

Alberta Breast Cancer Program Adjuvant Systemic Therapy Guidelines

- July 2011 Revision -

Adjuvant Systemic Therapy

Options in Lymph Node Negative Breast Cancer

Risk Categories for Lymph Node Negative Breast Cancer

NEGATIVE PROGNOSTIC RISK FACTORS	<ul style="list-style-type: none"> ▪ HER2 over-expression (i.e. HER2+) ▪ Grade 3 ▪ Hormone receptor negative disease ▪ Age < 35 years ▪ Presence of lymph/vascular invasion
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RISK CATEGORY	DEFINITION
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 lower or higher 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)

Adjuvant Systemic Therapy Options in Lymph Node Negative Breast Cancer

		Hormone Receptor (+)	Hormone Receptor (-)
HER(-)	Lower Risk	Observation* OR Endocrine Therapy	Observation *
	Intermediate Risk	Endocrine Therapy +/- Chemotherapy	Chemotherapy
	Higher Risk	Chemotherapy + Endocrine Therapy	Chemotherapy
HER2(+)		See Adjuvant Systemic Therapy for HER2(+) LN(-) Breast Cancer	

* Note: Systemic therapy may not be offered to patients in cases where:

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

Adjuvant Chemotherapy Options for HER2 Normal (HER2 Negative)

Lymph Node Negative Breast Cancer

HER2(-) LN(-)

Lower risk:

No chemotherapy generally recommended

Intermediate risk:

DCx4 or ACx4 or CMFx6

Higher risk:

DCx4 or FECx6 or ACx4 or CMFx6

(Evidenced-based Anthracycline/taxane containing regimen options may be used in selective circumstances)

Note: Non-anthracycline based regimens are preferred if there are cardiac risk concerns

Adjuvant Endocrine Therapy Options for HER2 Normal (HER2 Negative)

Lymph Node Negative Breast Cancer

Hormone Receptor Positive, HER2(-), LN(-)

See Adjuvant Endocrine Therapy Section

Adjuvant Systemic Therapy in HER2 Positive (HER2+) Lymph Node Negative Breast Cancer

	Hormone Receptor (+)	Hormone Receptor (-)
HER2+	Adjuvant Trastuzumab-Based Chemotherapy * + Endocrine Therapy	Adjuvant Trastuzumab-Based Chemotherapy *

• **See HER2(+) LN(-) Tumoral size Considerations / Discussions**

* Note: Systemic therapy may not be offered to patients in cases where:

- The patient has other significant co-morbidities which precludes the safe administration of adjuvant systemic therapy
- The patient has limited life expectancy

Adjuvant Systemic Therapy for HER2 Positive (HER2+) Lymph Node Negative Breast Cancer

HER2(+) LN(-) Tumoral Size Considerations:

<0.5 cm:

- ER (+): Consider endocrine therapy
- No trastuzumab-based adjuvant chemotherapy is generally recommended
[Special considerations may apply]

0.5 cm to 1 cm:

- ER (+): Consider endocrine therapy
[+/- chemotherapy / trastuzumab may be offered in special circumstances]
- ER (-): Discuss chemotherapy / trastuzumab

> 1 cm:

- ER (+): Discuss chemotherapy / trastuzumab and endocrine therapy
- ER (-) : Discuss chemotherapy / trastuzumab

Adjuvant Chemotherapy Options for HER2 Positive (HER2+) Lymph Node Negative Breast Cancer

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 (as per HERA)
- Evidence based Anthracycline-containing regimen → Taxane + concurrent Trastuzumab

- Trastuzumab duration = 1 year (17 cycles)
- Concurrent trastuzumab therapy (generally given with taxanes) is preferred to sequential therapy
- Non-anthracycline based regimens are preferred if there are cardiac risk concerns
- Single agent (monotherapy) adjuvant trastuzumab alone (i.e. without chemotherapy) is not recommended due to lack of level 1 evidence

Adjuvant Endocrine Therapy Options for HER2 Positive (HER2+) Lymph Node Negative Breast Cancer

Hormone Receptor Positive, HER2(+), LN(-)

See Adjuvant Endocrine Therapy Section

Adjuvant Endocrine Therapy (for Hormone Receptor Positive Disease Only)

Patient Group	Recommended Treatment
<p>Pre-menopausal</p>	<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 practitioners in the use of AIs in this population as these types of patients were not included in the postmenopausal 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 <ul style="list-style-type: none"> • Patients who have had bilateral oophorectomy should be considered to be postmenopausal and treated accordingly (see Adjuvant Endocrine Therapy – Postmenopausal Recommendations) • 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.

Adjuvant Endocrine Therapy (for Hormone Receptor Positive Disease Only)

Patient Group	Recommended Treatment
Post-menopausal	<p>Tam x 2-3 years → AI x 3-2 years (Total = 5 years adjuvant endocrine therapy)</p> <p>Alternative options:</p> <ul style="list-style-type: none"> • Upfront AI x 5 years • Tamoxifen X 5 years (if an AI is contraindicated) <p>In cases of AI intolerance an alternate AI may be used or the patient can be switched back to tamoxifen (provided that there is no contraindication to do so)</p>
Extended Adjuvant Endocrine Therapy	<p>For <u>postmenopausal</u> patients with early stage, hormone receptor positive tumors who have already 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 <p>[note: only 3 yrs of extended adjuvant AI is funded provincially, as such, any additional medications beyond this would require patient or 3rd party funding]</p>
General Comments	<ul style="list-style-type: none"> • Endocrine therapy should not be given concurrently with adjuvant chemotherapy • At this time, no evidence exists for the standard use of fulvestrant in the adjuvant setting

Adjuvant Systemic Therapy

Options in Lymph Node Positive Breast Cancer

Adjuvant Systemic Therapy Options in Lymph Node Positive Breast Cancer

	Hormone Receptor (+)	Hormone Receptor (-)
HER2(-)	Chemotherapy + Endocrine Therapy	Chemotherapy
HER2(+)	Chemotherapy + Trastuzumab + Endocrine Therapy	Chemotherapy + Trastuzumab

* Systemic therapy may not be offered to patients in cases where:

- The patient has other significant co-morbidities which precludes the safe administration of adjuvant systemic therapy
- The patient has limited life expectancy

Adjuvant Chemotherapy in Lymph Node Positive Breast Cancer

General Comments

Adjuvant Chemotherapy:

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

HER2+ Adjuvant Chemotherapy Regimens:

- Concurrent trastuzumab therapy (generally given with taxanes) is preferred to sequential trastuzumab therapy
- Single agent (monotherapy) adjuvant trastuzumab alone (i.e. without chemotherapy) is not recommended due to lack of level 1 evidence
- Adjuvant Trastuzumab duration = 1 year (17 cycles) is currently recommended with regular cardiac monitoring
- Non-anthracycline based regimens are preferred if there are cardiac risk concerns

Adjuvant Chemotherapy in Lymph Node Positive Breast Cancer

<p>HER2(-)</p>	<ul style="list-style-type: none"> • FEC – D or • TAC (with G-CSF support) <p><u>Other evidence based options include:</u></p> <ul style="list-style-type: none"> • AC – P (weekly) • DC X 4 • FEC x 6 <p><u>Special considerations:</u></p> <ul style="list-style-type: none"> • Non-anthracycline based regimens are preferred if there are cardiac risk concerns (DCx4 or CMFx6) • In frail patients – consider weekly paclitaxel regimens rather than q3weekly docetaxel
<p>HER2(+)</p>	<ul style="list-style-type: none"> • FEC-DH* [* 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] • or Docetaxel / Carboplatin / Trastuzumab (DCbH X 6) <p><u>Other evidence based options include:</u></p> <ul style="list-style-type: none"> • AC x 4 → (q3wk Docetaxel or qwk Paclitaxel) x 4 and concurrent Trastuzumab • Any standard adjuvant breast cancer chemotherapy → sequential trastuzumab (as per HERA trial) <p><u>Special considerations</u></p> <ul style="list-style-type: none"> • Non-anthracycline based regimens are preferred if there are cardiac risk concerns (DCbH or DC/H)

**Adjuvant Endocrine Therapy Options for
Lymph Node Positive Breast Cancer**

Hormone Receptor Positive, HER2(+), LN(+)

See Adjuvant Endocrine Therapy Section

Adjuvant Endocrine Therapy (for Hormone Receptor Positive Disease Only)

Patient Group	Recommended Treatment
<p>Pre-menopausal</p>	<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 practitioners in the use of AIs in this population as these types of patients were not included in the postmenopausal 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 <ul style="list-style-type: none"> • Patients who have had bilateral oophorectomy should be considered to be postmenopausal and treated accordingly (see Adjuvant Endocrine Therapy – Postmenopausal Recommendations) • 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.

Adjuvant Endocrine Therapy (for Hormone Receptor Positive Disease Only)

Patient Group	Recommended Treatment
Post-menopausal	<p>Tam x 2-3 years → AI x 3-2 years (Total = 5 years adjuvant endocrine therapy)</p> <p>Alternative options:</p> <ul style="list-style-type: none"> • Upfront AI x 5 years • Tamoxifen X 5 years (if an AI is contraindicated) <p>In cases of AI intolerance an alternate AI may be used or the patient can be switched back to tamoxifen (provided that there is no contraindication to do so)</p>
Extended Adjuvant Endocrine Therapy	<p>For <u>postmenopausal</u> patients with early stage, hormone receptor positive tumors who have already 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* <p>[* note: as per the AHS-Cancer Care Outpatient Cancer Drug Benefit Program listing, only 3 years of extended adjuvant AI are funded provincially, as such, any additional medications beyond 3 years would require patient or 3rd party funding]</p>
General Comments	<ul style="list-style-type: none"> • Endocrine therapy should not be given concurrently with adjuvant chemotherapy • At this time, no evidence exists for the standard use of fulvestrant in the adjuvant setting

Abbreviation 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)