



BC Cancer Clinical Pharmacy Guide

Dual Modality BC Cancer Protocols

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Introduction

BC Cancer has combined modality protocols for several tumour sites where radiation therapy (RT) treatment is delivered with systemic cancer drug therapy. They are referred to as dual modality protocols and have protocol codes ending in “RT”. One of the goals of combined (or dual) modality treatment is to limit local disease using RT, and control systemic disease using systemic drug therapy.

These protocols may involve oral cancer drugs (e.g., CNAJZRT), parenteral drugs (e.g., HNLAART), or a combination of both (e.g., GICART).

Note: for the purposes of BC Cancer protocols, the terms radiation, irradiation, and radiotherapy are used interchangeably.

Definitions

Concurrent RT

RT delivered in conjunction with cancer drugs.

Consolidative RT

RT which is utilized to kill any residual cancer cells after initial RT, surgery, stem cell transplant or systemic therapy.

Concomitant boost RT

A type of accelerated fractionation where a daily dose of radiation is given over multiple sessions per day over a shorter period of time.

Pelvic irradiation

RT delivered to the pelvic region – can be for gynecological cancers, prostate, bladder, anal or rectal cancers.

Radical RT

High doses of radiation that are used to cure cancer. It is also called curative intent RT.

External beam thoracic radiotherapy or thoracic irradiation

RT is given to the chest region in lung cancer patients.

Palliative RT

A wide range of symptoms from advanced, incurable or metastatic cancers can be treated with palliative radiation therapy. The goal of palliative RT is to control or prevent symptoms from occurring which provides patients a better quality of life. Some symptoms benefitting from palliative RT include:

- bone pain due to metastases
- dysphagia related to locally advanced thoracic cancer
- pain from spinal cord compression
- neurological symptoms such as seizures, nausea, vomiting, headaches etc., from brain metastases
- dysphagia, bleeding, airway compromise due to head and neck tumours
- vaginal bleeding, pelvic pain due to pelvic tumours
- bleeding from skin lesions related to either primary skin cancers or metastatic disease to skin

Radiosensitization

Some cancer drugs act as radiosensitizers and can potentiate the toxic effects of radiation therapy. The mechanism of radiosensitization varies based on the agent. BC Cancer dual modality protocols use radiosensitizers with RT to exploit this enhanced toxicity and may lower the overall amount of RT needed for treatment. Combined treatment has been shown to increase disease control and increase survival rates in conditions such as head and neck cancers, lung and gynecological malignancies.

Examples of commonly used radiosensitizers in BC Cancer protocols include chemotherapeutic agents such as capecitabine, cisplatin, etoposide, fluorouracil and temozolomide. The immunotherapy agent cetuximab is also used in BC Cancer protocols.

Some dual modality protocols that use chemotherapeutic agents as radiosensitizers to potentiate the toxic effects of radiation therapy may order cancer drug therapy to be given on days with RT **only**. Refer to the below *Treatment* section excerpt from the GOCXCRT protocol:

TREATMENT:

note: Since Cisplatin is used in this protocol as a radio-sensitizing agent, it is to be administered on a day on which radiation therapy is delivered, preferably on day 1 or 2 of the 5-day radiation. Radiation should be targeted to start shortly after Cisplatin is complete: ideally less than 2 hours, but may be given up to four hours, after completion of infusion. If radiation therapy is cancelled, do not give Cisplatin that day; postpone until radiation therapy resumes.

Drug	Dose	BC Cancer Administration Guidelines
Cisplatin	40 mg/m ²	IV in NS 500 mL with mannitol 30 g and magnesium sulfate 2 g, over 1 h

Repeat weekly x 5 cycles (also see under **RADIATION THERAPY**).

Interpretation:

- If RT is cancelled, cisplatin should NOT be given.

Other dual modality protocols order cancer drug therapy to be given on days patient is not receiving RT in addition to RT days. Refer to the below *Treatment* section excerpt from the HNLACETR protocol:

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
cetuximab (first dose)	400 mg/m ² (loading dose) on day minus 7 from radiation start date	IV over 2 hours (use 0.2 micron in-line filter) (maximum infusion rate 10 mg/min) Observe for 1 hour post-infusion**
	THEN	
cetuximab (subsequent dose)	250 mg/m ² on days 1, 8, 15, 22, 29 and 36 with concurrent radiation*	IV over 1 hour (use 0.2 micron in-line filter) (maximum infusion rate 10 mg/min) Observe for 1 hour post-infusion**

* cetuximab may be given on:

- days 1, 8, 15, 22 and 29 if radiation is given over 5 weeks, or
- days 1, 8, 15, 22, 29, 36 and 43 if radiation is given over 7 weeks

Interpretation:

- Cetuximab loading dose of 400 mg/m² is given on day minus 7 of radiation therapy start date (one week prior to starting RT).
- On day 1 of treatment cycle, radiation therapy begins and can be administered for 5 to 7 weeks.
- Cetuximab 250 mg/m² is given once weekly with concurrent RT for 5 to 7 weeks.

- The total number of cetuximab doses given during RT depends on the total duration of RT. For example, if RT is being given for 5 weeks, 5 doses of cetuximab will be given during RT, 1 dose each on days 1, 8, 15, 22, and 29 of treatment cycle. If RT is being given for 7 weeks, 7 doses of cetuximab will be given, 1 dose each on days 1, 8, 15, 22, 29, 36, and 43 of treatment cycle.

Interpreting the RT Treatment Section

The different types of radiation therapy treatments used at BC Cancer are discussed in the Radiation Therapy section of Module 6.

Refer to the below *Pelvic Irradiation* section excerpt from the GIAVCRT protocol for an example of radiation therapy treatment interpretation:

Pelvic Irradiation:

- 4500 cGy in 25 fractions over 5 weeks
- Followed at the Radiation Oncologist's discretion by a boost of 540 cGy to the tumour bed and immediately adjacent lymph nodes, plus 2 cm.
- When feasible, a final boost of 360 cGy may be given to the tumour bed, plus 2 cm. No small bowel may be treated within this volume.

Interpretation:

- A total dose of 4500 centigray (cGy) is given as 25 divided doses (180 cGy per dose per day) over a course of 5 weeks (weekdays only).
- Once RT is completed, an additional single dose of 540 cGy can be delivered to a small area encompassing the tumour bed and immediately adjacent lymph nodes, plus 2 cm of surrounding area.
- Another additional single dose of 360 cGy can be delivered to the tumour bed, plus 2 cm of surrounding area. The small bowel is a critical organ at risk (OAR) which limits the amount of radiation that can be given to avoid long term radiation induced toxicity.

Interpreting the Cancer Drug Treatment Section

Dose

It is important to note that when cancer drug therapy is delivered at the same time as RT, the drug dose(s) may need to be lower than when the drug is administered alone to minimize the risk of cumulative toxicities. Dual modality protocols must be used for patients receiving both

drug therapy and RT concurrently. Careful coordination of dose and timing of all RT and cancer drug treatments, and monitoring of treatment toxicities, is required.

Refer to the Option 1 *Treatment* section excerpt below from the dual modality protocol GIRCRT.

CYCLE: WEEK Option 1	CHEMOTHERAPY		
	Drug	Dose	BC Cancer Administration Guideline
Radiation: 25 fractions over 5 weeks*			
Cycle 1	capecitabine [†]	825 mg/ m ² BID on each RT day (Total daily dose=1650 mg/m ²)	PO. Second dose should be taken 10-12 hours after the first dose. Given on the days that RT is given for the duration of Radiation Therapy, beginning on the first day of RT and ending on the last day of RT.
SURGERY			
Cycles 2–7**	capecitabine [†]	1250 mg/m ² BID (Total daily dose = 2500 mg/m ²) x 14 days	PO

*May take 5-6 weeks
**Cycle 2 starts 4-8 weeks after surgery. Cycle is 21 days.

Interpretation:

- Cycle 1 consists of both chemotherapy and radiation therapy given concurrently. Note: for Cycle 1, the patient receives smaller doses of capecitabine 825 mg/m² orally twice daily on days of RT only (not on weekends or statutory holidays) beginning on the first day of RT and ending on the last day of RT treatment. Larger doses of capecitabine 1250 mg/m² BID can be given in Cycles 2-7, when chemotherapy is administered alone following RT.
- Duration of Cycle 1 is 5-6 weeks, depending on the number of statutory holidays and the number of weekdays in that time period, as required to complete 25 fractions of RT. Typically lab tests are ordered once weekly during RT.
- Once Cycle 1 is completed, patient can undergo surgery. Patient is assessed within 4-8 weeks after surgery and is then started on Cycle 2.
- Cycles 2-7 consist of chemotherapy ONLY. Patient receives a higher dose of capecitabine orally twice daily for 14 days, then has 7 days off treatment, after which the next cycle starts.
- Duration of each cycle from Cycles 2-7 is 21 days. Typically, lab tests are ordered every three weeks, prior to each treatment Cycle.

Treatment Timing

Noting the RT treatment start and end dates is necessary for dual modality protocols that ask for cancer drug therapy to be given during RT. Some may ask for drug therapy to be delivered:

- on days with RT only

(e.g., continuously as in GICART or once weekly as in HNNLAPRT)

- on specific days before, during or after RT treatment

(e.g., HNLACETRT , LULACATRT)

- on days with and without RT

(e.g., CNAJTZRT).

Additionally, appropriate lab test results need to be available to pharmacy to align with the dispensing schedule.

Dosing on Days with RT only

Refer to the *Treatment* section excerpt below from the dual modality protocol GICART, where parenteral and oral chemotherapy is given concurrently with radiation therapy:

mitomycin	10 mg/m ² on Day 1 Week 1 and on Day 29 Week 5 (Week 5 mitomycin is optional) (Maximum dose = 20 mg)				IV push	
capecitabine*	825 mg/m ² BID on each RT day (Days 1-5, 8-12, 15-19, 22-26, 29-33 and continue until last day of RT) Note: capecitabine treatment is completed on the last day of RT (Total daily dose=1650 mg/m ²)				PO. Second dose should be taken 10-12 hours after the first dose	
Week	1	2	3	4	5	6
Radiation therapy**	X	X	X	X	X	1/2
capecitabine	X Days 1-5	X Days 8-12	X Days 15-19	X Days 22-26	X Days 29-33	Continue until last day of RT
mitomycin	X Day 1				X Day 29 (mitomycin optional)	

**** Radiotherapy: 50.4 Gy in 28 fractions (over 5 ½ weeks, no gap)**

Interpretation:

- Mitomycin 10 mg/m² (maximum dose 20 mg) is given on Day 1 and optionally on Day 29.
- Capecitabine 825 mg/m² BID is given on all days with RT only (not weekends and/or statutory holidays) beginning on the first day of RT and ending on the last day of RT treatment.
- Duration is 5-6 weeks, depending on number of statutory holidays and the number of weekdays in that time period, as required to complete 28 fractions of RT. Typically lab tests are ordered once weekly during RT.

Dosing Once Weekly

Refer to the *Treatment* section excerpt below from the LULACATRT protocol, where parenteral chemotherapy is only given once weekly during RT.

Note: smaller doses of chemotherapy are used when given once weekly concurrent with RT:

Concurrent with radiation therapy: starting the first day of radiation therapy (note: lower drug doses with weekly dosing schedule)		
Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	45 mg/m ²	IV in 100 to 250 mL NS over 1 hour (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)
CARBOplatin	Dose = AUC 2 x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes
Repeat <u>weekly</u> x 6 weeks concurrent with radiation therapy		
Optional consolidation chemotherapy: starting about 4 weeks after completion of concurrent chemoradiation therapy (note: regular drug doses with 3-weekly dosing schedule)		
Drug	Dose	BC Cancer Administration Guideline
PACLitaxel	200 mg/m ²	IV in 250 to 500 mL NS over 3 hours (use non-DEHP bag and non-DEHP tubing with 0.2 micron in-line filter)
CARBOplatin	Dose = AUC 6 x (GFR* + 25)	IV in 100 to 250 mL NS over 30 minutes
Repeat every <u>3 weeks</u> x 2 cycles		
... RADIATION THERAPY: 60 Gy external beam thoracic radiotherapy in 30 fractions over 6 weeks		

Interpretation of concurrent chemotherapy with radiation therapy section:

- Cycle 1 (weeks 1 to 6) are considered the concurrent therapy. Cycles 2 and 3 are the optional consolidation chemotherapy.
- Paclitaxel and carboplatin are given once weekly during radiation therapy.
- Duration of concurrent treatment is approximately 6 weeks, depending on number of statutory holidays and the number of weekdays in that time period, as required to complete 30 fractions of RT.

Interpretation of the optional consolidation chemotherapy section:

- 4 weeks after completing concurrent therapy, patient can receive additional chemotherapy ONLY at the discretion of the physician.
- Consolidation chemotherapy is given to eliminate any cancer cells left over after initial treatment.
- Cycle 2 is given 4 weeks after the completion of concurrent therapy.
- Cycle 3 is given 3 weeks after Cycle 2.

Dosing Continuously

Refer to the *Treatment* section excerpt below from the CNAJ TZRT protocol, where oral chemotherapy is given throughout the duration of RT treatment. Note: smaller daily doses of chemotherapy are used when given concurrently with RT.

Drug	Dose*	BC Cancer Administration Guideline
temozolomide	<p>Concomitant with RT: 75 mg/m² po daily preferably 1 h prior to RT especially in the first week of treatment, and in A.M. on days without RT until completion of RT (usual duration 6 weeks)</p> <p>Adjuvant treatment starting 4 wks after RT: 150 mg/m² once daily x 5 d (d 1 to 5) every 28 d x 6 cycles</p>	PO
Dose may be increased to 200 mg/m ² for the second cycle of adjuvant therapy if no significant hematologic, hepatic or other toxicity is noted (see below)		

Interpretation of concurrent chemotherapy with radiation therapy section:

- Weeks 1 to 6 are considered the concurrent therapy. Cycles 1-6 of adjuvant treatment are started 4 weeks after RT.

- Temozolomide 75 mg/m² PO daily is given on ALL days, with or without RT, preferably 1 hour prior to RT treatment on days with RT, and in the morning on days without RT.
- Duration of concurrent treatment is approximately 6 weeks, depending on number of statutory holidays and the number of weekdays in that time period.

Interpretation of the adjuvant chemotherapy section:

- 4 weeks after completing the concurrent therapy, patient can receive temozolomide 150 mg/m² PO daily x 5 days every 28 days for 6 cycles.
- If Cycle 1 is well tolerated, the temozolomide dose can be increased to 200 mg/m² for subsequent cycles.

Dose Modifications

As both RT and cancer drug therapy can individually cause toxicities, their combination puts patients at increased risk of more severe toxicities. For example, radiation therapy for breast cancer can cause radiation dermatitis. Patients receiving concurrent RT and cancer drug therapy are at increased risk of developing more severe radiation dermatitis.

Patients require monitoring for toxicities throughout dual modality treatment. Medical oncologists, radiation oncologists, nurse practitioners, general practitioners in oncology (GPO) and oncology nurses may be involved in the routine weekly assessments throughout combined RT and cancer drug treatment. Radiation therapists screen the patient prior to each RT treatment, referring them for assessment when needed.

Prior Irradiation

When RT is delivered to a large surface area of the body or to a location with large bone marrow reserve (e.g., long bones), the immunosuppressive side effects can be long lasting. This prior radiotherapy can impact toxicity in future cancer drug treatments as noted in the below *Precautions* section excerpt from the GIFIRINOX protocol:

Prior pelvic radiotherapy or radiotherapy to greater than 15% of the bone marrow bearing area may increase the degree of myelosuppression associated with this regimen, and caution is recommended in these cases. Close monitoring of the CBC is essential.

Interpretation:

- Hematological toxicity may be more pronounced in patients who have had pelvic RT or RT to their long bones; close monitoring of hematological counts is required.

Concurrent Irradiation

During dual modality treatment, systemic therapy can be held or omitted due to low blood counts or other side effects. RT, on the other hand, may continue and be completed unless the patient experiences severe toxicities related directly to RT.

Refer to the *Precautions* section excerpt below from the BC Cancer protocol [GIAVCRT](#):

PRECAUTIONS:

1. Patients may experience severe toxicity while receiving concurrent Chemotherapy and Radiation Therapy. Capecitabine and radiation may have to be interrupted until toxicity has improved to grade 1 or less. The dose of capecitabine should be adjusted according to the tables upon restarting chemoradiation. It is important that the patient receive the full Radiation Therapy component. The major toxicity during concurrent Chemotherapy and Radiation Therapy is severe diarrhea, usually during week 4. The patient should be monitored to ensure that dehydration does not occur. Note that diarrhea may result in increased INR and the risk of bleeding in patients on warfarin.

Interpretation:

- Chemotherapy and radiation therapy can be held or interrupted. However, the full dose of planned RT is delivered regardless of whether the full dose of concurrent chemotherapy is received. RT is generally not interrupted but the prescriber may delay based on their assessment.
- Capecitabine dose modification may be required once toxicity is resolved. Subsequent dose will depend on the toxicity grade and number of times it occurred as outlined in the *Dose Modification* section of the protocol.
- The most common toxicity seen during concurrent capecitabine and RT is diarrhea and it manifests later during the treatment. Other toxicities may be limited by the low doses of chemotherapy used during concurrent therapy.
- Diarrhea puts patients at risk of dehydration, and patients on warfarin at risk of increased INR and bleeding. Further Instructions for monitoring and treating both are given in the *Precautions* section of the protocol.

It is important to note that there can be different dose modification parameters for the concurrent and adjuvant portions of the same dual modality treatment.

For example, the [CNAJ TZRT](#) protocol has different doses and dose modifications for concomitant versus adjuvant treatment. During concurrent treatment, temozolomide 75

mg/m² is given with RT but may be discontinued for toxicity. During adjuvant treatment, temozolomide 150 mg/m² is given once daily x 5 days each cycle, and the dose may be increased to 200 mg/m² if well tolerated, or reduced to 100 mg/m² for toxicity, or discontinued.

Refer to the *Dose Modification* parameters for concomitant versus adjuvant treatment in the excerpts below from the CNAJ TZRT protocol:

Hematologic and hepatic dose modification parameters for Concomitant Temozolomide with RT:

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
1.0 to less than 1.5	or	75 to less than 100	Delay temozolomide until counts recover
less than 1.0	or	less than 75	Discontinue temozolomide

Bilirubin (micromol/L)		ALT	Dose
less than 25	and	less than or equal to 2.5 x ULN	100%
greater than or equal to 25	or	greater than 2.5 x ULN	Delay***

*** Follow LFTs weekly and re-institute temozolomide at 75 mg/m² if Bilirubin recovers to less 25 micromol/L and ALT recovers to less than or equal to 2.5 x ULN

Note: Dose reductions below 75 mg/m² are not permitted. Radiation Therapy to continue without temozolomide until recovery of LFTs.

Interpretation of dose modifications for concurrent RT and chemotherapy:

- Concurrent temozolomide can be given at full dose of 75 mg/m², if ANC is 1.5 x 10⁹/L or more AND platelets are 100 x 10⁹/L or more AND bilirubin is less than 25 micromol/L AND if ALT is 2.5 x ULN or less prior to Day 1 of start of concurrent therapy.
- If weekly labs show ANC is 1.5 x 10⁹/L or more AND platelets are 100 x 10⁹/L or more AND bilirubin is less than 25 micromol/L AND if ALT is 2.5 x ULN, temozolomide can continue at 100% dose.

- If ANC is between 1.0 to less than 1.5 x 10⁹/L OR platelets are 75 to less than 100 x 10⁹/L, concurrent temozolomide should be delayed until counts recover. CBC should be checked weekly.
- If ANC is less than 1.0 x 10⁹/L OR platelets are less than 75 x 10⁹/L, concurrent temozolomide should be discontinued.
- Dose reductions are not allowed.
- There is no change in dose or schedule of RT and it continues as planned.

Hematological dose modification parameters for Adjuvant Temozolomide alone:

Day 1:

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose
greater than or equal to 1.5	and	greater than or equal to 100	100%
less than 1.5	or	less than 100	Delay*

* Follow CBC weekly and re-institute temozolomide at one dose level lower (150 mg/m² or 100 mg/m²) if ANC recovers to greater than 1.5 x 10⁹/L and platelets recover to greater than 100 x 10⁹/L within 3 weeks

Day 22:

ANC (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose
greater than or equal to 1.0	and	greater than or equal to 50	100%
less than 1.0	or	less than 50	Reduce one dose level**

**Dose levels are 200 mg/m², 150 mg/m² and 100 mg/m²

Interpretation of hematologic dose modifications for chemotherapy alone:

- Adjuvant temozolomide starts 4 weeks after completion of RT. Temozolomide is given once daily on days 1 to 5 of each cycle, every 28 days for 6 cycles.
- The first adjuvant temozolomide cycle can be given at full dose of 150 mg/m² if ANC is 1.5 x 10⁹/L or more AND platelets are 100 x 10⁹/L or more prior to Cycle 1 Day 1 of adjuvant temozolomide.
- If Cycle 1 temozolomide at 150 mg/m² is well tolerated, the dose can be increased to 200 mg/m² for subsequent cycles at the discretion of the prescriber.
- For subsequent cycles, Day 22 CBC is also checked.

- Patient can receive 100% planned dose if Day 22 counts are adequate (ANC is $1.0 \times 10^9/L$ or more AND platelets are $50 \times 10^9/L$ or more), **along with** adequate counts prior to Day 1 of next cycle (ANC $1.5 \times 10^9/L$ or more AND platelets $100 \times 10^9/L$ or more).
- If Day 22 counts are low (ANC less than $1.0 \times 10^9/L$ or platelets less than $50 \times 10^9/L$), the dose for next cycle should be reduced by 1 dose level. If platelets fall below $20 \times 10^9/L$, a platelet transfusion may be needed.
- If counts are still low prior to Day 1 of next cycle (ANC less than $1.5 \times 10^9/L$ or platelets less than $100 \times 10^9/L$), treatment should be delayed. Once counts recover, the patient may be restarted at the lower dose level.
- Dose reductions below 100 mg/m^2 are not permitted. Temozolomide should be discontinued for repeat Grade 3 or 4 hematologic toxicity at the 100 mg/m^2 dose level (ANC less than $1 \times 10^9/L$, platelets less than $50 \times 10^9/L$).

Hepatic dose modification parameters for Adjuvant Temozolomide alone:

Bilirubin (micromol/L)		ALT	Dose
less than 25	and	less than or equal to $2.5 \times \text{ULN}$	100%
25 to 85	or	2.6 to $5 \times \text{ULN}$	Reduce one dose level**
greater than 85	or	greater than $5 \times \text{ULN}$	Delay***

** Dose levels are 200 mg/m^2 , 150 mg/m^2 and 100 mg/m^2

*** Follow LFTs weekly and re-institute temozolomide at 100 mg/m^2 if Bilirubin recovers to less than 85 micromol/L and ALT recovers to less than $5 \times \text{ULN}$

- Note: Dose reductions below 100 mg/m^2 are not permitted. Temozolomide should be discontinued for repeat Bilirubin greater than 85 micromol/L and repeat ALT greater than $5 \times \text{ULN}$

Interpretation of hepatic dose modifications for chemotherapy alone:

- Adjuvant temozolomide can be given at full dose if bilirubin is less than 25 micromol/L AND if ALT is $2.5 \times \text{ULN}$ or less prior to Day 1 of adjuvant treatment.
- If bilirubin increases to 25 to 85 micromol/L OR if ALT increases to 2.6 to $5 \times \text{ULN}$, temozolomide dose should be reduced by one dose level.
- If bilirubin increases to greater than 85 micromol/L OR if ALT increases to greater than $5 \times \text{ULN}$, temozolomide should be delayed until the counts recover, and the temozolomide dose should be reduced to the lowest dose level of 100 mg/m^2 .

- Dose reductions below 100 mg/m² are not permitted. Temozolomide should be discontinued for repeat Grade 3 or 4 hepatic toxicity at the 100 mg/m² dose level (bilirubin greater than 85 micromol/L, ALT greater than 5 x ULN)

As with all dose modifications, the full clinical picture of the patient should be considered. See Module 3 for a detailed discussion of lab test interpretation. Work through [Case Study 12](#) to practice clinically reviewing a dual modality protocol.

Radiation and Cancer Drug Treatment Plans not included in Dual Modality Protocols

Cancer drugs and radiation therapy may both be recommended as part of a comprehensive patient treatment plan outside of a designated dual modality protocol. Patients who are to receive radiation as part of the treatment plan are referred to a radiation oncologist for consideration of RT.

Timing of radiation and cancer drug treatment varies depending on a number of factors such as toxicity of combined treatment, need for surgery, control of cancer symptoms or site of cancer.

- In patients with breast cancer who have undergone surgery and will receive adjuvant chemotherapy and RT, RT will usually follow chemotherapy to reduce toxicity.
- When a patient with advanced cancer is receiving cancer drug treatment and requires RT for management of brain metastases, drug therapy can be completed first or interrupted so the patient can receive RT.

In some instances, both radiation and drug therapy may be given concurrently using separate protocols. It is important to carefully check dosing regimens and monitor the patient in these cases. Individual BC Cancer protocols and Cancer Drug Manual monographs may contain information that is helpful in determining the safety of radiation therapy given concurrently with cancer drug therapy.

Refer to the *Radiation* section of the [BRAJTR](#) protocol to determine when trastuzumab may be considered safe to be given during RT.

Radiation:

For patients with indications for radiation, the radiation treatment should be given at the usual time after the completion of the chemotherapy with the trastuzumab continued during the radiation therapy. There has been no increased toxicity reported in the clinical trials at this time, but there is no long term data; therefore, patients should be monitored. There have been no studies of concurrent trastuzumab and internal mammary node radiation, so it is unclear at this time whether there would be an enhanced risk of cardiotoxicity. If there is an anticipated need for internal mammary node radiation, it may be helpful to discuss the overall treatment program and timing with the treating radiation oncologist at the outset of chemotherapy.

Interpretation:

- Trastuzumab given according to BRAJTR protocol, every 3 weeks **after completion of chemotherapy**, can be continued during radiation therapy unless there is a need for internal mammary node radiation.
- For patients that require internal mammary node radiation, the overall treatment program and timing should be discussed with the treating radiation oncologist to determine enhanced risk of cardiotoxicity.
- If patient receives trastuzumab while undergoing radiation therapy, they should be monitored for long term effects.

Other examples of exceptional circumstances found in the BC Cancer resources included below.

- The *Dosage Guidelines* section of the Doxorubicin CDM monograph mentions that doxorubicin and concurrent RT are generally not recommended. However, the *Eligibility/Tests* section of the SAAJA protocol clarifies that there can be exceptions. Select patients with non-metastatic operable soft tissue sarcoma that are receiving doxorubicin, may receive radiation therapy concurrently with doxorubicin instead of the usual practice of receiving RT following doxorubicin.
- Patients with locally advanced or metastatic prostate cancer being treated with RT or brachytherapy usually receive a LHRH agonist as per protocol GUPLHRH at the same time as RT.

When patients are receiving radiation and cancer drug therapy concurrently, it is important that all members of the involved health care team coordinate the patient's care to minimize toxicity.