Beleid MERKEL CEL CARCINOMEN

1. Diagnose

APO onderzoek met immunohistochemie om primaire huidpathologie te bewijzen (dd lymfoom, metastasen)

Volledig huidnazicht, palpatie klierstreken, labo (uitgebreid, met NSE tumormerker), PET-CT, sentinel lymph node biopsy (SNB) (indien klinisch N0)

SNB: positivity rate is ~20% voor T1 en 40%-50% voor T2

2. TNM stadiëring

Overgenomen uit UpToDate®

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed (eg, curetted)
T0	No evidence of primary tumor
Tis	*In situ* primary tumor
T1	Maximum clinical tumor diameter ≤2 cm
T2	Maximum clinical tumor diameter >2 but ≤5 cm
T3	Maximum clinical tumor diameter >5 cm
T4	Primary tumor invades fascia, muscle, cartilage, or bone

Regional lymph nodes (N)	
Clinical (N)	
N category	**N criteria**
NX	Regional lymph nodes cannot be clinically assessed (eg, previously removed for another reason, or because of body habitus)
N0	No regional lymph node metastasis detected on clinical and/or radiologic examination
N1	Metastasis in regional lymph node(s)
N2	In-transit metastasis (discontinuous from primary tumor; located between primary tumor and draining regional nodal basin, or distal to the primary tumor) **without** lymph node metastasis
N3	In-transit metastasis (discontinuous from primary tumor; located between primary tumor and draining regional nodal basin, or distal to the primary tumor) **with** lymph node metastasis

Distant metastasis (M)	
Clinical (M)	
M category	**M criteria**
M0	No distant metastasis detected on clinical and/or radiologic examination
M1	Distant metastasis detected on clinical and/or radiologic examination
M1a	Metastasis to distant skin, distant subcutaneous tissue, or distant lymph node(s)
M1b	Metastasis to lung
M1c	Metastasis to all other visceral sites

Prognostic stage groups			
Clinical stage group (cTNM)			
When T is...	**And N is...**	**And M is...**	**Then the stage group is...**
Tis	N0	M0	0
T1	N0	M0	I
T2-3	N0	M0	IIA
T4	N0	M0	IIB
T0-4	N1-3	M0	III
T0-4	Any N	M1	IV

Primary tumor (T)	
T category	**T criteria**
TX	Primary tumor cannot be assessed (eg, curetted)
T0	No evidence of primary tumor
Tis	*In situ* primary tumor
T1	Maximum clinical tumor diameter ≤2 cm
T2	Maximum clinical tumor diameter >2 but ≤5 cm
T3	Maximum clinical tumor diameter >5 cm
T4	Primary tumor invades fascia, muscle, cartilage, or bone

Regional lymph nodes (N)	
Pathological (pN)	
pN category	**pN criteria**
pNX	Regional lymph nodes cannot be assessed (eg, previously removed for another reason or **not** removed for pathological evaluation)
pN0	No regional lymph node metastasis detected on pathological evaluation
pN1	Metastasis in regional lymph node(s)
pN1a(sn)	Clinically occult regional lymph node metastasis identified only by sentinel lymph node biopsy
pN1a	Clinically occult regional lymph node metastasis following lymph node dissection
pN1b	Clinically and/or radiologically detected regional lymph node metastasis, microscopically confirmed
pN2	In-transit metastasis (discontinuous from primary tumor; located between primary tumor and draining regional nodal basin, or distal to the primary tumor) **without** lymph node metastasis
pN3	In-transit metastasis (discontinuous from primary tumor; located between primary tumor and draining regional nodal basin, or distal to the primary tumor) **with** lymph node metastasis

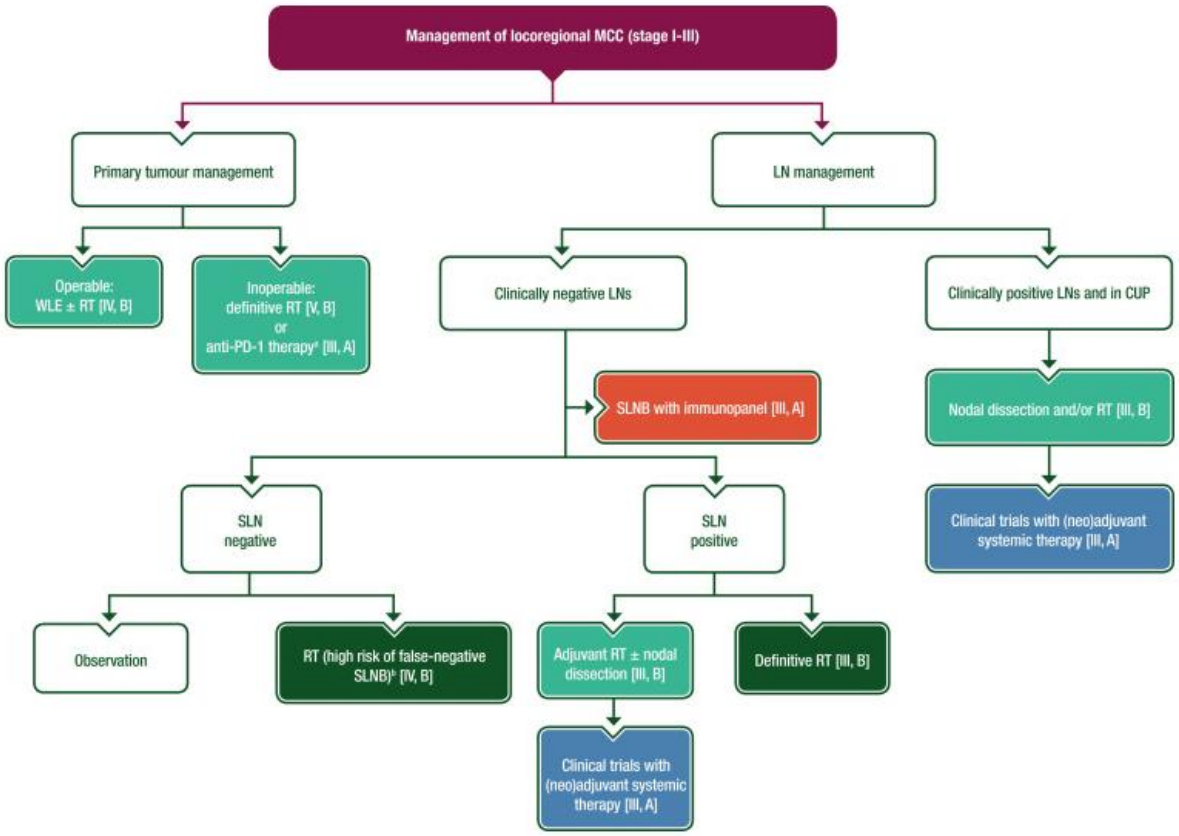
Distant metastasis (M)	
Pathological (M)	
M category	**M criteria**
M0	No distant metastasis detected on clinical and/or radiologic examination
pM1	Distant metastasis microscopically confirmed
pM1a	Metastasis to distant skin, distant subcutaneous tissue, or distant lymph node(s), microscopically confirmed
pM1b	Metastasis to lung, microscopically confirmed
pM1c	Metastasis to all other distant sites, microscopically confirmed

Prognostic stage groups			
Pathological stage group (pTNM)			
When T is...	**And N is...**	**And M is...**	**Then the stage group is...**
Tis	N0	M0	0
T1	N0	M0	I
T2-3	N0	M0	IIA
T4	N0	M0	IIB
T1-4	N1a(sn) or N1a	M0	IIIA
T0	N1b	M0	IIIA
T1-4	N1b-3	M0	IIIB
T0-4	Any N	M1	IV

3. Behandeling

3.1 Locoregionaal

ESMO guidelines



3.1.1 Primaire tumor

<u>Heelkunde</u>

Brede excisie met 1-2 cm marge.

Als 1-2 cm technisch niet haalbaar is: 0.5-1.0 cm met adjuvante radiotherapie

Sentinel lymph node biopsy (SNB)

<u>Primaire radiotherapie (brede marges 3-5 cm)</u> (thv het aangezicht tot 2 cm in functie van anatomie/toxiciteit)

Alternatief voor heelkunde indien inoperabel letsel

<u>Adjuvante radiotherapie</u> bij patiënten met volgende risicofactoren:

- primaire tumor ≥1 cm
- primaire tumor in hoofdhals regio
- positieve of nipte snedevlakken (marges < 1 cm)
- lymfovasculaire invasie
- immuungecompromitteerde patiënt

- satellietletsels
- positieve lymfeklieren
  NB: Indien SNB (technisch) niet mogelijk → adjuvante radiotherapie tumorbed + regionale klierstreek te overwegen

Dosis schema radiotherapie

- 50-56 Gy zo negatieve sectievlakken
- 56-60 Gy zo microscopisch positieve sectievlakken
- 60 to 66 Gy zo macroscopisch positieve sectievlakken, inoperable primaire letsels of inoperable regionale lymfeklieren

3.1.2 Lymfeklieren

1. Klinisch negatieve klieren: steeds sentinel lymphnode biopsy te doen
2. Klinisch positieve klieren (of positieve sentinel):
   - histologisch te bevestigen (niet nodig indien positieve sentinel)
   - lymfeklierevidement
   - (adjuvante) radiotherapie
     - 50-56 Gy bij positieve sentinel
     - 60-66 Gy bij multipele aangetaste lymfeklieren en/of aanwezigheid van kapseldoorbraak
     - Geen radiotherapie: te overwegen bij lage tumor burden op sentinel lymphnode biopsy of bij enkel 1 macroscopisch aangetaste lymfeklier zonder kapseldoorbraak
     - Geen sentinel lymphnode biopsy of evidement en klinisch evidente lymfadenopathie: 60-66 Gy
       (Ref: NCCN guidelines)

3.2 Gemetastaseerde ziekte

- 1ste lijn: immuuntherapie onder vorm van Avelumab (=anti-PD-L1 antibody, Bavencio®), tweewekelijkse IV toediening (of studiedeelname)
- 2de lijn: chemotherapie (platinum-etoposide) (of studiedeelname)

4. Follow-up

Klinisch onderzoek van huid en lymfeklieren:

- eerste 3 jaar om de 3-6 maanden
- jaar 4 en jaar 5: om de 6 maanden
- na 5 jaar: om de 12 maanden

PET-CT:

- eerste 3 jaar om de 6-12 maanden
- na 3 jaar: ifv risico-inschatting