

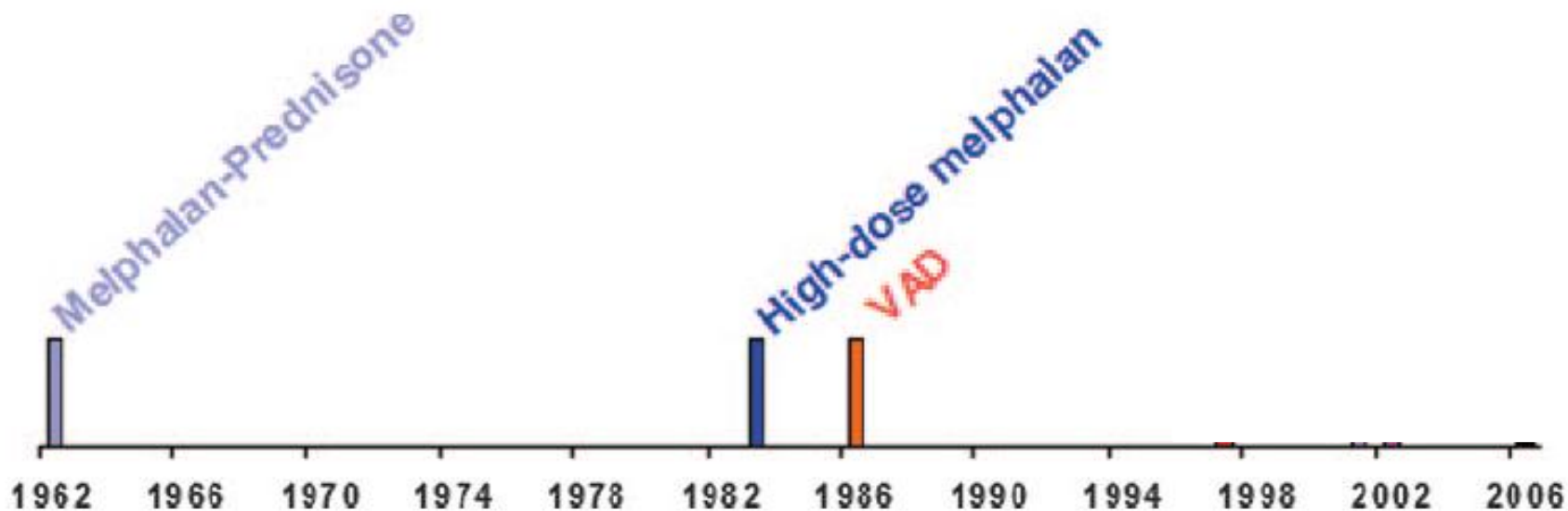
# **Medici e Pazienti Contro il Mieloma**

**Gli effetti collaterali: il paziente di cosa deve preoccuparsi e come può collaborare?**

**Monica Galli  
UO Ematologia - HPG23 - Bergamo**



# Primi Trattamenti Attivi nel Mieloma Multiplo



# Effetti collaterali del cortisone

- If taking dexamethasone 40 mg PO daily, days 1–4, 9–12, 17–21, consider 50% dose reduction if any grade 2 or grade 3 steroid toxicity occurs.
  - If dose is already reduced, consider reducing dose frequency days 1–4 and 15–18, at a dose of dexamethasone 20 mg PO each day if grade 2 or grade 3 toxicity persists.
  - Consider further reduction to days 1–4 each month if grade 2 or grade 3 toxicity persists.
  - Consider dexamethasone 40 mg at weekly intervals.
  - Consider stopping steroids if grade 2 or grade 3 toxicity persists despite dose reductions.
- If taking dexamethasone 40 mg PO daily, days 1–4 and 15–18, follow dose reduction schedule as above, starting with 50% dose decrease with the first evidence of grade 2 or grade 3 toxicity.
  - Consider further reduction to days 1–4 each month if grade 2 or grade 3 toxicity persists.
  - Consider stopping steroids if grade 2 or grade 3 toxicity persists despite dose reductions.
- If taking dexamethasone 40 mg PO daily, days 1–4, consider steroid taper if grade 2 or grade 3, such as
  - 40 mg PO days 1–3, then 20 mg PO day 4, 12 mg PO day 5, 8 mg PO day 6, and 4 mg PO day 7
- If taper is ineffective and grade 2 or grade 3 toxicities persist, consider dexamethasone 20 mg PO daily days 1–4.

## Body Image

Weight gain, increased appetite  
Cushingoid appearance  
Hirsutism or alopecia

## Cardiovascular

Edema

## Constitutional

"Let down" effect after discontinuing steroids  
Flushing or sweating  
Insomnia

## Dermatologic

Acneform rash  
Thinning of skin

## Endocrine

Steroid-induced hyperglycemia  
Adrenal insufficiency  
Hypogonadism

## Gastrointestinal

Gastric or duodenal ulcer  
Heartburn (dyspepsia)  
Flatulence  
Taste alteration (dysgeusia)  
Hiccoughs (hiccups, singultus)

## Immune

Leukocytosis  
Infection

## Musculoskeletal

Proximal myopathy  
Osteonecrosis (avascular necrosis)  
Osteopenia or osteoporosis  
Muscle cramping

## Ophthalmic

Blurred vision  
Cataracts

## Psychiatric

Personality changes and mood alterations (anxiety)  
Hyperactivity

## Sexual Dysfunction



# Tossicità ematologica di grado 3 e 4 (anemia, piastrinopenia, neutropenia)

---

Trasfusioni di globuli rossi;  
EPO

Trasfusioni di concentrati piastrinici;  
(Agenti trombopoietici)

G-CSF;  
Farmaci Antibiotici, Antivirali, Antifungini

**Modifica della dose dei farmaci anti-Mieloma**



# Complicanze gastrointestinali: Nausea e Vomito

ADVERSE EVENT	GRADE 1 (MILD)	GRADE 2 (MODERATE)	GRADE 3 (SEVERE)	GRADE 4 (LIFE THREATENING OR DISABLING)
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated < 24 hours	Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or total parenteral nutrition indicated 24 hours	Life-threatening consequences
Vomiting	1 episode in 24 hours	2–5 episodes in 24 hours; IV fluids indicated < 24 hours	6 episodes in 24 hours; IV fluids or total parenteral nutrition indicated 24 hours	Life-threatening consequences

VARIABLE	NAUSEA	VOMITING
Patient characteristics	Age younger than 50 Female Nausea and vomiting during previous anticancer treatments Sweating, dizziness, or warmth after last anticancer treatment	More likely in children than in adults Female History of motion sickness and anxiety History of emesis and dehydration caused by cancer therapy
Diet	Current or prior heavy alcohol use	Current or prior heavy alcohol use
Medications	Chemotherapy, opioids, levodopa, digitalis, pilocarpine, nicotine, non-steroidal anti-inflammatory agents, antibiotics, and iron supplements	Chemotherapy, opioids, levodopa, digitalis, pilocarpine, nicotine, and non-steroidal anti-inflammatory agents
Comorbidities	Older patients with declining organ function and multiple illnesses and conditions, bowel obstruction, brain metastases, or gastrointestinal infections or bleeding	Bowel obstruction; brain metastases; gastrointestinal infections or bleeding; electrolyte imbalance
Medical procedures	Radiation therapy	Radiation therapy



# Complicanze Gastrointestinali: Nausea e Vomito

- Eat small amounts of food throughout the day and eat before getting too hungry.
- Eat dry foods such as dry cereal, toast, or crackers without liquids, especially first thing in the morning.
- Avoid heavy, high-fat, and greasy meals before anticancer therapy.
- Consider avoiding favorite foods, as they may no longer be favorite foods if they become associated with nausea.
- Don't lie flat for at least two hours after eating.
- Fresh air and loose clothing may be helpful after eating.
- Exercising after eating may increase discomfort.
- Avoid strong odors.
- Distraction
- Suggest patients relax and try to keep their minds off therapy by using soothing music, relaxation tapes or CDs, progressive relaxation, guided imagery, or self-hypnosis.
- Acupuncture
- Biofeedback
- Systematic desensitization
- Consider how likely the therapy is to cause nausea in the absence of effective nausea treatment.

**Idratazione**

**Antiemetici**

**Desametasone**

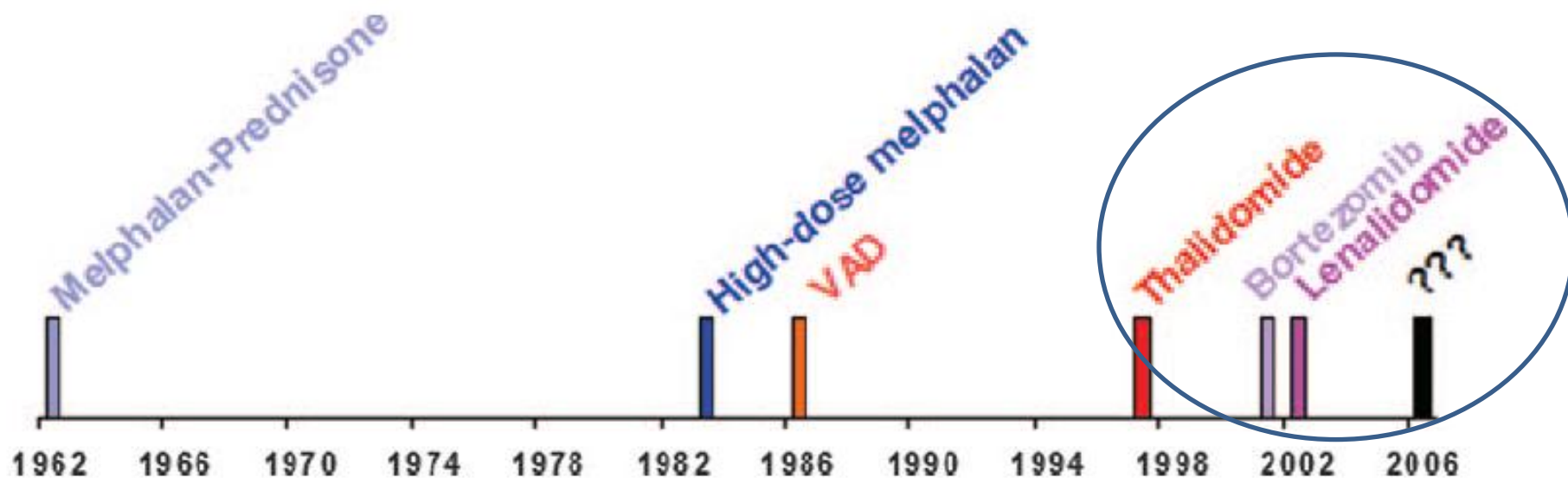
**NPT**

**Esclusione cause ostruttive**

**Eventuale ricovero**



# Nuovi Trattamenti nel Mieloma Multiplo



Negli ultimi 15 anni in aggiunta ai chemioterapici e al cortisone si sono resi disponibili molti nuovi farmaci, che migliorano in modo significativo i risultati della terapia del Mieloma Multiplo

Talidomide

Lenalidomide (Revlimid)

Pomalidomide (Imnovid)

Bortezomib (Velcade)

Carfilzomib (Kyprolis)

Elotuzumab

Daratumumab

Vorinostat





# Eventi Avversi Associati alle Terapie del Mieloma

		PN	Myopathy	VTE	Thrombocytopenia	Neutropenia	Lymphopenia	Anemia	Decreased NK cells	Infection	Pneumonia	Fatigue	Nausea	Diarrhea	Constipation	2° primary malignancy	High blood glucose	Infusion reaction	Osteoporosis	Rash	Edema	Mood disorders
PIs	Bortezomib	X			X				X		X	X	X	X								
	Carfilzomib				X	X	X	X		X	X	X	X								X	
IMiDs	Thalidomide	X		X	X	X					X	X		X					X	X		
	Lenalidomide			X	X	X		X	X		X	X	X	X	X				X	X		
	Pomalidomide			X	X	X		X			X	X		X					X			
Chemotherapy	Cyclophosphamide				X	X		X	X			X			X							
	Melphalan				X	X		X				X	X		X							
Corticosteroids	Dexamethasone		X	X					X			X				X		X		X	X	
	Prednisone		X	X					X			X				X		X		X	X	
DACis	Panobinostat				X	X	X	X		X	X		X									
	Vorinostat				X			X			X	X	X									
mAbs	Elotuzumab							X		X	X	X	X			X	X					
	Daratumumab				X			X									X					

NK natural killer, PN peripheral neuropathy, VTE venous thromboembolism



# Tossicità Ematologica di Grado 3 e 4

Farmaco	Anemia (%)	Piastrinopenia (%)	Neutropenia (%)
Talidomide	16	4	13
Lenalidomide	8	10	21
Bortezomib	10	29	15

Trasfusioni di globuli rossi; EPO

Trasfusioni di concentrati piastrinici; (Agenti trombopoietici)

G-CSF; Farmaci Antibiotici, Antivirali, Antifungini

**Modifica della dose dei farmaci anti-Mieloma**



# Modifiche alla Dose dei Farmaci

Risk factor	0	1	1 + occurrence of grade 3-4 hematologic AE	≥2
Dose level	0	-1	-2	-2
	LEVEL 0	LEVEL -1	LEVEL -2	
Prednisone	2 mg/kg Days 1-4 of a 4-6 week cycle 60 mg/ m <sup>2</sup> Days 1-4 of a 6 week cycle	1 mg/kg Days 1-4 of a 4-6 week cycle 30 mg/ m <sup>2</sup> Days 1-4 of a 6 week cycle	0.3 mg/kg Days 1-4 of a 4-6 week cycle 10 mg/m <sup>2</sup> Days 1-4 of a 6 week cycle	
Dexamethasone	40 mg Day 1, 8, 15, 22 of a 28-day cycle	20 mg Day 1, 8, 15, 22 of a 28-day cycle	10 mg Day 1, 8, 15, 22 of a 28-day cycle	
Melphalan	0.25 mg/kg Days 1-4 of a 4-6 week cycle 9 mg/ m <sup>2</sup> Days 1-4 of a 6 week cycle	0.18 mg/kg days 1-4 of a 4-6 week cycle 7.5 mg/ m <sup>2</sup> days 1-4 of a 6 week cycle	0.13 mg/kg Days 1-4 of a 4-6 week cycle 5 mg/ m <sup>2</sup> Days 1-4 of a 6 week cycle	
Thalidomide	100-200 mg/day	50-100 mg/day	50 mg qod - 50 mg/day	
Lenalidomide	25 mg Days 1-21 of a 28-day cycle	15 mg Days 1-21 of a 28-day cycle	10 mg Days 1-21 of a 28-day cycle	
Bortezomib	1.3 mg/m <sup>2</sup> twice weekly Days 1,4,8,11 every 3 weeks	1.3 mg/m <sup>2</sup> once weekly Days 1, 8, 15, 22 every 5 weeks	1.0 mg/m <sup>2</sup> once weekly Days 1, 8, 15, 22 every 5 weeks	

AE: adverse events.



# Complicanze Gastrointestinali

**Table 2. Incidence of Gastrointestinal Events in Patients With Multiple Myeloma Receiving Novel Therapies**

TOXICITY	LENALIDOMIDE <sup>a</sup> (TWO STUDIES, N = 346)		THALIDOMIDE <sup>a</sup> (OPEN-LABEL STUDY, N = 102)		BORTEZOMIB (PHASE III TRIAL, N = 331)	
	ALL GRADES (%)	GRADE 3 <sup>b</sup> (%)	ALL GRADES (%)	GRADE 3 <sup>b</sup> (%)	ALL GRADES (%)	GRADE 3 <sup>b</sup> (%)
Constipation	39	2	55	8	42	2
Diarrhea	29	2	12	1	57	7
Nausea	22	< 2 <sup>c</sup>	28	5	57	2
Vomiting	10	< 2 <sup>c</sup>	12	2	35	3

<sup>a</sup> Administered in combination with dexamethasone

<sup>b</sup> No grade 4 events were reported.

<sup>c</sup> Only grade 3 and 4 adverse events with an incidence of  $\geq 2\%$  were reported.

*Note.* Based on information from Celgene Corporation, 2007a, 2007b; Millennium Pharmaceuticals, Inc., 2007.



# Complicanze Gastrointestinali: Stipsi e Dissenteria

## Stipsi:

**Talidomide e Velcade**

## Dissenteria:

**Velcade**

VARIABLE	CONSTIPATION	DIARRHEA
Patient characteristics	Adults older than 65 years Sedentary or bedridden	Adults older than 65 years Recent stay in a hospital or nursing home.
Diet	Low-fiber diet Poor fluid intake	Herbal supplements, including milk thistle, aloe, cayenne, saw palmetto, and ginseng
Medications	Particularly opioids and dexamethasone; also antacids, antiemetics, antiseizure medications, and iron supplements	Laxatives, antibiotics, antacids containing magnesium, colchicine, propranolol, diuretics, angiotensin-converting enzyme inhibitors, and antidepressants
Comorbidities	Diabetes, hypertension, hypothyroidism, tumor pressing on spinal cord, bowel obstruction, and peripheral neuropathy	History of irritable bowel syndrome, colitis, or diverticulitis; and graft-versus-host disease following bone marrow transplantation
Medical procedures	Surgery involving the intestinal tract	Surgery involving the intestinal tract or bone marrow transplantation



# Neuropatia Periferica

## Talidomide e Velcade

Peripheral neuropathy severity	Potential action based on recent phase III studies	
	Bortezomib	Thalidomide
Grade 1 (paresthesia, weakness and/or loss of reflexes) without pain or loss of function	If the patient is on a biweekly schedule <sup>a</sup> : reduce current bortezomib dose by one level or prolong dosing interval to once weekly If the patient is already on a weekly schedule: reduce current bortezomib dose by one level	Continue to monitor patient with clinical examination. Consider reducing dose if symptoms worsen. However, dose reduction is not necessarily followed by improvement of symptoms
Grade 2 (interfering with function but not with activities of daily living)	If the patient is on a biweekly schedule: reduce current bortezomib dose by one level or prolong dosing interval to once weekly If the patient is already on a weekly schedule: reduce current bortezomib dose by one level or consider temporary discontinuation of bortezomib. If the neuropathy resolves to grade 1 or better, once-weekly treatment with reduced bortezomib dose may be restarted if the benefit-to-risk ratio is favorable	Reduce dose or interrupt treatment and continue to monitor the patient with clinical and neurological examination. If no improvement or continued worsening of the neuropathy, discontinue treatment. If the neuropathy resolves to grade 1 or better, the treatment may be restarted, if the benefit/risk is favorable
Grade 3 (interfering with activities of daily living)	Discontinue bortezomib <sup>b</sup>	Discontinue thalidomide
Grade 4 (sensory neuropathy that is disabling or motor neuropathy that is life-threatening or that leads to paralysis)	Discontinue bortezomib <sup>b</sup>	Discontinue thalidomide



# Reazioni Cutanee

---

Talidomide (46%)  
Lenalidomide (27%):  
**Rash**



Velcade (20%):  
**Nodulazioni**



**Riduzione dosaggio / Interruzione  
del farmaco**

**Identificare il farmaco responsabile**



# Modifiche allo stile di vita

---

**Controllare il peso corporeo**

**Limitare il consumo di alcool e sigarette**

**Limitare l'assunzione di sale e zuccheri semplici**

**Seguire una dieta ricca di frutta e verdura e povera di grassi (soprattutto saturi)**

**Svolgere attività fisica regolare**





# Attività Fisica

---

## What to do:

- Do as much daily self-care as possible.
- Take a walk every day.
- Try to do a specific prescribed activity regimen that is approved by your doctor.
- Eat a nutritious diet, drink plenty of fluids, and get plenty of rest.
- Keep a log or journal of your activity.
- Notify your healthcare provider about sudden onset of pain, progressive weakness, headaches, blurred vision, numbness, and tingling.

## What not to do:

- Stay in bed with little movement.
- Let others do for you what you can do for yourself.
- Force yourself to exercise if you are having symptoms from your disease or treatment.
- Try to perform any exercise without first asking the nurse, doctor, or physical therapist.
- Move any joint or body part if it is painful.



# Complicanze Psicosociali - 1

SYSTEM AND ADVERSE EVENT	GRADE 1 (MILD)	GRADE 2 (MODERATE)	GRADE 3 (SEVERE)	GRADE 4 (LIFE THREATENING OR DISABLING)	GRADE 5 (DEATH)
<b>Constitutional</b> "Let-down" effect (fatigue <sup>a</sup> )	Mild fatigue over baseline	Moderate or causing difficulty with some activities of daily living	Severe fatigue interfering with activities of daily living	Disabling	Not applicable
Flushing	Asymptomatic	Symptomatic	Not applicable	Not applicable	Not applicable
Sweating (diaphoresis)	Mild and occasional	Frequent or drenching	Not applicable	Not applicable	Not applicable
Insomnia	Occasional difficulty sleeping, not interfering with function	Difficulty sleeping; interfering with function but not interfering with activities of daily living	Frequent difficulty sleeping; interfering with activities of daily living	Disabling	Not applicable



# Complicanze Psicosociali - 2

SYSTEM AND ADVERSE EVENT	GRADE 1 (MILD)	GRADE 2 (MODERATE)	GRADE 3 (SEVERE)	GRADE 4 (LIFE THREATENING OR DISABLING)	GRADE 5 (DEATH)
<b>Sexual dysfunction</b>					
Erectile dysfunction	Decrease in erectile function (frequency or rigidity of erections) but erectile aids not indicated	Decrease in erectile function (frequency or rigidity of erections) but erectile aids indicated	Decrease in erectile function (frequency or rigidity of erections) but erectile aids not helpful; penile prosthesis indicated	Not applicable	Not applicable
Libido	Decrease in interest but not affecting relationship; intervention not indicated	Decrease in interest and adversely affecting relationship; intervention indicated	Not applicable	Not applicable	Not applicable



# Complicanze Psicosociali - 3

SYSTEM AND ADVERSE EVENT	GRADE 1 (MILD)	GRADE 2 (MODERATE)	GRADE 3 (SEVERE)	GRADE 4 (LIFE THREATENING OR DISABLING)	GRADE 5 (DEATH)
Psychiatric					
Personality changes	Change, but not adversely affecting patient or family	Change; adversely affecting patient or family	Mental health intervention indicated	Change harmful to others or self; hospitalization indicated	Death
Mood alteration <sup>b</sup>	Mild mood alteration not interfering with function	Moderate mood alteration interfering with function but not interfering with activities of daily living; medication indicated	Severe mood alteration interfering with activities of daily living	Suicidal ideation; danger to self or others	Death

## Gruppi di supporto



# Vaccinazioni

---

Anti-influenzale	ogni anno
Anti-pneumococcica	ogni 5 anni
Anti-tetanica	ogni 10 anni



# Grazie per l'attenzione



Azienda Ospedaliera  
Papa Giovanni XXIII  
Bergamo

