Sentinel Node Biopsy (SLNB) IS Standard of Care

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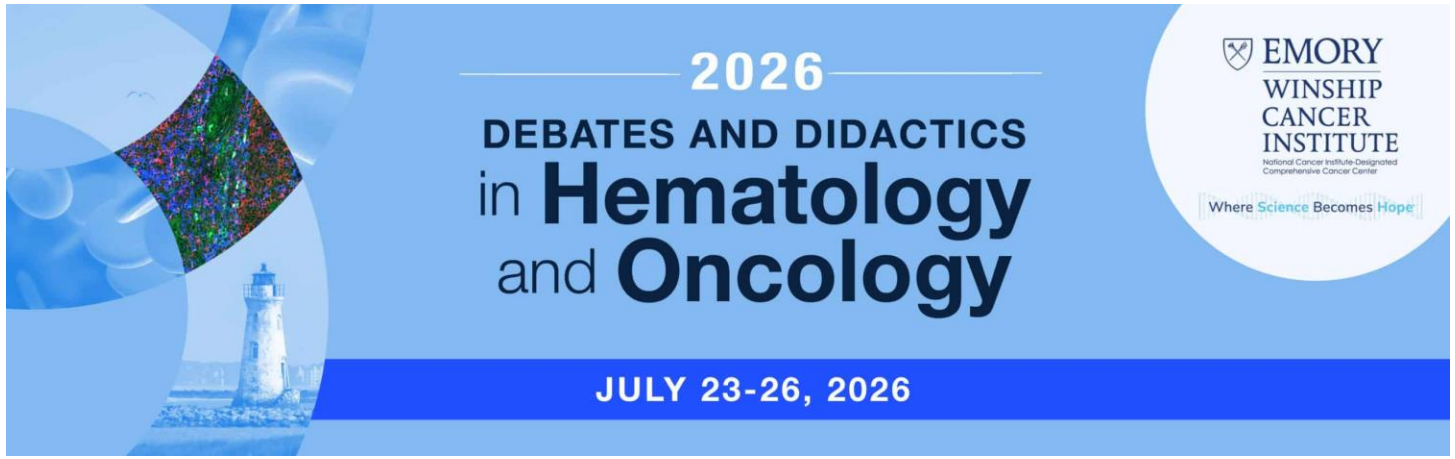
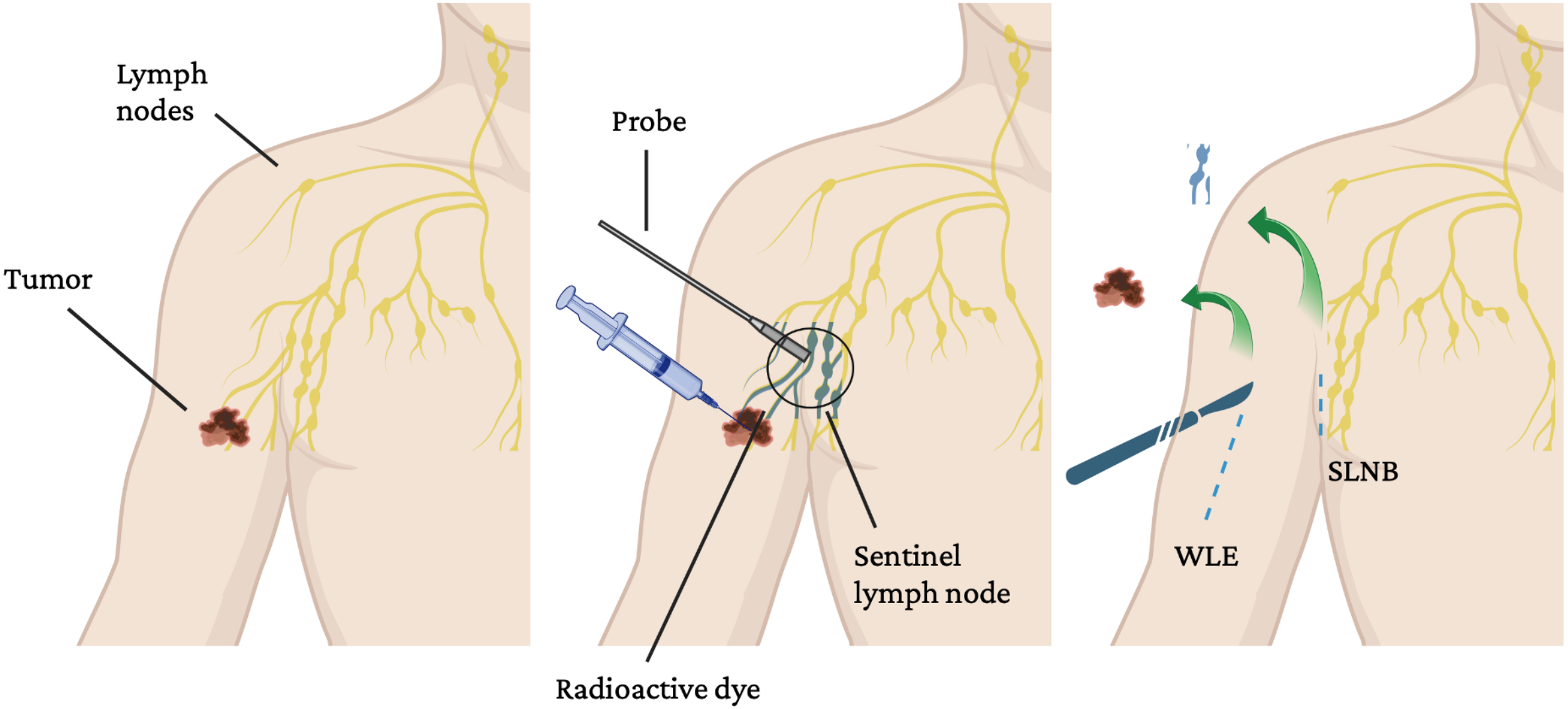


What is a sentinel lymph node biopsy (SLNB)?



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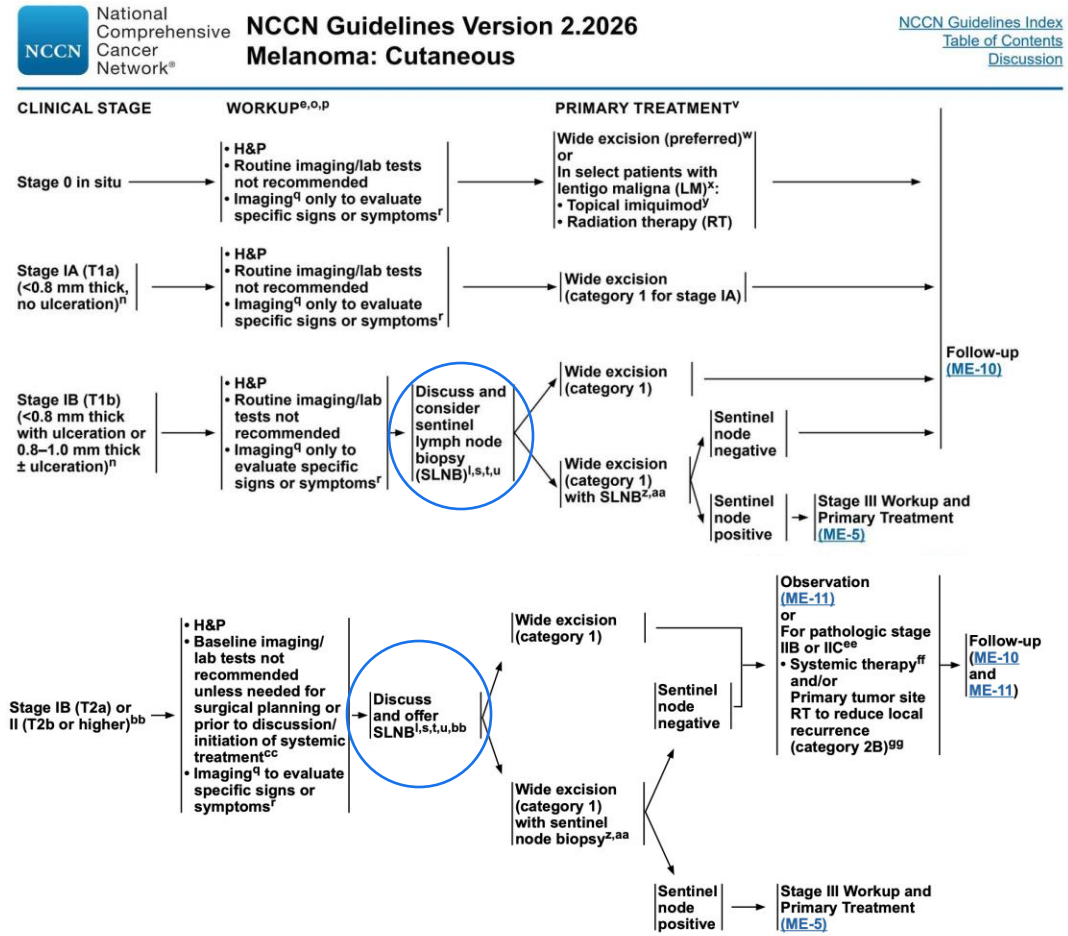
SLNB IS Standard of Care for Melanoma

- NCCN: "SLNB should be discussed with all patients with clinical stage Ib or II melanoma
- SLNB provides unmatched staging accuracy, regional disease control, a survival signal, and is the gateway to modern adjuvant therapy discussion – no alternative achieves all of these.



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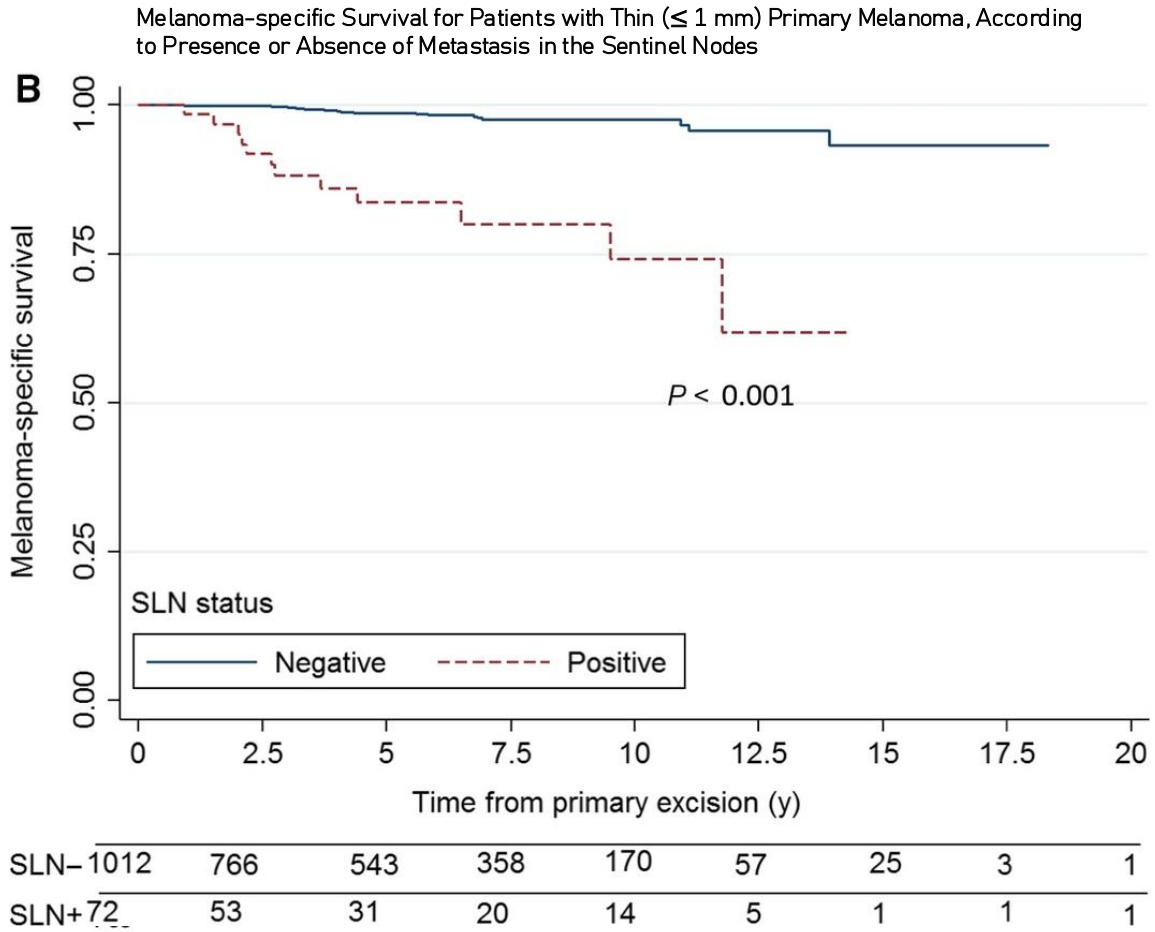
SLNB is the Most Powerful Prognostic Tool Available

- SLN status is the single strongest predictor of survival in clinically localized melanoma, superior to any primary tumor feature alone
- No imaging modality, GEP test, or nomogram can replace the pathologic information provided by SLNB.
- NCCN explicitly states:
  - "Nodal basin US is not a substitute for SLNB" and
  - "predictive GEP testing should not replace surgical oncology discussion of pathologic staging with SLNB"



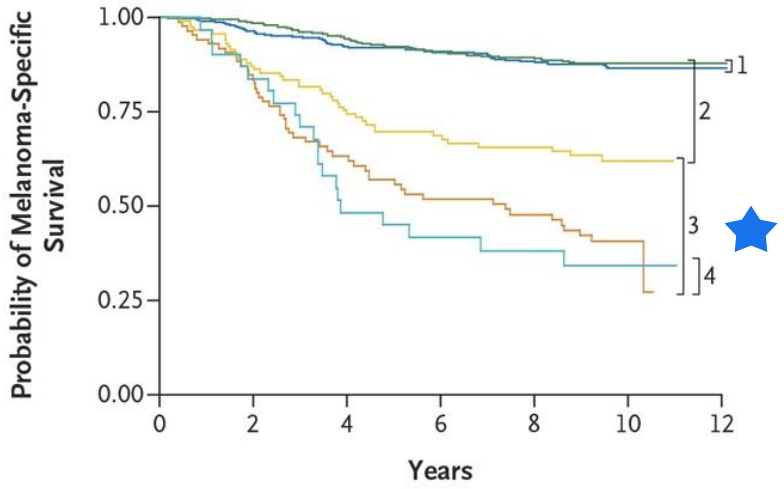
Morton et al, *NEJM* 2014; Tejera-Vaquerizo et al, *Cancer Medicine* 2019

MSLT-I – The Landmark Randomized Clinical Trial

- Randomized ~2,000 patients with melanoma ≥ 1.0 mm to WLE + SLNB vs WLE + observation (immediate lymphadenectomy if nodal metastases +)
- SLNB improved disease-free survival (p = 0.009 for intermediate thickness)
- Among node-positive patients with intermediate-thickness melanoma (1.2 – 3.5 mm), those identified by SLNB and treated with immediate lymphadenectomy had dramatically better melanoma-specific survival vs those who developed clinically palpable nodes during observation: HR 0.56, p = 0.006
- Overall ITT HR for melanoma death was 0.88 (95% CI 0.68 – 1.12) – trend toward benefit but underpowered (would need ~6,576 patients for 80% power)

C Melanoma-Specific Survival, Intermediate-Thickness Melanomas

	No. of Events/ Total No.	Rate (%) Yr 5	Yr 10
OBS, no nodal recurrence	48/413	92.0±1.4	86.6±1.8
OBS, nodal recurrence	49/87	57.5±5.4	41.5±5.6
SNB, true neg.	63/612	92.3±1.1	88.0±1.4
SNB, pos.	41/122	69.8±4.4	62.1±4.8
SNB, false neg.	20/31	45.2±8.9	34.4±8.7



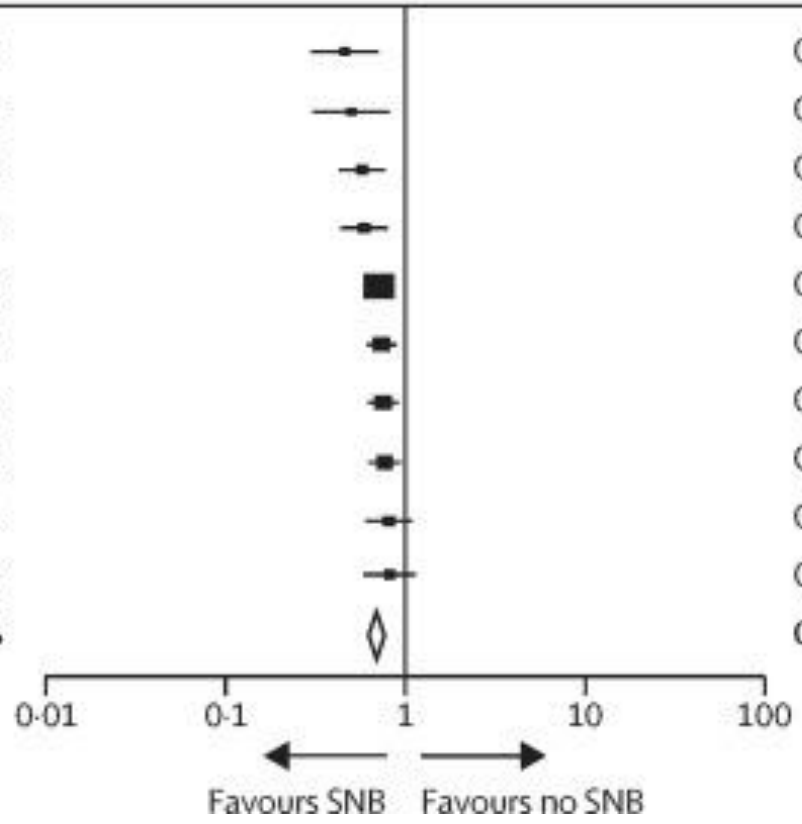
No. at Risk							
OBS, no nodal recurrence	413	375	339	311	282	175	4
OBS, nodal recurrence	87	73	51	40	36	16	0
SNB, true neg.	612	570	511	448	395	243	5
SNB, pos.	122	100	81	68	60	31	0
SNB, false neg.	31	26	15	12	10	6	0

Morton et al, *NEJM* 2006, 2014

2026 Meta-Analysis – The Survival Question Answered

C

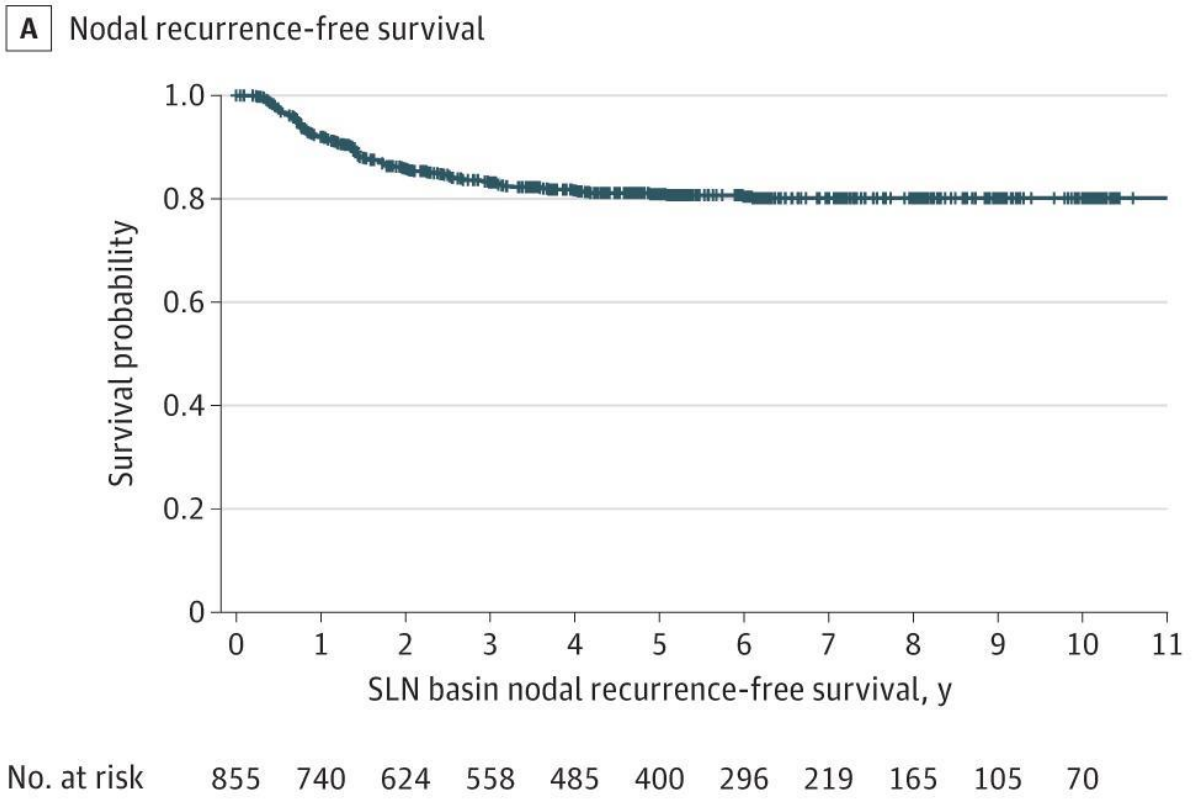
	log (HR)	SNB total	No SNB total	Weight	Fixed HR (95% CI)
Chang (2019)[19]	−0·777 (0·22)	127	51	2·8%	0·46 (0·30–0·71)
Hsu (2023)[20]	−0·693 (0·25)	161	66	2·2%	0·50 (0·31–0·82)
Rajeh (2023)[33]	−0·553 (0·152)	780	260	5·9%	0·58 (0·43–0·77)
Ribero (2015)[23]	−0·528 (0·155)	178	172	5·6%	0·59 (0·44–0·80)
van der Ploeg (2014)[27]	−0·337 (0·064)	2909	2931	33·1%	0·71 (0·63–0·81)
Boada (2018)[25]	−0·301 (0·099)	376	376	13·8%	0·74 (0·61–0·90)
Morton (2014),[6] 3·6+ mm Breslow	−0·288 (0·099)	173	117	13·8%	0·75 (0·62–0·91)
Morton (2014),[6] 1·2–3·5 mm Breslow	−0·261 (0·105)	770	500	12·3%	0·77 (0·63–0·95)
Koskivuo (2017)[22]	−0·211 (0·155)	305	616	5·6%	0·81 (0·60–1·10)
Calista (2013)[28]	−0·198 (0·17)	533	224	4·7%	0·82 (0·59–1·14)
Total (95% CI)		**6312**	**5313**	**100·0%**	**0·71 (0·66–0·76)**
Heterogeneity: χ^2=11·74, df=9 (p=0·23); I^2=23%					
Test for overall effect: Z=9·39 (p<0·00001)					



Varey et al, *Lancet Oncology* 2026

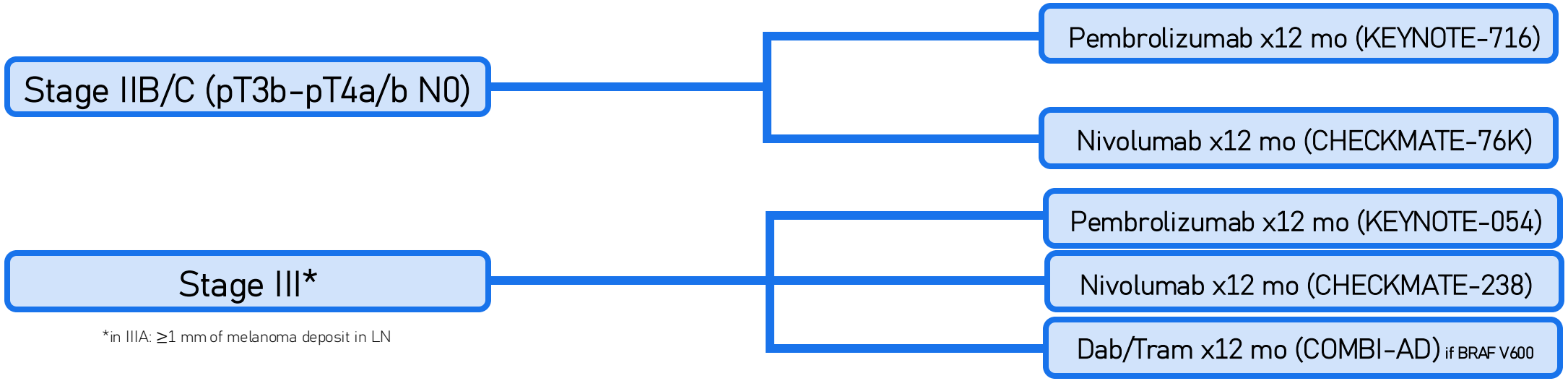
MSLT-II: SLNB is Therapeutic, Not Just Diagnostic

- SLNB prevents regional node field recurrence in ~80% of patients with sentinel node metastases
- Without SLNB, patients who develop clinically palpable nodal disease require more extensive surgery (therapeutic lymph node dissection) with significantly greater morbidity including lymphedema and wound complications
- The false-negative rate of SLNB is only ~5%



Crystal et al, JAMA Surgery 2022; Faries et al, NEJM 2017

Gateway to Adjuvant Therapy – You Cannot Treat What You Cannot Stage



*in IIIA: ≥1 mm of melanoma deposit in LN

- FDA-approved adjuvant therapies for melanoma are stage-dependent
- Clinical trial eligibility for most adjuvant/neoadjuvant melanoma trials requires known SLN status
- Omitting SLNB means flying blind in the adjuvant therapy decision – exposing patients to either unnecessary treatment toxicity or missed therapeutic opportunity

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Low Morbidity – A Favorable Risk-Benefit Profile

Procedure	Overall Complication Rate	Lymphedema	Serious/Long-term Toxicity
SLNB	**11-17%** (mostly minor)	1.3-4.3%	Very low
Completion Lymph Node Dissection	24-67%	15-30% long-term	Wound complications, chronic lymphedema
Therapeutic Lymphadenectomy (if SLNB omitted and nodes later become palpable)	Higher than CLND after SLNB	Higher than CLND	More extensive surgery, delayed treatment

Moody et al, *Euro Jour Surg Onc*, 2017; Roaten et al, *Arch Surg*, 2005

Addressing the Opposition

"MSLT-I didn't show overall survival benefit"

- It was underpowered (needed ~6,576 patients, enrolled 1,661).
- The 2026 meta-analysis of 40,287 patients now shows a statistically significant survival benefit (HR 0.86, $p < 0.0001$)

"Adjuvant immunotherapy works regardless of nodal status, so why biopsy?"

- Without SLNB, regional node-field relapse rates are 20-27% with ICI alone vs 7-9% with SLNB + ICI for T3b/T4 melanomas.
- SLNB and adjuvant therapy are complimentary, not interchangeable

"GEP tests can replace SLNB"

- NCCN explicitly states GEP testing should NOT replace SLNB
- No GEP test provides pathologic staging, regional disease control, or the prognostic granularity of SLN tumor burden measurement

"It's just a staging procedure"

- It is staging AND therapy:
- 80% of definitive basin clearance, survival benefit, and the essential gateway to personalized adjuvant treatment decisions

Key Takeaways

- SLNB is the rare procedure that simultaneously:
  1. provides the most accurate staging
  2. delivers therapeutic regional disease control
  3. enables evidence-based adjuvant therapy decisions
  4. now associated with a statistically significant survival benefit
  5. all the above, with low morbidity

SLNB is not merely standard of care; it is indispensable