Oncology Board Review

Brenda Shinar, MD

Question 1.

- A; Counseling and genetic testing

Manage a patient with newly diagnosed breast cancer who meets criteria for genetic testing

- Inheirited genetic mutations account for <10% of all breast cancers
  - BRCA 1 and 2
  - Li-Fraumeni
  - Cowden syndrome
- Results of testing may determine surgical planning:
  - Breast conserving surgical resection with intensive surveillance for a second breast primary and ovarian cancer
  - Prophylactic bilateral mastectomy and SO without surveillance

Who to test?

Personal history of breast cancer PLUS (NOT all criteria are listed):

- Diagnosed ≤ age 45
- Diagnosed ≤ age 50
  - ≥ 1 first, second, or third degree relative with breast ca dx ≤ age 50 or
  - ≥ 1 first,second, or third degree relative with ovarian, PPC, or fallopian tube cancer at any age or
  - 2 or more breast primaries
- Diagnosed age ≤ 60
  - with triple negative breast cancer (ER-PR-Her2-)

Question 2.

- B; 5-Fluorouracil, leucovorin, and oxaliplatin (FOLFOX)

Manage stage III colon cancer

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NCCN Guidelines Version 3.2013 Staging Colon Cancer

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Colon Cancer Table of Contents
Discussion

Table 1. Definitions for T, N, M

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria[a]
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into the pericolorectal tissues
T4a	Tumor penetrates to the surface of the visceral peritoneum[b]
T4b	Tumor directly invades or is adherent to other organs or structures[b,c]

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1-3 regional lymph nodes
N1a	Metastasis in one regional lymph node
N1b	Metastasis in 2-3 regional lymph nodes
N1c	Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in four or more regional lymph nodes
N2a	Metastasis in 4-6 regional lymph nodes
N2b	Metastasis in seven or more regional lymph nodes

Distant Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis
M1a	Metastasis confined to one organ or site (eg, liver, lung, ovary, nonregional node)
M1b	Metastases in more than one organ/site or the peritoneum

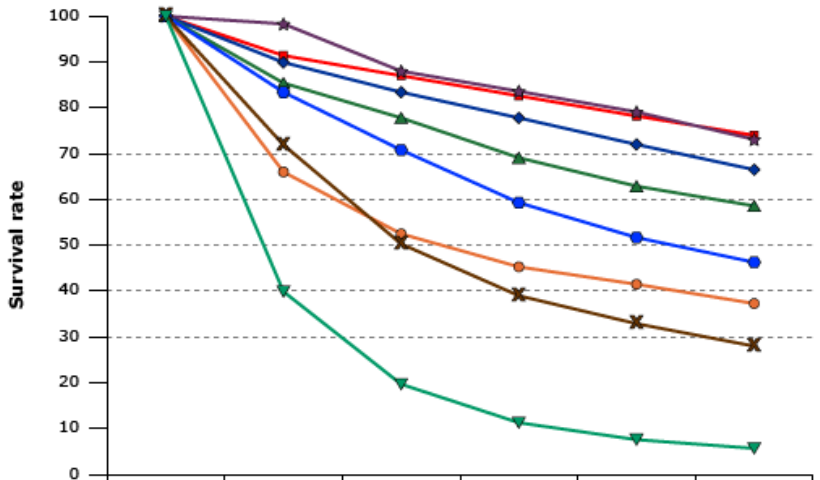
Table 2. Anatomic Stage/Prognostic Groups

Stage	T	N	M	Dukes*	MAC*
0	Tis	N0	M0	-	-
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1-T2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3-T4a	N1/N1c	M0	C	C2
	T2-T3	N2a	M0	C	C1/C2
	T1-T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3-T4a	N2b	M0	C	C2
	T4b	N1-N2	M0	C	C3
IVA	Any T	Any N	M1a	-	-
IVB	Any T	Any N	M1b	-	-

Note: cTNM is the clinical classification, pTNM is the pathologic classification. The y prefix is used for those cancers that are classified after neoadjuvant pretreatment (e.g., ypTNM). Patients who have a complete pathologic response are ypT0N0cM0 that may be similar to Stage Group 0 or I. The r prefix is to be used for those cancers that have recurred after a disease-free interval (rTNM).

*Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (Any TN1 M0 and Any T N2 M0). MAC is the modified Astler-Coller classification.

Observed survival rates for 28,491 cases with adenocarcinoma of the colon



	0	1	2	3	4	5
I	100.0	91.4	87.0	82.6	78.2	74.0
IIA	100.0	89.9	83.4	77.8	72.0	66.5
IIB	100.0	85.4	77.8	69.1	62.9	58.6
IIC	100.0	66.0	52.5	45.3	41.5	37.3
IIIA	100.0	98.3	88.0	83.6	79.1	73.1
IIIB	100.0	83.4	70.8	59.3	51.7	46.3
IIIC	100.0	71.9	50.3	39.0	32.9	28.0
IV	100.0	39.9	19.7	11.3	7.6	5.7

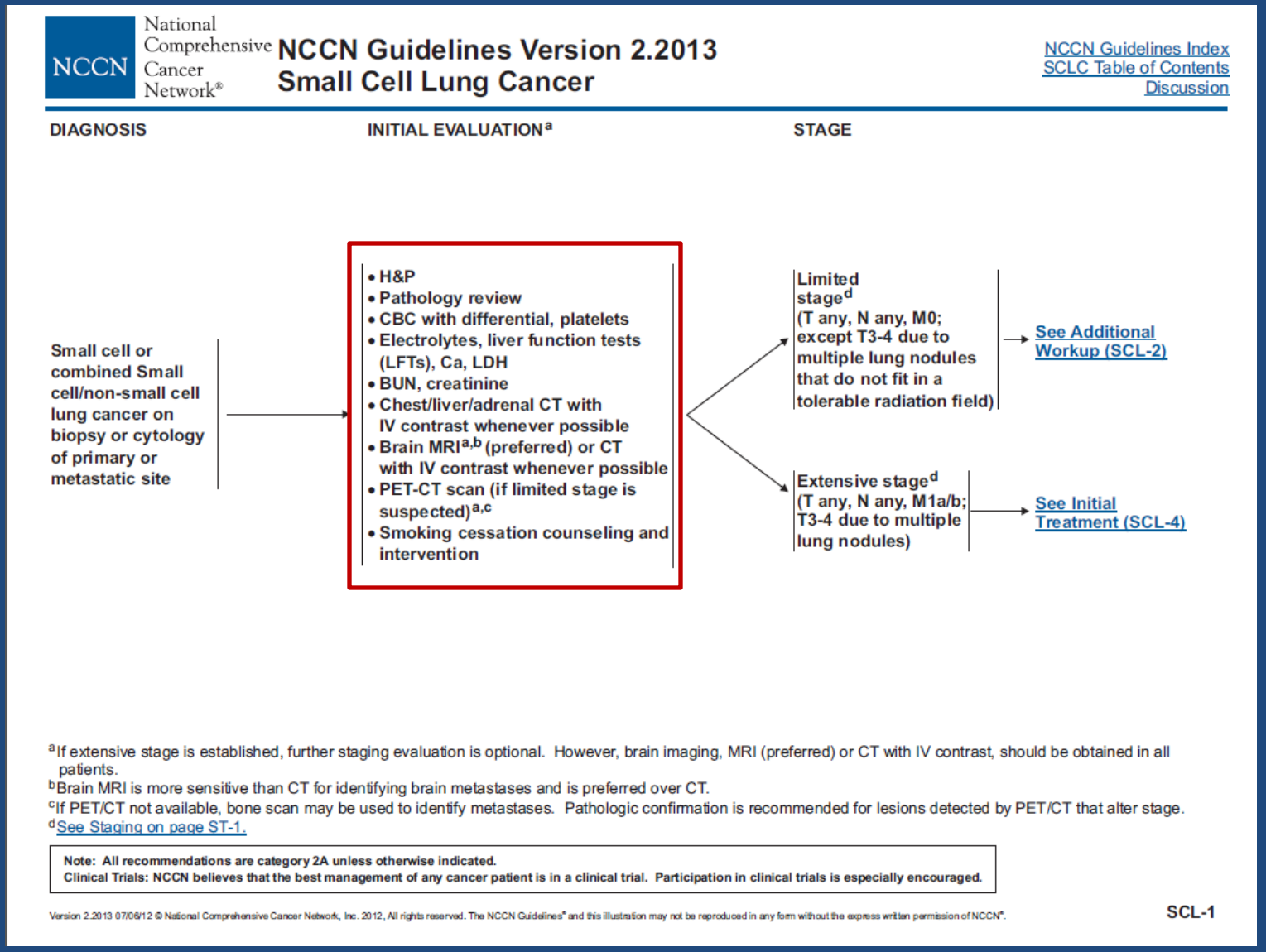
Years from diagnosis

- Adjuvant chemotherapy has been shown to improve survival in stage III (node positive) colon cancer
  - 30% reduction in disease recurrence
  - 20-30% reduction in mortality
- Adjuvant chemo should be started within 6 to 8 weeks of surgery
- A 6 month course of oxaliplatin-based regimen (FOLFOX) is preferred (superior to 5-FU and leukovorin alone)
- Radiation therapy is not used in stage III colon cancer, but is used in stage II and III rectal cancer

Question 3.

- A; Chemotherapy with adjunctive radiation therapy

Diagnose and Manage Limited Stage Small Cell Lung Cancer



TNM staging system for lung cancer (7th edition)

Primary tumor (T)	
T1	Tumor ≤3 cm diameter, surrounded by lung or visceral pleura, without invasion more proximal than lobar bronchus*
T1a	Tumor ≤2 cm in diameter
T1b	Tumor >2 cm but ≤3 cm in diameter
T2	Tumor >3 cm but ≤7 cm, or tumor with any of the following features:
	Involves main bronchus, ≥2 cm distal to carina
	Invades visceral pleura
	Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
T2a	Tumor >3 cm but ≤5 cm
T2b	Tumor >5 cm but ≤7 cm
T3	Tumor >7 cm or any of the following:
	Directly invades any of the following: chest wall, diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium, main bronchus <2 cm from carina (without involvement of carina)
	Atelectasis or obstructive pneumonitis of the entire lung
	Separate tumor nodules in the same lobe
T4	Tumor of any size that invades the mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, or with separate tumor nodules in a different ipsilateral lobe
Regional lymph nodes (N)	
N0	No regional lymph node metastases
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural or pericardial effusion
M1b	Distant metastasis (in extrathoracic organs)

Limited Stage is I-IIIB except for T3 and T4

Stage groupings			
Stage IA	T1a-T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T1a,T1b,T2a	N1	M0
	T2b	N0	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a,T1b,T2a,T2b	N2	M0
	T3	N1,N2	M0
	T4	N0,N1	M0
Stage IIIB	T4	N2	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1a or M1b

NCCN Guidelines Version 2.2013
Small Cell Lung Cancer

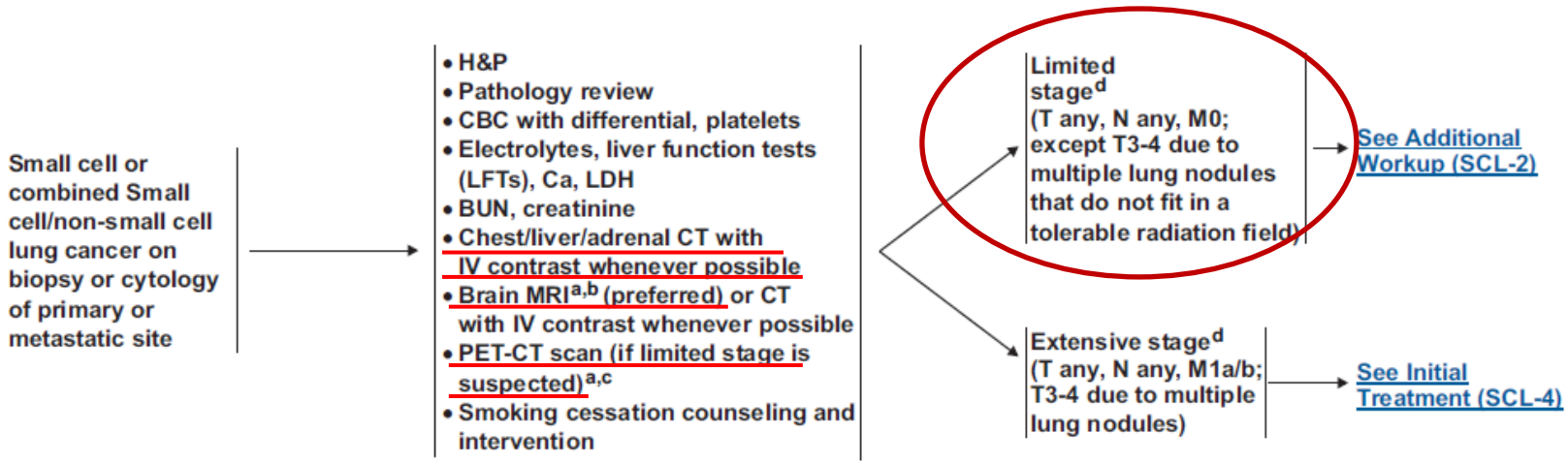
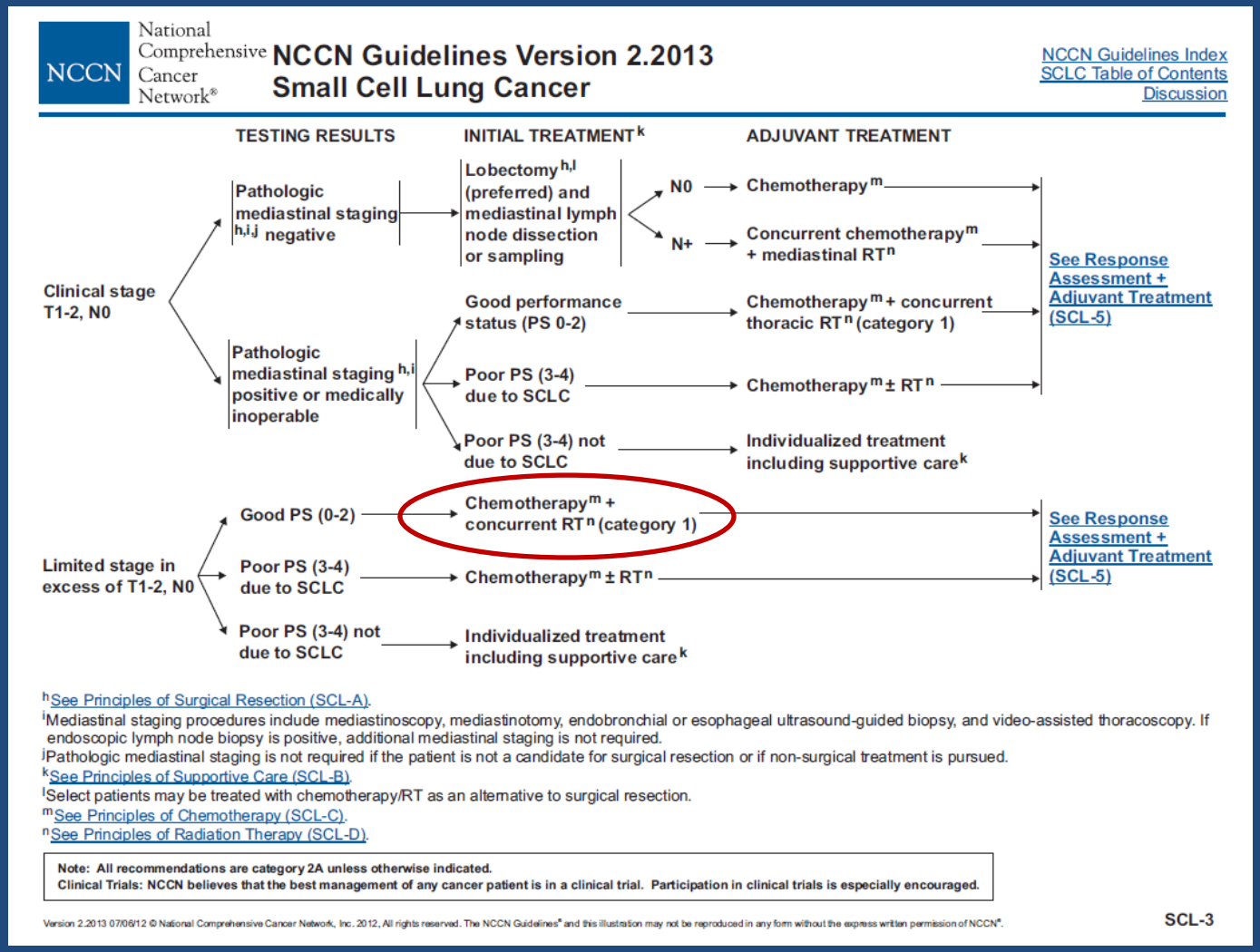


Table 1 **- Definition of small cell lung cancer consists of two stages:**
(1) Limited-stage: AJCC (7th edition) Stage I-III (T any, N any, M0) that can be safely treated with definitive radiation doses. Excludes T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan.
(2) Extensive-stage: AJCC (7th edition) Stage IV (T any, N any, M 1a/b), or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan.

[a] If extensive stage is established, further staging evaluation is optional. However, brain imaging, MRI (preferred) or CT with IV contrast, should be obtained in all patients.
[b] Brain MRI is more sensitive than CT for identifying brain metastases and is preferred over CT.
[c] If PET/CT not available, bone scan may be used to identify metastases. Pathologic confirmation is recommended for lesions detected by PET/CT that alter stage.
[d] See Staging on page ST-1.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Manage limited-stage small cell lung cancer



Don't forget to add prophylactic whole brain radiation in this patient!

Question 4.

- C; Surgery and adjuvant chemotherapy

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NCCN Guidelines Version 2.2013 Staging Non-Small Cell Lung Cancer

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Discussion

Table 1. Definitions for T, N, M*

T	Primary Tumor
TX	Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤ 3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)[a]
	T1a Tumor ≤ 2 cm in greatest dimension
	T1b Tumor > 2 cm but ≤ 3 cm in greatest dimension
T2	Tumor > 3 cm but ≤ 7 cm or tumor with any of the following features:[b] Involves main bronchus, ≥ 2 cm distal to the carina Invades visceral pleura Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
	T2a Tumor > 3 cm but ≤ 5 cm in greatest dimension
	T2b Tumor > 5 cm but ≤ 7 cm in greatest dimension
T3	Tumor > 7 cm or one that directly invades any of the following: chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus < 2 cm distal to the carina[a] but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe
T4	Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; separate tumor nodule(s) in a different ipsilateral lobe

N	Regional Lymph Nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

M	Distant Metastasis
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
	M1a Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural (or pericardial) effusion[c]
	M1b Distant metastasis

[a] The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximally to the main bronchus, is also classified as T1.

[b] T2 tumors with these features are classified T2a if ≤ 5 cm or if size cannot be determined, and T2b if > 5 cm but ≤ 7 cm

[c] Most pleural (and pericardial) effusions with lung cancer are due to tumor. In a few patients, however, multiple cytopathologic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is nonbloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging element and the patient should be classified as T1, T2, T3, or T4.

*Used with permission. Goldstraw P, Crowley J, Chansky K, et al. The IASLC Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumors. J Thorac Oncol 2007;2:706-714.

Treat a patient with early-stage non-small cell lung cancer (NSCLC)

NCCN Guidelines Version 2.2013 Staging
Non-Small Cell Lung Cancer

Table 2. Anatomic Stage and Prognostic Groups

Occult Carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
Stage IV	Any T	Any N	M1a
	Any T	Any N	M1b

Surgery is indicated for patients with stage I and II disease with no mediastinal involvement.

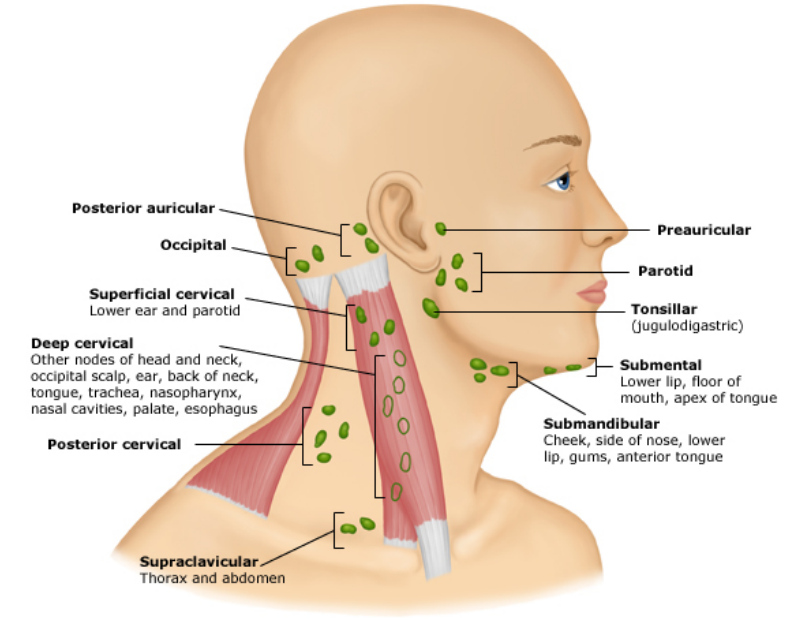
Adjuvant chemotherapy with a cisplatin-based regimen should be given to patients with surgically resected NSCLC in stage II to reduce recurrent disease and mortality. (5% reduction in risk of death at 5 years).

Adjuvant chemotherapy should be considered in high risk stage 1B patients after surgery for benefit.
(> 4 cm, et cetera)

Question 5.

- A; endoscopic evaluation of the oropharynx

Evaluate a patient for head and neck cancer

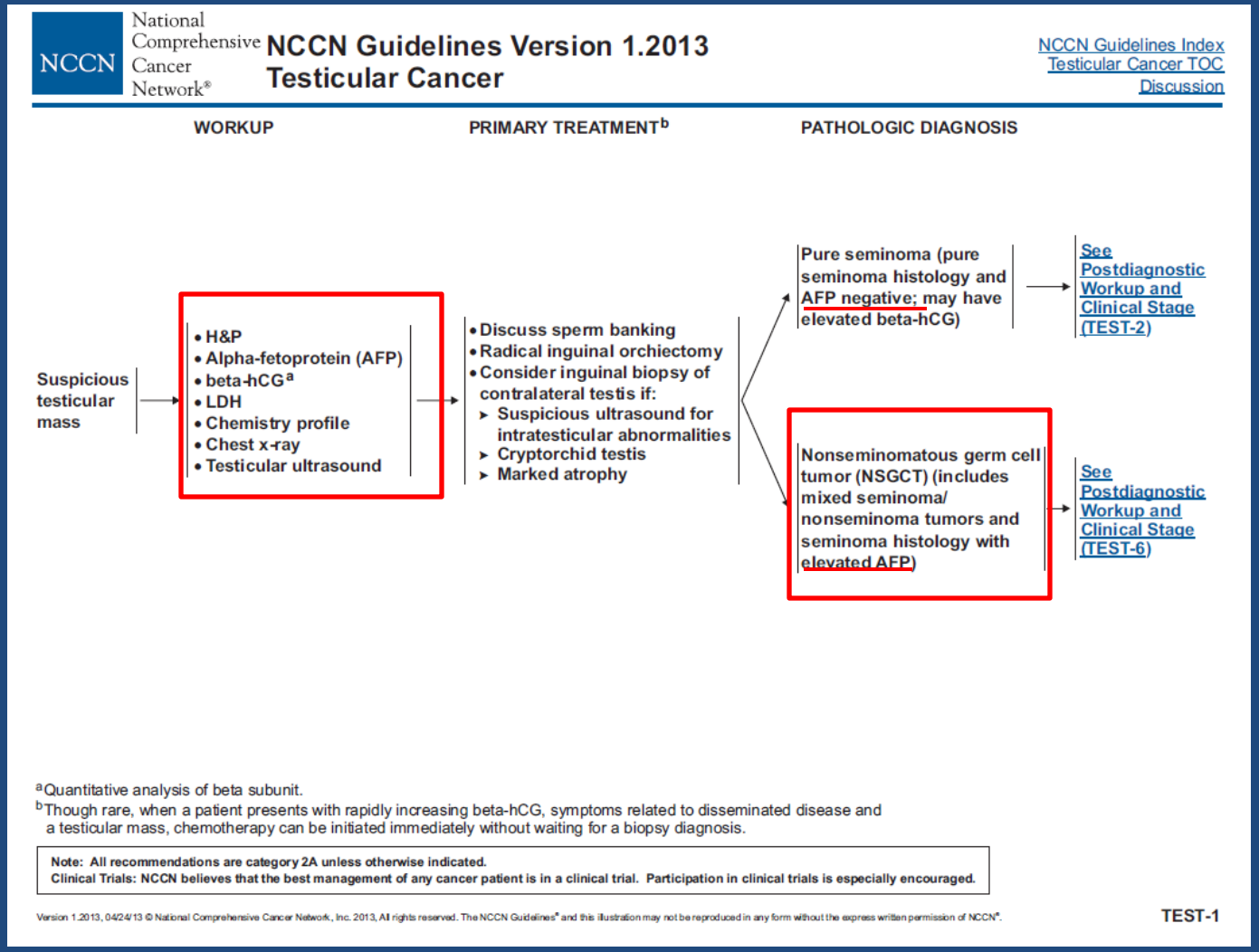


- FIRST step would be ENT consult for triple scope endoscopy to look for a primary cancer; if the endoscopy is negative, pursue FNA of node
- Excisional biopsy of node would potentially alter tissue planes needed for better resection
- PET/CT could be done AFTER tissue diagnosis is made

Question 6.

- C; Nonseminoma germ cell tumor

Diagnose Testicular Cancer:
AFP is the KEY to Pathology!



Question 7.

- A; Chemotherapy and radiation therapy

Manage a patient with early-stage Hodgkin lymphoma

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NCCN Guidelines Version 1.2013 Staging Hodgkin Lymphoma

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Discussion

Table 1

Definitions of Stages in Hodgkin's Disease[1]

Stage I Involvement of a single lymph node region (I) or localized involvement of a single extralymphatic organ or site (I_E).

Stage II Involvement of two or more lymph node regions on the same side of the diaphragm (II) or localized involvement of a single associated extralymphatic organ or site and its regional lymph node(s), with or without involvement of other lymph node regions on the same side of the diaphragm (II_E).

Note: The number of lymph node regions involved may be indicated by a subscript (eg, II_3).

Stage III Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized involvement of an associated extralymphatic organ or site (IIIE), by involvement of the spleen (III_S), or by both (III_{E+S}).

Stage IV Disseminated (multifocal) involvement of one or more extralymphatic organs, with or without associated lymph node involvement, or isolated extralymphatic organ involvement with distant (nonregional) nodal involvement.

A No systemic symptoms present
B Unexplained fevers >38°C; drenching night sweats; or weight loss >10% of body weight (within 6 months prior to diagnosis)

Adapted from **Carbone PP, Kaplan HS, Musshoff K, et al. Report of the Committee on Hodgkin's Disease Staging Classification. Cancer Res 1971;31(11):1860-1.**

For most patients with early stage, favorable disease, (lack of B symptoms, bulky disease), treatment with combined chemo and radiation is preferred.

Manage a patient with early-stage Hodgkin lymphoma

Favorable prognosis — As described above, cooperative research groups have used varying definitions of favorable prognosis early stage disease. The following treatment options are generally used in patients with favorable prognosis stage I-II disease. There are differences in relapse rates and toxicity between treatment approaches. (See "Treatment of favorable prognosis early (stage I-II) classical Hodgkin lymphoma".)

- ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) for three (preferred) to four cycles, followed by involved field irradiation to 30 Gy with fields encompassing the initially involved lymph node site (involved-site radiation therapy). This approach has the lowest relapse rate.
- ABVD for two cycles, followed by involved-field (or perhaps involved-site) irradiation with 20 Gy may be sufficient treatment for patients with favorable disease as defined by the GHSG. This regimen has lower toxicity.
- ABVD for four to six cycles without radiation therapy. This is an emerging option for patients at risk of long-term complications from radiotherapy. However, this option is associated with higher recurrence rates compared with combined modality therapy. There are several trials studying the use of ABVD alone versus ABVD and radiation therapy in patients who are PET negative after two to three cycles of chemotherapy. Two of these trials (EORTC H10 trial and UK RAPID trial) show fewer early recurrences in patients assigned to combined modality therapy. The impact on late toxicities and survival is not yet known. Both trials need much longer follow-up before firm recommendations can be made regarding the role of PET scanning in making initial treatment decisions. (See "Treatment of favorable prognosis early (stage I-II) classical Hodgkin lymphoma", section on 'Chemotherapy alone'.)

Hodgkin Lymphoma International Prognostic Score (IPS)

The International Prognostic Score for Hodgkin lymphoma

One point is given for each of the characteristics below present in the patient, for a total score ranging from zero to seven

- Serum albumin <4 g/dL
- Hemoglobin <10.5 g/dL
- Male gender
- Age >45 years
- Stage IV disease
- White blood cell count ≥15,000/microL
- Absolute lymphocyte count <600/microL and/or <8 percent of the total white blood cell count

When applied to an initial group of 5141 patients with advanced Hodgkin lymphoma treated prior to 1992 with combination chemotherapy with or without radiation therapy, five-year overall survival (OS) and freedom from progression (FFP) rates according to score were as follows[1]:

Score	Five-year FFP, percent	Five-year OS, percent
0	84	89
1	77	90
2	67	81
3	60	78
4	51	61
5 or more	42	56

When applied to 740 patients with advanced Hodgkin lymphoma treated with curative intent with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) from 1980 to 2010, five-year OS and FFP rates according to score were as follows[2]:

Score	Five-year FFP, percent	Five-year OS, percent
0	88	98
1	84	97
2	80	91
3	74	88
4	67	85
5 or more	62	67

≥ 4 risk factors in stage III and IV disease changes the preferred chemo regimen!

Question 8.

- D; No further treatment

Manage early-stage melanoma

Risk factors for melanoma:

- Personal history of melanoma
- Family history
- Intermittent, intense sun exposure (> 5 sunburns as a child: risk 2x)
- Multiple atypical moles

Primary tumor (T)	
TX	Primary tumor cannot be assessed (eg, curettaged or severely regressed primary)
T0	No evidence of primary tumor
Tis	Melanoma in situ
T1	≤1.0 mm
	a: without ulceration and mitoses <1/mm^2
	b: with ulceration or mitoses ≥1/mm^2
T2	1.01-2.0 mm
	a: without ulceration
	b: with ulceration
T3	2.01-4.0 mm
	a: without ulceration
	b: with ulceration
T4	>4.0 mm
	a: without ulceration
	b: with ulceration
Regional lymph nodes (N)	
NX	Patients in whom the regional nodes cannot be assessed (eg, previously removed for another reason)
N0	No regional metastases detected
N1	One lymph node
	a: micrometastases*
	b: macrometastases•
N2	Two or three lymph nodes
	a: micrometastases*
	b: macrometastases•
	c: in-transit met(s)/satellite(s) without metastatic lymph nodes
N3	Four or more metastatic lymph nodes, or matted lymph nodes, or in-transit met(s)/satellite(s) with metastatic lymph node(s)
Distant metastasis (M)	
M0	No detectable evidence of distant metastases
M1a	Metastases to skin, subcutaneous, or distant lymph node, normal serum LDH
M1b	Lung metastases, normal LDH
M1c	Metastasis to other visceral metastases with a normal LDH, or any distant metastases and an elevated LDH

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Melanoma

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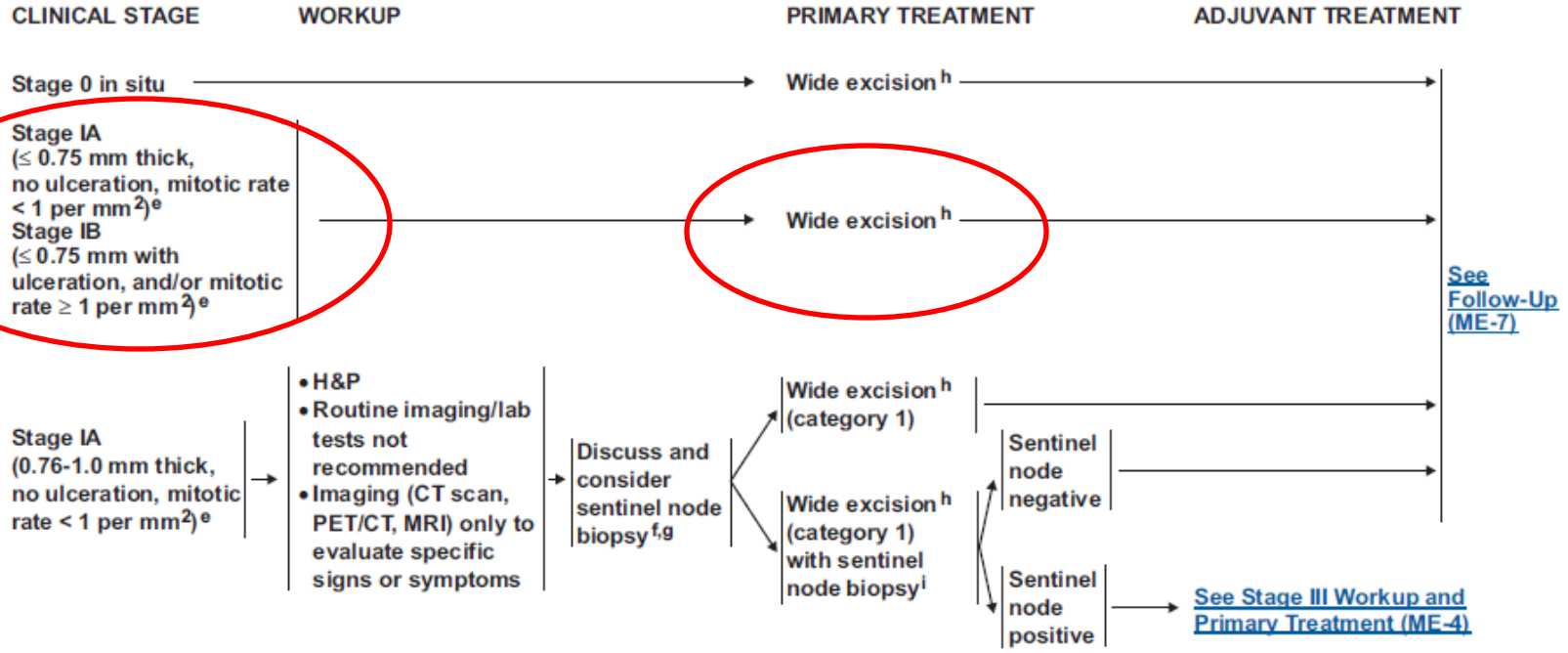


[e]In general, SLNB is not recommended for primary melanomas ≤ 0.75 mm thick, unless there is significant uncertainty about the adequacy of microstaging. For melanomas 0.76-1.0 mm thick, SLNB may be considered in the appropriate clinical context. In patients with thin melanomas (≤ 1.0 mm), apart from primary tumor thickness, there is little consensus as to what should be considered "high-risk features" for a positive SLN. Conventional risk factors for a positive SLN, such as ulceration, high mitotic rate, and LVI, are very uncommon in melanomas ≤ 0.75 mm thick; when present, SLNB may be considered on an individual basis.

[f]Decision to perform SLNB may be based on significant patient comorbidities, patient preference or other factors.

[g]Sentinel node biopsy is an important staging tool, but the impact of SLNB on overall survival is unclear.

[h]See Principles of Surgical Margins for Wide Excision of Primary Melanoma (ME-B).

[i]Sentinel lymph nodes should be evaluated with multiple sectioning and immunohistochemistry.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

PRINCIPLES OF SURGICAL MARGINS FOR WIDE EXCISION OF PRIMARY MELANOMA

Tumor Thickness	Recommended Clinical Margins[2]
In situ[1]	0.5 cm
≤ 1.0 mm	1.0 cm (category 1)
1.01 - 2 mm	1-2 cm (category 1)
2.01 - 4 mm	2.0 cm (category 1)
> 4 mm	2.0 cm (category 1)

- Margins may be modified to accommodate individual anatomic or functional considerations.

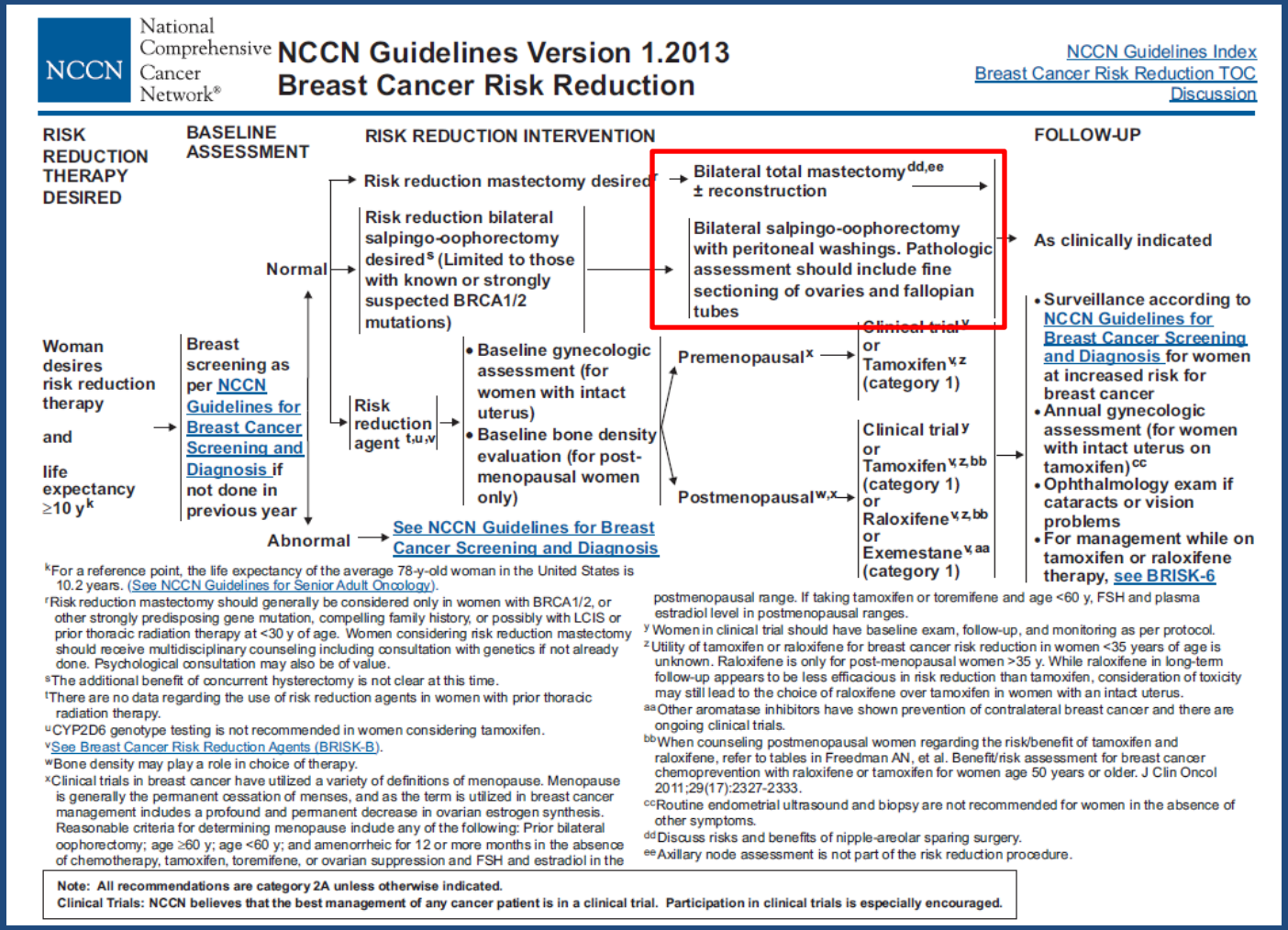
Common Follow-up Recommendations For All Patients:

- At least annual skin exam for life
- Educate patient in monthly self skin exam (and monthly lymph node self exam for Stage IA - IV NED)
- Routine blood tests are not recommended
- Radiologic imaging is indicated to investigate specific signs or symptoms
- Follow-up schedule influenced by risk of recurrence, prior primary melanoma, and family history of melanoma, and includes other factors, such as atypical moles/dysplastic nevi, and patient/physician concern.

Question 9.

- B; Bilateral salpingo-oopherectomy and bilateral mastectomy

Manage a patient with the BRCA gene mutation who is at increased risk for developing ovarian cancer



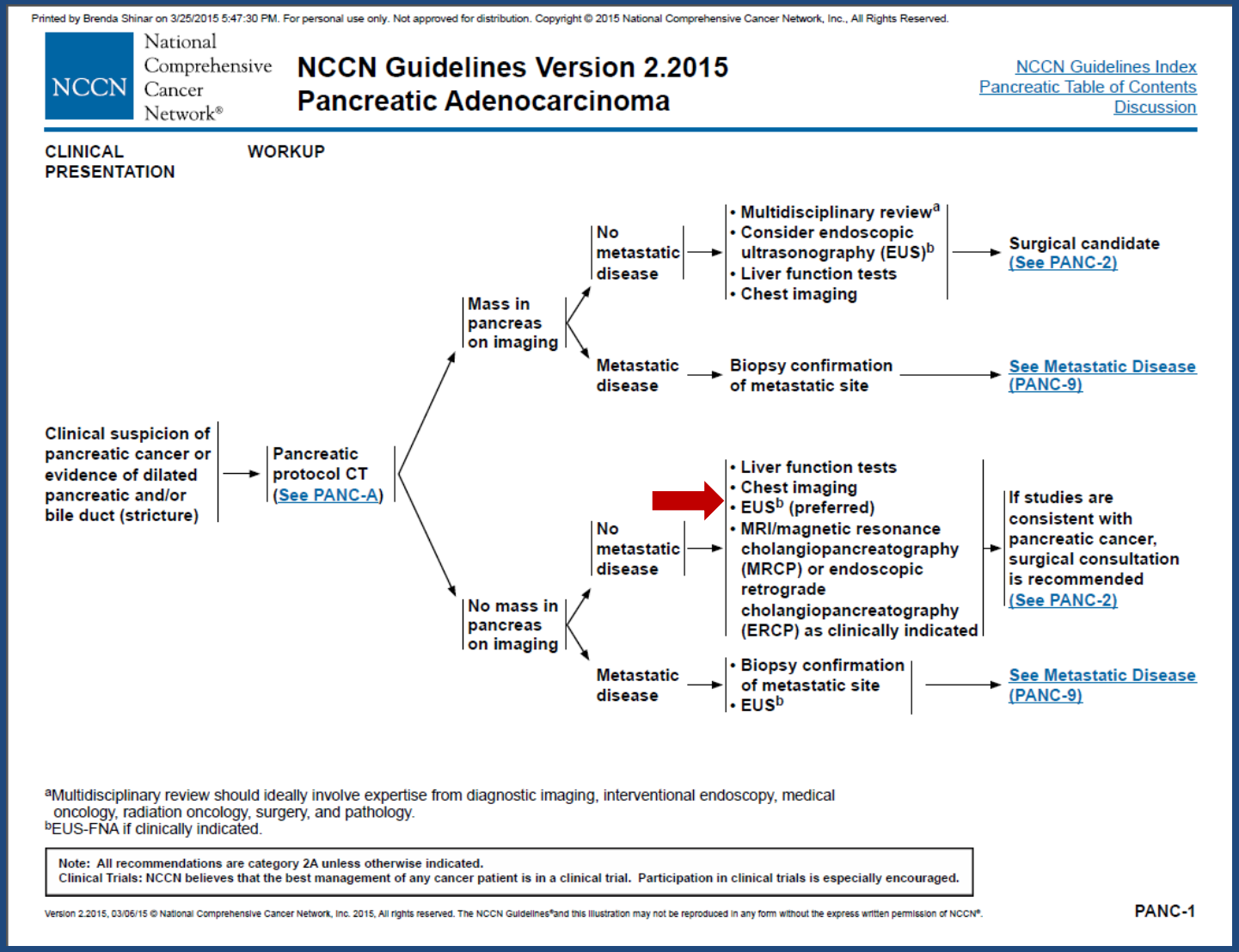
Risk reduction mastectomy reduces the risk of breast cancer > 90%

Risk reduction bilateral salpingo-oopherectomy should be done by age 35-40 after childbearing and reduces the risk of ovarian and breast cancer

Question 10.

- C; Perform endoscopic ultrasound of the pancreas

Diagnose pancreatic cancer using endoscopic ultrasound



Question 11.

- A; Contrast-enhanced CT

Diagnose and manage hepatocellular carcinoma

Indications for surveillance for hepatocellular carcinoma

Cirrhosis from any cause

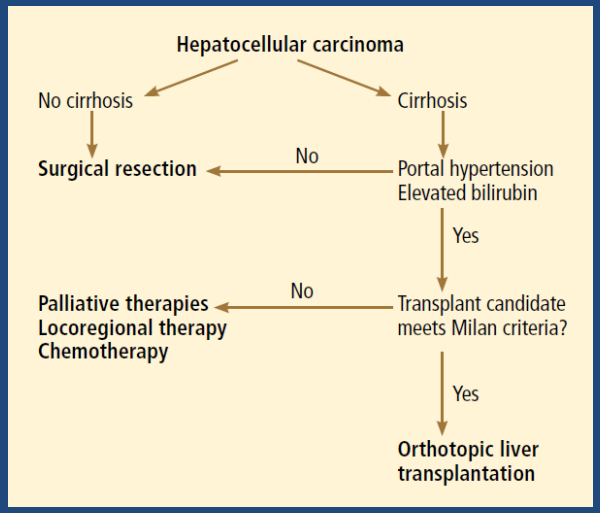
Asian male hepatitis B carriers over age 40

Asian female hepatitis B carriers over age 50

Hepatitis B carriers with a family history of hepatocellular carcinoma

African and North American blacks with hepatitis B

ADAPTED FROM BRUIX J, SHERMAN M; PRACTICE GUIDELINES COMMITTEE, AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES. MANAGEMENT OF HEPATOCELLULAR CARCINOMA. HEPATOLOGY 2005; 42:1208–1236, WITH PERMISSION FROM JOHN WILEY AND SONS.



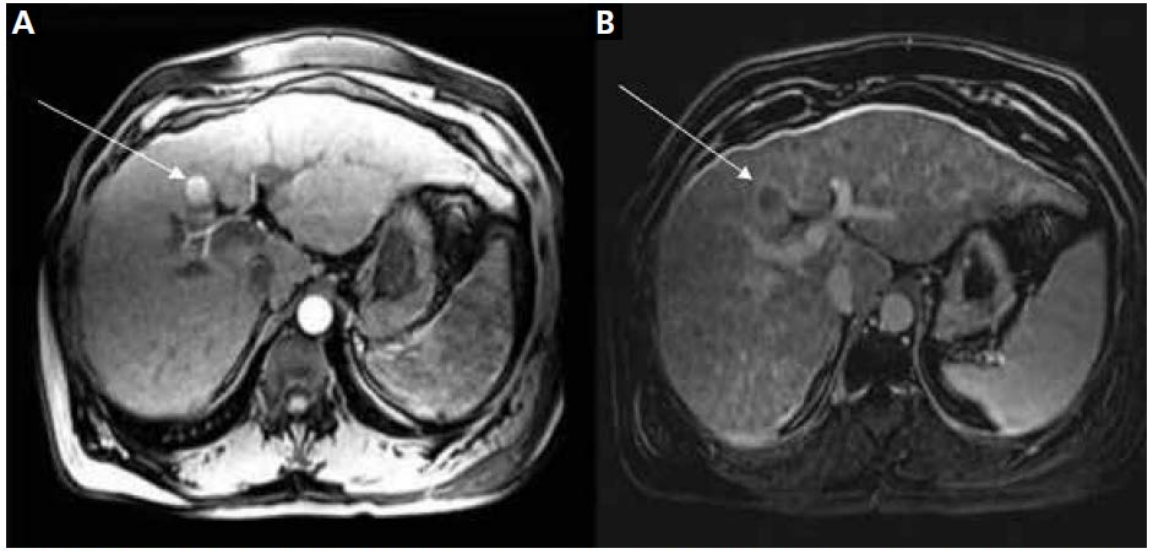


FIGURE 2. Left, arterial hyperenhancement of hepatocellular carcinoma seen on dynamic computed tomography. Right, venous-phase washout of contrast medium.

TABLE 2

Treatments for hepatocellular carcinoma

Surgical resection [a]

Orthotopic liver transplantation [a,b]

Locoregional therapies

Ablative therapies

- Radiofrequency ablation [a]
- Percutaneous ethanol injection
- Microwave ablation, cryotherapy, laser ablation
- Electroporation, light-activated drug therapy

Perfusion-based therapies

- Transarterial chemoembolization
- Transarterial chemoembolization with doxorubicin-eluting beads
- "Bland" embolization
- Radioembolization

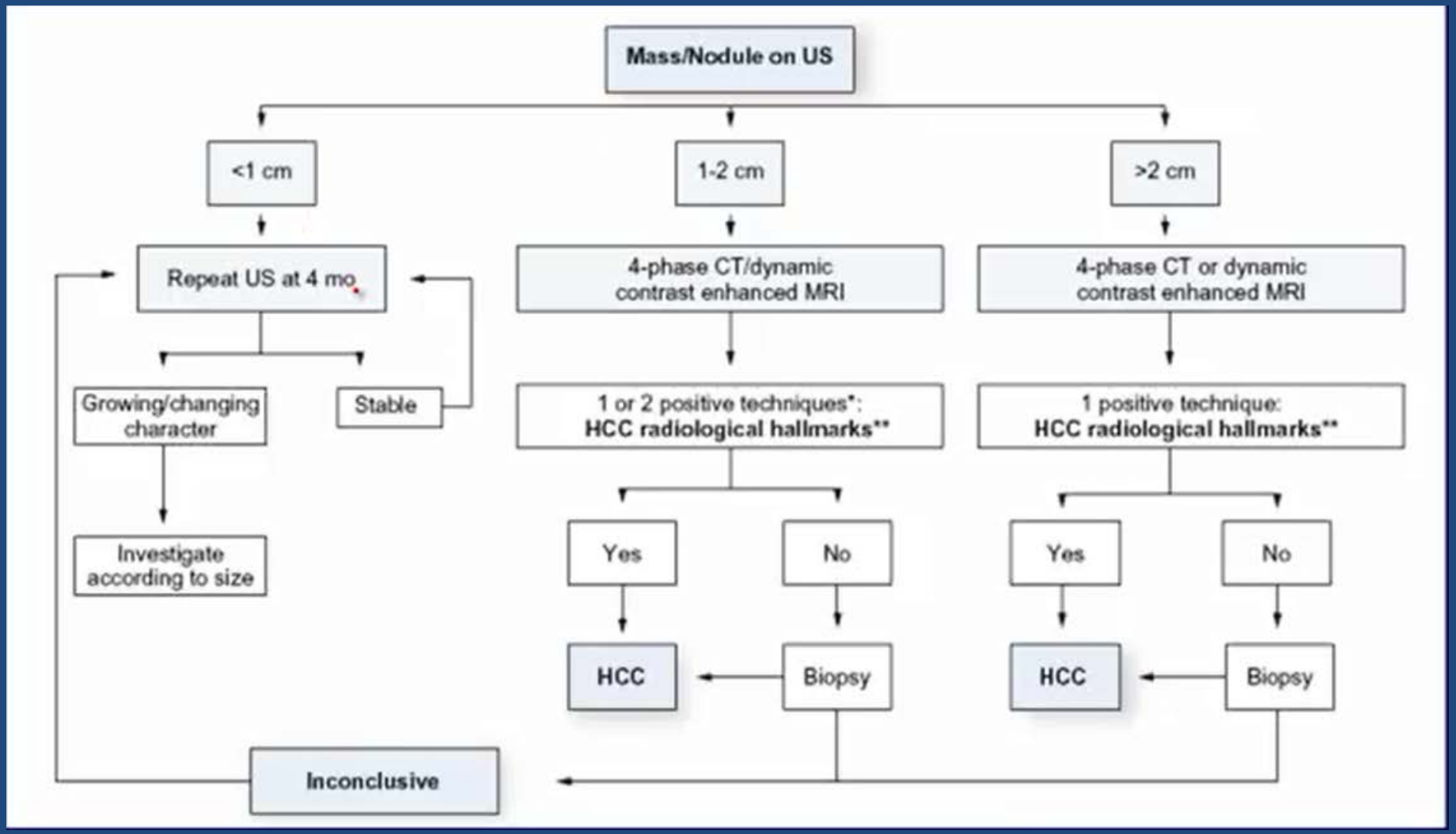
Systemic chemotherapy

Sorafenib

Doxorubicin, everolimus, bevacizumab

[a] Potentially curative treatment for hepatocellular carcinoma

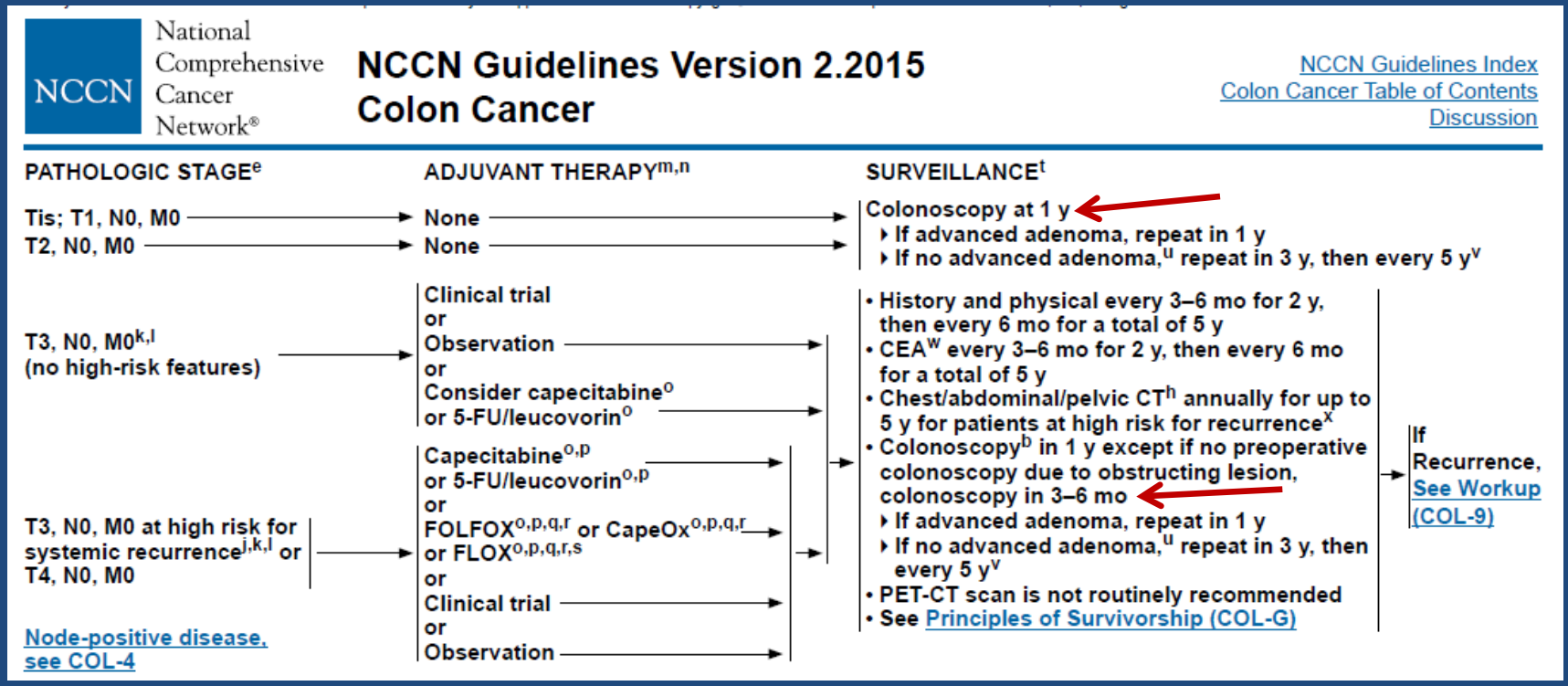
[b] Patient must meet the Milan criteria, ie, a solitary lesion < 5 cm or three lesions (with the largest < 3 cm), no vascular invasion, and no extrahepatic spread


Mass/Nodule on US
<1 cm
1-2 cm
>2 cm
Repeat US at 4 mo
4-phase CT/dynamic contrast enhanced MRI
4-phase CT or dynamic contrast enhanced MRI
Growing/changing character
Stable
1 or 2 positive techniques*: HCC radiological hallmarks**
1 positive technique: HCC radiological hallmarks**
Investigate according to size
Yes
No
Yes
No
HCC
Biopsy
HCC
Biopsy
Inconclusive

Question 12.

- B; Colonoscopy in 1 year

Manage post-colorectal cancer surveillance



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PATHOLOGIC STAGE[e]	ADJUVANT THERAPY[m,n]	SURVEILLANCE[t]
Tis; T1, N0, M0	None	Colonoscopy at 1 y ▸ If advanced adenoma, repeat in 1 y ▸ If no advanced adenoma,[u] repeat in 3 y, then every 5 y[v]
T2, N0, M0	None	
T3, N0, M0[k,l] (no high-risk features)	Clinical trial or Observation or Consider capecitabine[o] or 5-FU/leucovorin[o]	• History and physical every 3–6 mo for 2 y, then every 6 mo for a total of 5 y • CEA[w] every 3–6 mo for 2 y, then every 6 mo for a total of 5 y • Chest/abdominal/pelvic CT[h] annually for up to 5 y for patients at high risk for recurrence[x] • Colonoscopy[b] in 1 y except if no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3–6 mo ▸ If advanced adenoma, repeat in 1 y ▸ If no advanced adenoma,[u] repeat in 3 y, then every 5 y[v] • PET-CT scan is not routinely recommended • See Principles of Survivorship (COL-G)
T3, N0, M0 at high risk for systemic recurrence[j,k,l] or T4, N0, M0	Capecitabine[o,p] or 5-FU/leucovorin[o,p] or FOLFOX[o,p,q,r] or CapeOx[o,p,q,r] or FLOX[o,p,q,r,s] or Clinical trial or Observation	

If Recurrence, See Workup (COL-9)

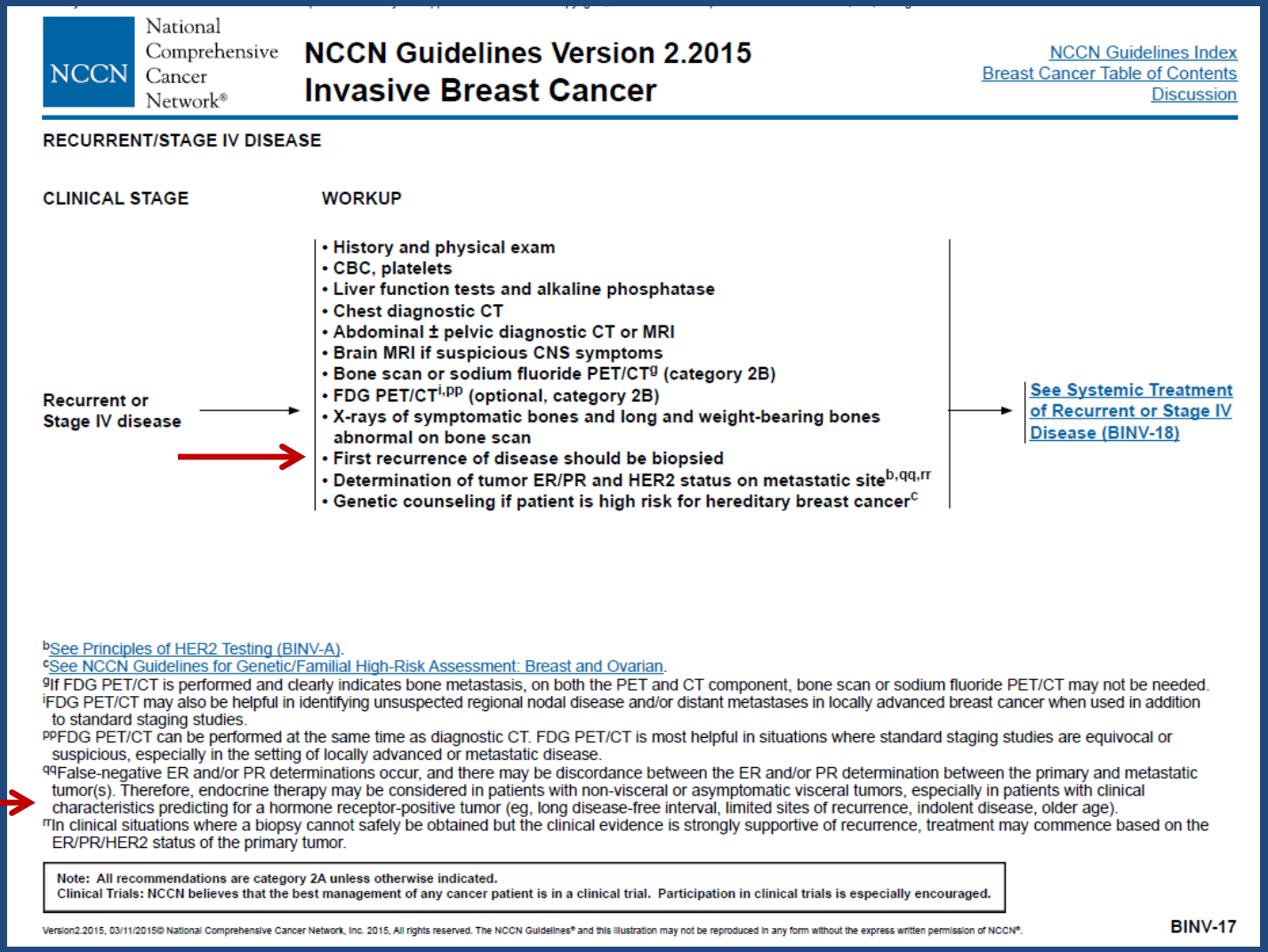
Node-positive disease, see COL-4

80% of recurrent cancers recur in 3 years and 95% recur in 5 years!

Question 13.

- B; Bone biopsy

Manage a patient with recurrent breast cancer



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Invasive Breast Cancer

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RECURRENT/STAGE IV DISEASE

CLINICAL STAGE	WORKUP
Recurrent or Stage IV disease	• History and physical exam • CBC, platelets • Liver function tests and alkaline phosphatase • Chest diagnostic CT • Abdominal ± pelvic diagnostic CT or MRI • Brain MRI if suspicious CNS symptoms • Bone scan or sodium fluoride PET/CT[g] (category 2B) • FDG PET/CT[i,pp] (optional, category 2B) • X-rays of symptomatic bones and long and weight-bearing bones abnormal on bone scan • First recurrence of disease should be biopsied • Determination of tumor ER/PR and HER2 status on metastatic site[b,qq,rr] • Genetic counseling if patient is high risk for hereditary breast cancer[c]

→ See Systemic Treatment of Recurrent or Stage IV Disease (BINV-18)

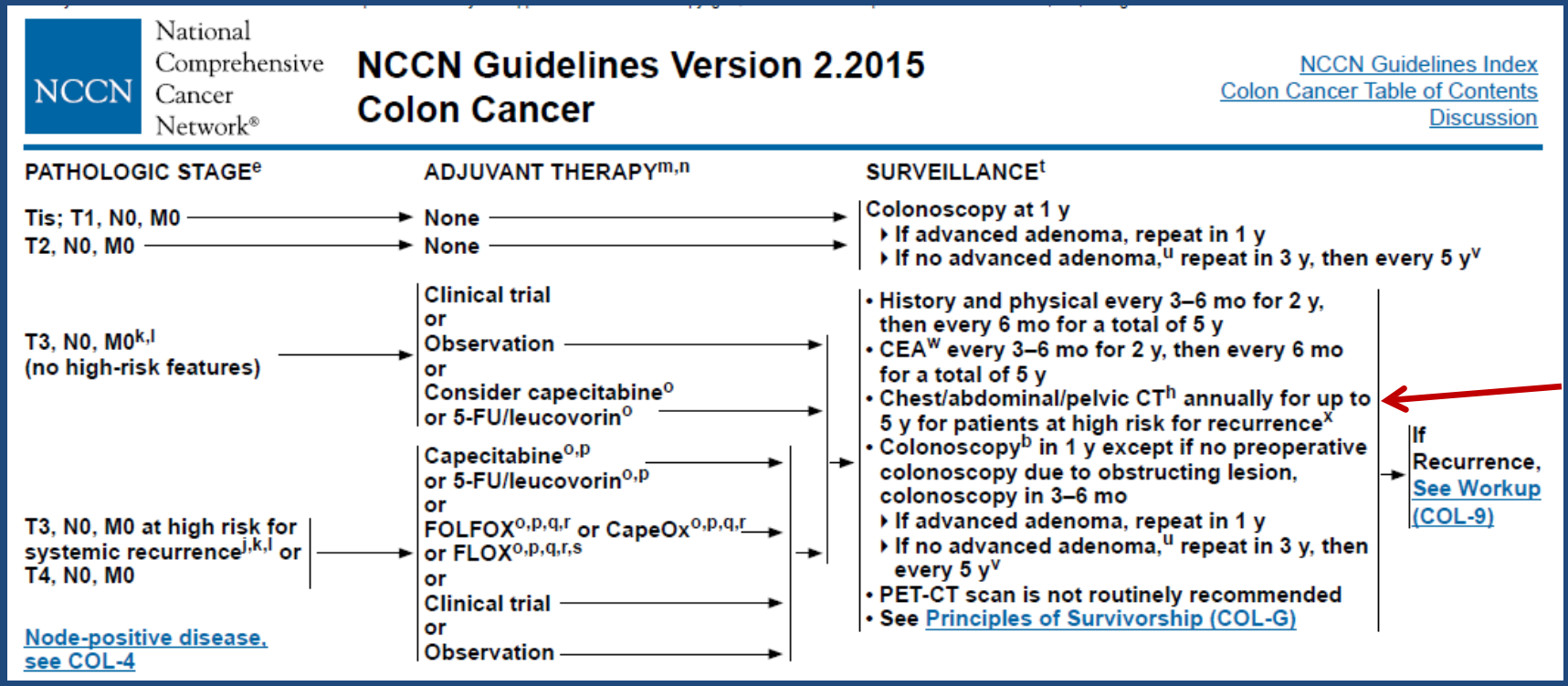
[b] See Principles of HER2 Testing (BINV-A).
[c] See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian.
[g] If FDG PET/CT is performed and clearly indicates bone metastasis, on both the PET and CT component, bone scan or sodium fluoride PET/CT may not be needed.
[i] FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases in locally advanced breast cancer when used in addition to standard staging studies.
[pp] FDG PET/CT can be performed at the same time as diagnostic CT. FDG PET/CT is most helpful in situations where standard staging studies are equivocal or suspicious, especially in the setting of locally advanced or metastatic disease.
[qq] False-negative ER and/or PR determinations occur, and there may be discordance between the ER and/or PR determination between the primary and metastatic tumor(s). Therefore, endocrine therapy may be considered in patients with non-visceral or asymptomatic visceral tumors, especially in patients with clinical characteristics predicting for a hormone receptor-positive tumor (eg, long disease-free interval, limited sites of recurrence, indolent disease, older age).
[rr] In clinical situations where a biopsy cannot safely be obtained but the clinical evidence is strongly supportive of recurrence, treatment may commence based on the ER/PR/HER2 status of the primary tumor.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Question 14.

- A; CT annually for 3 years

Manage post-colorectal cancer surveillance

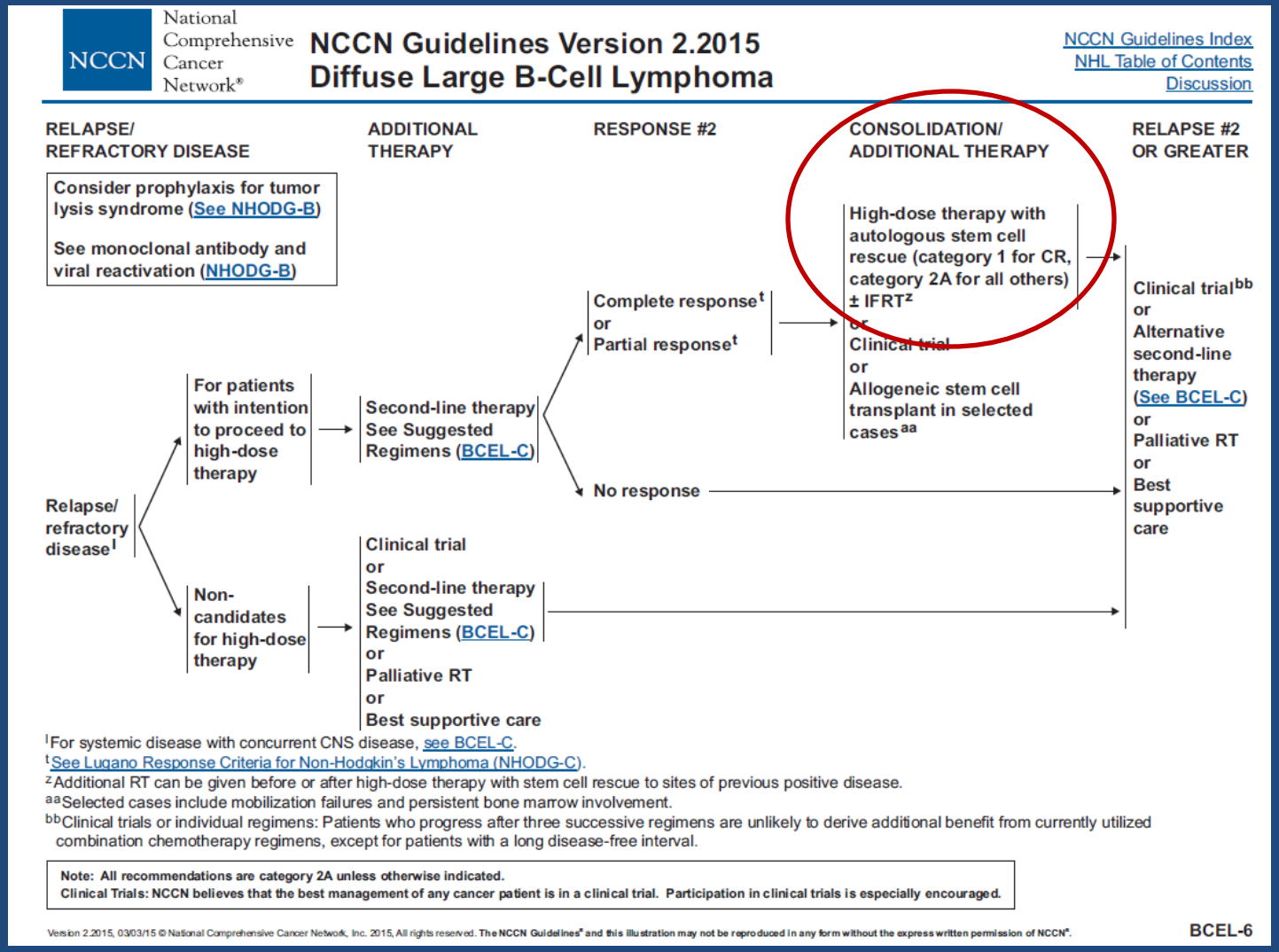


CT should be done with IV and oral contrast;
if contrast contraindicated, non-contrast CT of chest with
MRI of abdomen and pelvis with contrast is alternative;
High risk includes lymphatic or venous invasion or poorly differentiated tumor

Question 15.

- C; Autologous hematopoietic stem cell transplant

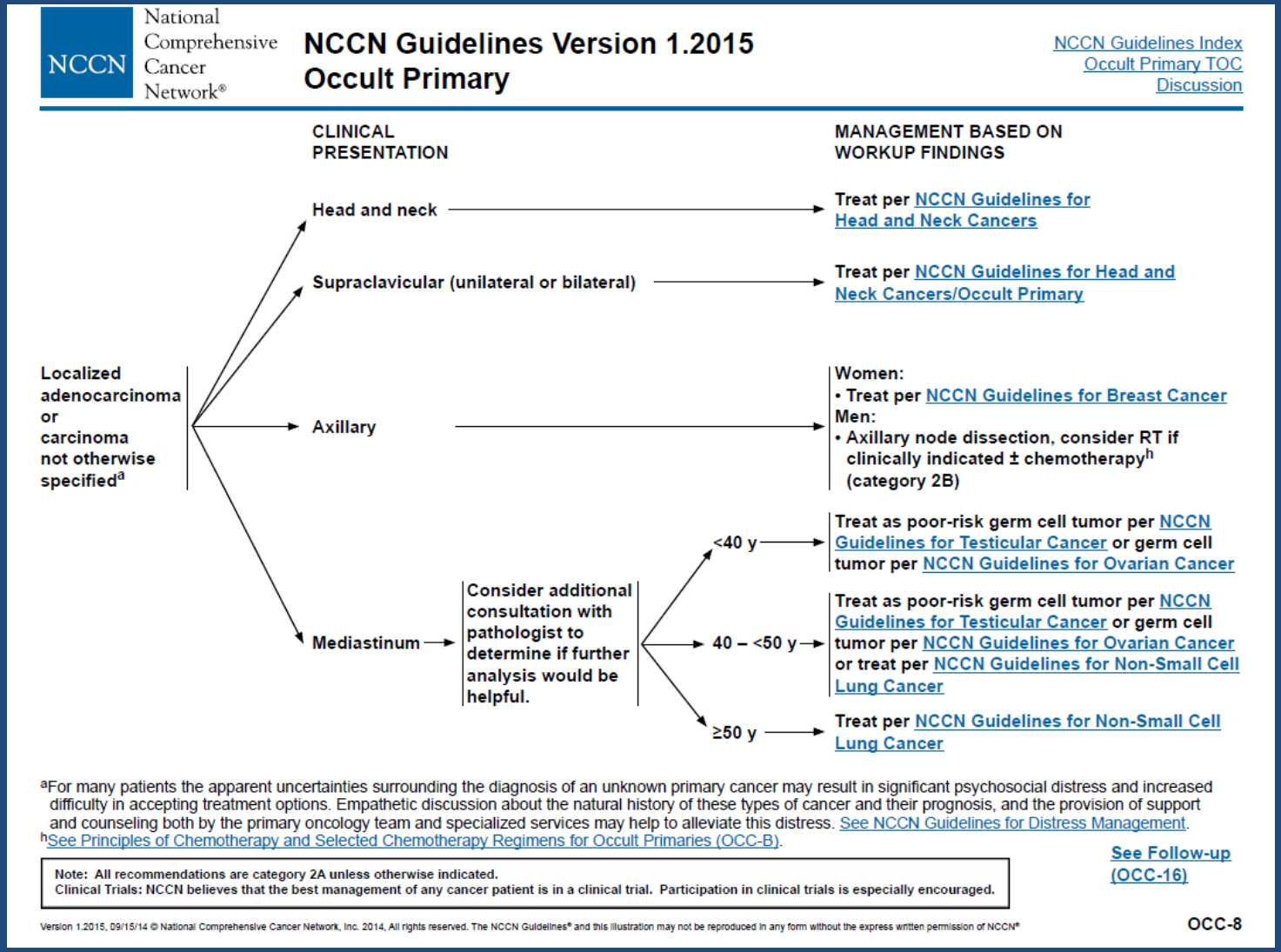
Treat a patient with recurrent, chemotherapy-sensitive diffuse large cell B-cell lymphoma



Question 16.

- E; Surgical debulking followed by chemotherapy

Manage cancer of unknown primary type



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Occult Primary

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Occult Primary TOC
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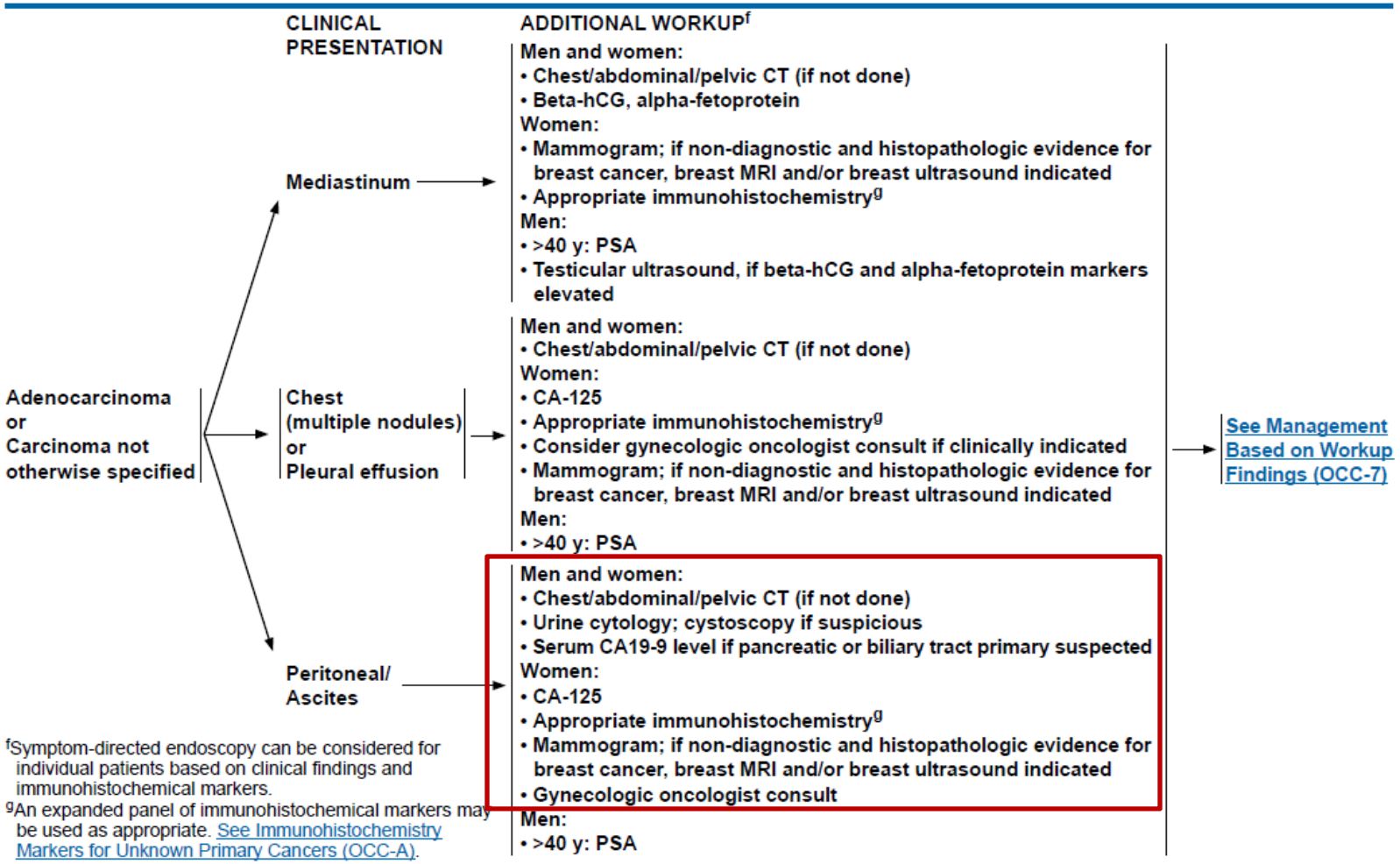

[f]Symptom-directed endoscopy can be considered for individual patients based on clinical findings and immunohistochemical markers.

[g]An expanded panel of immunohistochemical markers may be used as appropriate. See Immunohistochemistry Markers for Unknown Primary Cancers (OCC-A).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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Occult Primary

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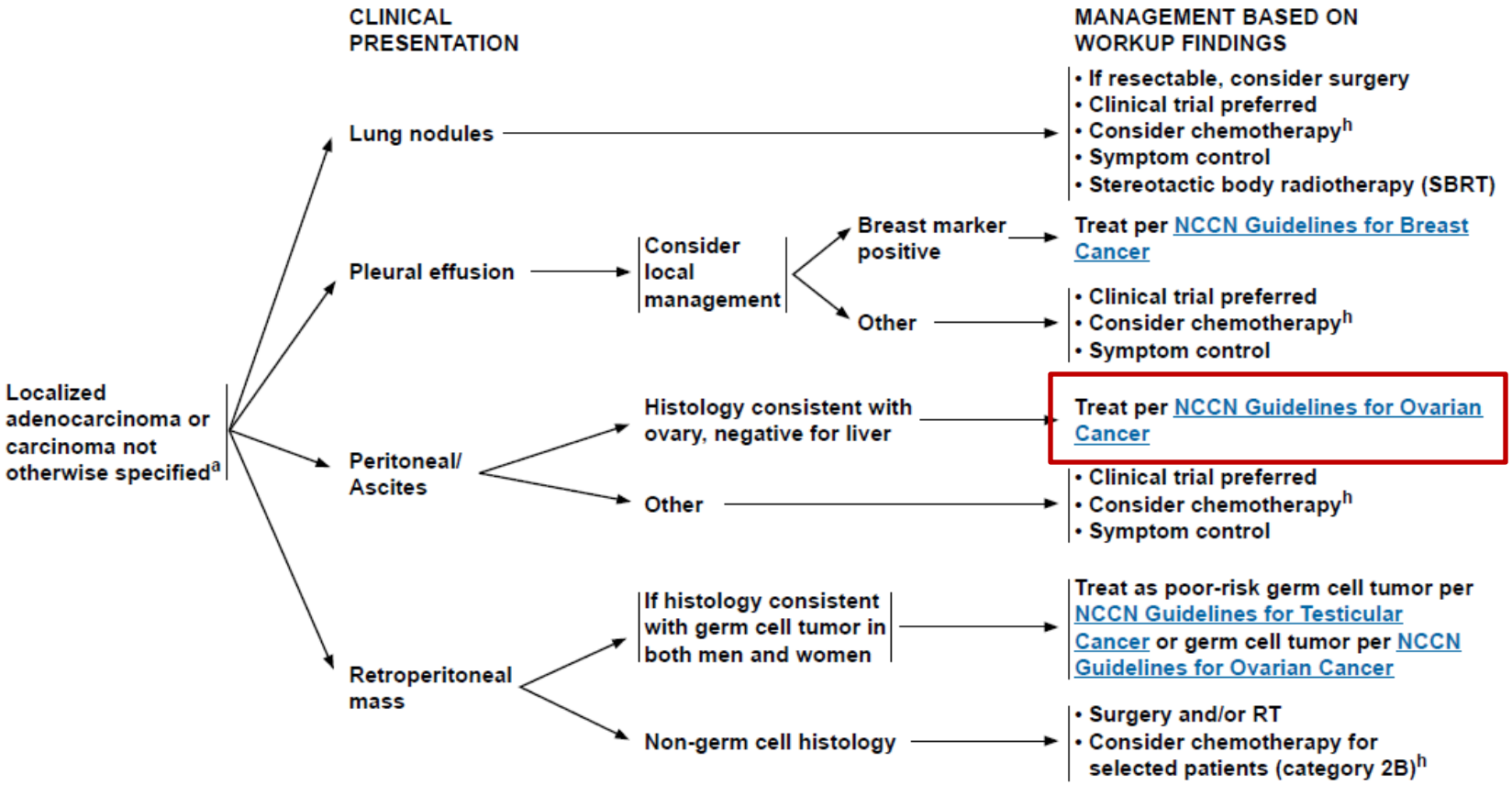


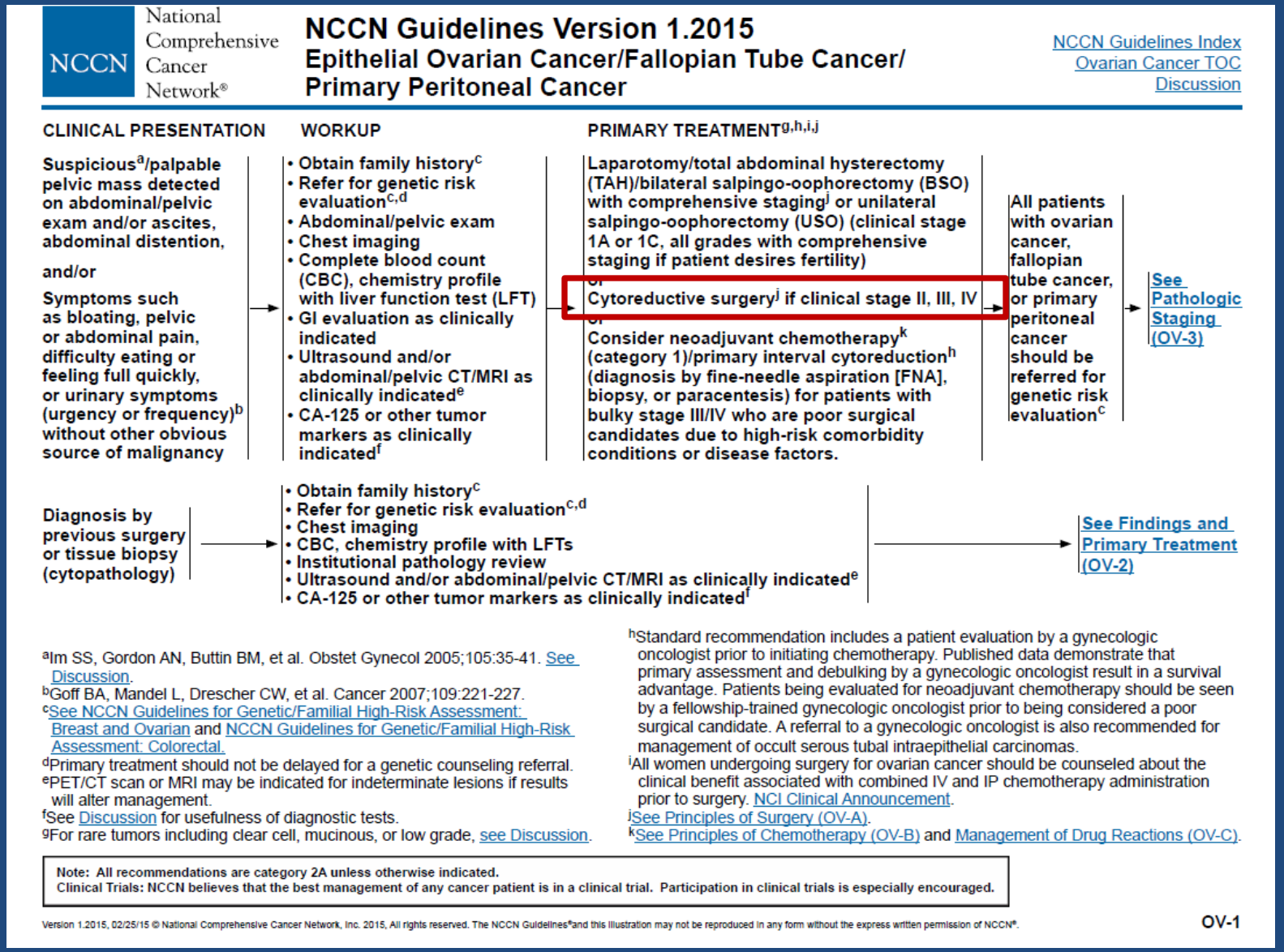
[a]For many patients the apparent uncertainties surrounding the diagnosis of an unknown primary cancer may result in significant psychosocial distress and increased difficulty in accepting treatment options. Empathetic discussion about the natural history of these types of cancer and their prognosis, and the provision of support and counseling both by the primary oncology team and specialized services may help to alleviate this distress. See NCCN Guidelines for Distress Management.

[h]See Principles of Chemotherapy and Selected Chemotherapy Regimens for Occult Primaries (OCC-B).

See Follow-up (OCC-16)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Peritoneal carcinomatosis + malignant ascites with no extraovarian site determined should be treated as stage III ovarian cancer.



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Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer

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Ovarian Cancer TOC
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CLINICAL PRESENTATION

Suspicious[a]/palpable pelvic mass detected on abdominal/pelvic exam and/or ascites, abdominal distention,

and/or

Symptoms such as bloating, pelvic or abdominal pain, difficulty eating or feeling full quickly, or urinary symptoms (urgency or frequency)[b] without other obvious source of malignancy

WORKUP

- Obtain family history[c]
- Refer for genetic risk evaluation[c,d]
- Abdominal/pelvic exam
- Chest imaging
- Complete blood count (CBC), chemistry profile with liver function test (LFT)
- GI evaluation as clinically indicated
- Ultrasound and/or abdominal/pelvic CT/MRI as clinically indicated[e]
- CA-125 or other tumor markers as clinically indicated[f]

PRIMARY TREATMENT[g,h,i,j]

Laparotomy/total abdominal hysterectomy (TAH)/bilateral salpingo-oophorectomy (BSO) with comprehensive staging[j] or unilateral salpingo-oophorectomy (USO) (clinical stage 1A or 1C, all grades with comprehensive staging if patient desires fertility)

or

Cytoreductive surgery[j] if clinical stage II, III, IV

or

Consider neoadjuvant chemotherapy[k] (category 1)/primary interval cytoreduction[h] (diagnosis by fine-needle aspiration [FNA], biopsy, or paracentesis) for patients with bulky stage III/IV who are poor surgical candidates due to high-risk comorbidity conditions or disease factors.

All patients with ovarian cancer, fallopian tube cancer, or primary peritoneal cancer should be referred for genetic risk evaluation[c]

→ See Pathologic Staging (OV-3)

Diagnosis by previous surgery or tissue biopsy (cytopathology)

- Obtain family history[c]
- Refer for genetic risk evaluation[c,d]
- Chest imaging
- CBC, chemistry profile with LFTs
- Institutional pathology review
- Ultrasound and/or abdominal/pelvic CT/MRI as clinically indicated[e]
- CA-125 or other tumor markers as clinically indicated[f]

→ See Findings and Primary Treatment (OV-2)

[a]Im SS, Gordon AN, Buttin BM, et al. Obstet Gynecol 2005;105:35-41. See Discussion.
[b]Goff BA, Mandel L, Drescher CW, et al. Cancer 2007;109:221-227.
[c]See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian and NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal.
[d]Primary treatment should not be delayed for a genetic counseling referral.
[e]PET/CT scan or MRI may be indicated for indeterminate lesions if results will alter management.
[f]See Discussion for usefulness of diagnostic tests.
[g]For rare tumors including clear cell, mucinous, or low grade, see Discussion.
[h]Standard recommendation includes a patient evaluation by a gynecologic oncologist prior to initiating chemotherapy. Published data demonstrate that primary assessment and debulking by a gynecologic oncologist result in a survival advantage. Patients being evaluated for neoadjuvant chemotherapy should be seen by a fellowship-trained gynecologic oncologist prior to being considered a poor surgical candidate. A referral to a gynecologic oncologist is also recommended for management of occult serous tubal intraepithelial carcinomas.
[i]All women undergoing surgery for ovarian cancer should be counseled about the clinical benefit associated with combined IV and IP chemotherapy administration prior to surgery. NCI Clinical Announcement.
[j]See Principles of Surgery (OV-A).
[k]See Principles of Chemotherapy (OV-B) and Management of Drug Reactions (OV-C).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Question 17.

- B; Androgen deprivation therapy (ADT) and radiation therapy

Treat high-risk, locally advanced prostate cancer

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NCCN Guidelines Version 2.2014 Staging Prostate Cancer

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Table 1.
TNM Staging System For Prostate Cancer
Primary Tumor (T)
Clinical

TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1		Clinically inapparent tumor neither palpable nor visible by imaging
	T1a	Tumor incidental histologic finding in 5% or less of tissue resected
	T1b	Tumor incidental histologic finding in more than 5% of tissue resected
	T1c	Tumor identified by needle biopsy (e.g., because of elevated PSA)
T2		Tumor confined within prostate*
	T2a	Tumor involves one-half of one lobe or less
	T2b	Tumor involves more than one-half of one lobe but not both lobes
	T2c	Tumor involves both lobes
T3		Tumor extends through the prostatic capsule**
	T3a	Extracapsular extension (unilateral or bilateral)
	T3b	Tumor invades the seminal vesicle(s)
T4		Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder, levator muscles, and/or pelvic wall.

*Note: Tumor found in one or both lobes by needle biopsy, but not palpable or reliably visible by imaging, is classified as T1c.

**Note: Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.

Pathologic(pT)*

pT2		Organ confined
	pT2a	Unilateral, involving one-half of one side or less
	pT2b	Unilateral, involving more than one-half of one side but not both sides
	pT2c	Bilateral disease
pT3		Extraprostatic extension
	pT3a	Extraprostatic extension or microscopic invasion of the bladder neck**
	pT3b	Seminal vesicle invasion
pT4		Invasion of bladder, rectum

*Note: There is no pathologic T1 classification.

**Note: Positive surgical margin should be indicated by an R1 descriptor (residual microscopic disease).

Regional Lymph Nodes (N)
Clinical

NX	Regional lymph nodes were not assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional lymph node(s)

Pathologic

PNX	Regional nodes not sampled
pN0	No positive regional nodes
pN1	Metastases in regional nodes(s)

Distant Metastasis (M)*

M0		No distant metastasis
M1		Distant metastasis
	M1a	Non-regional lymph node(s)
	M1b	Bone(s)
	M1c	Other site(s) with or without bone disease

*Note: When more than one site of metastasis is present, the most advanced category is used. pM1c is most advanced.

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Prostate Cancer

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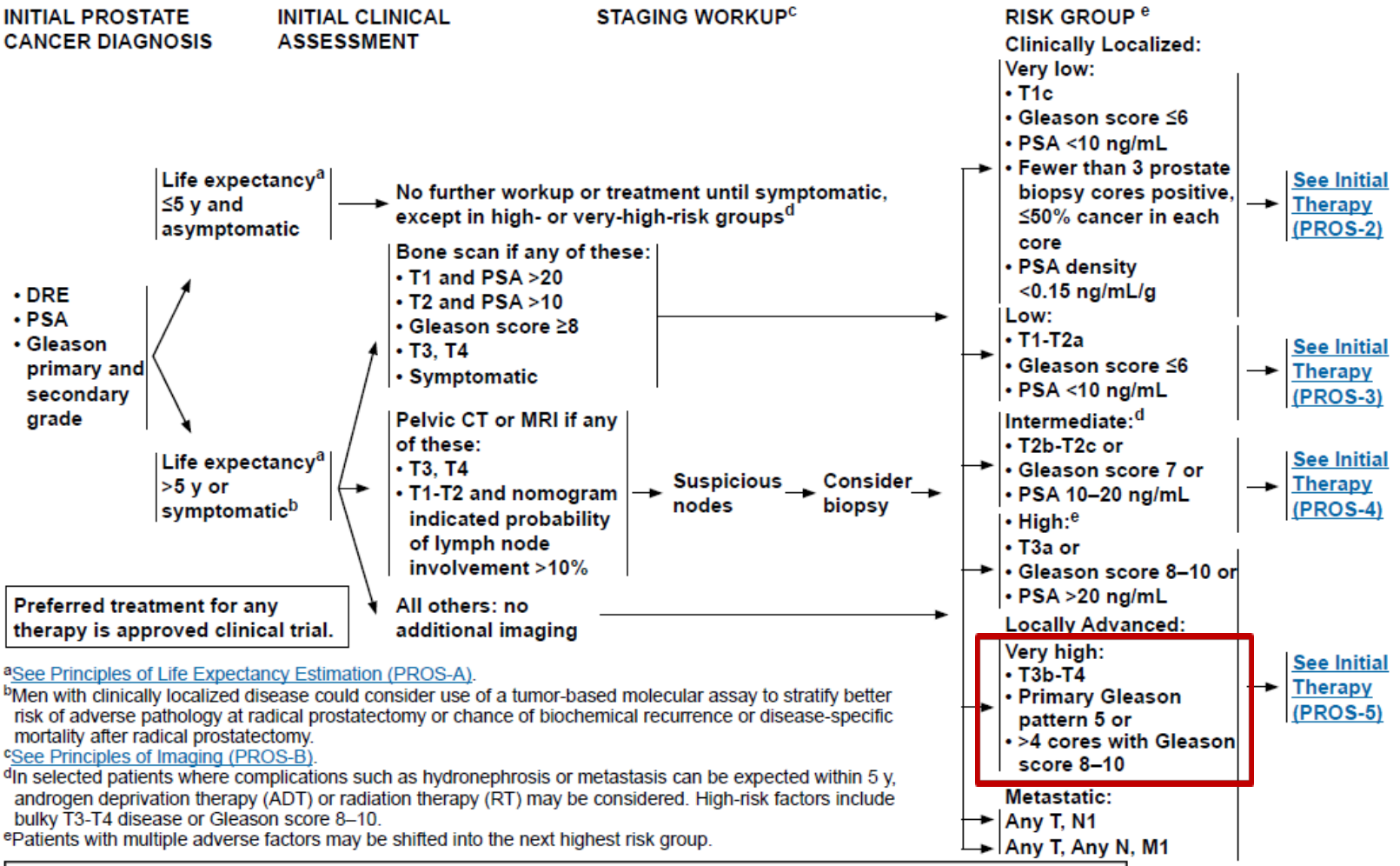

[a] See Principles of Life Expectancy Estimation (PROS-A).

[b] Men with clinically localized disease could consider use of a tumor-based molecular assay to stratify better risk of adverse pathology at radical prostatectomy or chance of biochemical recurrence or disease-specific mortality after radical prostatectomy.

[c] See Principles of Imaging (PROS-B).

[d] In selected patients where complications such as hydronephrosis or metastasis can be expected within 5 y, androgen deprivation therapy (ADT) or radiation therapy (RT) may be considered. High-risk factors include bulky T3-T4 disease or Gleason score 8–10.

[e] Patients with multiple adverse factors may be shifted into the next highest risk group.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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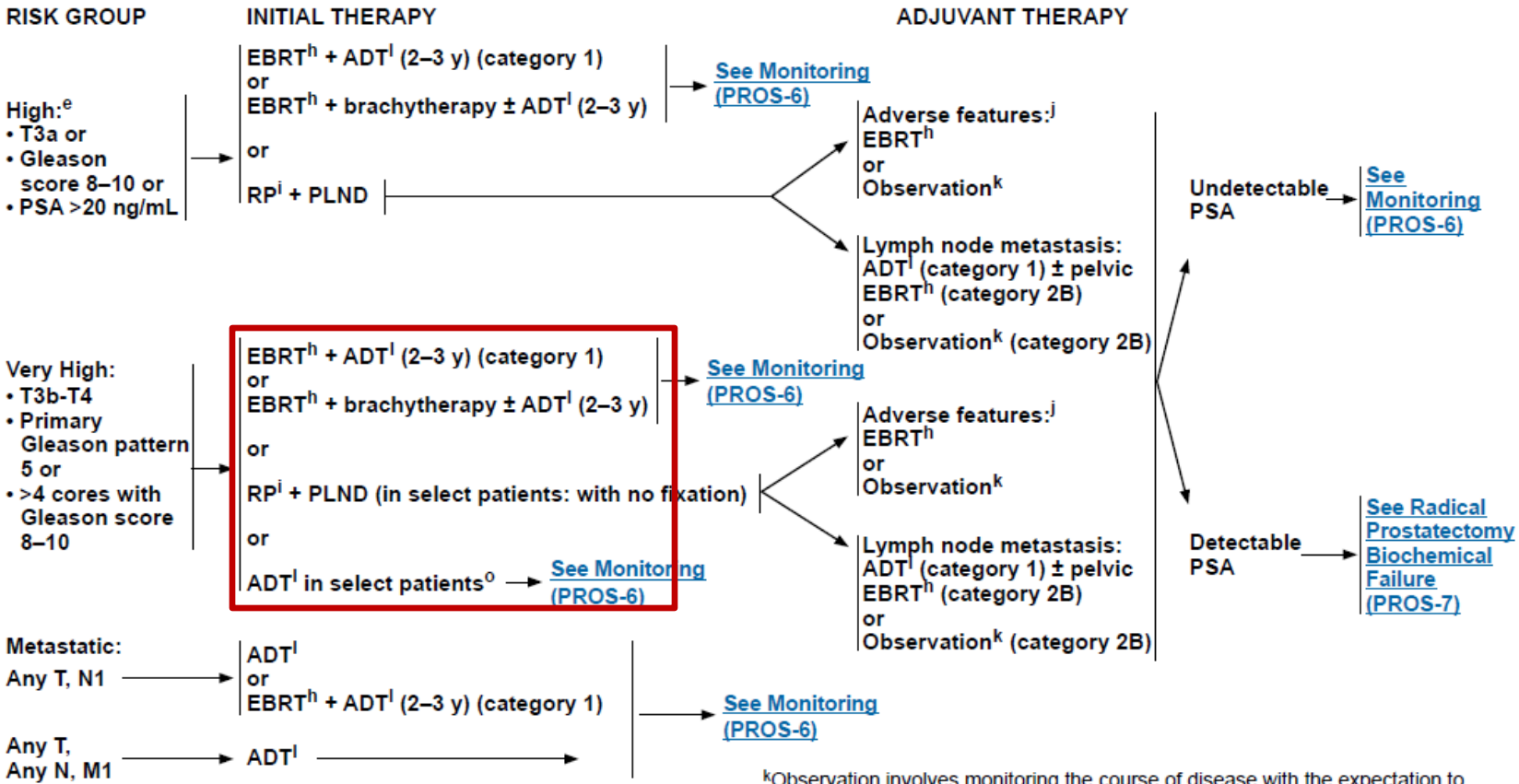

[e]Patients with multiple adverse factors may be shifted into the next highest risk group.
[h]See Principles of Radiation Therapy (PROS-D).
[i]See Principles of Surgery (PROS-E).
[j]Adverse laboratory/pathologic features include: positive margins, seminal vesicle invasion, extracapsular extension, or detectable PSA.

[k]Observation involves monitoring the course of disease with the expectation to deliver palliative therapy for the development of symptoms or a change in exam or PSA that suggests symptoms are imminent. See Principles of Active Surveillance and Observation (PROS-C).
[l]See Principles of Androgen Deprivation Therapy (PROS-F).
[o]Primary therapy with ADT should be considered only for patients who are not candidates for definitive therapy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Question 18.

- C; Surgical resection followed by chemotherapy

NCCN Guidelines Version 2.2013 Staging Non-Small Cell Lung Cancer

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Table 1. Definitions for T, N, M*

T	Primary Tumor
TX	Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor ≤ 3 cm in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)[a]
T1a	Tumor ≤ 2 cm in greatest dimension
T1b	Tumor > 2 cm but ≤ 3 cm in greatest dimension
T2	Tumor > 3 cm but ≤ 7 cm or tumor with any of the following features:[b] Involves main bronchus, ≥ 2 cm distal to the carina Invades visceral pleura Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
T2a	Tumor > 3 cm but ≤ 5 cm in greatest dimension
T2b	Tumor > 5 cm but ≤ 7 cm in greatest dimension
T3	Tumor > 7 cm or one that directly invades any of the following: chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus < 2 cm distal to the carina[a] but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe
T4	Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina; separate tumor nodule(s) in a different ipsilateral lobe

N	Regional Lymph Nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

M	Distant Metastasis
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural (or pericardial) effusion[c]
M1b	Distant metastasis

[a] The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximally to the main bronchus, is also classified as T1.

[b] T2 tumors with these features are classified T2a if ≤ 5 cm or if size cannot be determined, and T2b if > 5 cm but ≤ 7 cm

[c] Most pleural (and pericardial) effusions with lung cancer are due to tumor. In a few patients, however, multiple cytopathologic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is nonbloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging element and the patient should be classified as T1, T2, T3, or T4.

*Used with permission. Goldstraw P, Crowley J, Chansky K, et al. The IASLC Lung Cancer Staging Project: Proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumors. J Thorac Oncol 2007;2:706-714.

Treat a patient with early-stage non-small cell lung cancer (NSCLC)

NCCN Guidelines Version 2.2013 Staging
Non-Small Cell Lung Cancer

Table 2. Anatomic Stage and Prognostic Groups

Occult Carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
	T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
Stage IIIB	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
Stage IV	Any T	Any N	M1a
	Any T	Any N	M1b

Surgery is indicated for patients with stage I and II disease with no mediastinal involvement.

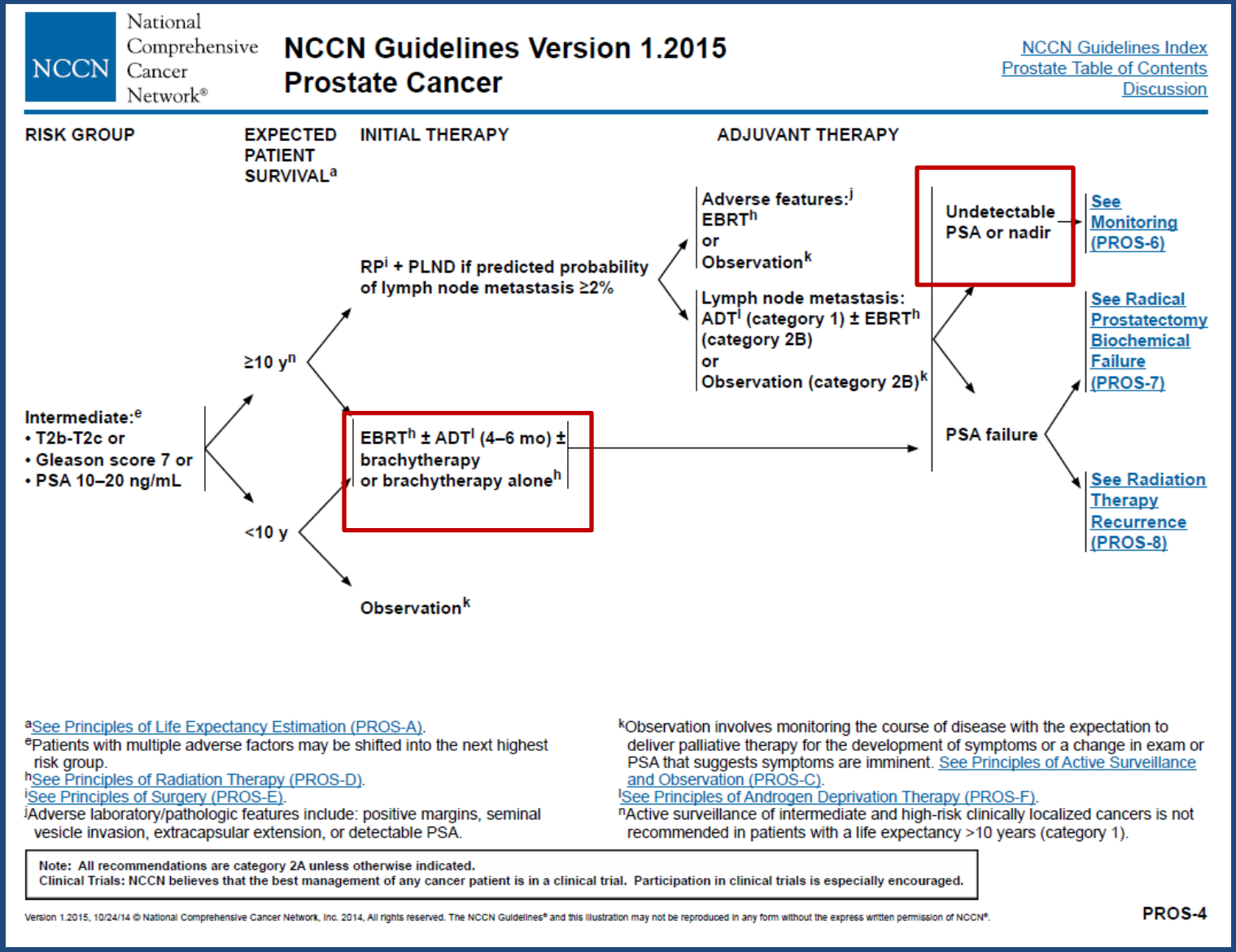
Adjuvant chemotherapy with a cisplatin-based regimen should be given to patients with surgically resected NSCLC in stage II to reduce recurrent disease and mortality. (5% reduction in risk of death at 5 years).

Adjuvant chemotherapy should be considered in high risk stage 1B patients after surgery for benefit.
(> 4 cm, et cetera)

Question 19.

- D; PSA measurement and digital rectal examination every 6 to 12 months

Manage prostate cancer follow up;
75% of recurrences occur within 5 years



[a] See Principles of Life Expectancy Estimation (PROS-A).
[e] Patients with multiple adverse factors may be shifted into the next highest risk group.
[h] See Principles of Radiation Therapy (PROS-D).
[i] See Principles of Surgery (PROS-E).
[j] Adverse laboratory/pathologic features include: positive margins, seminal vesicle invasion, extracapsular extension, or detectable PSA.
[k] Observation involves monitoring the course of disease with the expectation to deliver palliative therapy for the development of symptoms or a change in exam or PSA that suggests symptoms are imminent. See Principles of Active Surveillance and Observation (PROS-C).
[l] See Principles of Androgen Deprivation Therapy (PROS-F).
[n] Active surveillance of intermediate and high-risk clinically localized cancers is not recommended in patients with a life expectancy >10 years (category 1).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

PROS-4

Manage prostate cancer follow up;
75% of recurrences occur within 5 years

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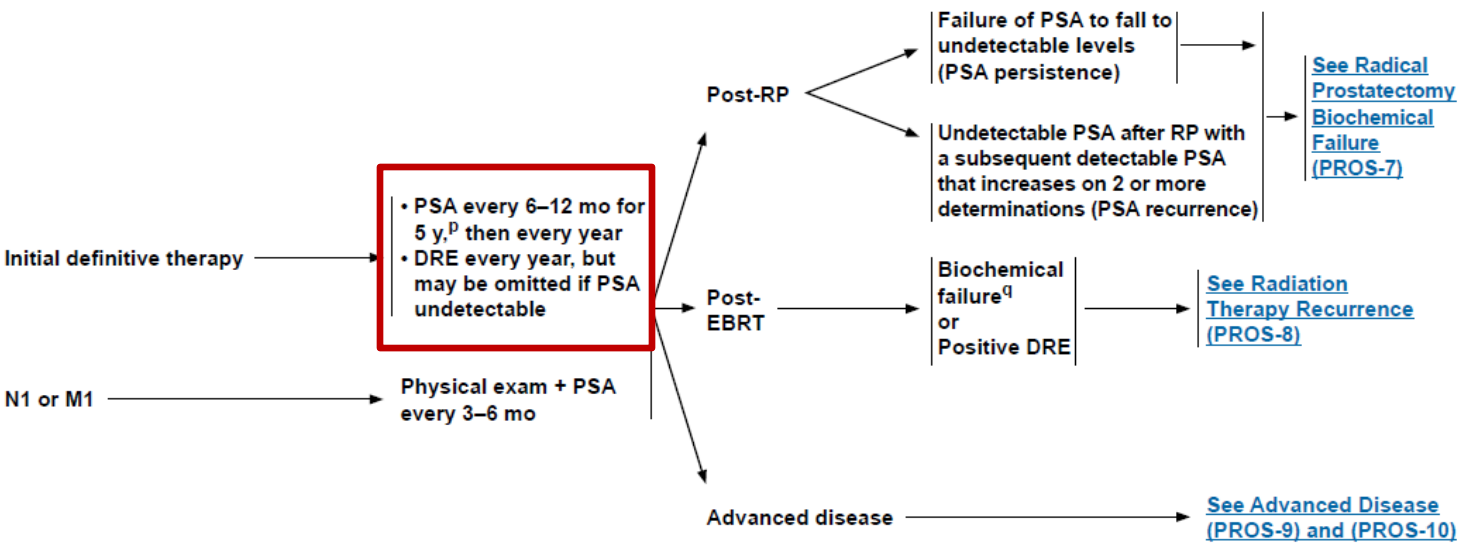

[p]PSA as frequently as every 3 mo may be necessary to clarify disease status, especially in high-risk men.

[q]RTOG-ASTRO (Radiation Therapy Oncology Group-American Society for Therapeutic Radiology and Oncology) Phoenix Consensus-1) PSA increase by 2 ng/mL or more above the nadir PSA is the standard definition for biochemical failure after EBRT with or without HT; and 2) A recurrence evaluation should be considered when PSA has been confirmed to be increasing after radiation even if the increase above nadir is not yet 2 ng/mL, especially in candidates for salvage local therapy who are young and healthy. Retaining a strict version of the ASTRO definition allows comparison with a large existing body of literature. Rapid increase of PSA may warrant evaluation (prostate biopsy) prior to meeting the Phoenix definition, especially in younger or healthier men.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Question 20.

- D; Obtain Pap smear in 2 years

Summary of Recommendations

Population	Page Numbers	Recommended Screening Method*	Management of Screen Results	Comments
Aged <21 y	521-522	No screening		HPV testing should not be used for screening or management of ASC-US in this age group
Aged 21-29 y	522-523	Cytology alone every 3 y	HPV-positive ASC-US† or cytology of LSIL or more severe: Refer to ASCCP guidelines[2] Cytology negative or HPV-negative ASC-US†: Rescreen with cytology in 3 y	HPV testing should not be used for screening in this age group
Aged 30-65 y	523-529	HPV and cytology "cotesting" every 5 y (preferred)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines[2] HPV positive, cytology negative: Option 1: 12-mo follow-up with cotesting Option 2: Test for HPV16 or HPV16/18 genotypes • If HPV16 or HPV16/18 positive: refer to colposcopy • If HPV16 or HPV16/18 negative: 12-mo follow-up with cotesting Cotest negative or HPV-negative ASC-US: Rescreen with cotesting in 5 y	Screening by HPV testing alone is not recommended for most clinical settingst
		Cytology alone every 3 y (acceptable)	HPV-positive ASC-US† or cytology of LSIL or more severe: Refer to ASCCP guidelines[2] Cytology negative or HPV-negative ASC-US†: Rescreen with cytology in 3 y	
Aged >65 y	529-531	No screening following adequate negative prior screening		Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y
After hysterectomy	531	No screening		Applies to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 20 y or cervical cancer ever
HPV vaccinated	531-533	Follow age-specific recommendations (same as unvaccinated women)		

ASCCP, American Society for Colposcopy and Cervical Pathology; ASC-US, atypical squamous cells of undetermined significance; CIN2, cervical intraepithelial neoplasia grade 2; HPV, human papillomavirus; LSIL, low-grade squamous intraepithelial lesion.

* Women should not be screened annually at any age by any method.

† ASC-US cytology with secondary HPV testing for management decisions.