

Oncology Board Review

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Question 1.

- B; Digital mammography with 3D tomography

Breast cancer screening for Average Risk Women

Modalities of screening:

- Self breast exam (N)
- Clinical breast exam (N, I, Y)
- Mammography (Y)
 - Film (almost historic)
 - Digital 2D
 - Digital 3D; less recall rates (more specificity than sensitivity with dense breasts)
- Ultrasound (N)
- MRI (Y in High risk only)

Risk assessment:

- Average risk = <15% lifetime risk (1:7)
- High risk = 20-25% lifetime risk
 - Gail model risk assessment tool
 - Tyrer-Cuzik risk assessment

The Breast Cancer Risk Assessment Tool is an interactive tool designed by scientists at the National Cancer Institute (NCI) and the [National Surgical Adjuvant Breast and Bowel Project \(NSABP\)](#) to estimate a woman's risk of developing [invasive breast cancer](#). See [About the Tool](#) for more information.

The Breast Cancer Risk Assessment Tool may be updated periodically as new data or research becomes available.

Risk Tool

(Click a question number for a brief explanation, or [read all explanations.](#))

1. Does the woman have a medical history of any breast cancer or of [ductal carcinoma in situ \(DCIS\)](#) or [lobular carcinoma in situ \(LCIS\)](#) or has she received previous radiation therapy to the chest for treatment of Hodgkin lymphoma?
2. Does the woman have a mutation in either the [BRCA1](#) or [BRCA2](#) gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer?
3. What is the woman's age?
This tool only calculates risk for women 35 years of age or older.
4. What was the woman's age at the time of her first [menstrual period](#)?
5. What was the woman's age at the time of her first live birth of a child?
6. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?
7. Has the woman ever had a breast [biopsy](#)?
 - 7a. How many breast biopsies (positive or negative) has the woman had?
 - 7b. Has the woman had at least one breast biopsy with [atypical hyperplasia](#)?
8. What is the woman's race/ethnicity?
 - 8a. What is the sub race/ethnicity?

Calculate Risk >

Results (Breast Cancer Risk)

[New Risk Calculation](#)

Reminder: The Breast Cancer Risk Assessment Tool was designed for use by health professionals. If you are not a health professional, you are encouraged to print these results and discuss them with your health care provider.

[Print Page](#)

Limitations:

- These risk calculations have been validated for women in the U.S. who are screened regularly for breast cancer.
- Risk estimates do not allow one to say precisely which woman will develop breast cancer. In fact, some women who develop breast cancer may have lower estimated risks than some women who do not develop breast cancer.
- The BCRAT was not designed to estimate risk for:
 - Women with a prior diagnosis of breast cancer, [lobular carcinoma in situ \(LCIS\)](#), or [ductal carcinoma in situ \(DCIS\)](#).
 - Women who have received previous radiation therapy to the chest for treatment of Hodgkin lymphoma
 - Women with gene mutations in [BRCA1](#) or [BRCA2](#), or those who are known to have certain genetic syndromes that increase risk for breast cancer.

For women with any of the above medical history other methods to estimate breast cancer risk are better. See [About the Tool](#) section for a list of references.

- Recent immigrants from parts of rural Asia, such as rural China, probably have lower risks than projected by the tool.

Race/Ethnicity:

White

5 Year Risk of Developing Breast Cancer

- > This woman (age 46): 1.3%
- > Average woman (age 46): 1%

Explanation

Based on the information provided (see below), the woman's estimated risk for developing invasive breast cancer over the next 5 years is 1.3% compared to a risk of 1% for a woman of the same age and race/ethnicity from the general U.S. population. This calculation also means that the woman's risk of NOT getting breast cancer over the next 5 years is 98.7%.

Lifetime Risk of Developing Breast Cancer

- > This woman (to age 90): 11.5%
- > Average woman (to age 90): 11.8%

Explanation

Based on the information provided (see below), the woman's estimated risk for developing invasive breast cancer over her lifetime (to age 90) is 11.5% compared to a risk of 11.8% for a woman of the same age and race/ethnicity from the general U.S. population.

These results are based upon the following answers:

Personal factors

Woman's age: 46 Menarche: 14 Height (m): 1.72 Weight (kg): 76.8

Measurements Metric: Imperial:

Nulliparous: Parous: Unknown: Age at First Child: ?

No prior biopsy / no proliferative disease: Prior biopsy, result unknown: Hyperplasia (not atypia): Atypical hyperplasia: Lobular Carcinoma in Situ (LCIS):

Premenopausal: Perimenopausal: Postmenopausal: No information: Age at Menopause: ?

Ovarian cancer:

Competing mortality:

Risk Options

HRT use Length of use (years):

Never: 5 or more years ago: Less than 5 years ago: Current user:

Mammographic density (age 40+)

b. Scattered fibroglandular density

% Volpara® Volumetric Density* % VAS Percentage Density* BI-RADS® ATLAS Density*

Ashkenazi inheritance:

Genetic Testing

Male relatives

Half Sisters

Affected cousins

Affected Nieces

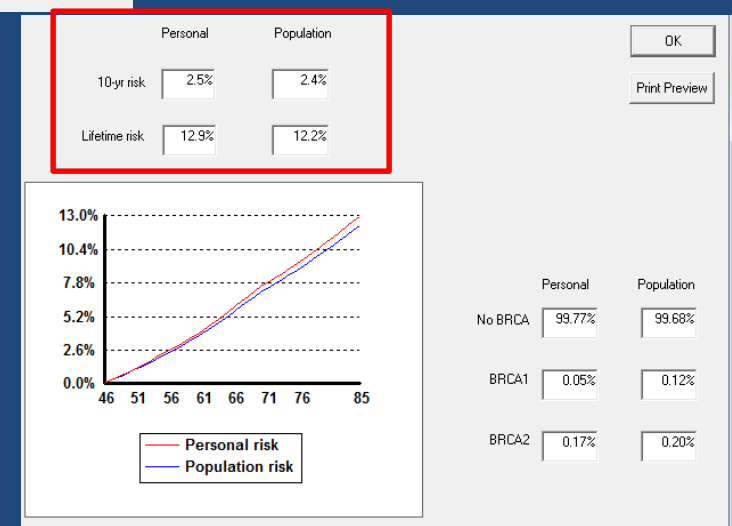
View Family History

IBIS Risk Evaluator v8.0

Tyrer-Cusik Model incorporates breast density.

IBIS Risk Evaluator

www.ems-trials.org/riskevaluator/



Risk and protective factors for developing breast cancer

	Risk group		
	Low risk	High risk	Relative risk
Risk factors			
Deleterious BRCA1/BRCA2 genes	Negative	Positive	3.0 to 7.0
Mother or sister with breast cancer	No	Yes	2.6
Age	30 to 34	70 to 74	18.0
Age at menarche	>14	<12	1.5
Age at first birth	<20	>30	1.9 to 3.5
Age at menopause	<45	>55	2.0
Use of contraceptive pills	Never	Past/current use	1.07 to 1.2
HRT (estrogen + progestin)	Never	Current	1.2
Alcohol	None	2 to 5 drinks/day	1.4
Breast density on mammography (percents)	0	≥75	1.8 to 6.0
Bone density	Lowest quartile	Highest quartile	2.7 to 3.5
History of a benign breast biopsy	No	Yes	1.7
History of atypical hyperplasia on biopsy	No	Yes	3.7
Protective factors			
Breast feeding (months)	≥16	0	0.73
Parity	≥5	0	0.71
Recreational exercise	Yes	No	0.70
Postmenopause body mass index (kg/m ²)	<22.9	>30.7	0.63
Oophorectomy before age 35 years	Yes	No	0.3
Aspirin	≥Once/week for ≥6 months	Nonusers	0.79

HRT: hormone replacement therapy.

Adapted from: Clemons M, Goss P. Estrogen and the risk of breast cancer. *N Engl J Med* 2001; 344:276.

Recommendations for Breast Cancer Screening for Average Risk Women

Society and expert recommendations for routine mammographic screening in women at average risk

Group (date)	Frequency of screening (years)	Initiation of screening		
		40 to 49 years of age	50 to 69 years of age	≥70 years of age
Government-sponsored groups				
US Preventive Services Task Force (2016) ^[1]	2	Individualize*	Yes	Yes, to age 74
Canadian Task Force on Preventive Health Care (2011) ^[2]	2 to 3	Recommend against*	Yes	Yes, to age 74
National Health Service, United Kingdom (2013) ^[3]	3	Yes, start age 47	Yes	Yes, to age 73
Royal Australian College of General Practitioners (2012) ^[4]	2	No (eligible but not targeted)	Yes	No (eligible but not targeted)
Medical societies				
American College of Obstetricians and Gynecologists (2011) ^[5]	1	Yes	Yes	Yes [¶]
American College of Physicians (2015) ^[6]	1 to 2	Individualize*	Yes	Yes, to age 74
American Academy of Family Physicians (2009) ^[7]	2	Individualize*	Yes	Yes, to age 74
American Cancer Society (2015) ^[8]	1 year age 45 to 54 2 years age ≥55	Yes, start age 45	Yes	Yes ^Δ
American College of Radiology (2013) ^[9]	1	Yes	Yes	Yes [◇]
Coalitions				
National Comprehensive Cancer Network (2014) ^[10]	1	Yes	Yes	Yes

* Women should be counseled about the harms and benefits of mammography; individualized decision based on risks and patient preference.

¶ Discuss with doctor and individualize decision after age 75.

Δ If in good health and life expectancy > 10 years.

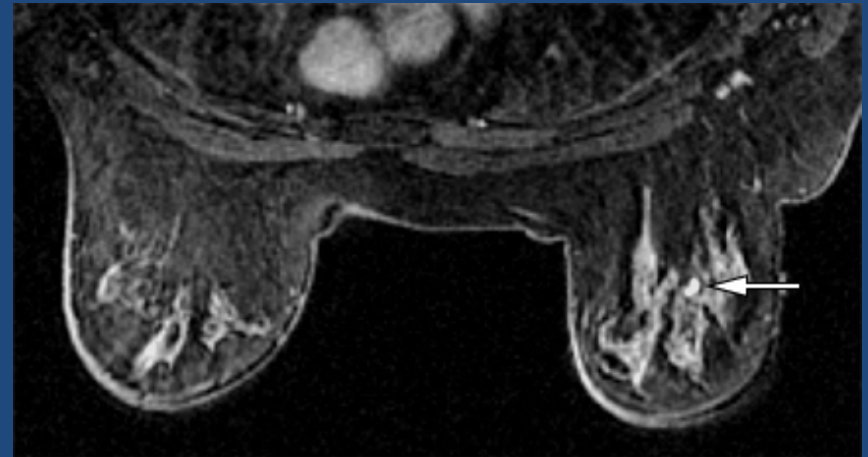
◇ Individualize to current health and life expectancy; if a woman is in reasonably good health and would be a candidate for treatment, then should continue screening.

Question 2.

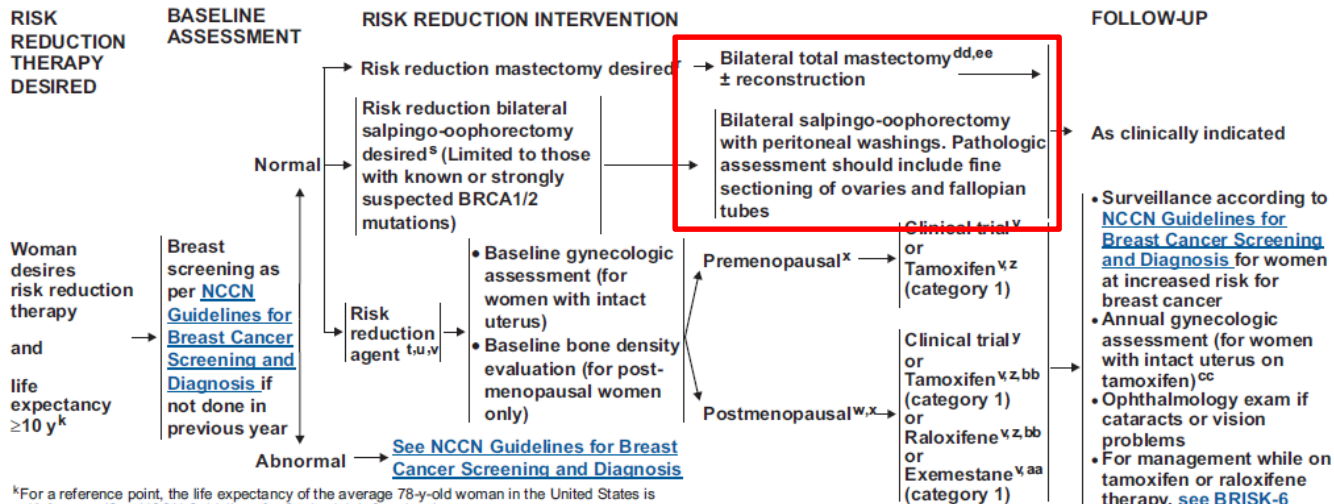
- D; Yearly digital mammogram and yearly MRI starting now

Cancer screening in BRCA positive women who have NOT undergone risk-reduction surgery

- Yearly mammogram starting at age 25
- Yearly breast MRI starting at age 25, 6 months after mammogram
- Transvaginal ultrasound (day 1-10 of cycle) and Ca-125 (day 5 of cycle) every 6 months (or 5-10 years before family member with cancer)
- Tamoxifen chemoprophylaxis
- OCPs may reduce risk of ovarian cancer but may increase risk of breast cancer



Manage a patient with the BRCA gene mutation who wishes to undergo risk reduction surgery



^kFor a reference point, the life expectancy of the average 78-y-old woman in the United States is 10.2 years. (See [NCCN Guidelines for Senior Adult Oncology](#)).

^dRisk reduction mastectomy should generally be considered only in women with BRCA1/2, or other strongly predisposing gene mutation, compelling family history, or possibly with LCIS or prior thoracic radiation therapy at <30 y of age. Women considering risk reduction mastectomy should receive multidisciplinary counseling including consultation with genetics if not already done. Psychological consultation may also be of value.

^eThe additional benefit of concurrent hysterectomy is not clear at this time.

^fThere are no data regarding the use of risk reduction agents in women with prior thoracic radiation therapy.

^gCYP2D6 genotype testing is not recommended in women considering tamoxifen.

^hSee [Breast Cancer Risk Reduction Agents \(BRISK-B\)](#).

ⁱBone density may play a role in choice of therapy.

^jClinical trials in breast cancer have utilized a variety of definitions of menopause. Menopause is generally the permanent cessation of menses, and as the term is utilized in breast cancer management includes a profound and permanent decrease in ovarian estrogen synthesis. Reasonable criteria for determining menopause include any of the following: Prior bilateral oophorectomy; age ≥ 60 y; age <60 y; and amenorrheic for 12 or more months in the absence of chemotherapy, tamoxifen, toremifene, or ovarian suppression and FSH and estradiol in the

postmenopausal range. If taking tamoxifen or toremifene and age <60 y, FSH and plasma estradiol level in postmenopausal ranges.

^yWomen in clinical trial should have baseline exam, follow-up, and monitoring as per protocol.

^zUtility of tamoxifen or raloxifene for breast cancer risk reduction in women <35 years of age is unknown. Raloxifene is only for postmenopausal women >35 y. While raloxifene in long-term follow-up appears to be less efficacious in risk reduction than tamoxifen, consideration of toxicity may still lead to the choice of raloxifene over tamoxifen in women with an intact uterus.

^{aa}Other aromatase inhibitors have shown prevention of contralateral breast cancer and there are ongoing clinical trials.

^{bb}When counseling postmenopausal women regarding the risk/benefit of tamoxifen and raloxifene, refer to tables in Freedman AN, et al. Benefit/risk assessment for breast cancer chemoprevention with raloxifene or tamoxifen for women age 50 years or older. *J Clin Oncol* 2011;29(17):2327-2333.

^{cc}Routine endometrial ultrasound and biopsy are not recommended for women in the absence of other symptoms.

^{dd}Discuss risks and benefits of nipple-areolar sparing surgery.

^{ee}Axillary node assessment is not part of the risk reduction procedure.

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.

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

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

Question 3.

- B; BRCA 1 and 2 testing

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

- Inherited 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 \leq age 45**
- **Diagnosed \leq age 50**
 - ≥ 1 first, second, or third degree relative with breast ca dx \leq 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-)**

Referral Screening Tool for Doctors= Breastcancergenescreen.org



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Health Care Providers

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What is Hereditary Breast and Ovarian Cancer Syndrome (HBOC)?

Although multiple factors have been associated with increased risk for breast and ovarian cancer, family history remains the most significant and consistent predictor of disease development (1-4). It is estimated that 2-7% of breast cancers, and 10-15% of ovarian cancers are the result of an inherited mutation in one of two major hereditary breast/ovarian cancer susceptibility genes, BRCA1 and BRCA2 (BRCA1/2). (5-11) Women who carry a mutation in one of the BRCA genes have a lifetime risk for breast cancer ranging from 45-90%, with over half occurring under the age of 50. (11-16) The risk for ovarian cancer in gene mutation carriers is as high as 30 fold that of the general population. (9, 11-17, 16)

Family history clues that indicate a possible risk for HBOC include a personal or family history of:

- Breast cancer diagnosed before the age of 50
- Ovarian cancer diagnosed at any age
- Both breast and ovarian cancer in the same person
- Bilateral or multiple primary breast cancers
- Ashkenazi Jewish heritage with a history of breast and/or ovarian cancer
- Presence of male breast cancer in the family
- A known BRCA1 or BRCA2 mutation identified in the family
- Breast cancer diagnosed prior to age 60 with triple negative pathology (ER -, PR -, HER2 -)

How will this knowledge benefit my patient?

- Potential benefits of identifying individuals at hereditary risk for breast and ovarian cancer are well-documented (18-31) and include management options for BRCA1/2 mutation carries such as:
 - Prophylactic mastectomy
 - Bilateral salpingoophorectomy
 - Breast MRI
 - Tamoxifen
- Identification of a BRCA1/2 mutation also allows for accurate testing of family members to identify who is and is not at increased risk for cancer.

Should I refer my patient for cancer genetic counseling?

Breastcancergenescreen.org



Breast Cancer Genetics Referral Screening Tool (B-RST™)

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Please print and take to your doctor for consultation.

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Screening Results:

Patient Name: N/A
Date of Screen: 3/28/2016
B-RST™ #: 1016437

B-RST™ Result = Positive Screen

What does this result mean?

- You have a 5-10% chance or greater to have a genetic mutation (change) in one of the BRCA genes.
- You are at increased risk for Hereditary Breast/Ovarian Cancer
 - [Read more about Hereditary Breast/Ovarian Cancer and Genetic Testing](#)
- Your risks for breast and/or ovarian cancer *may* be greatly increased over the general population.
- [Cancer Genetic Counseling](#) is recommended to carefully review your family history in more detail, assess cancer and genetic risks, and discuss the benefits and limitations of BRCA genetic testing.

Keep in mind that B-RST™ is a screen - not a "yes or no" diagnostic test.

This result does not mean that you will get cancer. It only means that you have a higher chance to have a BRCA mutation and may be at increased risk for developing early onset breast cancer or ovarian cancer.

Talk with your doctor if you have questions about your B-RST™ result, or require help in setting up a cancer genetic counseling appointment.

Note: People who screen positive on the B-RST™ may not be found to be good candidates for BRCA genetic testing when a comprehensive cancer risk assessment is performed.

[Resources To Locate a Cancer Genetics Professional](#)



Breast Cancer Genetics Referral Screening Tool (B-RST™)

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B-RST™ Score Interpretation

POSITIVE: Person has a 5-10% or *greater* chance of carrying a mutation in *BRCA1* or *BRCA2*, which are associated with substantially increased risks (10 fold or more) for early onset breast cancer and ovarian cancer. Referral for cancer genetic counseling is indicated.

Note: Individuals who screen positive on the B-RST™ may not be found to be appropriate candidates for *BRCA1/2* testing when a comprehensive cancer risk assessment is performed.

NEGATIVE: Person is *unlikely* to carry a *BRCA1/2* mutation.

LOW Risk = Based on family history, person's risks for breast/ovarian cancer expected to be at or below that of the general population.

MODERATE Risk = Persons who do not have a family history suggestive of *hereditary* cancer, but may have a risk for breast and/or ovarian cancer that is somewhat increased (~2-4 fold) above that of the general population. Further risk assessment and/or enhanced screening or prevention strategies may be appropriate for some of these individuals. (*Commun Oncol*, 2009; 6:373)

Disclaimers:

- This screening tool does not assess *non-familial* risk factors for breast or ovarian cancer.
- Changes in family history could result in a change in the risk score. B-RST™ should be re-run if additional cases of breast and/or ovarian cancer occur.
- In families with few females, single cases of ovarian cancer or early breast cancer may be related to a *BRCA1/2* mutation.
- There are other, less common hereditary causes of breast and ovarian cancer. A cancer genetics consultation should be pursued if:
 - There are multiple individuals with cancer in multiple generations
 - Cancers are of an usually early age of onset
 - Rare or unusual cancers or tumors have occurred (examples: cancer of adrenal glands, medullary thyroid cancer, hamartomatous polyps, paragangliomas)

Question 4.

- B; Bone biopsy

Manage a patient with recurrent breast cancer



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NCCN Guidelines Version 2.2015 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 \(BINV-18\)](#)

^bSee Principles of HER2 Testing (BINV-A).

^cSee NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian.

^gIf 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.

ⁱFDG 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 5.

- C; Low-dose chest CT

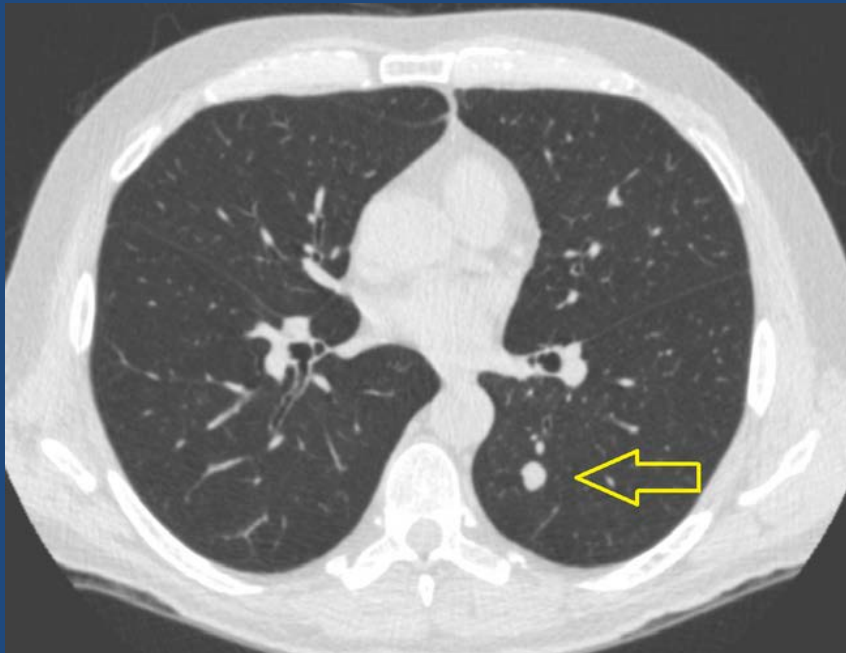
Lung cancer screening with annual low-dose chest CT

Who to screen:

- Age 55-80 years
- ≥ 30 pack years smoking
- Quit 15 years ago or less

Modalities to screen

- CXR- No benefit
- **Low dose (2 mSv vs 7 mSv radiation dose) chest CT**
- Relative mortality reduction of 20%
 - Screening 1000 patients over 6 years, 3.9 deaths prevented
 - 8.6 million screens may save 12,000 deaths from lung cancer per year



Question 6.

- B; Mediastinoscopy

Diagnose and Manage Limited Stage Small Cell Lung Cancer



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NCCN Guidelines Version 2.2013
Small Cell Lung Cancer

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DIAGNOSIS

INITIAL EVALUATION^a

STAGE

Small cell or combined Small cell/non-small cell lung cancer on biopsy or cytology of primary or metastatic site

- H&P
- Pathology review
- CBC with differential, platelets
- Electrolytes, liver function tests (LFTs), Ca, LDH
- BUN, creatinine
- Chest/liver/adrenal CT with IV contrast whenever possible
- Brain MRI^{a,b} (preferred) or CT with IV contrast whenever possible
- PET-CT scan (if limited stage is suspected)^{a,c}
- Smoking cessation counseling and intervention

Limited stage^d
(T any, N any, M0; except T3-4 due to multiple lung nodules that do not fit in a tolerable radiation field)

[See Additional Workup \(SCL-2\)](#)

Extensive stage^d
(T any, N any, M1a/b; T3-4 due to multiple lung nodules)

[See Initial Treatment \(SCL-4\)](#)

^aIf 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.

^bBrain MRI is more sensitive than CT for identifying brain metastases and is preferred over CT.

^cIf 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.

DIAGNOSIS

INITIAL EVALUATION^a

STAGE

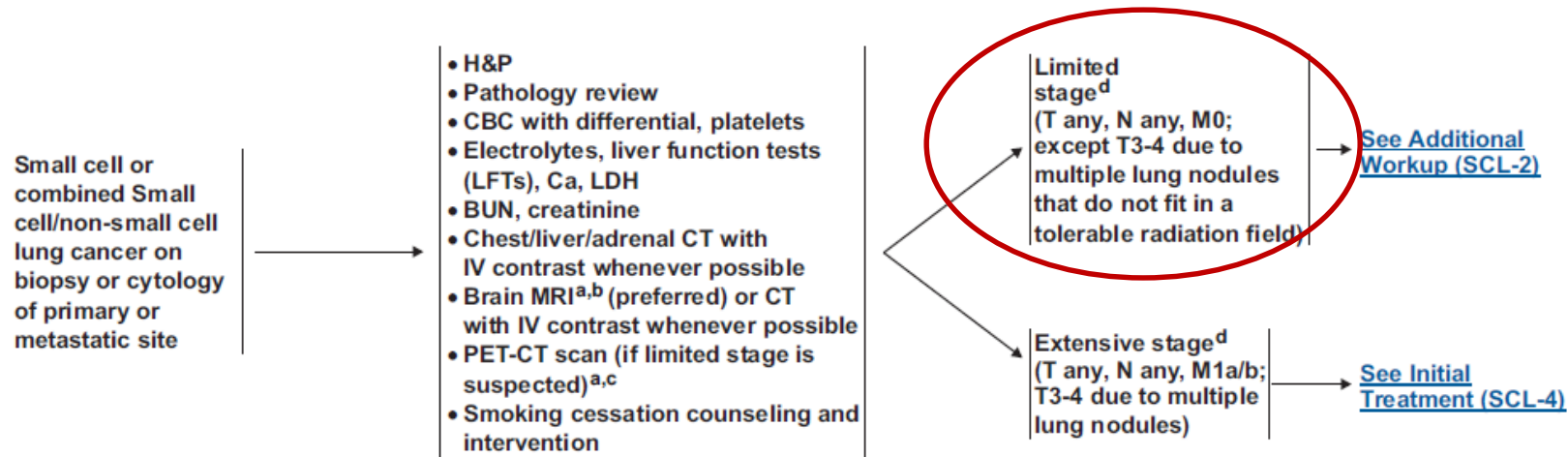


Table 1 - Definition of small cell lung cancer consists of two stages:

(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.

^aIf 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.

^bBrain MRI is more sensitive than CT for identifying brain metastases and is preferred over CT.

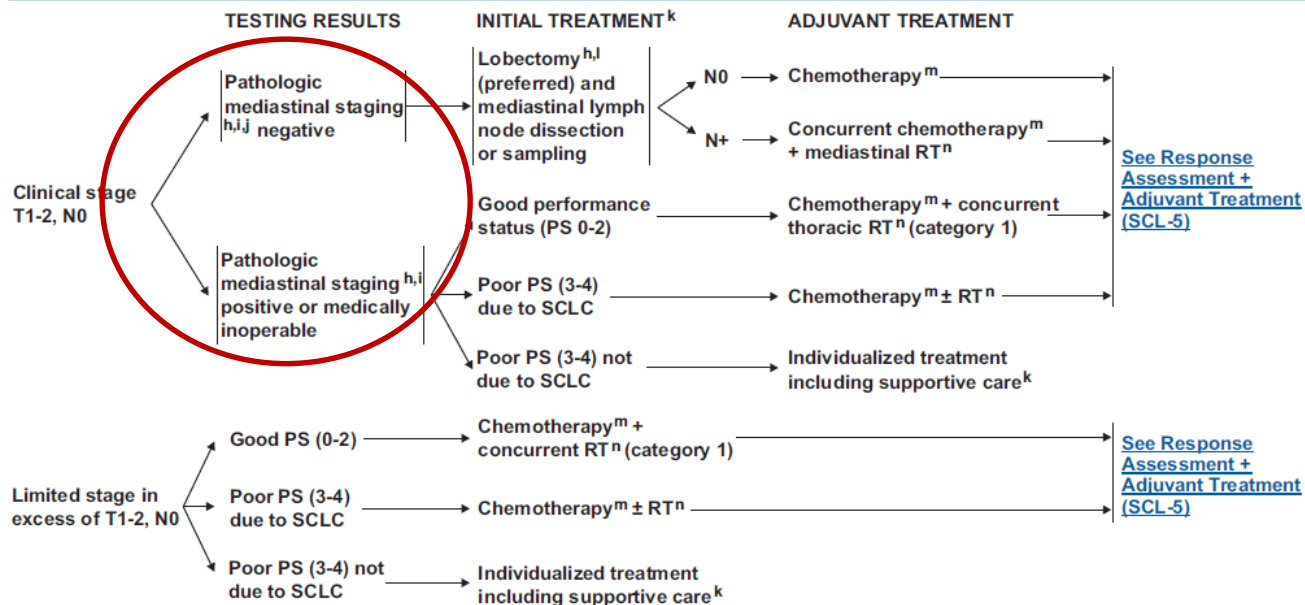
^cIf PET/CT not available, bone scan may be used to identify metastases. Pathologic confirmation is recommended for lesions detected by PET/CT that alter stage.

^d[See Staging on page ST-1.](#)

Note: All recommendations are category 2A unless otherwise indicated.

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Manage limited-stage small cell lung cancer



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

^hSee Principles of Surgical Resection (SCL-A).

ⁱMediastinal staging procedures include mediastinoscopy, mediastinotomy, endobronchial or esophageal ultrasound-guided biopsy, and video-assisted thoracoscopy. If endoscopic lymph node biopsy is positive, additional mediastinal staging is not required.

^jPathologic mediastinal staging is not required if the patient is not a candidate for surgical resection or if non-surgical treatment is pursued.

^kSee Principles of Supportive Care (SCL-B).

^lSelect patients may be treated with chemotherapy/RT as an alternative to surgical resection.

^mSee Principles of Chemotherapy (SCL-C).

ⁿSee Principles of Radiation Therapy (SCL-D).

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 7.

- C; Surgery and adjuvant chemotherapy

Table 1. Definitions for T, N, M*

T	Primary Tumor	N	Regional Lymph Nodes
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	NX	Regional lymph nodes cannot be assessed
T0	No evidence of primary tumor	N0	No regional lymph node metastasis
Tis	Carcinoma in situ	N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
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	N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
T1a	Tumor ≤2 cm in greatest dimension	N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)
T1b	Tumor >2 cm but ≤3 cm in greatest dimension	M	Distant Metastasis
T2	Tumor >3 cm but ≤7 cm or tumor with any of the following features: ^b	MX	Distant metastasis cannot be assessed
	Involves main bronchus, ≥2 cm distal to the carina	M0	No distant metastasis
	Invades visceral pleura	M1	Distant metastasis
	Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung	M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural (or pericardial) effusion ^c
T2a	Tumor >3 cm but ≤5 cm in greatest dimension	M1b	Distant metastasis
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		

^aThe 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.

^bT2 tumors with these features are classified T2a if ≤5 cm or if size cannot be determined, and T2b if >5 cm but ≤7 cm.

^cMost 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.

NCCN Guidelines Version 5.2017 Non-Small Cell Lung Cancer

PATHOLOGIC DIAGNOSIS OF NSCLC

INITIAL EVALUATION

CLINICAL STAGE

NSCLC →

- Pathology review^a
- H&P (include performance status + weight loss)^b
- CT chest and upper abdomen with contrast, including adrenals
- CBC, platelets
- Chemistry profile
- Smoking cessation advice, counseling, and pharmacotherapy
- ▶ Use the 5 A's Framework: Ask, Advise, Assess, Assist, Arrange
<http://www.ahrq.gov/clinic/tobacco/5steps.htm>
- Integrate palliative care^c (See [NCCN Guidelines for Palliative Care](#))

- Stage IA, peripheral^d (T1ab, N0) → [See Pretreatment Evaluation \(NSCL-2\)](#)
- Stage I, peripheral^d (T2a, N0); central^d (T1ab-T2a, N0);
Stage II (T1ab-T2ab, N1; T2b, N0); stage IIB (T3, N0)^e → [See Pretreatment Evaluation \(NSCL-2\)](#)
- Stage IIIA (T3, N1) → [See Pretreatment Evaluation \(NSCL-4\)](#)
- Stage IIB^f (T3 invasion, N0);
Stage IIIA^f (T4 extension, N0-1; T3, N1) → [See Pretreatment Evaluation \(NSCL-7\)](#)
- Stage IIIA^f (T1-3, N2) → [See Pretreatment Evaluation \(NSCL-7\)](#)
- Separate pulmonary nodule(s) (Stage IIB, IIIA, IV) → [See Treatment \(NSCL-9\)](#)
- Multiple lung cancers → [See Pretreatment Evaluation \(NSCL-11\)](#)
- Stage IIB^f (T1-3, N3) mediastinal CT positive
Contralateral (lymph nodes ≥1 cm) or palpable supraclavicular lymph nodes → [See Pretreatment Evaluation \(NSCL-12\)](#)
- Stage IIB^f (T4, N2-3) on CT → [See Pretreatment Evaluation \(NSCL-12\)](#)
- Stage IV (M1a)^c (pleural or pericardial effusion) → [See Pretreatment Evaluation \(NSCL-13\)](#)
- Stage IV (M1b)^c
Limited sites with resectable lung lesion → [See Systemic Therapy \(NSCL-16\)](#)
- Stage IV (M1b)^c disseminated metastases → [See Systemic Therapy \(NSCL-16\)](#)

^aSee [Principles of Pathologic Review \(NSCL-A\)](#).

^bEnhanced frailty or geriatric assessments may predict complications better following treatment modalities, particularly surgery. A preferred frailty assessment system has not been established.

^cTemel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small cell lung cancer. *N Engl J Med* 2010;363:733-742.

^dBased on the CT of the chest: Peripheral = outer third of lung; Central = inner two thirds of lung.

^eT3, N0 related to size or satellite nodules.

^fFor patients considered to have stage IIB and stage III tumors, where more than one treatment modality (surgery, radiation therapy, or chemotherapy) is usually considered, a multidisciplinary evaluation should be performed.

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

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 IIIA	T1a	N2	M0
Stage 0	Tis	N0	M0		T1b	N2	M0
Stage IA	T1a	N0	M0		T2a	N2	M0
	T1b	N0	M0		T2b	N2	M0
Stage IB	T2a	N0	M0		T3	N1	M0
Stage IIA	T2b	N0	M0		T3	N2	M0
	T1a	N1	M0		T4	N0	M0
	T1b	N1	M0		T4	N1	M0
	T2a	N1	M0		Stage IIIB	T1a	N3
Stage IIB	T2b	N1	M0			T1b	N3
	T3	N0	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 8.

- B; Fecal immunochemical testing every year

Characteristics of colorectal cancer screening strategies*

Screening method	Frequency [¶]	Evidence of efficacy	Other considerations
Stool-based tests			
gFOBT	Every year	RCTs with mortality end points: <ul style="list-style-type: none"> High-sensitivity versions (eg, Hemoccult SENSА) have superior test performance characteristics than older tests (eg, Hemoccult II) 	<ul style="list-style-type: none"> Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT ^Δ	Every year	Test characteristic studies: <ul style="list-style-type: none"> Improved accuracy compared with gFOBT Can be done with a single specimen 	<ul style="list-style-type: none"> Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT-DNA	Every one or three years [◇]	Test characteristic studies: <ul style="list-style-type: none"> Specificity is lower than for FIT, resulting in more false-positive results, more diagnostic colonoscopies, and more associated adverse events per screening test Improved sensitivity compared with FIT per single screening test 	<ul style="list-style-type: none"> There is insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative diagnostic colonoscopy; may potentially lead to overly intensive surveillance due to provider and patient concerns over the genetic component of the test
Direct visualization tests			
Colonoscopy ^Δ	Every 10 years	Prospective cohort study with mortality end point	<ul style="list-style-type: none"> Requires less frequent screening Screening and diagnostic follow-up of positive findings can be performed during the same examination
CT colonography [§]	Every five years	Test characteristic studies	<ul style="list-style-type: none"> There is insufficient evidence about the potential harms of associated extracolonic findings, which are common
Flexible sigmoidoscopy	Every five years	RCTs with mortality end points: <ul style="list-style-type: none"> Modeling suggests it provides less benefit than when combined with FIT or compared with other strategies 	<ul style="list-style-type: none"> Test availability has declined in the United States
Flexible sigmoidoscopy with FIT ^Δ	Flexible sigmoidoscopy every 10 years plus FIT every year	RCT with mortality end point (subgroup analysis)	<ul style="list-style-type: none"> Test availability has declined in the United States Potentially attractive option for patients who want endoscopic screening but want to limit exposure to colonoscopy

FIT: fecal immunochemical test; FIT-DNA: multitargeted stool DNA test; gFOBT: guaiac-based fecal occult blood test; RCT: randomized clinical trial.

* Although a serology test to detect methylated *SEPT9* DNA was included in the systematic evidence review, this screening method currently has limited evidence evaluating its use (a single published test characteristic study met inclusion criteria, which found it had a sensitivity to detect colorectal cancer of <50%).^[1] It is therefore not included in this table.

Question 9.

- B; 5-Fluorouracil, leucovorin, and oxaliplatin (FOL-FOX)

Manage stage III colon cancer



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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	<u>Tumor invades through the muscularis propria into the pericolorectal tissues</u>
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	<u>Metastasis in 1-3 regional lymph nodes</u>
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	<u>No distant metastasis</u>
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

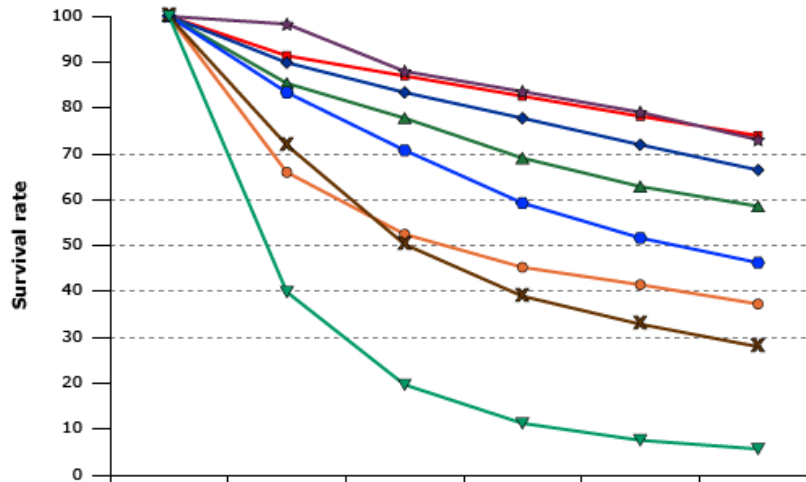
Table 2. Anatomic Stage/Prognostic Groups

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
IIIC	T1-T2	N2b	M0	C	C1
	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 10.

- A; CT annually for 3 years

Manage post-colorectal cancer surveillance

NCCN	National Comprehensive Cancer Network®	NCCN Guidelines Version 2.2015 Colon Cancer		NCCN Guidelines Index Colon Cancer Table of Contents Discussion
PATHOLOGIC STAGE ^e	ADJUVANT THERAPY ^{m,n}	SURVEILLANCE ^t		
Tis; T1, N0, M0 T2, N0, M0	None 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		
T3, N0, M0 ^{k,l} (no high-risk features)	Clinical trial or Observation or Consider capecitabine ^o or 5-FU/leucovorin ^o	<ul style="list-style-type: none"> • 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^d in 1 y except if no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3–6 mo  		
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	<ul style="list-style-type: none"> ▶ 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) 		
Node-positive disease, see COL-4		If Recurrence, See Workup (COL-9)		

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

Manage post-colorectal cancer surveillance



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PATHOLOGIC STAGE ^e	ADJUVANT THERAPY ^{m,n}	SURVEILLANCE ^t
Tis; T1, N0, M0 T2, N0, M0	None 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
T3, N0, M0 ^{k,l} (no high-risk features)	Clinical trial or Observation or Consider capecitabine ^o or 5-FU/leucovorin ^o	<ul style="list-style-type: none"> • 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^d in 1 y except if no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3–6 mo <ul style="list-style-type: none"> ▶ 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](#)

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;

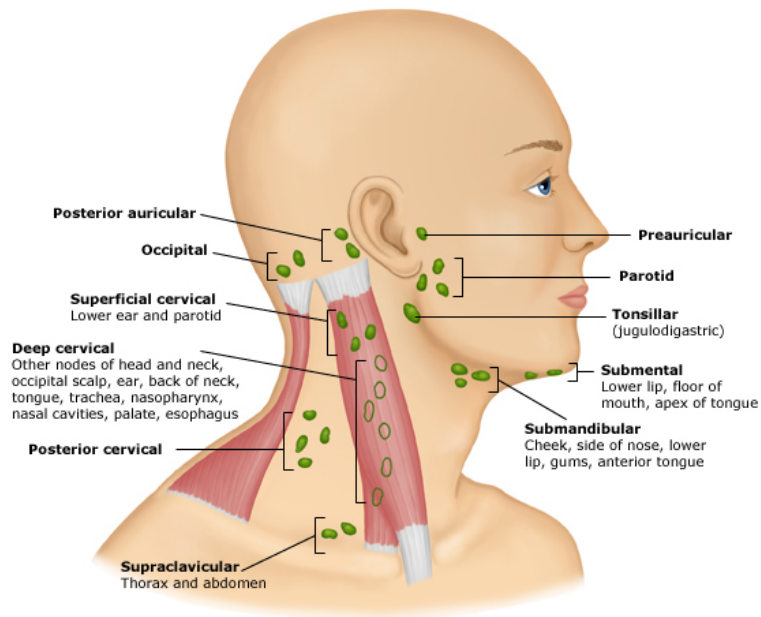
High risk includes lymphatic or venous invasion or poorly differentiated tumor

Question 11.

- A; Endoscopic evaluation of the oropharynx

Evaluate a patient for head and neck cancer

Lymph nodes of the head and neck



This drawing schematically depicts the major lymph nodes in the head and neck area that are likely to be enlarged on physical examination in patients with various local or systemic diseases. The major nodal groups are shown here in bold, with the areas draining into these nodal groups noted when appropriate. While enlargement of both the left and right supraclavicular lymph nodes may reflect disease in the thorax, left supraclavicular nodal enlargement, because of its drainage pattern, may also reflect the presence of abdominal involvement (ie, Virchow's node).

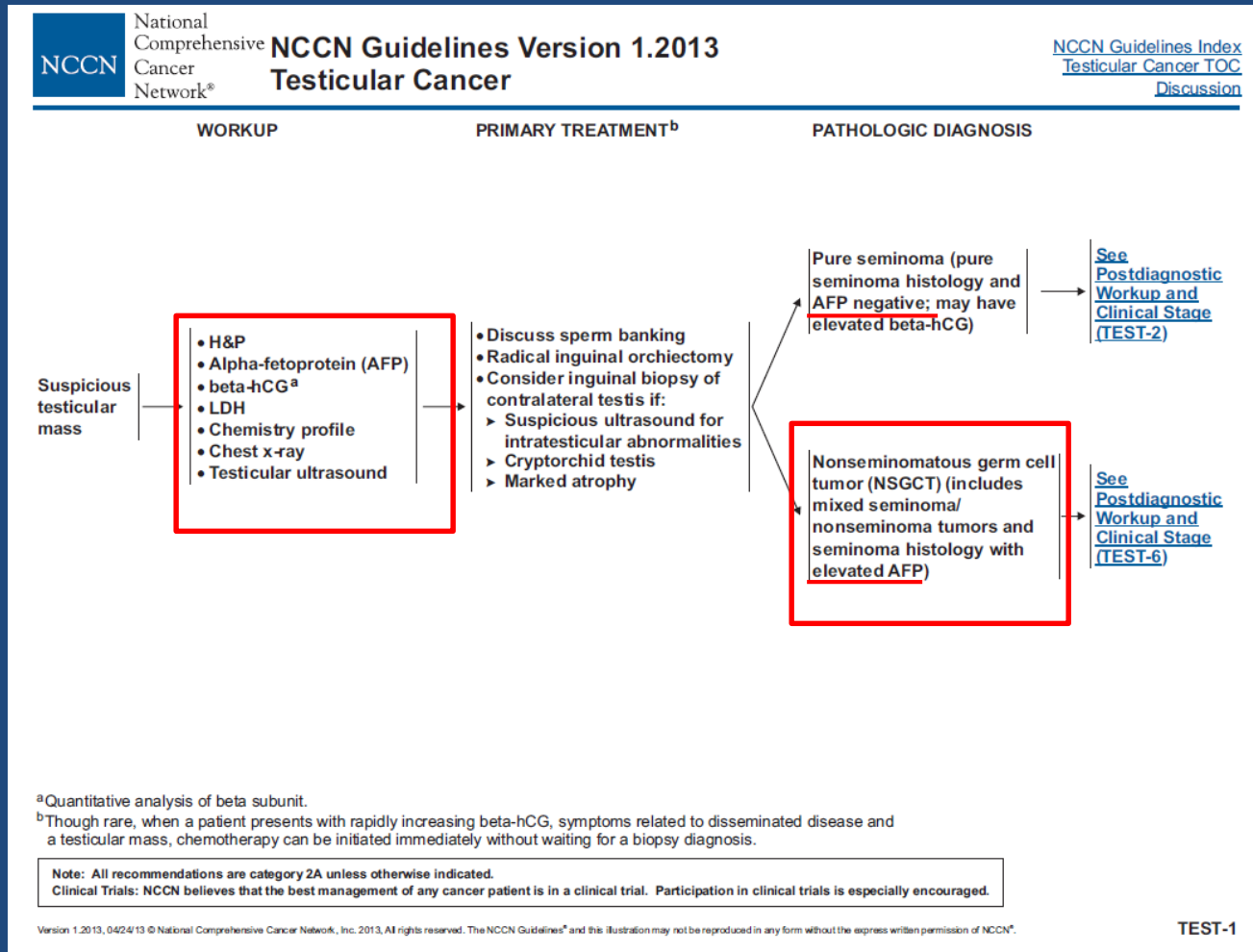
- **FIRST** step would be ENT consult for triple scope endoscopy to look for a primary cancer; **if the endoscopy is negative, pursue FNA of node**
- Excisional biopsy of node would potentially alter tissue planes needed for better resection
- PET/CT could be done **AFTER** tissue diagnosis is made

Question 12.

- C; Non-seminoma germ cell tumor

Diagnose Testicular Cancer:

NO AFP is the KEY to NON-Seminoma Pathology!



Question 13.

- 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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Table 1

Definitions of Stages in Hodgkin's Disease¹

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, II₃).

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 (III_E), 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 $\geq 15,000/\mu\text{mL}$

Absolute lymphocyte count <600/ μmL 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 14.

- C; Autologous hematopoietic stem cell transplant

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



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NCCN Guidelines Version 2.2015 Diffuse Large B-Cell Lymphoma

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RELAPSE/
REFRACTORY DISEASE

ADDITIONAL
THERAPY

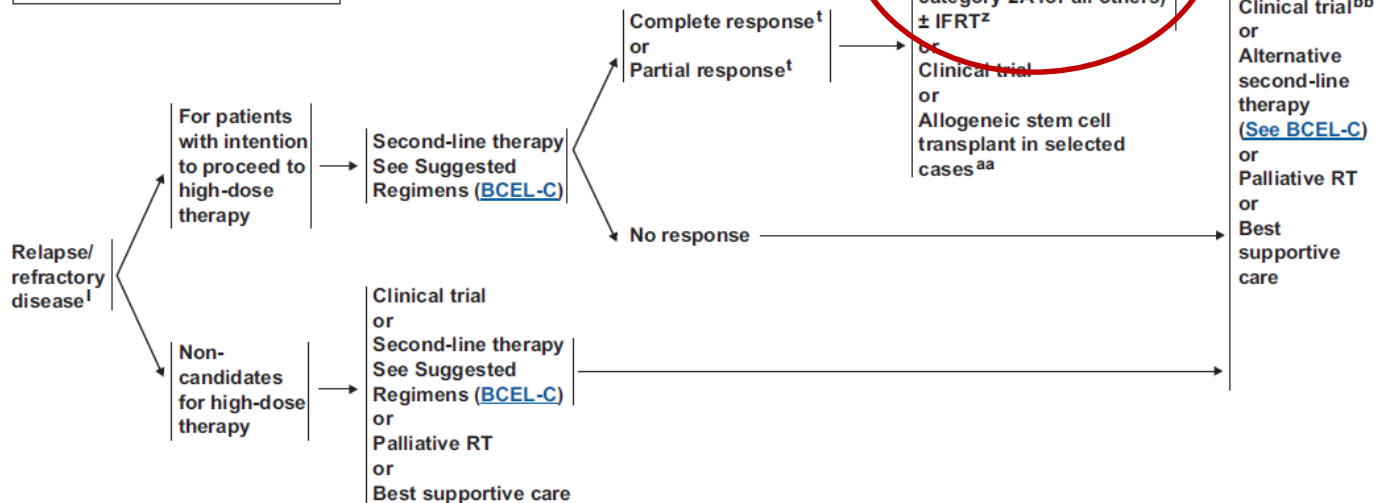
RESPONSE #2

CONSOLIDATION/
ADDITIONAL THERAPY

RELAPSE #2
OR GREATER

Consider prophylaxis for tumor lysis syndrome ([See NHODG-B](#))

See monoclonal antibody and viral reactivation ([NHODG-B](#))



¹For systemic disease with concurrent CNS disease, [see BCEL-C](#).

^t[See Lugano Response Criteria for Non-Hodgkin's Lymphoma \(NHODG-C\)](#).

^zAdditional RT can be given before or after high-dose therapy with stem cell rescue to sites of previous positive disease.

^{aa}Selected cases include mobilization failures and persistent bone marrow involvement.

^{bb}Clinical trials or individual regimens: Patients who progress after three successive regimens are unlikely to derive additional benefit from currently utilized combination chemotherapy regimens, except for patients with a long disease-free interval.

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 15.

- D; No further treatment



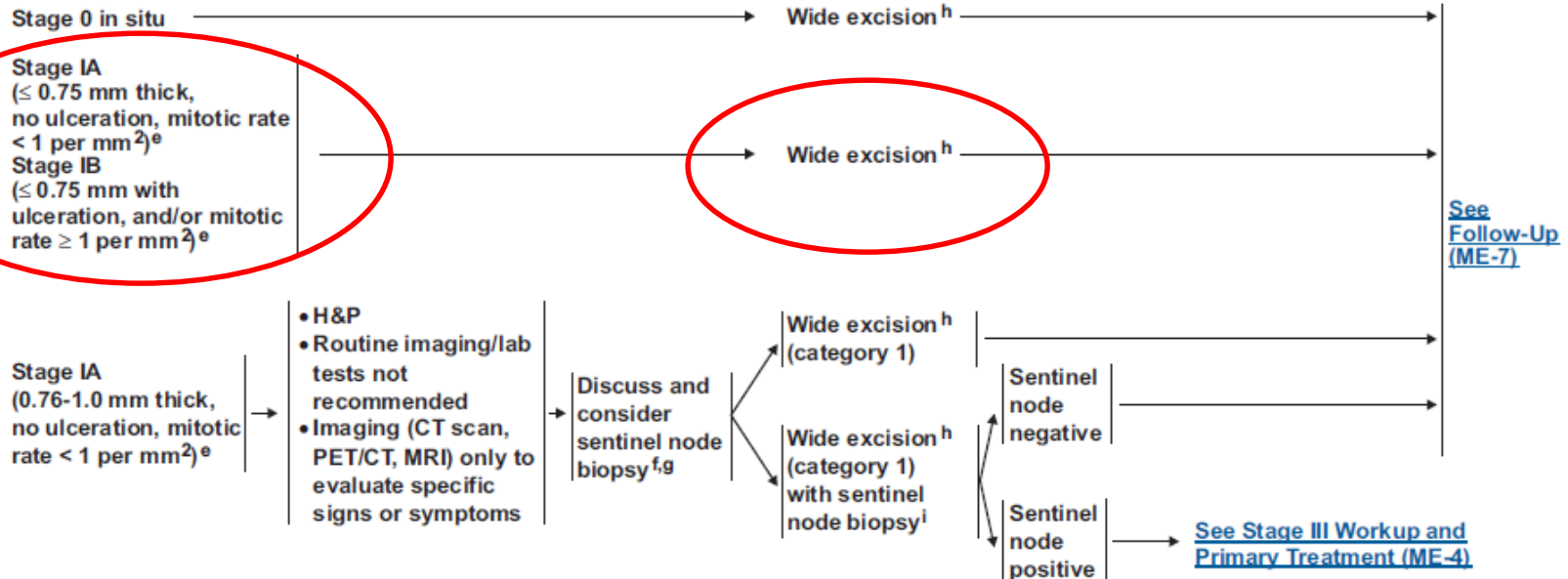
RISK FACTORS FOR MELANOMA DEVELOPMENT*

Male sex¹
Age >60 years
Phenotypic Predisposition <ul style="list-style-type: none"> • Atypical mole/dysplastic nevus pattern² • Increased mole count (particularly large nevi)³ • Sun-sensitive phenotype/tendency to sunburn³ • Red hair-blue eyes/Fitzpatrick skin type I/pheomelanin predominant phenotype³
Personal Medical History/Comorbidities <ul style="list-style-type: none"> • Multiple and/or blistering sunburns^{3,4} • Precancer/cancers,^{5,6} especially: <ul style="list-style-type: none"> ▶ Actinic keratosis/non-melanoma (keratinocyte) skin cancer (eg, basal cell and squamous cell carcinomas)³ ▶ Childhood cancer⁷ • Immunosuppression/immune perturbation related to: <ul style="list-style-type: none"> ▶ Solid organ transplantation^{3,8,9} ▶ Hematopoietic cell transplantation⁹ ▶ Human immunodeficiency virus/acquired immunodeficiency syndrome¹⁰ • Rare Genodermatoses <ul style="list-style-type: none"> ▶ Xeroderma pigmentosum¹¹
Genetic Predisposition <ul style="list-style-type: none"> • Presence of melanoma susceptibility polymorphisms (including CDKN2A, CDK4, MC1R, and other as yet undefined germline mutations)³ • Family history of melanoma, especially if multiple
Environmental Factors <ul style="list-style-type: none"> • Tanning bed use^{3,13,14} • Residence in sunnier climate/latitude nearer equator¹⁵ • Intermittent, intense sun exposure (for truncal/extremity melanomas, often observed with associated increased nevus count)³ • Chronic sun exposure (for head/neck/arm melanomas, often associated with lower nevus count)

Manage early-stage melanoma

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

CLINICAL STAGE WORKUP PRIMARY TREATMENT ADJUVANT TREATMENT



^eIn 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.

^fDecision to perform SLNB may be based on significant patient comorbidities, patient preference or other factors.

^gSentinel node biopsy is an important staging tool, but the impact of SLNB on overall survival is unclear.

^hSee [Principles of Surgical Margins for Wide Excision of Primary Melanoma \(ME-B\)](#).

ⁱSentinel 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

<u>Tumor Thickness</u>	<u>Recommended Clinical Margins²</u>
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.

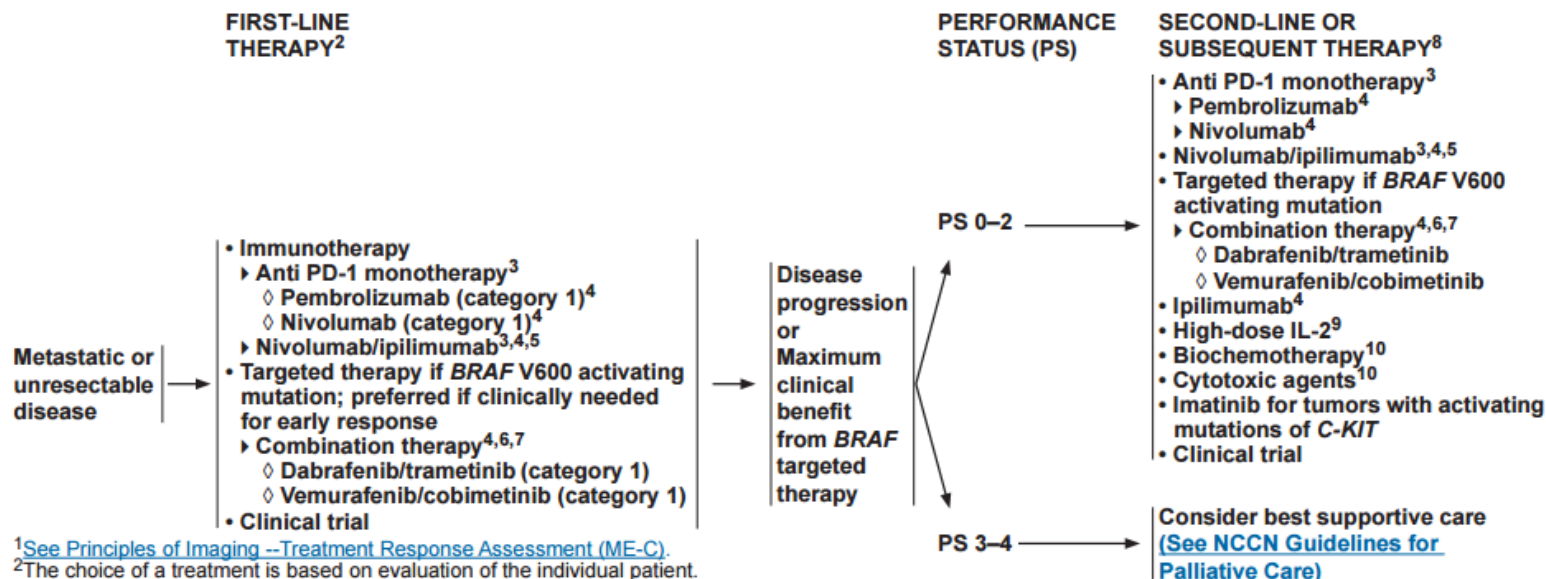
Common Follow-up Recommendations For All Patients:

- 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 16.

- A; BRAF V600 mutation analysis

SYSTEMIC THERAPY FOR METASTATIC OR UNRESECTABLE DISEASE¹



¹See [Principles of Imaging --Treatment Response Assessment \(ME-C\)](#).

²The choice of a treatment is based on evaluation of the individual patient.

³The use of PD-L1 as a biomarker for selection of anti-PD-1 therapy and/or nivolumab/ipilimumab combination therapy is an emerging research issue with non-uniform application among the NCCN Member Institutions (category 2B).

⁴See [Management of Toxicities of Immunotherapy and Targeted Therapy \(ME-H\)](#).

⁵Nivolumab/ipilimumab combination therapy is associated with improved ORR and PFS compared with single-agent nivolumab or ipilimumab, at the expense of significantly increased toxicity. Compared to single-agent therapy, the impact of nivolumab/ipilimumab combination therapy on overall survival is not known. The phase III trial of nivolumab/ipilimumab versus either nivolumab or ipilimumab monotherapy was conducted in previously untreated patients with unresectable stage III or IV melanoma.

⁶In previously untreated patients with unresectable Stage IIIC or Stage IV disease, *BRAF*/MEK inhibitor combination therapy was associated with improved PFS and response rate, and in preliminary reports improved OS, when compared to *BRAF* inhibitor monotherapy.

⁷If *BRAF*/MEK inhibitor combination therapy is contraindicated, *BRAF*-inhibitor monotherapy with dabrafenib or vemurafenib are recommended options, especially in patients who are not appropriate candidates for checkpoint immunotherapy.

⁸For patients who experience progression of melanoma during or shortly after first-line therapy, consider second-line agents if not used first line and not of same class. For patients who progressed on single-agent checkpoint immunotherapy, nivolumab/ipilimumab combination therapy is a reasonable treatment option. For patients who experience disease control (CR, PR, or SD) and have no residual toxicity, but subsequently experience disease progression/relapse >3 months after treatment discontinuation, re-induction with the same agent or same class of agents may be considered.

⁹High-dose IL-2 should not be used for patients with inadequate organ reserve, poor performance status, or untreated or active brain metastases. For patients with small brain metastases and without significant peritumoral edema, IL-2 therapy may be considered (category 2B). Therapy should be restricted to an institution with medical staff experienced in the administration and management of these regimens.

¹⁰For a list of cytotoxic regimens and biochemotherapy regimens, see [\(ME-G 2 of 6\)](#).

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Question 17.

- D; Surgical resection of the pancreatic mass

Diagnose pancreatic cancer and send to surgery without delay

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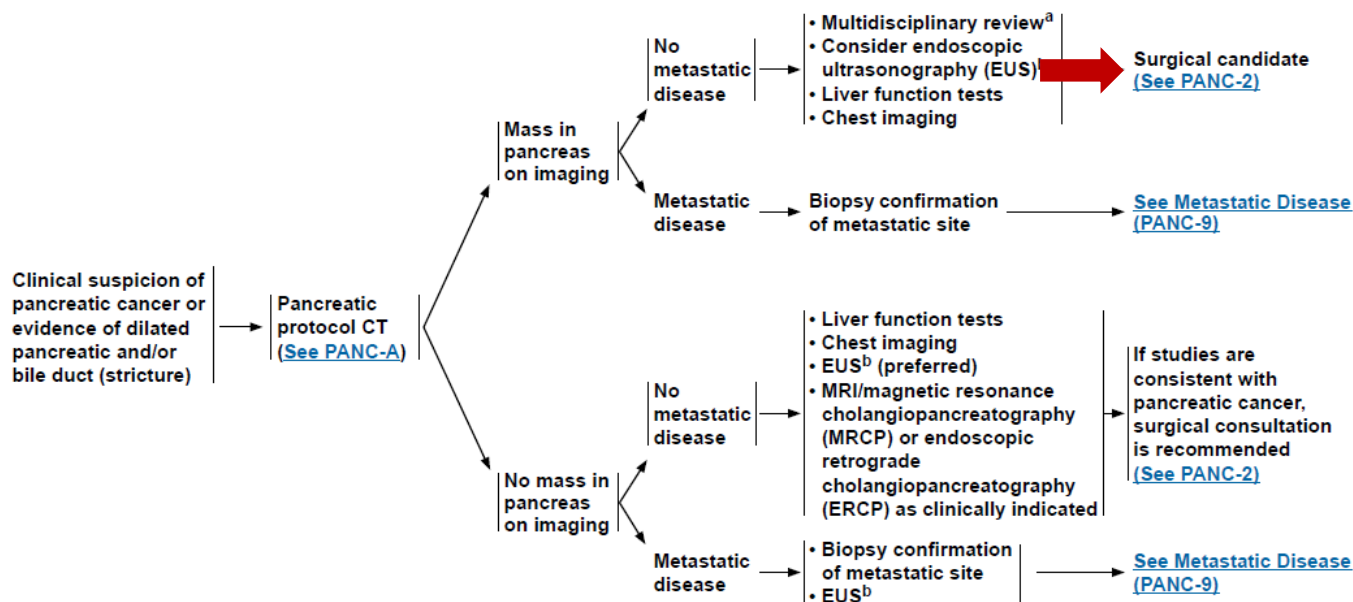


NCCN Guidelines Version 2.2015 Pancreatic Adenocarcinoma

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CLINICAL PRESENTATION

WORKUP



^aMultidisciplinary review should ideally involve expertise from diagnostic imaging, interventional endoscopy, medical oncology, radiation oncology, surgery, and pathology.

^bEUS-FNA if clinically indicated.

Note: All recommendations are category 2A unless otherwise indicated.
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Question 18.

- 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

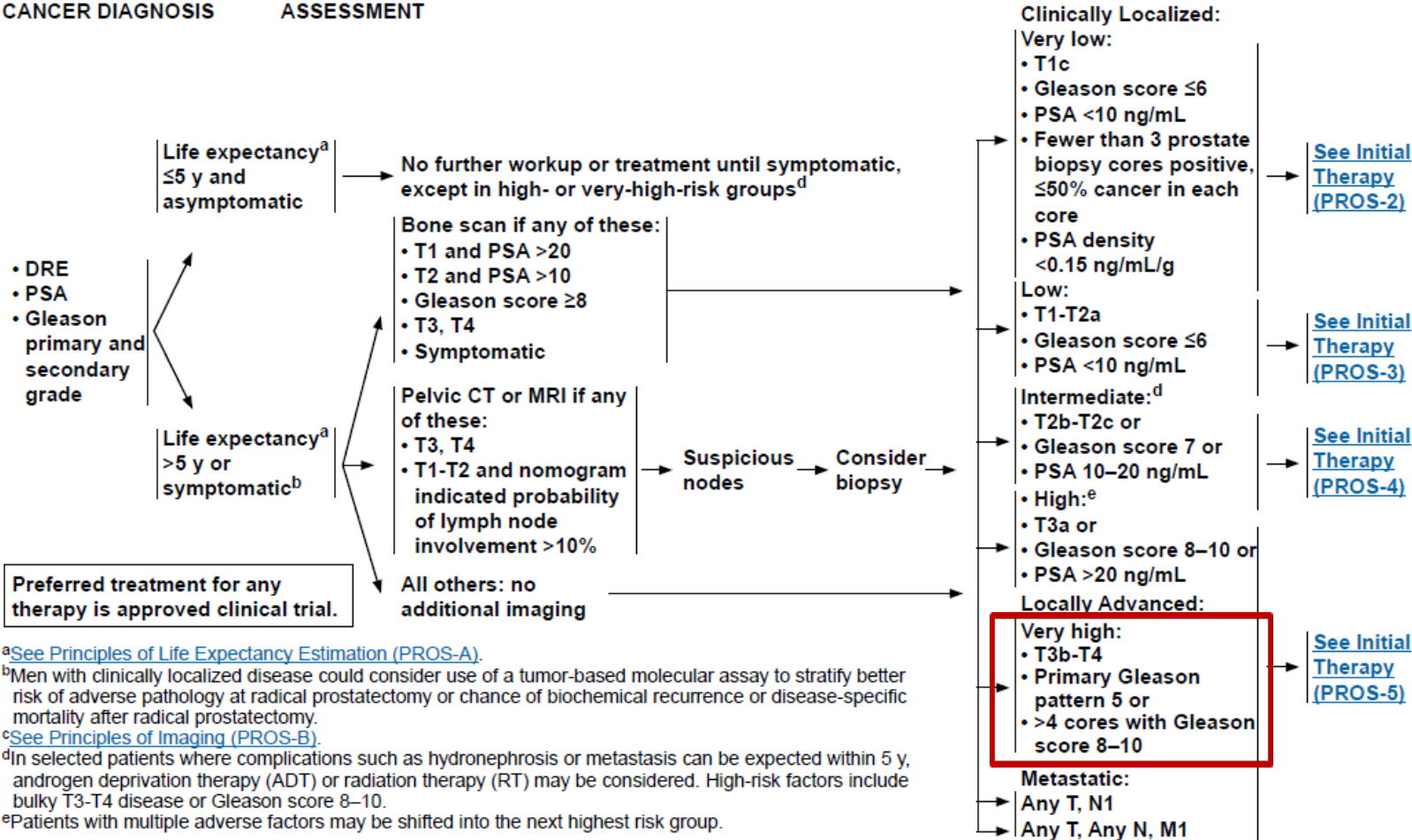
*Note: When more than one site of metastasis is present, the most advanced category is used. pM1c is most advanced.

INITIAL PROSTATE CANCER DIAGNOSIS

INITIAL CLINICAL ASSESSMENT

STAGING WORKUP^c

RISK GROUP^e



^aSee Principles of Life Expectancy Estimation (PROS-A).

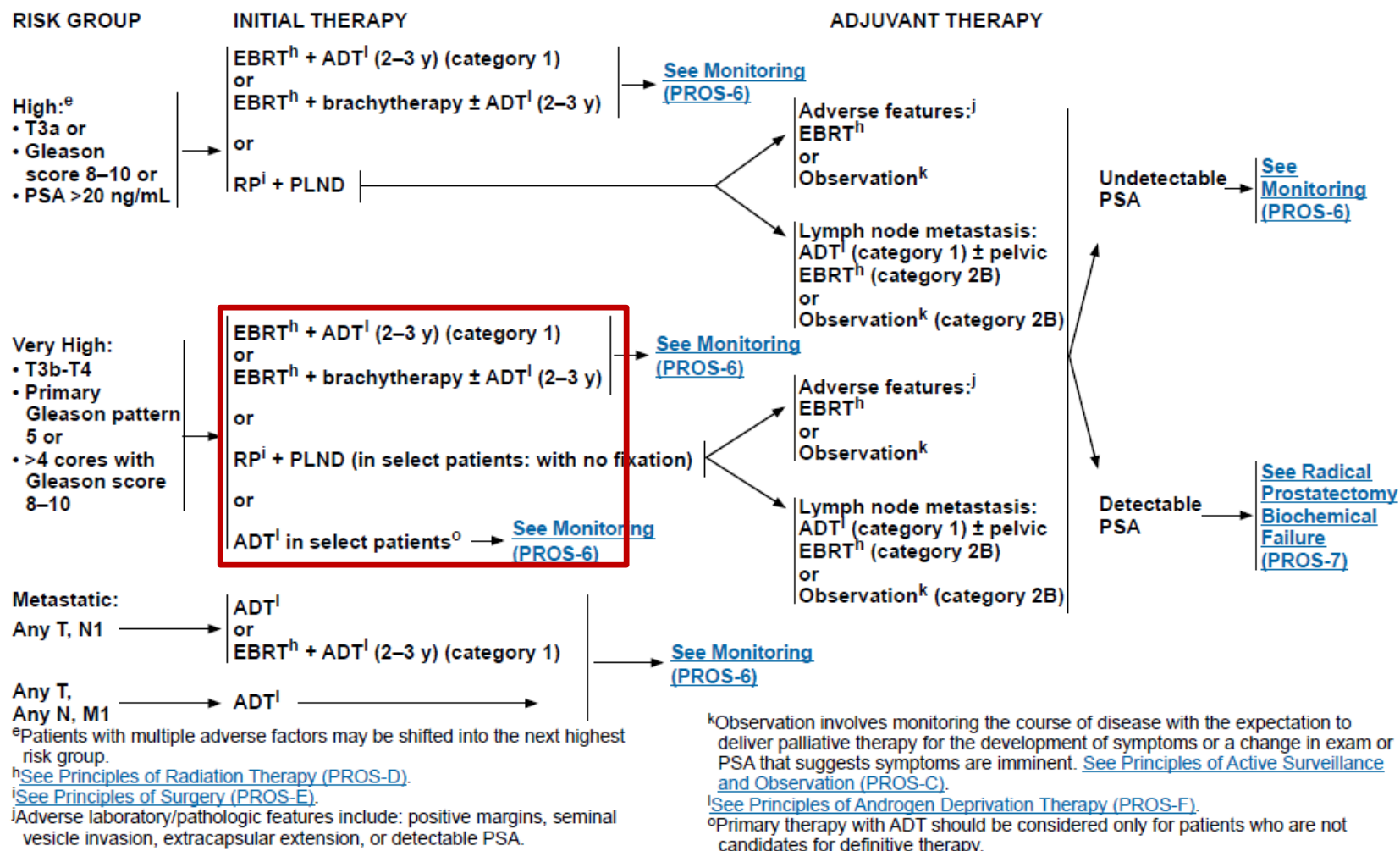
^bMen with clinically localized disease could consider use of a tumor-based molecular assay to stratify better risk of adverse pathology at radical prostatectomy or chance of biochemical recurrence or disease-specific mortality after radical prostatectomy.

^cSee Principles of Imaging (PROS-B).

^dIn 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.

^ePatients 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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Question 19.

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

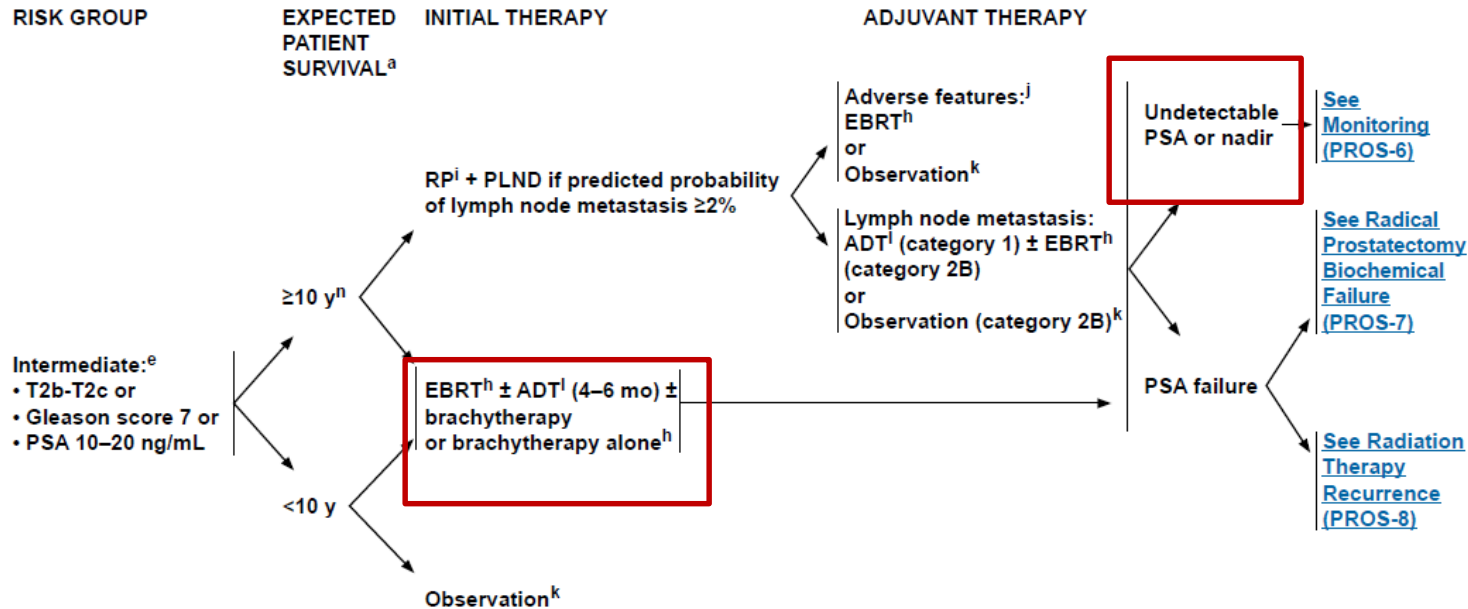
Manage prostate cancer follow up; 75% of recurrences occur within 5 years



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^aSee [Principles of Life Expectancy Estimation \(PROS-A\)](#).

^ePatients with multiple adverse factors may be shifted into the next highest risk group.

^hSee [Principles of Radiation Therapy \(PROS-D\)](#).

ⁱSee [Principles of Surgery \(PROS-E\)](#).

^jAdverse laboratory/pathologic features include: positive margins, seminal vesicle invasion, extracapsular extension, or detectable PSA.

^kObservation 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 \(PROS-C\)](#).

^lSee [Principles of Androgen Deprivation Therapy \(PROS-F\)](#).

ⁿActive 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.

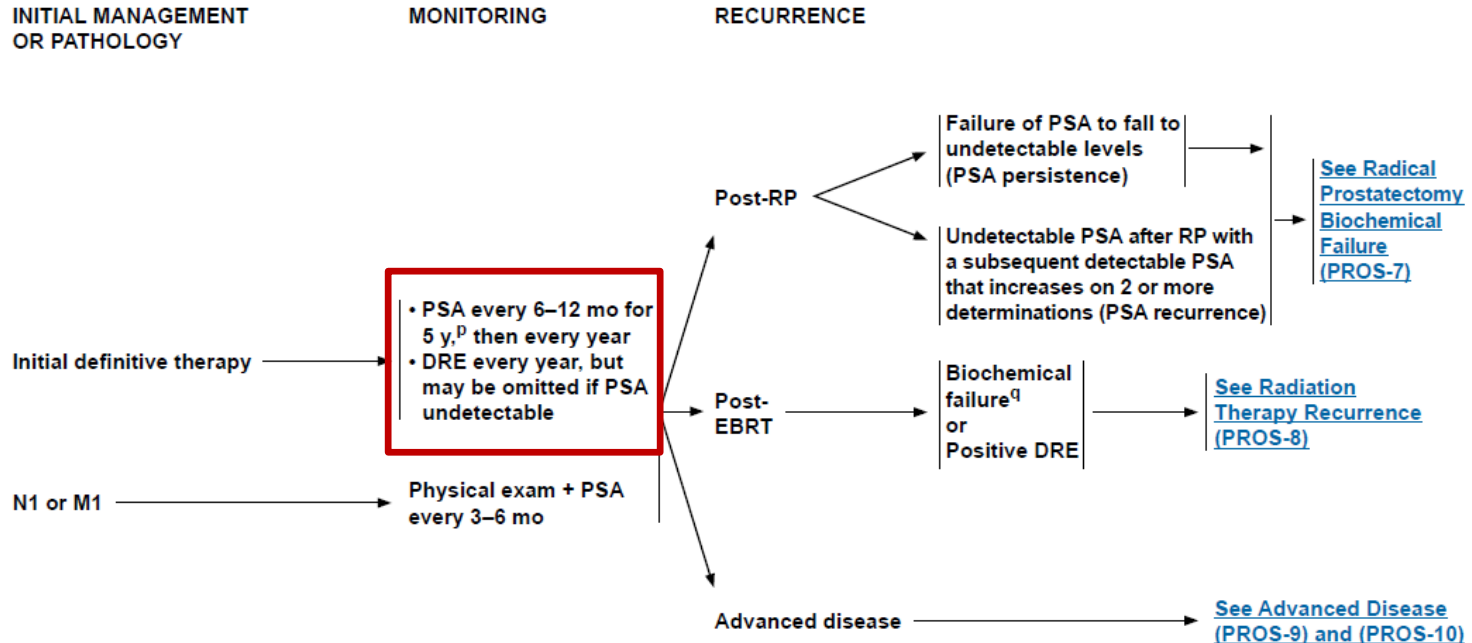
Manage prostate cancer follow up; 75% of recurrences occur within 5 years



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

^aRTOG-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 <ul style="list-style-type: none"> • 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 settings†
		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.