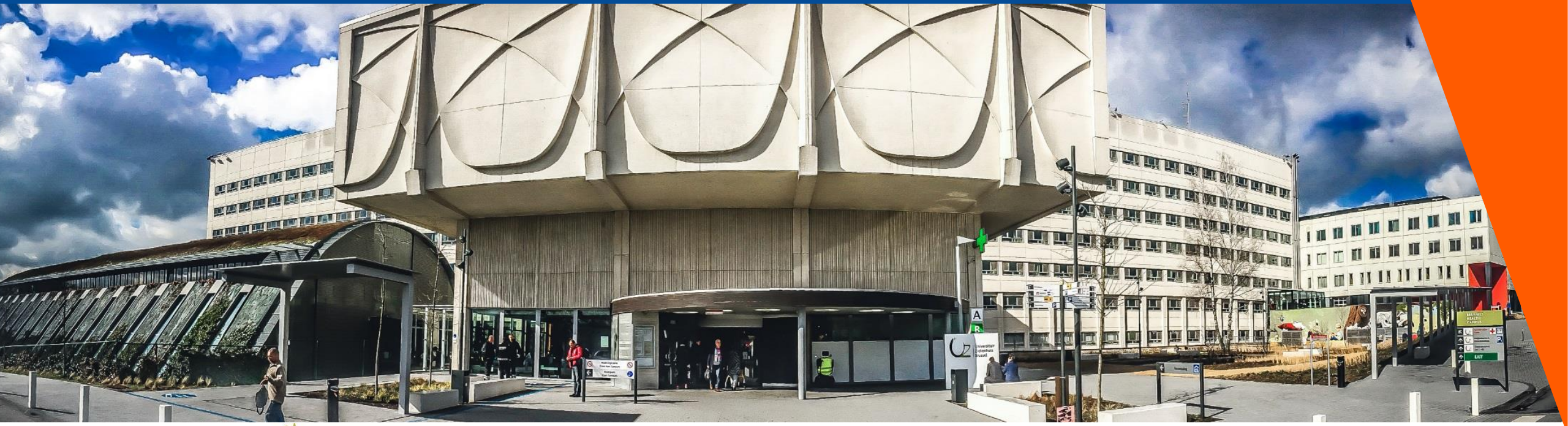
Cutane AE in de longoncologie
Eerste hulp bij huidtoxiciteit

Dr. Jolien Kessels
Staflid dermatologie
Department of Dermatology
Universitair Ziekenhuis Brussel



VRIJE UNIVERSITEIT BRUSSEL

Universitair Ziekenhuis Brussel





Dermatoloog, UZ Brussel

Huidtumoren
Cutane lymfomen
Huidbijwerkingen van oncologische therapieën

Disclosures

Personal financial compensation (speaker fee): Bristol Myers Squibb (BMS), AMGEN, La Roche Posay (L'Oreal), Pierre Fabre, Johnson & Johnson, Astra Zeneca

Advisory board: Sun Pharma, Johnson & Johnson

Consulting: Bioderma, La Roche Posay (L'Oreal)

Research funding: Kom op Tegen Kanker, LEO Pharma, Wetenschappelijk Fonds Willy Gepts

No artificial intelligence (AI) was used for researching, drafting or lay-out of this presentation

Please respect my patients' privacy! ☺



But feel free to take pictures of slides that do not include clinical photos

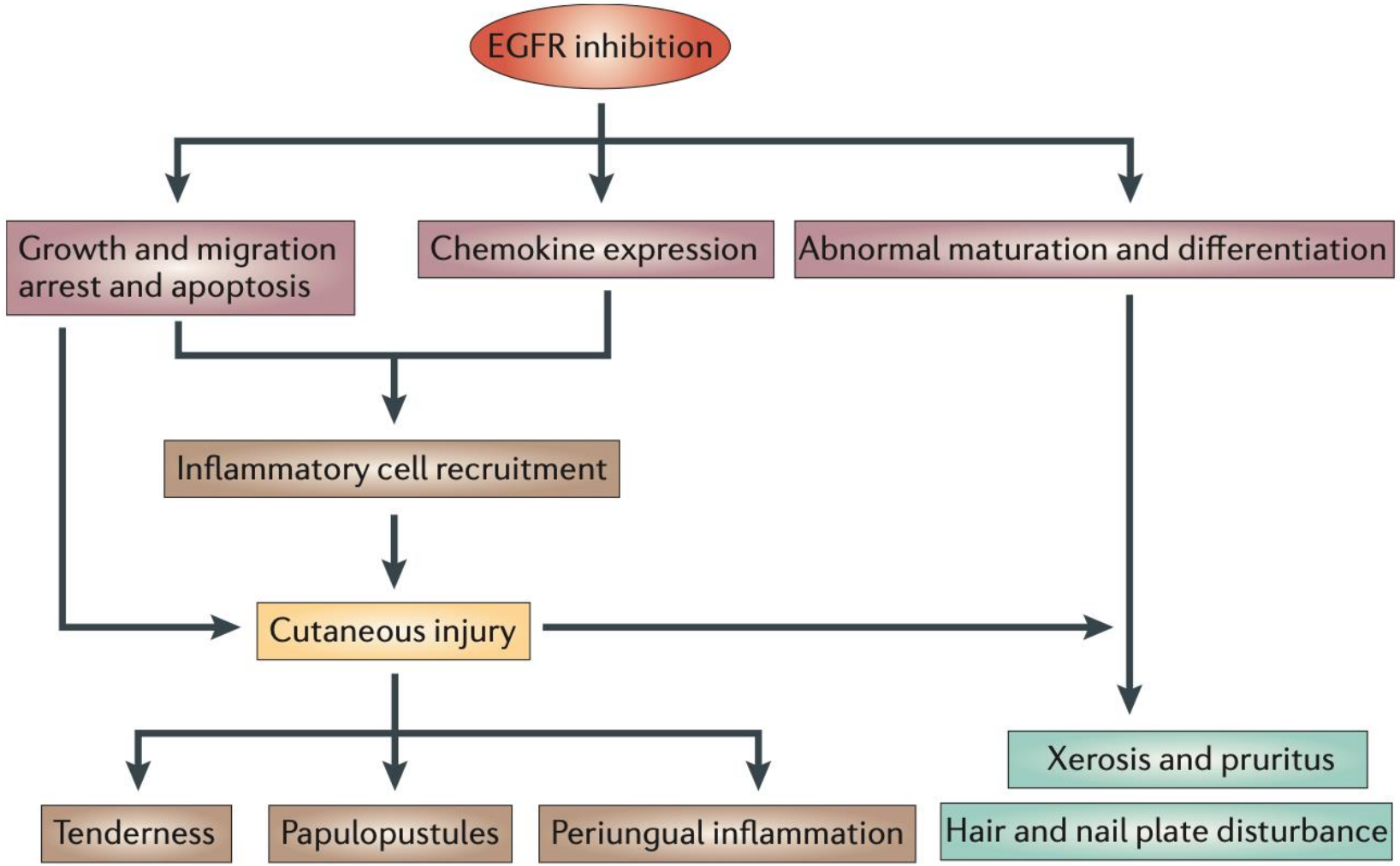
The agenda

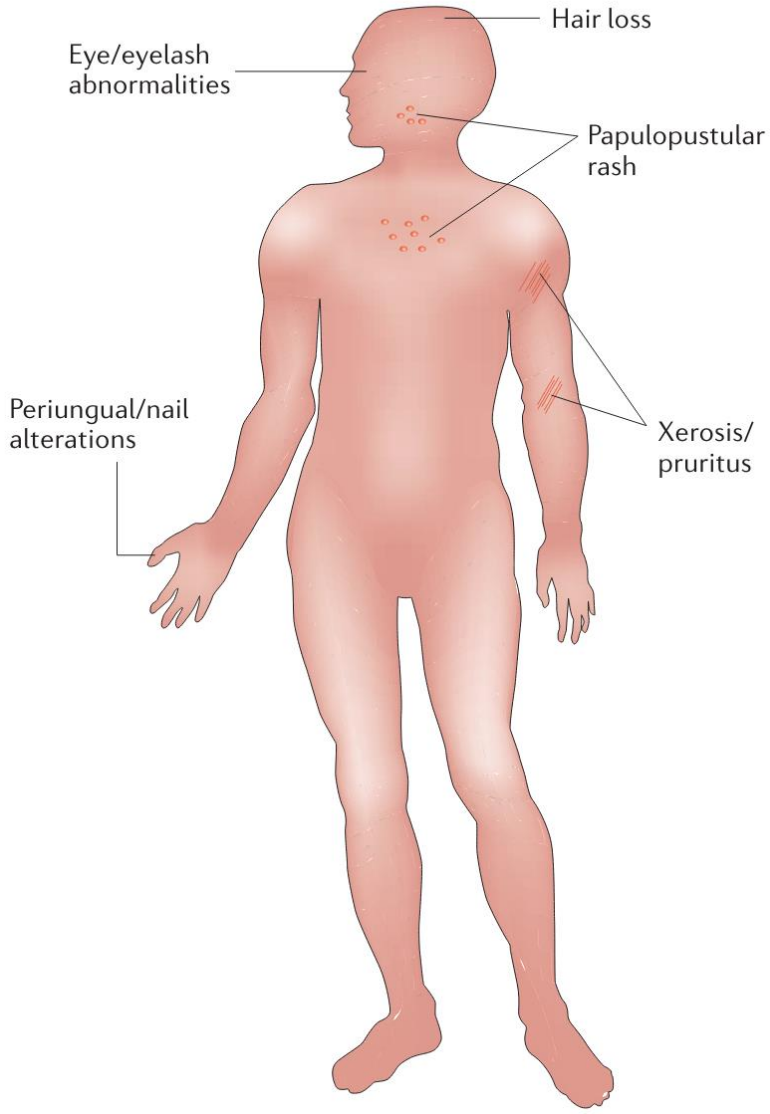
- EGFR-i
- New molecules - amivantamab
- Checkpoint inhibitors

The agenda

- **EGFR-i**
- New molecules - amivantamab
- Checkpoint inhibitors

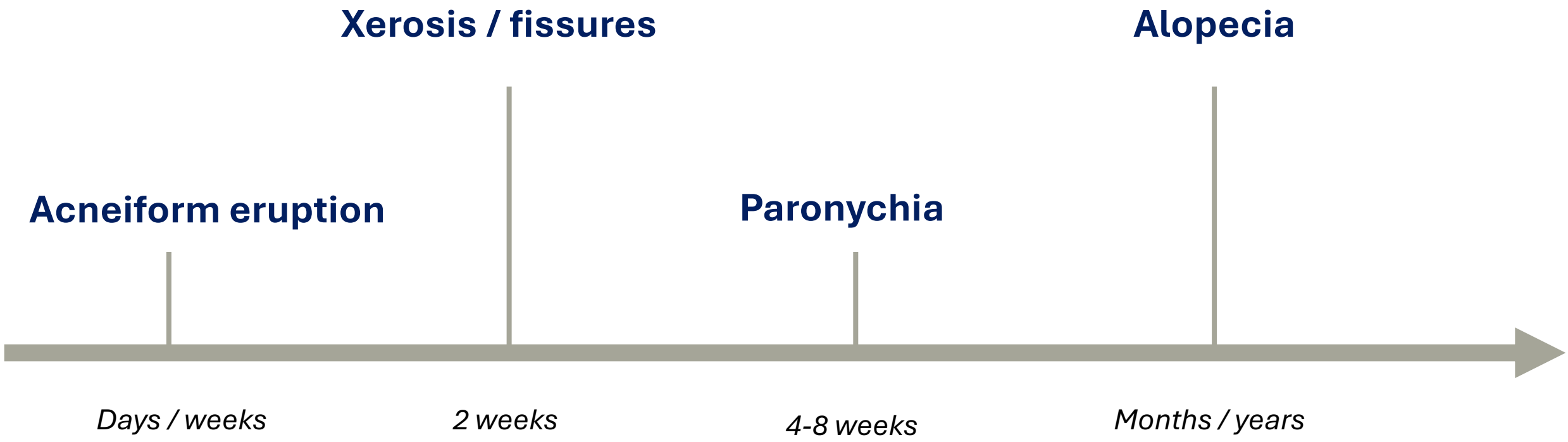
EGFRi is responsible for several cutaneous AEs





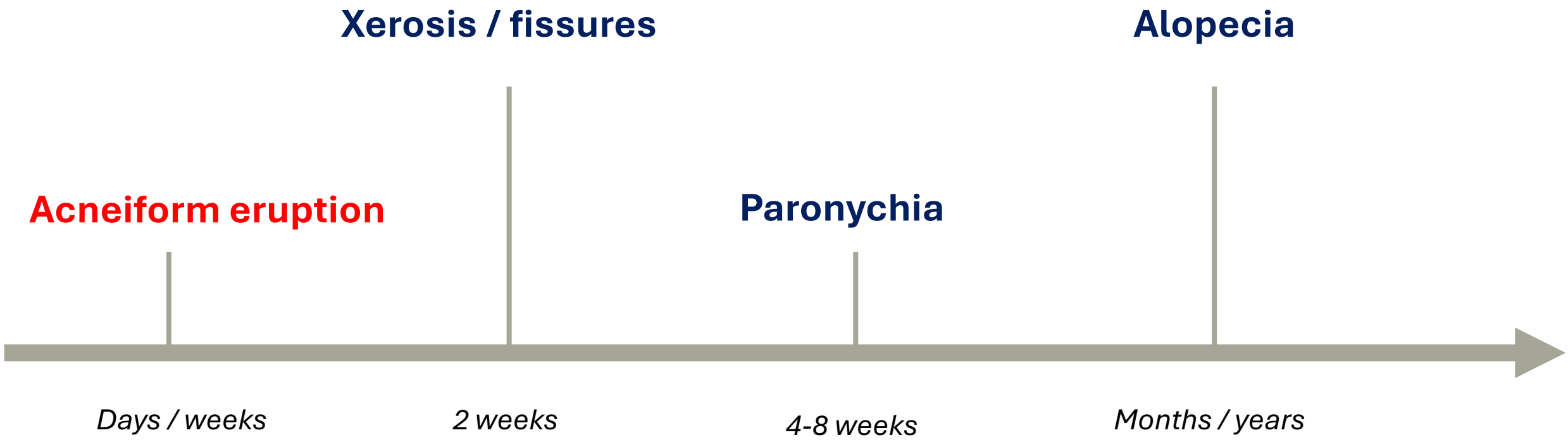
Lacouture et al. NEJM 2006

When does skin toxicity occur with EGFRi?



Lacouture et al. NEJM 2006
Lacouture et al. Ann. Of. Oncol. 2020

When does skin toxicity occur with EGFRi?



Lacouture et al. NEJM 2006
Lacouture et al. Ann. Of. Oncol. 2020

Case illustration

- 60 yo woman
- **Stage IV lung adenocarcinoma** ($EGFR^{mut}$) with node- and brain metastases
- R/ **erlotinib** (Tarceva) = EGFRi-TKI
- Three weeks after initiation of treatment: onset of itchy rash



Photo: UZB dept. of dermatology

Case illustration

Photo: UZB dept. of dermatology

- 60 yo woman
- **Stage IV lung adenocarcinoma** ($EGFR^{mut}$) with node- and brain metastases
- R/ **erlotinib** (Tarceva) = EGFRi-TKI
- Three weeks after initiation:



Grade 2 acneiform rash < EGFR-i TKI

Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)
		
		
		

Lacouture et al. Clinical Colorectal Cancer. 2018

Acneiform eruption: take to work messages

- Major impact on QoL
- Start after +- 2 weeks, peaks after 4-6 weeks



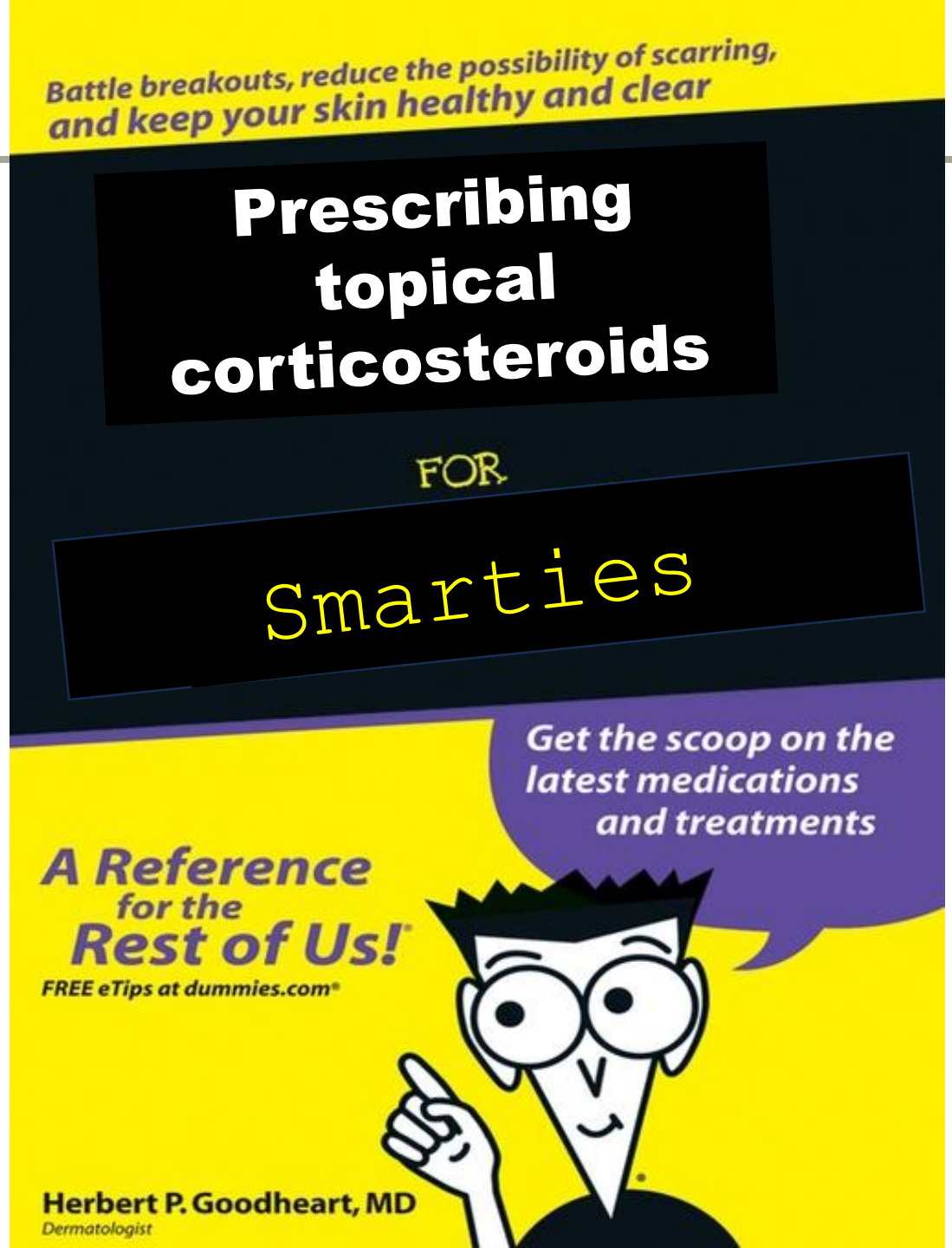
- Take bacterial swab for culture
  → Surinfections are frequent

- **Grade 1**: topical metronidazole (2% in CMG, or Rozex ® cream 0.75%)
- **Grade 2**: add cycline antibiotic and/or mild/moderate topical CS
- **Grade 3**: switch to moderate/potent CS and add cycline antibiotic OR isotretinoin

- Adapt your vehicle choice of topical CS to the body site involved

- Preventive treatment can be considered in some cases, but avoid long-term use of topical CS

CS: corticosteroid


Battle breakouts, reduce the possibility of scarring, and keep your skin healthy and clear
Prescribing topical corticosteroids
FOR
Smarties
Get the scoop on the latest medications and treatments
A Reference for the Rest of Us!
FREE eTips at dummies.com
Herbert P. Goodheart, MD
Dermatologist

Choice of topical corticosteroid

- Dependant on potency (low, intermediate, high), body site (genitalia vs. palms/soles), the vehicle (cream/lotion/ointment), and concentration

Body site

Thin

Eyelids

Genitalia

Face

Intertriginous folds

Trunk/extremities

Palms/soles

Thick

Potency

Low potency

Hydrocortisone

Triamcinolone acetonide

Mometasone furoaat

Betamethasone valeraat

Betamethasone diproprionaat

Clobetasole proprionaat

Strong potency

Choice of topical corticosteroid

Potency

BCFi
BELGISCH CENTRUM VOOR
FARMACOTHERAPEUTISCHE INFORMATIE

15.2.1. Zeer sterk werkzame preparaten

15.2.2. Sterk werkzame preparaten

15.2.3. Matig werkzame preparaten

15.2.4. Zwak werkzame preparaten

Choice of topical corticosteroid

- Dependant on the vehicle (cream/lotion/ointment), potency (low, intermediate, high), body site (genitalia vs. palms/soles) and concentration

Vehicle

Liquid

Lotion

Gel

Mousse

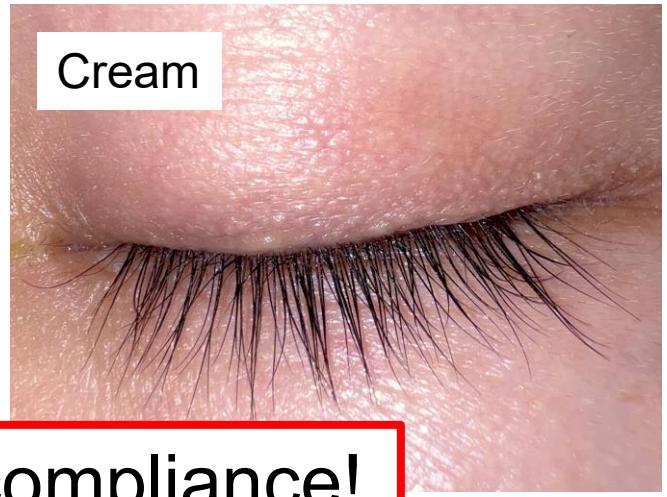
Cream

Ointment

Solid

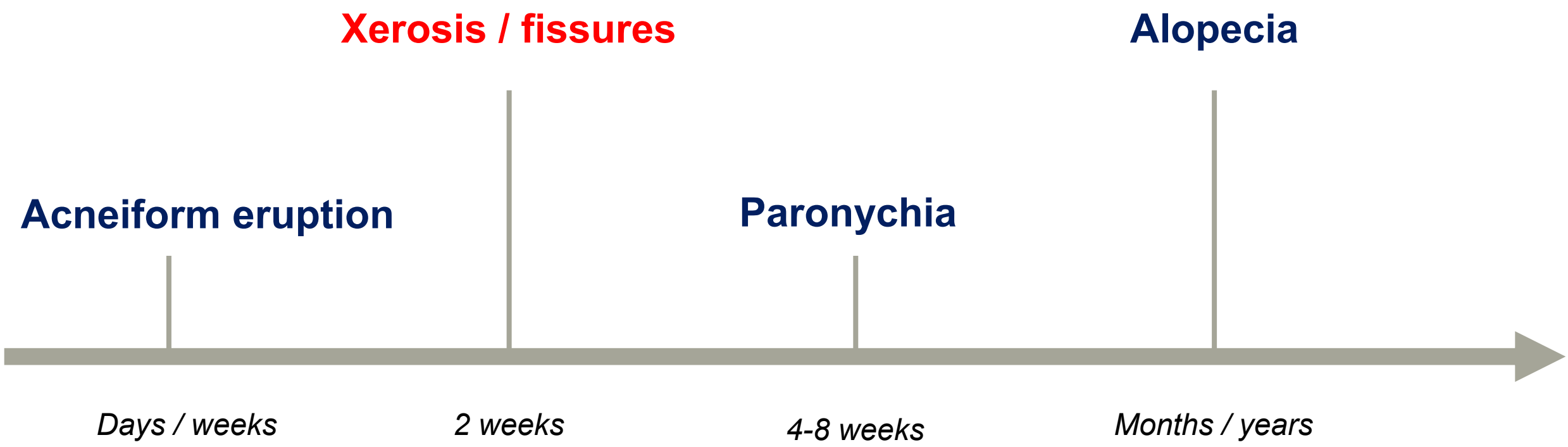






Choosing the right vehicle will improve compliance!

When does skin toxicity occur with EGFRi?

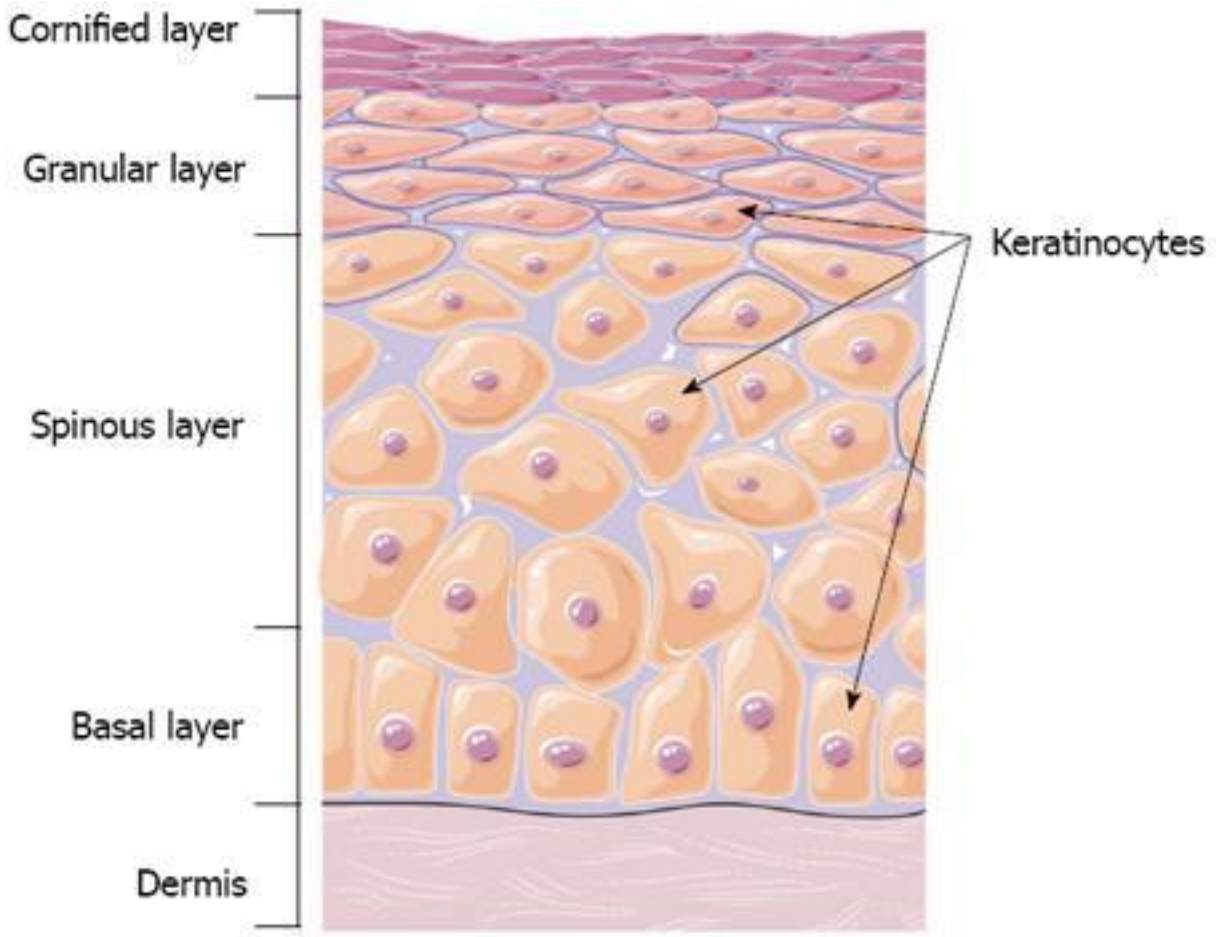


Lacouture et al. NEJM 2006
Lacouture et al. Ann. Of. Oncol. 2020

Eczema / xerosis / fissures

- Due to **abnormal keratinocyte differentiation**
  - Disturbed stratum corneum
  - Interference of sebaceous gland function
- **Loss of the water-retaining function** of the epidermis
- Postmitotic epidermal cells **require 14 days** to reach the stratum corneum

- → **Dryness / xerosis / fissures**



Case illustration

- 61 yo woman
- Stage IV lung adenocarcinoma ($EGFR^{mut}$)
- R/ osimertinib (Tagrisso ®)



Photo: UZB dept. of dermatology

Eczema / xerosis / fissures: take to work messages

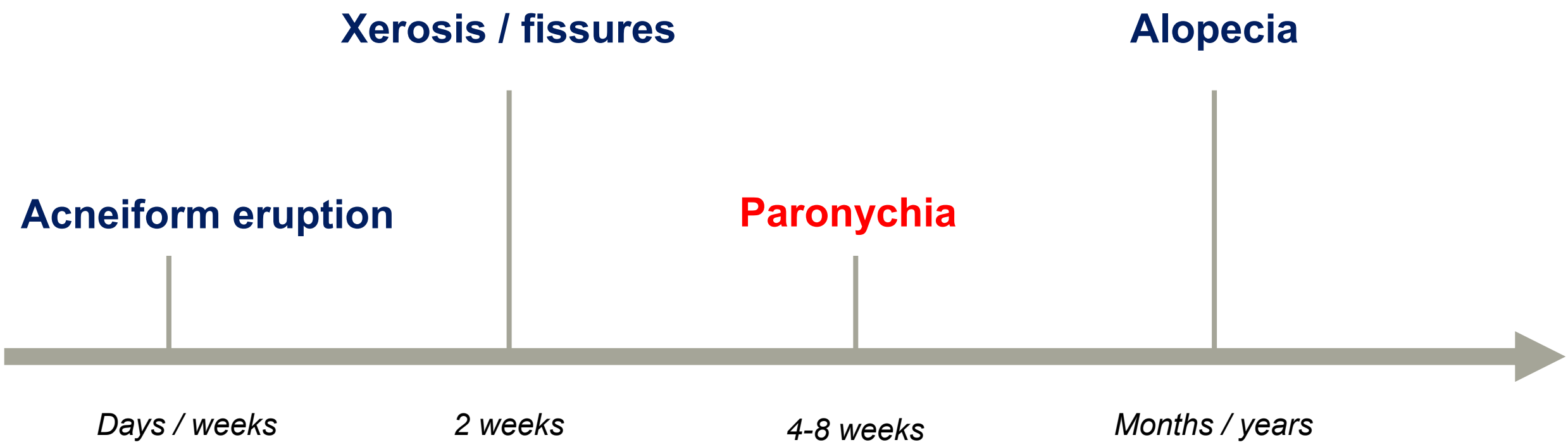
- Prevention is key
  - Bland emollients and showel oil
  - Gloves for ALL household tasks (incl. peeling fruit/vegetables)

- Take bacterial swabs in case of oozing/crusting eczema

- Hard callus/fissures: urea 30-50% (Xerial SVR)

- In case of active inflammation without surinfection: potent topical CS

When does skin toxicity occur with EGFRi?



Lacouture et al. NEJM 2006
Lacouture et al. Ann. Of. Oncol. 2020

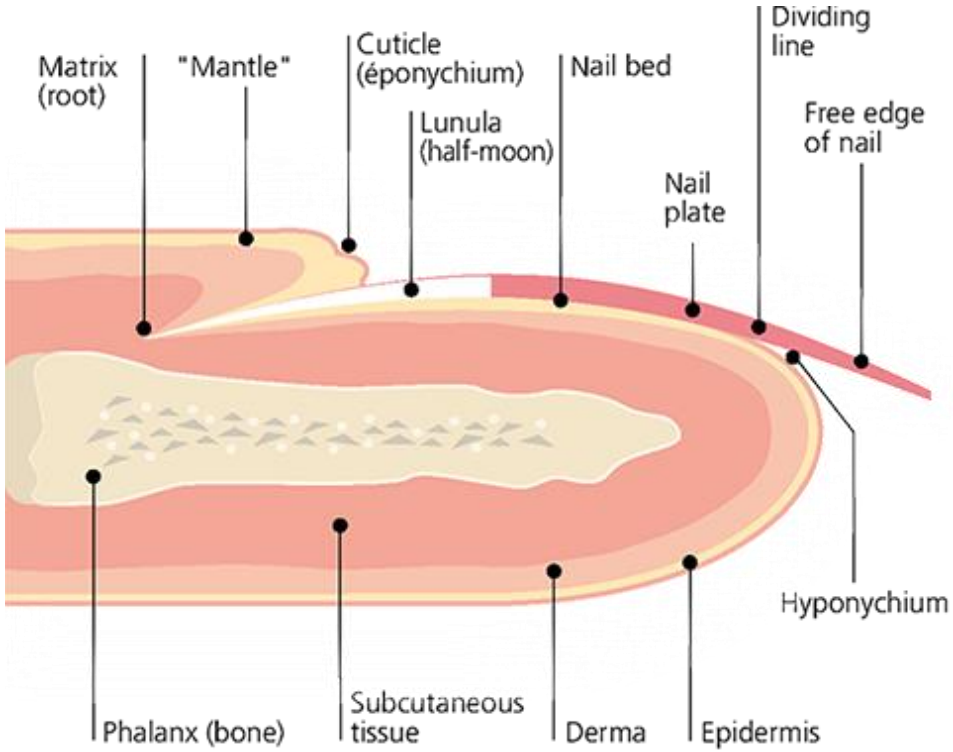
Paronychia

- Cutaneous appendages are largely dependent on EGFR signalling for normal development and function

- Develops 4-8 weeks after initiation of treatment

- Acute versus chronic

- Prevention:
  - Cutting nails straight and not too short
  - Appropriate shoes



Lacouture et al. Ann. Of. Oncol. 2020

Case illustrations

Photo: UZB dept. of dermatology



Acute

Several weeks after start panitumumab



Subacute / chronic

Ongoing treatment with cetuximab

Case illustrations

Photo: UZB dept. of dermatology



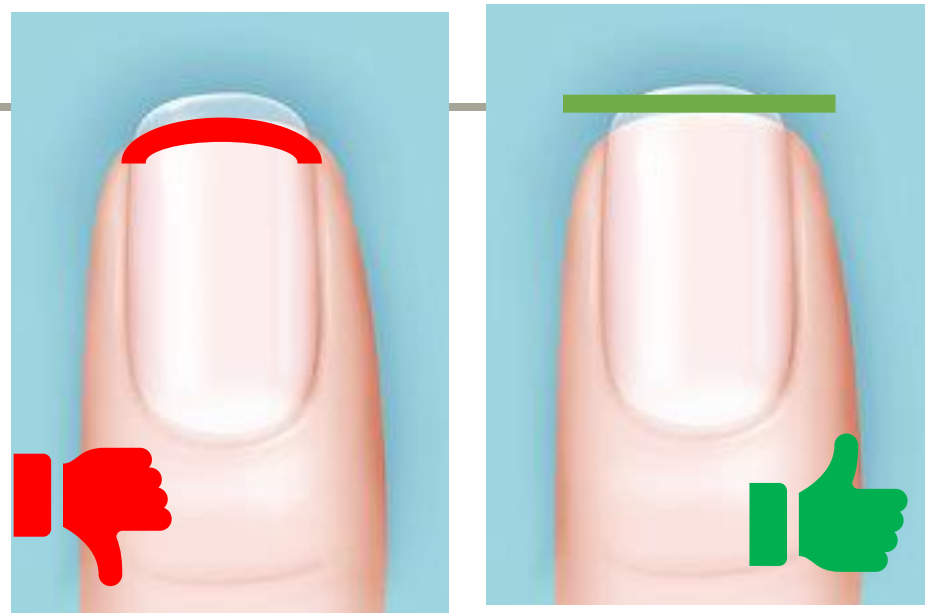
Acute paronychia





Zilvernitraat stokjes
Worden geactiveerd door contact met vocht of water

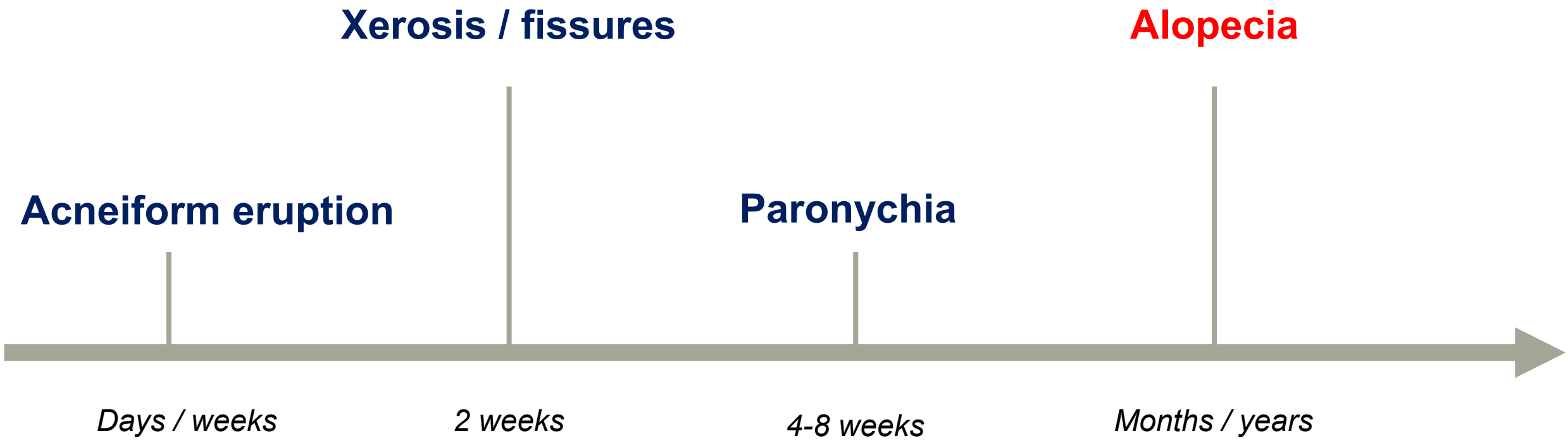
Paronychia: take to work messages



- **Prevention!**
  - Cutting nails straight and not too short
  - Appropriate shoes
- Use potent topical CS
- Use antiseptics (i.e. betadine baths)
- Use silver nitrate for pyogenic granulomas
- Avoid surgery



When does skin toxicity occur with EGFRi?



Lacouture et al. NEJM 2006
Lacouture et al. Ann. Of. Oncol. 2020

Alopecia

Photo: UZB dept. of dermatology

- Usually a diffuse non-scarring (reversible) alopecia (in theory…)
- Occurs months to years after start of therapy



Lacouture et al. NEJM 2006


WITH GREAT POWER
COMES GREAT
RESPONSIBILITY...


With new drugs comes new skin toxicity...

The agenda

- EGFR-i
- New molecules - **amivantamab**
- Checkpoint inhibitors

Amivantamab

- “Scalp rash”: erosive pustular dermatosis of the scalp





George et al. JAAD Case Rep. 2024; Senterre et al. Case Rep Dermatol. 2025

Amivantamab

- Majority of skin AEs are classical EGFRi related
- Scalp rash required prompt medical attention: potent topical CS, interrupt treatment, consider oral CS
- Rapid progression and slow healing

Management of amivantamab skin toxicity

Enhanced Versus Standard Dermatologic Management With Amivantamab-Lazertinib in *EGFR*-Mutated Advanced NSCLC: The COCOON Global Randomized Controlled Trial

Oral doxycycline or minocycline (100 mg twice daily; weeks 1–12)
Ceramide-based moisturizer (on body and face at least daily)
Clindamycin 1% (on scalp daily; weeks 13–52) **feasability?**
Chlorhexidine 4% (on fingernails and toenails daily) **NS**

➔ **Practical recommendations adapted to the Belgian underway (BJMO)**

Cho et al. *J Thorac Oncol* 2025
DM=dermatolologic management

The agenda

- EGFR-i
- New molecules - amivantamab
- **Checkpoint inhibitors**

Case illustration

- 75 yo man
- Stage IV NSCLC
- R/ pembrolizumab
- AE: hypophysitis and thyroiditis
- Recently: progressive rash with blistering, itch +++





Photo: Dr Kessels – UZB dept. of dermatology







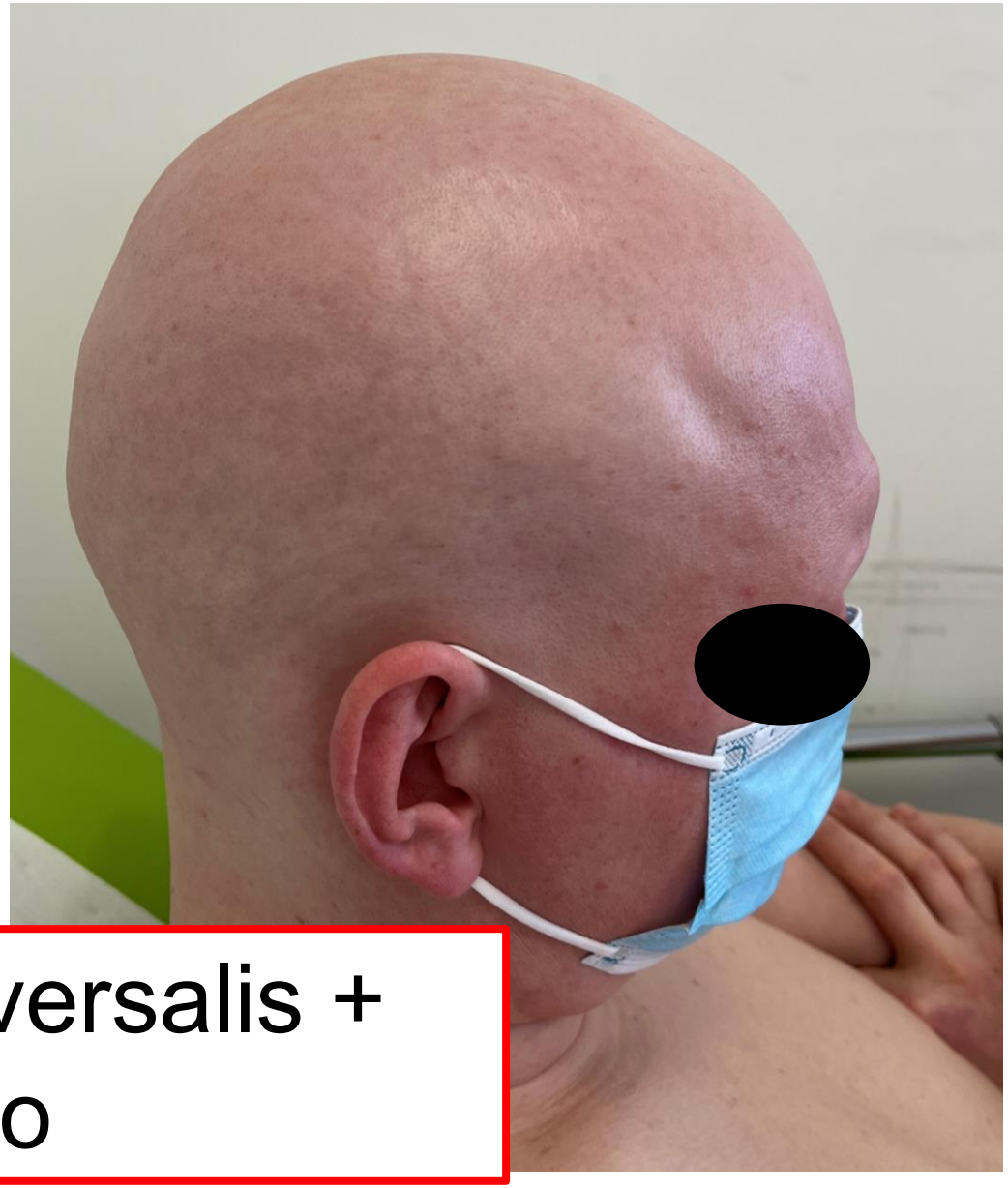
Bullous pemphigoid < checkpoint inhibitor

Photo: Dr Kessels – UZB dept. of dermatology

Checkpoint inhibitors & skin

Photo: Dr Kessels – UZB dept. of dermatology





Alopecia universalis + vitiligo

Checkpoint inhibitors & skin







Skin & nail psoriasis

Photo: UZB dept. of dermatology

Checkpoint inhibitors & skin







Erosive lichen planus

Photo: Prof. Grosber / UZB dept. of dermatology

Checkpoint inhibitors & skin

Photo: Dr Kessels – UZB dept. of dermatology



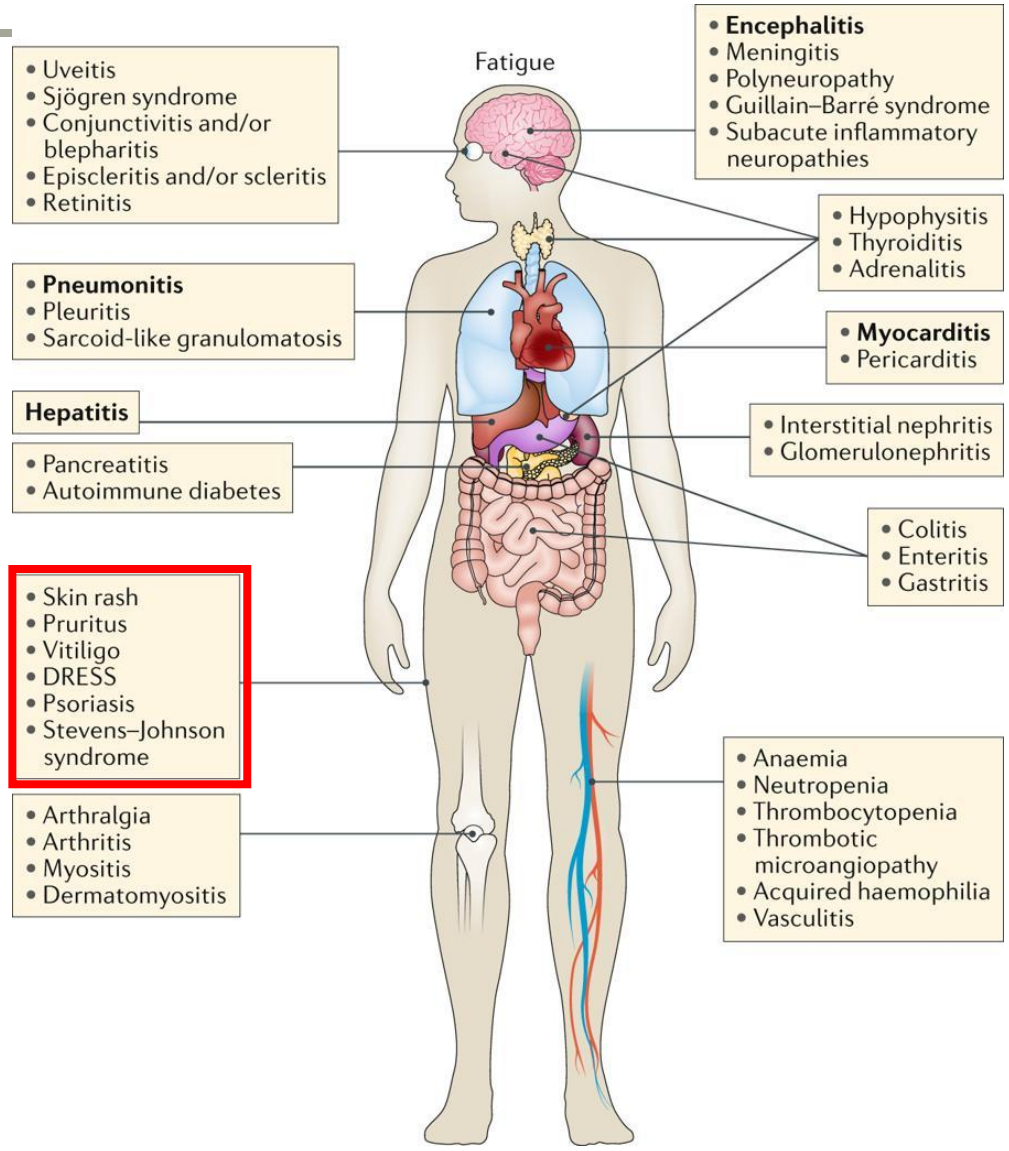




Subacute lupus erythematosus

Checkpoint inhibitors & skin

- Skin toxicity: among the most frequent irAE
- Develop **early** in the course of treatment
- Most frequent: rash, pruritis, vitiligo (> melanoma patients)
  - →Usually grade 1-2
  - →Emollient
  - →Topical CS if itchy: Elocom® 1x/day, 2 weeks
- Less frequent: alopecia areata, lichenoid reactions, psoriasiform eruptions
- Stevens-Johnson syndrome, DRESS



Long et al. Immune checkpoint inhibitors in melanoma. Lancet 2021
Haanen et al. Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines 2017

Checkpoint inhibitors & skin

Photo: Prof. Grosber / UZB dept. of dermatology







Checkpoint inhibitors & skin



Stevens-Johnson syndrome



Photo: Prof. Grosber / UZB dept. of dermatology

Stevens-Johnson Syndrome (SJS) <10% BSA
Toxic Epidermal Necrolysis (TEN) > 30% BSA

SJS – TEN overlap syndrome: continuum

- Prodromal phase: flu-like symptoms, fever, malaise
- Skin findings:
  - Mucosal erosions
  - Dusky macules
  - Positive Nikolsky sign on erythematous skin
  - Blisters / erosions



+- Neutrophilia, lymfopenia, cytolysis, renal impairment

Slide: courtesy of Prof. Dr. M. Grosber, UZB

Stevens-Johnson Syndrome (SJS)
Toxic Epidermal Necrolysis (TEN)

Mortality: 25-35%

Culprit drugs:

- Antibiotics: cotrimoxazol, β-Lactams, tetracyclins, chinolones
- Anti-epileptics: carbamazepine, fenytoïne, fenobarbital, lamotrigine
- Antiretrovirals: nevirapine, abacavir
- NSAID's: oxicam group
- Allopurinol
- Checkpoint inhibitors

Some of your patients with symptomatic brain metastases or lymphopenia may be on one of these medications!





Photo: Huidziekten.nl

Red flags: severe cutaneous adverse reactions (SCARs)



- Generalized skin eruptions that are **painful** (**itch =/= pain**)
- Skin **blistering**, epidermal **erosion (+ Nikolsky sign)**
- Skin eruptions with **systemic** involvement (fever, reduced general condition, organ involvement, lab abnormalities)
- Skin eruptions with **mucosal** involvement

Checkpoint inhibitors: take to work messages

- Skin toxicity is very common with ICB
- It can occur early or late in the treatment

- Reactions can range from **relatively benign …** (rash, eczema, psoriasis)
- **… to potentially life-treatening** (SJS, TEN, systemic lupus)
- In case of doubt: take a skin biopsy

- **Beware** of skin reactions with altered general state, blistering, and/or fever

SJS: Stevens Johnson Syndrome
TEN: toxic epidermal necrolysis



Questions?