Consensus or Controversy? Investigator Perspectives on Practical Issues and Research Questions in Multiple Myeloma

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Module 1: Up-Front Treatment for Transplant-Eligible Patients

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Induction therapy: 55 yo, transplant eligible, standard-risk MM

If you use bortezomib (BTZ), how would you initially administer BTZ?

	Standard risk	BTZ administration
 DR BENSINGER	CyBorD	Twice weekly, IV
 DR DIMOPOULOS	VTD	Twice weekly, SubQ
 DR KRISHNAN	RVD	Weekly, IV or twice weekly, subQ
 DR RAJE	RVD	Twice weekly, SubQ
 DR STEWART	CyBorD	Weekly (continuous), subQ

If previous 55-yo patient with standard-risk MM receives RVD, how would you initially administer BTZ?

 DR BENSINGER	Twice weekly, IV
 DR DIMOPOULOS	Twice weekly, subQ
 DR KRISHNAN	Weekly, IV
 DR RAJE	Twice weekly, subQ
 DR STEWART	Weekly (continuous), subQ

BTZ to be administered for 2 weeks every 3 weeks in above selected schedules/ methods of administration except where noted

Induction therapy if 55-yo patient has *del(17p)*?

 DR BENSINGER	CyBorD
 DR DIMOPOULOS	VTD
 DR KRISHNAN	RVD
 DR RAJE	RVD
 DR STEWART	RVD

Induction therapy if 55-yo patient has *renal failure*?


DR BENSINGER — CyBorD


DR DIMOPOULOS — VTD


DR KRISHNAN — CyBorD


DR RAJE — CyBorD


DR STEWART — CyBorD

If previous 55-yo patient with renal failure receives CyBorD, how would you initially administer BTZ?

 DR BENSINGER	Twice weekly, IV
 DR DIMOPOULOS	Twice weekly, subQ
 DR KRISHNAN	Weekly, IV
 DR RAJE	Twice weekly, subQ
 DR STEWART	Weekly (continuous), IV

BTZ to be administered for 2 weeks every 3 weeks in above selected schedules/ methods of administration except where noted

Cytogenetic abnormalities considered high risk

 DR BENSINGER	Hypodiploidy, del(13q), t(4;14), t(14;16), t(14;20), del(17p), amplification of 1q
 DR DIMOPOULOS	Hypodiploidy, t(4;14), del(17p)
 DR KRISHNAN	Hypodiploidy, t(14;16), t(14;20), del(17p)
 DR RAJE	Hypodiploidy, t(4;14), t(14;16), del(17p)
 DR STEWART	Hypodiploidy, t(4;14), t(14;16), t(14;20), del(17p)

Induction therapy: 80 yo, standard-risk MM

 DR BENSINGER	RD/Rd
 DR DIMOPOULOS	RVD lite
 DR KRISHNAN	RD/Rd
 DR RAJE	RVD lite
 DR STEWART	Rd

Preemptive dose reductions recommended for older patients?

	Preemptive dose reduction?	How?
 DR BENSINGER	Yes	>75 years: lenalidomide 15 mg, dexamethasone 20 mg
 DR DIMOPOULOS	Yes	
 DR KRISHNAN	Yes	Reduce the lenalidomide dose, use subQ BTZ
 DR RAJE	Yes	Lenalidomide 15 mg, low-dose dexamethasone, weekly BTZ
 DR STEWART	Yes	Lenalidomide 15 mg, dexamethasone 20 mg, BTZ 1.3 mg/m^2 weekly

80-yo patient with standard-risk MM receives RVD lite, how would you initially administer BTZ?

If the patient receives CyBorD, how would you initially administer BTZ?

	BTZ – Normal renal function?	BTZ – Renal failure?
 DR BENSINGER	Weekly, subQ	Weekly, IV
 DR DIMOPOULOS	Weekly, subQ	Twice weekly, subQ
 DR KRISHNAN	Weekly, subQ	Weekly, IV
 DR RAJE	Weekly, subQ	Twice weekly, subQ
 DR STEWART	Weekly (continuous), subQ	Weekly (continuous), IV

BTZ to be administered for 2 weeks every 3 weeks in above selected schedules/methods of administration except where noted

Induction therapy if patient has del(17p)?

Induction therapy if patient has *renal failure*?

	Del(17p)	Renal failure
 DR BENSINGER	RVD lite	VD
 DR DIMOPOULOS	RVD lite	VD
 DR KRISHNAN	VD	VD
 DR RAJE	RVD lite	VD
 DR STEWART	RVD lite	CyBorD

Module 2: Maintenance/ Consolidation Therapy and the Impact of Adverse Cytogenetics

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Consolidation treatment for younger patients with standard-risk MM who respond to induction therapy and ASCT?

 DR BENSINGER	No
 DR DIMOPOULOS	Yes, VTD for all or most patients
 DR KRISHNAN	Yes, RVD or CRD for select patients
 DR RAJE	Yes, RVD for all or most patients
 DR STEWART	No

Consolidation treatment for younger patients with high-risk MM who respond to induction therapy and ASCT?

 DR BENSINGER	No
 DR DIMOPOULOS	Yes, VTD for all or most patients
 DR KRISHNAN	Yes, RVD for select patients
 DR RAJE	Yes, RVD for all or most patients
 DR STEWART	No

Do you generally consolidate with the induction regimen?

 DR BENSINGER	I generally don’t recommend consolidation
 DR DIMOPOULOS	Yes
 DR KRISHNAN	Yes
 DR RAJE	Yes
 DR STEWART	I generally don’t recommend consolidation

Maintenance treatment for younger patients who respond to induction therapy and ASCT?

 DR BENSINGER	Yes, for select patients, if not in CR
 DR DIMOPOULOS	No
 DR KRISHNAN	Yes, for all or most patients, if not in CR or high risk
 DR RAJE	Yes, for most patients
 DR STEWART	Yes, for all patients

55 yo with standard-risk MM achieves CR after RVD induction/ASCT: Post-transplant maintenance?

Post-transplant maintenance therapy if the patient has *del(17p)*?

	Standard risk	Del(17p)
 DR BENSINGER	No	BTZ
 DR DIMOPOULOS	No	Lenalidomide/BTZ
 DR KRISHNAN	Lenalidomide	BTZ
 DR RAJE	Lenalidomide	Lenalidomide/BTZ
 DR STEWART	Lenalidomide	Lenalidomide/BTZ

Duration of maintenance therapy with standard-risk MM?

Duration of maintenance therapy with del(17p)?

	Standard risk	Del(17p)
 DR BENSINGER	I don't generally recommend maintenance	2 years
 DR DIMOPOULOS	I don't generally recommend maintenance	2 years
 DR KRISHNAN	Until disease progression	2 years
 DR RAJE	Until disease progression	Until disease progression
 DR STEWART	2 years	2 years

Maintenance therapy: 80 yo w/ standard-risk MM achieves CR after RVD lite induction?

Maintenance therapy if patient has *del(17p)*?

	Standard risk	Del(17p)
 DR BENSINGER	No	BTZ +/- dexamethasone
 DR DIMOPOULOS	RVD lite	RVD lite
 DR KRISHNAN	Lenalidomide +/- dexamethasone	BTZ +/- dexamethasone
 DR RAJE	RVD lite	RVD lite
 DR STEWART	Lenalidomide +/- dexamethasone	RVD lite

When do you start maintenance therapy for transplant-ineligible patients receiving LEN- or BTZ-based therapy?

 DR BENSINGER	After patient achieves maximal response
 DR DIMOPOULOS	I generally don't recommend maintenance in this setting
 DR KRISHNAN	After 6 cycles
 DR RAJE	After 8 cycles
 DR STEWART	After patient achieves maximal response

Duration of maintenance therapy: 80 yo with standard-risk MM?

Duration of maintenance therapy: 80 yo with del (17p)?

	Standard risk	Del(17p)
 DR BENSINGER	No	2 years
 DR DIMOPOULOS	1 year	1 year
 DR KRISHNAN	Until disease progression	2 years
 DR RAJE	Until disease progression	Until disease progression
 DR STEWART	2 years	2 years

Proportion of patients receiving lenalidomide maintenance needing dose adjustment/discontinuation?

Most common causes for dose adjustment/ discontinuation?

	Dose adjustment/ discontinuation	Reasons
 DR BENSINGER	70%	Cytopenias, infection
 DR DIMOPOULOS	Not using lenalidomide maintenance	N/A
 DR KRISHNAN	25%	Cytopenia
 DR RAJE	10%	Low counts and fatigue
 DR STEWART	20%	Rash, fatigue, generalized weakness, diarrhea, muscle cramping, recurrent infection

Module 3: Carfilzomib and Other Novel Proteasome Inhibitors

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Efficacy of carfilzomib (CFZ) versus bortezomib?

 DR BENSINGER	About the same
 DR DIMOPOULOS	CFZ is more efficacious
 DR KRISHNAN	About the same
 DR RAJE	About the same
 DR STEWART	About the same

Have you used CFZ as part of front-line therapy off protocol?

 DR BENSINGER	No
 DR DIMOPOULOS	No
 DR KRISHNAN	No
 DR RAJE	No
 DR STEWART	Yes, if paid for by insurance

Sufficient evidence to use CFZ as front-line therapy?

 DR BENSINGER	Yes
 DR DIMOPOULOS	No
 DR KRISHNAN	No
 DR RAJE	No
 DR STEWART	Yes

Do you believe CFZ is associated with…

	Cardiac toxicity?	Pulmonary toxicity?	Peripheral neuropathy?
 DR BENSINGER	No	No	Yes, minor
 DR DIMOPOULOS	Yes	No	No
 DR KRISHNAN	Yes	Yes	No
 DR RAJE	Yes	Yes	No
 DR STEWART	Yes	No	No

Situations in which you generally conduct cardiac screening prior to administering CFZ?

 DR BENSINGER	History of cardiac disease, on cardiac meds or symptoms suggesting cardiac disease
 DR DIMOPOULOS	History of CHF, CAD, arrhythmia
 DR KRISHNAN	Older patients or those with prior cardiac history
 DR RAJE	Significant cardiac history
 DR STEWART	We don’t routinely conduct cardiac screening

Can CFZ be safely administered to patients with renal failure?

 DR BENSINGER	Yes
 DR DIMOPOULOS	Yes
 DR KRISHNAN	Yes
 DR RAJE	Yes
 DR STEWART	Yes

Next treatment for younger patient with disease progression at end of 2nd year of LEN maintenance after ASCT?

Next immediate treatment if the patient above had received no maintenance therapy after ASCT?

	LEN maintenance	No LEN maintenance
 DR BENSINGER	BTZ	BTZ
 DR DIMOPOULOS	BTZ	LEN
 DR KRISHNAN	Possibly RVD or CyBorD	CyBorD or RVD
 DR RAJE	CFZ	LEN or CFZ
 DR STEWART	CFZ	BTZ

Next treatment for 80 yo with disease progression at end of 2nd year of BTZ maintenance after Rd induction?

 DR BENSINGER	LEN
 DR DIMOPOULOS	LEN
 DR KRISHNAN	Pomalidomide
 DR RAJE	LEN or pomalidomide
 DR STEWART	Pomalidomide

Next treatment for 80 yo with disease progression at end of 2nd year of LEN maintenance after Vd induction?

 DR BENSINGER	BTZ
 DR DIMOPOULOS	BTZ
 DR KRISHNAN	Pomalidomide
 DR RAJE	BTZ or CFZ or pomalidomide depending on patient-specific variables
 DR STEWART	BTZ

How would you compare the peripheral neuropathy associated with…

	Weekly IV BTZ	SubQ BTZ	CFZ	Ixazomib
 DR BENSINGER	7	5	1	3
 DR DIMOPOULOS	6	3	0	0
 DR KRISHNAN	3	3	0	1
 DR RAJE	4	2	0	1
 DR STEWART	6	4	0	2

(0, negligible – 10, very significant)

Module 4: Pomalidomide and Other Emerging Agents

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Sequence of CFZ and pomalidomide (POM) for younger patient with prior response to BTZ and LEN?

Sequence CFZ and POM for an older patient?

	Younger patient	Older patient
 DR BENSINGER	CFZ first	CFZ first
 DR DIMOPOULOS	Either equally likely first	Either equally likely first
 DR KRISHNAN	POM first	POM first
 DR RAJE	Either equally likely first	Either equally likely first
 DR STEWART	Either equally likely first	POM first

Clinical factors used to determine whether to use CFZ or POM for recurrent MM?

 DR BENSINGER	History of thrombotic complications, cardiac disease, age of patient, distance from treatment center
 DR DIMOPOULOS	None
 DR KRISHNAN	Renal failure, thrombosis, cytopenias, convenience
 DR RAJE	Comorbidities and prior therapy
 DR STEWART	Prior response, prior toxicity, genetic risk, compliance, convenience

What agents do you combine with POM in the relapsed/refractory setting?

 DR BENSINGER	Dexamethasone, sometimes BTZ or CFZ
 DR DIMOPOULOS	Low-dose dexamethasone
 DR KRISHNAN	BTZ, doxorubicin, CFZ
 DR RAJE	CLAPD, BTZ, dexamethasone
 DR STEWART	CFZ, BTZ, dexamethasone, cyclophosphamide

Module 5: Bone-Directed Therapy; Smoldering Myeloma

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Recommended bone-targeted therapy for patients with bone involvement?

How long do you generally continue treatment beyond initial therapy?

	Bone-targeted Tx	Duration/frequency
 DR BENSINGER	Zoledronic acid	Indefinitely
 DR DIMOPOULOS	Zoledronic acid	2 years
 DR KRISHNAN	Zoledronic acid	I stop and restart if disease progresses
 DR RAJE	Zoledronic acid	Indefinitely
 DR STEWART	Zoledronic acid	2 years

Do you recommend bone-targeted therapy for patients with no clinical evidence of bone involvement?

 DR BENSINGER	Yes, for most patients
 DR DIMOPOULOS	Yes, for most patients
 DR KRISHNAN	Yes, for most patients
 DR RAJE	Yes, for most patients
 DR STEWART	No

Recommendation for a 65-year-old woman with high-risk smoldering myeloma?

 DR BENSINGER	Close follow-up
 DR DIMOPOULOS	Close follow-up
 DR KRISHNAN	MRI or PET/CT
 DR RAJE	Close follow-up
 DR STEWART	Close follow-up

In what situations, if any, do you treat patients with smoldering myeloma?

 DR BENSINGER	Rapidly rising M protein or symptoms of bone discomfort without lytic disease or hypercalcemia
 DR DIMOPOULOS	I don’t treat smoldering myeloma
 DR KRISHNAN	I don’t treat smoldering myeloma
 DR RAJE	I don’t treat smoldering myeloma
 DR STEWART	I don’t treat smoldering myeloma

When treating smoldering myeloma, what systemic therapy do you generally recommend?

 DR BENSINGER	LEN
 DR DIMOPOULOS	I don’t treat smoldering myeloma
 DR KRISHNAN	I don’t treat smoldering myeloma
 DR RAJE	I don’t treat smoldering myeloma
 DR STEWART	I don’t treat smoldering myeloma