### Grading Toxicity

#### Oral Mucositis

<table>
<thead>
<tr>
<th>Grade</th>
<th>Toxicity</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (Mild)</td>
<td>Asymptomatic or mild symptoms; intervention not indicated</td>
<td>Consider additional antiviral and antifungal coverage</td>
</tr>
<tr>
<td>Grade 2 (Moderate)</td>
<td>Moderate pain or ulcer; oral intake not interfereing</td>
<td>Anticipate immunotherapy to continue</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>Severe pain; interfering with oral intake</td>
<td>Anticipate possible alternative treatment(s)</td>
</tr>
<tr>
<td>Grade 4 (Potentially Life-Threatening)</td>
<td>Life-threatening consequences; urgent intervention indicated</td>
<td>Need for dental work (e.g., root canal, tooth extraction)</td>
</tr>
<tr>
<td>Grade 5 (Death)</td>
<td>Grade 5 (Death)</td>
<td>Pain with swallowing/throat pain</td>
</tr>
</tbody>
</table>

#### Dry Mouth (Xerostomia)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Toxicity</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (Mild)</td>
<td>Symptomnatic (e.g., dry or thick saliva)</td>
<td>Consider antimicrobial prophylaxis (sulfamethoxazole/trimethoprim double dose M/W/F; single dose if used daily) or alternative if sulfa-allergic (e.g., atovaquone [Mepron®] 1500 mg po daily)</td>
</tr>
<tr>
<td>Grade 2 (Moderate)</td>
<td>Moderate symptoms; oral intake alterations (e.g., requires saltwash, another lubricant, diet limited to purees and/or soft, moist foods); unstimulated saliva &lt;0.2 mL/min</td>
<td>Encourage vigilant oral hygiene</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>Severe symptom not adequately ameliorated</td>
<td>Monitor hydration status</td>
</tr>
<tr>
<td>Grade 4 (Potentially Life-Threatening)</td>
<td>Life-threatening consequences; urgent intervention indicated</td>
<td>Identify barriers to adherence</td>
</tr>
<tr>
<td>Grade 5 (Death)</td>
<td>Grade 5 (Death)</td>
<td>Oral care</td>
</tr>
</tbody>
</table>

### Management (including anticipatory guidance)

#### Overall Strategy
- Assess for other etiology of mucositis or dry mouth: candidiasis; ask patient about new medications (particularly antihistamines), herbs, supplements, etc.
- Assess patient & family understanding of toxicity and rationale
- Identify barriers to adherence

#### Interventions in at-risk patients
- Advise basic oral hygiene:
  - Tooth brushing (soft toothbrush, avoid toothpaste with whitening agents)
  - Use of dental floss daily
  - >1 mouth rinses to maintain oral hygiene (avoid commercial mouthwashes or those with alcohol)
- If patient wears dentures, assess for proper fit, area of irritation, etc.
- Dental referral if necessary
- Assess patient & family understanding of prevention strategies and rationale
- Identify barriers to adherence

#### Mucositis
- Urgent oral hygiene
  - Increase frequency of brushing to Q4 hours and at bedtime
  - If unable to tolerate brushing, advise chlorhexidine gluconate 0.12% or sorbic acid bismuthoates mixture
    - 1 tsp bismuthoate in 8 ounces of water
  - ½ tsp salt and 2 tbsp sodium bicarbonate dissolved in 4 cups of water
- Encourage intake of cool, fluid food intake
- Nonpharmacologic
  - Sugarless gum
  - Sugarless hard candies
  - Natural lemon
  - Pharmacologic
    - Saliva stimulants (XyliMelts®)
    - Lactobacillus
    - Cevimeline HCI
- Nonpharmacologic
  - Corticosteroid rinses
  - 2% viscous lidocaine applied to lesions 15 minutes prior to meals
  - 2% morphine mouthwash
  - 2% doxepin mouthwash
  - “Miracle Mouthwash”: 0.5% doxepin mouthwash
- Pharmacologic
  - Oral solids or liquids
  - Encourage water intake
  - Monitor hydration status
- Nutrition referral if appropriate
- Avoid antimetabolites or other hematotoxic agents
- Avoid alcohol, caffeine, spicy foods
- Avoid foods that are hot, spicy, acidic
- Avoid toothpaste with whitening agents
- Avoid morphine mouthwashes
- If persistent, consider biopsy or endoscopic evaluation

#### Corticosteroids

* Steroid taper instructions/protocol as a guide but not an absolute

- Taper should consider patient’s current symptom profile
- Close follow-up in person or by phone
- Consider additional antiviral and antifungal coverage
- Avoid antimetabolites or other hematotoxic agents
- Avoid alcohol, caffeine, spicy foods
- Avoid foods that are hot, spicy, acidic
- Avoid toothpaste with whitening agents
- Avoid morphine mouthwashes
- If persistent, consider biopsy or endoscopic evaluation

#### Long-term high-dose steroids

- Assess for other etiology of mucositis (amphotericin B liposomal/trimethoprim double dose M/W/F; single dose if used daily) or alternative if sulfasalazine (e.g., azathioprine [Imuran®] 1500 mg po daily)
- Consider additional antiviral and antifungal coverage
- Avoid antimetabolites or other hematotoxic agents
- Avoid alcohol, caffeine, spicy foods
- Avoid foods that are hot, spicy, acidic
- Avoid toothpaste with whitening agents
- Avoid morphine mouthwashes
- If persistent, consider biopsy or endoscopic evaluation

#### Nutritional support

- Evaluate gut status (e.g., lacteal fistula, ileoceleal fistula, etc.)
- Inability to adequately aliment orally, tube feeding or total parenteral nutrition indicated; unstimulated saliva <0.1 mL/min
- Life-threatening consequences; urgent intervention indicated
- 0.2 mL/min
- >1 mouth rinses to maintain oral hygiene (purees and/or soft, moist foods)
- Other lubricants, diet limited to purees and/or soft, moist foods
- Inability to adequately aliment orally; tube feeding or total parenteral nutrition indicated; unstimulated saliva <0.1 mL/min
- Life-threatening consequences; urgent intervention indicated
- 0.2 mL/min
- >0.2 mL/min
- Grade 1 (Mild)
- Grade 2 (Moderate)
- Grade 3 (Severe)
- Grade 4 (Potentially Life-Threatening)
- Grade 5 (Death)

*Risk patients

#### Dental referral if necessary

- Identify barriers to adherence

#### Anticipatory guidance regarding use of pharmacologic agents

- Anticipate possible alternative treatment(s)
- Anticipate possible alternative treatment(s)
- Anticipate immunotherapy to continue
- Anticipate immunotherapy to be discontinued for Grade 2 event any Grade 0-1 event
- Immunotherapy to be discontinued for Grade 2 events persisting >12 weeks (ipilimumab or pembrolizumab, nivolumab) or any recurrent Grade 3 event (pembrolizumab, nivolumab)