


RECOGNITION AND MANAGEMENT OF TOXICITIES OF ORAL THERAPEUTICS IN HEMATOLOGIC MALIGNANCIES



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No disclosures

Objectives

- Increase knowledge of toxicities of oral therapeutics in hematologic malignancies
- Identify how to recognize toxicities of oral hematologic medications
- Understand the treatment interventions for the toxicities when on oral hematologic medications if they occur

Oral cancer treatment

- In next 5 years, 1/3 of all oncology/hematology treatments will be in the oral form
- These patients will require frequent office visits and support
- There are not data/guidelines for all aspects of care related to oral oncolytics
- Insurance coverage will be an issue

Guidelines and Resources

- Chemotherapy and Biotherapy Guidelines and Recommendations for Practice – ONS 2014
- 2010 ONS Oral Chemotherapy Online Program and Oral Chemotherapy Toolkit
- Moore S., Brandt M.L. (2010). Adherence to oral therapies for cancer: helping your patients stay on course toolkit. Oncology Nursing Society.

Pretreatment Evaluation

- Labs and imaging studies are needed for baseline evaluation and dosing of medications
- Evaluation of patient and home environment to give the best chance for compliance and efficacy
- Review of current medications for possible drug interactions.
- Assuring the patient understands their regimen/plan

Take careful and thorough history

*** ASK ABOUT SIDE EFFECTS AT EACH VISIT ***

What are the symptoms - describe in detail :

onset, timing, intensity, location, frequency, duration, radiation (pain), alleviating/aggravating factors

- Compare to past symptoms – worse, better, same
- Also ask caregiver's input – especially helpful if patient has memory issues

Pomalidomide

- Exact mechanism is unclear; may be related to immunomodulatory, antiangiogenic and anti-inflammatory properties
- Indicated for MM in pts who have had at least 2 prior therapies – and progression of disease within 60 days of completing last therapy
- Starting dose 4mg po daily on days 1-21/28 day cycle 2 hours before or 2 hours after a meal
- If in combination with Dexamethasone 20-40mg days 1-8-15-22/28 day cycle

Pomalidomide SE

- Hepatotoxicity: including fatalities. Monitor LFTs monthly
- Hypersensitivity reactions: angioedema and severe dermatologic reactions have been reported. Discontinue for angioedema or severe dermatologic reactions.
- Tumor lysis syndrome: Monitor patients at risk and take appropriate precautions.
- Thromboembolism, neutropenia, anemia, constipation/diarrhea, nausea/vomiting, dyspnea, URI, back pain, edema, neuropathy
- Avoid co-administration of strong CYP1A2 inhibitors (Cipro) or reduce dose of pomalidomide

Lenalidomide

- Exact mechanism is unclear but may be related to immunomodulatory, antiangiogenic, or antineoplastic properties
- For use with MM with Dex or transfusion-dep anemia 2/2 MDS
- 25mg capsule po daily 1-21/28 day cycle
- Dose adjusted for CrCl < 60ml/min.
- For patients with del 5q myelodysplastic syndrome, monitor CBC weekly for 1st 8 weeks then monthly thereafter.

Lenalidomide SE

- Significant increased risk of DVT, PE, MI, CVA in pts with MM on lenalidomide and dex so anti-thrombotic prophylaxis
- Hepatotoxicity: monitor LFT
- TLS: monitor pts at high risk
- Cutaneous reactions including fatalities: angioedema, Steven's Johnson's syndrome, toxic epidermal necrolysis
- SE: diarrhea, fatigue, anemia, constipation, neutropenia, leukopenia, peripheral edema, insomnia muscle cramps/spasms, back pain, nausea, pyrexia, URI, bronchitis, rash, dizziness, dyspnea, tremor, decreased appetite, headache

Bosutinib

- BCR-ABL Tyrosine kinase inhibitor – causes apoptosis
- Newly diagnosed chronic phase Ph+ CML: 400mg tablets po once daily with food
- Ph+ CML with resistance to prior therapy: 500mg tablet po daily with food
- SE: HA, diarrhea, nausea/vomiting, abdominal pain, thrombocytopenia, anemia, neutropenia, rash, pyrexia, fatigue, increased ALT and AST (LFTs monthly for first 3 months), edema, pericardial effusion
- Avoid grapefruit juice, PPIs

Acalabrutinib

- Small molecule Bruton tyrosine kinase inhibitor – inhibits malignant B-cell proliferation
- Mantle cell lymphoma who have received one prior therapy
- 100mg capsule Q12 hours with water and with/without food

- Do not use with PPIs
- Stagger dosing with H2 receptor blockers and antacids

Acalabrutinib SE

- Anemia, thrombocytopenia, neutropenia, hemorrhage, atrial fib, HA, diarrhea/constipation, nausea/vomiting, abdominal pain, fatigue, myalgia, bruising, rash
- Monitor CBC monthly during treatment

Enasidenib

- Small molecule inhibitor of isocitrate dehydrogenase 2
- Relapsed or refractory AML
- 100mg tablet orally once daily with/without food
- Labs including CBC with diff, BMP, Ca, PO₄, uric acid baseline and every 2 weeks for 3 mos.
- **BLACK BOX WARNING** that adverse reaction of differentiation syndrome can occur

Enasidenib SE

- Differentiation Syndrome (tx with corticosteroid therapy). Symptoms are fever, dyspnea, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, lymphadenopathy, bone pain and hepatic, renal, or multi-organ dysfunction.
- Nausea, vomiting, diarrhea, anorexia, leukocytosis, elevated bilirubin, hypokalemia or hypophosphatemia

Midostaurin

- Multikinase inhibitor – causes apoptosis
- In combination with other meds for tx of adult patients with newly diagnosed AML whom are FLT3 mutation positive
- Aggressive systemic mastocytosis with associated hematologic neoplasm or mast cell leukemia
- 50mg capsule po twice daily with food on days 8-21 of each cycle of induction with cytarabine and daunorubicin and on days 8-21 of each cycle of consolidation with high dose cytarabine for AML.
- SE: Febrile neutropenia, myelosuppression, pneumonitis, nausea/vomiting, mucositis, headache, musculoskeletal pain, epistaxis, device related infection, hyperglycemia, URI, interstitial lung disease and QT prolongation
- Lab abnormalities: LFTs increased, Cr increased, hypernatremia, hypocalcemia, increased uric acid

Venetoclax

- Anti-apoptotic protein
- Chronic lymphocytic leukemia with 17p deletion who have received at least one prior therapy
- 20mg po daily for 7 days followed by ramp up dosing to the recommended daily dosing of 400mg daily. Taken with meal and water.
- SE: TLS, pneumonia, febrile neutropenia, hemolytic anemia, thrombocytopenia.
- Pyrexia, peripheral edema, hypokalemia, nausea, vomiting, headache, cough, back pain

Ibrutinib

- Selective inhibitor of Bruton's tyrosine kinase
- CLL who have received at least one other therapy, mantle cell lymphoma who have received one prior therapy, CLL/SLL, Waldenstrom's
- 420mg po daily (3x 140mg capsules daily) with glass of water
- SE: TLS, cytopenias (check CBC monthly)
diarrhea/constipation, nausea, bruising, URI, fatigue, musculoskeletal pain, rash, pyrexia, peripheral edema, arthralgia, stomatitis, sinusitis, dizziness

Idelalisib

- Small molecule inhibitor of phosphoinositide-3 kinase (PI3K) delta
- Relapsed CLL in combination with rituximab, relapsed follicular B-cell NHL who have received at least 2 prior therapies, relapsed SLL who have received 2 prior therapies
- 150mg tablet po BID with/without food
- SE: diarrhea, pyrexia, fatigue, nausea, cough, pneumonia, abdominal pain, chills, rash, neutropenia

Idelalisib SE

- Fatal/serious Hepatotoxicity-monitor hepatic function prior to and during tx.
- Fatal/serious severe diarrhea/colitis
- Fatal/serious pneumonitis
- Fatal/serious infections
- Fatal/serious intestinal perforation
- Severe cutaneous reactions
- Anaphylaxis

Ponatinib

- Multiple TKI inhibitor incl. BCR-ABL
- Adult patients with chronic phase, accelerated phase, or blast phase CML that is resistant or intolerant to prior TKI therapy or Ph+ALL that is resistant or intolerant to prior TKI therapy.
- 45mg po once daily tablet.
- SE: HTN, rash, abdominal pain, fatigue, headache, dry skin, constipation, arthralgia, nausea, pyrexia, cytopenias, lymphopenia, leukopenia

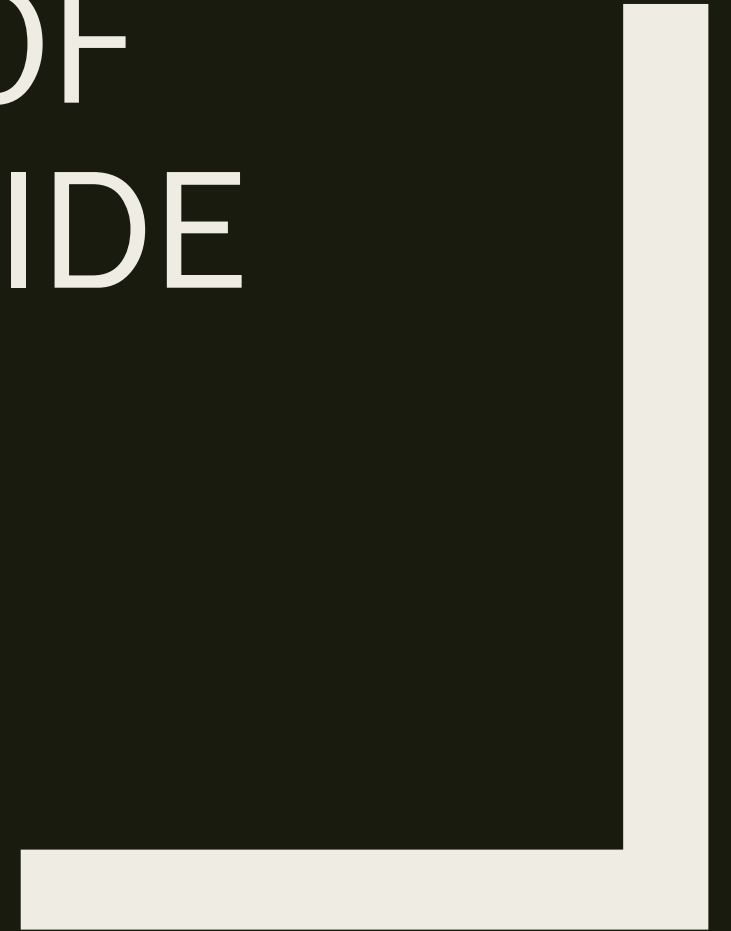
Ponatinib SE

- Arterial occlusion (stop drug)
- Venous thromboembolism
- Heart failure-monitor heart function
- Hepatotoxicity (monitor LFTs)
- HTN, Pancreatitis (monitor serum lipase monthly), neuropathy, ocular toxicity (eye exam at baseline and periodic during tx), fluid retention, cardiac arrhythmia, myelosuppression (CBC every 2 weeks for 3 months then monthly)-ANC >1000, plt >50,000, TLS, RPLS, compromised wound healing and GI perforation (interrupt therapy in pts undergoing surgery)

Ixazomib

- Proteasome inhibitor
- In combination with lenalidomide and dexamethasone for MM in patients who have received at least one prior therapy
- 4mg po capsule on days 1, 8,15/28 day cycle 1 hour before or 2 hours after meal (Hepatic impairment: reduce dose to 3mg, Renal impairment: reduce dose to 3mg)
- SE: thrombocytopenia (monitor monthly), GI toxicities (diarrhea, constipation, nausea, vomiting), peripheral neuropathy, peripheral edema, rash, hepatotoxicity, back pain

MANAGEMENT OF TOXICITIES AND SIDE EFFECTS



Cancer-related fatigue

- Defined as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and that significantly interferes with usual functioning.
- Tends to fluctuate over the course of treatment and may be present for months or years after cessation of treatment.
- Treat the underlying causes that we have measures for (anemia, comorbid conditions, emotional distress, nutritional deficiencies, sleep problems)

Nausea and vomiting

- Anticipatory: days/hours prior to chemo - benzos
- Refractory: any point in tx. Cycle – consider metoclopramide 20 mg QID (dopamine agonist) or Olanzapine 10 mg daily x 5 days (multiple receptors)
- Prochlorperazine 10mg po Q6hrs
- Ondansetron 8mg po Q8hrs (5-HT₃) (QTc interval prolongation)
- Rolapitant 200mg po on day 3 (NK-1 with 180 hr $\frac{1}{2}$ life)
- Aprepitant (NK-1 receptor antagonist) acute and delayed phase emesis
- Palonsetron (second generation 5-HT₃ receptor agonist) acute and delayed phase emesis

Bowels

■ Constipation

- *Miralax 17gms in 4-8 oz. water/juice daily-can increase to twice daily if needed*
- *Can add senokot-S 1-4 at HS if needed*

■ Diarrhea

- *Lomotil 2 tablets QID (maximum dose)*
- *Immodium 2 tablets QID (maximum dose)*

Peripheral Neuropathy

- Gabapentin up to 3600mg/24 hours divided TID
- Cymbalta 60mg po daily
- Lyrica 75mg po BID to begin
- Alpha lipoic acid 600mg po daily
- Compounded topical creams

Conclusion

- Assess for SE at every visit
- Always take a thorough history of symptoms
- Early interventions can prevent succession to toxicities

THANK YOU!

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