

Rol systemische therapie bij niet-melanoma tumoren van de huid

Ipodium 09/03/2024

Systemische therapie bij niet-melanoma tumoren van de huid

Standaardtherapie lokale tumoren:

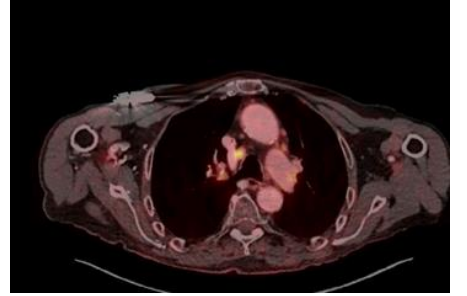
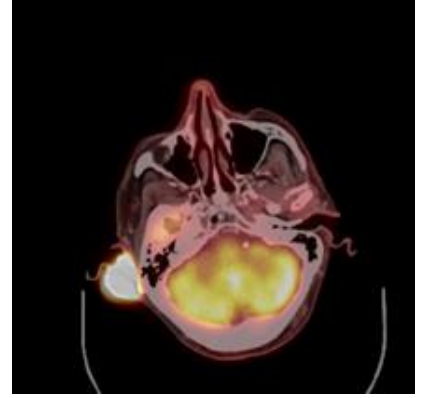
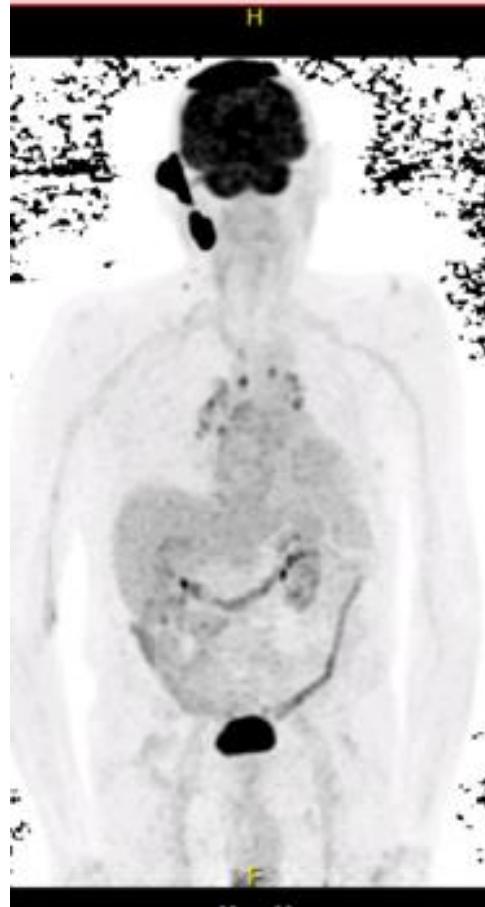
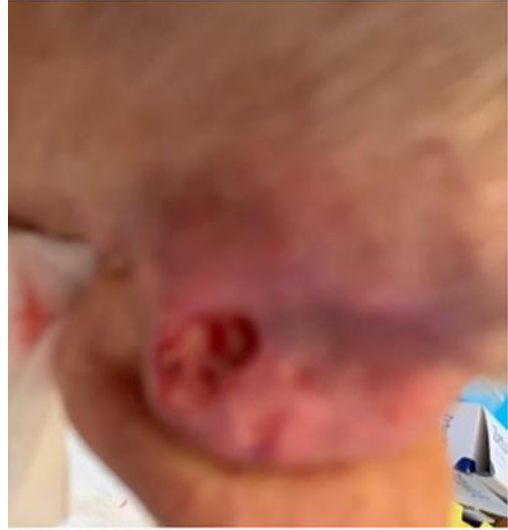
- Resectie met negatieve sectievlakken
- Radiotherapie

Rol systemische therapie zo niet meer lokaal te behandelen/
gemetastaseerd

- Chemotherapie
- Immunotherapie
- TKI

Casus: man, 82 j

- Medische voorgeschiedenis:
- AHT, PTCA met stent LAD, VKF
- 2017: resectie invasief spinocellulair carcinoma scalp gr 1, pT3, recoupe toont negatieve sectievlakken
- 06/2019: recidief thv scalp, resectie
- 11/2019: recidief thv scalp; resectie (invasiediepte niet te beoordelen)
- 07/2020: retroauriculaire AP rechts, grote wonde thv scalp > foto



Casus:

- Bilan toont eveneens mediastinale adenopathieën
- APO: invasief spinocellulair carcinoma gr 2, TPS score 3
- 31/07/2020: start PDL-1 inhibitor cemiplimab (Libtayo[®])
via medical need
- Na 2 m reeds tekens van respons > foto's
- Globaal goede tolerantie, wel vermoeidheid, jeuk
- 08/2022: stop owv toename vermoeidheid



Casus: man, 88j



systemische therapie bij spinocellulair carcinoma van de huid (SCC): therapie

- 5% pt met spinocellulair carcinoma zijn niet lokaal behandelbaar/M+
- Risicofactoren: T, lvi, pni, gr 3, IS, recidief (na RT)
- Geen echte chemostandaard, meestal cisplatinumbevattende schema's of cetuximab (EGFR-I)
- rr: 15 tot 18%, gemiddelde overleving 8 tot 15 m *

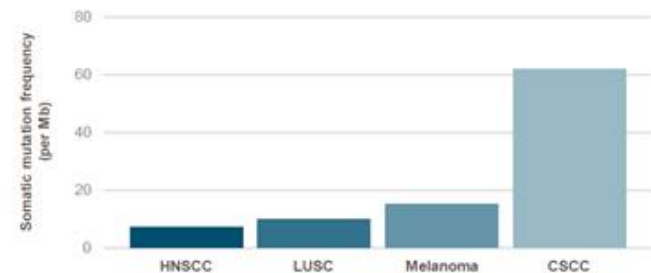
* C, Lance Covery et al, cancer med 2020 Oct;9(20):7381-7387. doi: 10.1002/cam4.3146. Epub 2020 Jun 24.

systemische therapie bij spinocellulair carcinoma van de huid (SCC): immunotherapie

The high mutation burden of advanced CSCC supports the evaluation of PD-1 inhibition¹⁻³

A high mutation burden can lead to neoantigen formation, which can increase the likelihood of immune recognition of tumour cells. In response, tumour cells utilize immune checkpoint interaction to evade recognition.⁴⁻⁶

Mutation burden of the tumour genome in aggressive CSCC in comparison with melanoma and other squamous tumour types¹

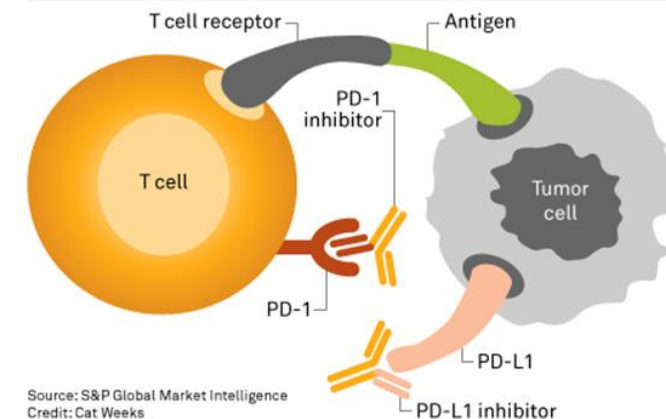


CSCC has one of the highest mutation burdens in the landscape of more than 100 tumour types.⁷



CSCC, cutaneous squamous cell carcinoma; HNSCC, head and neck squamous cell carcinoma; LUSC, lung squamous cell carcinoma; Mb, megabase; PD-1, programmed death receptor-1.

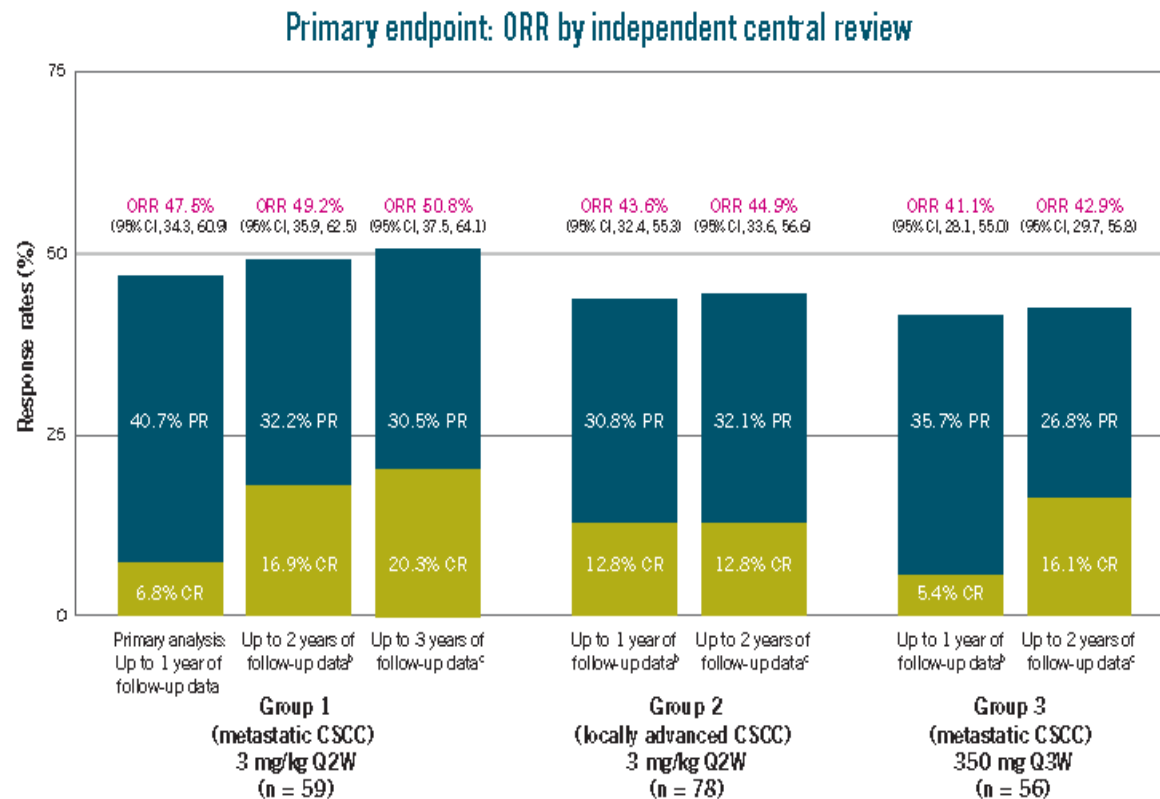
PD-1 inhibitors: Merck & Co. Inc.'s Keytruda; Bristol-Myers Squibb's Opdivo.
PD-L1 inhibitors: AstraZeneca's Imfinzi; Pfizer and Merck KGaA's Bavencio; Roche's Tecentriq.



Source: S&P Global Market Intelligence
Credit: Cat Weeks

systemische therapie bij spinocellulair carcinoma van de huid: immunotherapie

- Study 1540 (n: 193; Ia/mCSCC): efficacy
- Study 1423 (n:591> 219 cscC): safety



Ongoing respons:

at 12 months or longer 87.8%

at 24 months or longer 69,4%

systemische therapie bij spinocellulair carcinoma van de huid: immunotherapie

- nevenwerkingen: ernstig bij 8.6% pt; nood tot stop r/ bij 5.8% pt
- meest voorkomende nw: vermoeidheid, jeuk, huiduitslag, diarree

Toekomst: neo-adjuvant gebruik cemiplimab bij CSCC?

F2 n:79, 2 tot 4 toedieningen cemiplimab gevolgd door heelkunde: pCR 51%*

* N D Gross et al, N Engl J Med 2022; 387:1557-1568

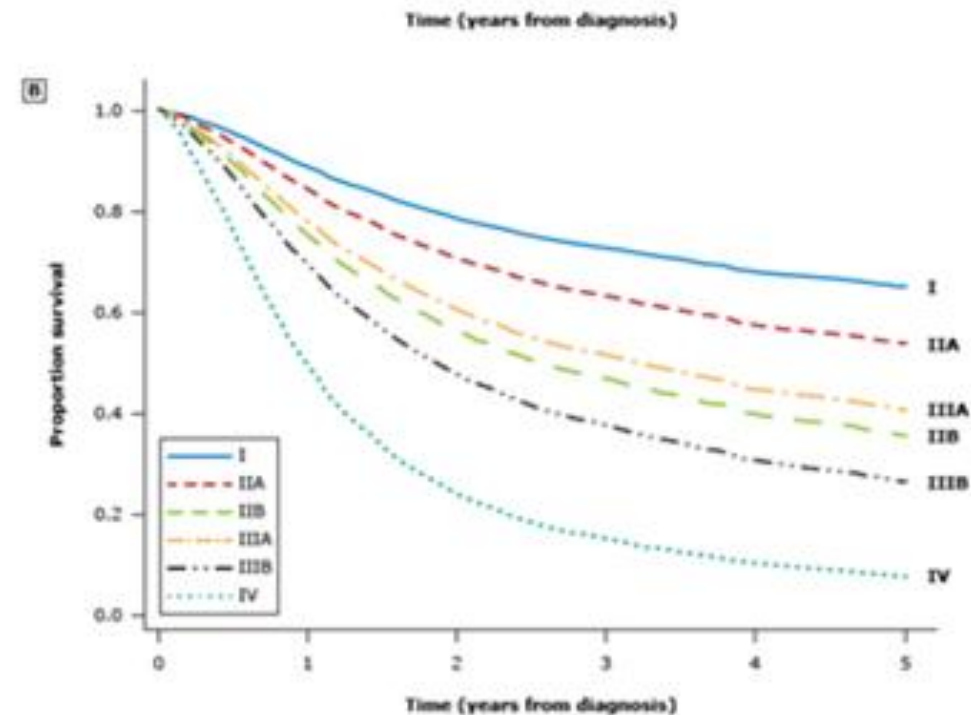
systemische therapie bij Merkelceltumoren

- Zeldzaam (doch ↑)
- RF: chronische zonblootstelling; IS en hemato, ouderdom
- Ethio: polyomavirusinfectie (60-80%)
- Moeilijke differentiele diagnose: lipoma, cyste, kerato-acanthoma, BSC, SCC,...
- APO: dd lymfoom, melanoma, kleincellig carcinoma
- > IHC: CK20 (!), NSE, CgA
- Lokaal: resectie (+sentinel) +/- RT of externe Rt



systemische therapie bij Merkelceltumoren

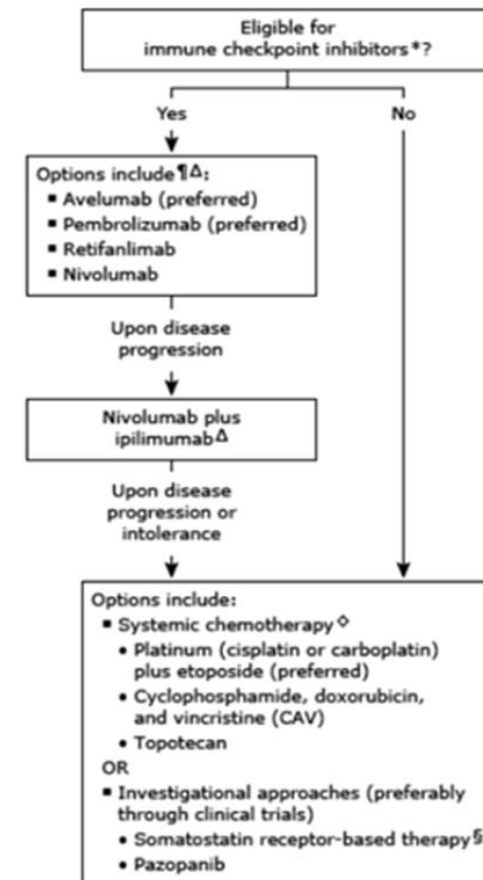
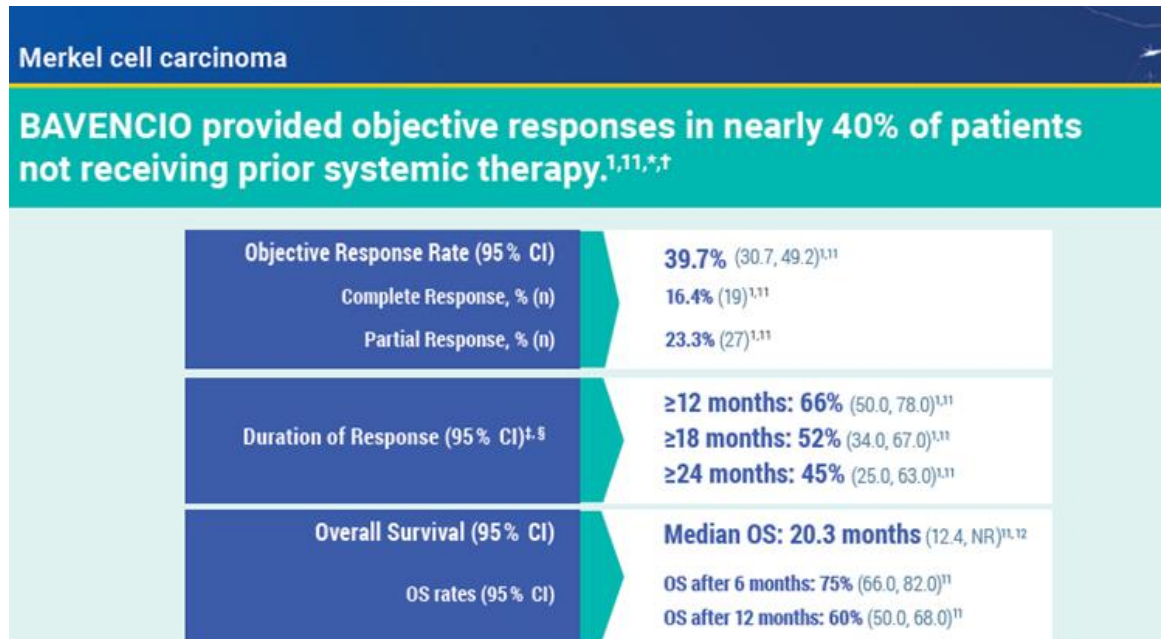
- slechte prognose in gevorderde setting
- locale AP, huid op afstand, longM+,
andere viscerale M+, subc m



Pathological stage	5-year OS	95% CI
I	62.8%	59.6 to 65.8%
IIA	54.6%	49.3 to 59.7%
IIB	34.8%	25.6 to 44.1%
IIIA	40.3%	37.5 to 43.0%
IIIB	26.8%	23.4 to 30.4%
IV	13.5%	11.0 to 16.3%

systemische therapie bij Merkelceltumoren

- IO: avelumab (Bavencio®), pembrolizumab, nivolumab
Javelin Merkel 200: F2; n: 116 met avelumab
- Chemotherapie: hoge RR (tot 60%) doch kortdurend, toxiciteit
- Toekomst: luthetiumdotate?



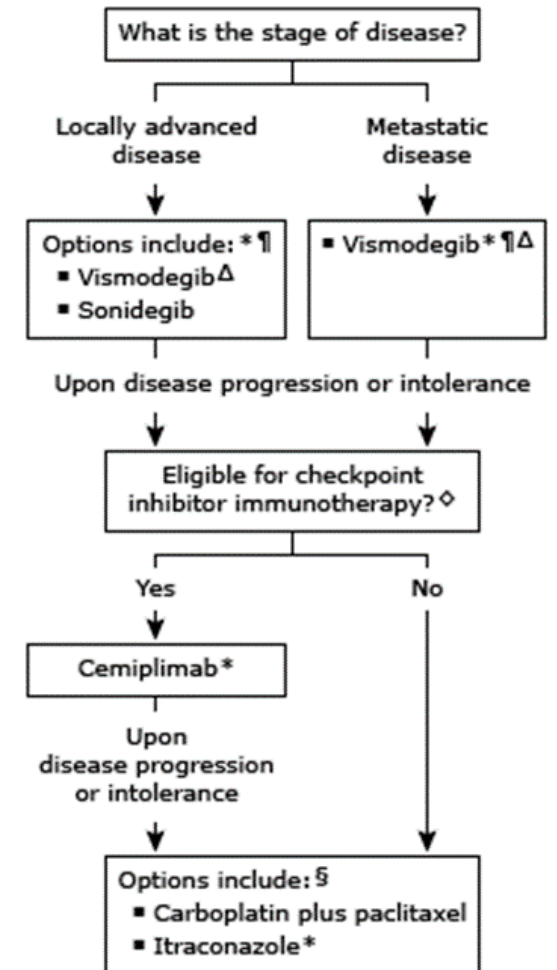
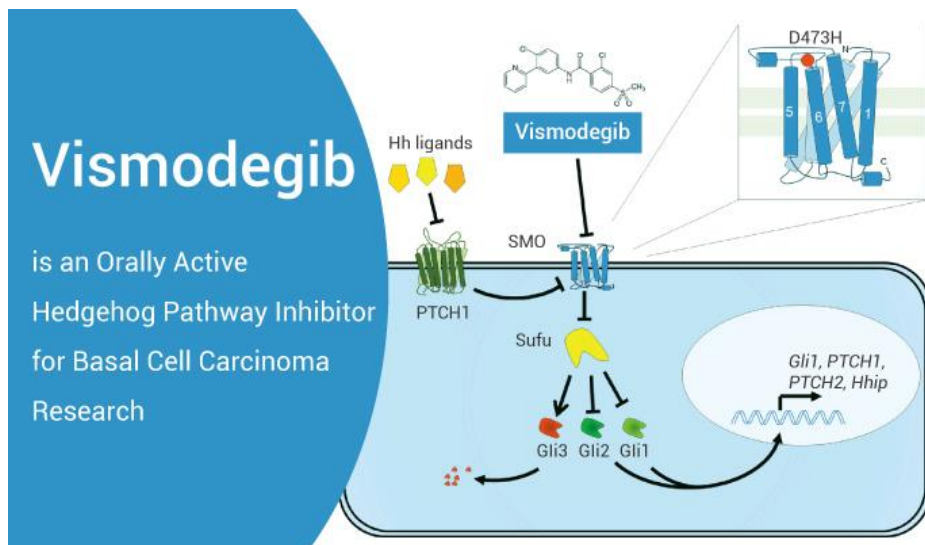
systemische therapie bij basocellulaire tumoren (BSC)

- Zelden M+, vooral lokaal destructief
- UV blootstelling (zonnebank), IS, genetisch
- Behandeling: LOCAAL!

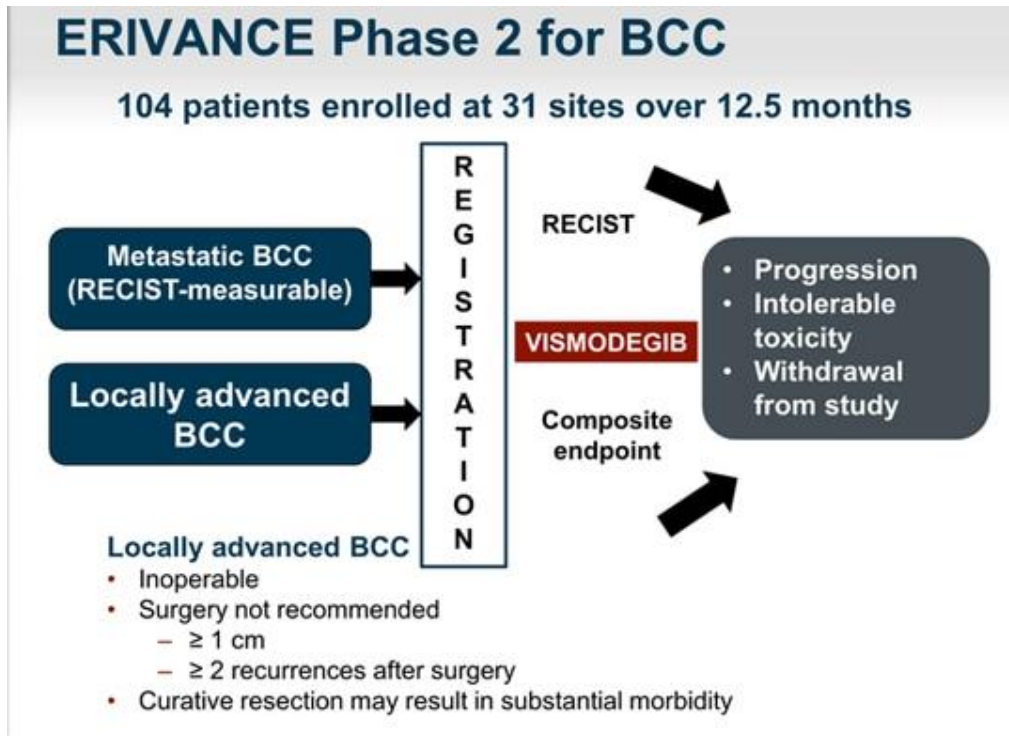


systemische therapie bij basocellulaire tumoren (BSC)

- Zo niet met locale therapie te behandelen:
 - Vismodegib (Erivedge©)
 - IO (cemiplimab)
 - (chemo)



systemische therapie bij basocellulaire tumoren (BSC)



Objective response rate by independent review from ERIVANCE^{1*}

	laBCC (n=63)	mBCC (n=33)
ORR	43% (n=27)	30% (n=10)
(95% CI)	(30.5-56.0)	(15.6-48.2)
Complete response	21% (n=13)	0% (n=0)
Partial response	22% (n=14)	30% (n=10)
Median duration of response (months)	7.6	7.6
(95% CI)	(5.7-9.7)	(5.6-NE)

Incidence of common adverse reactions ($\geq 10\%$): Pooled analysis of 4 studies (N=138)^{1-3,4}

Adverse reactions occurring in $\geq 10\%$ of advanced BCC patients	Grade 1 (%) (Mild)	Grade 2 (%) (Moderate)	Grade 3 (%) (Severe)	Grade 4 (%) (Disabling or life-threatening)	All grades (%)
Muscle spasms	51.4%	16.7%	3.6%	–	72%
Alopecia	49.3%	14.5%	N/A	N/A	64%
Change in taste (dysgeusia)	34.1%	21.0%	N/A	N/A	55%
Weight loss	25.4%	12.3%	7%	N/A	45%
Fatigue	27.5%	6.5%	5%	0.7%	40%
Nausea	23.9%	5.8%	0.7%	–	30%
Diarrhea	21.7%	6.5%	0.7%	–	29%
Decreased appetite	15.2%	8.0%	2.2%	–	25%
Constipation	17.4%	3.6%	–	–	21%
Arthralgias	11.6%	3.6%	0.7%	–	16%
Vomiting	10.9%	2.9%	–	–	14%
Loss of taste (ageusia)	8.0%	2.9%	N/A	N/A	11%

Adverse reactions reported using Medical Dictionary for Regulatory Activities preferred terms and graded using National Cancer Institute Common Terminology Criteria for Adverse Events v3.0 for assessment of toxicity. N/A=not applicable, this grade does not exist for this adverse reaction.

Besluit: beter voorkomen dan...dank voor uw aandacht!

