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Positive Quality Intervention: Managing TKI-Induced Hand-Foot Skin Reaction

Description: Hand-foot skin reaction (HFSR) is one of the most common cutaneous adverse events caused by protein tyrosine kinase inhibitors (TKIs). It is important to prevent and manage this side effect in an effort to avoid dose reductions or treatment interruptions and reduced quality of life.

Background: The risk of developing HFSR varies widely across targeted TKIs. This is likely related to inhibition of different pathways, vascular damage and potential additive effects from combination regimens, including non-TKI oncolytic therapy. HFSR develops within the first 2-4 weeks of TKI therapy in the majority of patients.[1] The clinical appearance and distribution of TKI-associated HFSR differs from that of chemotherapy-associated hand-foot syndrome (HFS), which classically manifests as diffuse palmoplantar erythema, edema, and neuropathic pain with possible progression to desquamation, erosion, and ulceration. Palms of the hands are more commonly involved in the presentation of HFS. In contrast, HFSR affects flexural and pressure-bearing areas resulting in hyperkeratotic lesions, particularly in the soles of the feet.[2,3] Symptoms usually begin with dysesthesia and erythema that is worsened by mechanical or thermal stress followed by increasing pain and callus-like thickening in the erythematous areas.[4] Lesions are described as tender and scaling, with a peripheral halo of erythema, yellowish and hyperkeratotic plaques, or callus-like blisters (which usually do not contain fluid), typically localized to areas of pressure.[5] This can significantly impact a patient's quality of life as hand and foot toxicity can impair mobility, balance, activities of daily living, and psychosocial well-being – many of which are already ongoing struggles in the oncology population. It is important to recognize those patients at risk for development of HFSR in order to provide prevention and management techniques to optimize clinical outcomes.

PQI Process:

- Identify patients starting TKI therapy and evaluate risk for development of HFSR, including comorbid conditions associated with poor circulation
- Prevention tips prior to treatment initiation
  - Physical examination on the condition of the hands and feet
  - Consider referral to podiatrist or dermatologist for removal of preexisting hyperkeratotic areas or calluses on palms or soles
  - Moisturize 3 times per day (e.g., nondeodorant, fragrance-free, alcohol-free, oil-based creams)
  - Consider twice daily application of moisturizing emollient creams containing keratolytics to preexisting areas[4]
    - Ammonium lactate 12%
    - Urea 10-20%
    - Salicylic acid 3-6%
- After patients start therapy, monitor symptoms of HFSR on a biweekly basis
- Grade and initiate treatment for HFSR as symptoms develop according to NCCN CTCAE Criteria[6] and impact on quality of life[3]

Grade 1	**Continue TKI at current dose**
Minimal skin changes or dermatitis (e.g., erythema, edema, or hyperkeratosis) without pain	▪ Conduct thorough patient interview to confirm follow through on recommendations provided prior to treatment initiation ▪ Urea 20% cream BID ▪ Super-high potency topical corticosteroid (e.g., clobetasol propionate 0.5%) once daily

Grade 2	**Continue TKI at current dose**
Skin changes (e.g., peeling, blisters, bleeding, fissures, edema, or hyperkeratosis) with pain; interferes with ADL	▪ Continue supportive care as with Grade 1 ▪ Super-high potency topical corticosteroid BID ▪ Topical lidocaine 4-5% ▪ Oral analgesics (e.g., NSAIDs, GABA agonists) ▪ Consider dose modification
Grade 3	**Interrupt TKI**
Severe skin changes (e.g., peeling, blisters, bleeding, fissures, edema, or hyperkeratosis) with pain; unable to perform ADL	▪ Continue supportive care as with Grades 1 and 2 ▪ Hold treatment x 7 days or until resolution to ≤ Grade 1 ▪ Dose modification per prescribing information or provider discretion

Patient-Centered Activities:

- Counsel on the importance of measures to prevent and decrease severity of HFSR
- Emphasize a "3 C" approach
    - Control calluses
    - Comfort with cushions
    - Cover with creams
- Soak feet in a water bath with Epsom salt
- Educate on the proper (and gentle) use of tools, (e.g., pumice stones) for exfoliation and callus removal
- Avoid hot water, tight-fitting shoes or items that may rub, pinch, or cause friction
- Cushion pressure points with cotton socks, soft shoes and/or insoles
- Avoid use of urea-based or topical steroid agents on non-intact skin to prevent further irritation, breakdown or discomfort
- Caution patients on the increased risk of infection with a disrupted or inflamed skin barrier, as they are immunocompromised
- Monitor skin and call provider for worsening of severity

References:

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