

Leven met melanoom onder systemische behandeling:

DE HUID

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Dermatologie



Bijwerkingen medicatie algemeen

Maculopapulair
exantheem



Netelroos



Bijwerkingen chemotherapie

- Haarverlies
- Stomatitis
- Hand foot syndroom
- Nagelafwijkingen
- Droogte / jeuk
- Extravasatie
- EGFR inhibitoren: acneiforme rash
- ...
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BRAF inhibitoren

	Vemurafenib	Dabrafenib
'huiduitslag'	70%	22%
fotosensitiviteit	20%	3%
panniculitis	14%	Cases
millia / cysts	>50%	?
hyperkeratosen	25%	35%
palm / plant erythrodysesthesy	12%	18%
Kerato-acanthoom / spino	9% KA 14% SCC	12%
Haarveranderingen	31% alopecia 3,7% andere	28%
Atypische naevi / melanoma	3% atyp naevi 3% melanomen	2%
		E. Livingstone, EADO 2017

'Huiduitslag'



JAMA Dermatology, July 22, 2015

Zon overgevoeligheid

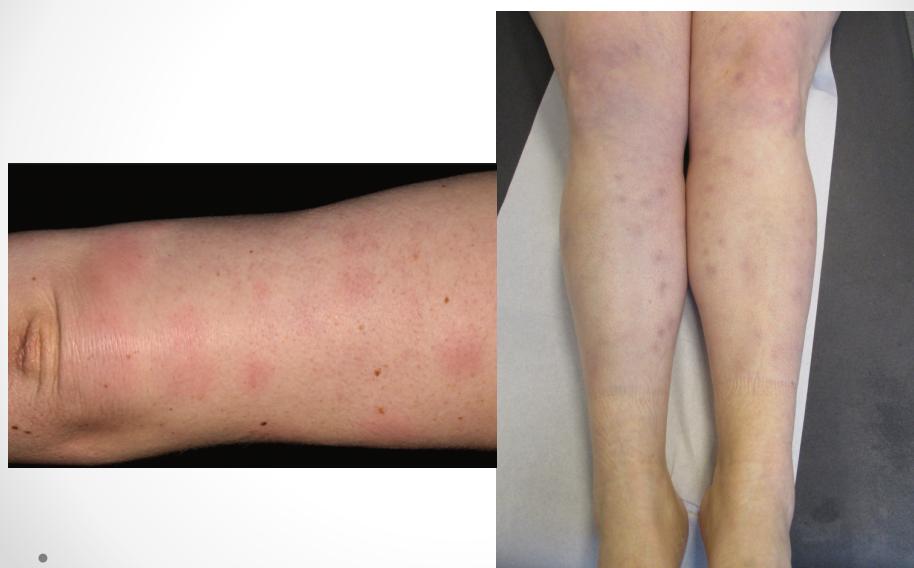


- Cave achter raam
- Cave in auto
- Cave lippen



JAMA Dermatology, July 22, 2015

Panniculitis



Cysten en milia



Ruze/verharde letsels



JAMA Dermatology, July 22, 2015

Kerato-acanthoom / Spinocellulair carcinoom



Reactie handen en voeten



Haarveranderingen

- Haarverlies / verdunning
- Verandering van haren
 - Krul
 - Kleur

Atypische moedervlekken en melanomen

- Vnl wild type

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MEK-inhibitoren

Flaherty KT et al, N Eng J Med 2012; 367:107-14

Table 3. Adverse Events.*

Adverse Event	Trametinib (N = 211)	Chemotherapy (N = 99)
	number of patients (percent)	
Rash	121 (57) Grade 2 40 (19) Grade 3 or 4† 16 (8)	10 (10) 3 (3) 0
Diarrhea	91 (43) Grade 2 13 (6) Grade 3 or 4† 0	16 (16) 3 (3) 2 (2)
Fatigue	54 (26) Grade 2 11 (5) Grade 3 8 (4)	27 (27) 7 (7) 3 (3)
Peripheral edema	54 (26) Grade 2 8 (4) Grade 3 2 (1)	3 (3) 0 0
Acneiform dermatitis	40 (19) Grade 2 20 (9) Grade 3 2 (1)	1 (1) 0 0
Nausea	38 (18) Grade 2 5 (2) Grade 3 2 (1)	37 (37) 10 (10) 1 (1)
Alopecia	36 (17) Grade 2 3 (1) Grade 3 1 (<1)	19 (19) 8 (8) 0
Hypertension	32 (15) Grade 2 6 (3) Grade 3 26 (12)	7 (7) 3 (3) 3 (3)
Constipation	30 (14) Grade 2 3 (1) Grade 3 0	23 (23) 5 (5) 1 (1)
Vomiting	27 (13) Grade 2 3 (1) Grade 3 2 (1)	19 (19) 4 (4) 2 (2)

* The safety analysis included all patients who underwent randomization and received at least one dose of a study drug (310 patients). The number of patients in the trametinib group and placebo in the chemotherapy group were not included in the safety population. Listed are the most common adverse events (occurring in ≥15% of patients) of any grade, along with grade 2 or 3 adverse events.
† One patient in the trametinib group had grade 4 rash, and one patient in the chemotherapy group had grade 4 diarrhea.



Immunotherapie

	Pembrolizumab	Nivolumab	Ipilimumab	Nivo + Ipi
Huid bijwerkingen	?	37,4-41,9%	43,5-58,7%	59,1-71,3%
Huiduitslag	13,4-20,7%	14,5-26,1%	14,5-26,1%	28,4-55%
Maculopapulaire rash	1,5-3,6%	2,7-17,4%	2,7-17,4%	11,8-16%
Pruritus	14,1-20,7%	24,4-35,4%	24,4-35,4%	33,2-47%
vitiligo	8,9-11%	1,6-8,7%	1,6-8,7%	6,7-11%

- Pontow MA et al. N Eng J Med 2015; 372:2006-17
- Larkin J et al. N Eng J Med 2015, may 31
- Robert C et al. N Eng J Med 2015; 372:2521-2532
- Hodi FS et al. N Eng J Med 2010; 363:711-23

'Rash'

- Maculopapulair exantheem
- DD andere huiduitslag
 - Lichenoide eruptie
 - Psoriasisiforme eruptie (vnl psoriasis inversa)
 - opstoot vooraf bestaande huidziekten (vnl auto-immuun gerelateerd)
 - rosacea



Nagels - Mond



vitiligo

- Ontstaat na enkele maanden behandeling
- Meestal diffuus, zelden lokaal
- Kan ook thv haren, thv littekens
- Irreversibel



Is er een link tussen IR huid bijwerkingen en respons op behandeling?

- Recente studies : link tussen skin rash / vitiligo en langere totale overleving en/of progressie vrije overleving
- verdere studies nodig

Sanlorenzo M et al. Pembrolizumab cutaneous adverse events and their association with disease progression. JAMA Dermatol 2015; 151:1206-1212

Freeman-Keller M et al. Nivolumab in resected and unresectable metastatic melanoma: characteristics of immune-related adverse events and association with outcomes. Clin Cancer Res 2016;22:886-94

Hua C, Robert C. Association of vitiligo with tumor response in patients with metastatic melanoma treated with pembrolizumab. JAMA Dermatol 2016;52:45-51

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Dank u voor uw
aandacht!