Management of Drug Side Effects

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Gist Day of Learning
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General Oncology-Pharmacology

DNA or protein transcription

Cellular Receptors

Tyrosine Kinase Domain

Kinase 1

Kinase 2

Kinase 3

Kinase 4

Migration, Differentiation, etc.
Pharmacology: Drug Side Effects

Target 1: Disease response

Target 2: QTc changes, constipation, etc.
Imatinib (Gleevec®)
Side Effects

- Fatigue
- Anemia
- Nausea or vomiting
- Diarrhea
- Edema/fluid retention
- Cramps
- Endocrine

- Rash/skin problems
- Joint pain
- Eyes
- Sensitive to sunlight
- Liver toxicity
- Myelotoxicity (blood counts)
- Neurotoxicity

Side Effects Are Dose Related
Side Effect Lineage

Time

Side Effects

Dose Exposure

2 weeks

1 month

2 months

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Nausea/Vomiting

Pro-Tips:
• Onset: Can happen upon initiation
• Take medication with food and large glass of water
• Take anti-nausea medication (ondansetron/prochlorperazine)
  • Nausea around dose: Take medication 30min prior to dose
  • Nausea throughout day: As needed, scheduled, or different medication

The Oncologist 2004; 9:271-281
Diarrhea

Pro-Tips:
- Onset: Can happen upon initiation
- Take Medication with food and large glass of water
- Antidiarrheal medications

The Oncologist 2004; 9:271-281
## Diarrhea

<table>
<thead>
<tr>
<th>Signs that you have diarrhea</th>
<th>Be sure to call Mayo Clinic Cancer Center right away if you have any of these signs</th>
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</thead>
<tbody>
<tr>
<td>• More stools per day than you had before starting chemotherapy</td>
<td>• Fever (a temperature of 100.5 degrees Fahrenheit or higher)</td>
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<tr>
<td>• Softer, looser, or more watery stool</td>
<td>• Flu-like symptoms</td>
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<tr>
<td>• Stomach pain or feeling weak</td>
<td>• Chills, Sweating, Feeling Hot</td>
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<tr>
<td>• More cramping and/or gas</td>
<td>• Severe stomach pain or cramps</td>
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</tbody>
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### What to Drink

- Drink at least 8 to 10 large glasses of fluid a day (water, Gatorade, Pedialyte, clear broth)
- Drink a little at a time, continuously throughout the day
- Limit fluids at mealtimes to 4 to 6 ounces
- Avoid milk or dairy products, alcohol, coffee and very hot or very cold fluids

### What to Eat

- Eat small meals frequently
- Follow the BRAT diet (Bananas, Rice, Applesauce, Toast)
- Avoid fatty or fried foods, spicy foods, high-fiber foods, raw fruits and vegetables, beans, chocolate
Diarrhea

Taking Medicine for your diarrhea
Imodium A-D® (Loperamide)

First Episode of Diarrhea

- Take 2 caplets (4mg) with first bowel movement of diarrhea
- Then take 1 caplet (2mg) every 4 hours or with each unformed stool
- Stop taking loperamide if you do not have a bowel movement for 12 hours.
  If diarrhea continues (more than 4 bowel movements in a 24 hour time frame), see directions for continued diarrhea

Continued Diarrhea

- Take 1 caplet (2mg) every 2 hours
- Stop taking loperamide if you do not have a bowel movement for 12 hours.
  If diarrhea continues (more than 4 bowel movements in a 24 hour time frame), please call the Mayo Clinic cancer center.

Mayo Clinic Cancer Center: 480-342-4800 or 480-301-8000 (after hours)
Swelling

- Edema is typically mild, but up to 50% of people could get swelling
- Found in lower extremities/under eyes → morning more common
- At Risk: Women, >65 years of age, cardiovascular/renal issues
- Timing: >400mg/day: ~ 1 month; ≤ 400mg/day: ~ 2 months

Pro Tips:
- Ice Pack, topical 1% hydrocortisone or 0.25% phenylephrine (eyes)
- Water Pills (Furosemide), Decrease salt (eyes/feet)
- Be judicious with time on your feet/prop up feet

The Oncologist 2004; 9:271-281
Rash

- Rash can vary in presentation (red/swollen bumps, dry skin, etc.): contact provider
- Location: forearms, trunk, and face (less common)
- At Risk: High doses, women

Pro Tips:
- Heavy Creams, antihistamines
- Steroids (if creams unresponsive)
- Dose adjustments

The Oncologist 2004; 9:271-281
Cramping

- **Risk:** 25-50% of people can experience cramps
  - Typically mild in presentation
- **Location:** Thighs, calves, feet, or hands
- **Presentation:** The cramps should not change pattern, frequency, or severity (if so contact provider). Have consistent triggers
- **Cause:** Exertion, night-time/sleep, low calcium/magnesium
- **Treatment:** Tonic water (quinine), calcium/magnesium supplementation, sports drinks, medications (NSAID, muscle relaxants)

The Oncologist 2004; 9:271-281
Eyes

• Periorbital swelling (see above)

• Changes in visual acuity:
  • Epiphora (tearing)
    • Cause: Lacrimal duct blockage, overproduction of tears
    • Management: Timing of dose, antihistamine drops
  • Dry eyes:
    • Management: Artificial tears

Bottom Line: If not improving, contact provider.
Side Effects

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- Neurotoxicity

Side Effects Are Dose Related
Sunitinib (Sutent ®) & Regorafenib (Stivarga ®)
Side Effects

- Fatigue
- Nausea or vomiting
- Diarrhea
- Sore Mouth
- Rash/skin problems
- Hypertension
- Voice

- Myelotoxicity (blood counts)
  - Neutropenia
  - Anemia
  - Thrombocytopenia
- Liver toxicity
- Cardio-toxicity
- Kidney toxicity

Side Effects Are Dose Related
Rash/Skin Problems

Skin

Inside Blood Vessel

Sunitinib

Fibroblast blockade

Trauma

Rash

• Presentation: Pain/redness on palms and soles → lesions
• Location: Heals of feet or joints in hands
• Timing: 2-4 weeks after initiation

Pro Tips:
• Avoid excess hot water
• Avoid excessive trauma/rigorous exercise in first month
• Avoid tight fitting shoes

Rash/Skin Problems

Prophylaxis

- Creams with urea
- Prevention measures

Grade 1: Minimal skin changes with out pain
- Prescription strength urea +/- steroid creams
- Prevention measure
- Follow up in 2 weeks

Grade 2: Skin changes (blisters, cracks, etc) with pain
- Prescription strength urea + steroid creams twice a day
- Prevention measures
- +/- pain medications
- Follow up in 2 weeks

Grade 3: Severe skin changes (blisters, cracks, etc) with pain
- Prescription steroid creams twice a day
- Prevention measures
- + pain medications
- Follow up in 2 weeks; hold medication

Sore Mouth: Pathophysiology

Injury → Activation → Signal Amplification → Ulceration → Healing

Time Frame: 5-7 days

*Normal Gut turnover is 7-14 days

Sonis ST. ASCO Education Book. 2013; e236-e240
Sore Mouth

• Pro Tips:
  • Prevention:
    • Oral Care
      • Soft tooth brush
      • Saline and/or sodium bicarbonate mouth rinses
  • Treatment:
    • Avoid spicy/acidic/abrasive foods
    • Prescriptions
Hypertension

- Timing: Early, within 1-6 weeks
- Risk Factors: Pre-existing hypertension, age >60 years, BMI >25 kg/m2
- Effect is based on dosing

Pro Tips:
- Monitor blood pressure daily especially in people underlying blood pressure/cardio issues
- Contact provider if blood pressure is consistently >130/80 or rapidly increasing blood pressure
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- Kidney toxicity

Side Effects Are Dose Related
Kidney/Liver/Heart Toxicity

- **Pro tips:**
  - Kidney: Monitor for changes in urine quality
  - Heart: Discuss cardiac medical history
  - Liver: Labs

= Protein
Questions & Discussion