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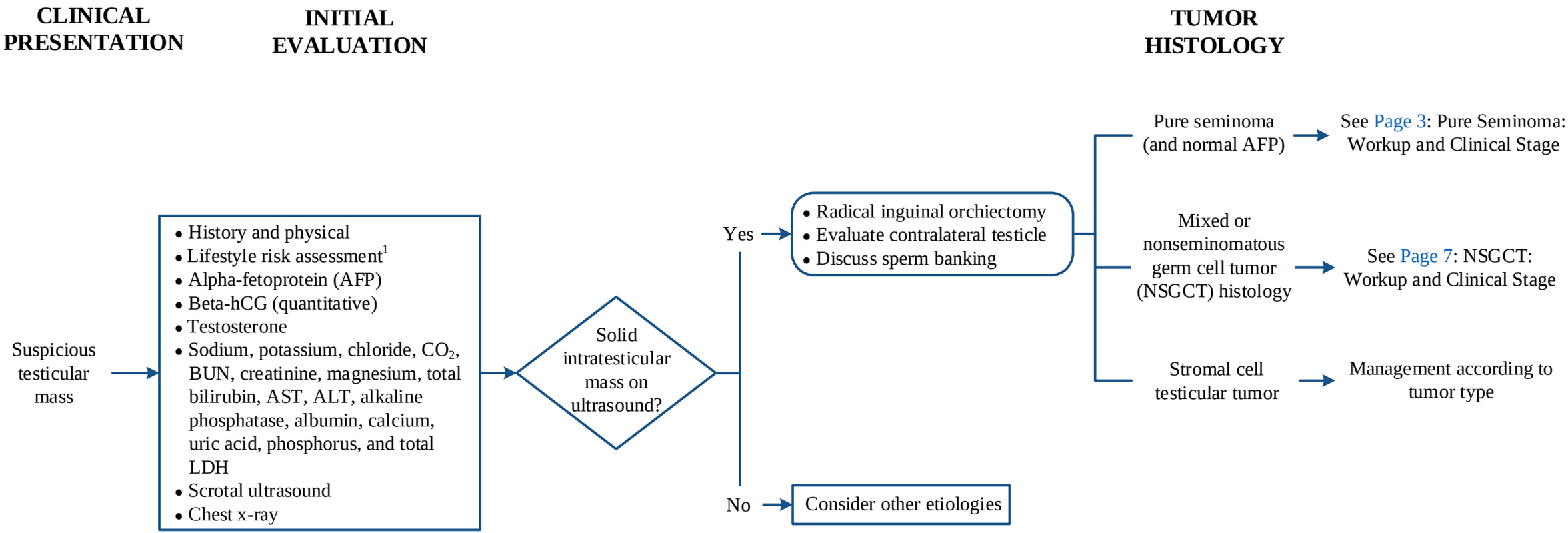
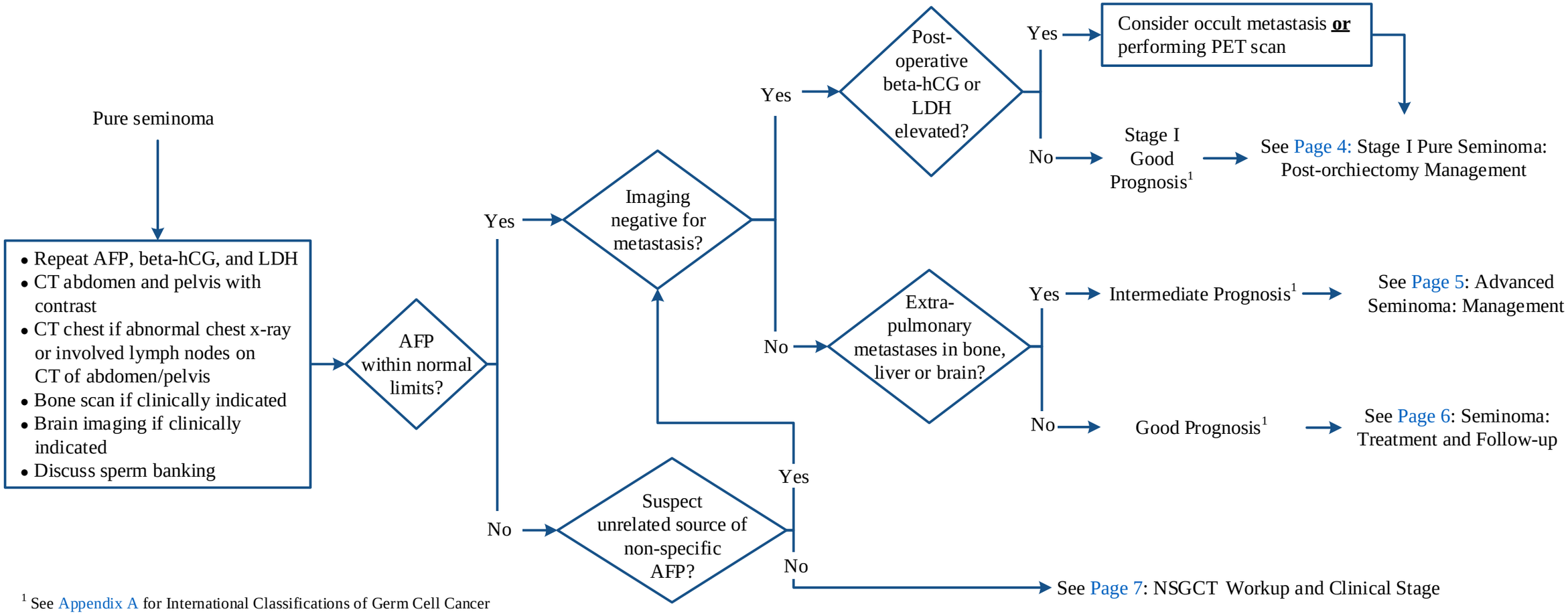
Note: Consider Clinical Trials as treatment options for eligible patients.



[1] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

Note: Consider Clinical Trials as treatment options for eligible patients.

HISTOLOGY **FURTHER WORK-UP**



[1] See Appendix A for International Classifications of Germ Cell Cancer

Note: Consider Clinical Trials as treatment options for eligible patients.

TUMOR MARKERS AND STAGING

TREATMENT

- Any pT/Tx
- N0
- M0
- S1-3

→ Stage IS:
- Beta-hCG **or** AFP elevated **and**
- Metastatic workup negative

→ Consider sperm banking

→ Any of the following present?
- Horseshoe or pelvic kidney
- Inflammatory bowel disease
- Prior radiation therapy

Yes →
Consider management options:
- Surveillance **or**
- Single-dose carboplatin AUC = 7 **or**
- Adjuvant carboplatin (AUC = 7) for 1 or 2 cycles

→ See Page 6: Seminoma: Treatment and Follow-up

No →
Most patients with clinical stage IA pure seminoma can be offered three options:
- Surveillance in compliant patients who are committed to long term follow-up **or**
- Radiation therapy to para-aortic lymph nodes with or without ipsilateral iliac lymph nodes **or**
- Adjuvant carboplatin (AUC = 7) for 1 or 2 cycles

→ See Page 6: Seminoma: Treatment and Follow-up

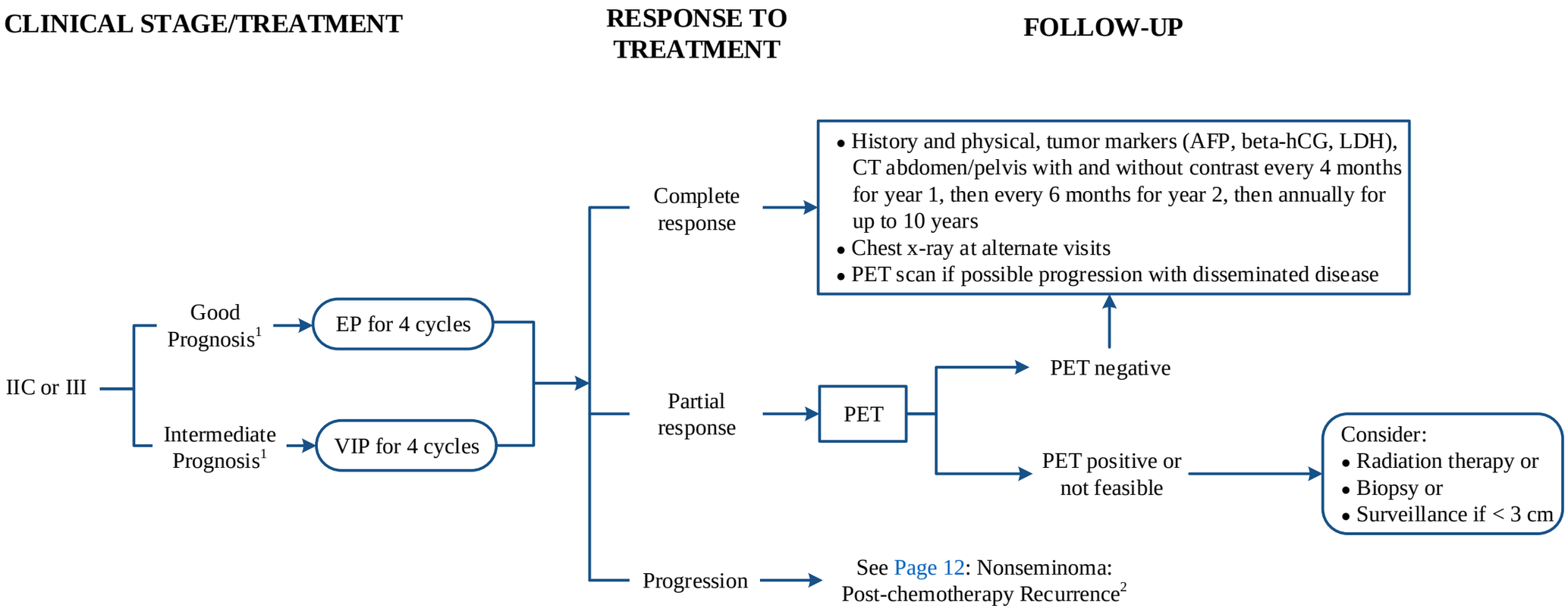
- Any pT/Tx
- N0
- M0
- S0

→ Primary tumor > 4 cm **or** pT3-4 ?

Yes → Consider sperm banking

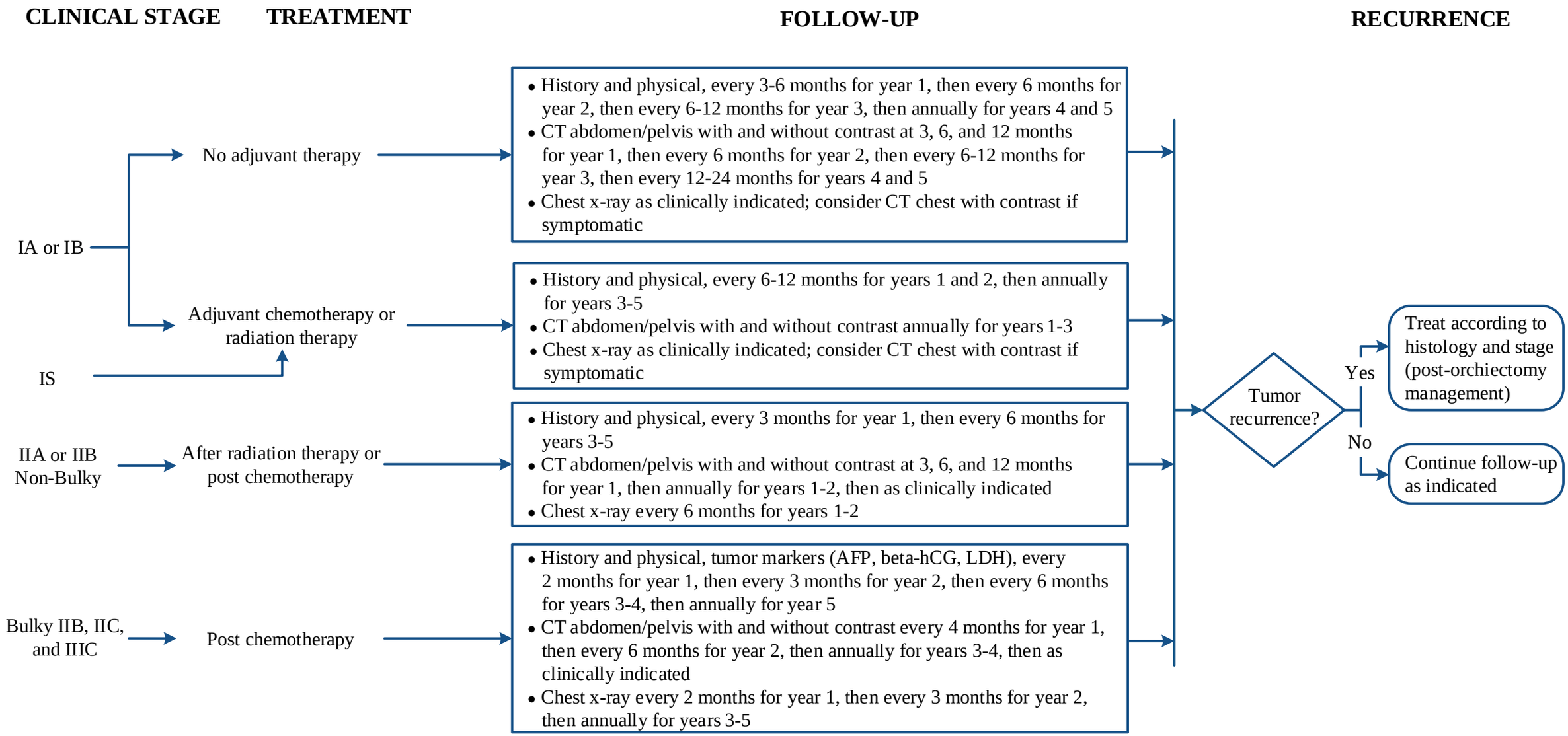
No → Consider sperm banking

Note: Consider Clinical Trials as treatment options for eligible patients.



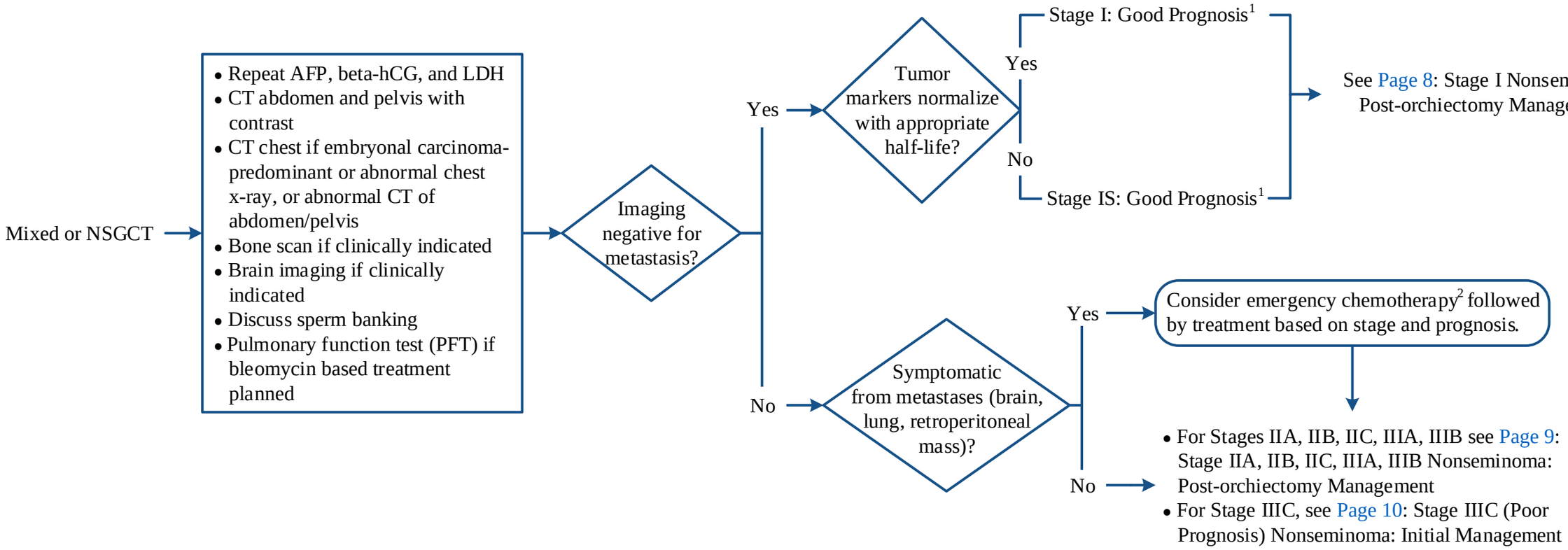
EP = etoposide and cisplatin
VIP = etoposide, ifosfamide, and cisplatin
[1] See Appendix A: International Classifications of Germ Cell Cancers
[2] Seminoma that is refractory to chemotherapy is rare and should be managed as nonseminoma

Note: Consider Clinical Trials as treatment options for eligible patients.



Note: Consider Clinical Trials as treatment options for eligible patients.

HISTOLOGY **FURTHER WORK-UP**



[1] See Appendix A: International Classifications of Germ Cell Cancer

[2] It is acceptable to administer emergency chemotherapy to selected patients with advanced metastatic NSGCT on the basis of clinical presentation before orchiectomy, and without a tissue diagnosis

Note: Consider Clinical Trials as treatment options for eligible patients.

TUMOR MARKERS AND STAGING

MANAGEMENT OPTIONS

- Any pT/Tx
- N0
- M0
- S1-3

→ Stage IS:
- Beta-hCG **or** AFP elevated **and**
- Metastatic workup negative

→ Consider sperm banking → 2 cycles BEP → See Page 11: Nonseminoma: Post-chemotherapy Management

- Any pT/Tx
- N0
- M0
- S0

→ High risk features[1]?

Yes → High Risk – probability of recurrence is approximately 50% → Consider sperm banking → Embryonal carcinoma predominant?

- **Yes** → Consider management options:
  - Surveillance (in compliant patients, pT1-2) **or**
  - Adjuvant chemotherapy (1-2 cycles BEP)
- **No** → Consider management options:
  - Surveillance (in compliant patients, pT1-2)
  - Prophylactic RPLND
  - Adjuvant chemotherapy (1-2 cycles BEP)

No → Average Risk – probability of recurrence is approximately 30% → Consider sperm banking → Consider management options:
- Surveillance (in compliant patients)
- Prophylactic RPLND

→ See Appendix B: IA, IB Nonseminoma Surveillance

BEP = bleomycin, etoposide, and cisplatin
RPLND = retroperitoneal lymph node dissection

[1] High Risk Features (in the primary tumor):
- Lymphovascular invasion
- Invasion of tunica vaginalis
- Invasion of spermatic cord or scrotum (pT3-4)
- Embryonal carcinoma predominant

Testicular Cancer

Stage IIA, IIB, IIC, IIIA, IIIB Nonseminoma: Post-orchiectomy Management

Note: Consider Clinical Trials as treatment options for eligible patients.

TUMOR MARKERS AND STAGING

- **Stage IIA, IIB**
  - Any pT/Tx
  - N1-3
  - M0
  - S0-1
- **IIC, IIIA and IIIB**
  - Any pT/Tx
  - Any N, M1a, S0-2, or N1-3, M0, S2

PRETREATMENT WORKUP

- Baseline pulmonary function testing
- Consider baseline audiometry testing
- Consider sperm banking

S1
- Total LDH < 1.5 times upper limit of normal **and**
- Beta-hCG < 5,000 mIU/mL **and**
- AFP < 1,000 ng/mL?

Yes → Good Prognosis[1]

No →

S2
- Total LDH 1.5-10 times upper limit of normal **or**
- Beta-hCG 5,000-50,000 mIU/mL **or**
- AFP 1,000-10,000 ng/mL

→ Intermediate Prognosis[1]

S3
- Total LDH > 10 times upper limit of normal **or**
- Beta-hCG > 50,000 mIU/mL **or**
- AFP > 10,000 ng/mL

→ Poor Prognosis[1]

TREATMENT

Good Prognosis[1]:

- Stage IIA, IIB **and**
- N0 (markers not elevated) **and**
- Teratoma component in primary tumor **and**
- Not embryonal carcinoma predominant tumor?

Yes → Surgical option: retroperitoneal lymph node dissection
- Stage IIA → Surveillance → See Appendix B: IA, IB Nonseminoma Surveillance
- Stage IIB → EP for 2 cycles → See Page 11: Nonseminoma: Post-chemotherapy Management

No →
- BEP for 3 cycles **or**
- EP for 4 cycles

→ See Page 11: Nonseminoma: Post-chemotherapy Management

Stage IIC, IIIA →
- BEP for 3 cycles **or**
- EP for 4 cycles

→ See Page 11: Nonseminoma: Post-chemotherapy Management

Intermediate Prognosis[1] →
- BEP for 4 cycles **or**
- Clinical trial

→ See Page 11: Nonseminoma: Post-chemotherapy Management

Poor Prognosis[1] → See Page 10: Stage IIIC (Poor Prognosis) Nonseminoma: Initial Management

EP = etoposide and cisplatin
BEP = bleomycin, etoposide, and cisplatin

[1] See Appendix A: International Classifications of Germ Cell Cancer

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Note: Consider Clinical Trials as treatment options for eligible patients.

TUMOR MARKERS AND STAGING

IIIC, Poor Prognosis:

- Any pT/Tx, Any N, M1b[1], Any S
- Total LDH > 10 times upper limit of normal **or**
- Beta-hCG > 50,000 mIU/mL **or**
- AFP > 10,000 ng/mL

TREATMENT

To avoid delay in the start of chemotherapy, the diagnosis can be made on clinical grounds and orchiectomy can be deferred

Respiratory distress **or** symptomatic brain metastases?

Yes

- Patient with respiratory distress
  - Vincristine and cisplatin
  - EP (limit to 3 days in unstable patient)
- Patient with symptomatic brain metastases
  - Primary chemotherapy with **or** without surgery if clinically indicated

No

- Baseline pulmonary function testing
- Consider baseline audiometry testing
- Consider sperm banking

- Clinical trial preferred **or**
- BEP for 4 cycles

Tumor markers normalized or plateau[2]?

Yes → See Page 11: Nonseminoma: Post-chemotherapy Management

No → Additional chemotherapy → Tumor markers normalized or plateau[2]?

After first cycle, continue for a minimum of 4 cycles:

First line
- Clinical trial (preferred) **or**
- BEP **or**
- VIP **or**

Second line
- TIP **or**
- High dose chemotherapy regimens **or**
- Stem cell transplant **or**
- Clinical trial (preferred)

EP = etoposide and cisplatin
BEP = bleomycin, etoposide, and cisplatin
VIP = etoposide, ifosfamide, and cisplatin
TIP = paclitaxel, ifosfamide, and cisplatin

[1] M1b - Distant metastases other than to non-regional lymph nodes and lungs

[2] Plateau: The observed rate of decline in tumor markers should be compared to the expected serum half-lives of 5-7 days (AFP) and 2-3 days (beta-hCG). It is common to see a slower rate of decline after the second cycle of chemotherapy. A continued rate of decline that is much less than the expected half life and does not normalize should be interpreted as a plateau. The decision to stop chemotherapy should be based on clinical judgement, taking into consideration the clinical status of the patient, which of the markers are elevated, extent of elevation, and after ruling out potential sources of spurious elevation.

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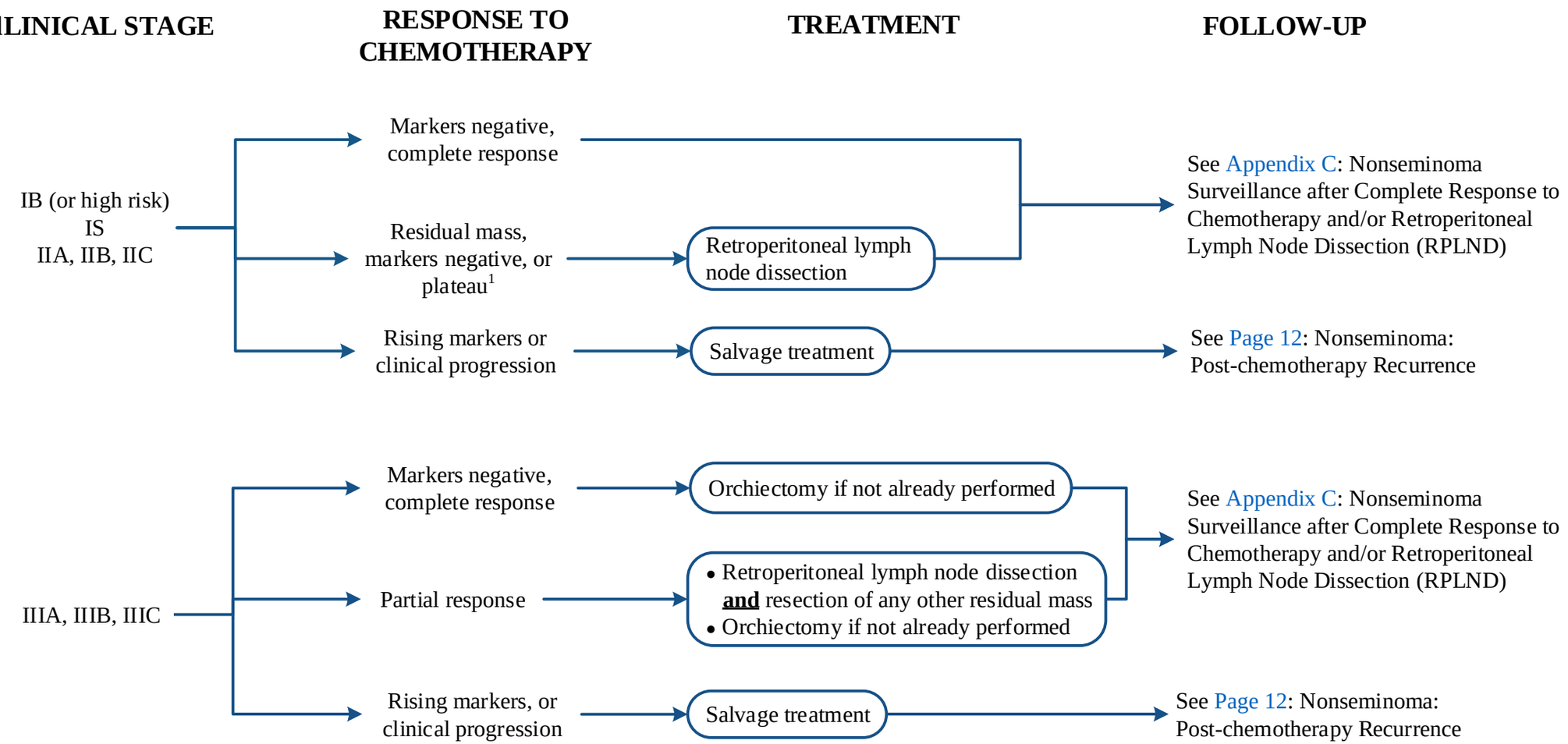
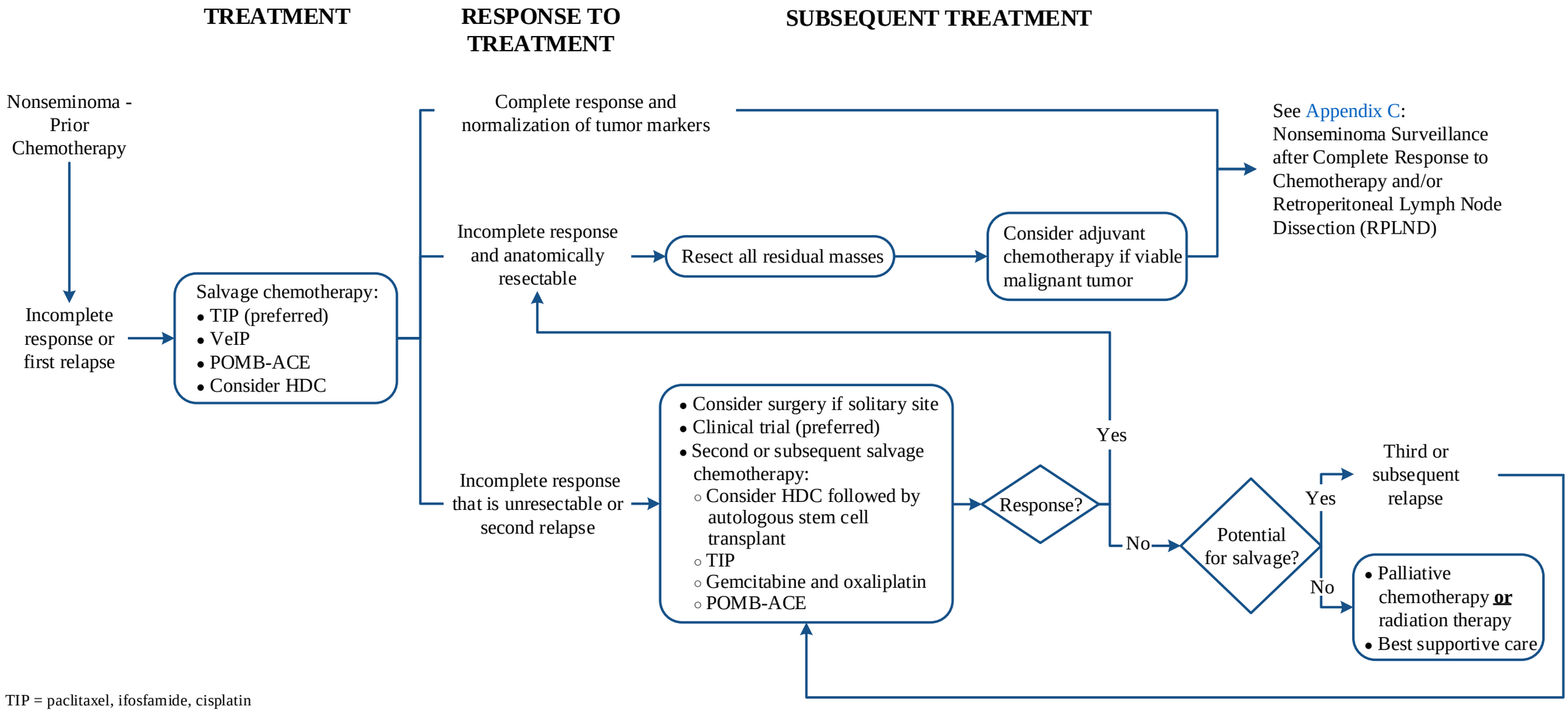
Note: Consider Clinical Trials as treatment options for eligible patients.



[1] Plateau: The observed rate of decline in tumor markers should be compared to the expected serum half-lives of 5-7 days (AFP) and 2-3 days (beta-hCG). It is common to see a slower rate of decline after the second cycle of chemotherapy. A continued rate of decline that is much less than the expected half life and does not normalize should be interpreted as a plateau. The decision to stop chemotherapy should be based on clinical judgement, taking into consideration the clinical status of the patient, which of the markers are elevated, extent of elevation, and after ruling out potential sources of spurious elevation.

Note: Consider Clinical Trials as treatment options for eligible patients.



TIP = paclitaxel, ifosfamide, cisplatin
VeIP = vinblastine, ifosfamide, cisplatin, mesna
POMB-ACE = cisplatin, vincristine, methotrexate and bleomycin alternaing with actinomycin-D, cyclophosphamide, and etoposide
HDC = high-dose chemotherapy

APPENDIX A: International Classifications for Germ Cell Cancers[1]

		Nonseminoma	Seminoma
GOOD PROGNOSIS	**FEATURES**	Testes/retroperitoneal primary **and** No non-pulmonary visceral metastases **and**	Any primary site **and** No non-pulmonary visceral metastases **and**
	All Good Markers: • **AFP**	< 1,000 ng/mL **and**	Normal
	• **Beta-hCG**	< 5,000 iu/L (1,000 ng/mL) **and**	Any value
	• **LDH**	< 1.5 times upper limit of normal	Any value
INTERMEDIATE PROGNOSIS	**FEATURES**	Testes/retroperitoneal primary **and** No non-pulmonary visceral metastases **and**	Any primary site **and** Non-pulmonary visceral metastases **and**
	Markers any of: • **AFP**	≥ 1,000 and ≤ 10,000 ng/mL **or**	Normal
	• **Beta-hCG**	≥ 5,000 iu/L and < 50,000 iu/L **or**	Any value
	• **LDH**	≥ 1.5 times normal and ≤ 10 times normal	Any value
POOR PROGNOSIS	**FEATURES**	Mediastinal primary **or** Non-pulmonary metastases	No patients classified as poor prognosis
	Markers any of: • **AFP**	> 10,000 ng/mL **or**	
	• **Beta-hCG**	≥ 50,000 iu/L (10,000 ng/mL) **or**	
	• **LDH**	> 10 times normal	

[1] From the International Germ Cell Consensus Classification from the International Germ Cell Cancer Collaborative Group

APPENDIX B: IA, IB Nonseminoma Surveillance

Year	Visits, Markers, and Chest X-ray	CT Abdomen/Pelvis with and without contrast
1	Every 1-2 months	Every 4 months
2	Every 2-3 months	Every 6 months
3	Every 3 months	Every 6 months
4	Every 4 months	Annually
5	Every 6 months	Annually
6 and above	Annually	Annually

APPENDIX C: Nonseminoma Surveillance after Complete Response to Chemotherapy and/or Retroperitoneal Lymph Node Dissection (RPLND)

Year	Visits, Markers, and Chest X-ray	CT[1] Abdomen/Pelvis with and without contrast
1	Every 2-3 months	Every 6 months
2	Every 2-3 months	Every 6-12 months
3	Every 4 months	Annually
4	Every 6 months	Annually
5	Every 6-12 months	Annually
6 and above	Annually	Every 12-24 months

[1] CT scans for patients treated with chemotherapy. Baseline CT scan for patients status post RPLND.

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Continued on next page

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DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Genitourinary Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Ana Aparicio, MD (Genitourinary Medical Oncology)
John Araujo, MD (Genitourinary Medical Oncology)
Tharakeswara K. Bathala, MD (Abdominal Imaging Department)
Seungtaek Choi, MD (Radiation Oncology)
Paul Corn, MD (Genitourinary Medical Oncology)
Olga N. Fleckenstein♦
Eric Jonasch, MD (Genitourinary Medical Oncology)
Karen Hoffman, MD (Radiation Oncology)
Jose Karam, MD (Urology)
Deborah Kuban, MD (Radiation Oncology)Ŧ
Christopher Logothetis, MD (Genitourinary Medical Oncology)
Yago Nieto, MD (Stem Cell Transplantation)
Louis Pisters, MD (Urology)Ŧ
Padmanee Sharma, MD (Genitourinary Medical Oncology)
Arlene O. Siefker-Radtke, MD (Genitourinary Medical Oncology)
Nizar M. Tannir, MD (Genitourinary Medical Oncology)
Shi-Ming Tu, MD (Genitourinary Medical Oncology)Ŧ
John Ward, MD (Urology)
Mary Lou Warren, DNP, RN, CNS-CC♦
Amado Zurita-Saavedra, MD (Genitourinary Medical Oncology)

Ŧ Core Development Team Lead
♦ Clinical Effectiveness Development Team