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**Table SI. Test definitions for true-positive, true-negative, false-positive, and false-negative results**

		Histological confirmation or clinical and/or radiological follow-up	
		Presence of metastasis	Absence of metastasis
<b>Image-guided biopsies</b>	<b>IGB (+)</b>	with a diagnosis of melanoma metastasis confirmed by histopathology (complete lymph node dissection, partial or complete excision) or clinical and/or radiological follow-up for a minimum of 4 months.	with a diagnosis of melanoma metastasis negated by histopathology (benign lesion, malignancy other than melanoma) or clinical and/or radiological follow-up for a minimum of 4 months.
	<b>IGB (-)</b>	with a diagnosis of benign, non-atypical lesion, but with posterior detection of metastatic disease by histopathology (complete lymph node dissection, partial or complete excision, SLNB) or radiological exploration confirmed during a minimum follow-up time of 4 months.	with a diagnosis of benign, non-atypical lesion confirmed by histopathology (complete lymph node dissection, partial or complete excision, SLNB) and/or radiological follow-up for a minimum of 4 months.

Abbreviations: IGB, image-guided biopsy; SLNB, sentinel lymph node biopsy.

**Table SII. Characteristics of image-guided biopsies falsely diagnosed as melanoma (false-positives)**

Case	Age at IGB, sex	Primary melanoma subtype, location	IGB tissue type, location	IGB technique	IGB findings	Histological/radiological confirmation	Follow-up
1	39, M	Acral, finger	Lymph nodes, axillary	US-FNAC	Scarce atypical cells, compatible with melanoma metastasis, S-100 positive	Complete lymph node dissection. No metastasis in 22 lymph nodes identified, no evidence of disease in subsequent ultrasound. No inflammatory or regressive changes reported.	8 years, 9 months. No evidence of disease
2	64, M	Superficial spreading, lower limbs	Lymph nodes, inguinal	US-FNAC	Malignant cells indicative of melanoma metastasis	Complete lymph node dissection. No metastasis in 13 lymph nodes identified. Extensive cicatricial changes associated with granulomatous reaction to a foreign body, focally abscesified	4 years, 3 months. 1 year nivolumab treatment. No evidence of disease
3	74, M	Superficial spreading, head and neck	Lymph nodes, cervical	US-FNAC	Melanoma metastases with abundant necrosis, macroscopically dark liquid	Complete lymph node dissection. Absence of metastasis in 9 cervical lymph nodes identified. No inflammatory or regressive changes reported.	11 months. Treatment initiated during clinical trial, progression 5 months after IGB with suprarrenal and gallbladder metastasis.

4	49, F	Nodular, trunk	Subcutaneous	CT-FNAC	Scarce atypical cells, suspicious of melanoma metastasis	Mass excision. Fibro-histiocitary proliferation proliferant fasciitis type. Adjacent foreign body reaction.	2 years, 9 months. The mass was finally diagnosed as a high-grade fusiform sarcoma, resistant to surgery, chemotherapy and radiotherapy.
5	69, M	Superficial spreading, head and neck	Lymph nodes, cervical	US-FNAC	Melanoma metastasis	Complete lymph node dissection. No metastasis in 21 cervical lymph nodes identified. No inflammatory or regressive changes reported.	12 years, 3 months. No evidence of disease
6	28, M	Superficial spreading, head and neck	Lymph nodes, cervical	US-FNAC	Malignant cells indicative of melanoma metastasis	Radiological follow-up without evidence of metastasis.	7 years, 10 months. Relapse 8 years after IGB with disseminated metastasis (lung, bone). Clinical trial and subsequent treatment with pembrolizumab and bone radiotherapy initiated.

Abbreviations: M, male; F, female; IGB, image-guided biopsy; US-FNAC, ultrasound guided fine needle aspiration cytology; CT-FNAC, computerized tomography guided fine needle aspiration biopsy.

**Table SIII. Characteristics of false-negative, repeated, and inconclusive image-guided biopsies**

<b>IGB characteristics</b>	<b>False-negative, n (%)</b>	<b>Second IGB, n (%)</b>	<b>Inconclusive, n (%)</b>
Total	32	19	49
<b>Moment of IGB</b>			
Staging	8 (25.0%)	3 (15.8%)	9 (18.0%)
Follow-up	24 (75.0%)	16 (84.2%)	41 (82.0%)
<b>IGB technique</b>			
US-FNAC	18 (56.2%)	13 (68.4%)	45 (90.0%)
CT-FNAC	8 (25.0%)	4 (21.1%)	2 (4.0%)
US-CNB	2 (6.2%)	0 (0.0%)	0 (0.0%)
CT-CNB	4 (12.5%)	2 (10.5%)	3 (6.0%)
<b>Tissue location of IGB</b>			
Lymph nodes	15 (46.9%)	11 (57.9%)	29 (58.0%)
Subcutaneous	6 (18.8%)	2 (10.5%)	14 (28.0%)
Lung	7 (21.9%)	2 (10.5%)	1 (2.0%)
Liver	2 (6.2%)	2 (10.5%)	1 (2.0%)
Bone	2 (6.2%)	2 (10.5%)	2 (4.0%)
Other	0 (0.0%)	0 (0.0%)	3 (6.0%)
Insufficient sample	0	5 (26.3%)	-
Mean tumor burden, mm (SD)	18.19 (11.18)	17.56 (11.31)	19.80 (14.71)

Abbreviations: IGB, image-guided biopsy; US-FNAC, ultrasound-guided fine-needle aspiration cytology; US-CNB, ultrasound-guided core-needle biopsy; CT-FNAC, computerized tomography-guided fine-needle aspiration cytology; CT-CNB, computerized tomography-guided core-needle biopsy; SD, standard deviation.