THE ART OF CRT

Weekly CRT AE Management Guide for Patients With Unresectable Stage III NSCLC

This guide was developed with Dr Victoria Villaflor, MD, and nurse practitioner Lauren Bere based on their experiences and practice. It should not take the place of your clinical judgement. These are general recommendations for educational purposes only. Individual recommendations for patients may vary.

GET STARTED
About this Guide

Victoria Villaflor, MD

As a lung cancer specialist, I see many patients with Stage III unresectable non-small cell lung cancer (NSCLC). With so many of my patients receiving chemoradiation therapy (CRT), I had to figure out approaches to safely deliver CRT in hopes of improving my patients’ outcomes.

I was inspired to create this guide for several reasons. First, I had several conversations with peers who often reach out for strategies on how to overcome toxicities their patients experience while on CRT. Currently, there is not a good knowledge base on how to handle potential CRT side effects. Additionally, I have seen several patients with unresectable Stage III NSCLC searching for a second opinion who were not offered CRT as a treatment option. In fact, research has shown that many patients are not given the option of curative-intent CRT. As an avid patient advocate, I find that unacceptable. I feel that if cancer care teams were more readily able to control symptoms, they might be more willing to treat patients with unresectable Stage III NSCLC with CRT.

As such, the purpose of this guide is to provide real-world guidance on the struggles we are up against with CRT and to provide solutions to better help patients get through these treatments and avoid treatment delays.

I hope this guide will inspire the health care community to have more confidence in their ability to successfully treat patients with CRT by controlling symptoms and being aware of the potential pitfalls. It is my hope that this guide will help care teams navigate their patients through CRT.

Lauren Bere, NP-C

As a nurse practitioner, I have worked in the unresectable Stage III NSCLC setting for three years. I collaborate with a variety of thoracic oncologists and have the opportunity to treat patients with standard-of-care treatment, as well as in clinical trials. Through this experience, I can ensure that we are always pursuing the latest, most effective, data-driven treatments.

We were inspired to create this guide to reach all patients with unresectable Stage III NSCLC. This is a unique patient population in that they require an aggressive, multidisciplinary approach to treatment: chemoradiation therapy. This approach can be curative, which in the world of cancer, we do not have the privilege of seeing very often. Because of this, it is important to offer patients this therapy option if applicable, even while knowing that the treatment is extensive. With the correct systems and processes in place, these patients could get their cure.

I hope that this guide can assist providers in navigating through the CRT process. The more comfortable we all are with a treatment, the more likely we are to recommend the therapy, resulting in more curative outcomes. I completely understand the hesitation with the CRT process, as it is extensive and can be tumultuous. However, through education and ongoing discussion, these barriers can be broken and more patients can have access to this curative-intent treatment.

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# INTRODUCTION

**Overall Strategies for Success**

**Pre-existing Comorbidities & Treatment Considerations**

**CRT Adverse Events: Why it Happens, Why it Matters, & What to Do**

**Proactive Management: What to Do Before Starting CRT**

**Nutrition Strategies for Success**

# WEEKLY GUIDE

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INTRODUCTION

Overall Strategies for Success: AE Management During CRT

Optimize patient performance status as quickly as possible before treatment since concurrent chemoradiotherapy (CRT) can potentially worsen pre-existing conditions

Proactive management of adverse events (AEs) versus reactive management can reduce acuity of AEs

Pre-authorize and fill medications before treatment so they are available when the patients need them

**AEs throughout concurrent CRT**
- **Weeks 1-2**: Lowest acuity
- **Week 3**: Increased acuity
- **Weeks 4-6**: Continual worsening
- **Weeks 7-8**: Worsening but stabilizing
- **Weeks 9-12**: Reduction

Proactive AE management throughout concurrent CRT will provide patients with an improved opportunity to complete therapy.
INTRODUCTION

Overall Strategies for Success: Literacy, Logistics, & Financials

**Literacy**
- Assess patient literacy and start with simple educational information
- Provide prioritized lists (medication, nutrition, etc)
- Educate and involve the family to help retain information

**Transportation & Lodging**
- Work with social workers and nurse navigators
- Provide information on transportation assistance (ACS, Uber, Lyft)
- Provide information on housing assistance (Hope Lodge, Airbnb)
- Ensure patients make transportation arrangements before CRT begins

**Financial Burden**
- Facilitate interactions between patients and social workers and/or advocacy groups to identify financial aid resources

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# Pre-existing Considerations

## INTRODUCTION

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*General guidance gathered from discussions with a physician and nurse based on their opinions and experience. ACE=angiotensin-converting enzyme; ARB=angiotensin II receptor blocker; COPD=chronic obstructive pulmonary disease; CRT=chemoradiotherapy; EKG=electrocardiogram; PCP=primary care physician; PPI=proton pump inhibitor; UTI=urinary tract infection.*

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## Pre-existing Comorbidities & Treatment Considerations

### What to expect:
- Patient may be overwhelmed or fearful of treatment

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### Reflux

<table>
<thead>
<tr>
<th>Why it Matters for CRT</th>
<th>What to Do</th>
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</thead>
<tbody>
<tr>
<td>CRT can cause esophagitis, and pre-existing reflux can exacerbate esophagitis</td>
<td>Start high-dose PPI 2x daily* and esophagus-coating anti-ulcer medication (eg, sucralfate) 4x daily</td>
</tr>
<tr>
<td>CRT can also cause reflux and exacerbate esophagitis</td>
<td>Consider a dopamine antagonist as a promotility</td>
</tr>
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CRT Adverse Events: Why it Happens, Why it Matters, & What to Do

What to expect:
- Patients may experience the following AEs during the course of concurrent CRT

Fatigue

Why it Happens & Why it Matters
- Chemotherapy and radiation can cause fatigue
- Can lead to dehydration/weight loss, which can compound fatigue
- Can prevent exercise, which can compound fatigue
- Can lead to patient-initiated treatment breaks, which leads to worse outcomes

What to Do
- Encourage proper hydration and nutrition
- Encourage patients to remain active
- Counsel against treatment breaks due to fatigue

*General guidance gathered from discussions with a physician and nurse based on their opinions and experience.

IV=intravenous; NCCN=National Comprehensive Cancer Network; PPI=proton pump inhibitor.

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General Management:

- See patients at least once a week (Weeks 1–9 at minimum) to monitor for toxicities
- Send patients home with orders updated at each appointment, including an updated appointment calendar and other standing orders (eg, medication changes, calorie goals, exercise instructions)
- Treatment interruptions result in worsened outcomes
  » Breaks in radiation should be avoided as best as possible
**INTRODUCTION**

**Nutrition Strategies for Success**

- Instruct patients to **eat 5–6 small meals throughout the day** rather than 3 big meals
- Ensure patients **drink fluids in between meals** to prevent filling up during meals
- Suggest patients **set alarms on their phones** reminding them to eat*
- Encourage patients to **use a calorie tracker** to get a better understanding of how much they are actually eating per day*  

<table>
<thead>
<tr>
<th>DON’T’s</th>
<th>DO’s</th>
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<tbody>
<tr>
<td>Spicy foods</td>
<td>Bland foods</td>
</tr>
<tr>
<td>Acidic foods</td>
<td>Season with herbs*</td>
</tr>
<tr>
<td>» Tomatoes (tomato sauce, ketchup, tomato soup)</td>
<td>» Basil, oregano, cilantro, etc</td>
</tr>
<tr>
<td>» Citrus, berries, orange juice, cranberry juice, etc</td>
<td>» Soft and easy to swallow foods</td>
</tr>
<tr>
<td>» Vinegar</td>
<td>» Yogurt and pudding</td>
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<tr>
<td>Hard or crunchy foods</td>
<td>» Applesauce</td>
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<tr>
<td>» Nuts, pretzels, chips, and crusty breads</td>
<td>» Pre-made smoothies</td>
</tr>
<tr>
<td>Foods that can worsen reflux</td>
<td>» Cottage cheese with blended or canned fruit</td>
</tr>
<tr>
<td>» Broccoli and cauliflower</td>
<td>» Oatmeal</td>
</tr>
<tr>
<td>» Lime</td>
<td>» Mashed potatoes</td>
</tr>
<tr>
<td>» Chocolate</td>
<td>» Hard-boiled eggs</td>
</tr>
<tr>
<td>» Caffeine</td>
<td>» Hummus</td>
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<tr>
<td>Alcohol or carbonated fluids</td>
<td>» Soft protein sources like fish, scrambled eggs, soups and stews, nut butters, and ground meat</td>
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<tr>
<td></td>
<td>» Avocado</td>
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<tr>
<td></td>
<td>» Heavy cream and ice cream</td>
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<td></td>
<td>» Mayonnaise</td>
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<tr>
<td></td>
<td>» Tofu (add to soups or blend into smoothies)</td>
</tr>
</tbody>
</table>

**DON'T’s**  
- Spicy foods  
- Acidic foods  
  » Tomatoes (tomato sauce, ketchup, tomato soup)  
  » Citrus, berries, orange juice, cranberry juice, etc  
  » Vinegar  
- Hard or crunchy foods  
  » Nuts, pretzels, chips, and crusty breads  
- Foods that can worsen reflux  
  » Broccoli and cauliflower  
  » Lime  
  » Chocolate  
  » Caffeine  
- Alcohol or carbonated fluids

**DO’s**  
- Bland foods  
- Season with herbs*  
  » Basil, oregano, cilantro, etc  
- Soft and easy to swallow foods  
  » Pasta with white cream sauce or butter and sage  
  » Yogurt and pudding  
  » Applesauce  
  » Pre-made smoothies  
  » Cottage cheese with blended or canned fruit  
  » Oatmeal  
  » Mashed potatoes  
  » Hard-boiled eggs  
  » Hummus  
  » Soft protein sources like fish, scrambled eggs, soups and stews, nut butters, and ground meat  
  » Avocado  
  » Heavy cream and ice cream  
  » Mayonnaise  
  » Tofu (add to soups or blend into smoothies)  
- Smoothies and/or protein powders  
- Increase fiber intake

*General guidance gathered from discussions with a physician and nurse based on their opinions and experience.
Week 1 CRT: What to Expect from AEs & How to Manage Them

What to expect:

• Energy level should not change and side effects may be nonexistent to minimal during Week 1
• Patients will still be grasping the extent of treatment and may experience anxiety as treatment begins, which will start to subside by end of Week 1

Nausea

What to Expect

• May see early signs of nausea
• Higher degree of nausea may be experienced with cisplatin regimen

How to Manage

• Follow NCCN guidelines for nausea management*
• Use anti-nausea medications based on chemotherapy emetogenicity
• Administer IV fluids as appropriate

*General guidance gathered from discussions with a physician and nurse based on their opinions and experience. IV=intravenous; NCCN=National Comprehensive Cancer Network; PPI=proton pump inhibitor.
Use Week 1 as additional opportunity to ensure that patients understand treatment and what they need to do to ensure success.

Instead of YES/NO questions, ask specific, open-ended questions regarding hydration, nutrition, and exercise:

eg, “How are you getting all of your calories?” versus “Are you eating?”

Ensure that patients have all medications filled and ready at their home (eg, antiemetics).

Note that serotonin receptor antagonists can cause side effects, including constipation and headaches.

» AEs may lead to increased nausea and other issues.

*General guidance gathered from discussions with a physician and nurse based on their opinions and experience.

†Starting point: Use formulas for estimating daily calories/protein goals. Adjust based on individual patient metabolism.
### WEEKLY GUIDE

#### Week 2 CRT: What to Expect from AEs & How to Manage Them

**What to expect:**

- Patients will be settling into their routines and likely tolerating treatment well at this point, but may experience difficulty swallowing or pain toward end of Week 2
- Patients who were symptomatic due to large tumors may begin to feel better as the tumor shrinks*
- Continue to be proactive while AEs are minimal (eg, have medications filled ahead of time)

<table>
<thead>
<tr>
<th>Nausea</th>
<th>Pain</th>
<th>Reflux</th>
<th>Thrush Infection</th>
</tr>
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</table>

**Nausea**

**What to Expect**

- May see early signs or worsening of nausea
- Higher degree of nausea may be experienced with cisplatin regimen

**How to Manage**

- Follow NCCN guidelines for nausea management*
- Use anti-nausea medications based on chemotherapy emetogenicity
- Administer IV fluids as appropriate

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*General guidance gathered from discussions with a physician and nurse based on their opinions and experience. GABA = gamma-aminobutyric acid; IV = intravenous; NCCN = National Comprehensive Cancer Network; PPI = proton pump inhibitor.*
• Let patients know difficulty swallowing = pain

• Ensure patients have their medications in place by asking questions like, “What does your medication cabinet look like?”

• It is Dr Villaflor’s opinion that oxycodone is ideal for pain management because of its small pill size and because it presents less issues for patients with renal and hepatic dysfunction*

• Patients may refuse to take pain medication because of addiction fears from media coverage
  » Coach patients on the importance of temporary pain medication to minimize dehydration, malnutrition, and fatigue

• Encourage patients to log pain medication use (frequency, dosage, etc) to aid in titrating as symptoms get worse

*General guidance gathered from discussions with a physician and nurse based on their opinions and experience.

†Starting point: Use formulas for estimating daily calories/protein goals. Adjust based on individual patient metabolism.

‡Radiation works by oxidation; therefore, radiation works better if hemoglobin is >10 g/dL.
What to expect:

- Patients will start experiencing subtle early signs of AEs (e.g., difficulty swallowing, slight weight loss)
- It is imperative to address AEs before the first signs and symptoms occur, because they become more difficult to manage as time progresses
- Symptoms will worsen throughout Week 3 and AEs will increase in acuity by end of Week 3
- Patients may refuse to take necessary pain medication

### Nausea

**What to Expect**

- May see early signs or worsening of nausea
- Higher degree of nausea may be experienced with cisplatin regimen

**How to Manage**

- Follow NCCN guidelines for nausea management*
- Use anti-nausea medications based on chemotherapy emetogenicity
- Administer IV fluids as appropriate

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*General guidance gathered from discussions with a physician and nurse based on their opinions and experience.

1. If patients continue to have mucositis despite PPI use, consider the possibility of a yeast or viral (CMV) infection. Confirm with endoscopy and treatment with an antifungal or antiviral.

2. BUN/creatinine ratio <20:1 or poor skin turgor indicates dehydration.

CMV = cytomegalovirus; GABA = gamma-aminobutyric acid; IV = intravenous; NCCN = National Comprehensive Cancer Network; PPI = proton pump inhibitor.
Week 3 CRT: Tips & Additional Considerations

- Patients may start experiencing subtle early signs of AEs (e.g., difficulty swallowing, slight weight loss) and they may progressively worsen throughout the week.

- It is imperative to address at the early signs of AEs before symptoms increase and become difficult to manage.

- Ask patients how symptoms have changed from the previous week (versus asking for symptoms)*

- Let patients know difficulty swallowing = pain

- Patients may refuse to take pain medications because of addiction fears from media coverage.

  » Coach patients on the importance of temporary pain medication to minimize dehydration, malnutrition, and fatigue.

- Educate patients to log pain medication use (frequency, dosage, etc.) to aid in titrating as symptoms get worse.

*General guidance gathered from discussions with a physician and nurse based on their opinions and experience.
What to expect:

- Patients will experience increased acuity of AEs in Week 4, with severity continually increasing through Weeks 5–6

**Nausea**

**What to Expect**

- May see worsening of nausea caused by increased mucus* and dehydration
- Higher degree of nausea may be experienced with cisplatin regimen

**How to Manage**

- Follow NCCN guidelines for nausea management*
- Use anti-nausea medications based on chemotherapy emetogenicity
- Administer IV fluids as appropriate

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*BUN/creatinine ratio <20:1 or poor skin turgor indicates dehydration.
CMV=cytomegalovirus; GABA=gamma-aminobutyric acid; IV=intravenous; NCCN=National Comprehensive Cancer Network; PPI=proton pump inhibitor.
WEEKLY GUIDE

Weeks 4-6 CRT: Tips & Additional Considerations

- Consistently ask patients about their exercise routine and increase daily goal (up to 30 minutes daily)
- Consistently ask about hydration and nutrition
  » Consult a nutritionist if patients are struggling with nutrition
- Consistently ask patients about the frequency of bowel movements
  » Patients should be having one good bowel movement daily with adequate stool consistency (not small pellets)
- Ask about urination frequency and color to monitor for dehydration (dark urine = dehydration)
- As the weeks progress, check for mental fatigue and encourage importance of continuous treatment
- Patients may want to take treatment breaks as symptoms get worse
  » Encourage patients to show up to treatment*
  » Remind patients of the progress they have made*
- Patients with pre-existing comorbidities may experience amplified but similar side effects
  » Ensure that these patients are more aggressively managed so they can continue treatment*
- Educate patients to log pain medication use (frequency, dosage, etc) to aid in titrating as symptoms gets worse

Remind patients of the progress they have made!

*General guidance gathered from discussions with a physician and nurse based on their opinions and experience.
†Starting point: Use formulas for estimating daily calories/protein goals. Adjust based on individual patient metabolism.
‡Radiation works by oxidation; therefore, radiation works better if hemoglobin is >10 g/dL.
Weeks 7-8 (1-2 weeks post-CRT): What to Expect from AEs & How to Manage Them

What to expect:

- Although concurrent CRT is no longer being administered, AEs may continue to worsen during Weeks 7–8
- It is imperative to continue to see patients and aggressively/proactively treat for AEs

### Nausea

**What to Expect**

- May see worsening of nausea caused by increased mucus* and dehydration
- Higher degree of nausea may be experienced with cisplatin regimen

**How to Manage**

- Follow NCCN guidelines for nausea management*
- Use anti-nausea medications based on chemotherapy emetogenicity
- Administer IV fluids as appropriate

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WEEKLY GUIDE

Weeks 7-8 (1–2 weeks post-CRT): Tips & Additional Considerations

• Maintain same level of vigilance in AE management even though concurrent CRT is not being administered

• Manage patient expectations*
  » Patients may incorrectly expect AEs to improve since they are not receiving CRT*

• Continue to ask patients about hydration, nutrition, and activity
  » Educate patients on continuing good habits during the weeks following CRT*

• Patients may want to come off medications (eg, pain medication)
  » Educate patients on the importance of continuing medications and even titrating up as symptoms continue toward peak

• Educate patients to log pain medication use (frequency, dosage, etc) to aid in titrating as symptoms get worse

• Weeks 8–9 (3 weeks post-CRT) ideal time to initiate post-CRT immune-oncology (IO) therapy for eligible patients

• Consolidation chemotherapy is not recommended following concurrent CRT

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†Starting point: Use formulas for estimating daily calories/protein goals. Adjust based on individual patient metabolism.
‡Radiation works by oxidation; therefore, radiation works better if hemoglobin is >10 g/dL.
What to expect:

- AEs will generally start to improve at the beginning of Week 9
- Weeks 8-9 (3 weeks post-CRT) are ideal time to initiate post-CRT IO therapy for eligible patients
- Emphasize that the AEs expected with IO therapy differ from those seen with CRT
  » Educate patients on AEs associated with IO therapy
  » Inform patients regarding who to call and when if experiencing one
- Patients will start to feel 80% to normal by Week 12 (close to how they were feeling at approximately Week 3 of CRT)

Nutrition:

- Patients still need to avoid acidic foods until 6 weeks post-CRT (Week 12) as the esophagus continues to heal

Medications:

- Esophagus-coating anti-ulcer medication (eg, sucralfate) can be reduced usually starting 3-4 weeks post-CRT (Weeks 9-10)*
- PPIs can also be tapered down starting 3-4 weeks post-CRT (Weeks 9-10) but some patients may need to stay on longer depending on severity of reflux*
- Pain medications should be tapered down slowly to avoid rebound pain and withdrawals
- Remaining medications can be tapered as symptoms improve but may not occur until Weeks 11-12*
# Key Takeaways

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<thead>
<tr>
<th><strong>Patient health and comorbidities should be optimized prior to initiation of CRT</strong></th>
<th><strong>Proactive management of CRT AEs is crucial</strong> — if you wait until AEs worsen, it may be too late to control or reverse</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Without adequately addressing early pain control, a cascade of issues can occur</strong></td>
<td><strong>Assigning AE management responsibility, including early and frequent communication between medical oncology and radiation oncology teams, is essential</strong></td>
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Zarxio® (filgrastim-sndz) injection, for subcutaneous or intravenous use [prescribing information]. East Hanover, NJ: Amgen Inc; April 2018.

Zofran® (ondansetron) for oral use [prescribing information]. East Hanover, NJ: Novartis Pharmaceutical Corporation; October 2017.