Melanoma Institute Australia

VCCC Alliance
Overcoming cancer together

COURSE GLOSSARY

Melanoma Biology

Glossary of Key Terms

Translating Science to Clinical Practice

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Glossary of Key Terms

A

Acral lentiginous melanoma
A subtype of cutaneous melanoma arising on glabrous skin (palms, soles, nail beds)

Acral skin
Glabrous (hairless) skin found on the palms, soles, and nail beds.

Adjuvant therapy
Treatment given after definitive surgery with curative intent, to reduce the risk of recurrence.

Age-standardised rate (ASR)
An incidence or mortality rate adjusted for differences in the age distribution of populations, enabling valid comparisons across groups and over time.

Angiogenesis
The formation of new blood vessels, which tumours exploit to sustain growth and facilitate haematogenous metastasis.

B

BAP1
BRCA1-associated protein 1 — a tumour suppressor gene. Germline mutations in BAP1 are associated with uveal melanoma susceptibility and other malignancies. Somatic loss of BAP1 is a strong predictor of metastatic risk in uveal melanoma.

Basement membrane
The thin layer of extracellular matrix separating the epidermis from the dermis.

Biopsy — excisional
Complete surgical removal of a suspicious lesion with a small margin of normal tissue. The preferred diagnostic technique as it provides the most accurate Breslow thickness and staging information.

Biopsy — incisional / punch
Partial removal of a lesion. Used when complete excision is not feasible. May underestimate Breslow thickness and complicate definitive treatment planning.

Biopsy — shave
A technique in which the lesion is shaved off. May be therapeutic if performed to sufficient depth but is often a partial biopsy. Depth assessment can be limited.

BRAF
A gene that provides instructions for making a protein involved in cell growth signalling, which transmits signals from the cell surface to the nucleus to regulate cell division, differentiation, and survival. A component of the MAPK signalling pathway.

BRAF V600E
The most common BRAF point mutation, a valine-to-glutamate substitution at codon 600. Found predominantly in low-CSD (superficial spreading) melanomas. Targetable with BRAF inhibitors combined with MEK inhibitors.

BRAF V600K
A valine-to-lysine substitution at BRAF codon 600. More common in high-CSD (lentigo maligna-type) melanomas. Also targetable with BRAF/MEK inhibitor combinations.

Breslow thickness
The vertical distance in millimetres from the top of the melanoma (or from the base of an ulcer) to the deepest tumour cells. The single most important prognostic factor in localised melanoma and the primary determinant of T stage. Accurately assessed only on complete excision.

C

CDKN2A
Cyclin-dependent kinase inhibitor 2A — a tumour suppressor gene encoding p16. Germline mutations confer a major hereditary melanoma predisposition. Somatic loss facilitates escape from cellular senescence during melanoma development.

Checkpoint inhibitor (ICI)
Immune checkpoint inhibitor — a class of immunotherapy drugs that block inhibitory signals on T cells (PD-1, CTLA-4, LAG-3), allowing the immune system to mount or sustain an anti-tumour response.

Clark level
A historical classification (levels I–V) describing the anatomical depth of melanoma invasion into skin layers. Largely superseded by Breslow thickness but still reported on pathology reports.

Clinical staging
Staging based on physical examination, clinical assessment of lymph nodes, and imaging findings, prior to pathological confirmation. Provides an estimate of disease extent but cannot identify microscopic spread.

Complete lymph node dissection (CLND)
Surgical removal of all lymph nodes in a nodal basin following a positive SLNB or clinically detected nodal disease.

CSD melanoma
Melanoma arising on chronically sun-damaged skin; subdivided into high-CSD and low-CSD subtypes based on degree of cumulative UV exposure. See also: High-CSD melanoma; Low-CSD melanoma.

Cutaneous melanoma
Melanoma arising from the skin. The predominant form of melanoma in Australia. Includes superficial spreading, nodular, lentigo maligna, acral lentiginous, and desmoplastic subtypes, among others.

Cytokine release syndrome (CRS)
A systemic inflammatory response caused by rapid immune activation.

D

De novo melanoma
Melanoma that arises on previously normal-appearing skin, without an identifiable precursor naevus.

Dermis
The layer of skin beneath the epidermis, containing collagen, blood vessels, lymphatics, and nerves.

Dermoscopy
A non-invasive skin surface microscopy technique using polarised light and magnification to aid clinical differentiation of benign from malignant lesions. A key tool in initial assessment of suspicious pigmented lesions.

Desmoplasia
A local reaction causing growth of dense fibrous connective tissue (stroma) around tumour cells

Dysplastic naevus
A melanocytic naevus with atypical architectural and cytological features

Dysplastic naevus syndrome
A clinical phenotype characterised by multiple dysplastic naevi (typically >5), associated with an approximately 10-fold increased melanoma risk.

E

Epidermis
The outermost layer of the skin, containing keratinocytes and melanocytes.

F

Field effect
The concept that histologically normal-appearing melanocytes surrounding a primary tumour may be partially biologically transformed and at risk of further malignancy.

Fine needle aspiration (FNA)
A minimally invasive technique using a fine needle to obtain cells from a suspicious lymph node or lesion for cytological assessment.

Fitzpatrick skin type
A classification system (Types I–VI) categorising skin colour and its response to UV exposure.

G

GNA11 / GNAQ
Genes encoding G-protein alpha subunits. Activating mutations in GNAQ or GNA11 are the primary oncogenic drivers in uveal melanoma distinct from the MAPK pathway mutations seen in cutaneous melanoma.

H

Haematogenous spread
Metastasis via the bloodstream, allowing distant organ involvement.

High-CSD melanoma
Melanoma arising from skin with chronic sun damage.

HLA-A*02:01
A human leukocyte antigen subtype present in approximately 45% of individuals of European descent.

I

Immunogenicity
The capacity of a tumour to be recognised and attacked by the immune system.

Immunosuppression
A state of reduced immune system activity.

Immunotherapy
A broad term for treatments that harness or modify the immune system to fight cancer.

In situ melanoma
Melanoma confined to the epidermis, with no breach of the basement membrane.

In-transit metastasis
Cutaneous or subcutaneous melanoma deposits in the region between the primary tumour and the regional nodal basin, beyond the primary site.

Immune-related adverse event (irAE)
Adverse effects arising from checkpoint inhibitor-driven immune activation affecting normal tissues. Can involve any organ system; commonly skin, gut, liver, lung, and endocrine glands.

K

KIT
A receptor tyrosine kinase encoded by the KIT gene, a component of the MAPK pathway. KIT mutations or amplifications are the predominant driver in acral and mucosal melanomas.

L

Local recurrence
Re-emergence of melanoma at or very near the site of the primary tumour.

Low-CSD melanoma
Melanoma arising on skin with minimal cumulative sun damage, typically from intermittent UV exposure.

Lymphoscintigraphy
A nuclear medicine imaging technique using a radioactive tracer injected near the primary melanoma to map the draining lymphatics and identify the sentinel lymph node(s) prior to SLNB.

Lymphovascular invasion
Histological evidence of melanoma cells within lymphatic or blood vessel lumens.

M

MAPK pathway
Mitogen-activated protein kinase pathway — a normal intracellular signalling cascade controlling cell division, differentiation, and survival.

Multidisciplinary team (MDT)
A team of healthcare professionals from different specialties (surgery, medical oncology, radiation oncology, pathology, radiology, nursing, and allied health) who collaborate to plan and review melanoma patient care.

Melanin
The pigment produced by melanocytes that absorbs UV radiation and protects the skin's DNA from UV-induced damage.

Melanocyte
Specialised pigment-producing cells located in the basal layer of the epidermis, in hair follicles, and in mucosae. The cell of origin for all melanomas.

Melanoma-specific survival (MSS)
A survival measure that counts only deaths attributed to melanoma, excluding deaths from other causes. Distinguished from overall survival (OS).

Microsatellite
A deposit of tumour cells discontinuous from the primary melanoma, found within the dermis or subcutaneous tissue.

Mitotic rate (TMR)
Tumour mitotic rate — the number of mitotic figures per mm^2 of tumour, reflecting the rate of cell division.

Molecular testing
Genomic analysis of tumour tissue to identify actionable mutations.

Mucosal melanoma
Melanoma arising from mucosal surfaces (nasal, oral, anorectal, vulvar).

Mucosal surface
The moist lining of body cavities (e.g. nasal passages, oral cavity, vulva, gastrointestinal tract).

N

Naevus (pl. naevi)
A benign melanocytic lesion (mole).

Neoadjuvant therapy
Treatment given before definitive surgery, with the aim of downstaging disease, improving surgical outcomes, and enabling assessment of pathological response.

Neoantigen
An abnormal protein produced by tumour cells due to somatic mutations, which may be recognised as foreign by the immune system. High tumour mutational burden produces more neoantigens, driving immunogenicity and checkpoint inhibitor responsiveness.

Neurotropism (perineural invasion)
Invasion of melanoma cells along nerve sheaths. Associated with increased local recurrence risk, particularly in desmoplastic melanoma. Not incorporated into AJCC staging as it is not prognostic for distant spread.

NF1
Neurofibromatosis type 1 gene — a negative regulator of the MAPK pathway.

Nodular melanoma
A historically recognised subtype characterised by rapid vertical growth from the outset, without a preceding radial growth phase. No longer strictly recognised as a separate subtype in modern pathway-based classification but remains in common clinical and pathological use.

Non-CSD melanoma
Melanoma arising independent of cumulative UV exposure: includes acral, mucosal, and uveal subtypes.

NRAS
Neuroblastoma RAS viral oncogene homologue — the second most commonly mutated gene in cutaneous melanoma after BRAF.

P

Pathological complete response (pCR)
Absence of residual viable tumour cells in surgical specimens following neoadjuvant therapy.

Pathological response (neoadjuvant)
Standardised histological assessment of tumour response following neoadjuvant therapy, recording the percentage of residual viable tumour and pattern of response. Critical for prognostication and guiding postoperative management.

Pathological staging
Staging determined after histological examination of the surgically removed primary tumour and regional lymph nodes.

Pathology report — synoptic
A structured, standardised format for reporting melanoma histological features, ensuring consistency and completeness across reports.

PD-1 (Programmed cell death protein 1)
An inhibitory receptor on T cells. When bound by PD-L1 (on tumour or immune cells), it suppresses T cell activity.

PD-L1
Programmed death-ligand 1 — expressed on tumour cells and immune cells; binds PD-1 to suppress T cell activity.

R

Recurrence-free survival (RFS)
The time from definitive treatment to documented disease recurrence or death from any cause.

Regression (tumour)
Histological evidence of prior immune-mediated tumour destruction: fibrosis, melanophage accumulation, and vascular proliferation where tumour cells once existed.

Relative risk
A measure comparing the likelihood of developing a disease between two groups.

S

Satellite metastasis
Discrete tumour nests separated from the primary melanoma by normal dermis. Classified as N-stage disease (Stage III or higher).

Sentinel lymph node biopsy (SLNB)
A surgical procedure to identify and remove the SLN(s) for histological assessment.

Sentinel lymph node (SLN)
The first draining lymph node(s) from the primary tumour site, identified via lymphoscintigraphy and intraoperative blue dye or gamma probe detection.

Surgical margin
The distance between the edge of the tumour and the cut edge of the surgical specimen, as measured histologically. Clinical margins for WLE are determined by Breslow thickness; histological margins are assessed by the pathologist.

Surveillance
Scheduled follow-up of melanoma patients to detect recurrence of melanoma, or new primary melanomas.

T

TILs (Tumour-infiltrating lymphocytes)
Immune cells (primarily T cells) that have migrated into the tumour.

TMB (Tumour mutational burden)
The total number of somatic mutations per megabase of a tumour genome.

TNM system
Tumour–Node–Metastasis classification system. The internationally standardised framework for melanoma staging, with each component (T, N, M) combining to yield an overall stage (I–IV) that guides prognosis and treatment.

Tumour microenvironment (TME)
The local cellular and molecular environment surrounding tumour cells, including immune cells, stromal cells, blood vessels, and signalling molecules. The TME influences tumour growth, immune evasion, and treatment response.

U

Ulceration
Full thickness absence of the overlying epidermis with associated host reaction above the primary tumour, as assessed histologically.

Uveal melanoma
Melanoma arising from the uveal tract of the eye (choroid ~90%, ciliary body ~6%, iris ~4%). Driven by GNAQ/GNA11 mutations, not UV radiation.

UV radiation (UVR)
Radiation emitted primarily by the sun (and artificial sources). The single largest modifiable risk factor for cutaneous melanoma.

UV signature mutation
A specific pattern of DNA mutations caused by UV radiation exposure. Absent in acral, mucosal, and uveal melanomas, confirming their non-UV-driven aetiology.

W

Wide local excision (WLE)
Surgical re-excision of the primary melanoma site with a standardised clinical margin of normal skin, determined by Breslow thickness.

Common Abbreviations

AJCC	American Joint Committee on Cancer
AIHW	Australian Institute of Health and Welfare
ASR	Age-standardised rate
BRAFi	BRAF inhibitor
CLND	Complete lymph node dissection
CNS	Central nervous system
CRS	Cytokine release syndrome
CSD	Cumulative sun damage
CT	Computed tomography
CTLA-4	Cytotoxic T-lymphocyte-associated protein 4
FNA	Fine needle aspiration
ICI	Immune checkpoint inhibitor
IHC	Immunohistochemistry
irAE	Immune-related adverse event
LAG-3	Lymphocyte activation gene-3
MAPK	Mitogen-activated protein kinase
MDT	Multidisciplinary team
MEKi	MEK inhibitor
MHC	Major histocompatibility complex
MIA	Melanoma Institute Australia
MRI	Magnetic resonance imaging
MSS	Melanoma-specific survival
OS	Overall survival
PBS	Pharmaceutical Benefits Scheme
pCR	Pathological complete response
PD-1	Programmed cell death protein 1
PD-L1	Programmed death-ligand 1
PET	Positron emission tomography
RFS	Recurrence-free survival
SLN	Sentinel lymph node
SLNB	Sentinel lymph node biopsy
TIL	Tumour-infiltrating lymphocyte
TLND	Therapeutic lymph node dissection
TMB	Tumour mutational burden
TME	Tumour microenvironment
TMR	Tumour mitotic rate
TNM	Tumour–Node–Metastasis
UVR	Ultraviolet radiation
WLE	Wide local excision

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