredient: oxaliplatin

Powder for solution for infusion inactive ingredients: lactose monohydrate
Concentrate for solution for infusion inactive ingredients: water for injection

Manufactured by:
sanofi-aventis U.S. LLC

Bridgewater, NJ 08807

Eloxatin is also manufactured by Ben Venue Laboratories Cleveland, OH 44146-0568 for sanofi-aventis U.S. LLC

Revised: Month/Year