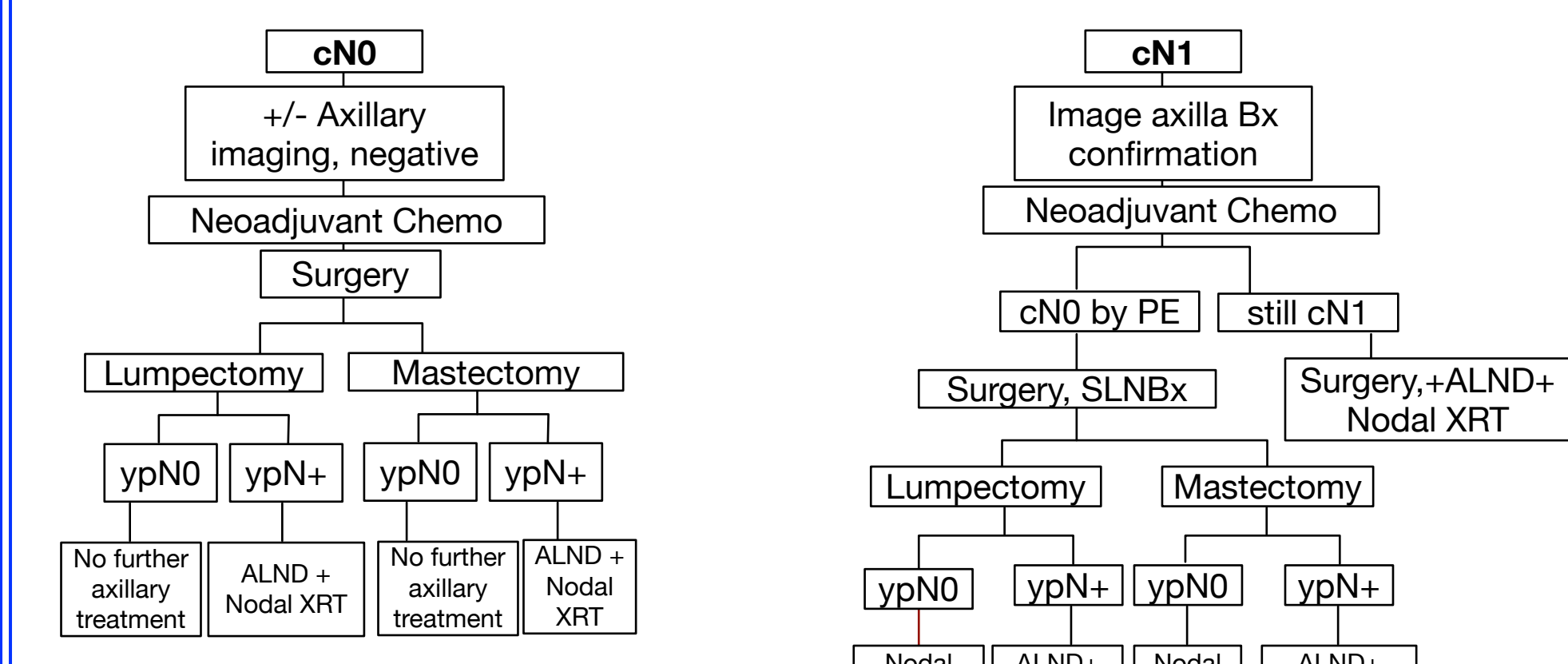


Current standard for axillary management for patients treated with neoadjuvant systemic therapy, **both chemotherapy and endocrine therapy alike.**

Management of the Axilla and Neoadjuvant Endocrine Therapy vs. Chemotherapy

Figure 1 Management of the Axilla



The current standards for axillary management for patients treated with neoadjuvant systemic therapy, both chemotherapy and endocrine therapy alike. However, it is important to note that those treated with neoadjuvant endocrine therapy do not meet inclusion criteria for these clinical trials. The three most commonly used definitions of pathologic complete response—ypT0 ypN0 (absence of invasive cancer and in-situ cancer in the breast and axillary nodes), ypT0is ypN0 (absence of invasive cancer in the breast and axillary nodes, irrespective of ductal carcinoma in situ), and ypT0is (absence of invasive cancer in the breast irrespective of ductal carcinoma in situ or nodal involvement) (October, 2020)

Figure 2

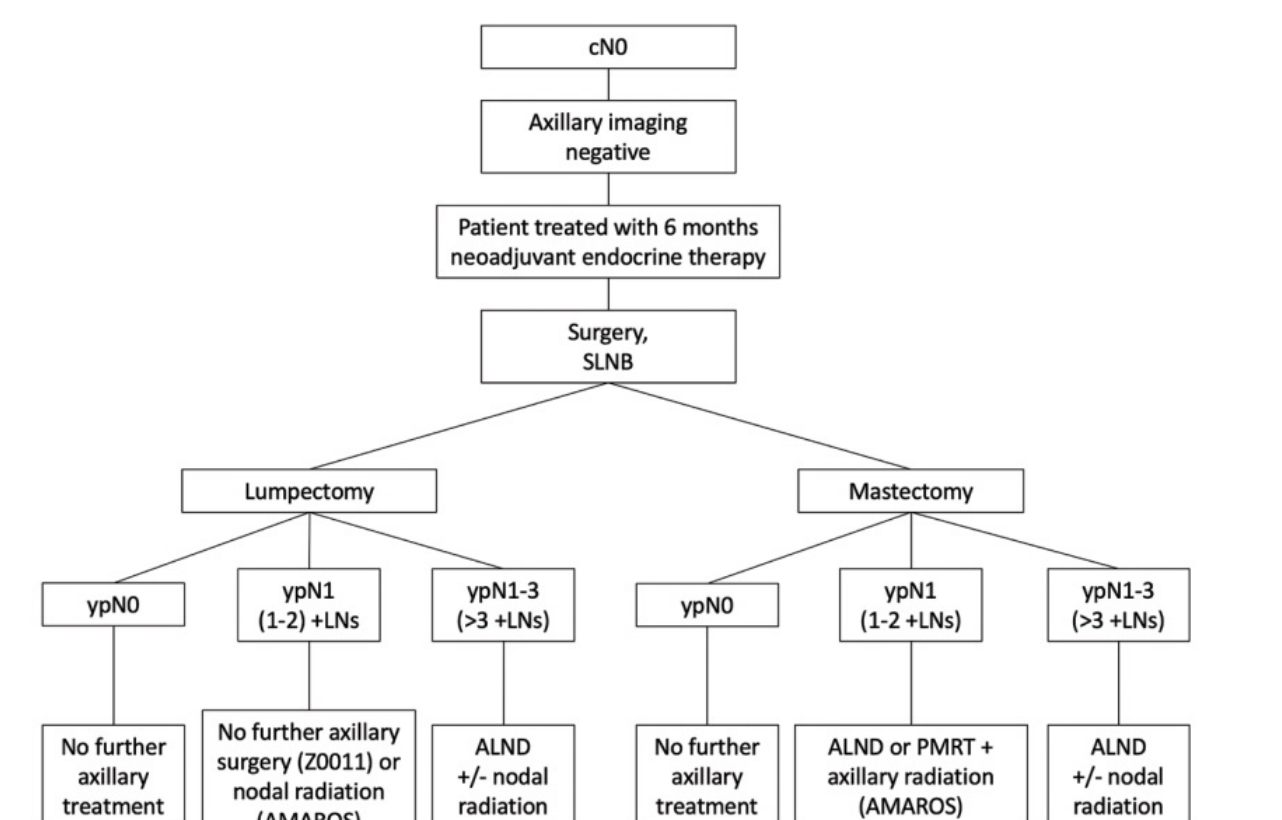


Figure 2. This figure depicts a suggested axillary management algorithm for hormone receptor-positive cN0 patients, treated with neoadjuvant endocrine therapy. While pretreatment axillary ultrasound is recommended, it is not critical for this algorithm, because these patients would have met Z0011/AMAROS criteria if surgery were their primary treatment (provided they have CT1-2 breast tumors). ALND, axillary lymph node dissection; cT, clinical tumor category; LN, lymph node; NET, neoadjuvant endocrine therapy; SLNB, sentinel lymph node biopsy; ypN, pathological node status.

Figure 3

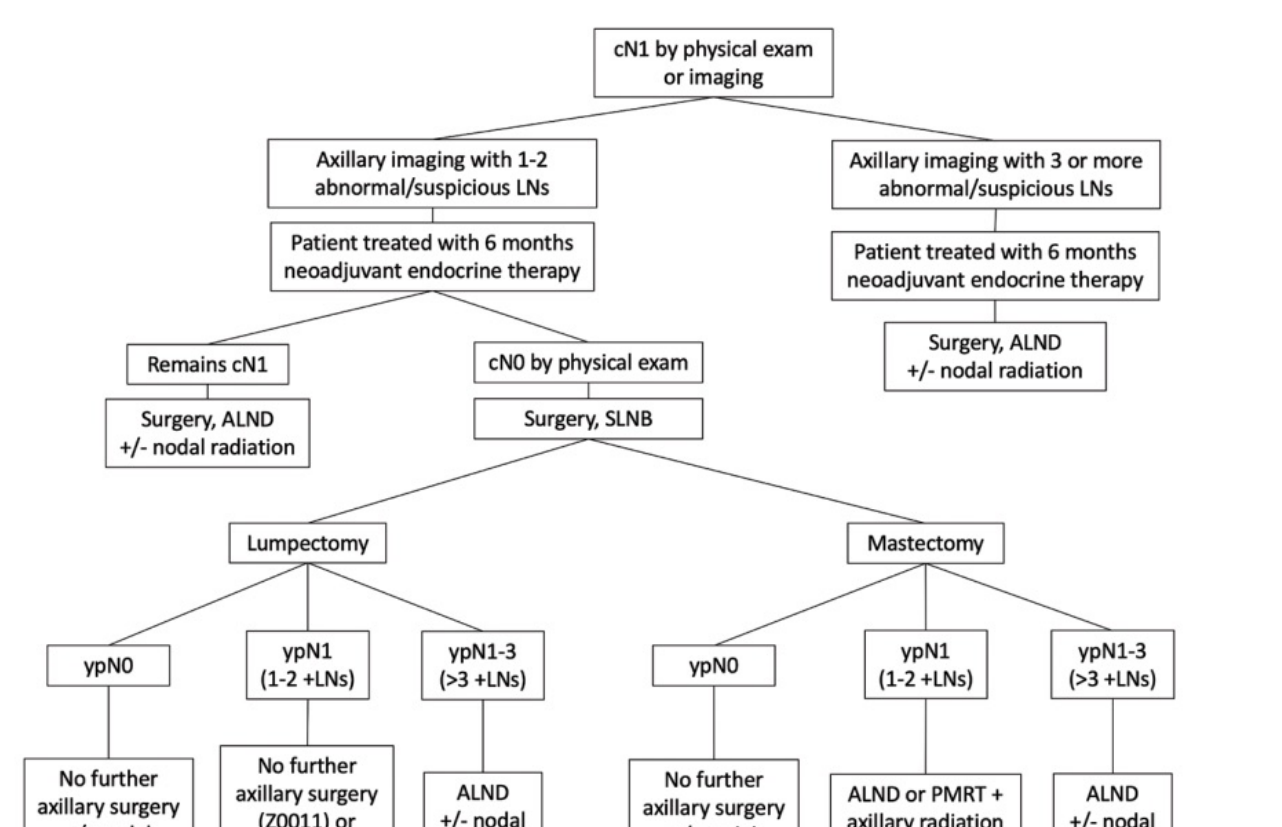


Figure 3. This figure depicts a suggested axillary management algorithm for hormone receptor-positive cN1 patients, treated with neoadjuvant endocrine therapy. This algorithm is predicated on thorough pretreatment axillary imaging, to include at least ultrasound, to characterize the patient's presenting nodal disease burden, and to select patients with minimal nodal disease for thoughtful declassification of axillary surgery. ALND, axillary lymph node dissection; cN, clinical node status; LN, lymph node; NET, neoadjuvant endocrine therapy; SLNB, sentinel lymph node biopsy; ypN, pathological node status.

Strategies to Optimize Axillary Surgery in Patients With Breast Cancer Receiving Neoadjuvant Endocrine Therapy October 13, 2020

Axillary Management After Neoadjuvant Endocrine Therapy for Hormone Receptor-Positive Breast Cancer: 2020

Review: The Present and Future of Neoadjuvant Endocrine Therapy for Breast Cancer Treatment 2021

How Effective is Neoadjuvant Endocrine Therapy (NET) in Downstaging the Axilla and Achieving Breast-Conserving Surgery? : 2020 (Morrow et al.)

Efficacy of neoadjuvant endocrine therapy compared with neoadjuvant chemotherapy in pre-menopausal patients with oestrogen receptor-positive and HER2-negative, lymph node-positive breast cancer: 2020

De-escalated chemotherapy versus endocrine therapy plus pertuzumab + trastuzumab for HR+/HER2+ early breast cancer (BC): First efficacy results from the neoadjuvant WSG-TP-II study.

New SUGGESTED management for hormone receptor-positive cN0 patients, post neoadjuvant endocrine therapy.

New SUGGESTED management for hormone receptor-positive cN1 patients, post neoadjuvant endocrine therapy.

POETIC Trial: ΔKi67 due to AI for 2 wks post B

Ki67	Diagnostic Core	Operative Core	Recurrence Rate
High	High	19%	
High	Low	9%	
Low	Low	4%	

ASCO 2021

ASCO 2021

NET 2020

NET 2020

Adjuvant Rx

Predict duration of endocrine Rx w BCI

GIM4 trial

Decision: NET or NCT

Consider Neoadjuvant Endocrine Therapy (NET)

Factors and considerations favoring neoadjuvant endocrine therapy (NET)

- Grade 1-2
- Absence of LVI by D2-40?
- ER+, PgR ≥20, Ki67 < 20
- Low Genomic Score
- cN0-1
- consider: Z0011 or AMAROS

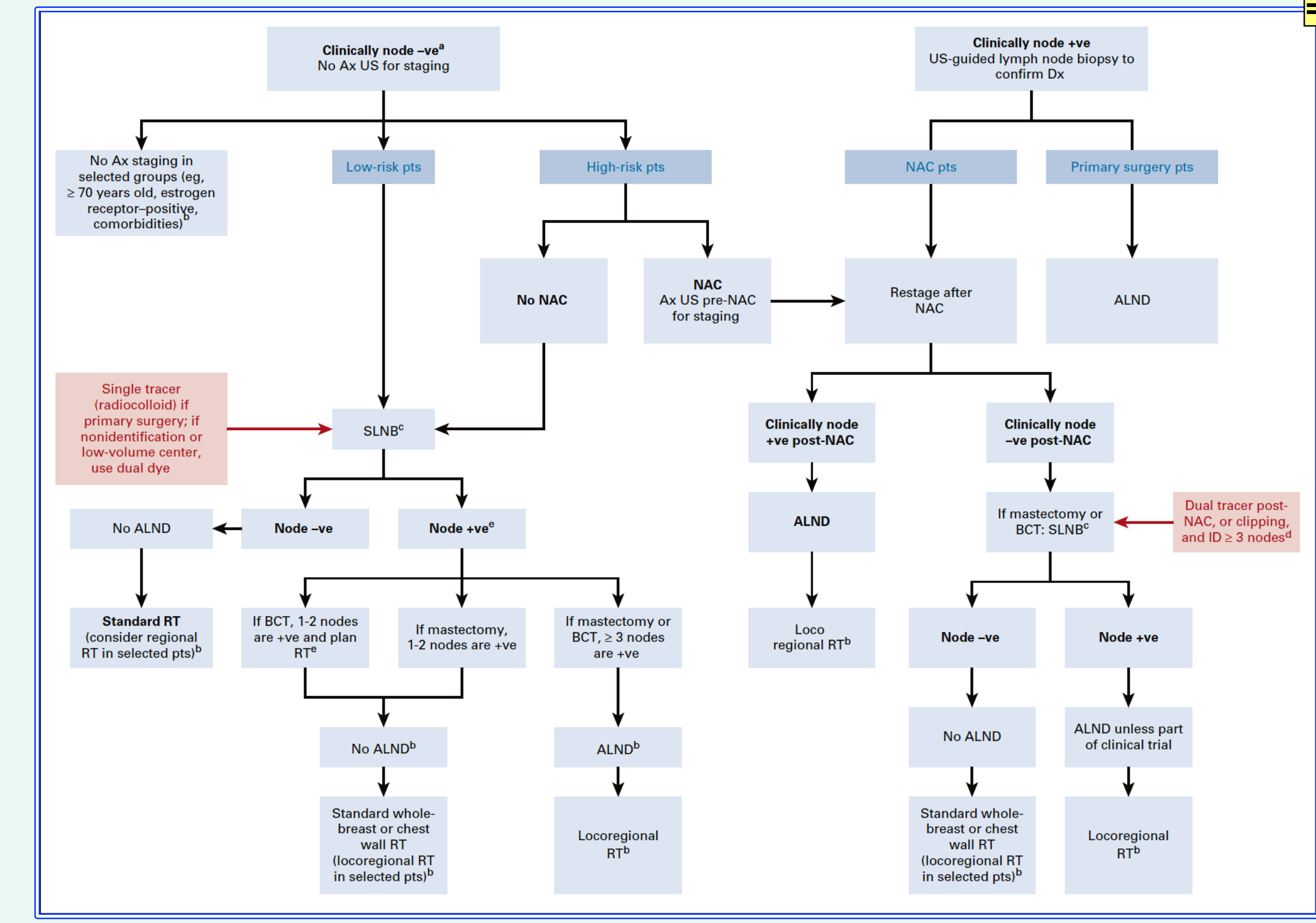
Consider Neoadjuvant Chemotherapy (NCT)

Factors favoring neoadjuvant chemotherapy (NCT)

- Grade 2-3
- LVI by D2-40 present?
- ER+ PgR < 20 Ki67 ≥ 20
- High Genomic Recurrence Score
- cN ≥ 2
- consider: B51 or A011202

Increasing genomic-based Recurrence Score →

Management of the Axilla in Early-Stage Breast Cancer: Ontario Health (Cancer CareOntario) and ASCO Guideline 2021



Deciding when to use adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer

Neoadjuvant endocrine therapy: A potential strategy for ER-positive breast cancer

Table 2 The optimal duration and optimal endocrine agents of neoadjuvant endocrine therapy

Clinical trial	Patient characteristics	Treatment arms (n)	Duration	Primary endpoint	ORR	BCS rate
Krausz-Strohbe et al ¹ , 2008	ER+ and/or PR+ Postmenopausal	LET 2.5 mg/d (33)	4-8 mo	OR by clinical palpation, mammography, ultrasound, and BCS	55% vs 24% at 4 and > 4 mo	71% vs 80% at 4 and > 4 mo
Foote et al ² , 2014	ER+ Postmenopausal	EHE (102)	3 mo vs 6 mo	OR by clinical palpation at 3 and 6 months	58.7% vs 68.3%	61.8% vs 70.6% (P = 0.02)
Carpenter et al ³ , 2014	ER+ and/or PR+ Postmenopausal	LET 2.5 mg/d (146)	3-12 mo	Optimal duration to -	-	7.5 mo
Eisemann et al ⁴ , 2001 (PC24)	ER+ and/or PR+ Postmenopausal	(A) LET 2.5 mg/d (162); (B) TAM 20 mg/d (223)	4 mo	OR by clinical palpation	55% vs 36% (P < 0.001)	45% vs 35% (P = 0.02)
Smith et al ⁵ , 2005 (IMPACT)	ER+ Postmenopausal	(A) ANA 1 mg/d (115); (B) TAM 20 mg/d (108)	12 wk	OR by ultrasound	37% vs 36% (P = 0.87)	41% vs 31% (P = 0.23)
Casalini et al ⁶ , 2006 (TRIOACT)	ER+ and/or PR+ Postmenopausal	(A) ANA 1 mg/d (225); (B) TAM 20 mg/d (223)	3 mo	OR by ultrasound	50.0% vs 46.2% (P = 0.037)	38.1% vs 29.9% (P = 0.11)
Singh et al ⁷ , 2015	ER+ and/or PR+ Premenopausal	(A) EHE (76); (B) TAM 20 mg/d (75)	3 mo	OR by clinical palpation	76.3% vs 49% (P = 0.05)	36.9% vs 20% (P = 0.05)
Kuter et al ⁸ , 2012 (NEWEST)	ER+ Postmenopausal	(A) FUL 500 mg/16 wk (109); (B) FUL 250 mg/16 wk (102)	16 wk	Expression of Ki67	17.4 vs 11.8% at week 4; 22.9 vs 20.6% at week 16	-
Quenet-Turner et al ⁹ , 2015	ER+ Postmenopausal	(A) ANA 1 mg/d (81); (B) FUL 500 mg/16 wk (79)	6 mo	OR by clinical palpation	58.9% vs 53.8%	58.9% vs 50%
Goussard et al ¹⁰ , 2014 (CARMENA 02)	ER+ and/or PR+ Postmenopausal	(A) ANA 1 mg/d (99); (B) FUL 500 mg/16 wk (95)	6 mo	OR by clinical palpation	52.6% vs 36.8%	57.6% vs 50% (P = 0.5 not significant)
Ellis et al ¹¹ , 2011 (ACOSOG Z1031)	ER+ (Allred score ≥ 8) Postmenopausal	(A) EHE 25 mg/d (124); (B) LET 2.5 mg/d (126); (C) ANA 1 mg/d (125)	16-18 wk	OR by clinical palpation	69.1% vs 62.9% vs 74.8%	45.2% vs 40% vs 48.7%
Tortorella et al ¹² , 2007	ER+ T2-T3N0-1 Postmenopausal	LET 2.5 mg/d plus Goserelin 11.25 mg/3 mo (52)	4 mo	OR by clinical palpation	50%	47%
Manola et al ¹³ , 2012 (STAGE)	ER+ and/or PR+ Postmenopausal	(A) ANA 1 mg/d (106); (B) goserelin 3.6 mg/16 wk (106); (C) TAM 20 mg/d (106); (D) goserelin 3.6 mg/16 wk (106)	24 wk	OR by ultrasound	70.4% vs 50.5% (P = 0.006)	85.7% vs 67.6%
Dhillon et al ¹⁴ , 2019 (TRENDS)	ER+ and/or PR+ Postmenopausal	(A) Ergosterin + letrozole (26); (B) degarelix + letrozole (25)	6 mo	Time to optimal CPS	46.2% vs 44.0%	52.2% vs 42.3%

Neoadjuvant Endocrine Therapy in Clinical Practice: A Review Sept 21, 2021

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