HONG KONG COLLEGE OF MEDICAL NURSING
香 港 內 科 護 理 學 院

Non-Surgical Treatment of Lung Cancer:

Update on Nursing Management of Treatment-Induced Side Effects

Wong Sin Ting

RN, BScN, MScHC, PgDHSM, FHKAN (Medical– Oncology)

Disclosure

- No honorarium is received for the nurse lecture

Non-Surgical Treatment of Lung Cancer

- Radiotherapy
- Chemotherapy
- Targeted Therapy

Radiotherapy

- Dosage and fractionation depends on histopathology, stage of disease and treatment aim
- Chemotherapy may be added concurrently or as adjuvant treatment

Radiotherapy

- Standard external beam RT
- Stereotactic body radiation
- Prophylactic cranial irradiation

- Standard fractionation
- Accelerated hyperfractionation

Five Grades Describe Severity of Adverse Event: NCI CTCAE version 4.02

Grade 1	Mild: asymptomatic or mild symptoms, clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate: minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental ADL
Grade 3	Sever or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL
Grade 4	Life-threatening consequence: urgent intervention indicated
Grade 5	Death related to adverse event

Radiotherapy: Acute Side Effects

- Cough

- Decreased function of cilia & mucus-secreting glands causing bronchial mucosa irritation, oedema & hypervascularity

- Oesophagitis

- Irritation & inflammation of the lining of oesophagus within the RT field

- Dyspnoea
- Skin reactions
- Fatigue

Radiotherapy: Late/Delayed Side Effects

- Radiation pneumonitis & fibrosis
- Radiation myelopathy
- Cardiac injury
- Oesophageal injury

Chemotherapy

- Cisplatin/Carboplatin
- Etoposide
- Paclitaxel
- Gemcitabine
- Pemetrexed
- Vinorelbine
- Topetecan ……..

Common Side-effects

- Myelosuppression
- Gastrointestinal and mucosal side effects
- Cutaneous toxicity
- Alopecia
- Nephrotoxicity
- Neurotoxicity ……

Pemetrexed

Before treatment:

- Vitamin B12 1000 μg IMI one week before starting treatment and repeat every 9 weeks during chemo
- Folic acid 5 mg po daily start at one week before treatment and stop at 3 weeks after last dose

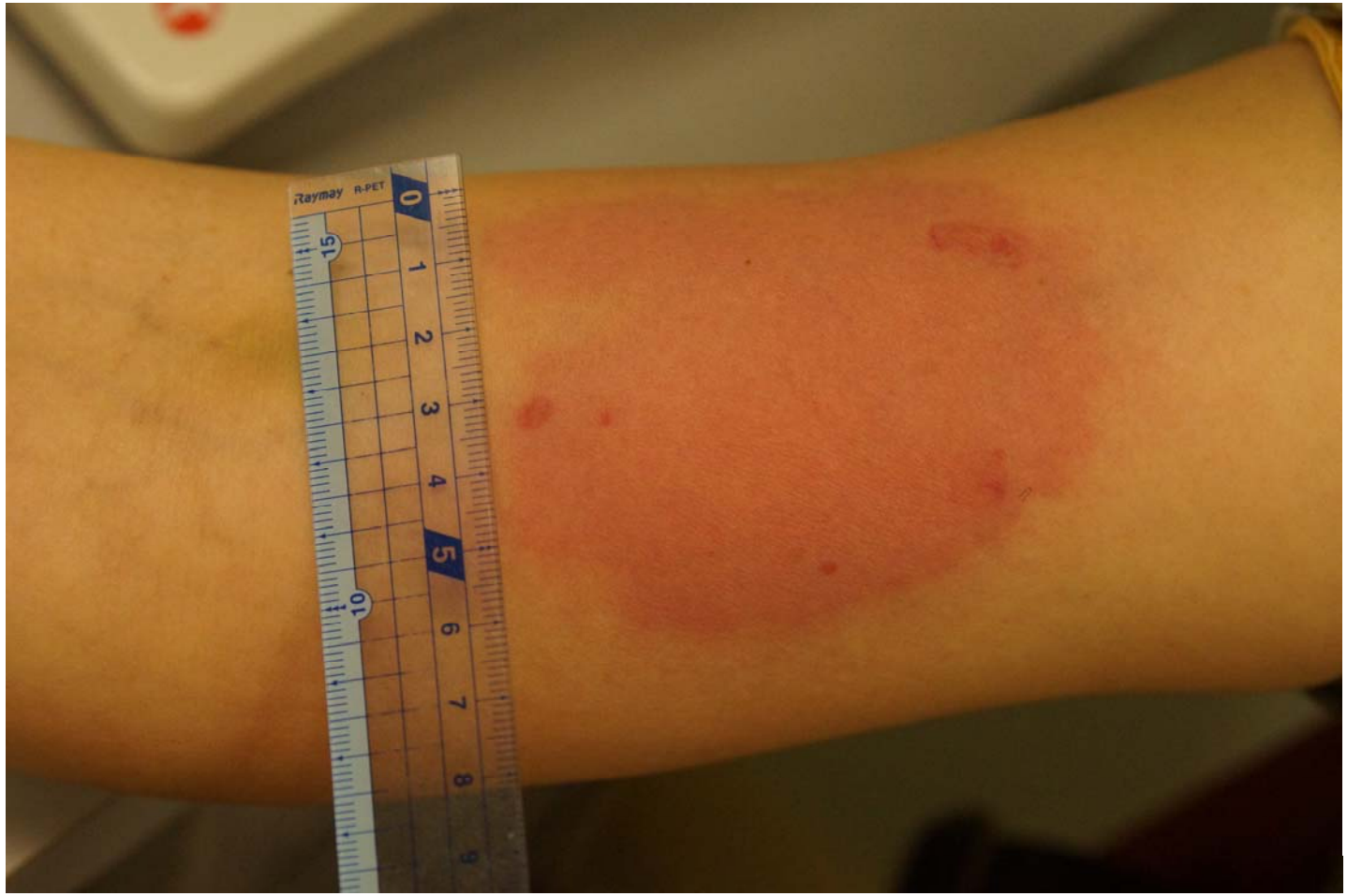
Alimta Product Info. EUSPC12NOV2012

Vinorelbine

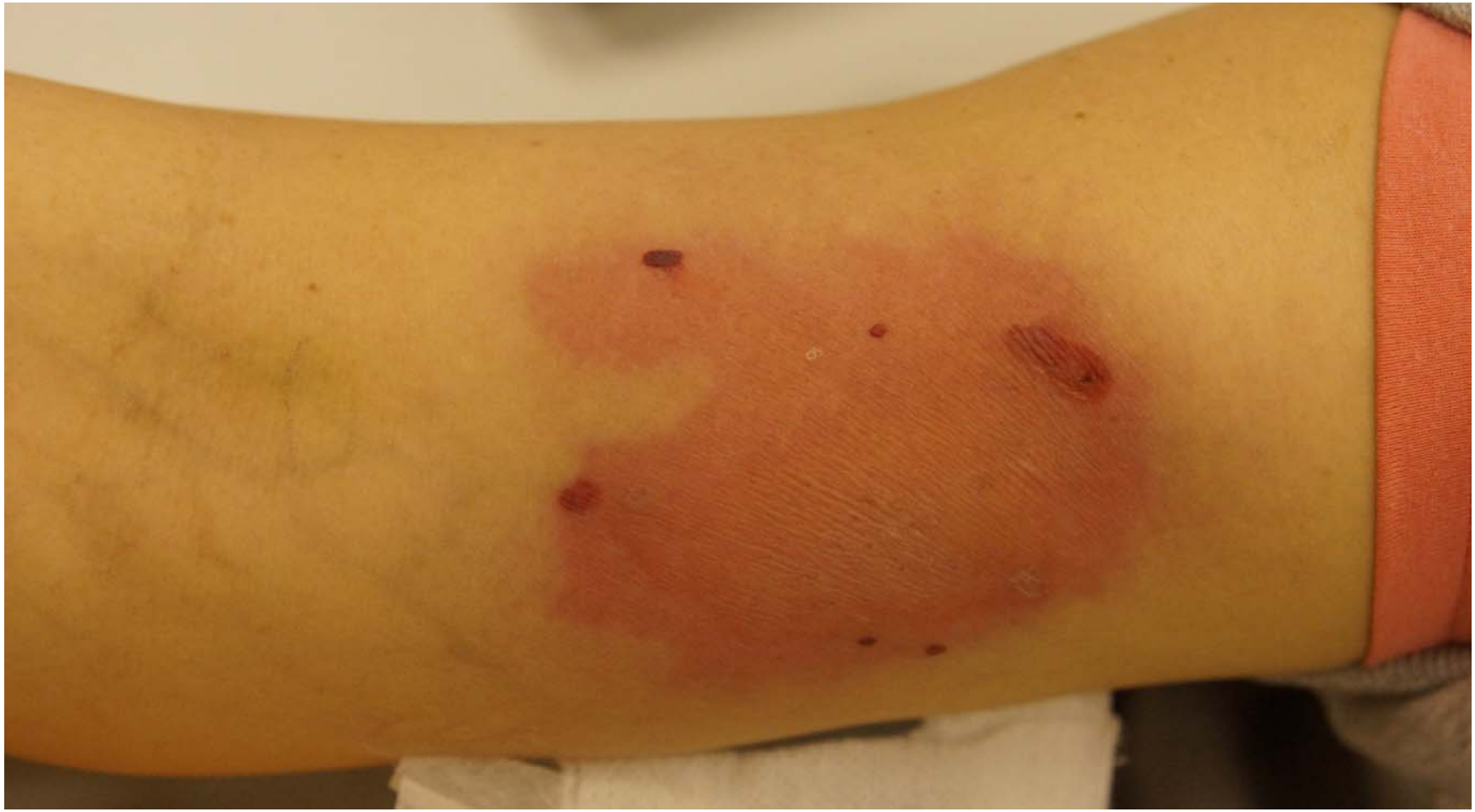
- Both as an irritant & vesicant
- Skin discoloration, chemical irritation, blistering or even skin sloughing
- Use of central venous access device for infusion with concurrent flushing using normal saline is recommended

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3773891/

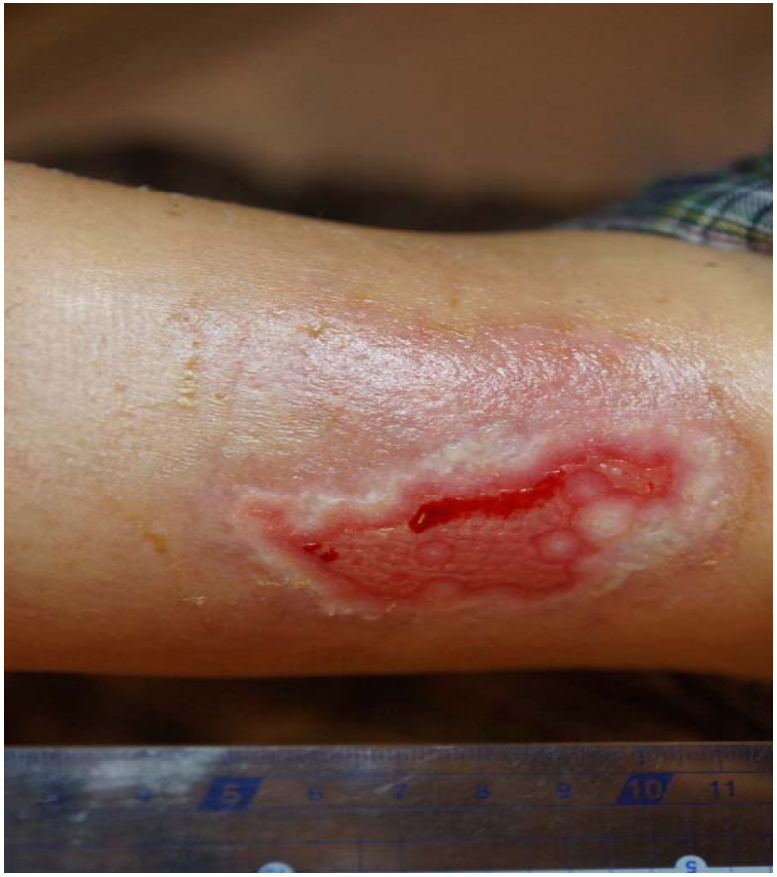
Vinorelbine (Day 6)



Vinorelbine (Day 8)



Vinorelbine (Day 22)



Vinorelbine

接受 Vinorelbine 治療病人出院指引

1. Vinorelbine 是一種起皰性的化療藥物，如滲漏出血管外,可導致嚴重的皮下組織損害，少數病人更因而需要接受手術,割除受損組織.
2. 請於出院後密切注意化療注射針口及相連血管的狀況，如針口或相連血管出現**變紅/增加痛楚/起水泡/潰瘍等狀請盡早求醫. 請特別注意上述徵狀可能於藥物注射後翌日甚至一兩星期後才出現.**
3. 求醫前可使用暖包或暖毛巾敷治以減輕症狀.
4. 為免受感染,切勿自行刺穿水泡.
5. 辦工時間(星期一至星期五早上九時至下午六時)可致電 22556112 聯絡 K6N 病房護理人員，非辦工時間請往急症室求診.

Discharge Guideline for Patients Receiving Vinorelbine Administration

1. Vinorelbine is a vesicant that has a potential to cause blistering, severe tissue damage when extravasated. A few patients may even need to have surgical debridement to remove the injured tissue.
2. Please closely observe the condition of the infusion site and along its blood vessel. **In case if there is increase redness/pain/blister formation/ulceration, please seek medical advice immediately. Please be aware that the above symptoms may occur on the next day or even 1-2 weeks after treatment.**
3. Warm compress can be applied to relieve the symptoms before seeking medical advice.
4. To minimize risk of infection, never attempt to aspirate the blister by yourself.
5. Contact K6N Chemotherapy Day Centre Nursing Staff on 22556112 in office hour (Mon-Fri 09:00-18:00) or seek medical advice in nearby A&E Department in non-office hour.

Queen Mary Hospital discharge guidelines for Vinorelbine

FDA Approved Targeted Therapy for Lung Cancer

- Bevacizumab
- Crizotinib
- Erlotinib
- Gefitinib
- *Afatinib
- *Ceritinib

*Afatinib and Ceritinib have not been registered in Hong Kong, updated in Aug 2014
http://www.dh.gov.hk/cindex.html

Common Toxicities

- Skin: acne-like rash, xerosis (dry skin), itchiness, nail changes, hair change
- Diarrhea

EGFR inhibitor-associated rash

- Various terms in different studies
- Rash
- Acne
- Acne-like skin rash
- Acneiform skin reaction
- Acneiform follicular rash
- Maculopapular rash
- Monomorphic pustular leasion
- Folliculitis
- …….

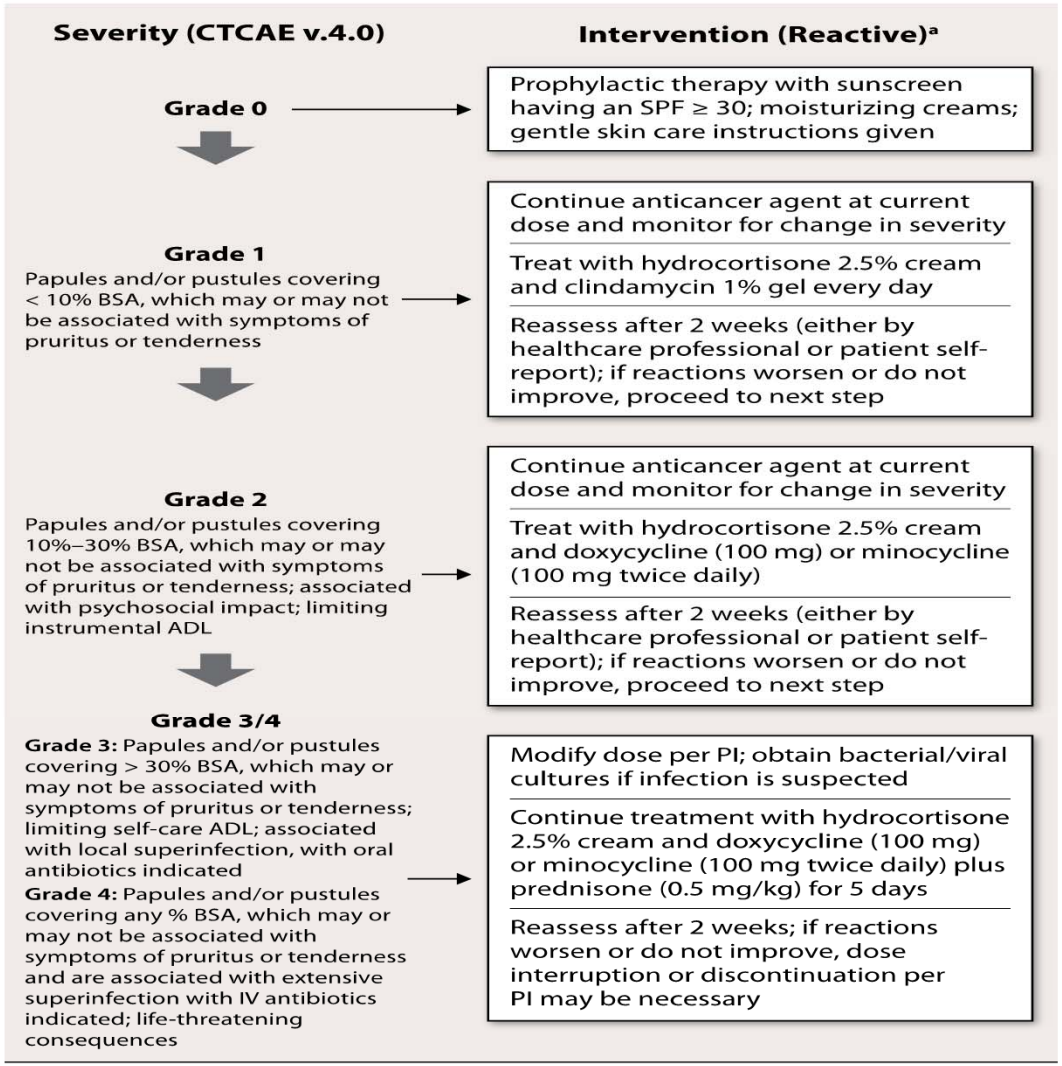
Characteristics

- An eruption containing of papules (a small raised pimple) and pustules (a small pus-filled blister)
- Typically appears on face, scalp, upper chest & back
- Unlike acne, the rash does not present with whitehead or blackhead
- Itchiness is common in EGFR-induced acneiform but is absent in acne vulgaris
- Scalp involvement is rare in acne vulgaris but also frequent in patients receiving EGFR inhibitors

CTCAE Grading of Selected Skin and Subcutaneous Tissue Disorders

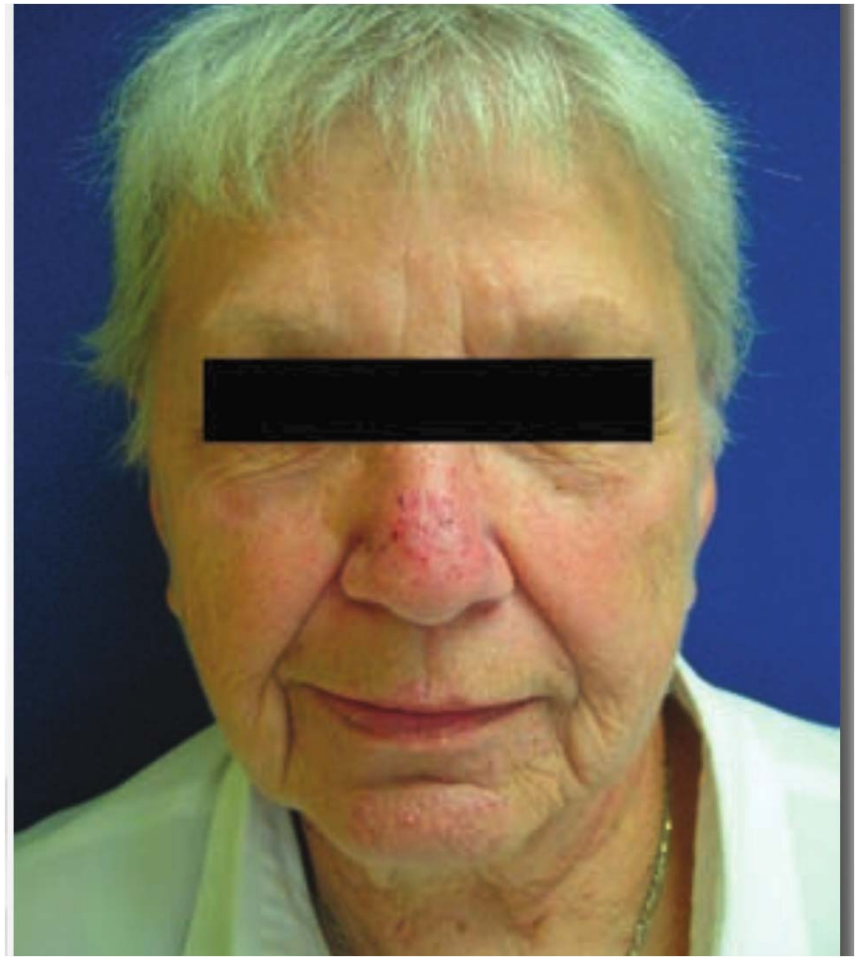
DISORDER	GRADE 1	GRADE 2	GRADE 3	GRADE 4	GRADE 5
Palmar-plantar erythrodysesthesia syndrome[a] *Definition:* a disorder characterized by redness, marked discomfort, swelling, and tingling in the palms of the hands or the soles of the feet	Minimal skin changes or dermatitis (eg, erythema, edema, or hyperkeratosis) without pain	Skin changes (eg, peeling, blisters, bleeding, edema, or hyperkeratosis) with pain; limiting instrumental ADL	Severe skin changes (eg, peeling, blisters, bleeding, edema, or hyperkeratosis) with pain; limiting self-care ADL		
Rash, acneiform *Definition:* a disorder characterized by an eruption of papules and pustules, typically appearing in the face, scalp, upper chest, and back	Papules and/or pustules covering < 10% of BSA, which may or may not be associated with symptoms of pruritus or tenderness	Papules and/or pustules covering 10%–30% of BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL	Papules and/or pustules covering > 30% of BSA, which may or may not be associated with symptoms of pruritus or tenderness; limiting self-care ADL; associated with local superinfection, with oral antibiotics indicated	Papules and/or pustules covering any % of BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection, with IV antibiotics indicated; life-threatening consequences	Death
Paronychia *Definition:* a disorder characterized by an infectious process involving the soft tissues around the nail	Nail fold edema or erythema; disruption of the cuticle	Localized intervention indicated; oral intervention indicated (eg, antibiotic, antifungal, antiviral); nail fold edema or erythema with pain; associated with discharge or nail plate separation; limiting instrumental ADL	Surgical intervention or IV antibiotics indicated; limiting self-care ADL		

Treatment Algorithm for Papulopustular Rash



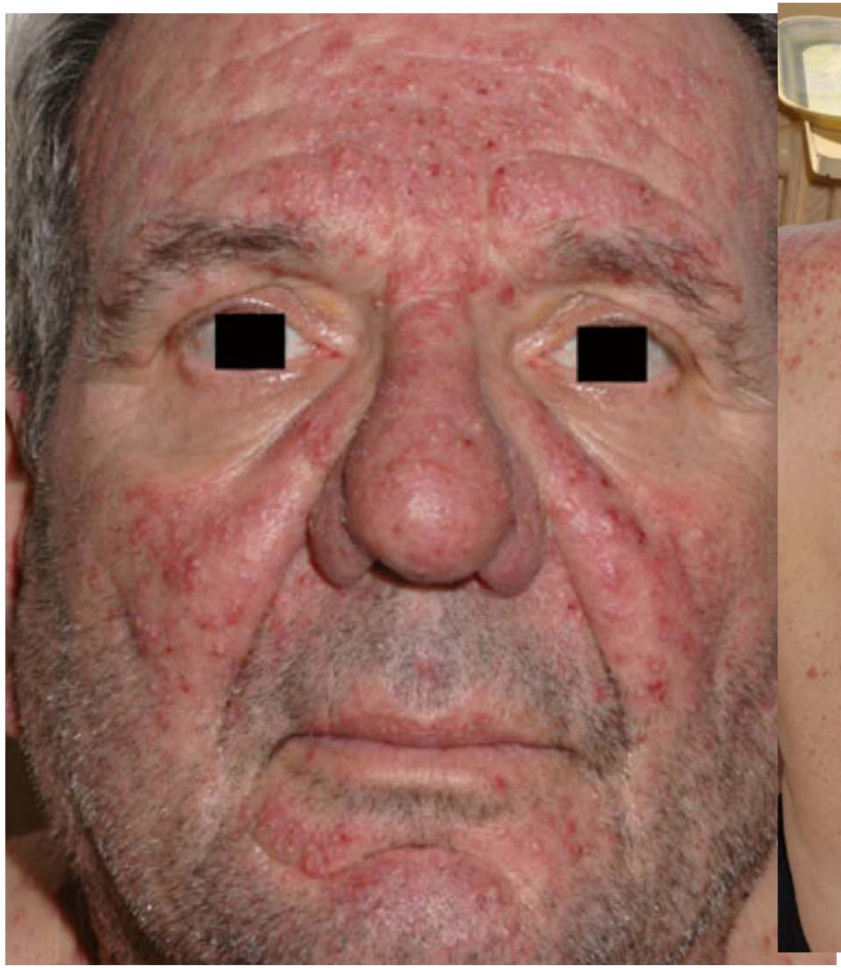
Balagula et al (2010)

Grade 1

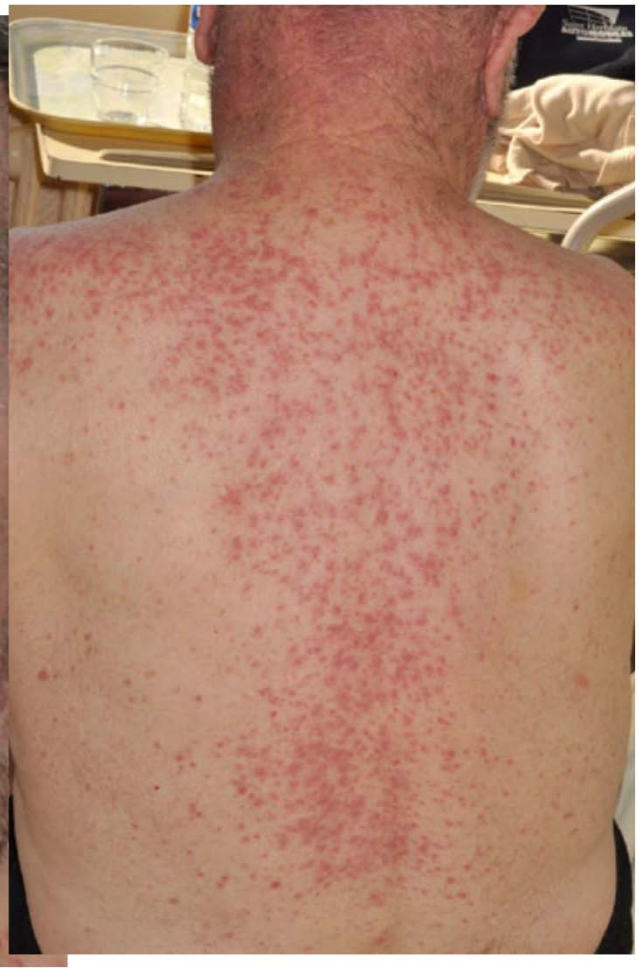


Oncologist, 2007;
Roche, 2009

Grade 2



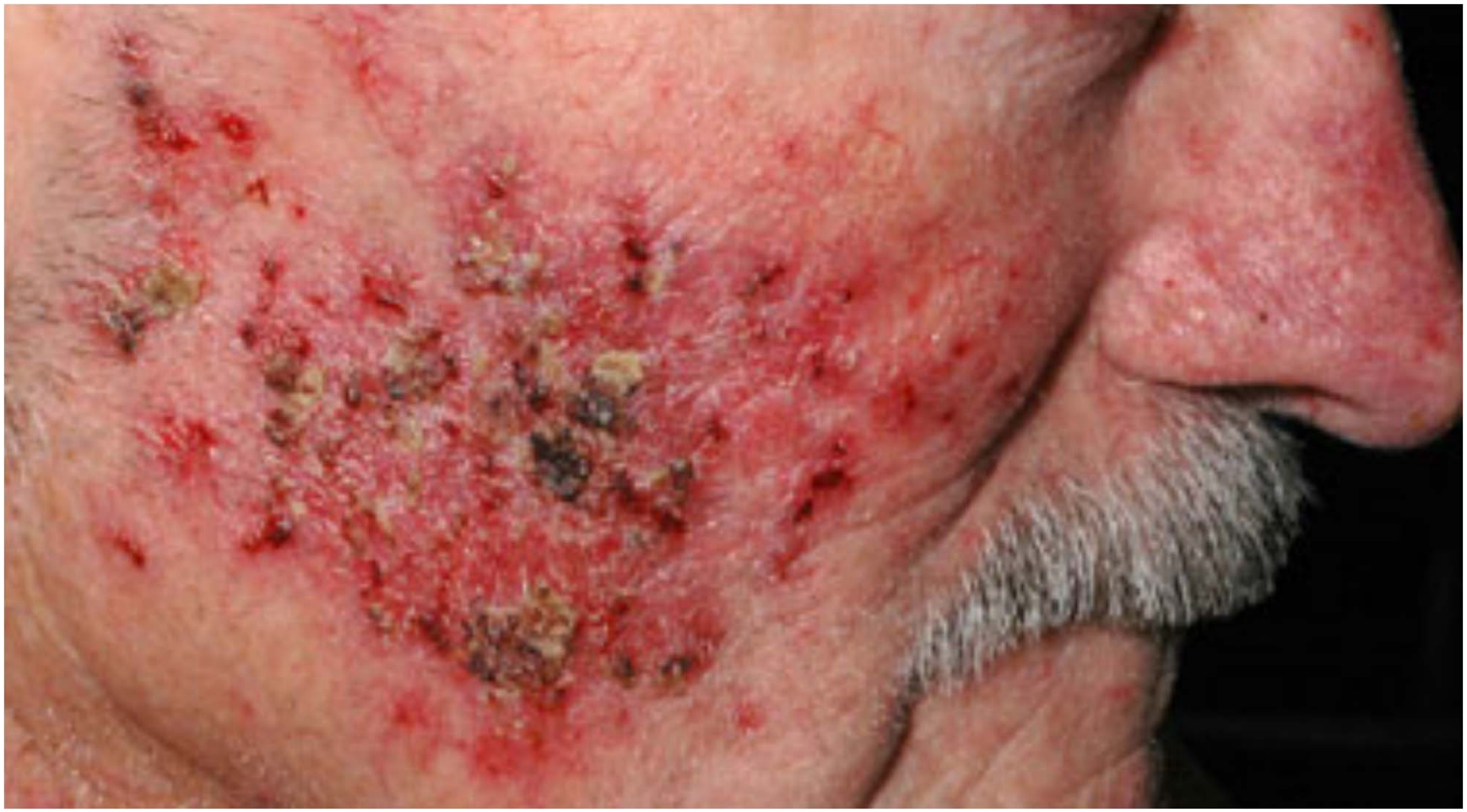
Facial location: especially localized in mid-face region



Dorsal location: ‘V’ shaped arrangement in upper trunk

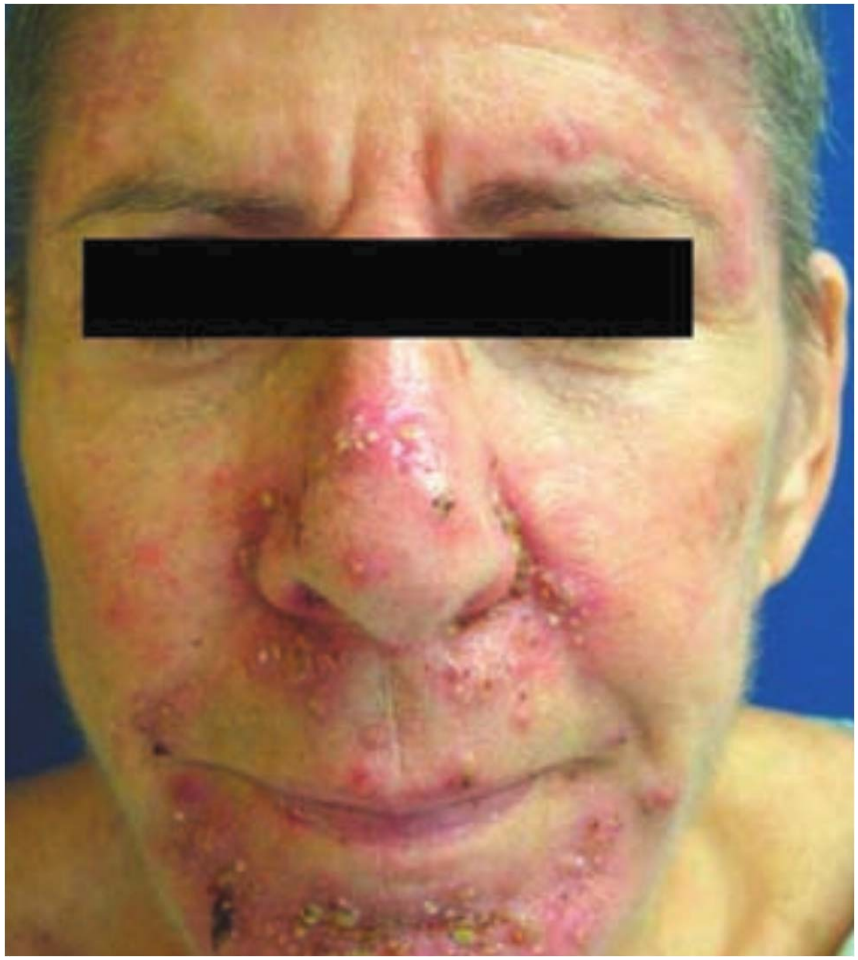
(Peuvrel et al, 2012)

Grade 2



Crust formation without impetiginisation (Peuvrel et al, 2012)

Grade 2



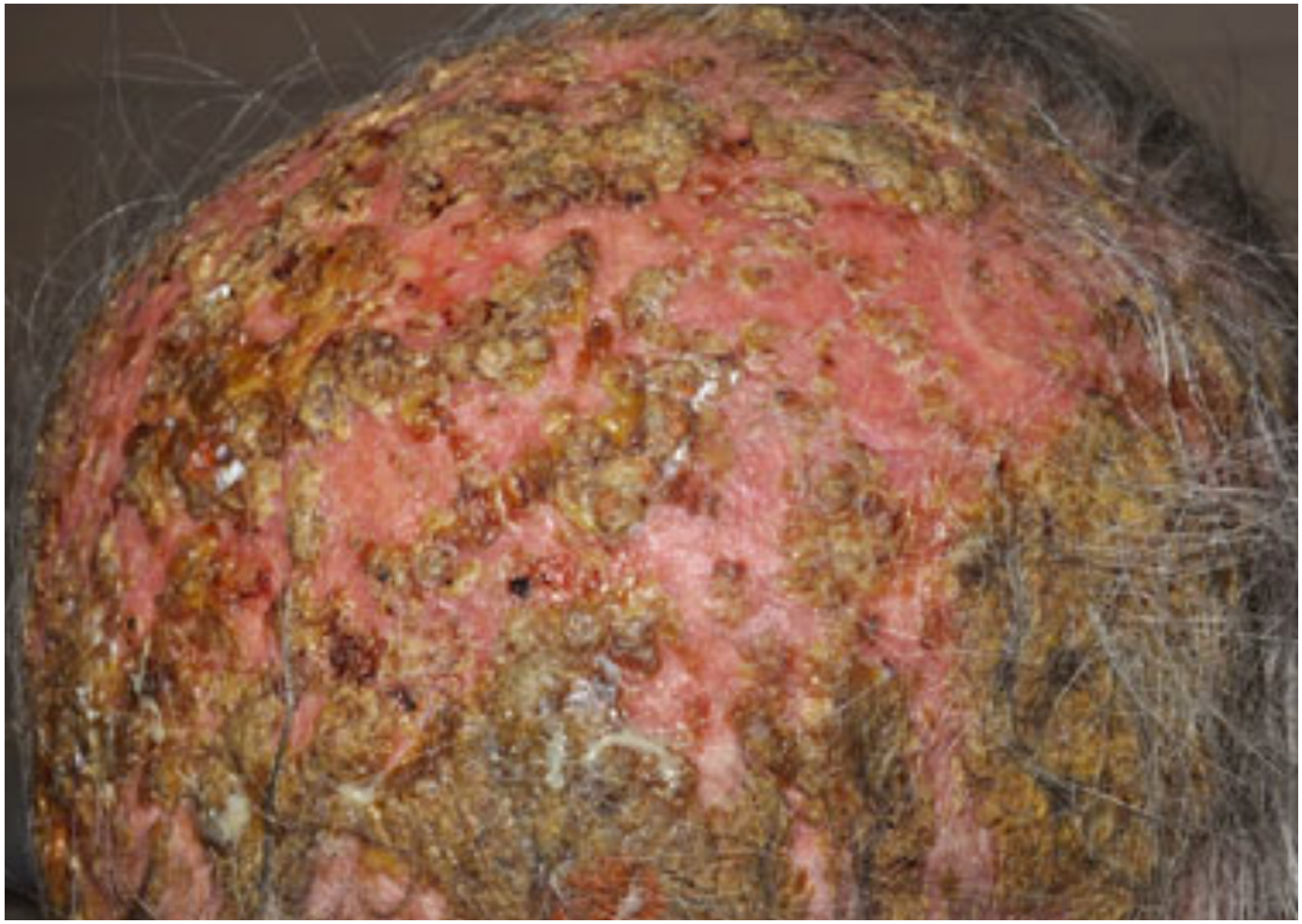
Continue EGFR inhibitor at current dose and monitor for change in severity; continue treatment of skin reaction with the following:

Hydrocortisone 2.5% cream‡ or clindamycin 1% gel or pimecrolimus 1% cream PLUS doxycycline 100 mg BID or minocycline 100 mg BID

Reassess after 2 weeks; if reactions worsen or do not improve, proceed to next step

Oncologist, 2007;
Roche, 2009

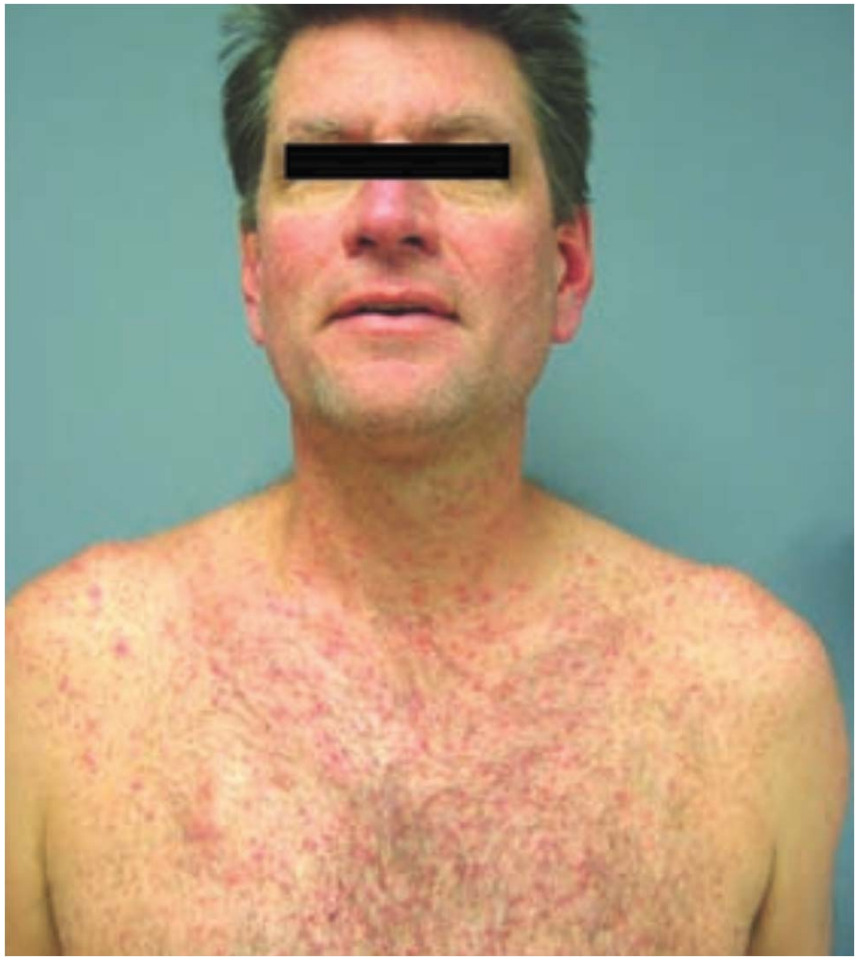
Grade 3



Impetiginised confluent honey-color crust with purulent discharge

(Peuvrel et al, 2012)

Grade 3



Reduce EGFR-inhibitor dose per label and monitor for change in severity; continue treatment of skin reaction with the following:

Hydrocortisone 2.5% cream‡ or clindamycin 1% gel or pimecrolimus 1% cream PLUS doxycycline 100 mg BID or minocycline 100 mg BID PLUS methylprednisolone dose pack

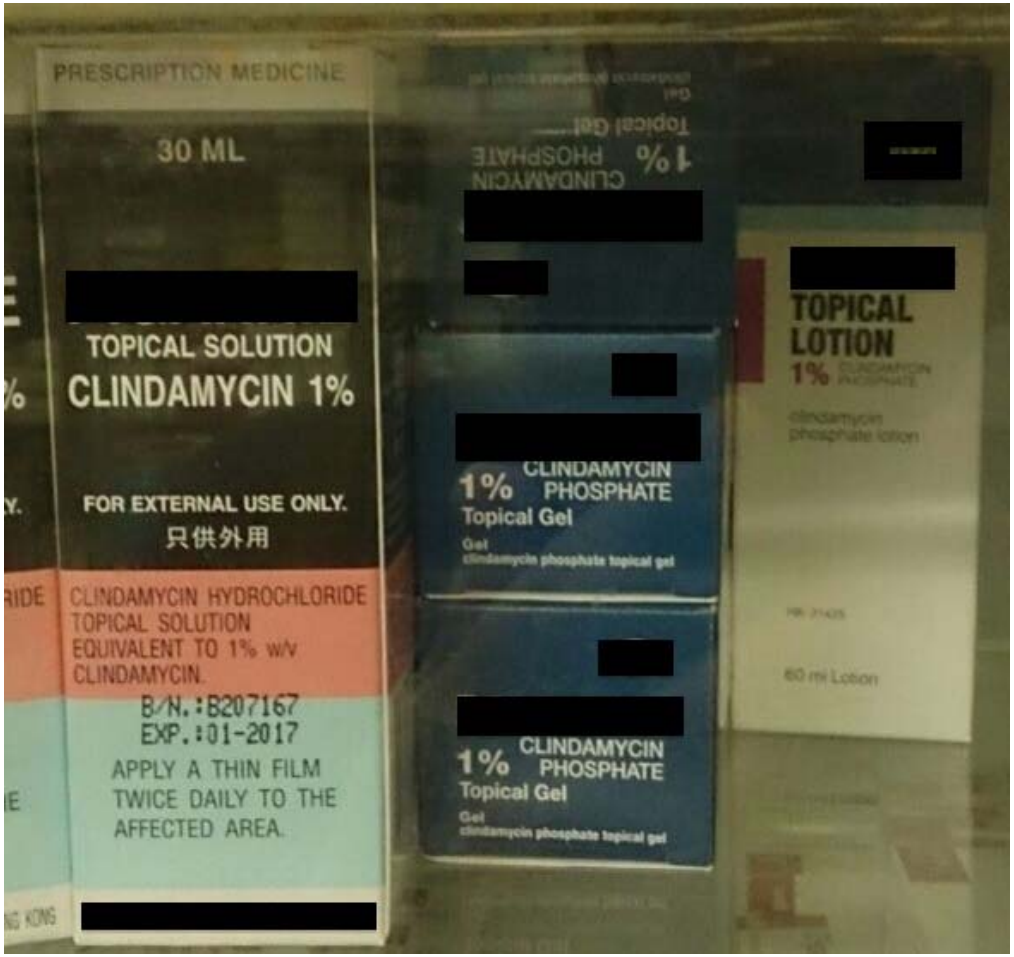
Reassess after 2 weeks; if reactions worsen, dose interruption or discontinuation may be necessary

Oncologist, 2007;
Roche, 2009

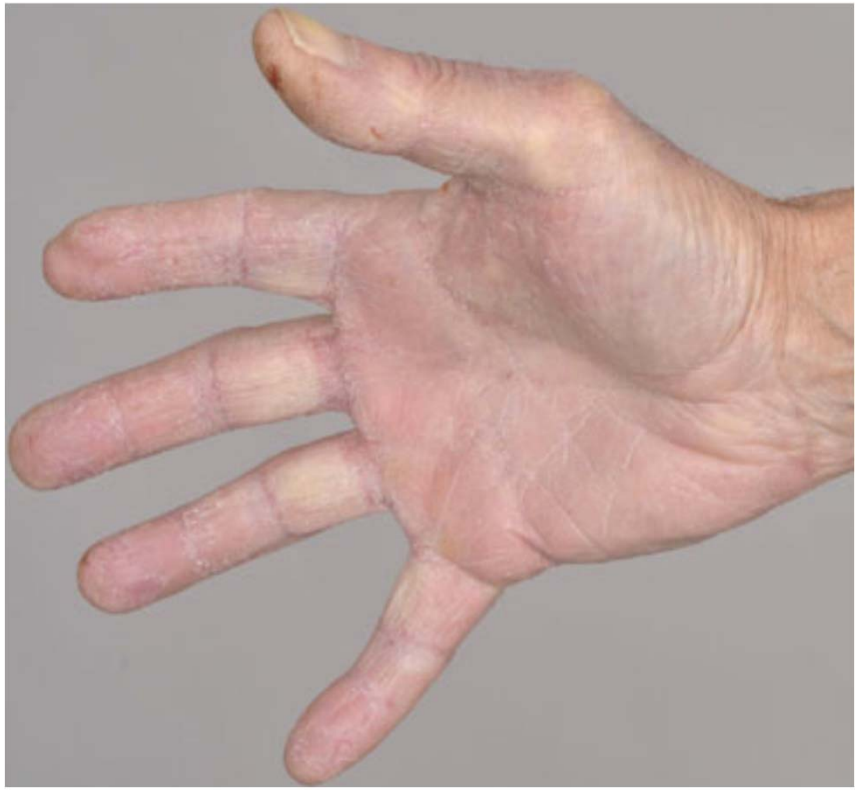
Local guidelines from Queen Mary Hospital

Grade	Descriptions	EGFR inhibitor Interruption?	Treatment suggestions
1 (Mild)	Localized MP rash, minimal symptoms, no impact on ADL, no superinfection	No	Topical treatment (face): - Benzoyl peroxide cream BD LA - Clindamycin cream 1% 30mL BD LA - Metronidazole cream 0.75% 15G QD LA Topical treatment (trunk or limbs): - Hydrocortisone 1% cream 15G BD LA - Clindamycin cream 1% 30mL BD LA - Metronidazole cream 0.75% 15G QD LA
2 (Mod)	Generalized rash, mild symptoms and signs (including fissure and paronychia), mildly affect ADL, with no superinfection	No	Topical treatment: - As For Grade 1 (For treatment of **Fissure* & *Paronychia*, refer to below) Systemic treatment: - Doxycycline 100mg QD - Tetracycline 500mg BD - Minocycline 100mg QD (or BD for more severe case)
3 (Severe)	Generalized rash, severe symptoms, interfering ADL, superinfections; Ulcerative rash, or affect mucosa e.g. eye pain	Yes	Consult senior for dose reduction, with reference to package insert of the respective EGFR inhibitors Consider dermatologist consultation for other possible DDx and specialist management of complications
Comments	- give hydrocortisone cream esp. when there is eczema; limit time of use to <= 2 weeks - must give warning regarding sun-exposure avoidance when using tetracycline group antibiotics		
*Fissures	Treat with topical antiseptic e.g. Fusidic acid ointment +/- wet gauze e.g. Fucidin Intertulle		
Paronychia	Advise patient to avoid tight-fitting shoes. There is no proven benefit of trimming with surgery Prevent infection with topical antiseptic / antifungal e.g. Fusidic acid ointment Topical steroid may be added in severe cases e.g. Hydrocortisone 1% cream 15G BD LA		

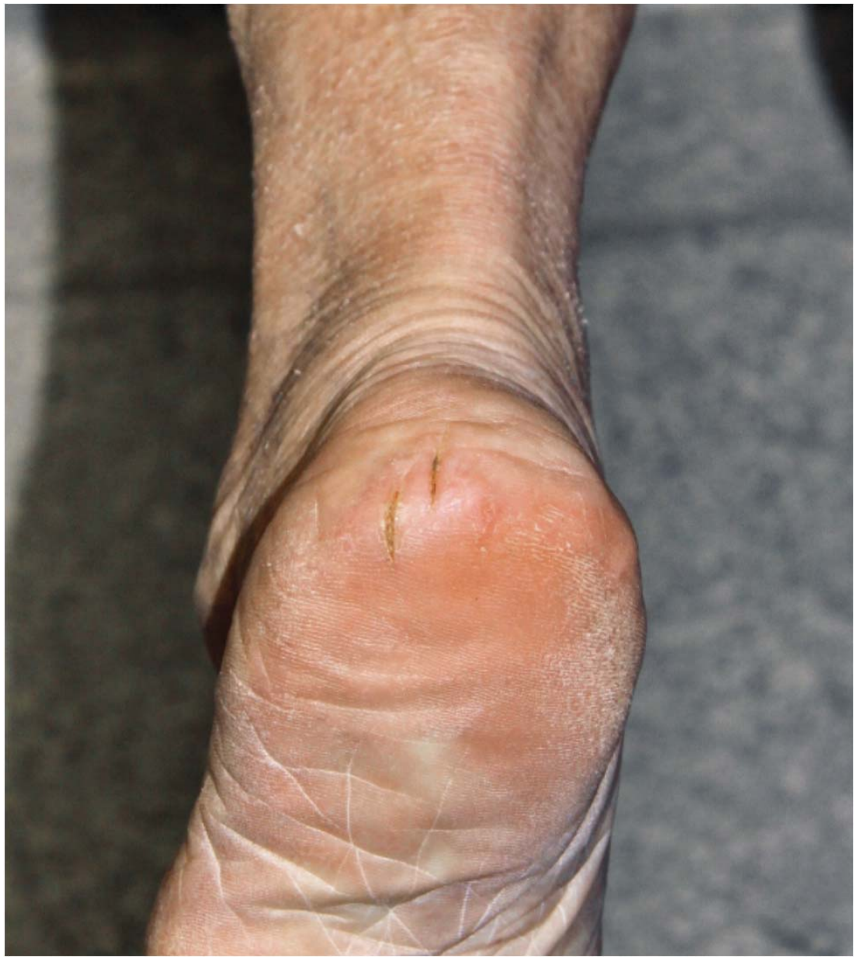
Topical Clindamycin
(With Cetylstearyl alcohol as emulsifying agent, but ethanol-free)



Xerosis



(Peuvrel et al, 2012)



(Bonny et al, 2011)

Xerosis

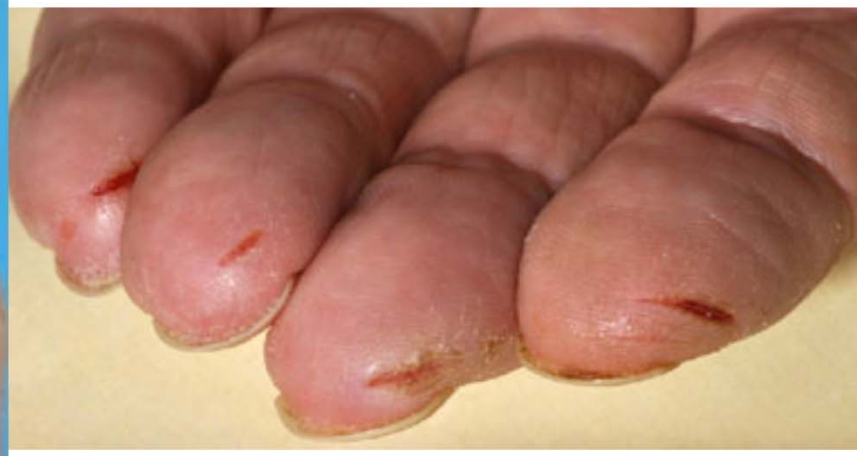
- mild – moderate: thick non-alcohol based moisturizing cream without fragrance or potential irritants
- Scaly area: greasy cream can be used on limbs but are cautioned on face, chest & extremely hairy areas (risk of folliculitis secondary to occlusion)
- Severe condition with inflammation: topical steroid cream

Sun protection

- Physical protection
- Use of sun screen
- Not to use on damaged or broken skin

Fissure

(Balagula et al, 2010)

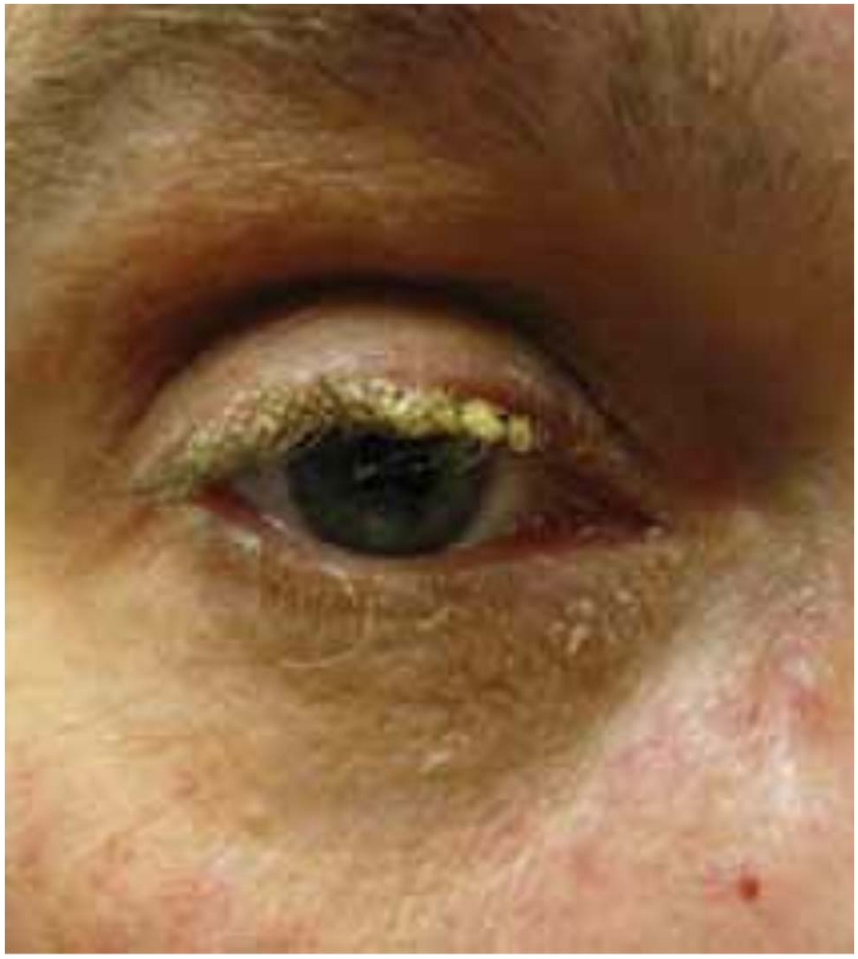


(Peuvrel et al, 2012)

Fissure

- Late side-effect, occurring around 30-60 days after start therapy
- Painful with risk of infection
- Thick moisturizer, barrier cream, topical steroid
- Protective footwear

Trichomegaly



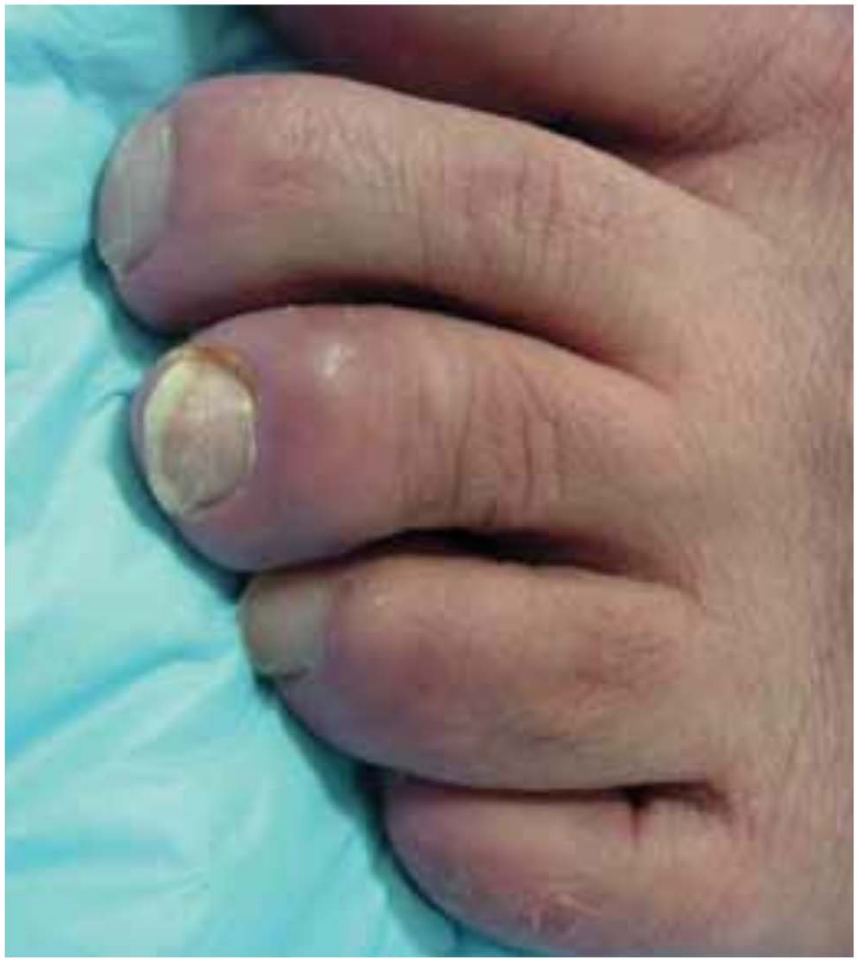
(Balagula et al, 2010)

- Increased length, thickness, stiffness, curling of eyelashes
- Create visual discomfort
- Intermittent cutting of eyelashes to a shorter length to promote comfort
- Risk of trichias (misdirection of eyelashes towards the globe) and corneal ulceration

Paronychia

- Tender, edematous & often purulent inflammation of nail fold
- Fingernails & toenails may be affected, most commonly on the first digits
- Delayed onset, usually 4-8 weeks after start of therapy
- Decreased epidermal thickness with a thin stratum corneum results in increased skin fragility
- Retention and penetration of nail plate fragments into the periungual tissues, resulting into foreign body reaction and subsequent inflammation

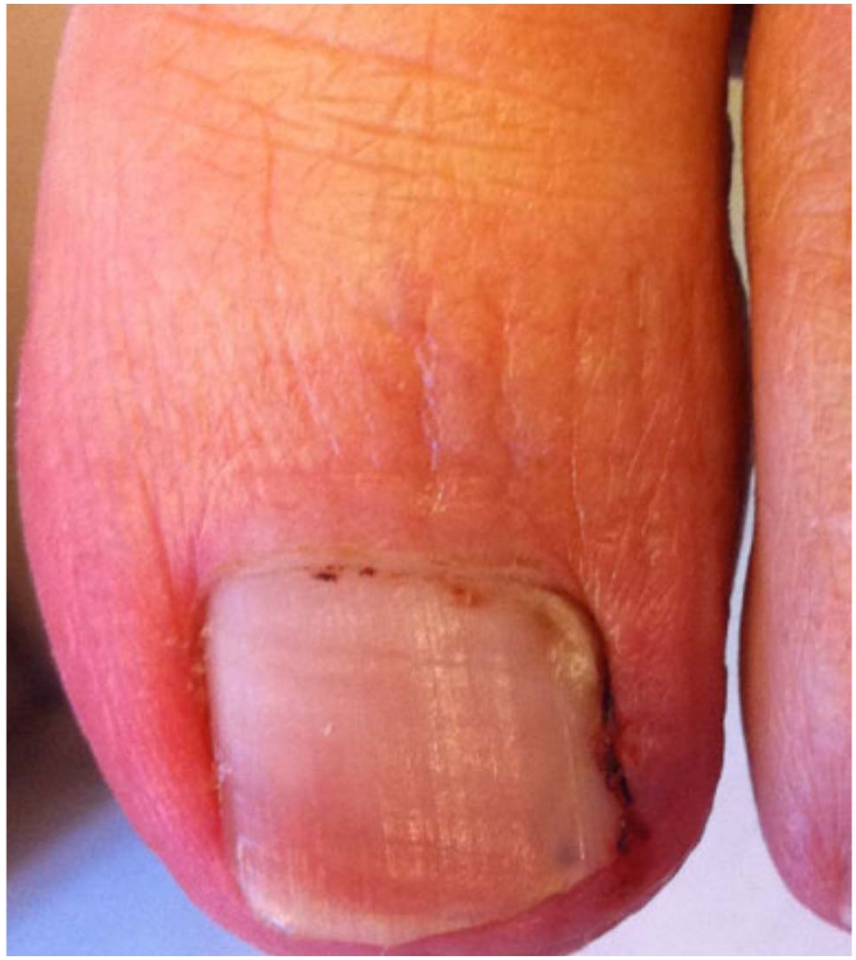
Paronychia



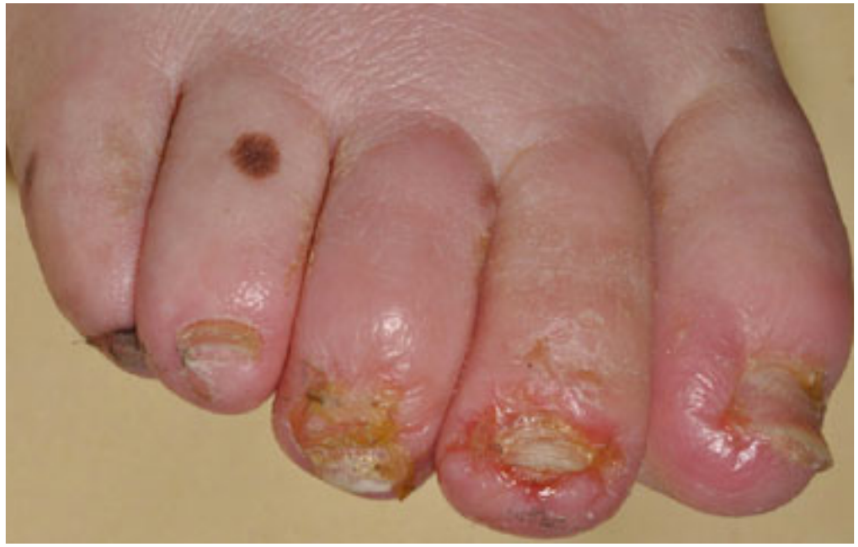
Severity (CTCAE v.4.0)	Intervention
Grade 0	Prophylaxis with moisturizing creams; gentle skin care instructions given
Grade 1 Nail fold edema or erythema; disruption of the cuticle	Continue anticancer agent at current dose and monitor for change in severity Treat with topical antibiotics and vinegar soaks[a] Reassess after 2 weeks (either by healthcare professional or patient self-report); if reactions worsen or do not improve, proceed to next step
Grade 2 Localized intervention indicated; oral intervention indicated (eg, antibiotic, antifungal, antiviral); nail fold edema or erythema with pain; associated with discharge or nail plate separation; limiting instrumental ADL	Continue anticancer agent at current dose and monitor for change in severity Treat with topical antibiotics and vinegar soaks[a] plus weekly silver nitrate applications Reassess after 2 weeks (either by healthcare professional or patient self-report); if reactions worsen or do not improve, proceed to next step
Grade 3 Surgical intervention or IV antibiotics indicated; limiting self-care ADL	Modify dose per PI; obtain bacterial/viral cultures if infection is suspected Continue treatment with systemic antibiotics and weekly silver nitrate applications; consider nail avulsion Reassess after 2 weeks; if reactions worsen or do not improve, dose interruption or discontinuation per PI may be necessary

(Balagula et al, 2010)

Paronychia



Grade 2 paronychia



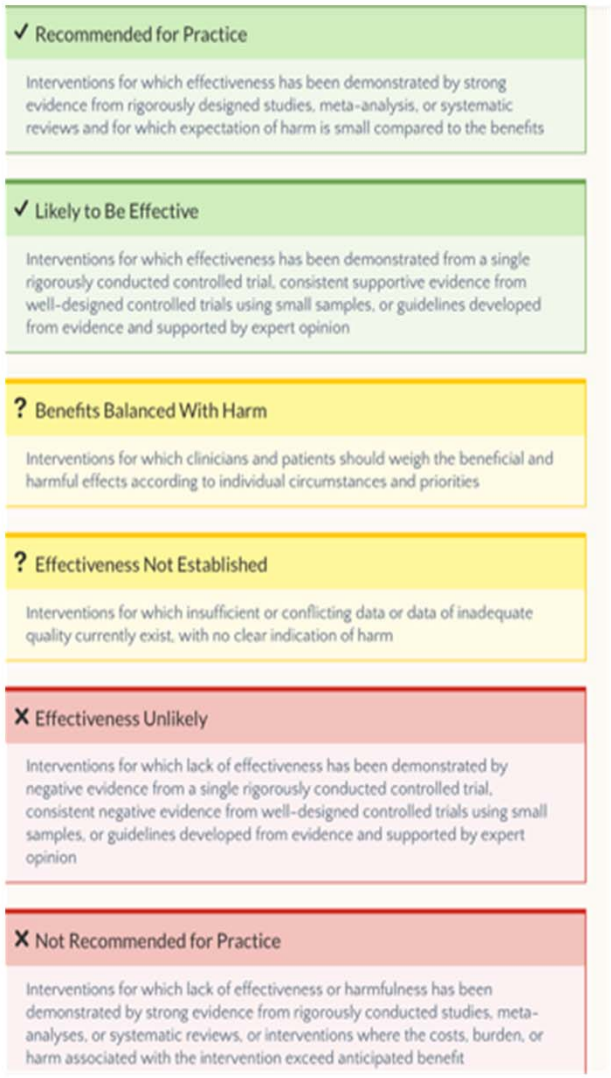
Grade 3 paronychia with superimposed infection

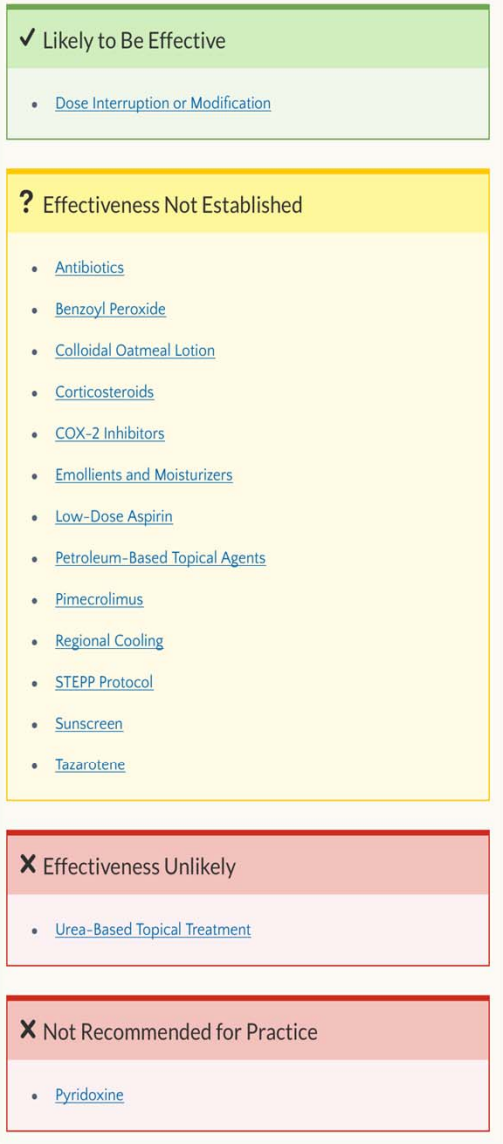
(Peuvrel et al, 2012)

Paronychia

- Encourage preventive measures: keep hands & feet dry, wearing gloves & comfortable shoes, avoid friction & pressure on nail fold or manipulation of nail
- High morbidity: significant pain, functional limitation, impairment of ADL

ONS: Putting Evidence into Practice





Diarrhea

CTCAE V 4.0*					
Adverse Event	Grade				
Diarrhea	1	2	3	4	5
	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline Not interfering with ADLs	Increase of >=7 stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADLs	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by frequent and watery bowel movements.					

*U.S. Department of Health and Human Services. National Institutes of Health. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0

Afatinib

- 95% of patients had diarrhea

(Medscape, 2014)

Afatinib has not yet registered in HK up to Aug 2014

Diarrhea

- Exclude other causes of diarrhea to avoid inappropriate treatment discontinuation
- Exclude concomitant use of laxative
- Mistakenly using an anti-diarrheal agent to treat diarrhea caused by infection can intensify diarrhea severity & infectious complication

Diarrhea

- Replace fluid and electrolytes
- Lorepamide and Octreotide are the only drugs with established efficacy in managing treatment-induced diarrhea

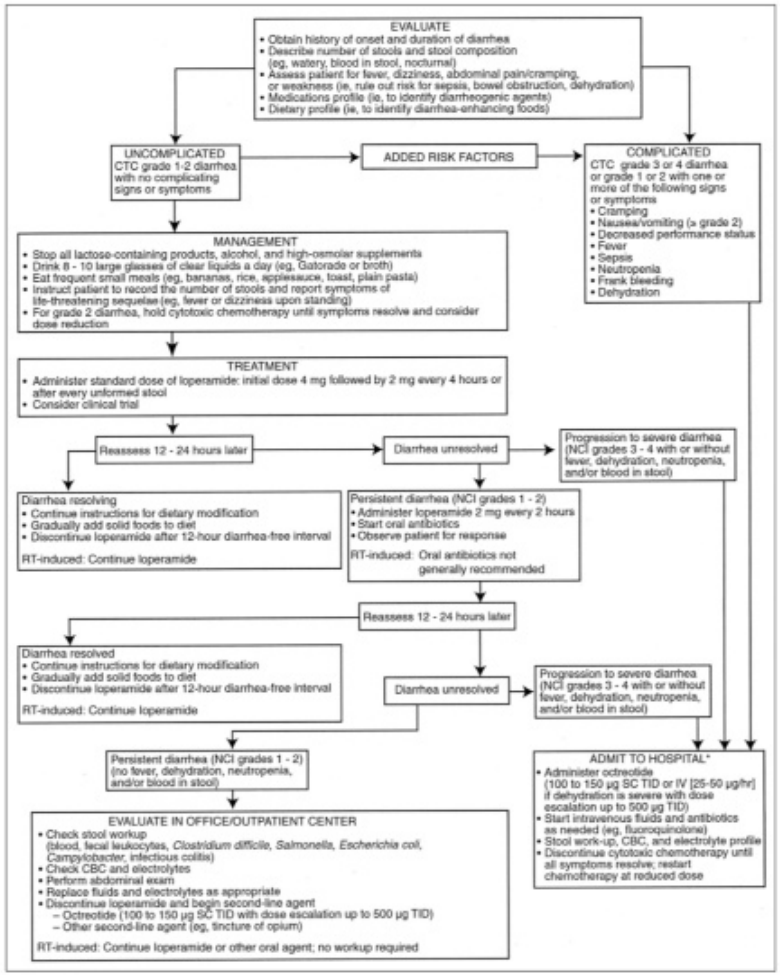


Fig 1. Proposed algorithm for the assessment and management of treatment-induced diarrhea. *For radiation-induced cases and select patients with CID, consider intensive outpatient management, unless the patient has sepsis, fever, or neutropenia. CTC, Common Toxicity Criteria; NCI, National Cancer Institute; RT, radiotherapy; SC, subcutaneous; tid, three times per day; IV, intravenous; CBC, complete blood count; CID, chemotherapy-induced diarrhea. Adapted with permission from Kornblau et al[11].

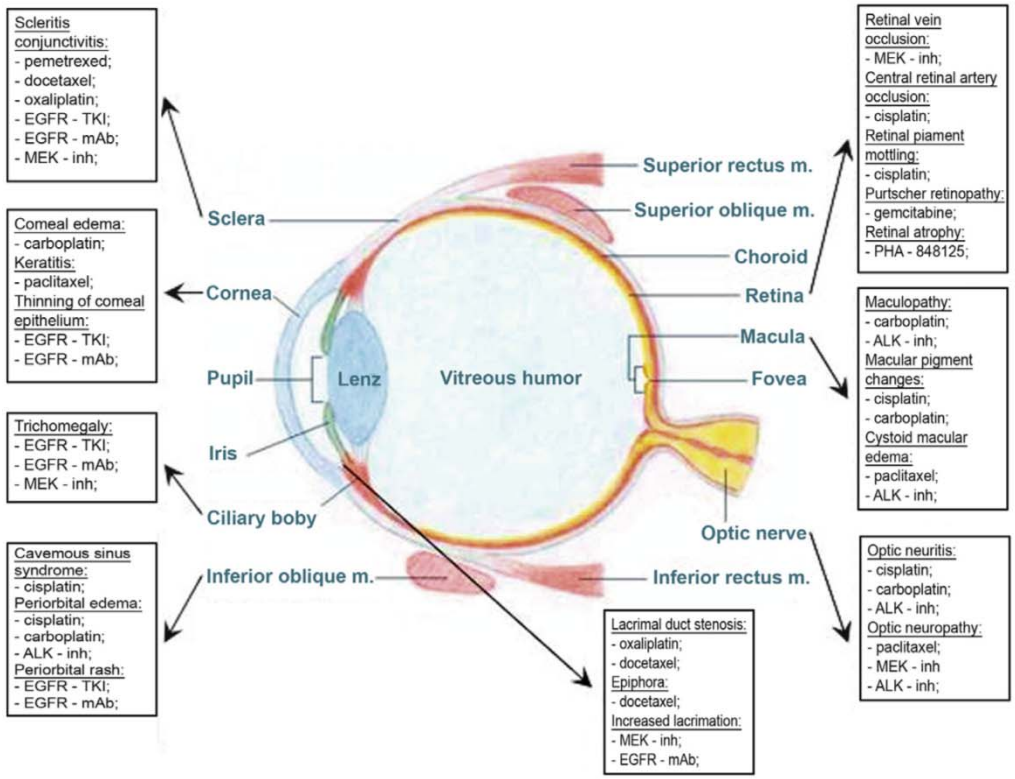


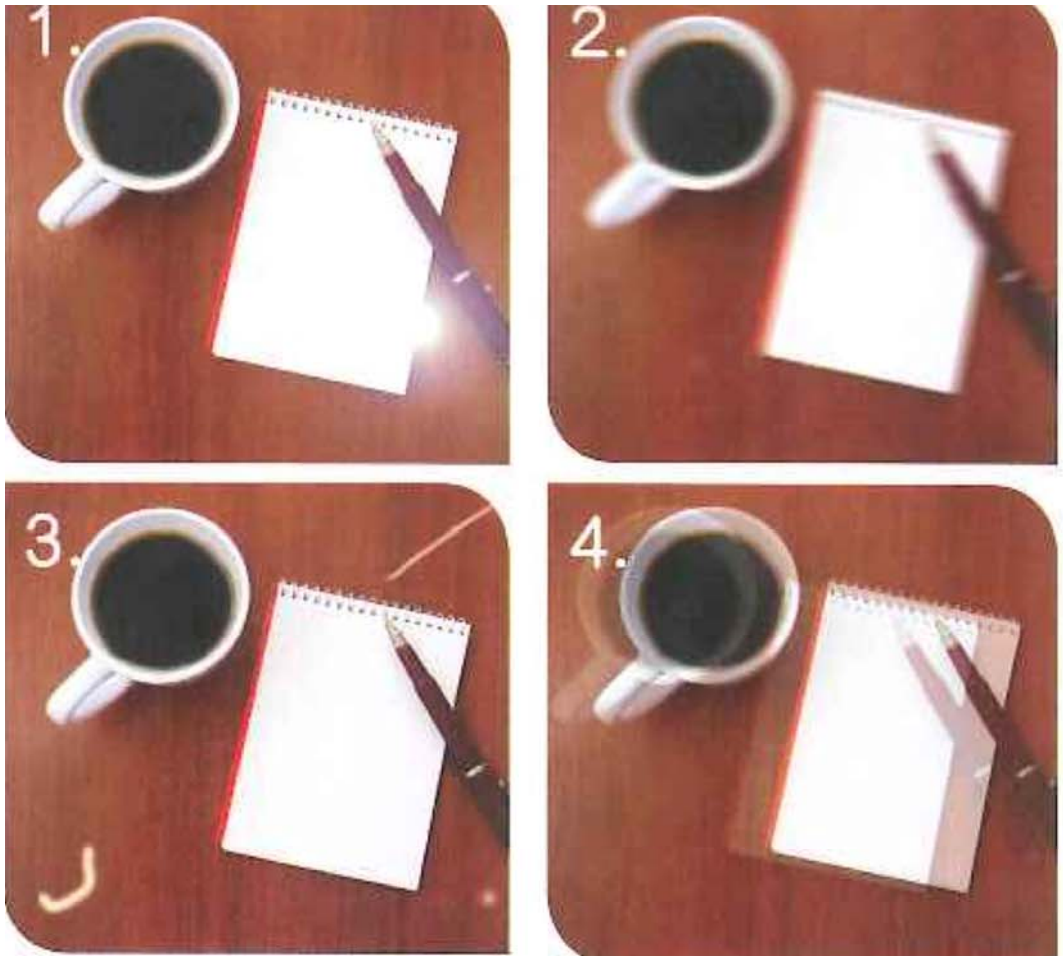
Fig. 1. Anatomic drawing of the eye and anticancer drugs associated with ocular disorders (ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; mAbs, monoclonal antibodies; MEK, mitogen-activated protein kinase; TKIs, tyrosine kinase inhibitors).

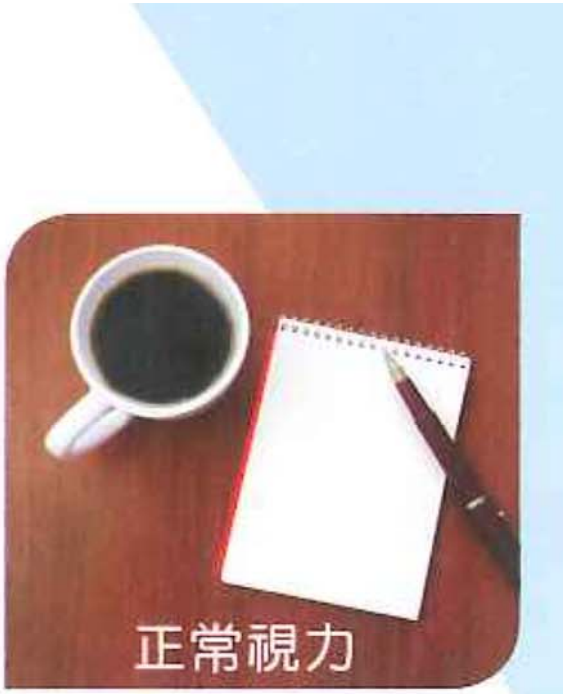
Crizotinib

- ≈ 62% of patients had visual changes with unknown cause
- Occurs within a few weeks after start of therapy
- Blurred vision
- Diplopia
- Floaters
- Increased sensitivity to light
- Trailing lights in peripheral vision field

(Meloskin, 2012)

Crizotinib





Pfizer, 2013

Crizotinib

- Effect not permanent
- Not threatening to vision
- Ophthalmologist consultation if needed

"Take two just before you go to bed and two just before you wake up."

"Don't take any of these red pills, and if that doesn't work, don't take any of the blue ones."

Potential Factors for Non-compliance for Oral Targeted Therapy

- Advanced age
- Chronic condition
- Cognitive impairment
- Depression
- Low literacy
- Lack of social support
- Cost

Implications of Non-compliance

- Attribution of patient's worsening condition to absence of drug activity
- Increased medical visits, hospitalization, LOS
- Clinical trials: misleading results, inconsistent response rates, potentially erroneous dosing recommendations
- Increased toxicity
- Decreased therapeutic efficacy

Bring Home Message

- Pre-treatment education for patients and family members
- Early identification of toxicities
- Updated knowledge of various new novel agents