

# **Bothered Bowels, Sugar Spikes and Tingly Toes**

**BEING ON THE LOOKOUT FOR TREATMENT TOXICITIES**

# Disclosure

- No relationships with commercial interests

# Mitigating Potential Bias

- Not applicable

# References

- BC Cancer Agency Cancer Drug Manual
  - Drug monographs
  - Patient education handouts

<http://www.bccancer.bc.ca/health-professionals/professional-resources/cancer-drug-manual/drug-index>

- Myeloma Canada

[www.myeloma.ca](http://www.myeloma.ca)

# Learning Objectives

- List the common toxicities patients encounter while receiving treatment for Multiple Myeloma
- Identify which toxicities are associated with each drug class and why
- Describe how these toxicities are experienced
- Gather some assessment tools for toxicity identification

# Know Baseline Symptoms

## Disease Related

- Calcium elevation
- Renal dysfunction
- Anemia
- Bone pain
- Fatigue
- Infection
- Peripheral Neuropathy

## Treatment Related

- Myelosuppression
- Peripheral neuropathy
- Diarrhea/Bowel changes
- Fatigue
- Hyperglycemia
- Deep vein thrombosis
- Shingles

# Patient Assessments

- Know the individuals' disease
  - presentation of disease
  - baseline
- Know the co-morbidities
- Know the treatment plan
- Know the bloodwork
- **Know individual treatment toxicities**



# “Know Mr. CRAB”



- **C** = hypercalcemia
- **R** = renal insufficiency
- **A** = anemia
- **B** = bone lesions

# Treatment Modalities

- (1) Radiation
- (2) Bisphosphonates
- (3) Steroids
- (4) Chemotherapy/Alkylating agents
- (5) Proteasome Inhibitors
- (6) Immune modulators
- (7) Monoclonal Antibodies



# (1) Radiation Therapy

- KNOW if pt is experiencing bone pain at presentation
- Any fractures?
- LOCAL TREATMENT:
  - to damage myeloma cells
  - Pain control
  - Spinal cord compression
  - Solitary plasmacytoma
  - Post-surgical radiation

# Radiation Treatment Toxicities

- WHY?** Causes double stranded breaks in DNA
- Confined to anatomic area of treatment
  - Treatment variables affect tolerance
    - Radiation dermatitis
    - fatigue
  - Usually single #s, 5-10#s





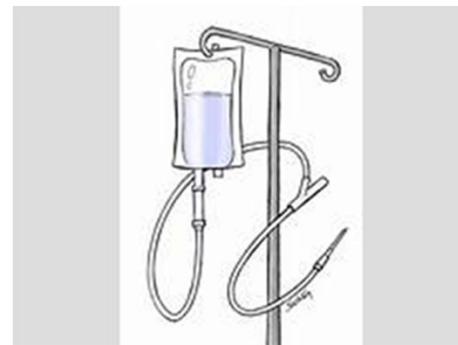
# Being on the Lookout



- **ASSESSMENT:**
  - Education: Late effects
  - Pain control
  - Acute flare/tissue swelling
  - skin assessment

## (2) Bisphosphonates

- Osteoclast and osteoblast dysregulation in Myeloma
- agents work by inhibiting osteoclastic activity
- Emergent use vs Therapeutic use
- **Zoledronic acid**
- **Pamidronate**



# Bisphosphonate Treatment Toxicities

- Flu like illness:
  - Arthralgias
  - Fatigue
  - Fever
  - Nausea
- Nephrotoxicity
- Hypocalcemia
- **Osteonecrosis of the jaw (ONJ)**





# Being on the Lookout

- **ASSESSMENT:**

- Understand baseline + comorbidities
- Lab review: Cr, Ca<sup>+</sup>, Alb, Cr Clearance re: dose
- Baseline dental exam ideal
- “pain, loose teeth, numb or heavy jaw”



# Oral Exam

- Look for open sores that don't heal
- Assess Oral hygiene
- Treat tooth or gum infections promptly
- Proper denture fit



# Osteonecrosis of Jaw

## (3) Systemic Glucocorticoids

- Have an antiinflammatory and an antimyeloma affect
- Steroids can be used alone or in combination
- **Prednisone**
- **Dexamethasone**

# Steroid Treatment Toxicities

- **WHY?** many systemic effects on many organ systems. Result largely from increased expression of regulatory and antiinflammatory proteins
- Frequency and severity of side effects related to respective dose and duration of therapy

# Steroid Treatment Toxicities

- Weight gain
- Skin thinning and purpura
- **Mood changes**
- Insomnia
- **Hyperglycemia**
- **Heartburn**
- Swelling/fluid retention
- Leg cramps
- Myopathy





# Being on the Lookout

- **ASSESSMENT:**

- Med review
- Patient education: hyperglycemia symptoms
- Monitor VS (BP) and weight
- Monitor bloodwork: glucose, lipids
- Activity level
- Discuss changes in mood
- Explore sleep hygiene

Date of Completion: \_\_\_\_\_ Name: \_\_\_\_\_ Date of Birth: \_\_\_\_\_



**1. Edmonton Symptom Assessment System (ESAS):**

Please circle the number that best describes:

1.	No pain	0	1	2	3	4	5	6	7	8	9	10	Worst possible pain
2.	Not tired	0	1	2	3	4	5	6	7	8	9	10	Worst possible tiredness
3.	Not nauseated	0	1	2	3	4	5	6	7	8	9	10	Worst possible nausea
4.	Not depressed	0	1	2	3	4	5	6	7	8	9	10	Worst possible depression
5.	Not anxious	0	1	2	3	4	5	6	7	8	9	10	Worst possible anxiety
6.	Not drowsy	0	1	2	3	4	5	6	7	8	9	10	Worst possible drowsiness
7.	Best appetite	0	1	2	3	4	5	6	7	8	9	10	Worst possible appetite
8.	Best feeling of wellbeing	0	1	2	3	4	5	6	7	8	9	10	Worst possible feeling of wellbeing
9.	No shortness of breath	0	1	2	3	4	5	6	7	8	9	10	Worst possible shortness of breath
10.	Other problem:	0	1	2	3	4	5	6	7	8	9	10	

**2. Canadian Problem Checklist:**

Please check all of the following items that have been a concern or problem for you in the past week including today:

<b>Emotional:</b>	<b>Practical:</b>	<b>Informational:</b>
<input type="checkbox"/> Fears / Worries	<input type="checkbox"/> Work / School	<input type="checkbox"/> Understanding my illness and/or treatment
<input type="checkbox"/> Sadness	<input type="checkbox"/> Finances	<input type="checkbox"/> Talking with the health care team
<input type="checkbox"/> Frustration/Anger	<input type="checkbox"/> Getting to and from appointments	<input type="checkbox"/> Making treatment decisions
<input type="checkbox"/> Changes in appearance	<input type="checkbox"/> Accommodation	<input type="checkbox"/> Knowing about available resources
<input type="checkbox"/> Intimacy / Sexuality	<input type="checkbox"/> Child / Family / Elder care	<input type="checkbox"/> Quitting smoking
<input type="checkbox"/> Coping		<input type="checkbox"/> Medications
<input type="checkbox"/> Change in sense of self	<b>Physical:</b>	
<input type="checkbox"/> Loss of interest in everyday things	<input type="checkbox"/> Concentration / Memory	<b>Social/Family:</b>
	<input type="checkbox"/> Sleep	<input type="checkbox"/> Feeling a burden to others
<b>Spiritual:</b>	<input type="checkbox"/> Weight	<input type="checkbox"/> Worry about family / friends
<input type="checkbox"/> Meaning / Purpose of life	<input type="checkbox"/> Constipation / Diarrhea	<input type="checkbox"/> Feeling alone
<input type="checkbox"/> Faith	<input type="checkbox"/> Swallowing	<input type="checkbox"/> Relationship difficulties
	<input type="checkbox"/> Falling / Loss of balance	

**Additional Question:**

Have you smoked in the past six weeks?  Yes  No

\*DRAFT November 2011, adapted from: Cancer Journey Action Group, Canadian Partnership Against Cancer's recommendations for screening for distress, May 2009

## (4) Chemotherapy

- Reduce the number of plasma cells in the bone marrow and the proteins they produce
- cycles of alternating treatment and rest periods
- Usually given in combination with steroids
- **Cyclophosphamide**
- **Melphalan**



# Chemotherapy Treatment Toxicities

- Myelosuppression
- Infection
- Mouth sores
- GI disturbance
- Bowel changes
- Hemorrhagic cystitis
- Hair loss/thinning



# Being on the Lookout

- **ASSESSMENT:**
  - Monitor bloodwork: CBC, Cr, LFTs
  - Rule out infection
  - Weight prior to every cycle
  - Urinary changes
  - Hydration: aim for 2L/day
  - Diet review: grapefruit juice + cyclo

Date of Completion: \_\_\_\_\_ Name: \_\_\_\_\_ Date of Birth: \_\_\_\_\_



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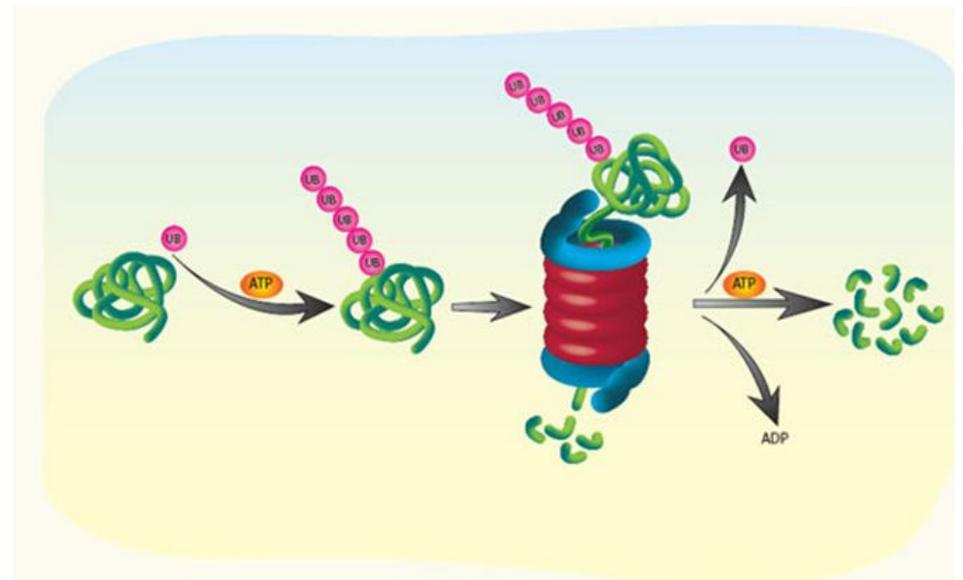
\*DRAFT November 2011, adapted from: Cancer Journey Action Group, Canadian Partnership Against Cancer's recommendations for screening for distress, May 2009

## (5) Proteasome Inhibitors “Mibs”

- block the activity of proteasomes
- **Bortezomib (SQ)**
- **Carfilzomib (IV)**
- **Ixazomib (PO)**



Proteasome



# “Mibs” Treatment Toxicities

## **BORTEZOMIB**

- **Peripheral Neuropathy**
- Fatigue
- Nausea
- Diarrhea
- Thrombocytopenia
- Hypotension
- **Herpes Zoster Reactivation**

## **CARFILZOMIB**

- Fatigue
- Nausea
- Anemia/thrombocytopenia
- Dyspnea
- Diarrhea
- Fever
- Cardiac toxicity
- Herpes Zoster Reactivation



# Being on the Lookout



- **ASSESSMENT:**

- self-report PN Assessment Tool prior to each cycle
- Sensory changes: sensation, reflexes
- Motor changes: strength, Check gait
- check safety strategies
- Monitor bloodwork: CBC, Cr, LFTs, bilis
- Diet review: avoid green tea
- Skin check: rashes, Bortezomib injection site
- Antiviral prophylaxis



# Herpes Zoster

# A Word about Peripheral Neuropathy

- Multifactorial: disease/comorbidity/treatment
- Nerve cells are more sensitive
- Sensory nerves at increased risk
- Onset and resolution of symptoms variable
- “decreased sensation”
- “burning” or “tingling” in the hands and feet
- “dexterity changes”
- “feel imbalanced”



## Typical Peripheral Neuropathy Symptoms

- ✓ Loss of Feeling
  - ✓ Freezing
  - ✓ Tingling
  - ✓ Hyper Sensitivity
  - ✓ Sharp Jabbing Pain
  - ✓ Burning Sensation
  - ✓ Numbness
- 

<https://www.therapysocks.com/images/PNS600b.jpg>



# Neurotoxicity Assessment Tool

	Not at all	A little	Some what	Quite a bit	Very much
I have numbness or tingling in my hands	0	1	2	3	4
I have numbness or tingling in my feet	0	1	2	3	4
I feel discomfort in my hands	0	1	2	3	4
I feel discomfort in my feet	0	1	2	3	4
I have joint pain or muscle cramps	0	1	2	3	4
I feel weak all over	0	1	2	3	4
I have trouble hearing	0	1	2	3	4
I get a ringing or buzzing in my ears	0	1	2	3	4
I have trouble buttoning buttons	0	1	2	3	4
I have trouble feeling small objects	0	1	2	3	4
I have trouble walking	0	1	2	3	4

<http://img.medscape.com/fullsize/migrated/574/717/colson.fig2.gif>



# Grading Peripheral Neuropathy

- **Grade 1** paresthesia and/or loss of reflexes, without pain or loss of function
- **Grade 1 with pain or Grade 2** interfering with function, but not with activities of daily living
- **Grade 2 with pain or Grade 3** interfering with activities of daily living
- **Grade 4** permanent sensory loss that interferes with function

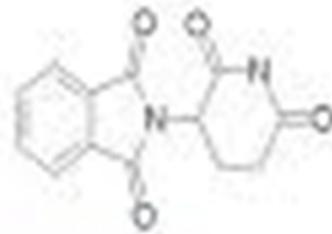
[http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Lymphoma-Myeloma/MYBORPRE\\_Protocol\\_1Oct2016.pdf](http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Lymphoma-Myeloma/MYBORPRE_Protocol_1Oct2016.pdf)

## (6) Immune Modulators

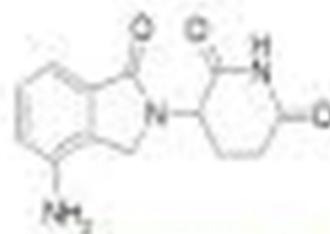
- -"IMiDs"
- Interfere with the underlying processes that promote the growth and reproduction of myeloma cells
- Impact the functioning of the immune system
- **Thalidomide**
- **Lenalidomide**
- **Pomalidomide**

# IMiDs

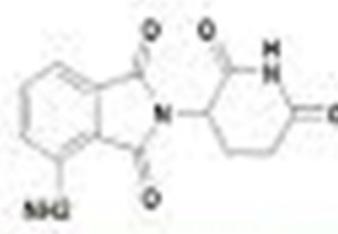
## IMiD Structures



**Thalidomide**  
100–200 mg/d  
Neuropathy  
Constipation  
Sedation  
DVT



**Lenalidomide**  
15–25 mg/d  
Myelosuppression  
Skin rash  
DVT



**Pomalidomide**  
2–4 mg/d  
Myelosuppression

Side effects

Potency



# Thalidomide - Teratogenicity



1. McBride WC: Thalidomide & Congenital Abnormalities. Lancet. 1961;11:1358
2. Lenz W: Thalidomide & Congenital Abnormalities. Lancet. 1962;1:45

# IMiD Treatment Toxicities

## LENALIDOMIDE

- Myelosuppression
- Skin rash
- **DVT**
- Bowel changes
- Fatigue
- **Teratogenicity**
- **Hypothyroidism**
- Hepatitis B Reactivation
- **Secondary Malignancies**

## POMALIDOMIDE

- Myelosuppression
- Fatigue
- DVT

# Venous Thromboembolism

- individual risk of developing a VTE
- appropriate thromboprophylaxis
- Risk Factors:
  - Obesity
  - Immobility
  - Recent surgery
  - Comorbidities (cardiac, diabetes, renal etc)



# Being on the Lookout

- **ASSESSMENT:**
  - Understand risk category + contraception plan
  - Monitor bloodwork: CBC, Cr, LFTs, TSH
  - Rule out infection
  - Bowel regimen
  - Skin check
  - VTE assessment



# VTE Assessment

## **DVT:**

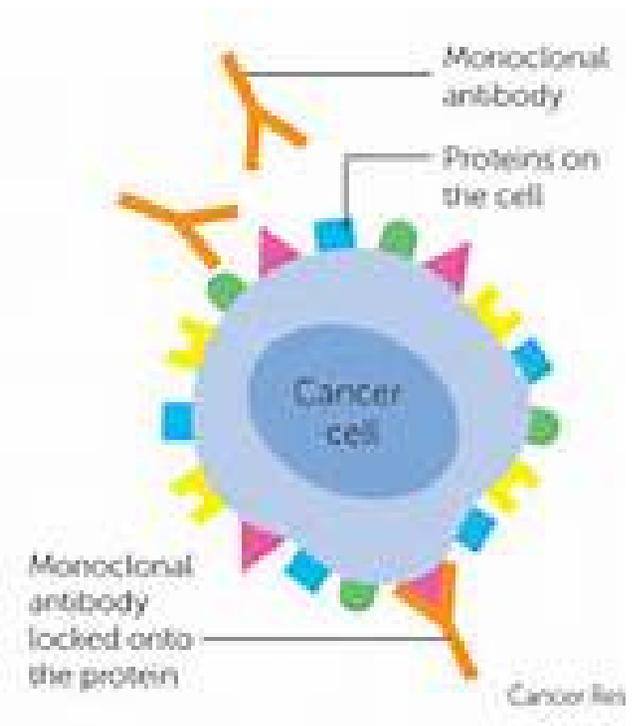
- Swelling
- Erythema
- Pain

## **Pulmonary Embolism:**

- Chest pain
- SOB
- Tachycardia
- Hemoptysis

# (7) Monoclonal Antibodies

- -“MABs”
- Glycoprotein specific
- **Denosumab: RANKL**
  - Inhibits osteoclast formation, Function + survival
- **Daratumumab: CD38**
  - inhibits cell growth and can lead to cell lysis



# “Mabs” Treatment Toxicities

## DENOSUMAB

- Flu like illness:
  - Arthralgias, Fatigue
  - Fever , nausea
- Osteonecrosis of the jaw (ONJ)
- Nephrotoxicity
- Hypocalcemia, anemia

## DARATUMUMAB

- Severe infusion reaction
- Respiratory symptoms
- Myelosuppression
- Fatigue
- Pyrexia
- Infections
- Arthralgias/myalgias



# Being on the Lookout

- **ASSESSMENT:**
  - Ensure baseline T+S
  - allergic response
  - Comorbidity review (COPD)
  - Med review: ensure antiviral prophylaxis



# Infection

- Myeloma pts already at increased risk for infection
- **WHY?** Suppression of normal plasma cell function and therapy induced
- **ASSESSMENT:**
  - ROS
  - Episodes of fever/chills
  - Immunizations: yearly flu, pneumococcal

# Take Home Message

- Know Mr. CRAB!
- Remember prophylaxis:  
viral + dvt
- Safety paramount with IMIDs
- Talk about peripheral neuropathy at every encounter!



# Questions

