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Adjunctive Urea-based Cream can reduce hand-foot skin reactions and improve quality of life in patients treated with multikinase inhibitor sorafenib

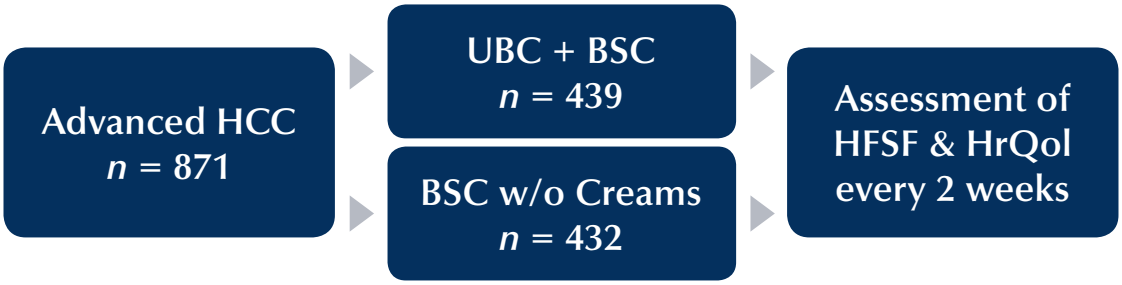
Ren Z, et al. Randomized controlled trail of the prophylactic effect of Urea-based cream, J Clin Oncol 2015;33:894-900

AIM

The multikinase inhibitor sorafenib has high rates of hand-foot skin reaction (HFSR) during the treatment of hepatocellular carcinoma (HCC) with HFSR being one of the most common adverse events leading to dose reduction. The aim of the study was to examine if an adjunctive Urea-based cream (UBC = Eucerin® UreaRepair 10% Urea Lotion) can reduce the incidence and severity of HFSR in patients with advanced HCC and improve patient quality of life compared with best supportive care (BSC).

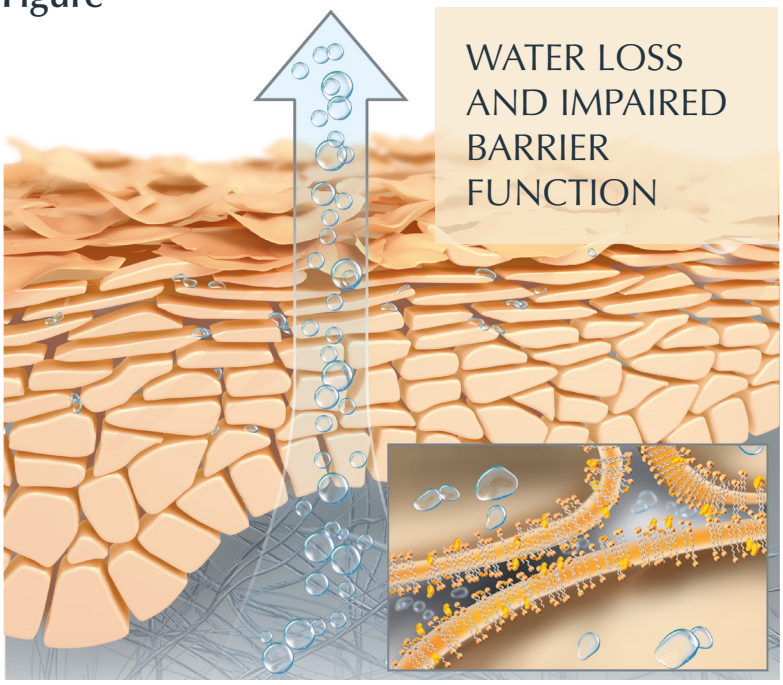
PATIENT AND METHOD

In this randomized, open-label trial, 871 patients with advanced HCC throughout China were treated with 10% UBC three times per day plus best supportive care (BSC; *n* = 439) or BSC alone excluding all creams (*n* = 432), starting on day 1 of sorafenib treatment, for up to 12 weeks. HFSF was assessed every 2 weeks and at 14 weeks for patients completing the study. Once HFSR occurred, patients were allowed any cream, including a UBC.

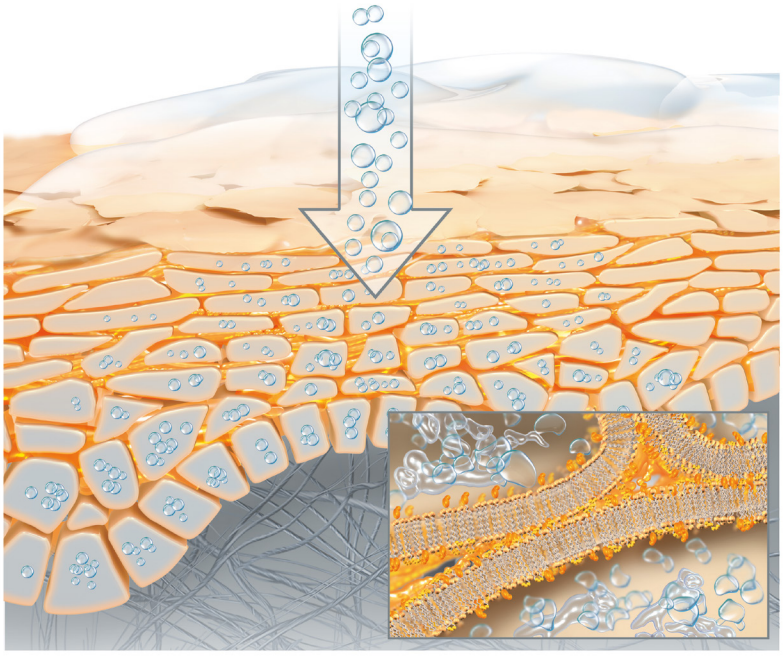


Creams containing urea are widely used to treat hyperkeratotic conditions, including psoriasis, and have been recommended for TKI-related HFSR.[1] Urea is considered the gold standard in the treatment of Xerosis cutis due to its extensive data and good efficacy.[2]

Figure[2]



DRY SKIN



TREATED SKIN

PRINCIPLES OF TREATMENT

LIPID LAYER ON THE SKIN SURFACE

SUPPLY OF MOISTURE (NMF, HUMECTANTS)

REPLENISHMENT OF INTERCELLULAR BARRIER LIPIDS

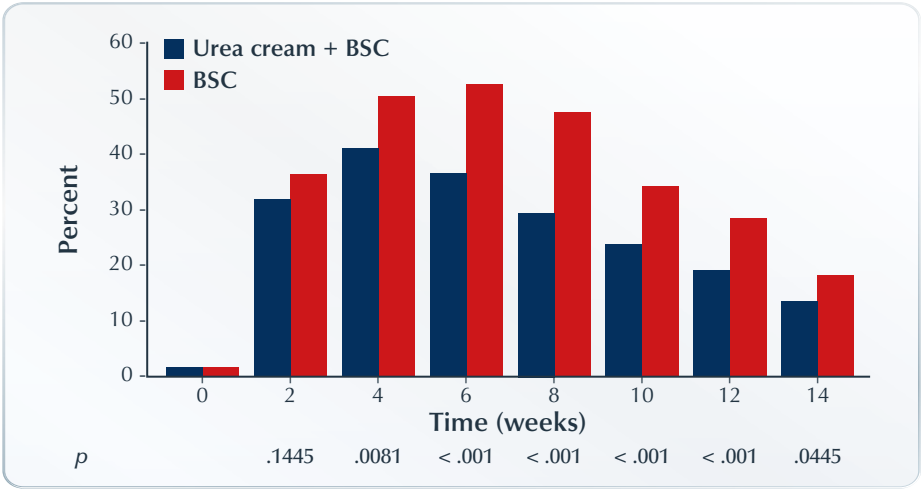
GOLD STANDARD UREA FOR THERAPY OF DRY SKIN

Based on available scientific data, urea (synonym: carbamide) is the gold standard in the treatment of xerosis cutis. Not only does urea effectively hydrate the skin, it also improves the barrier function as well as the skin´s own defense and hydration mechanisms. It increases the penetration of active ingredients into the skin and has antipruritic and -at higher concentrations- keratolytic effects.[2]

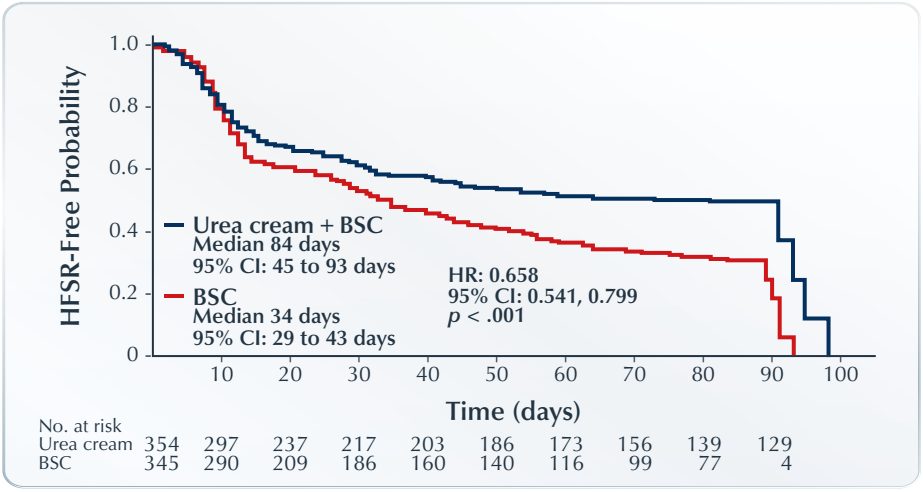
1. Lacouture ME, Wu S, Robert C, et al. Evolving strategies for the management of hand-foot skin reaction associated with the multitargeted kinase inhibitors sorafenib and sunitinib. Oncologist 2008;13:1001-1011. **2.** Augustin M, et al. Diagnosis and treatment of xerosis cutis – a position paper, JDDG 2019, DOI: 10.1111/ddg.13906.

RESULTS

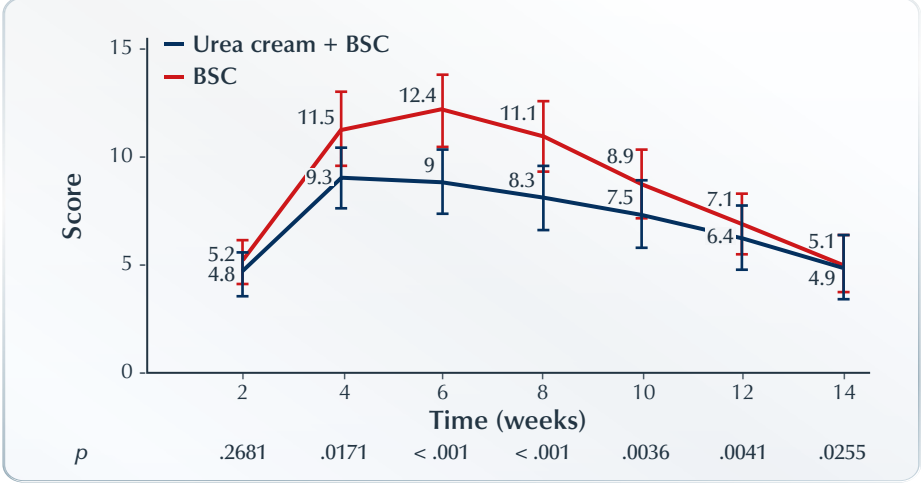
The 12-week incidence of any grade HFSR was significantly lower in the UBC group versus the BSC-alone group (56.0% v 73.6%, p <0.001), as was the incidence of grade ≥2 HFSR (20.7% v 29.2%, p = 0.004). Median time to first occurrence of HFSR was significantly longer in the UBC group than the BSC-alone group (84 v 34 days, respectively; p <0.001) with a significant reduction in HFSR occurrence by week 12 of treatment. Analysis of HF-QoL Questionnaires showed that the HFSR symptom score was lower at each study visit from week 4 to week 14 in patients treated with UBC plus BSC versus BSC alone, indicating a lower symptom burden in the former group. In addition, the HFSR daily activity score was lower at weeks 6 and 8 in patients receiving UBC plus BSC, indicating that HFSR had a reduced impact on these patients' daily activities.



Prevalence of any-grade hand-foot skin reaction at each study visit. Statistical analysis was conducted using the X^2 test. BSC, best supportive care.



Kaplan-Meier analysis of time to first hand-foot skin reaction (HFSR) event in patients who received urea-based cream plus best supportive care (BSC) and patients who received BSC alone. HR, hazard ratio.



Hand-Foot Reaction Quality of Life outcomes. HFSR-symptoms, indicating symptom burden over time in patients who received urea cream plus BSC and in patients who received BSC alone. Scores expressed as mean SE.

CONCLUSION

HFSR may be severe enough to require TKI dose reduction and to seriously impair activities of daily living. Despite relatively high HFSR rates, the management of HFSR has been reactive rather than proactive. Recent consensus recommendations by an international, interdisciplinary expert panel included the use of over-the-counter creams and moisturizers during treatment with TKIs.

The rates of any grade and grade ≥2 HFSR were significantly lower in the UBC plus BSC group than in the BSC-alone group, with similar reductions in each grade of HFSR severity. Moreover, UBC significantly extended the median time to first occurrence of HFSR, decreasing its risk through week 12 by 34%. Moreover, UBC improved patient HFSR-associated quality of life during sorafenib treatment, reducing HFSR symptoms and their impact on daily activities.

S-3 Guideline supportive therapy for oncology patients

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OFFICIAL S3-GUIDELINE RECOMMENDATION: BASIC CARE WITH 5-10% UREA AT LEAST 2 X DAILY IS RECOMMENDED FOR PROPHYLAXIS OF XEROSIS CUTIS, HAND FOOT SYNDROM, RADIODERMATITIS AND PRURITUS DURING ONCO-THERAPY
