

Managing TKI toxicities in lung cancer

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Disclosures

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2020 “available” TKIs in the US (some off label)

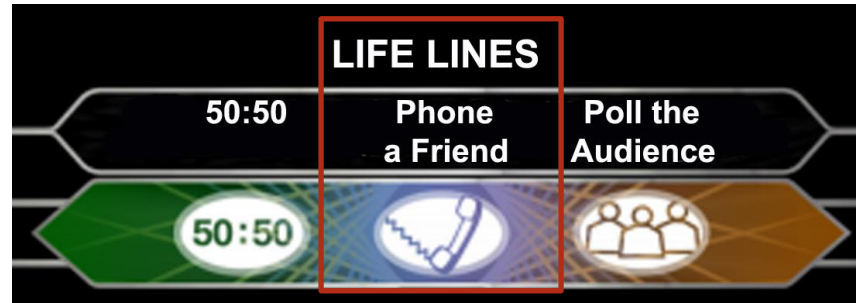
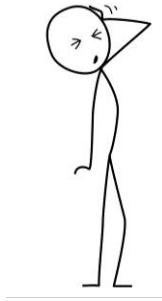
- EGFR
 - Osimertinib
 - Erlotinib
 - Afatinib
 - Gefitinib
 - Dacomitinib
- ALK
 - Alectinib
 - Brigatinib
 - Lorlatinib
 - Crizotinib
 - Ceritinib
- ROS1
 - Crizotinib
 - Entrectinib
 - Ceritinib
 - Lorlatinib
- BRAF
 - Vemurafenib
 - Dabrafenib
 - Dabrafenib + trametinib
- MET e14 and amp
 - Crizotinib
 - Capmatinib
 - Cabozantinib
- RET
 - Selpercatinib
 - Cabozantinib
 - Vandetinib
 - Alectinib
 - Ponatinib
- NTRK
 - Larotrectinib
 - Entrectinib
- HER2
 - Afatinib
 - Dacomitinib

More coming every month.....lots of very active compounds in late stages of development



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Colleagues
Pharmacists
Patient groups



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Some toxicities are common across a class

EGFR TKIs	ALK TKIs	MET TKIs	RET TKIs	NTRK TKIs
Rash	Bradycardia	LE edema (not responsive to diuretics)	Dry mouth	Weight gain
Diarrhea	Muscle aches	Nausea	HTN	Dizziness, ataxia



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Some toxicities are “unusual”, and you should “warn” your patient about them

Drug	Crizotinib	Alectinib, lorlatinib	1 st /2 nd gen EGFR TKIs
Reaction	Flashing lights at night, halos	Weight gain	Kinky hair, trichomegaly
Management	Usually nothing	Dose reduce if bothersome	Usually nothing, careful trimming of eyelashes (!)



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Management strategy must match pattern of tox

Very common and/or
early onset



Prophylactic treatment;
dose escalation



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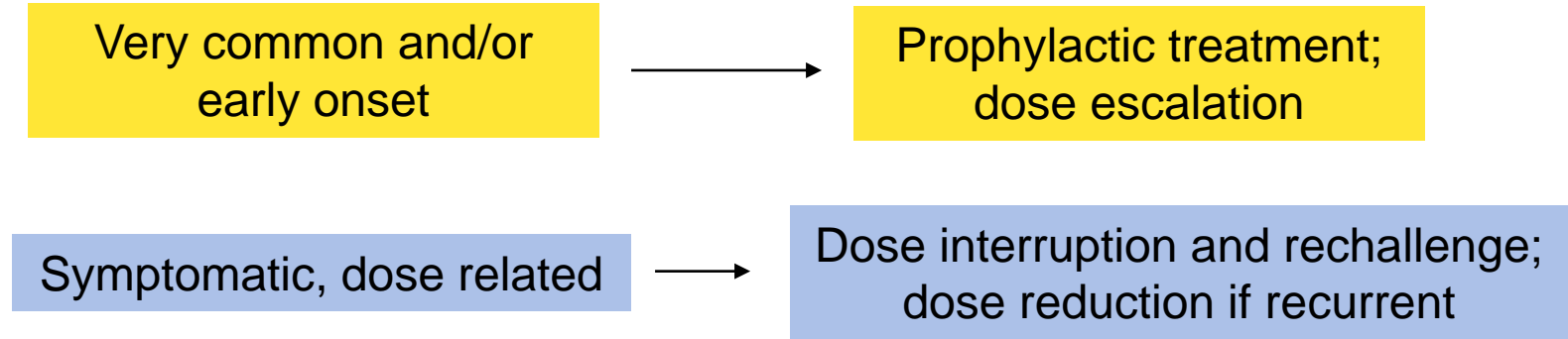
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Examples of Prophylactic Treatment; Dose Escalation

- Afatinib, dacomitinib: prophylactic antibiotics for rash
- Lorlatinib: prophylactic statin if elevated cholesterol at BL
- Lorlatinib: start w/ dose reduction if underlying mood or other psych disorder and increase as tolerated
- Brigatinib: start at lower dose x 1 week and escalate to reduce risk of ILD



Management strategy must match pattern of tox



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Examples of Dose Interruption and Re-challenge

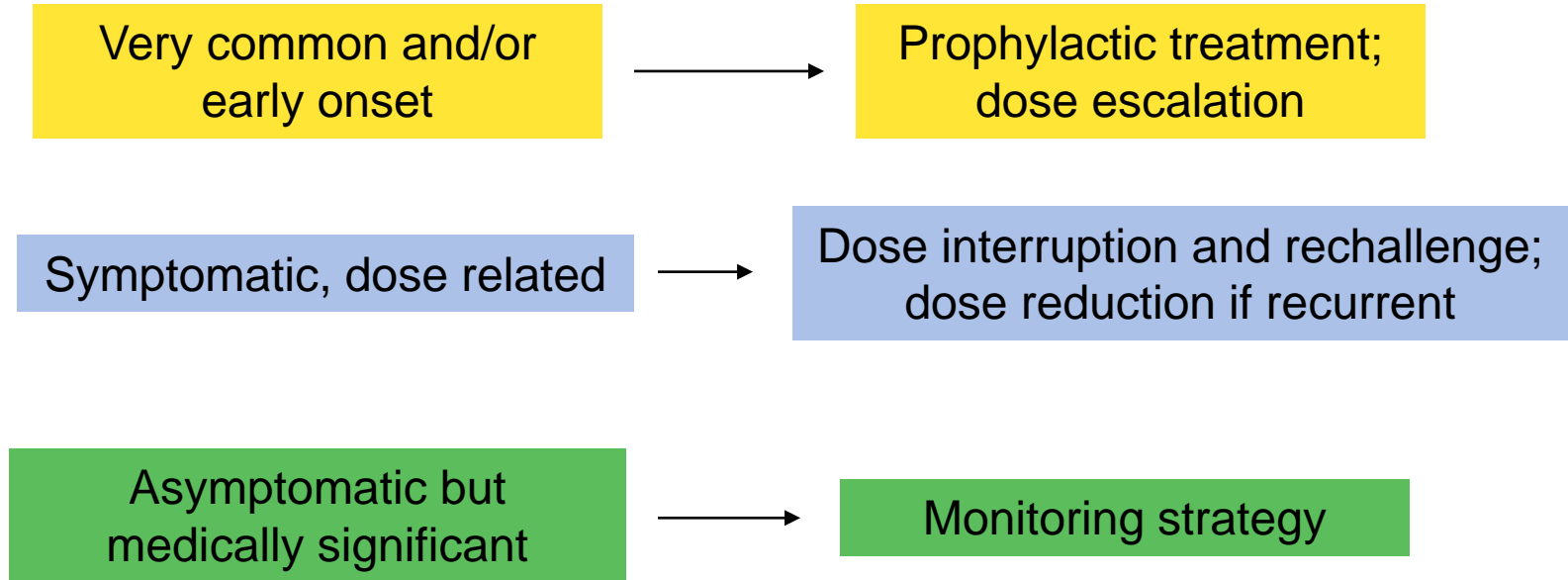
- Any EGFR TKI causing paronychia
- Any EGFR TKI causing rash
- Entrectinib and body aches



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Management strategy must match pattern of tox



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Examples of Monitoring Strategies

- Osimertinib: echocardiograms if underlying heart dz
- Lorlatinib: monitor cholesterol and treat if rising
- Almost all TKIs: following LFTs for hepatotoxicity



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Finally: Collect successful strategies from patients, and pass them along!

- Calf muscle cramps: compression socks, tonic water
- Brittle nails: vitamin E (oral)
- Scalp irritation: tea tree oil (topical)
- Fatigue: take med in PM instead of AM (if QD dosing)
- Muscle aches: aggressive oral hydration

