Clinical Management

Selecting a Specific Regimen:

- **Patient factors**
  - Age
  - Frailty
  - Other medical problems
  - Prior experience with drug/drug class

- **Disease factors**
  - Molecular profile
  - Pattern of organ involvement
  - Other risk factors

- **Medication factors**
  - Specific toxicities
  - Out-of-pocket costs
Is Less More?

- Yes, if toxicity of regimen is greater and negates the benefit of improved disease control
- No, continuous therapy associated with better outcomes when toxicity is comparable
- Aim for maximizing tolerability

“Less”
- Treatment toxicities
- Shorter length of treatment
- Fewer drugs

“More”
- Quality of Life
- MRD
- Response Rates
- Survival (OS/PFS)
Goals of Therapy

- Improve organ function
- Relieve pain and disease-related symptoms
- Maintain activity and function
- Disease Control: Deeper responses improve outcomes in transplant-eligible and transplant-ineligible patients
  - Minimal residual disease (MRD) negativity is prognostic for PFS & OS
  - MRD can be achieved in patients not undergoing ASCT
- Balance quality of life and achieving deep response
Comorbidities in MM

- Incidence of comorbidities increase with age
- Comorbidity is associated with increased mortality in both younger and elderly patients with MM
- Comorbidities increase vulnerability to therapy toxicities

- Managing comorbidities in MM requires attention to the individual patient
- Select therapy wisely, avoid drugs that worsen specific comorbidities
- Upfront dose modifications
- Close follow-up!

Mr. Jones is a 63M who presents with back pain. Imaging reveals a new compression fracture at T11 and multiple additional lytic lesions. He has a mild anemia, no hypercalcemia and preserved renal function. SPEP significant for 3.2 g/dL IgG kappa M-protein, kappa free light chain 732 mg/L. Bone marrow biopsy shows 40% plasma cells with standard-risk cytogenetics.

Mr. Jones is started on the following regimen for the treatment of newly diagnosed MM:

- **Lenalidomide** 25 mg po Days 1-14
- **Bortezomib** 1.3 mg/m² sc Days 1, 4, 8, 11
- **Dexamethasone** 20 mg po Days 1, 2, 4, 5, 8, 9, 11, 12

After one cycle he returns to your office in follow-up. His pain is well-controlled but he complains of insomnia.
Why Does Sleep Matter?

- Adequate sleep quality plays a central role in maintaining individuals’ physiological and mental health.
- Poor sleep quality and duration has been linked with a range of outcomes such as increased risk of infection, cardiovascular disease, diabetes, cognitive impairment, metabolic dysfunction, and mood-related disorders such as depression and anxiety.
- Disturbed mood has been found to be associated with fatigue severity, which might be further exacerbated by MM medications such as steroids.
Sleep and MM

- Pain
- Steroids
- Peripheral neuropathy
- Psychological distress
Steroids

The MM treatment course is distinguished by continuous, high-dose steroid usage.

This prolonged exposure makes MM patients particularly vulnerable to:

- Insomnia
- Mood alteration
- Change in body composition - loss of lean muscle, gain of visceral adipose tissue
- Increased appetite
- Weight gain
- Hyperglycemia
- Hyperlipidemia

All of these issues are modifiable or potentially preventable side effects that can affect long-term survival and QOL.
Steroids – Dose Reductions

Rd-R v Rd - 9 x 28-day cycles

- Rd-R
  - Lenalidomide 25 mg Days 1-21
  - Dexamethasone 20 mg Days 1, 8, 15, 22

- Lenalidomide maintenance 10 mg Days 1-21 days until disease progression

- Continuous Rd – until disease progression
  - Lenalidomide 25 mg Days 1-21
  - Dexamethasone 20 mg Days 1, 8, 15, 22

- EFS 10.4 vs 6.9 months (HR 0.70, p=0.02)
- OS at 3 years 74% v 63% (HR=0.73, p=0.06)
- No differences in OR or PFS
- Fewer dose reductions in Rd-R

Steroids - Clinical Management

- Keep communication open with patient and caregivers
  - Discuss symptoms such as insomnia, mood swings, hyperglycemia
  - Discuss timing of taking steroids – AM preferred

- Dose-adjust, as necessary

- Consider upfront dose modifications for older/frail patients
Mr. Jones returns to clinic to initiate Cycle 4

On review of systems:

• He reports worsening numbness of the soles of his feet

• He describes the sensation as feeling as though he is walking on sand
Peripheral Neuropathy

• Route of administration – IV vs SC

• Dose reduce!

• Treatments:
  • Anti-depressants (TCAs, SNRIs) and anti-convulsants (gabapentin, pregabalin) are first-line
  • These drugs can be used in combination with opioids
  • As with opioids, response to analgesics may vary according to the etiology of neuropathic pain and the individual patient: failure to control pain with one agent in a particular class does not mean the entire class of medications will not work
  • Patient education should emphasize the trial and error nature of the treatment so patients do not get discouraged
  • Doses should be increased until the analgesic effect is achieved, adverse effects become unmanageable, or the conventional maximum dose is reached
  • Drug selection may be influenced by other symptoms and comorbidities. For example, a sedating drug may be useful in a patient in whom insomnia is a problem
  • Consider cannabinoids and medical marijuana
Mr. Jones returns to clinic at Day 100 post-autologous stem cell transplant

He has recovered well from this treatment and is prepared to begin lenalidomide maintenance today

On review of symptoms, he reports:

• Has trouble “shutting off mind”, worries about disease recurrence
• Reports fears of not being able to see his youngest daughter get married
• Worries about his financial welfare and being able to continue to work for a few more years to save a little more money for his wife
Antidotes to Stress

• Mind body therapies- meditation, yoga, tai chi, prayer, acupuncture/acupressure
• Exercise – aerobic and strength training
• Balanced nutrition
• Positive emotions, humor, gratitude
• Support – relationships / social connectedness
• Restorative sleep
Cancer itself can be an isolating experience physically and emotionally

- Long treatment sessions
- Being immunocompromised during therapy may require limiting exposure to the outside world
- Emotional isolation can occur due to lack of peer group with similar experience, a sense of vulnerability
When is Social Support Needed?

Through all phases of cancer

• From work up
• Diagnosis
• Active treatment
• Rehabilitation
• Survivorship
• End of life
Mr. Jones returns to clinic for follow-up

- He remains in a CR after induction therapy with RVD and autologous stem cell transplant.

- He has been on lenalidomide maintenance for 2 years

- On review of symptoms:
  - He reports post-prandial diarrhea
  - Episodes are accompanied by fecal urgency
Lenalidomide-Related Diarrhea

- Commonly observed during long-term maintenance therapy on lenalidomide

- Bile acid malabsorption (BAM)
  - Excess bile acids are not absorbed in the small intestine and enter the large intestine causing symptoms of loose, watery stool, bloating, and inability to control bowel movements

- Lactose intolerance

- Recommend a stepwise approach:
  - First, try dietary modifications along with over-the-counter medications
  - If these changes are not enough, prescription medications may be necessary
Dietary Modifications:

**Avoid/Limit:**

- Fatty food (fried food, high-fat meals, oil-based salad dressing)

- Dairy products (milk, cheese, yogurt, ice-cream); Instead, try non-lactose or non-dairy/plant-based alternatives (soy, coconut, almond, oat milk)

**BRAT diet:**

B – Banana  
R – Rice  
A – Apple sauce  
T – Toast

- This bland “binding” food diet can decrease episodes of medication-induced diarrhea
Lenalidomide-Related Diarrhea

Over-the-counter medications/supportive agents:

Use to treat acute episodes:

• **Loperamide (Imodium A-D®)** – can help control acute episodes of diarrhea – take 4 mg (2 pills) by mouth initially, followed by 2 mg after each loose stool; can be safely taken up to 16 mg/day (8 pills)

May use as prevention:

• **Psyllium (Metamucil®)** – a bulk fiber can help make bowel movements more formed and less fluid

• **Probiotics/Lactobacillus acidophilus** – have shown some benefit
Lenalidomide-Related Diarrhea

Prescription medications:

Cholestyramine resin (Questran®) – available in powder form, take 4 g (1 packet) by mouth once daily initially, may need to increase to 2-3 times a day

• Colestipol (Colestid®) – available in tablet form, take 2 g (2 pills) by mouth once or twice daily, may need to increase to 2-3 times a day

• These medications are known as bile acid sequestrants and are commonly used to lower cholesterol, but they been shown to be effective for BAM as well

• Caution – some medications can bind to these agents and decrease absorption. Your pharmacist can help you identify if any medications need to be taken at a separate time.
Clinical Management

Supportive care
- Proteasome inhibitors/anti-CD38 antibodies: shingles prophylaxis
- IMiDs: blood clot prophylaxis
- Corticosteroids: consider GI prophylaxis
- Evidence of bone disease: zoledronic acid or denosumab (preferred if renal dysfunction)
  - *pain control / interventions such as vertebroplasty / kyphoplasty
- Infection prophylaxis:
  - Vaccines (pneumococcal, yearly influenza, shingles, COVID)
  - Antibiotics are actively being studied
  - IVIG if recurrent life-threatening infections or IgG<400
- Social Work
- Palliative Care
- Physical Therapy & Rehabilitative Medicine
Clinical Management of Toxicity

• Balance of achieving a deep response with quality of life
  – Dose adjust
• Consider all forms of toxicity:
  – Medication
  – Psychosocial
  – Financial
• Communication
  – Understand patient values and priorities
  – Ask patients and caregivers about symptoms
Thank you