

Myeloma Drug Access & Supportive Care Potpourri

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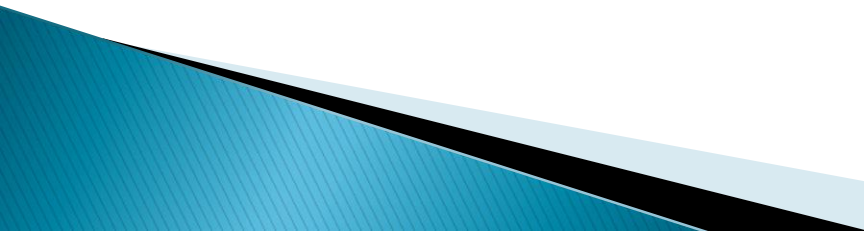
Disclosures

- ▶ Advisory board participant for lenalidomide in 2013

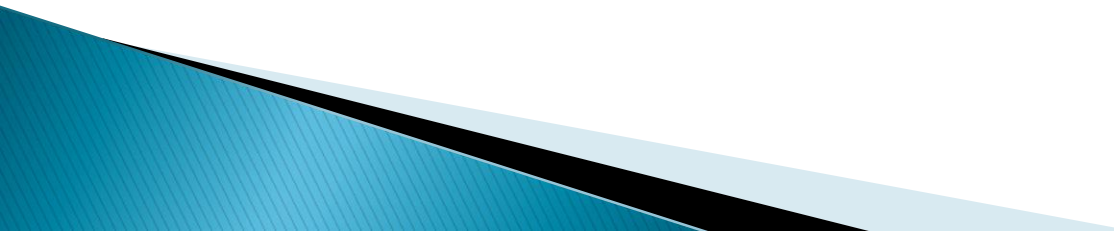
Mitigation of potential bias

- ▶ Not applicable

Learning objectives

- ▶ Understand the role of prophylaxis for herpes zoster
 - ▶ Be able to explain the role of venous thromboembolism (VTE) prophylaxis in patients taking immunomodulatory drugs
 - ▶ Discuss management, monitoring and dosing of bisphosphonates
 - ▶ Be able to identify the hallmark features of osteonecrosis of the jaw
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Learning objectives continued

- ▶ Discuss drug access issues for patients who live outside of Winnipeg
 - ▶ List the 3 different categories for Revaid patients
 - ▶ Discuss ways to minimize delays in drug access
 - ▶ Take a sneak peak of future drugs anticipated in multiple myeloma
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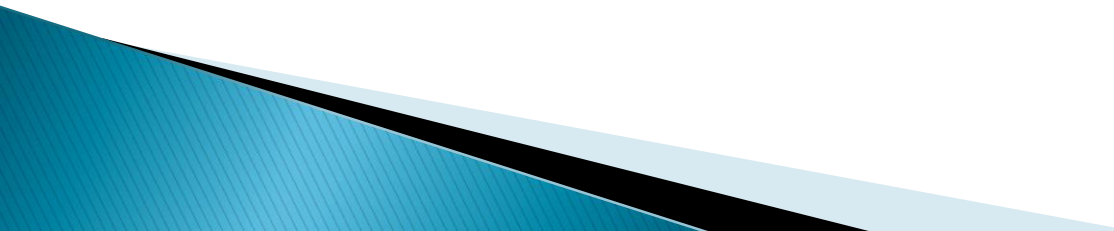
Herpes zoster prophylaxis

- ▶ 73 year old female presents to CancerCare Manitoba with newly diagnosed IgG multiple myeloma. The hematologist wants her to receive CBD (cyclophosphamide, bortezomib and dexamethasone) for 9 cycles.
- ▶ What supportive medication must be prescribed to this female?

Rates

- ▶ Result: Increased incidence of herpes zoster occurring on treatment was significantly higher in the bortezomib group (13%) compared to dexamethasone (5%).

Recommendations

- ▶ Start antiviral prophylaxis on day 1 of bortezomib-based regimen.
 - ▶ Valacyclovir 500mg orally daily
 - ▶ Dose adjusted to 500mg orally q2days in patients with renal function < 30 mL/min.
 - ▶ Patients continue taking their antiviral for 4 weeks after their last dose of bortezomib.
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Venous thromboembolism prophylaxis

- ▶ 71 year old female with IgG myeloma returns for a follow-up visit to CancerCare Manitoba. She sees the hematologist and is told she has relapsed disease. The doctor wants to start her on Rd (Revlimid and dexamethasone weekly).
- ▶ What should she be given for anticoagulation?

Background

- ▶ Immunomodulators (thalidomide, lenalidomide and pomalidomide) increase the risk of venous thromboembolic events (VTE)
- ▶ Adding dexamethasone to an immunomodulator increases the VTE risk.
- ▶ A risk–adapted strategy is used to select appropriate anticoagulation agent for patients on imid and steroid combination.

High risk category

Clinical factors:

- 1) Imid and previous personal history of VTE

Recommendation:

Prophylactic dose of low-molecular weight heparin or warfarin adjusted for an INR intensity target 2–3.

Intermediate risk

- ▶ IMiD and any VTE risk factors including (but not limited to):
 - Strong family history of VTE or known thrombophilia
 - Obesity
 - Prolonged immobilization
 - Additional medications with VTE (estrogens, Erythropoietin)

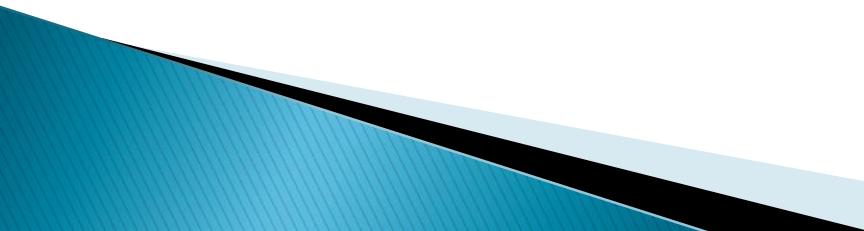
Intermediate risk continued

- 1) Low bleeding risk: Prophylactic dose of low molecular weight heparin or adjusted warfarin for INR of 2 to 3
- 1) High bleeding risk: Prior uncontrolled bleeding, platelets less than $80 \times 10^9/L$, difficult to control warfarin: recommend enteric coated aspirin 81 mg once daily

Low risk

- ▶ IMiD therapy is the only risk factor
- ▶ Recommend: Enteric coated aspirin 81 mg once daily

Bisphosphonates

- ▶ 56 year old male presents to myeloma clinic with IgA myeloma. The patient also has osteolytic lesions present on skeletal survey.
 - ▶ Should a bisphosphonate be given?
 - ▶ If so, how often and duration of treatment?
 - ▶ What should a patient be told about dental care during bisphosphonate treatment?
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Bisphosphonates

- ▶ The cause of bone destruction by osteolytic lesions is caused by two separate events:
- ▶ 1) Rapid growth of myeloma cells inhibits normal bone-forming cells and damages bone.
- ▶ 2) Osteoclast activity is increased and causes bone loss.

Recommendations

- ▶ For adult patients with active plasma cell myeloma, BP therapy should be administered to those with overt lytic bone destruction and/or vertebral and non-vertebral fractures from osteopenia as documented by imaging modalities.
- ▶ It is reasonable to start intravenous bisphosphonates in patients with multiple myeloma who do not have lytic bone disease if there is evidence of osteopenia or if they will be receiving therapy for their myeloma.

Recommendations

- ▶ Currently, pamidronate and zoledronic acid are the BPs used in patients with multiple myeloma
- ▶ Zoledronic acid is convenient as infusion is given over 15 minutes.
- ▶ Patients with CrCl less than 30 mL/min should not receive zoledronic acid. Those patients should receive pamidronate.

Recommendations

- ▶ Patients who have obtained less than a VGPR and/or those with active bone disease, further BP therapy at the 2 year mark needs to be assessed.
- ▶ After 2 years, patients without active bone disease can discontinue bisphosphonate therapy.
- ▶ For patients who have continued active bone disease after 2 years of bisphosphonate therapy, further BP therapy is recommended at the discretion of the prescribing physician.

Recommendations

- ▶ In patients who experience relapse with new bone disease, BP therapy should be reinstated.
- ▶ BP therapy should be discontinued in patients who experience osteonecrosis of the jaw.

Renal function dosing – zoledronic acid

Creatinine clearance	Zoledronic acid dose
Greater than 60 mL/minute	4 mg
50 to 59 mL/minute	3.5 mg
40 to 49 mL/minute	3.3 mg
30 to 39 mL/minute	3 mg
Less than 30 mL/minute	Not recommended

Recommend to monitor serum creatinine, calcium and albumin within 7 days before each zoledronic acid dose

Renal function dosing – pamidronate

Creatinine clearance	Recommended dose
30 mL/min or greater	90 mg over 2 hours
Less than 30 mL/min	30 to 90 mg over 4 hours

Recommend to check serum creatinine, calcium and albumin within 7 days before each pamidronate dose

Recommendations

- ▶ Osteonecrosis of the jaw can occur with bisphosphonates.

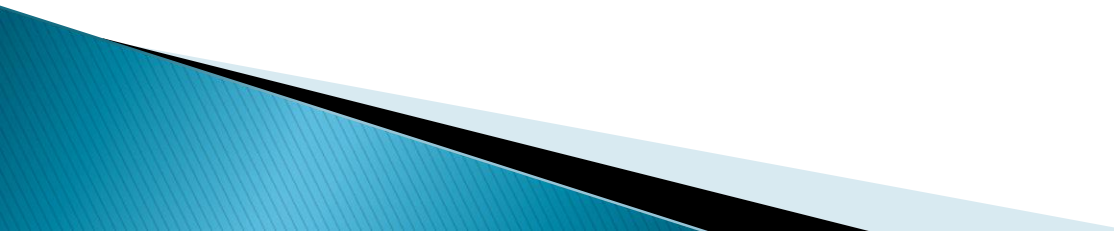
Recommendations:

- Comprehensive dental examination should be considered for all myeloma patients before commencing bisphosphonate therapy.
- Active oral infections should be treated and sites of high risk of infection should be eliminated.

Dental procedures

- ▶ While on therapy, patients should maintain excellent oral hygiene, avoid invasive dental procedures if possible and maintain yearly dental evaluations.

Revaid

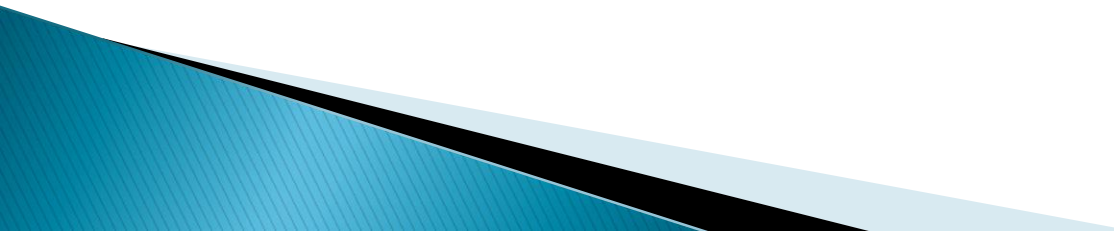
- ▶ Controlled distribution program.
 - ▶ Under this program, only prescribers and pharmacists registered with the program are able to prescribe and dispense the product.
 - ▶ Thalidomide, lenalidomide and pomalidomide can only be dispensed to patients who are registered and meet all the conditions of the Revaid program.
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Revaid

Patient Gender		
Male	Female*	
	<p>Has the patient naturally had a menstrual period in the last 12 months?</p>	<p>Does the patient have any one of the following?</p> <ul style="list-style-type: none"> • Patient has not had a menstrual period in > 12 consecutive months • Patient has had a hysterectomy • Patient has had a bilateral salpingo-oophorectomy • Patient has premature ovarian failure confirmed by a gynecologist • Patient is XY genotype • Patient has Turner syndrome and is unable to conceive • Patient has uterine agenesis
	YES	YES
Classify as a male patient	Classify as a Female of Child-Bearing Potential (FCBP)	Classify as a Female Not of Child-Bearing Potential (FNCBP)

Adopted from the Revaid forms

Revaid

- ▶ Only RevAid registered physicians can prescribe lenalidomide.
 - ▶ Hematologists at CCMB have RevAid and therefore are the ones that prescribe lenalidomide and pomalidomide.
 - ▶ Only RevAid registered pharmacies can dispense lenalidomide and pomalidomide.
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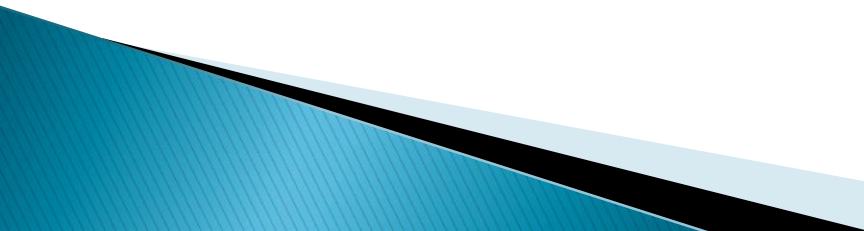
New drugs

- ▶ Three new drugs coming out for multiple myeloma
 - 1) Carfilzomib (intravenous)
 - 2) Ixazomib (oral)
 - 3) Daratumumab (intravenous)

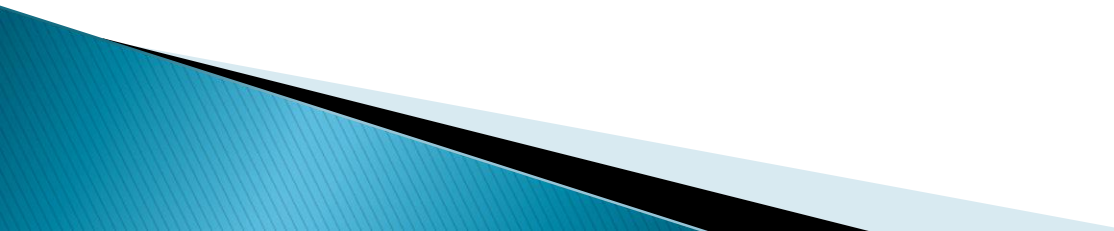
N.B. – different combinations



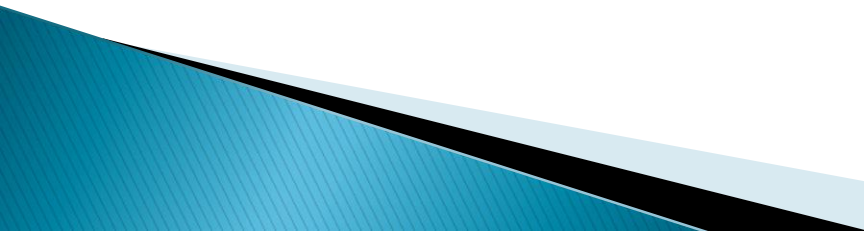
Carfilzomib

- ▶ A cousin to bortezomib
 - ▶ Given intravenously
 - ▶ Will be given in combination with lenalidomide and dexamethasone or dexamethasone alone for relapsed multiple myeloma
 - ▶ Not yet funded in Manitoba
 - ▶ All patients require hydration pre and post carfilzomib for cycle 1
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Ixazomib

- ▶ Cousin to bortezomib
 - ▶ Orally
 - ▶ In combination with lenalidomide and dexamethasone
 - ▶ Side effects: rash and peripheral neuropathy
 - ▶ Not funded in Manitoba as of yet
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Daratumumab

- ▶ Intravenous
 - ▶ Antibody against CD38 (present on myeloma cells)
 - ▶ Given as single-agent
 - ▶ Being studied in combination with lenalidomide and dexamethasone or bortezomib and dexamethasone
 - ▶ Relapsed multiple myeloma
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Questions / Discussion

