

National Comprehensive
Cancer Network[®]

Sarcoma

Version 1.2001

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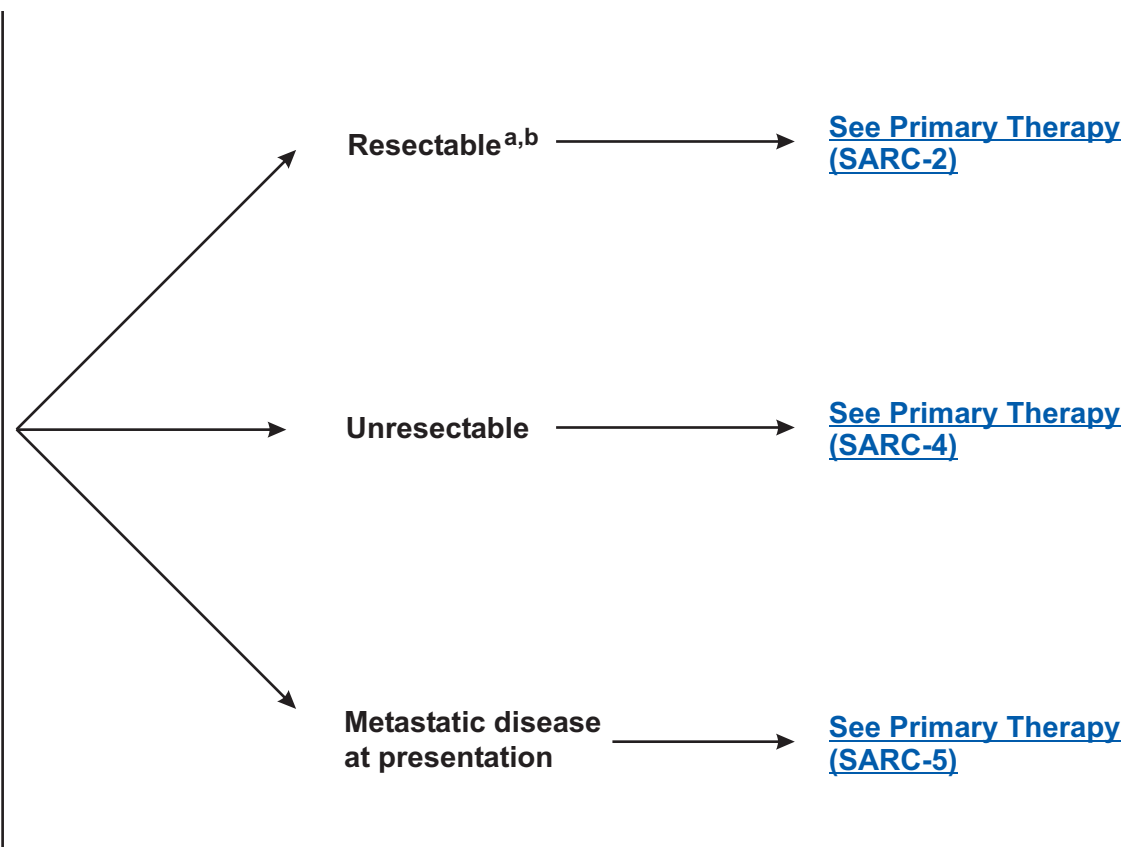
Clinical Trials: The NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN Categories of Consensus: All recommendations are Category 2A unless otherwise specified. See [NCCN Categories of Consensus](#)

These guidelines are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no representations nor warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way. These guidelines are copyrighted by National Comprehensive Cancer Network. All rights reserved. These guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2001.

WORK-UP

- All patients should be managed by a multidisciplinary team with expertise in sarcoma
- H&P
- Adequate imaging of primary tumor (MRI preferred [required for tumors ≥ 5 cm, optional depending on anatomic location for smaller tumors] $\pm$ CT)
 - › Plain radiograph of primary tumor (optional)
- Carefully planned biopsy (needle or incisional biopsy after adequate imaging, placed along longitudinal axis, with minimal dissection and careful attention to hemostasis)
 - › Biopsy should establish grade and histologic subtype
- Chest x-ray
- Chest CT (for patients in whom chemotherapy will be used preoperatively or postoperatively)



^a[See Sarcoma Surgery Principles \(SARC-A\).](#)

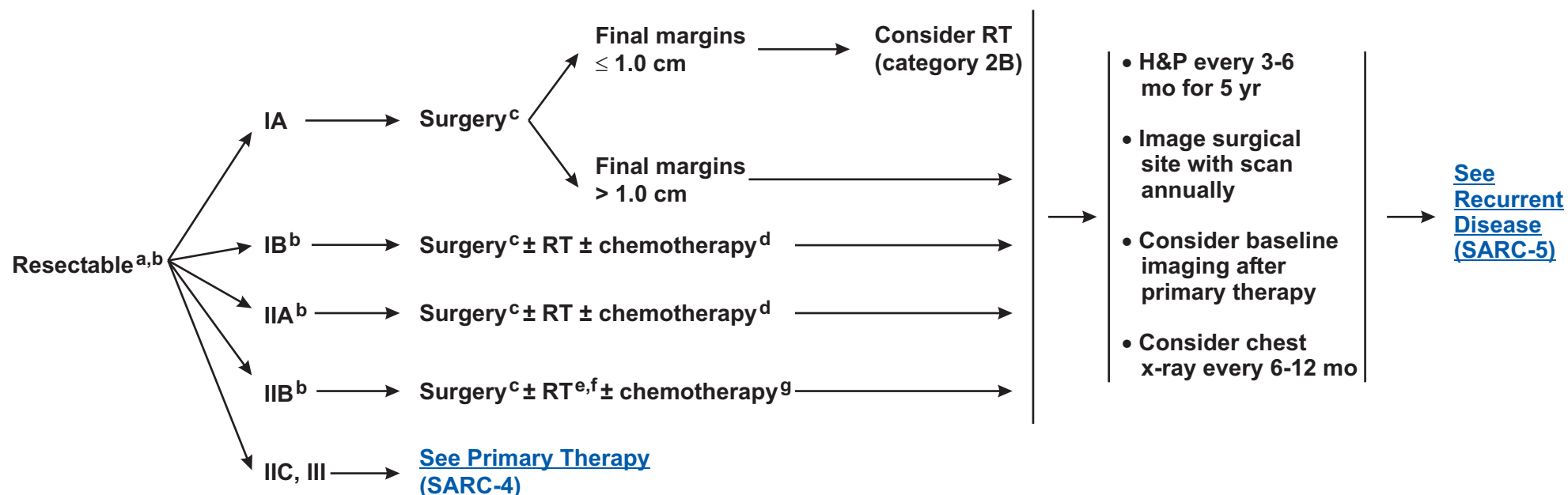
^bRandomized clinical trial data support the use of radiotherapy and/or chemotherapy as an adjunct to surgery in appropriately selected patients (category 1) based on an improvement in disease-free survival (although not overall survival). The preferred timing of treatment (preoperative vs postoperative) has not been defined.

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PRIMARY THERAPY

FOLLOW-UP



^aSee [Sarcoma Surgery Principles \(SARC-A\)](#).

^bRandomized clinical trial data support the use of radiotherapy and/or chemotherapy as an adjunct to surgery in appropriately selected patients (category 1) based on an improvement in disease-free survival (although not overall survival). The preferred timing of treatment (preoperative vs postoperative) has not been defined.

^cReresection, if feasible, may be necessary to render margins negative.

^dFor histologies with expected chemosensitivity, eg, myxoid/round cell liposarcoma.

^eSee [Radiotherapy Guidelines for High-Grade Extremity Sarcoma \(SARC-3\)](#).

^fConsider omission of RT for lesions that can be widely excised apart from critical structures.

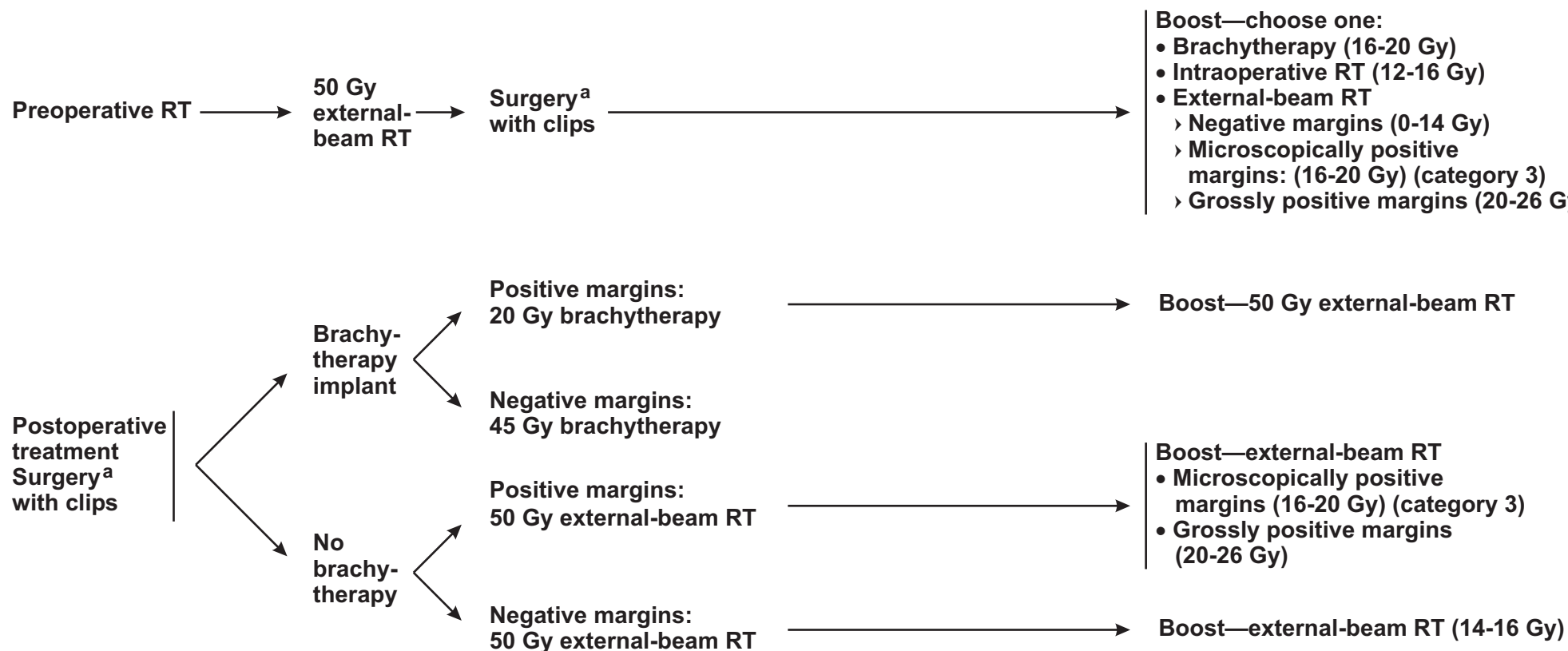
^gConsider chemotherapy for margins close to critical structures and at risk for significant decreased function.

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SARC-2

RADIOTHERAPY GUIDELINES FOR HIGH-GRADE EXTREMITY SARCOMA



^aSee Sarcoma Surgery Principles (SARC-A).

Back to Primary Therapy (SARC-1)

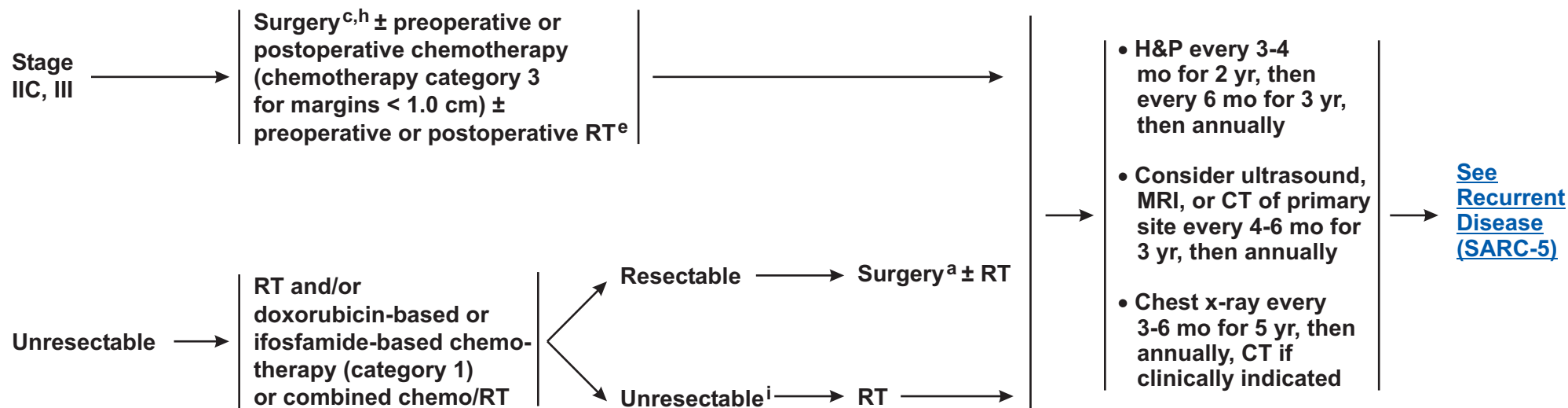
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SARC-3

PRIMARY THERAPY

FOLLOW-UP



^aSee [Sarcoma Surgery Principles \(SARC-A\)](#).

^cReresection, if feasible, may be necessary to render margins negative.

^eSee [Radiotherapy Guidelines for High-Grade Extremity Sarcoma \(SARC-3\)](#).

^hRandomized clinical trial data support the use of chemotherapy as an adjunct to surgery to improve disease-free survival (category 1).

ⁱMay include amputation, if needed.

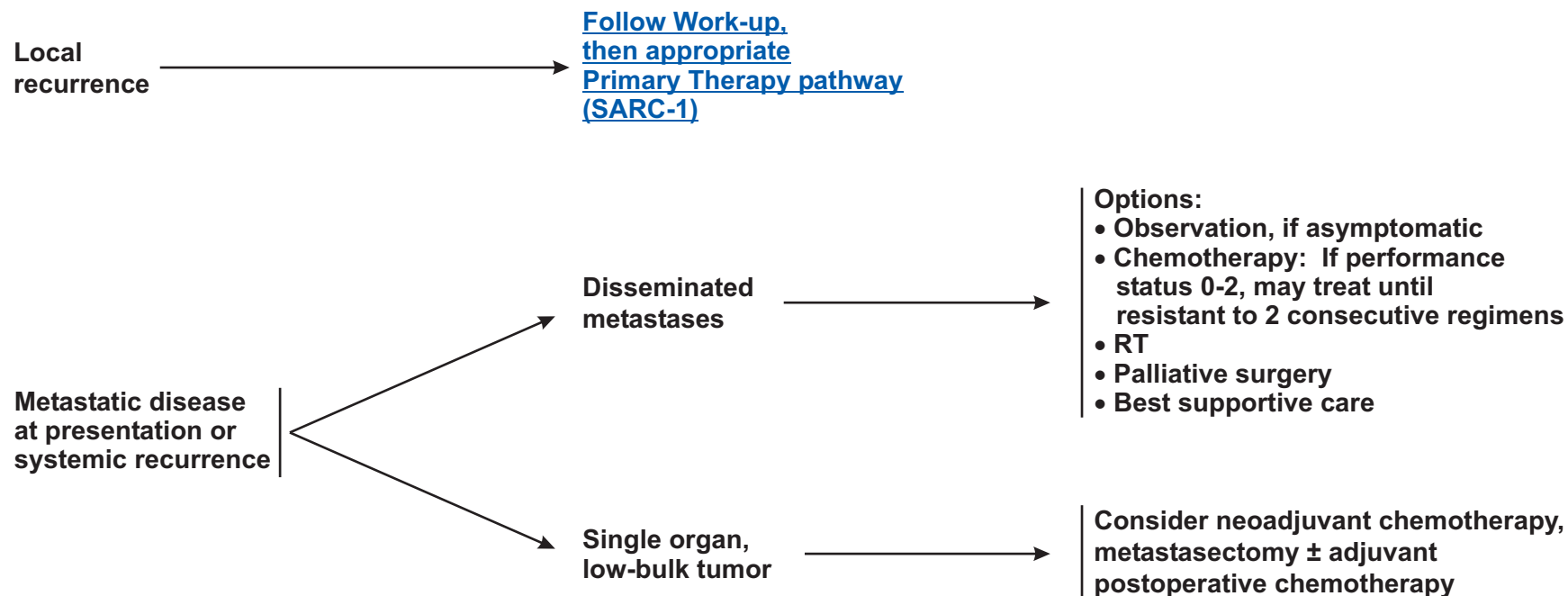
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RECURRENT DISEASE

PRIMARY THERAPY

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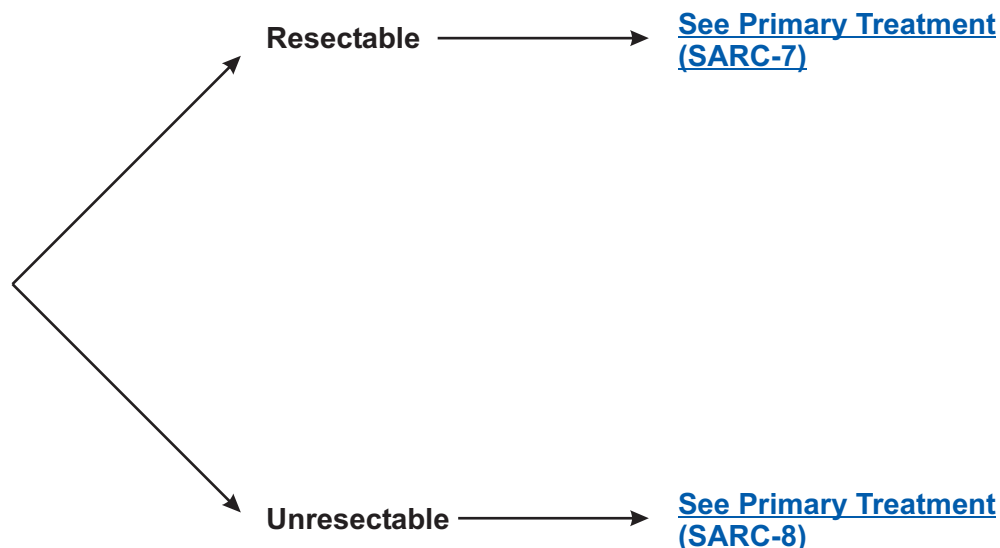
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SARC-5

WORK-UP

- All patients should be managed by a multidisciplinary team with expertise in sarcoma
- H&P
- Abdominopelvic CT with contrast, and/or MRI
- Preresection biopsy not necessarily required, based on degree of suspicion of other malignancies
- Chest x-ray
- Chest CT for patients in whom chemotherapy will be used preoperatively or postoperatively or as clinically indicated
- Endoscopy as indicated
- If retroperitoneal sarcoma found unexpectedly, do core biopsy only, and schedule patient for sarcoma team evaluation.

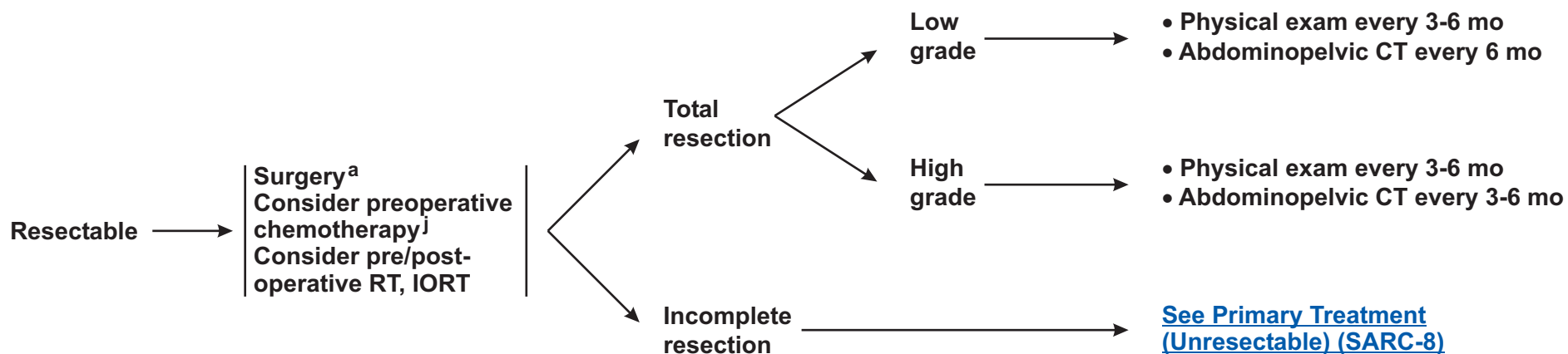


Note: All recommendations are category 2A unless otherwise indicated.

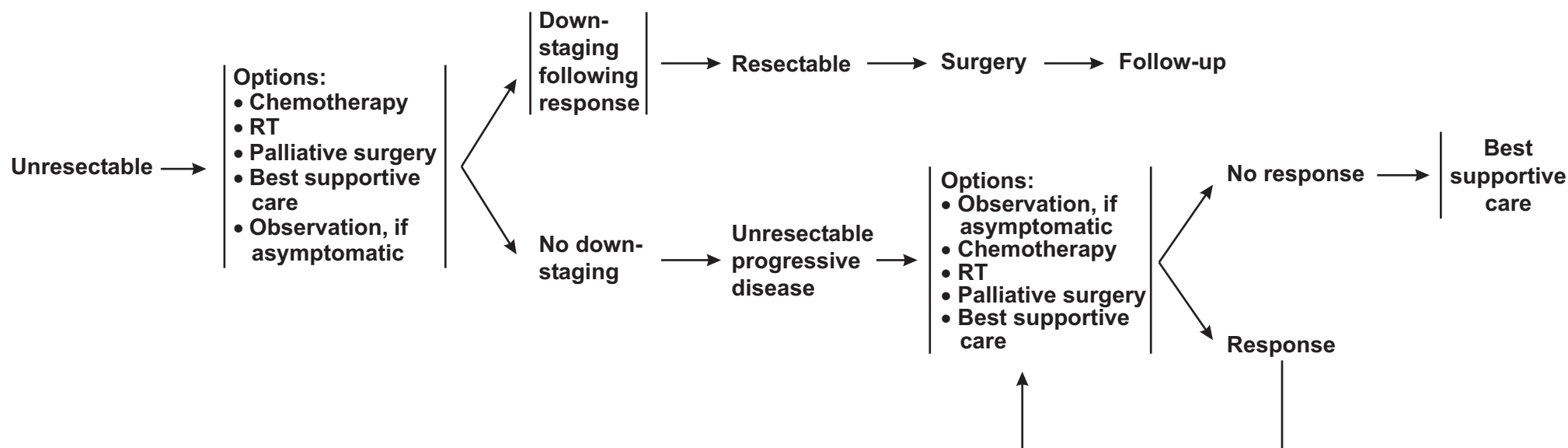
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

PRIMARY TREATMENT

FOLLOW-UP

^a[See Sarcoma Surgery Principles \(SARC-A\).](#)^jPostoperative chemotherapy is rarely given.[See Recurrent Disease \(SARC-9\)](#)[Back to the Sarcoma Table of Contents](#)**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.**SARC-7**

PRIMARY TREATMENT

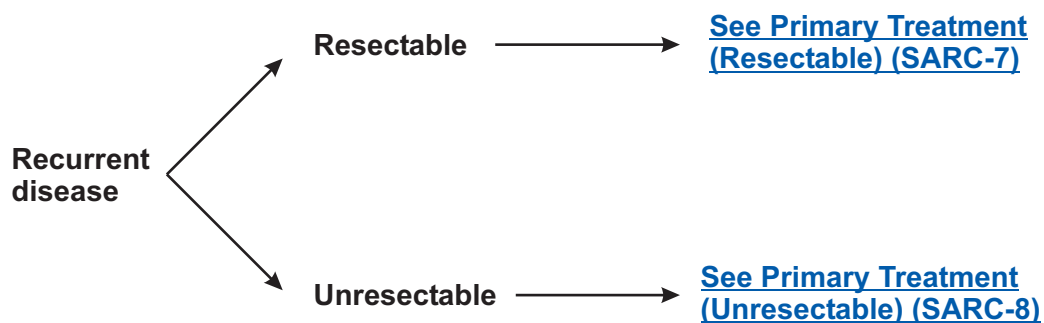
[See Recurrent Disease \(SARC-9\)](#)[Back to the Sarcoma Table of Contents](#)

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RECURRENT DISEASE

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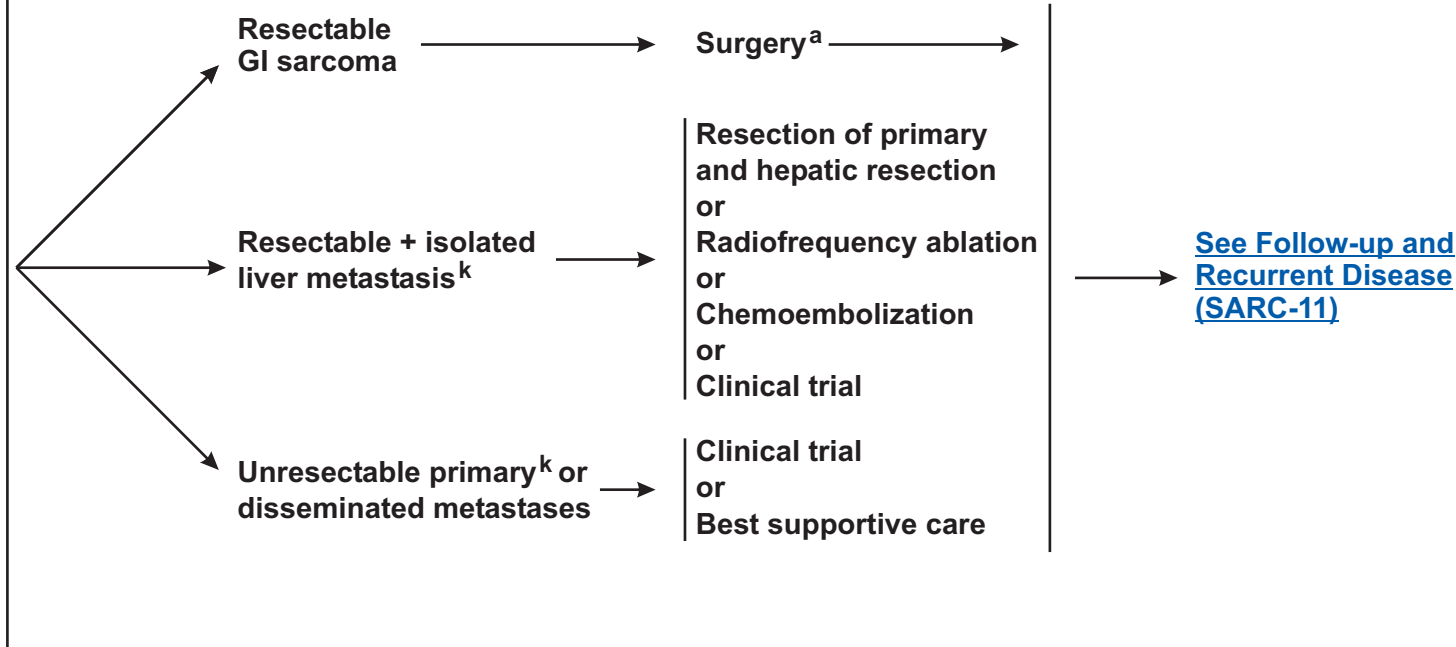
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

SARC-9

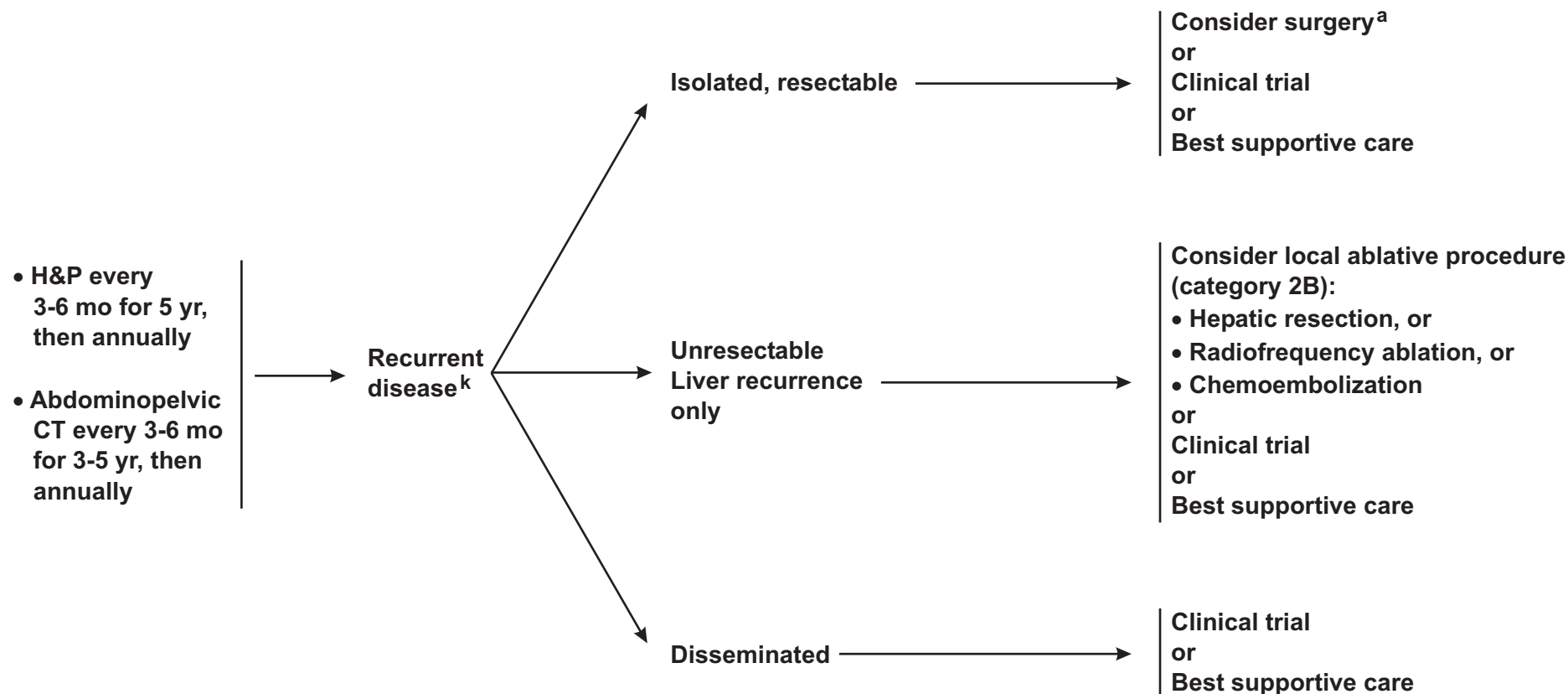
(GI stromal tumors or leiomyosarcomas of GI origin)

WORK-UP

- All patients should be managed by a multidisciplinary team with expertise in sarcoma
- H&P
- Abdominopelvic CT with contrast, and/or MRI
- With or without biopsy, based on degree of suspicion of other malignancies
- Chest x-ray
- Endoscopy as indicated
- Immunohistochemical staining of pathology specimen for C-KIT (CD 117)

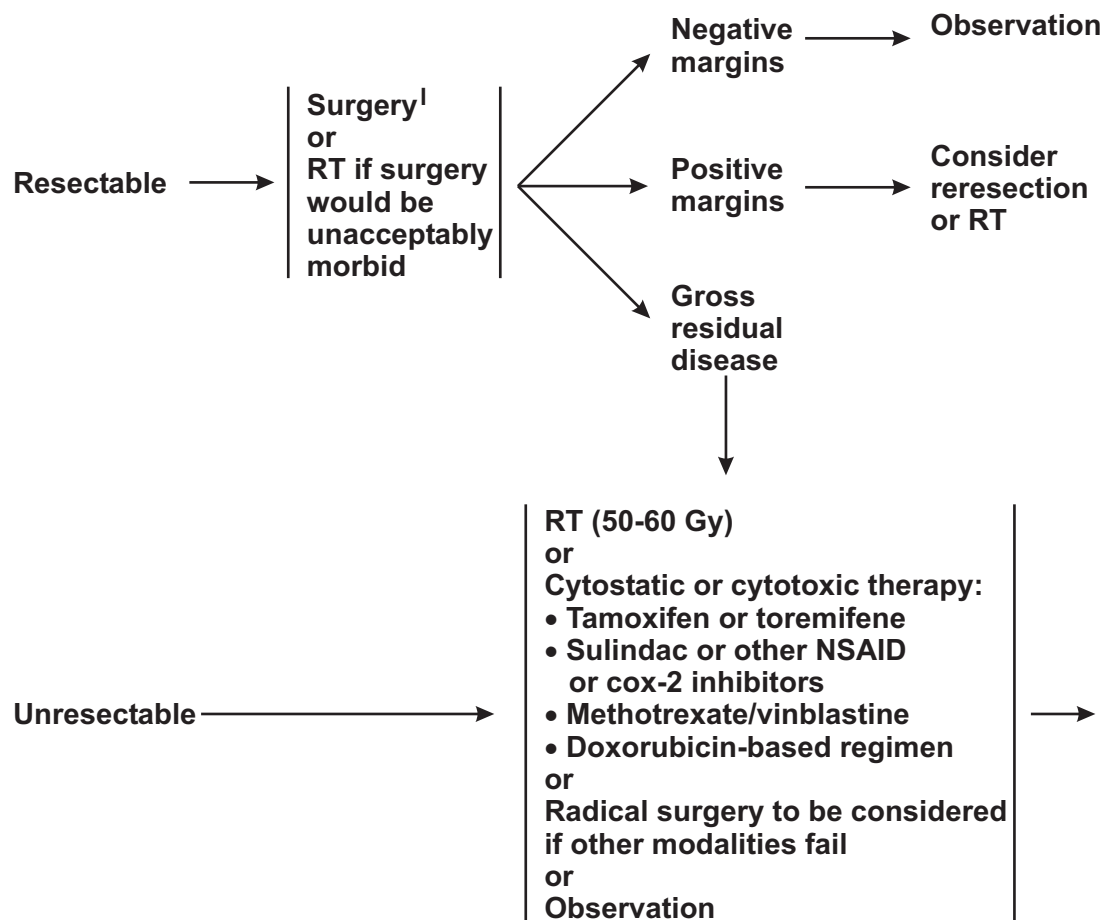
PRIMARY TREATMENT^a[See Sarcoma Surgery Principles \(SARC-A\).](#)^kRecent data strongly support the role of imatinib mesylate in the therapy of CD-117 positive GI stromal tumors (GIST). This will be discussed further in the 2002 version of the guidelines.**Note:** All recommendations are category 2A 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.

(GI stromal tumors or leiomyosarcomas of GI origin)

FOLLOW-UP**RECURRENT DISEASE**^aSee [Sarcoma Surgery Principles \(SARC-A\)](#).^kRecent data strongly support the role of imatinib mesylate in the therapy of CD-117 positive GI stromal tumors (GIST). This will be discussed further in the 2002 version of the guidelines.[Back to the Sarcoma Table of Contents](#)**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.

WORK-UP

- All patients should be managed by a multi-disciplinary team with expertise in sarcoma
- H&P
- CBC, platelets
- Chest x-ray
- Chest CT as clinically indicated

PRIMARY
TREATMENTADJUVANT
TREATMENT

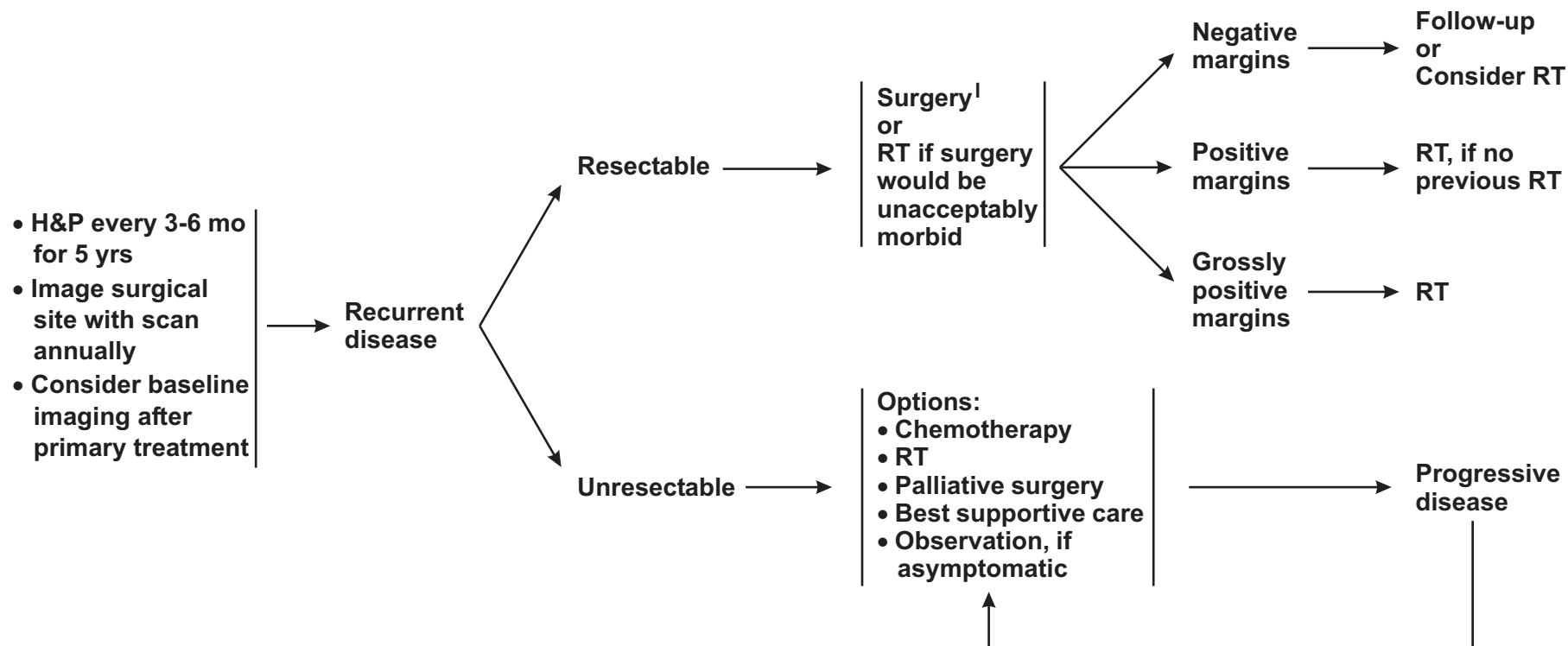
[†]For desmoids, microscopic positive margins may be acceptable if achieving negative margins would produce excessive morbidity.

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FOLLOW-UP

RECURRENT DISEASE



[†]For desmoids, microscopic positive margins may be acceptable if achieving negative margins would produce excessive morbidity.

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SARCOMA SURGERY PRINCIPLES

- Optimal margins and oncologic control; fascia-alone margins may be adequate
- Maximal function with minimal morbidity
- Limb sparing generally preferable
- If patient cannot be treated in accordance with these principles of sarcoma surgery, preoperative cytotoxic therapy (chemotherapy, RT) should be considered
- Pathology specimens should be reviewed again by pathologists with sarcoma expertise

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SARC-A

Staging

Table 1**1997 American Joint Committee on Cancer (AJCC) Staging System for Soft Tissue Sarcoma****Primary Tumor (T)**

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 5 cm or less in greatest dimension
T1a	Superficial tumor
T1b	Deep tumor
T2	Tumor more than 5 cm in greatest dimension
T2a	Superficial tumor
T2b	Deep tumor

Note: Superficial tumor is located exclusively above the superficial fascia without invasion of the fascia; deep tumor is located either exclusively beneath the superficial fascia, or superficial to the fascia with invasion of or through the fascia, or superficial and beneath the fascia. Retroperitoneal, mediastinal, and pelvic sarcomas are classified as deep tumors.

Regional Nodes (N)

NX	Regional lymph nodes cannot be assessed ^a
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

Distant Metastases (M)

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastases

Histopathologic Grade

GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

Stage Grouping**STAGE I**

A Low grade, small, superficial, deep	G12	T1a1b	N0	M0
B Low grade, large, superficial	G12	T2a	N0	M0

STAGE II

A Low grade, large, deep	G12	T2b	N0	M0
B High grade, small, superficial, deep	G34	T1a1b	N0	M0
C High grade, large, superficial	G34	T2a	N0	M0

STAGE III

High grade, large, deep	G34	T2b	N0	M0
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STAGE IV

Any metastasis	Any G	Any T	N1	M0
	Any G	Any T	N0	M1

^aBecause of the rarity of lymph node involvement in sarcomas, the designation NX may not be appropriate, and could be considered N0 if no clinical involvement is evident.

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Manuscript

NCCN Categories of Consensus

Category 1: There is uniform NCCN consensus, based on high-level evidence, that the recommendation is appropriate.

Category 2A: There is uniform NCCN consensus, based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 2B: There is nonuniform NCCN consensus (but no major disagreement), based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 3: There is major NCCN disagreement that the recommendation is appropriate.

All recommendations are category 2A unless otherwise noted.

Overview

Sarcomas constitute a diverse family of rare, but complex and distinct, diseases, typically segregated into two broad categories: (1) sarcomas of the bone and (2) soft tissue sarcomas. Typically, practice guidelines are developed for high-volume diseases. This is clearly not the case with sarcomas, because the annual incidence of these diseases in the United States is about 8,000 cases, and deaths due to sarcoma number about 4,400 cases per year (Greenlee et al, 2000). Collectively, sarcomas account for about 1% of all adult malignancies and 15% of pediatric malignancies.

The anatomic site of the primary disease represents an important variable that influences treatment and outcome. Soft tissue sarcomas of the extremities account for about one half of all

sarcomas. Gastrointestinal sarcomas make up about a quarter of the disease burden, and retroperitoneal sarcomas account for another 15% to 20%.

These practice guidelines address sarcoma management from the perspective of four disease subtypes: soft tissue extremity sarcomas, retroperitoneal (including nongastrointestinal visceral) sarcomas, desmoid tumors, and gastrointestinal sarcomas.

Current staging groups and nomenclature for classifying soft tissue sarcomas are given in Table 1 (Fleming et al, 1997). It should be noted that this staging system underwent changes in 1997 and these guidelines reflect the new categories. Because the standard primary treatment for most sarcomas is surgery, it is important to note sarcoma surgery principles: (1) The aim is to achieve optimal margins and oncologic control; fascia-alone margins may be adequate. (2) The goal is to preserve maximal function with minimal morbidity. (3) Limb sparing is preferable.

Because of variations in practice patterns and limited data from randomized clinical trials, many clinicians choose to augment surgery with other therapeutic modalities, notably adjuvant radiation therapy and adjuvant chemotherapy. When appropriate, the guidelines incorporate those adjuvant therapies that are supported by clinical trial data or extensive clinical experience.

Soft tissue Sarcomas of the Extremities

Work-up

Appropriate patients should be presented to a multidisciplinary sarcoma tumor board for evaluation prior to initiation of definitive therapy (Clasby et al, 1997). An essential element of the work-up is a history and physical examination. Laboratory tests have virtually no role.

Imaging studies are crucial to good clinical management of sarcomas. Magnetic resonance imaging (MRI) is preferable to computed tomography (CT) for large, deep tumors, but not necessarily for superficial, small tumors. Given the risk for hematogenous spread from a high-grade sarcoma to the lungs, imaging of the chest is key to accurate staging. Chest CT is the preferred imaging modality for patients who will be treated with preoperative or postoperative chemotherapy. Plain radiographic films of the primary lesion are considered optional.

A comprehensive evaluation should also include a carefully planned biopsy. A needle or excisional biopsy should be performed after the completion of adequate imaging studies. Enough tissue should be obtained to accurately assess histologic subtype and grade, because the latter will be used to determine the appropriate stage. On the other hand, the biopsy should entail minimal dissection so that there will not be any interference with definitive surgery.

On the basis of the initial work-up, the multidisciplinary team can assign the patient to one of the following three clinical paths, which determines the therapeutic choices and decisions to be made:

- Locally resectable tumor
- Unresectable tumor with no distant metastases
- Metastatic disease at the time of presentation

Primary Treatment for Resectable Tumors

Stage IA, IB, IIB: For small lesions of 5 cm or less (stage IA or IIB), surgery is the primary therapy, with adjuvant radiation therapy also being a consideration, based to some extent on tumor grade and also on margins and anatomy. This is also true for stage IB tumors (which are low grade but larger), for which surgery, with or without preoperative or postoperative radiotherapy and/or chemotherapy, is considered a reasonable therapeutic option.

Stage IIA: These large, low-grade, deep tumors are routinely treated with either preoperative or postoperative radiation therapy with or without chemotherapy, in addition to definitive surgery. Stage IIB patients are managed similarly.

Stage IIC, III: For large tumors of intermediate or high grade (stage IIC or III, > 5 cm), the panel recommends a combined modality approach utilizing preoperative or postoperative chemotherapy with or without preoperative or postoperative radiotherapy as adjuncts to primary surgery in most cases. Different centers use a variety of schedules and regimens. A recent study has demonstrated that adjuvant chemotherapy prolongs the disease-free interval, but does not improve overall survival, in these patients. For patients with margins less than 1 cm there was disagreement on the panel as to whether chemotherapy should routinely be applied. One management strategy commonly employed is neoadjuvant chemotherapy, with or without preoperative radiotherapy, if the patient has a good performance status (Pisters et al, 1997; Spiro et al, 1997), followed by definitive surgery, with or without postoperative radiotherapy (Rosenberg et al, 1982; Yang et al, 1998). Planning and performance of definitive surgery should take into account the possibility of adjuvant radiotherapy and the need for optimal dose delivery.

Adjuvant Treatment for Resectable Tumors

Adjuvant therapy varies according to the status of surgical margins, which, in turn, depends on expert processing of the resection specimen and careful examination of the specimen margins. Before margins can be proclaimed negative, the appropriate tools must be in place to ensure that the margins have been evaluated appropriately and adequately.

In patients with very small tumors and negative margins, no adjuvant therapy is required (Baldini et al, 1982). These patients can simply be followed according to the surveillance schedule outlined below. If

the margins are close to vital structures, or if a local recurrence would lead to major dysfunction, adjuvant radiotherapy can be utilized when the expected risk of complications is low.

If the surgical margins are positive (as often occurs when patients are referred to sarcoma centers following an attempted resection of a tumor that was not suspected to be a sarcoma), repeat resection is indicated. Less optimally, one could attempt to control the microscopic residual disease with radiotherapy if the patient has not received preoperative radiotherapy (but only if repeat resection might be expected to be excessively morbid) (Alektiar, et al, 2000).

The usual dose of radiation therapy, when employed preoperatively as an adjuvant modality, is 50 Gy, with boosts of external-beam, brachytherapy, or intraoperative RT postoperatively, unless the margins are negative (Sadoski, et al, 1993). There are several advantages of preoperative RT. First, the treatment volume is smaller because the likely extent of the disease is known and the tumor bed has not been manipulated (Nielsen, et al, 1991). Second, a multidisciplinary treatment plan is established prior to treatment. Third, the lack of delay in RT allows for the management of tumor cells prior to a tumor bed being flooded with growth factors. Finally, the tumor is smaller and surrounded by a pseudocapsule, which facilitates conservative resection (Barkley, et al, 1988). However, the main disadvantage of preoperative RT is the acute effect on wound healing (O'Sullivan, et al, 1999).

Postoperative external beam dosage will vary, depending on whether brachytherapy was also used. If no brachytherapy was used, 50 Gy can be delivered with boosts of 14-26 Gy, depending on the margin status. Many institutions are no longer giving a boost after preoperative or postoperative radiation to patients who have negative margins, based on local control rates that approach 95% with preoperative radiation at 50 Gy and negative margins (Sadoski, et al, 1993).

After a patient with stage IIB or IIIB disease has had optimal resection, with or without radiation therapy, the clinician and patient should discuss the use of adjuvant chemotherapy. Consensus is gradually emerging regarding the value of aggressive adjuvant chemotherapy in patients with high-grade sarcoma, although it is still not unanimous among NCCN sarcoma experts. Available evidence suggests that administration of adjuvant doxorubicin-based chemotherapy can prolong relapse-free survival in sarcoma patients (Bramwell et al, 1994; Tierney, 1997). However, intensive chemotherapy does not appear to improve overall survival and has clear toxicities. In certain other clinical situations, such as when close margins near vital areas make reresection difficult, chemotherapy may also be empirically employed.

Remarkably little data have been generated in the adjuvant setting regarding the combination of aggressively dosed ifosfamide plus doxorubicin supported by hematopoietic cytokine therapy. Results of recent trials appear to advocate this practice in selected patients who are at high risk of recurrence but otherwise in excellent health (Frustaci et al, 1999).

Primary Treatment for Unresectable Tumors

For unresectable extremity sarcomas, the guidelines recommend primary doxorubicin-based or ifosfamide-based chemotherapy, with or without neoadjuvant radiotherapy, to render the tumor potentially resectable (Pisters et al, 1997; Spiro et al, 1997). If the tumor shows a significant clinical response and becomes resectable, surgery becomes the primary modality. If the sarcoma remains unresectable, radiation therapy may be employed.

Surveillance

Surveillance is deemed important to detect recurrences that might still be potentially curable, and the guidelines outline a prudent follow-up schedule that avoids excessive testing. Low grade,

superficial or small tumors are routinely followed for 5 years with annual scanning of the primary site. Because higher-grade and larger tumors have a higher risk of dissemination, the surveillance recommendations for patients with these tumors are somewhat more intensive for the first 3 years following resection, with imaging every 4-6 months, the time period during which most of the risk of recurrence is clustered. Since these patients' risk never returns to zero, long-term annual follow-up is indicated, including consideration of annual MRI or CT scanning (Lewis et al, 1999). Chest x-rays are preformed every 3-6 months for 5 years, given the risk of metastatic disease in these high-grade lesions.

One change from the prior guidelines is the movement away from chest CT. This decision is based on information from the M. D. Anderson Cancer Center presented at the American Society for Clinical Oncology meeting in 2000, indicating that there is no cost or survival advantage obtained by following patients with chest CT scans (Fleming, et al, 2001, Porter, et al, 2000).

Management of Recurrence

The management of recurrent disease encompasses a heterogeneous group of patients and clinical scenarios. For a patient with a local recurrence, treatment should be the same as for patients with a new primary lesion (Singer et al, 1992).

For patients who present with metastatic disease or who develop a systemic recurrence after failure of primary therapy, the guidelines distinguish between widely disseminated metastases and limited metastases confined to a single organ. For patients who relapse or present with widely disseminated disease, a subsequent distinction is made between individuals who are asymptomatic and those who have symptoms.

One reasonable management option for asymptomatic patients would be to offer close observation with a “watchful waiting” strategy. Another equally reasonable alternative would be to offer

such patients palliative therapy--even “preemptive” palliation that might involve aggressive chemotherapy--before symptoms develop.

For symptomatic patients with disseminated metastases, most people would recommend moving directly to a palliative approach, defined broadly as “chemotherapy, radiotherapy, palliative surgery, or best supportive care.” The guidelines are intentionally nonspecific about this group of options because many different issues are factored into this decision (eg, patient performance status, specific clinical problems from the metastases, treatment availability), and specific details are best left to clinical judgment.

If a patient has progressive disease after first-line therapy and wishes to try second-line chemotherapy, the panel felt that option was reasonable. However, if a patient fails to respond to two consecutive chemotherapy regimens, the guidelines recommend best supportive care. Third-line chemotherapy would be used only for a patient who has derived clear clinical benefit from a prior chemotherapeutic intervention. The rationale behind this approach relates to the minuscule chance of response to third-line chemotherapy by patients who already have not benefitted from two prior chemotherapeutic regimens. However, for patients who have responded to chemotherapy, further trials could be considered as an option at the time of progression.

In contrast, a patient who presents with limited metastasis confined to a single organ warrants consideration for neoadjuvant chemotherapy, perhaps followed by metastasectomy. The guidelines purposely do not specify rules governing metastasectomy, which remains controversial for many cancers, including sarcoma. Several variables influence the decision to use metastasectomy, including the disease-free interval from original diagnosis to detection of the metastases, the patient's performance status, and the amount of prior therapy. Rather than address the fine points of metastasectomy decision making, the guidelines simply indicate that one should consider metastasectomy, with or without postoperative

chemotherapy, and leave the details to clinicians and individual institutions.

Retroperitoneal and Visceral Soft Tissue Sarcomas

Work-up

The initial evaluation work-up for retroperitoneal and visceral soft tissue sarcomas is similar to that for the extremity sarcomas and includes a history and physical examination, with presentation to a multidisciplinary sarcoma specialty review board. Recommended imaging studies include an abdominal and pelvic CT with contrast and/or an MRI and chest imaging (plain radiograph or CT). The need for a biopsy remains somewhat controversial, and this decision should be based on the clinician's degree of suspicion that other malignancies are present. The idea is to avoid inappropriate major resection of an intra-abdominal lymphoma or germ cell tumor, for example. Another clinical scenario occasionally encountered is the unexpected finding of a retroperitoneal sarcoma at the time of laparotomy. The recommendation in this situation is the performance of only a core biopsy to establish the diagnosis and the type and grade of tumor, with subsequent evaluation by a sarcoma team prior to undertaking definitive therapy.

Primary Therapy

Primary therapy depends on the resectability of the tumor. For patients with resectable tumors, surgery is standard therapy. Decisions about adjuvant/neoadjuvant chemotherapy or adjuvant radiotherapy are left to clinical judgment (Singer et al, 1995; Lewis et al, 1998).

Patients with unresectable tumors have several options, including chemotherapy with or without radiotherapy for palliation, the goal being tumor shrinkage to permit resection. Patients who have unresectable tumors that become resectable by downstaging with

chemotherapy and/or radiotherapy can undergo resection and then be followed. If patients remain unresectable because of disseminated metastatic disease, they should be treated as if they had recurrent disease.

Surveillance

Patients with low-grade tumors that have been successfully resected should have a follow-up physical examination every 3 to 6 months, a chest x-ray every 6 months, and an abdominal CT or MRI scan every 6 months. Patients with high-grade tumors that have been totally resected should have a physical examination every 3 to 6 months, as well as a chest x-ray and an abdominal CT or MRI scan every 3 to 6 months. Incomplete resection should be managed in the same fashion as unresectable disease. Patients who undergo successful resection following downstaging should be followed in the same as primary resection patients.

Treatment of Recurrence

For patients whose disease recurs after failed resection, the guidelines recommend the same management as outlined for primary disease. For patients whose recurrence is unresectable due to disseminated disease, management decisions depend on whether patients are symptomatic or asymptomatic (much the same as in the extremity sarcoma guidelines pathway). Watchful waiting may be considered for asymptomatic patients, and “preemptive” palliation may be offered if symptoms are expected to become problematic soon. For patients who are symptomatic, the palliative options are similar to those listed at this point in the pathway for extremity sarcomas.

Good rationale exists for supportive care in conjunction with some of the highly aggressive therapeutic regimens. Prospective data support the hypothesis that higher doses improve objective response rates. The response of sarcoma, in turn, does have an impact on outcomes--both functional outcomes and the ability of a

surgeon to provide palliation. Radiotherapy, palliative surgery, and best supportive care are among potential options that oncologists should discuss with symptomatic patients.

Second-line therapy for best supportive care may be considered for patients who have progressive disease despite first-line chemotherapy. If a patient derives no benefit from second-line therapy, off-protocol chemotherapy should cease in favor of symptomatic management with a “best supportive care” option. At almost any branch in the pathways, enrollment in a clinical trial should be considered if an appropriate trial is available.

Desmoid Tumors

Desmoid tumors can be described as locally aggressive fibromatoses or “benign malignancies.” Although desmoid tumors are not frank sarcomas, they often pose difficult decisions for patients, in terms of the amount of surgery required and the enormous resource management problems for institutions. They can be locally destructive, and in one series from Memorial Sloan-Kettering Cancer Center approximately 10% of patients died due to progressive disease (Posner, et al, 1989). Abdominal desmoids may be a component of the familial adenomatous polyposis syndrome, and in patients who have been treated with prophylactic colectomy, desmoids are a more significant cause of morbidity than colon cancer.

Work-up

The work-up for desmoid tumors is somewhat less intensive than for other sarcomas that have metastatic potential. In a sense, desmoid tumors are often locally metastatic, but they are not systemically metastatic.

Primary Treatment

The primary treatment for desmoid tumors is optimal surgery (Ballo et al, 1999). The guidelines have two main branches that depend on

whether a patient presents with resectable or unresectable disease. Regardless of whether surgical margins are positive or negative after resection, patients may be followed by observation alone. Radiotherapy offers another option for patients who have positive margins, if a subsequent relapse might lead to increased morbidity. If disease does recur, resection represents a reasonable strategy (the same as for primary management). In the case of unresectable disease, amputation should almost never enter into consideration. Functional outcomes are important, and alternatives to amputation may be open to patients who have unresectable desmoid tumors. For example, promising data exist for the use of cytostatic or cytotoxic therapy. Cytostatic options include tamoxifen and low-toxicity interventions, such as sulindac or other nonsteroidal anti-inflammatory agents, which have been reported to halt progression of these tumors (Wilcken and Tattersall, 1991; Thomas, et al, 1990; Izes, et al, 1996; Waddell, et al, 1983; Lackner, et al, 1997).

If cytostatic agents fail, consideration could turn to cytotoxic therapy with low-toxicity regimens, such as methotrexate with or without a vinca alkaloid (eg, vinblastine), or even a doxorubicin-based regimen with or without ifosfamide. Radiotherapy is another reasonable consideration, depending on the degree of debility, symptoms, and location of the affected area(s) (Weiss and Lackman, 1989; Skapek et al, 1998; Weiss, et al, 1999; Patel, et al, 1993; Lynch, et al, 1994; Seiter and Kemeny, 1993).

Treatment of Recurrence

Recurrent disease is managed in the same manner as recurrences of other sarcomas. If patients whose disease has relapsed are asymptomatic and have unresectable tumors, watchful waiting would be appropriate. If their disease progresses further, consideration could be given to radiotherapy with or without chemotherapy, because such patients presumably have not responded to lower-toxicity approaches. Similarly, if patients have progressive disease despite second-line chemotherapy, best

supportive care should be the preferred strategy outside of a clinical trial.

Gastrointestinal Sarcomas

Work-up

As with other sarcoma patients, those who have gastrointestinal sarcomas should be presented to a multidisciplinary tumor board for evaluation prior to initiation of definitive therapy. Essential elements of the work-up comprise the history and physical examination, abdominopelvic CT with contrast and/or MRI scan, a chest x-ray, and endoscopy as indicated. The decision to obtain a biopsy should be guided by the clinician's degree of suspicion. A new element in the work-up of these tumors is the staining of the pathologic specimen for c-kit (CD 117), because tumors with this immunohistochemical finding are sensitive to the new agent, STI-571.

Primary Treatment

Definitive surgery is the primary therapeutic modality for patients who have resectable gastrointestinal sarcomas without evidence of metastasis. For patients who have resectable primary disease and an isolated liver metastasis, definitive surgery should be performed for the primary disease. Several options exist for isolated liver lesions, including hepatic resection, radiofrequency ablation, and enrollment in a clinical trial.

Unresectable or disseminated gastrointestinal sarcomas have a poor prognosis. A major advance has been the finding that STI-571

produces durable remissions in this disease. A phase II study has demonstrated a 89% response rate (54% experienced partial response, 34% experienced stable disease) (Blanke, et al, 2001). Because this tumor had previously been considered to be resistant to conventional chemotherapy (Goss et al, 2000), this finding represents a major new avenue for investigation. Consideration should also be given to enrollment in an appropriate clinical trial, provision of best supportive care, or use of radiation therapy to reduce tumor burden and improve the chances of resectability.

Surveillance

Every patient, regardless of initial status at presentation or type of primary therapy, should have a thorough medical history and physical examination every 3 to 6 months for 5 years. At that point, the patient may then be followed annually. Similarly, an abdominopelvic CT scan should be repeated every 3 to 6 months for 3 to 5 years, and then annually thereafter.

Treatment of Recurrent Disease

The treatment options depend on the nature of the recurrence. If the recurrence is isolated and resectable, surgical resection may be considered. For a recurrence limited to the liver, consideration of a local ablative procedure is reasonable. As noted above, disseminated tumors should be treated with STI-571 if they are c-kit positive. Any patient who has a recurrence, regardless of presentation, should be considered a candidate for enrollment in a clinical trial, if an appropriate trial is available.

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