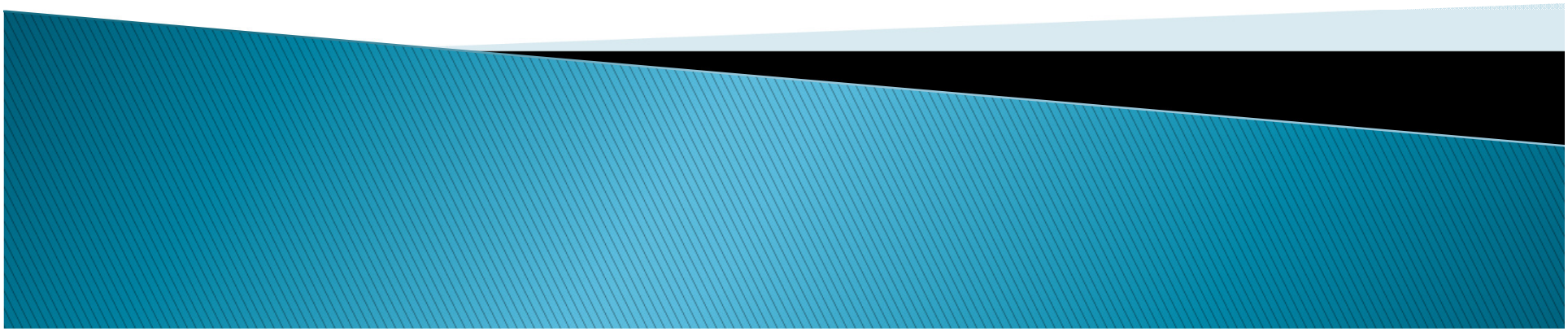
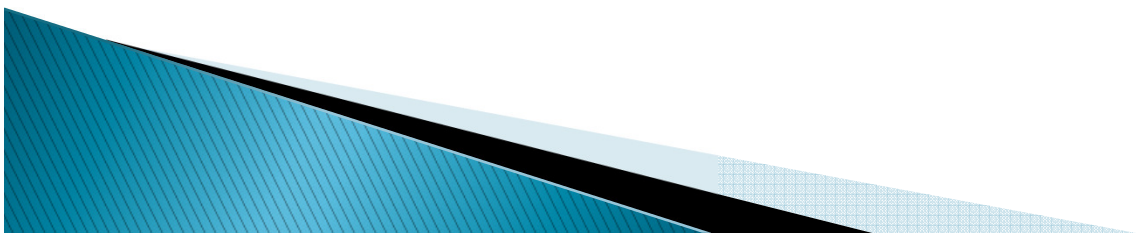
Myeloma Education Day

Dr. Vi Dao



Disclosures for Vi Dao

- Speakers Bureau/Honoraria:
  - Celgene
  - Pfizer

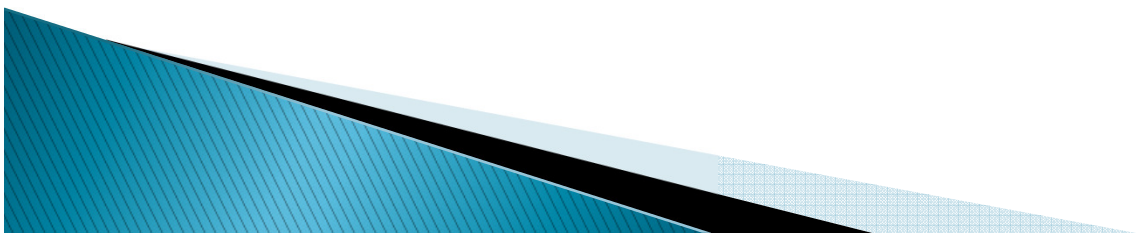


Mitigating potential bias

- All honoraria was donated to CCMB Professional Association Development Fund

Learning objectives

1. To be aware of the delegated responsibilities in the shared care model of the myeloma patient
2. To identify emergent (same day), urgent (same week) versus routine issues that needs to be communicated to the hematologist
3. To work through example of cases that illustrated communication issues and how to resolve them



Myeloma Journey: From referral to clinic visit (a 4 week process)

CCMB Referral Office to process referral
Fax: 204 786 0621
Phone: 204 787 2176

*Processing of referral may be delay if we are unable to get information **to determine the priority** of referral

~ 2 weeks

1. **Processed chart gets assign to Disease specific group (DSG)**
2. **MD will triage & chart gets assign to a clinic**

*Triage process usually occurs once per week unless emergent cases

~ 2 weeks

Clinic visit

*Myeloma Clinics:

1. Tuesday (Dr. Dao, Dr. Rimmer)
2. Wednesday (Dr. Minuk)
3. Friday (Dr. Kotb)

Triaging priorities in Myeloma Clinic

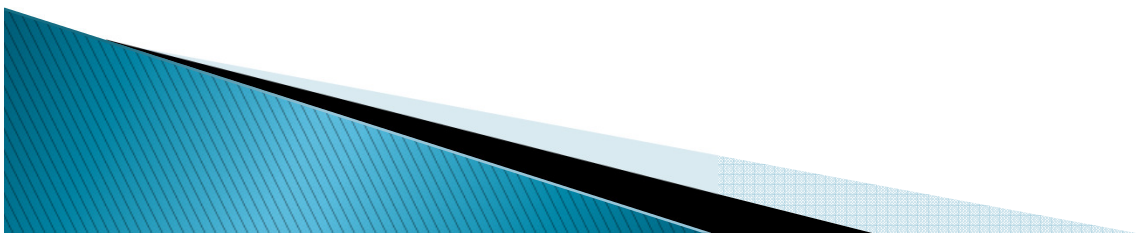
Priority	Examples	Goal/Time line

Emergent	• Bony involvement:
	  • Spinal cord compromise
	  • Unstable lesion with risk for pathological fracture
	  • Pain (plasmacytoma/lytic lesion)
	• Laboratory involvement:
	  • Hypercalcemia (>3mmol/L)
	  • Acute renal failure (needs serial creatinine values)
	  • Anemia is <u>not</u> considered Emergent as symptoms can be readily supported with transfusion *(but please let us know if transfusion has been arranged)*
		▪ Same day phone advice (Referral to surgery or radiation oncology)
		▪ Empiric treatment (bisphosphonate, steroid)
		▪ Further investigations with CT/MRI/Renal US or Blood/Urine tests
		▪ Clinic <1 week
		▪ May need to be hospitalized

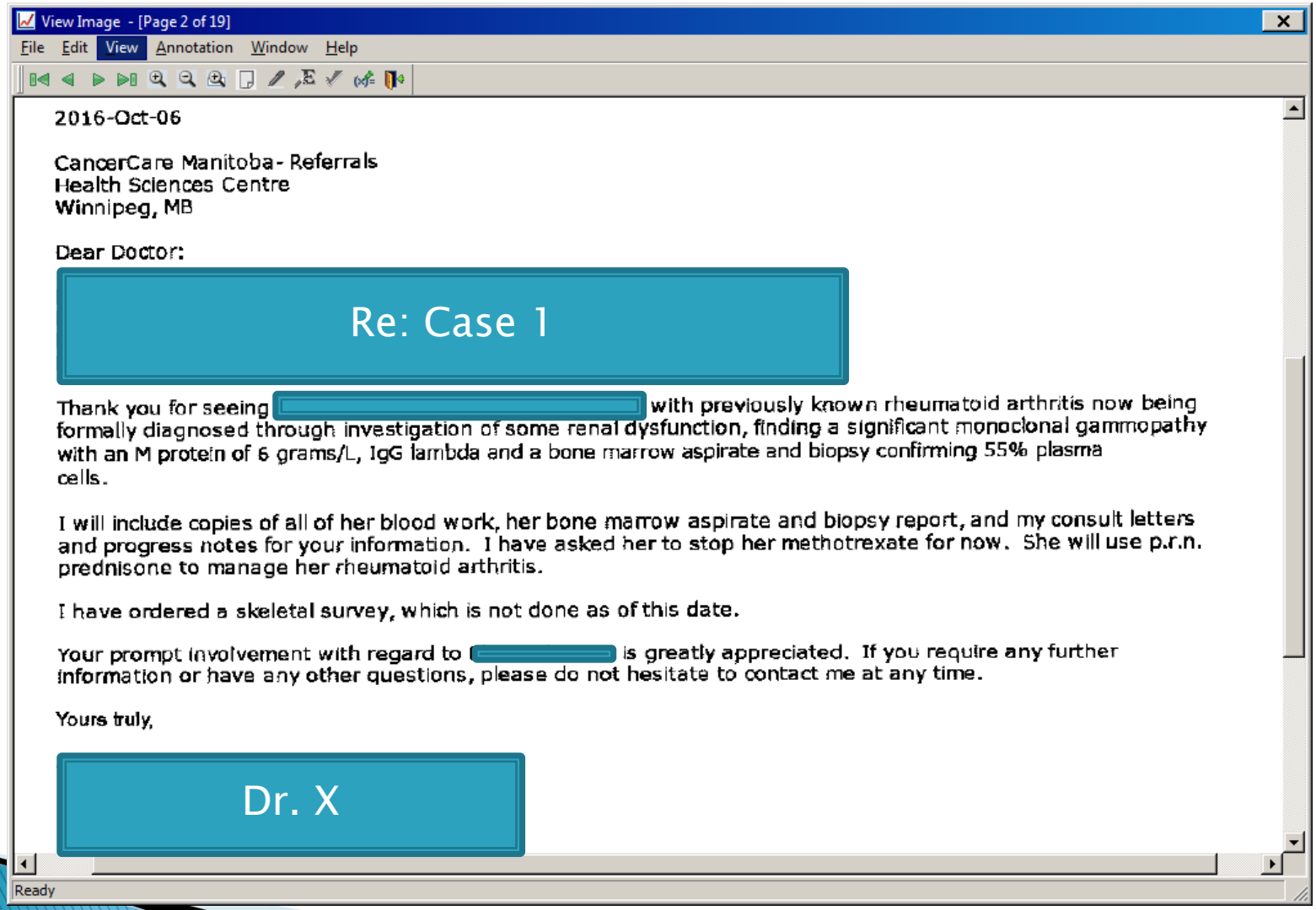
Urgent	All symptomatic or suspected myeloma that does not meet criteria for "emergent" as above	• To clinic in 2 weeks
Routine	• Asymptomatic (smoldering) myeloma • MGUS and query myeloma?	• To clinic within 4 weeks (or when results available)

What happens in the myeloma clinic?

- A team approach (~1 hour for new patient)
  - Including clerical to ensure all baseline investigations are completed with results to clinic
  - Nursing & pharmacist assessment
  - Clinical assistant/MD assessment with H&P dictated and plan outlined (using Physician Order Entry and/or Order Check List system)
- Bone marrow if needed should be done within 1 week (~30minutes time spot)
  - Same day if possible for rural patients, otherwise reschedule for a different day
- Appointment via TeleHealth is possible if requested and appropriate
- Treatment (if planned) should be scheduled within 2 weeks
  - Exception: to treat hypercalcemia or if emergent treatment is warranted (<24 hours)
- Follow up established (if required)



What does a great referral look like?



The components of the referral:

- It is legible & contains important demographics
  - Date of referral: Oct 6, 2016
  - Name of patient: Case 1
  - Name of referral doc: Dr. X
- It includes relevant medical information
  - RA on MTX
  - Old clinic notes & old labs
    - Hb 100
  - Info on why the investigation was initiated & results
    - "some renal dysfunction": creatinine 126
    - SPEP IgG lambda: 6g/L
    - Bone marrow: 55% plasma cell
- It includes the plan of Dr. X
  - "skeletal survey is ordered but no result"
  - "asked her to stop MTX" and "use Pred prn"

Great features

- Other important demographics
  - Name of GP (if not the same as the referring MD)
  - Name of relevant specialists involved in patient's care (Rheumatologist, Endocrine etc)
- The referring MD requested "prompt" involvement but it would be even more helpful to the referral if MD explain the specific concerns:
  - Concern regarding patient's symptoms: pain?
  - Concern regarding labs: renal failure, hypercalcemia, cytopenia etc

Features to improve upon

Case 1: How to get your referral seen earlier?

- Dr. X is not this patient's GP (although registered as GP in CCMB)
  - The patient's true GP may never get any notes from CCMB
- This referral was received at CCMB Referral Office on Oct 06, 2016 but not processed until Oct 12.
- *How can this processing time be shorten within the Referral Office?*
- Answer:
  - *by helping the Referral Office to correctly identify the priority of this referral*
  - this referral was *processed* immediately as it did not meet the emergent criteria
  - It may not be triage until another 7 days later

Case 1: How to shorten the wait time to the clinic visit?

- Answer: UPDATE YOUR REFERRAL with important changes in the patient's status
- With this referral NOT meeting criteria for "emergent" → would be have seen in 2 weeks
  - UNTIL review of most recent blood work on eChart by Referral Office done on Oct 12, 2016 showed: Hb 99 WBC 12 Plt 239
  - **Creatinine increased from 121 to 741**
- Now referral met "emergent" criteria at the time of triage and as such, was triaged on same date (instead of 7 days later)
- We find out that patient has been admitted for the last 4 days with vomiting and dehydration
- As such, request was made for the attending MD to PAGE the myeloma triage MD to discuss case. WHY?
  1. To discuss the etiology of the acute on chronic renal failure

     DDx: Prerenal ARF, hypercalcemia, cast nephropathy, post renal obstruction etc…
     - Add to ARF work up: calcium levels, Renal US, Urine tests
     - May initiate empiric treatment such as steroid while work up is pending, Nephrology involvement
  2. Advised baseline myeloma work up:
     - Free light chain assay and 24 hour urine tests to capture baseline data for future response assessment
  3. Patient was assigned to clinic visit Oct 19, 2016 via TH (7days as opposed to 14 days) → started chemotherapy on October 27, 2016

Case 2: Incomplete referral

18 July 2016

Appt. time: please arrange

This 73 years old woman was accidently hit by a TV remote control to her right forearm. Then she noticed a swelling on her arm. X-ray reported primary soft tissue malignancy with invasion the of adjacent bone. MRI is requested.

Your early attention to see her is very much appreciated.

Xray:

CONCLUSION: Large 4.2 x 9.4 cm soft tissue mass at the proximal right forearm, palmar aspect, as described above. There are extensive osseous changes involving the proximal to mid radial and ulnar shafts as well as the distal humeral shaft as described above. These findings are concerning for a possible primary soft tissue malignancy with invasion of the adjacent bone and/or possible bony metastatic involvement. It is recommended that a follow-up MRI of the right arm be performed for further evaluation.

The components of the referral:

- It is legible & contains important demographics
  - Date of referral
  - Name of patient
  - Name of referral doc
- It includes the problem (right arm swelling) and concerning xray finding
- Patient is needing an MRI and asking urgent intervention

Great features

- No mention of PMhx and other medications
- No mention how patient is doing (review of system)
  - ?Pain etc
- No mention of any exam findings

Features to improve upon

Case 2:

- CCMB received referral on July 19, 2016
- Assigned & triaged by surgical oncology group on July 26 → request CT/MRI
- CT done Aug 9,2016 (MRI still pending)
- Clinic visit with Surgical Onc scheduled for Aug 19 for biopsy of arm mass and thus, patient had "routine" blood work on Aug 12
- CBC: Hb 79 WBC 12 Plt 117 with 3% plasma cell
  - → Hematology DSG reassignment
    - History obtained over the phone: fatigue x 3 month and can't use right arm x 4 months with constipation
  - → calcium was added to above: 3.6, Creatinine 130.
  - Kappa 2078 and bone marrow showed 93% plasma cell
  - Admitted and treated within 24 hours

Case 3: Shared care patients followed by TeleHealth

Role of the hematologist

- Notes should clearly outline treatment plan
  - Regimen/Dose
  - Total Cycles
  - Supportive care
- Next appointment for follow up
- Investigations required as well as monitoring parameters
- With each cycle:
- Day 1 blood work (within 3 days of start)
- CBC retic fullbio SPEP and FLCI
- Every 3 month:
  - TSH if on IMiDs
  - Urine alb/Cr if on bisphosphonate
- What we are unable to do?
  - Advise regarding most new symptoms (such as SOB, pain, rash, hydration status etc)

Role of the CCP

- Assess patients prior to each cycle of treatment. What to assess for?

1. Toxicities
   - Dose modification of chemotherapy if needed
     - Change in renal function
     - Cytopenia (ANC, Plt, Hb)
     - Hypothyroidsim
     - Hyperglycemia & insomia
   - Increase supportive care (anti-nausea etc, pain control)
2. Response assessment
   - May need to change regimen if inadequate response or progressive disease
3. New symptoms
   - Pain – may indicate disease progression (needs imaging)
   - New comorbidities – may need adjustment of chemotherapy

When to pick up the phone?

Priority	Examples	Time line

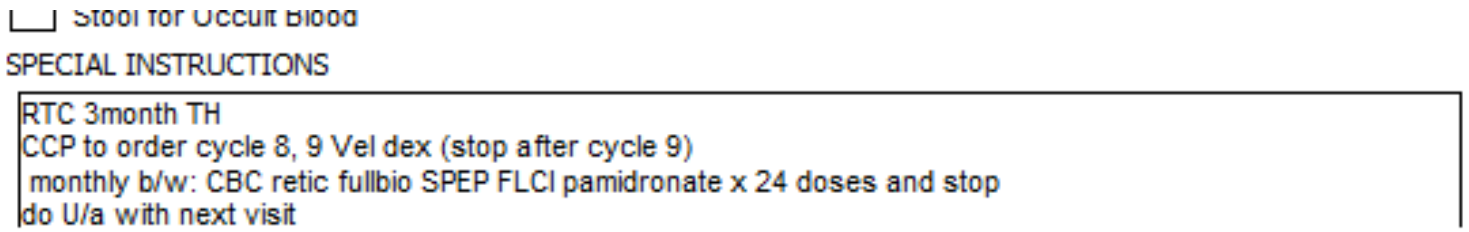
Emergent	• Bony involvement:
	  • Spinal cord compromise
	  • Unstable lesion with risk for pathological fracture
	• Laboratory involvement:
	  • Hypercalcemia (>3mmol/L)
	  • Acute renal failure
	  • Anemia is not considered Emergent as can be readily supported with transfusion if symptomatic
		▪ Same day phone advice
		▪ Needs to PAGE the responsible hematologist OR the person on call via HSC paging (204 787 2071)
		▪ We are not able to use our cell phone (reception is poor in certain areas)

Urgent	• Poor disease control (if unexpected)
	  • Inadequate response or progression
	• Change in health status (if unexpected)
	  • Change in renal function
	  • New comorbidities with poor PS
		• Needs to change treatment plan within 2-4 weeks
		• Call clinic RN line
		• Use email to alert us (make sure you see a response)
		• Page us as above

Routine	• Drug modification as per protocol
	  • Neuropathy & myelosuppression
	• Supportive care
	  • Pain control
	  • Anti nausea & GI side effects
	  • Hypothyroidism
	  • Hyperglycemia Rx
	  • VTE* (page/letter etc if advice re. anticoagulation is required)
		• ARIA notes is sufficient

Case 3: Shared care patients followed by TeleHealth

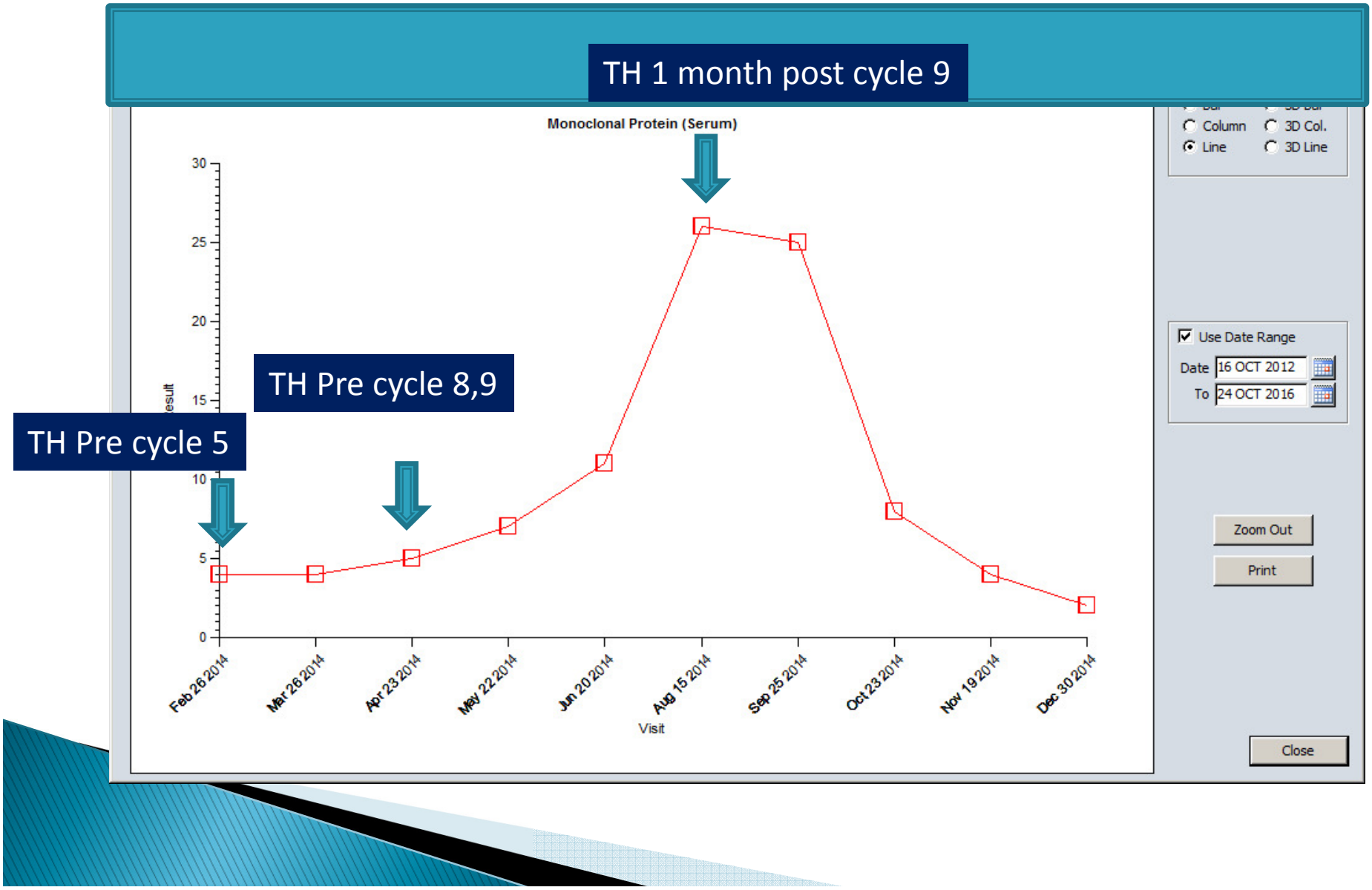
- 70M with oligosecretory myeloma, IgG K 11g/L diagnosed 2013
- Treatment:
- 1. Spine surgery/radiation for T8-9 compression fractures → paraplegic
- 2. Systemic chemotherapy with bortezomib/dexamethasone
  - Cycle 1-4: inpatient at HSC
  - Seen by myself via TH starting at cycle 5 Feb 2014: M band=4g/L → Partial response and once again, May 2014: M band stable 5g/L
  - Plan is to follow up with CCP pre cycle 8, 9 and I will see again 1 month post cycle 9
  - My Order check list (Shared care plan):


Stool for Occult Blood

SPECIAL INSTRUCTIONS

RTC 3month TH
CCP to order cycle 8, 9 Vel dex (stop after cycle 9)
monthly b/w: CBC retic fullbio SPEP FLCI pamidronate x 24 doses and stop
do U/a with next visit

Case 3: Shared care patients followed by TeleHealth



Case 4: Toxicities

- 84F with lambda myeloma diagnosed 2014
- Treatment:

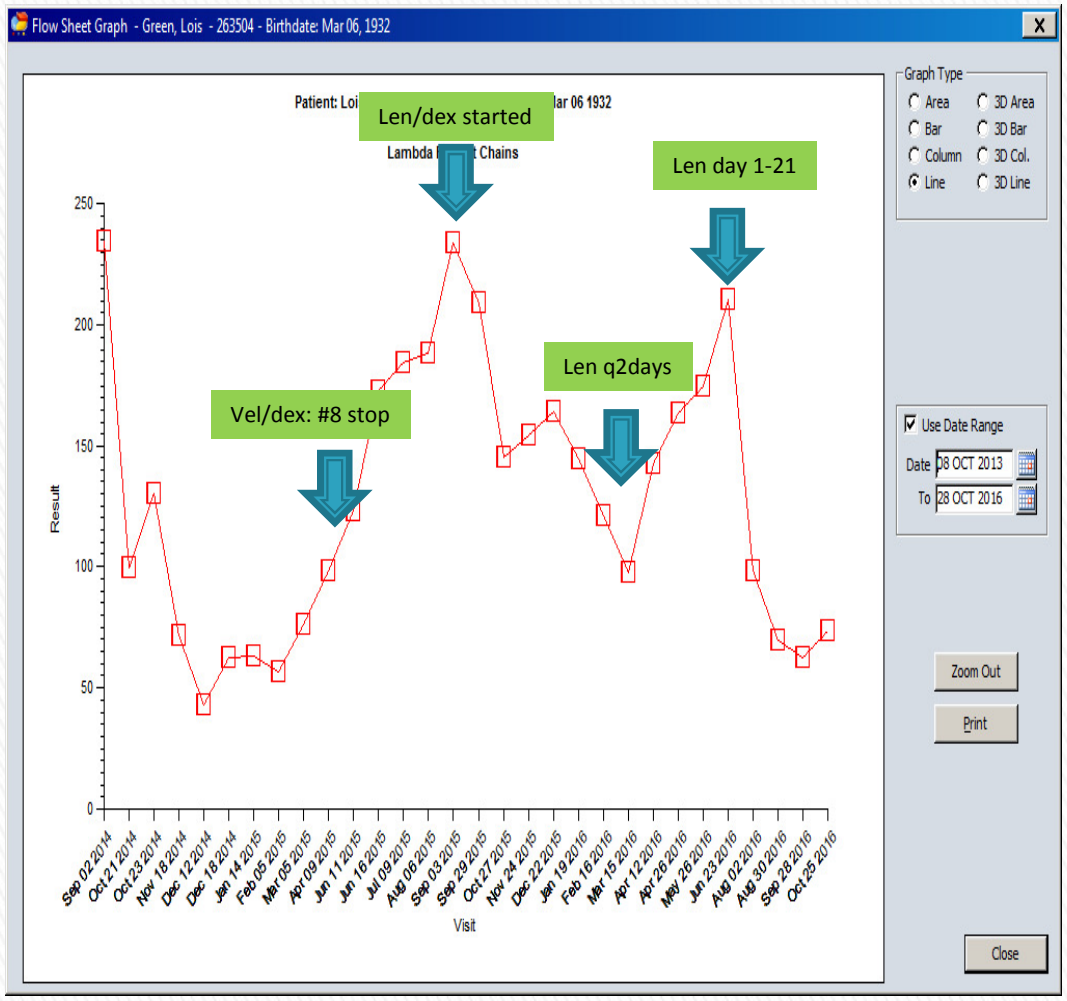
1. <u>CBD x 8 cycles</u>

- Cyclo omit due to neutropenia
- Stop at cycle 8 due to progressive disease

2. <u>Len/dex started</u>

Len10mg day 1-21

- At Cycle 6 – ANC 0.38
- Dose reduced to 10mg q2days from #6-10
- At cycle #11-15: len increased back to 10mg day 1-21
- But we are again noticing neutropenia (ANC 0.7)



Monitoring parameters: CBD

- For cycle 1 & 2:
  - Day 1 = CBC retic fullbio SPEP FLCI
    - Proceed with cyclo if ANC >1 AND plt >75 (for day 1,8,15,22)
    - Proceed with bortezomib if ANC >0.5 AND plt >30
  - Day 15 = CBC retic
    - Proceed with bortezomib if ANC >0.5 AND plt >30
- For cycle 3 and onward
  - Only need day 1 blood work as above
  - Will need day 15 CBC retic IF on day 1 b/w: ANC <1 OR plt <100

CBD: dose modification (adapted from BCCA)

1. Hematological:

ANC ($x10^9$/L)	Platelets ($x10^9$/L)	Bortezomib Dose
greater than or equal to 0.5	And greater than or equal to 30	100%
less than 0.5	Or less than 30	Consider delay until recovery checking CBC weekly; reduce dose to 1 mg/m^2 or consider once a week dosing (see above) at the same dose
reoccurrence of less than 0.5	reoccurrence of less than 30	Consider delay until recovery checking CBC weekly; further reduce dose to 0.7 mg/m^2 or consider once a week dosing (see above) at the same dose

For Cyclophosphamide (If using) lab on day 1

ANC ($x10^9$/L)	Platelets ($x10^9$/L)	Dose (cyclophosphamide)
greater than 1.0	greater than 80	100%
less than or equal to 1.0	less than or equal to 80	perform weekly CBC until recovery

2. Peripheral Neuropathy:

Severity of Peripheral Neuropathy Signs and Symptoms	Bortezomib Dose
Grade 1 (paresthesia and/or loss of reflexes) without pain or loss of function	100%
Grade 1 with pain or Grade 2 (interfering with function but not with activities of daily living)	Reduce dose to 1 mg/m^2
Grade 2 with pain or Grade 3 (interfering with activities of daily living	Delay until recovery. When resolved, reduce dose to 0.7 mg/m^2 weekly x 2 doses q 21 days or consider once weekly dosing (see above)
Grade 4 (permanent sensory loss that interferes with function)	Discontinue treatment

3. Hepatic Impairment:

	Bilirubin	AST	Bortezomib Dose
Mild	less than or equal to 1 x upper limit of normal	greater than the upper limit of normal	100%
	greater than 1 – 1.5 x upper limit of normal	Any	100%
Moderate	greater than 1.5-3 x upper limit of normal	Any	▪ Reduce dose to 0.7 mg/m^2 in the first cycle. ▪ Consider dose escalation to 1.0 mg/m^2 *or* further dose reduction to 0.5 mg/m^2 in subsequent cycles based on patient tolerability.
Severe	greater than 3 x upper limit of normal	Any	

*Bortezomib dose levels:
Weekly 1.5mg/m2 → 1.3mg/m2 → 1.0mg/m2 → 0.7mg/m2

CBD: dose modification (adapted from BCCA)

Diarrhea grading system

Grade 1	Grade 2	Grade 3	Grade 4
Increase of less than 4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 – 6 stools per day over baseline; IV fluids indicated for less than 24hrs; moderate increase in ostomy output compared to baseline; not interfering with activities of daily living	Increase of greater than 7 stools per day over baseline; incontinence; IV fluids for greater than 24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with activities of daily living	Life-threatening consequences (e.g., hemodynamic collapse)

Treatment of Diarrhea during cycle		
At first loose stool:	Start loperamide 2 mg po q 2 h while awake and q 4 h while sleeping. Continue around the clock until 12 h diarrhea free	• If diarrhea free greater than 12 h, stop loperamide. If new episode, retreat with loperamide. • If grade 3 diarrhea or diarrhea accompanied by mucus or dehydration, hold doses of Bortezomib (if applicable) and hydrate.

Diarrhea management: Next Cycle Dosing

Delay next cycle until diarrhea has resolved (less than 2 watery bowel movements / day)

Severity of diarrhea with last cycle:	Bortezomib dose this cycle
less than or equal to grade 2	no change from previous cycle
greater than or equal to grade 3 or associated with mucus or dehydration	Reduce dose to 80% of that used in the last course or consider once a week dosing. (if two dose reductions have already occurred further treatment with Bortezomib must be individualised and should only continue if a clearly useful clinical response in the myeloma has occurred)

Monitoring parameters: Imids (lenalidomide or pomalidomide)

- For cycle 1 & 2:
  - Day 1 = CBC retic fullbio SPEP FLCI
    - Proceed with cyclo if ANC >1 AND plt >75 (for day 1,8,15,22)
    - Proceed with bortezomib if ANC >0.5 AND plt >30
  - Day 15 = CBC retic
    - Proceed with bortezomib if ANC >0.5 AND plt >30
- For cycle 3 and onward
  - Only need day 1 blood work as above
  - Will need day 15 CBC retic IF on day 1 b/w: ANC <1 OR plt <100
  - TSH q3month

Lenalidomide: dose modification (adapted from BCCA)

Neutropenia

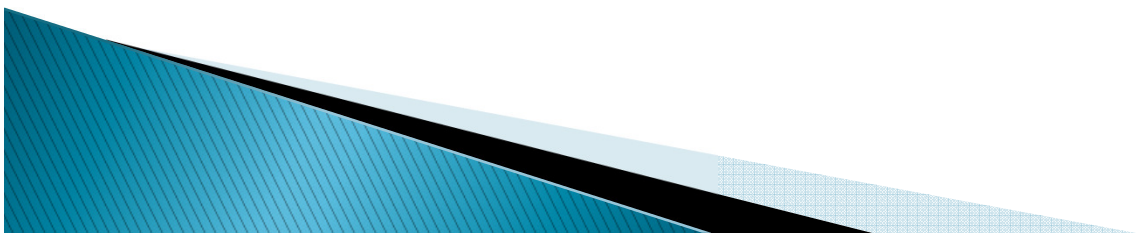
Initial dose*	ANC ($x10^9$/L)	Dose*
25 mg	**Day 1 of Cycle** less than 1	Hold until ANC greater than or equal to 1†, then resume at 25 mg dose plus filgrastim 5 mcg/kg; if filgrastim not available resume at 15 mg dosing (Filgrastim is not covered as a benefit at the BCCA)
	Day 15 of Cycle‡ less than 1	Omit for remainder of cycle; restart on Day 1 of next cycle at 15 mg dose if ANC greater than or equal to 1†
15 mg	**Day 1 of Cycle** less than 1	Hold until ANC greater than or equal to 1†, then resume at 10 mg dose
	Day 15 of Cycle‡ less than 1	Omit for remainder of cycle; restart on Day 1 of next cycle at 10 mg dose if ANC greater than or equal to 1†
10 mg	**Day 1 of Cycle** less than 1	Hold until ANC greater than or equal to 1†, then resume at 5 mg dose
	Day 15 of Cycle‡ less than 1	Omit for remainder of cycle; restart on Day 1 of next cycle at 5 mg dose if ANC greater than or equal to 1†
5 mg	**Day 1 of Cycle**	stop treatment

Estimated GFR (eGFR)* or Creatinine clearance (mL/min)	**Dose**
greater than 50	25 mg†
30-49	10 mg†‡
less than 30, not requiring dialysis	15 mg every other day for 21 days, then rest for 7 days (i.e. 28-day cycle)[4]
less than 30, dialysis dependent	15 mg three times a week for 21 days, then rest for 7 days (i.e. 28-day cycle)[4] (administer after dialysis)

What to monitor while on bisphosphonates?

- Proceed if acceptable renal function and calcium level *within 14 days*
- Do urine alb/cr q3month (look for FSGS)
  - *NOT urine protein/Cr
- Choice:

1. Zoledronic acid
2. Pamidronate (if estimated renal function is less than 30mL/min)
   - If 60-90mg: needs slower infusion (over 4 hour)
   - If 30mg: can infuse over 2 hour



Take home messages

1. Effective communication is key to providing good care (including referral and prompt reassessment)
2. If Emergent issue is suspected, needs to establish contact ASAP (within the same day)
3. With shared care model, CCP is the most responsible physician to supervise care including:
    1. Myeloma response
    2. Toxicities assessment
    3. Symptom management
4. The hematologist is responsible to provide optimization of regimen and advise regarding work up and modifications as needed