Management of Palmar-Plantar Erythrodysesthesia (PPE)

The cutaneous reaction termed palmar-plantar erythrodysesthesia (PPE) can be dose-limiting for some cytotoxics. The cytotoxics used that are most commonly implicated with PPE are 5-fluorouracil, capecitabine and liposomal doxorubicin.
Several kinase inhibitors are also associated with this side effect, for example sunitinib, sorafenib, axitinib, everolimus.

Patients should be advised to moisturise their hands and feet regularly throughout treatment with any of the above agents, and to minimise activities that put pressure on feet or hands if they start to develop sore hands or feet. Choice of moisturiser is patient preference. Examples of recommended moisturisers include urea-containing moisturisers e.g. Eucerin cream, or Udderly Smooth (available to purchase from St Luke's pharmacy, or via the internet)

Grading of PPE (CTC criteria)

Grade 1	Grade 2	Grade 3	Grade 4
Minimal skin changes (e.g. erythema) without pain	Skin changes (e.g., peeling, blisters, bleeding, oedema) or pain, not interfering with function	Ulcerative dermatitis or skin changes with pain, interfering with function	-

Management of patients who present with any Grade PPE:

- For information regarding delays and/or dose reductions of the chemotherapy according to grade of toxicity, refer to the relevant chemotherapy protocol and follow the advice given under "Dose Modifications".
- Regular moisturiser should be used to help reduce the dryness, as discussed above.
- No effective treatments for PPE have been verified in randomised clinical trials.
- There is limited and conflicting evidence as to the benefit of pyridoxine to reduce the severity of PPE induced by 5FU, capecitabine or liposomal doxorubicin, so allowing treatment to continue, and without having an adverse effect on clinical response.[1,2,3,4]
- There is no evidence to support the use of pyridoxine to manage PPE induced by kinase inhibitors.
- For Grade 1 or above PPE, patients on capecitabine, 5FU or liposomal doxorubicin may be tried on a course of pyridoxine 50mg po tds, which should continue for the remainder of the chemotherapy treatment *only if* a clinical benefit is noted.
- There is limited evidence that higher doses of pyridoxine can be tried[5]. However, this should not be routine practice until larger studies are carried out. Chronic high doses (200mg and above) of pyridoxine carry a risk of developing peripheral sensory neuropathies.
- Prophylactic pyridoxine is not to be used in patients who have never shown any symptoms of PPE.

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References: [1]Corrie, P et al; Br J Cancer 2012 ; 107 : 585 – 587
[2]Kang, Y et al, JCO 2010 ; 28 (24) : 3824 – 3829
[3]Von Gruenigen, V ; Cancer 2010 ; 116 (20) : 4735 - 4743
[4]Vail, DM et al; Clin Cancer Res 1998; 4 (6): 1567 – 1571
[5]Chalermchai, C et al; Asia-Pacific Journal of Clinical Oncology 2010; 6 (3): 155 - 160

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