Tebentafusp-tebn Care Step Pathway - Skin Toxicities

Assessment

Look:
- Does the patient appear uncomfortable?
- Does the patient appear unwell?
- Does the patient look sunburned?
- Is the patient scratching during the visit?
- Is skin integrity intact?
- Are there skin changes?
  - o Xerosis (dry skin)
  - o Changes in skin pigment or color
- Is there oral involvement of the rash?
- Does the patient look swollen?

Listen:
- Does the patient have pruritus with or without rash?
- Is there a rash with or without pruritus?
- Does the patient report swelling?
- Are symptoms interfering with ADLs?
- Are symptoms interfering with sleep?
- Have symptoms worsened?
- Does the patient report a burning sensation?

Recognize:
- Is there a history of dermatitis, pre-existing skin issues (psoriasis, eczema, wounds, prior radiation to region, etc.)?
- Laboratory abnormalities consistent with other etiologies (e.g., eosinophils on complete blood count, liver function abnormalities)

Grading Toxicity

MACULOPAPULAR RASH (aka morbilliform rash)

Definition: A disorder characterized by the presence of macules (flat) and papules (elevated); frequently affecting the upper trunk, spreading towards the center and associated with pruritus

Grade 1 (Mild)
Macules/papules covering <10% BSA with or without symptoms (e.g., pruritus, burning, tightness)

Grade 2 (Moderate)
Macules/papules covering 10-30% BSA with or without symptoms (e.g., pruritus, burning, tightness); having psychological effect and limiting instrumental ADLs; rash covering >30% BSA with or without mild symptoms

Grade 3 (Severe)
Macules/papules covering >30% BSA with or without associated symptoms; limiting self-care ADLs; skin sloughing covering <10% BSA

Grade 4 (Potentially Life-Threatening)
Papules/pustules covering any % BSA with or without symptoms and associated with superinfection requiring IV antibiotics; skin sloughing covering 10-30% BSA

PRURITUS

Definition: A disorder characterized by an intense itching sensation

Grade 1 (Mild)
Mild or localized; topical intervention indicated

Grade 2 (Moderate)
Widespread and intermittent; skin changes from scratching (e.g., edema, papulation, excoriations, lichenification [thick, leathery skin], oozing/crusts); limiting instrumental ADLs; oral intervention indicated

Grade 3 (Severe)
Widespread and constant; limiting self-care ADLs or sleep; systemic corticosteroid or immunosuppressive therapy indicated

Management

Overall Strategy
- Encourage use of moisturizers and non-irritating cleansers before patients start tebentafusp-tebn
- Assess for other etiology of rash: Ask patient about new medications, herbals, supplements, alternative/complementary therapies, lotions, etc.
- Educate patients that skin toxicity frequency and severity should drop drastically after the week 3 or week 4 dosages.
- Anticipate development of rash around 1 day after the first 3 dosages
- Advise patients that skin toxicity is very manageable. Very few people have to come off therapy because of this toxicity
- The likelihood of progression of skin toxicities to Grade 4 is very low (no cases reported in trials), but it's good to be aware of what more severe cases could look like

Grade 1 (Mild)
- Tebentafusp-tebn therapy to continue
- Oral antihistamines to be given for symptomatic patients (e.g., diphenhydramine HCL 25 mg PO q 6 hrs PRN)
- Provide oral analgesics for discomfort/pain (depending on labs, could be acetaminophen 500 mg PO q 6 hrs PRN, or ibuprofen 400 mg q 6 hrs PRN)
- Moderate potency topical corticosteroids may be used in some patients
- Advise vigilant skin care
  - o Twice daily applications of non-steroidal moisturizers or emollients applied to moist skin
  - o Moisturizers with ceramides and lipids are advised; however, if cost is an issue, petroleum jelly is also effective
  - o Soothing methods
    - § Cool cloth applications
    - § Topicals with cooling agents such as menthol or camphor
    - § Refrigerating products prior to application
  - o Avoid hot water; bathe or shower with tepid water
  - o Keep fingernails short
  - o Cool temperature for sleep
- Advise strict sun protection

Grade 2 (Moderate)
- Withhold tebentafusp-tebn until skin toxicity is Grade 1 or below (resume tebentafusp at same dosage level)
- High-potency topical corticosteroids to be used; if unresponsive to topical, consider low-dose oral corticosteroid (0.5 mg/kg to start)
- If patients are not responsive to oral corticosteroids, consider intravenous corticosteroids* (e.g., 2 mg/kg/day of methylprednisolone or equivalent)
- Oral antihistamines/oral anti-pruritics can be used (moderate to high-potency topical corticosteroids can be considered for rash alone)
- Provide oral analgesics for discomfort/pain (depending on labs, could be acetaminophen 500 mg PO q 6 hrs PRN, ibuprofen 400 mg q 6 hrs PRN, tramadol 50 mg q6 hrs PRN, or narcotics as needed)
- Advise vigilant skin care
  - o Gentle skin care
  - o Tepid baths; oatmeal baths
- Advise strict sun protection

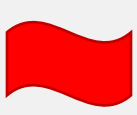
Grade 3 (Severe)
- Withhold tebentafusp-tebn until skin toxicity is Grade 1 or below (resume tebentafusp at same dosage level)
- Do not escalate dosage if Grade 3 skin reactions occur during initial dose escalation; resume escalation once dosage is tolerated
- High-potency topical corticosteroids to be used; if unresponsive to topical, consider low-dose oral corticosteroid (0.5 mg/kg to start)
- If patients are not responsive to oral corticosteroids, consider intravenous corticosteroids* (e.g., 2 mg/kg/day of methylprednisolone or equivalent)
- Provide oral analgesics for discomfort/pain (depending on labs, could be acetaminophen 500 mg PO q 6 hrs PRN, ibuprofen 400 mg q 6 hrs PRN, tramadol 50 mg q6 hrs PRN, or narcotics as needed, could escalate to hydroxyzine or doxepin if itching has progressed)
- Oral antihistamines/oral anti-pruritics can be used
- Consider dermatology consult
- Advise strict sun protection

Grade 4 (Potentially Life-threatening)
- Permanently discontinue tebentafusp-tebn for potentially life-threatening skin disease or any cases of SJS and TEN
- High-potency topical corticosteroids to be used (up to 2 mg/kg/day of prednisone); if unresponsive to topical, consider low-dose oral corticosteroid (0.5 mg/kg to start)
- If patients are not responsive to oral corticosteroids, consider intravenous corticosteroids* (e.g., 2 mg/kg/day of methylprednisolone or equivalent)
- Urgent dermatology consult +/- biopsy

*Administering Corticosteroids:

Corticosteroid taper instructions/calendar as a guide but not an absolute
- Taper should consider patient's current symptom profile
- Close follow-up in person or by phone, based on individual need & symptomatology
- Corticosteroids may cause indigestion; provide antacid therapy daily as gastric ulcer prevention while on corticosteroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage is >20 mg/day)
- Review corticosteroid medication side effects: mood changes (angry, reactive, hyperaware, euphoric, manic), increased appetite, interrupted sleep, oral thrush, fluid retention
- Be alert to recurring symptoms as steroids taper down & report them (taper may need to be adjusted)

RED FLAGS:
- **Extensive rash (>50% BSA), or rapidly progressive**
- **Anal, genitourinary, vaginal, or any mucous membrane involvement**
- **Concern for suprainfection**



ADLs = activities of daily living; BSA = body surface area; PO = by mouth; ICI = immune checkpoint inhibitor; SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis