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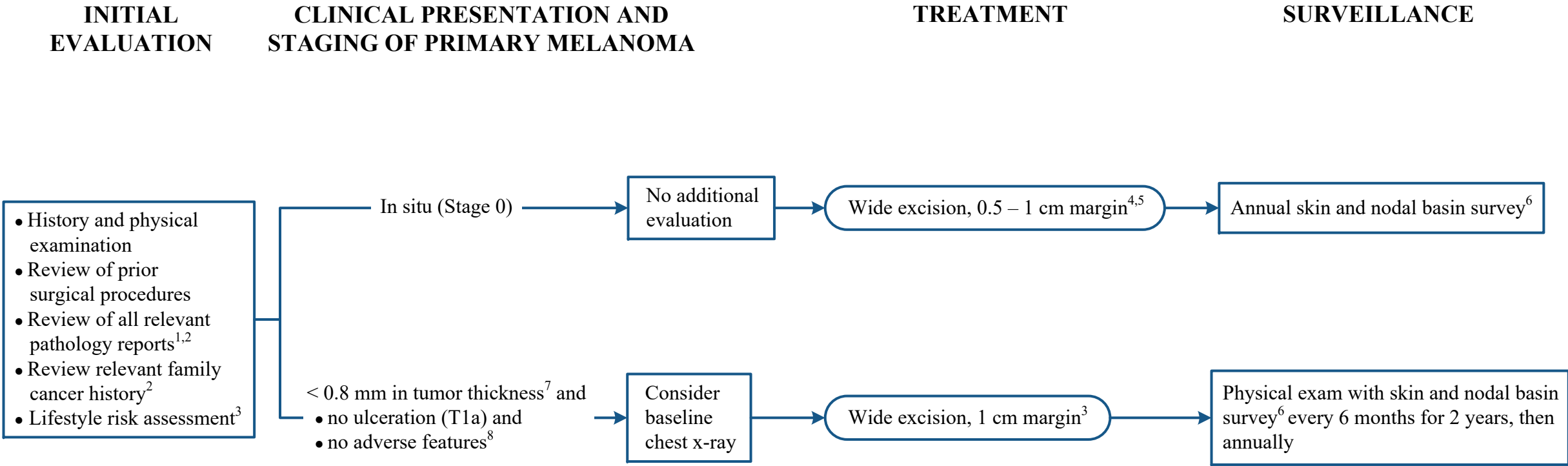
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CNS = central nervous system

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



¹ Refer to Review of Outside Pathology Material Policy (#CLN0605) as indicated

² Guidelines for germline testing to assess genetic predisposition for melanoma are rapidly evolving. At a minimum, patients with a history of three invasive cutaneous melanomas and/or high risk family history (multiple cutaneous melanomas, pancreatic, renal and/or breast cancer; astrocytoma; uveal melanoma and/or mesothelioma) should be offered genetic counseling (refer to [Genetic Counseling algorithm](#)).

³ See [Physical Activity, Nutrition, Obesity Screening and Management](#), and [Tobacco Cessation Treatment](#) algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

⁴ Consider function and cosmesis

⁵ Margins larger than 0.5 cm may be necessary for some, particularly large melanoma in situ, lentigo maligna type, lesions

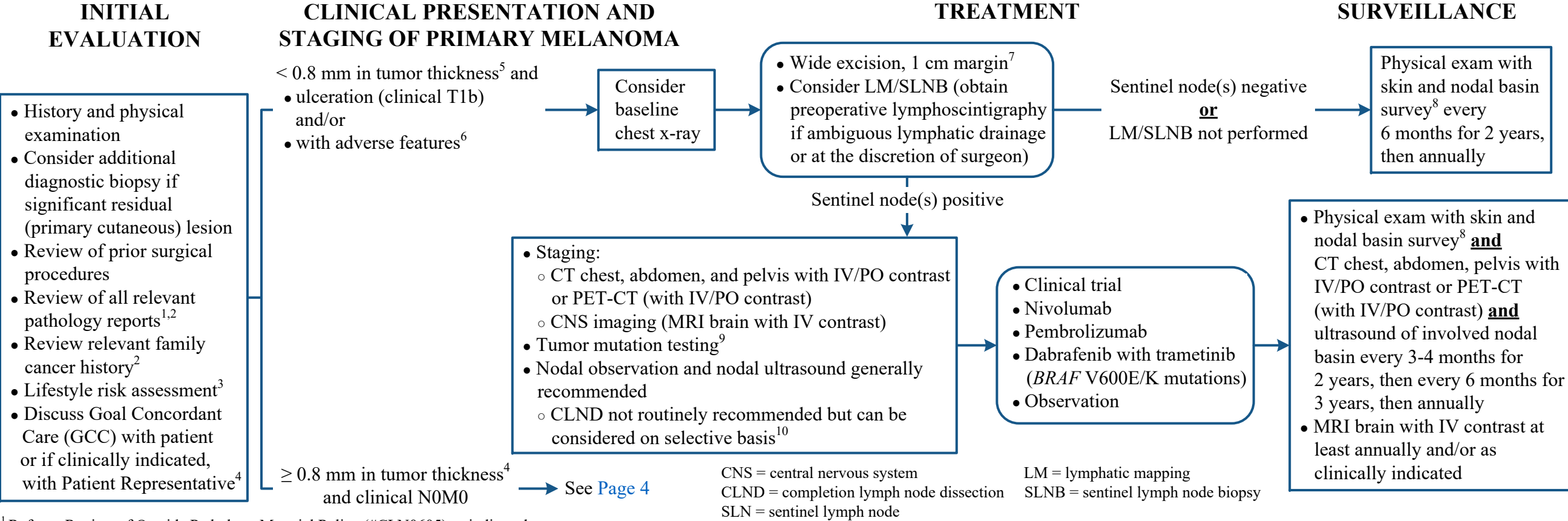
⁶ For patients with multiple complex nevi, history of multiple primary cutaneous melanomas or multiple non-melanoma skin cancers, Dermatology follow up is strongly recommended

⁷ Per AJCC 8th edition, the convention for rounding decimal values in the hundredth’s place is to round down those ending in 1 to 4 and to round up those ending in 5 to 9. For example, a melanoma measuring 0.75 mm in thickness would be recorded as 0.8 mm in thickness (*i.e.*, T1b), and those measuring from 0.95 to 1.04 mm would be rounded to 1 mm (*i.e.*, T1b).

⁸ Adverse features include: positive deep margins, lymphovascular invasion, young age or ≥ 2 mitoses/mm²

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⁷ Consider function and cosmesis

⁸ For patients with multiple complex nevi, history of multiple primary cutaneous melanomas or multiple non-melanoma skin cancers, Dermatology follow up is strongly recommended

⁹ Tumor mutation analysis includes at a minimum *BRAF*, *NRAS* and *KIT*

¹⁰ Randomized trials have failed to demonstrate survival benefit for routine CLND following a positive SLN. Although CLND is associated with improved regional control and in a minority of patients upstaging might impact clinical decision-making, post-hoc forest plot analyses of MSLT-2 have not definitely identified any subgroups of patients likely to derive a survival benefit; therefore, the vast majority of patients are no longer routinely offered CLND. One rare possible exception to this approach is for patients with limited access to follow-up.

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CLINICAL PRESENTATION AND STAGING OF PRIMARY MELANOMA

≥ 0.8 mm in tumor thickness¹ and clinical N0M0

- Consider preoperative ultrasound of regional nodal basin(s) if primary tumor greater than 4 mm or for ambiguous/equivocal regional basin(s) physical examination
- Baseline chest x-ray
- Consider cross-sectional imaging as clinically indicated for symptoms or T3b or T4 primary

- Wide excision with the following margins² based on tumor thickness¹
 - ≤ 1 mm: 1 cm margin
 - > 1-2 mm: 1-2 cm margin
 - > 2 mm: 2 cm margin
- LM/SLNB (obtain preoperative lymphoscintigraphy if ambiguous lymphatic drainage or at the discretion of surgeon)
- Multidisciplinary discussion for consideration of primary site adjuvant radiation therapy for high risk primaries³

Sentinel node(s) negative

Consider pembrolizumab or nivolumab for Stage IIB or IIC

SURVEILLANCE

- SLN-negative melanomas 0.8-1 mm
 - Physical exam with skin and nodal basin survey³ every 6 months for 2 years, then annually
- SLN-negative melanomas > 1 mm
 - Physical exam with skin and nodal basin survey⁴ every 3-4 months for 2 years, then every 6 months for 3 years, then annually
 - Consider chest x-ray, interval CT chest, abdomen, and pelvis with IV/PO contrast or PET-CT (with IV/PO contrast) and MRI brain with IV contrast, as clinically indicated

Sentinel node(s) positive

- Staging (if not already performed prior to surgery):
 - CT chest, abdomen, and pelvis with IV/PO contrast or PET-CT (with IV/PO contrast)
 - CNS imaging (MRI brain with IV contrast)
- Tumor mutation testing⁵
- Nodal observation and nodal ultrasound generally recommended
 - CLND not routinely recommended but can be considered on selective basis⁶

- Clinical trial
- Nivolumab
- Pembrolizumab
- Dabrafenib with trametinib (*BRAF* V600E/K mutations)
- Observation

- Physical exam with skin and nodal basin survey⁴ **and** CT chest, abdomen, pelvis with IV/PO contrast or PET-CT (with IV/PO contrast) **and** ultrasound of involved nodal basin every 3-4 months for 2 years, then every 6 months for 3 years, then annually
- MRI brain with IV contrast at least annually and/or, as clinically indicated

CNS = central nervous system

CLND = completion lymph node dissection

LM = lymphatic mapping

SLN = sentinel lymph node

SLNB = sentinel lymph node biopsy

¹ Per AJCC 8th edition, the convention for rounding decimal values in the hundredth's place is to round down those ending in 1 to 4 and to round up those ending in 5 to 9. For example, a melanoma measuring 0.75 mm in thickness would be recorded as 0.8 mm in thickness (*i.e.*, T1b), and those measuring from 0.95 to 1.04 mm would be rounded to 1 mm (*i.e.*, T1b).

² Consider function and cosmesis

³ High risk primaries include those with microsatellitosis, positive margins, or a combination of factors increasing the risk of local recurrence such as perineural invasion (PNI), > 4 mm thickness or an anatomically challenging area (*e.g.*, head and neck)

⁴ For patients with multiple complex nevi, history of multiple primary cutaneous melanomas or multiple non-melanoma skin cancers, Dermatology follow up is strongly recommended

⁵ Tumor mutation analysis includes at a minimum *BRAF*, *NRAS* and *KIT*

⁶ Randomized trials have failed to demonstrate survival benefit for routine CLND following a positive SLN. Although CLND is associated with improved regional control and in a minority of patients upstaging might impact clinical decision-making, post-hoc forest plot analyses of MSLT-2 have not definitely identified any subgroups of patients likely to derive a survival benefit; therefore, the vast majority of patients are no longer routinely offered CLND. One rare possible exception to this approach is for patients with limited access to follow-up.

Department of Clinical Effectiveness V8

Approved by The Executive Committee of the Medical Staff on 12/17/2024

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CLINICAL PRESENTATION/STAGING

Local recurrence, unknown primary melanoma (presenting as dermal, subcutaneous or nodal disease) or in-transit metastasis^{1,2}

- Review of all relevant pathology reports^{2,3}
- Review relevant family cancer history²
- CT chest, abdomen, pelvis with IV/PO contrast or PET-CT (with IV/PO contrast)
- CNS imaging (MRI brain with IV contrast)
- Tumor mutation testing⁴
- CBC with differential, comprehensive metabolic panel, LDH
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative⁵

Inadequately treated primary (local persistence or margin positive resection)

Refer to [Pages 2-4](#) for clinical presentation, staging, and treatment of primary melanoma

Resectable (isolated or limited) non-nodal locoregional metastasis⁶

- Consider clinical trial of neoadjuvant therapy or
- Local excision, negative margin
- Consider LM with SLNB
- Consider local postoperative adjuvant radiation therapy

Clinical nodal with or without clinical non-nodal locoregional metastasis, see [Page 6](#)
Multiple and/or unresectable satellite and/or in-transit metastases with or without clinical regional nodal disease, see [Page 7](#)

Distant metastasis, see [Pages 8-10](#)

TREATMENT

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- Consider staging/re-staging as clinically indicated:
 - CT chest, abdomen, and pelvis with IV/PO contrast or PET-CT (with IV/PO contrast)
 - CNS imaging (MRI brain with IV contrast)
- If SLNB performed and positive sentinel nodes:
 - Nodal observation and nodal ultrasound generally recommended
 - CLND not routinely recommended but can be considered on selective basis⁷
- For either positive or negative sentinel nodes or if SLNB not performed, consider the following:
 - Clinical trial
 - Nivolumab
 - Pembrolizumab
 - Dabrafenib with trametinib (*BRAF* V600E/K mutations)
 - Observation
 - Ipilimumab or ipilimumab with nivolumab if refractory to anti-PD-1 based therapy

SURVEILLANCE

- Physical exam with skin and nodal basin survey⁸ **and** chest x-ray **and** if SLNB positive, ultrasound of involved nodal basin every 3-4 months for 2 years, then every 6 months for 3 years, then annually
- CT chest, abdomen and pelvis with IV/PO contrast or PET-CT (with IV/PO contrast) and MRI brain with IV contrast at scheduled follow-up visits and/or, as clinically indicated

¹ If patient presents with clinically suspicious lymph node or nodule, and/or history of melanoma², consider fine needle aspiration and/or core needle biopsy to establish the diagnosis prior to excision to facilitate definitive treatment planning

² Guidelines for germline testing to assess genetic predisposition for melanoma are rapidly evolving. At a minimum, patients with a history of three invasive cutaneous melanomas and/or high risk family history (multiple cutaneous melanomas, pancreatic, renal and/or breast cancer; astrocytoma; uveal melanoma and/or mesothelioma) should be offered genetic counseling (refer to [Genetic Counseling algorithm](#)).

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CLND = completion lymph node dissection LM = lymphatic mapping

CNS = central nervous system SLN = sentinel lymph node SLNB = sentinel lymph node biopsy

⁶ Includes local recurrence, in-transit and/or satellite metastasis

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⁸ For patients with multiple complex nevi, history of multiple primary cutaneous melanomas or multiple non-melanoma skin cancers, Dermatology follow up is strongly recommended

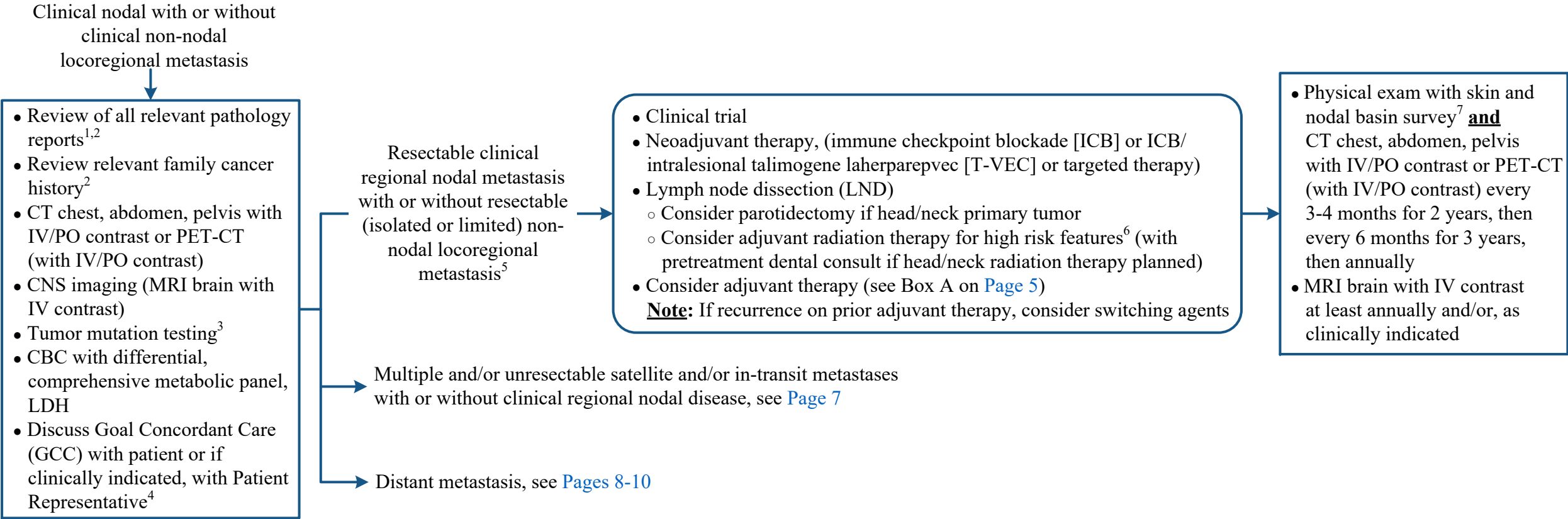
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CLINICAL PRESENTATION/STAGING

TREATMENT

SURVEILLANCE



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⁶ High-risk nodal features include:

- Lymph node number: 1+ parotid, 2+ other head and neck, 3+ axillary or inguinal **or**
- Lymph node deposit size: 3 cm+ head and neck, 4 cm+ axillary or inguinal **or**
- Extracapsular extension

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CLINICAL PRESENTATION/STAGING

TREATMENT

SURVEILLANCE

Multiple and/or
unresectable satellite and/or
in-transit metastases with or without
clinical regional nodal disease

- Review of all relevant pathology reports^{1,2}
- Review relevant family cancer history²
- CT chest, abdomen, pelvis with IV/PO contrast or PET-CT (with IV/PO contrast)
- CNS imaging (MRI brain with IV contrast)
- Tumor mutation testing³
- CBC with differential, comprehensive metabolic panel, LDH
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative⁴

- Consider clinical trial
- Systemic therapy as recommended on [Pages 9-11](#)
- Intralesional injection with talimogene laherparepvec (T-VEC) with or without immune checkpoint blockade
- Consider isolated limb infusion (ILI) for symptomatic patients refractory to other treatment modalities

Distant metastasis, see [Pages 8-10](#)

- Physical exam with skin and nodal basin survey⁵ **and** CT chest, abdomen, pelvis with IV/PO contrast or PET-CT (with IV/PO contrast) every 3-4 months for 2 years, then every 6 months for 3 years, then annually
- MRI brain with IV contrast at least annually and/or as clinically indicated

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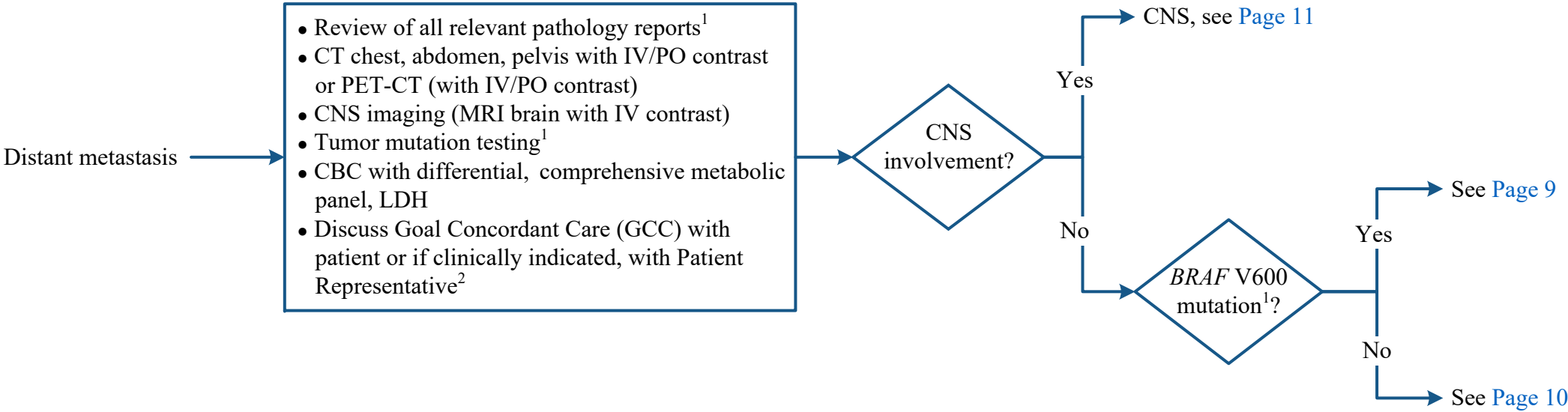
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CLINICAL PRESENTATION/STAGING

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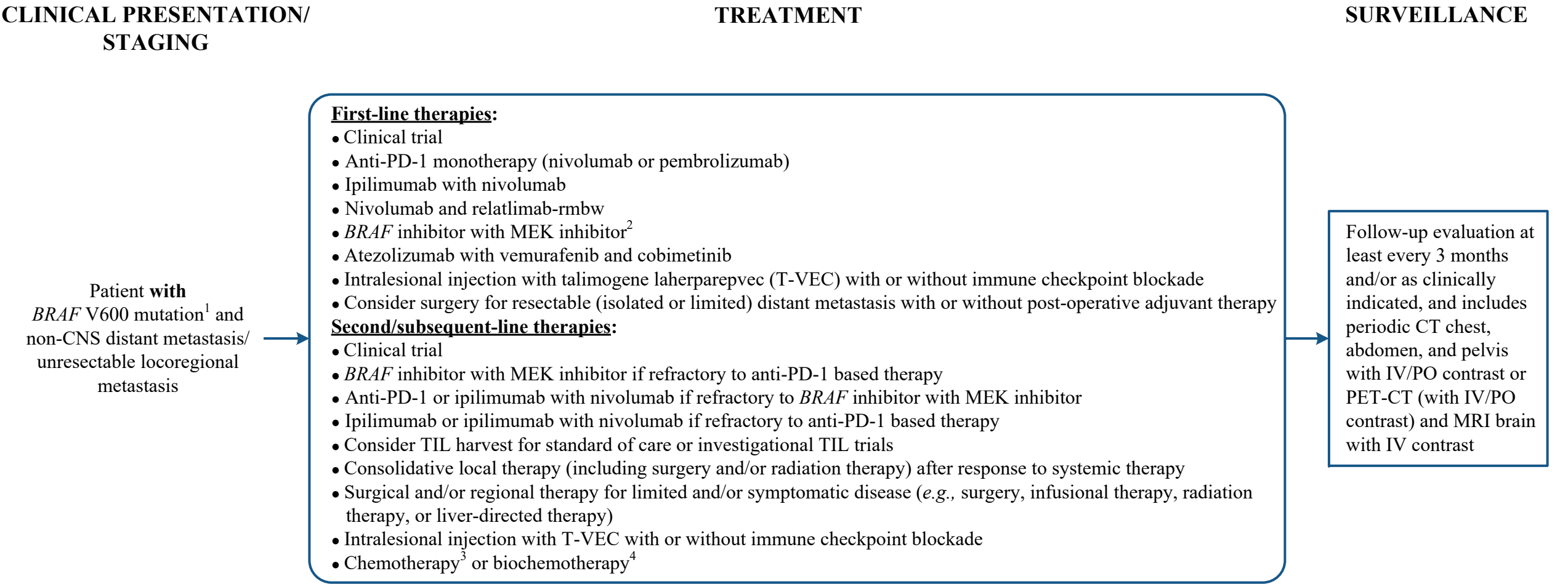
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CNS = central nervous system
TIL = tumor-infiltrating lymphocytes

¹ Tumor mutation analysis includes at a minimum *BRAF*, *NRAS* and *KIT*
² Regimens: dabrafenib with trametinib **or** vemurafenib with cobimetinib **or** encorafenib with binimetinib
³ Chemotherapy: CVD (cisplatin, vinblastine, dacarbazine), carboplatin in combination with paclitaxel, nab-paclitaxel, dacarbazine or temozolomide
⁴ Biochemotherapy: CVD plus interleukin-2 and interferon alpha

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CLINICAL PRESENTATION/
STAGING

TREATMENT

SURVEILLANCE

Patient **without**
BRAF V600 mutation¹ and
non-CNS distant metastasis/
unresectable locoregional
metastasis

First-line therapies:

- Clinical trial
- Anti-PD-1 monotherapy (nivolumab or pembrolizumab)
- Ipilimumab with nivolumab
- Nivolumab and relatlimab-rmbw
- Intralesional injection with talimogene laherparepvec (T-VEC) with or without immune checkpoint blockade
- Consider surgery for resectable (isolated or limited) distant metastasis with or without post-operative adjuvant therapy

Second/subsequent-line therapies:

- Clinical trial
- Ipilimumab or ipilimumab with nivolumab if refractory to anti-PD-1 based therapy
- FDA-approved *KIT* inhibitor for patients with targetable *KIT* mutation
- Consider TIL harvest for standard of care or investigational TIL trials
- Consolidative local therapy (including surgery and/or radiation therapy) after response to systemic therapy
- Surgical and/or regional therapy for limited and/or symptomatic disease (*e.g.*, surgery, infusional therapy, radiation therapy, or liver-directed therapy)
- Intralesional injection with T-VEC with or without immune checkpoint blockade
- Chemotherapy² or biochemotherapy³

Follow-up evaluation at
least every 3 months
and/or as clinically
indicated and includes
periodic CT chest,
abdomen, and pelvis
with IV/PO contrast or
PET-CT (with IV/PO
contrast) and MRI brain
with IV contrast

CNS = central nervous system
TIL = tumor-infiltrating lymphocytes

¹ Tumor mutation analysis includes at a minimum *BRAF*, *NRAS* and *KIT*
² Chemotherapy: CVD (cisplatin, vinblastine, dacarbazine), carboplatin in combination with paclitaxel, nab-paclitaxel, dacarbazine or temozolomide
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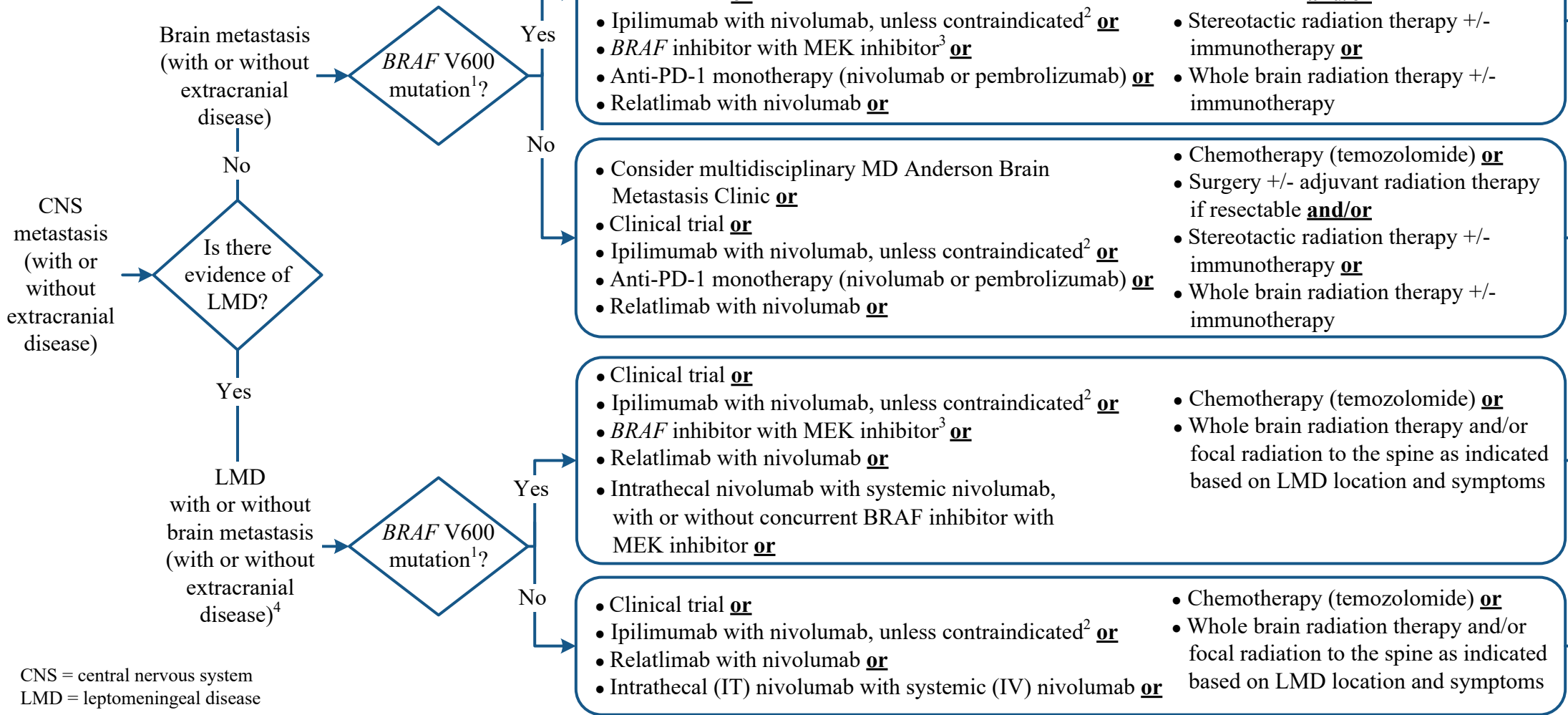
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**CLINICAL PRESENTATION/
STAGING**

TREATMENT

SURVEILLANCE



CNS = central nervous system
LMD = leptomeningeal disease

¹ Tumor mutation analysis includes at a minimum BRAF, NRAS and KIT
² Contraindications: receiving corticosteroids (at least dexamethasone 4 mg daily or equivalent) or is symptomatic requiring intervention
³ Regimens: Dabrafenib with trametinib **or** Vemurafenib with cobimetinib **or** Encorafenib with binimetinib
⁴ Refer to the [Solid Tumor Leptomeningeal Metastases algorithm](#)

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SUGGESTED READINGS

STAGING

Aloia, T. A., Gershenwald, J. E., Andtbacka, R. H., Johnson, M. M., Schacherer, C. W., Ng, C. S., . . . Mansfield, P. F. (2006). Utility of computed tomography and magnetic resonance imaging staging before completion in lymphadenectomy in patients with sentinel lymph node-positive melanoma. *Journal of Clinical Oncology*, 24(18), 2858-2865. <https://doi.org/10.1200/JCO.2006.05.6176>

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SURGERY FOR SENTINEL LYMPH NODE BIOPSY, REGIONAL AND DISTANT METASTASIS, AND LIMB PERFUSION

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SURGERY FOR SENTINEL LYMPH NODE BIOPSY, REGIONAL AND DISTANT METASTASIS, AND LIMB PERFUSION – continued

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SYSTEMIC THERAPY: CHEMOTHERAPY, IMMUNOTHERAPY, AND TARGETED THERAPY

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SUGGESTED READINGS - continued

SYSTEMIC THERAPY: CHEMOTHERAPY, IMMUNOTHERAPY, AND TARGETED THERAPY – continued

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SUGGESTED READINGS - continued

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ADJUVANT THERAPY FOR HIGH-RISK MELANOMA

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ADJUVANT THERAPY FOR HIGH-RISK MELANOMA – continued

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INTRATUMORAL THERAPY

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GENERAL

- MD Anderson Institutional Policy #CLN1202 - Advance Care Planning Policy
Advance Care Planning (ACP) Conversation Workflow (ATT1925)
MD Anderson Institutional Policy #CLN0604 – Review of Outside Pathology Material Policy

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DEVELOPMENT CREDITS

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

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