

Alberta Breast Cancer Program Adjuvant Systemic Therapy Guidelines

Updated
January 29, 2011

**Systemic Therapy
Recommendations for
Lymph Node Negative
Breast Cancer**

Risk Categories for Lymph Node Negative Breast Cancer

Risk Category	Risk Factor
NEGATIVE RISK FACTORS	<ul style="list-style-type: none"> - Age < 35 years - <u>HER2</u> over-expression (<u>HER2+</u>) - Presence of lymph/vascular invasion - Grade 3 - Hormone receptor negative disease (<u>ER +/- PR negative</u>)
Lower Risk	<ul style="list-style-type: none"> - < 1 cm with no negative risk factors - 1-2 cm, grade 1, no other negative risk factors
Intermediate Risk	<ul style="list-style-type: none"> - All other combinations of factors that do not fit into either the low or high risk criteria
Higher Risk	<ul style="list-style-type: none"> - 1 - 2 cm with any 2 or more Negative risk factors, - >2-3 cm with any 1 or more Negative risk factors, - >3 cm (regardless of other Negative risk factors) - Special consideration for HER2+ tumors (see below)

	Hormone Receptor (+)	Hormone Receptor (-)
Lower Risk	Observation* OR Hormonal Rx	Observation
Intermediate Risk	Hormonal Therapy +/- Chemotherapy	Chemotherapy
Higher Risk	Chemotherapy + Hormonal Therapy	Chemotherapy

* No systemic therapy may be offered to patients in cases where:

- Tumor is less than 1 cm or
- The patient has other significant co-morbidities which precludes the safe administration of adjuvant systemic therapy or
- The patient has limited life expectancy

Chemotherapy Options for Lymph Node Negative Breast Cancer

HER2(-) LN(-)

Lower risk:

Intermediate risk:

Higher risk:

No systemic therapy recommended

CMF or AC or DC

CMF or AC or DC or FEC x 6

HER2(+) LN(-)

Tumoral Size considerations:

<0.5 cm:

no further systemic therapy recommended

0.5 cm to 1 cm:

ER (+): consider endocrine therapy only

ER (-) - discuss chemotherapy/trastuzumab

> 1 cm: Discuss chemotherapy / trastuzumab +/- endocrine therapy (where applicable)

Chemotherapy options for HER2+ / lymph node negative:

• Non-Anthracycline based options:

– Docetaxel / Carboplatin / Trastuzumab (DCbH X 6) or

– Docetaxel / Cyclophosphamide / Trastuzumab (DC/H X 4)

• Anthracycline based options:

– AC x 4, or FEC X 6, followed by sequential trastuzumab

• Non-anthracycline regimens are preferred if there are cardiac risk factor concerns

• Trastuzumab duration = 1 year (17 cycles)

**Systemic Therapy
Recommendations for
Lymph Node Positive
Breast Cancer**

Risk Categories for Lymph Node Positive Breast Cancer

	Hormone Receptor (+)	Hormone Receptor (-)
HER2(-)	Chemotherapy + Hormonal Therapy	Chemotherapy
HER2(+)	Chemotherapy + Trastuzumab + Hormonal Therapy	Chemotherapy + Trastuzumab
<p>* No systemic therapy may be offered to patients in cases where:</p> <ul style="list-style-type: none"> - <u>The patient</u> has other significant co-morbidities which precludes the <u>safe administration of adjuvant systemic therapy or</u> - <u>The patient</u> has limited life expectancy 		

Lymph Node Positive Guidelines

Chemotherapy:

- A taxane containing therapeutic regimen is the preferred treatment option in cases of LN+ breast cancer wherever medically appropriate

HER2+ Chemotherapeutic Regimens:

- Concurrent trastuzumab therapy (generally given with taxanes) is preferred to sequential trastuzumab therapy
- One year of trastuzumab therapy (17 cycles) is currently recommended.

HER2(+)

Preferred:

- FEC-DH* or Docetaxel / Carboplatin / Trastuzumab (DCbH X 6)

* timing of trastuzumab addition (in relation to preceding anthracycline exposure) is at the discretion of the treating physician, in cases where concern about potentiating cardiotoxicity risk exist

Other evidence based options include:

- AC x 4 → (q3wk Docetaxel or qwk Paclitaxel) x 4 and Trastuzumab
- Any standard adjuvant breast cancer chemotherapy → sequential trastuzumab (as per HERA trial)

Special considerations

- If any cardiac risk or concern: Use DCbH or DC/H

HER2(-)

Preferred:

- FEC – D
- TAC (with G-CSF support)

Other evidence based options include:

- AC – P (weekly)
- DC X 4
- FEC x 6

Special considerations

- If any cardiac risk or concern: Use DC or CMF
- In frailer patients – consider weekly paclitaxel rather than q3weekly docetaxel

Endocrine Therapy (for Hormone Receptor Positive Disease only)

Patient Group	
Pre-menopausal	<p>Tamoxifen x 5 years*</p> <p>*In pre-menopausal patients who develop amenorrhea post chemotherapy:</p> <ul style="list-style-type: none">• No clinical trial information is currently available to guide us in the use of AIs in this population as these types of patients were not included in the <u>postmenopausal</u> adjuvant AI trials• Standard hormonal assays and/or monitoring algorithms are currently inadequate or unavailable to ensure that these types of patients are truly postmenopausal while on AIs <p>• Patients <u>who have had bilateral oophorectomy should be considered to be post-menopausal and treated accordingly</u> – see Post-menopausal endocrine therapy treatment guidelines</p> <p>• <u>Pending clinical trial confirmation, treatment with ovarian suppression with GnRH agonists is not generally indicated in the adjuvant setting, however, may be considered an option for pre-menopausal patients who have had hormone receptor positive breast cancer, and are eligible for adjuvant chemotherapy but decline chemotherapy OR where chemotherapy is contraindicated.</u></p>

Endocrine Therapy (for Hormone Receptor Positive Disease only)

Patient Group	
Post-menopausal	<p>Options:</p> <ul style="list-style-type: none">• Tam x 2-3 years → AI x 3-2 years <u>(Total = 5 years adjuvant endocrine therapy)</u> <p>Alternative options:</p> <ul style="list-style-type: none">• Upfront AI x 5 years• <u>Tamoxifen X 5 years (if an AI is contraindicated)</u>• <u>In cases of AI intolerance an alternate AI may be used or the patient could be switched back to tamoxifen (provided that there is no contraindication to do so)</u>
Extended Adjuvant Endocrine Therapy	<p>For patients with early stage, hormone receptor positive tumors who have completed 5 years of adjuvant Tamoxifen [either LN(+) or high risk LN(-)]</p> <ul style="list-style-type: none">• Consider AI x 3-5 years after completing 5 years of Tamoxifen
	<ul style="list-style-type: none">• At this time, no evidence exists for the standard use of fulvestrant in the adjuvant setting

Legend:

C= Cyclophosphamide

Cb= Carboplatin

D= Docetaxel

P= Paclitaxel

H = Trastuzumab (Herceptin®)

CMF = cyclophosphamide (oral), methotrexate, 5-FU

AC = adriamycin, cyclophosphamide

FEC = 5-FU, epirubicin, cyclophosphamide

FEC-D = FECx3 → Dx3

TAC = docetaxel, adriamycin, cyclophosphamide

DC = docetaxel, cyclophosphamide

DCbH = Docetaxel, Carboplatin, trastuzumab

DC/H= docetaxel, cyclophosphamide, trastuzumab

AI = Aromatase Inhibitor (anastrozole, letrozole or exemestane)