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MULTIPLE MYELOMA: EVERY YEAR A NEW STANDARD?

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When should treatment be initiated?

Potential New Myeloma or Smoldering Myeloma

Any Myeloma Defining Events?	**No Myeloma Defining Events (SMM)**	
• CRAB • ≥60% PC • FLC ≥100 • MRI >1	High Risk SSM (Median TTP ~2 years)	Intermediate or Low Risk SSM
	High Risk SSM Or Evolving SSM	
Treat as Myeloma	• *Early Therapy: Len or Rd* • *Clinical Trials* • *Observation*	*Observation*

Initial Treatment of Myeloma

Newly Diagnosed Myeloma

Not Transplant Candidate		**Transplant Candidate**
VRd x 9 months; *Len Maintenance until progression*	*Frail patients Rd x 1 year;* *Len Maintenance until progression*	*VRd x 3-4 cycles* *Transplant* *Len Maintenance (Standard risk)* *Bortezomib-based Maintenance (High risk)*

Newly Diagnosed Myeloma			
Len not available: ***VTd***	Acute renal failure: ***VCD***	High Risk MM in USA: ***KRd***	Other Situations: ***PAD, VMP***

Key questions

Can we improve on the VRd triplet?

- *Carfilzomib based (eg., KRd)*
- *Monoclonal Antibody based (eg., Drd)*
- *Alkylator based (eg., KCd)*

Should we use quadruplet [Dara-VMP (ALCYONE), Dara-VTd (Cassiopeia), KCRd (MRC XI)]?

- *Cost*
- *Toxicity*

Key questions

- OS is not practical
- Alternatives?
  MRD negative rate *plus* No evidence of survival impairment
  PFS benefit *plus* Trend to OS benefit (CASSIOPEIA)

Myeloma: Frontline Treatment

Newly Diagnosed Myeloma

Not Transplant Candidate		**Transplant Candidate**	
VRd x 8-12 cycles *(VTd/VCd if VRd not available)* *Len Maintenance* *Or* *DRd until progression*	*Frail patients Rd x 1 year;* *Len Maintenance until progression*	*VRd x 3-4 cycles or Dara based quadruplet*	
		In selected high-risk patients	
		Auto SCT *Maintenance:* *Len for std. risk;* *Bortezomib for high risk*	*VRd x 4 cycles* *Len Maintenance*

Based on CALGB 100104; S0777, IFM-2009, CTN 0702, HOVON, MAIA, CASSIOPEIA

Myeloma: First relapse

First Relapse: Consider salvage auto transplant in eligible patients

Not refractory to Lenalidomide*		Refractory to Lenalidomide	
DRd	*Alternatives: KRd, IRd, ERd*	*DVd or DPd*	*Alternatives: EPd, VCd, KPd, IPd, Pd*

*Relapse occurring while off all therapy, or while on small doses of single agent lenalidomide, or on bortezomib maintenance

Myeloma: Second or higher relapse

First Relapse options	Additional options
Any first relapse options that have not been tried (2 new drugs; triplet preferred)	• *VDT-PACE like anthracycline containing regimens* • *Melphalan* • *Bendamustine-based regimens* • *Adding Panobinostat* • *Quadruplet regimens*

*Relapse occurring while off all therapy, or while on small doses of single agent lenalidomide, or on bortezomib maintenance

Active Drugs in Multiple Myeloma

Old Drugs	Older Drugs (2003-2007)	Recently approved Drugs (2013-2015)	Future Drugs
• *Alkylators* • *Steroids* • *Interferon* • *Anthracyclines*	• *Bortezomib* • *Thalidomide* • *Lenalidomide* • *Liposomal doxorubicin*	• *Carfilzomib* • *Pomalidomide* • *Panobinostat* • *Ixazomib* • *Daratumumab* • *Elotuzumab*	*CAR-Ts* *GSK 2857916* *AMG 420* *Isatuximab* *Selinexor* *Venetoclax* *Filanesib* *LGH 447* *Dinaciclib* *Oprozomib* *Marizomib* *Melflufen*

Selection of Regimen (TRAP)	Principles
• Timing of the relapse • Response to prior therapy • Aggressiveness of the relapse • Performance status	• Prefer triplets • At least two new drugs • Consider transplant eligible patients • Clinical trials