

# First Line Treatment of Multiple Myeloma

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## Tenets

- **Tumor Stem Cell - Elusive**
  - MM germinal center-derived post-switch stage
- **Homing and Expansion in Bone Marrow (MM Strong Cross-Talk)**
  - Exploiting the microenvironment including OB/OC for survival: new target for therapy

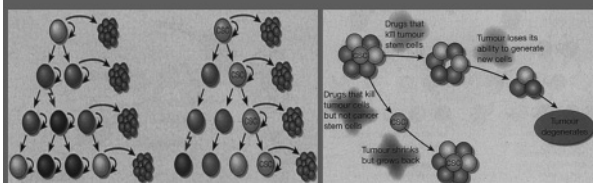
1

## Multi-Step Progression of Multiple Myeloma

	MGUS/Smoldering Myeloma	Intra-Medullary Myeloma	Malignant Myeloma
Stroma-dependence	+++	+++	+
Drug resistance	N/A	•Micro-environment •Stem cell	•Stem cell •Genetic changes
FISH Cytogenetics	Abnormal	Abnormal	Abnormal
Metaphase cytogenetics	Normal	Normal	Abnormal
Potential for long term disease control or cure	N/A	Good	Poor

3

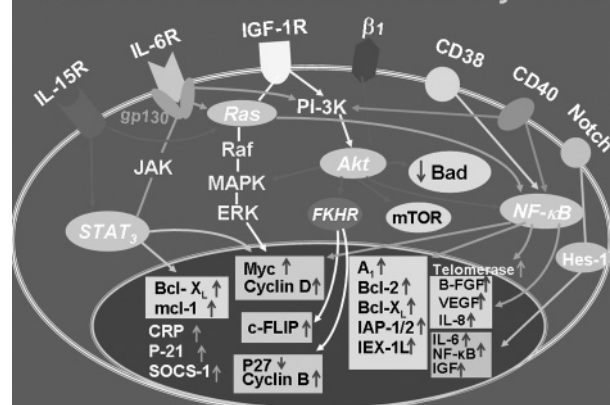
## Cancer Stem Cells



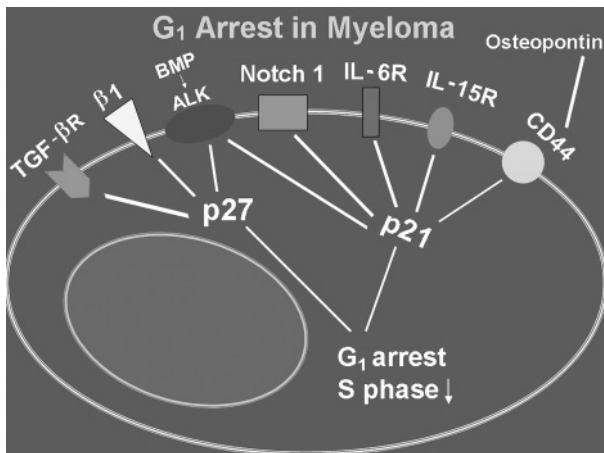
- Non-cycling
- Excellent detoxification

2

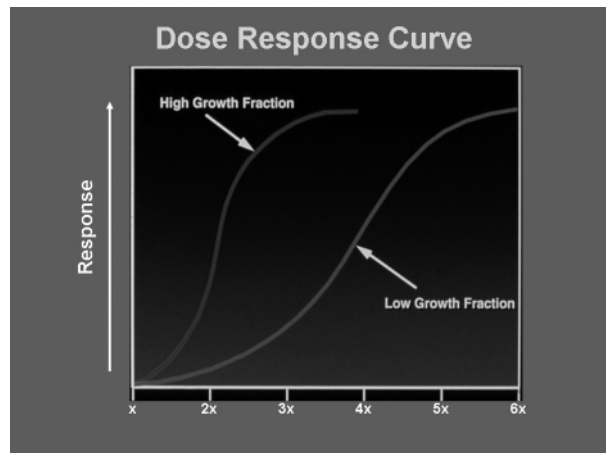
## Growth and Survival Control of Myeloma



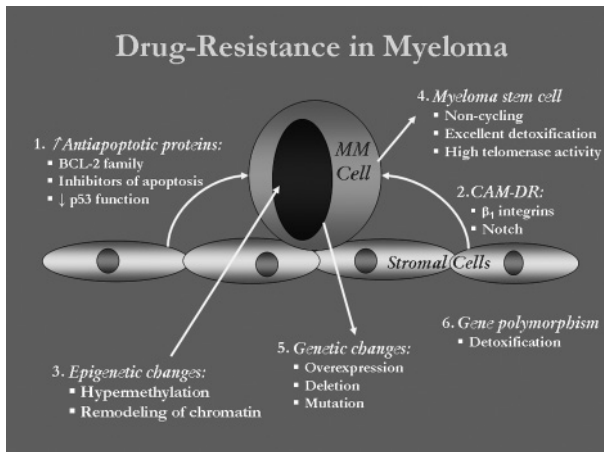
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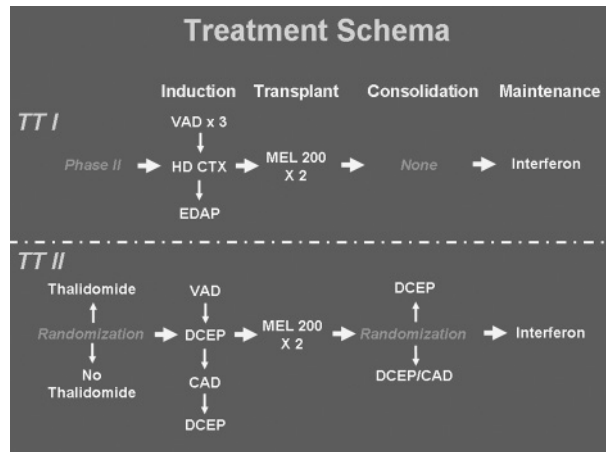
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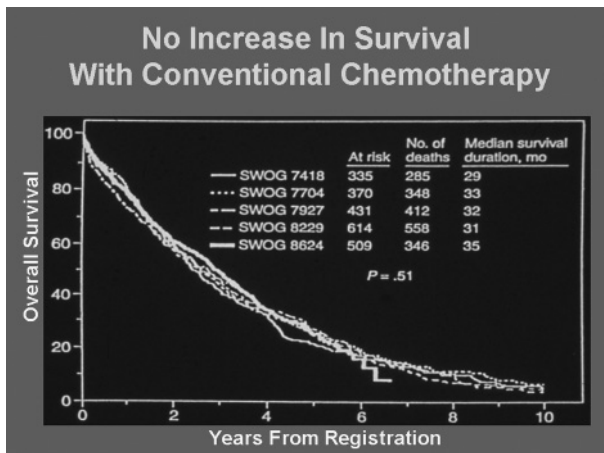
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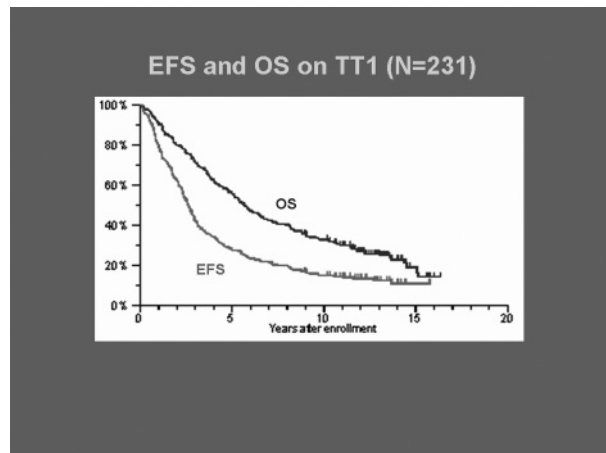
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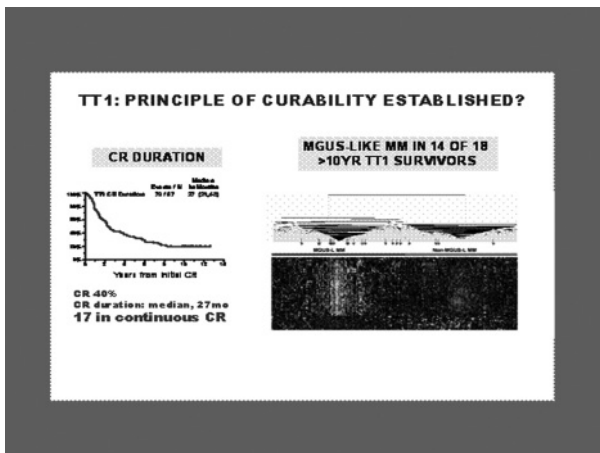
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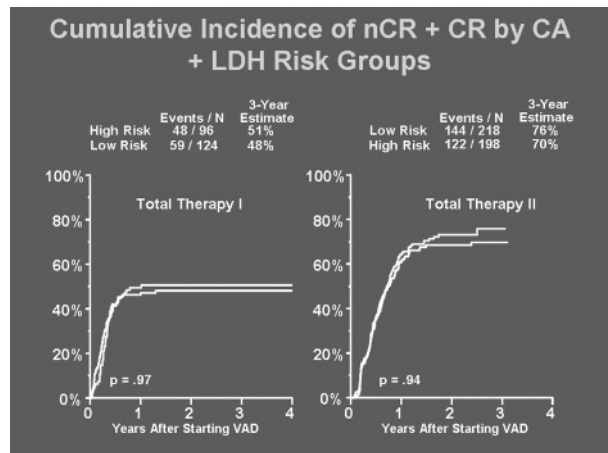
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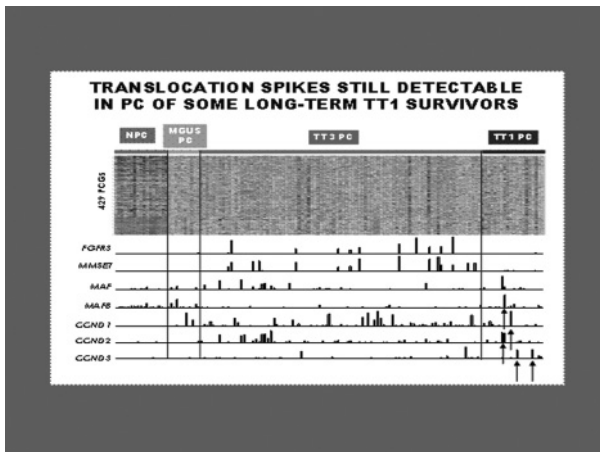
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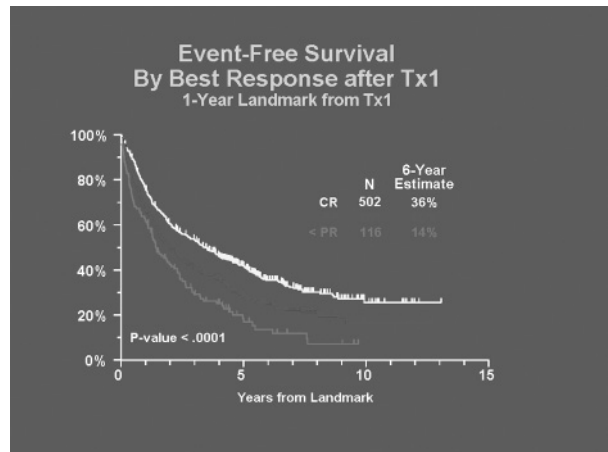
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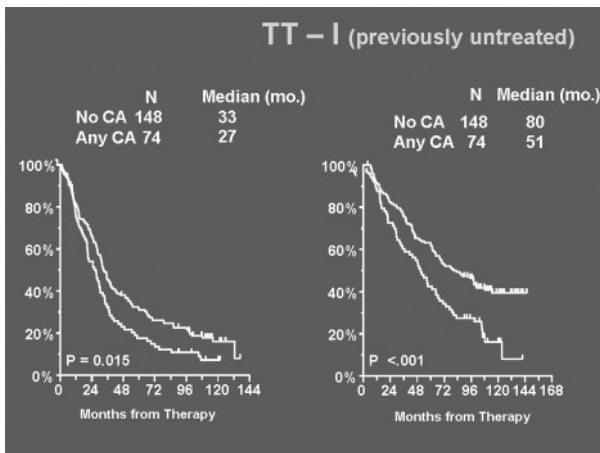
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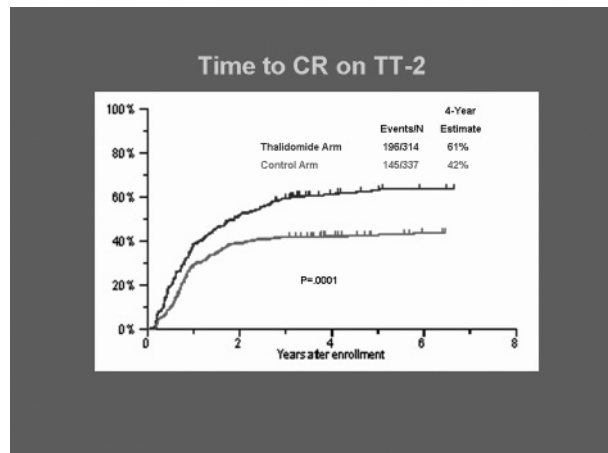
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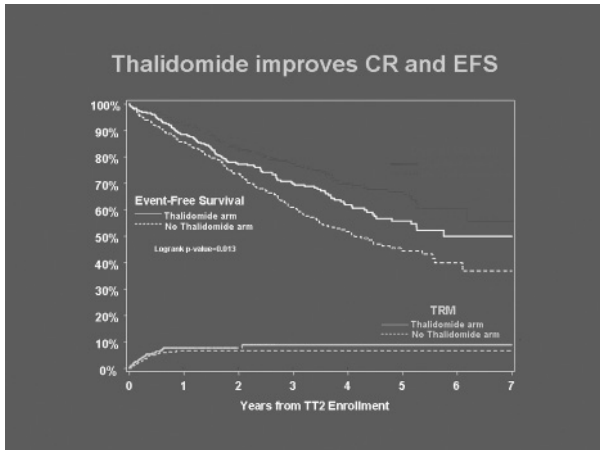
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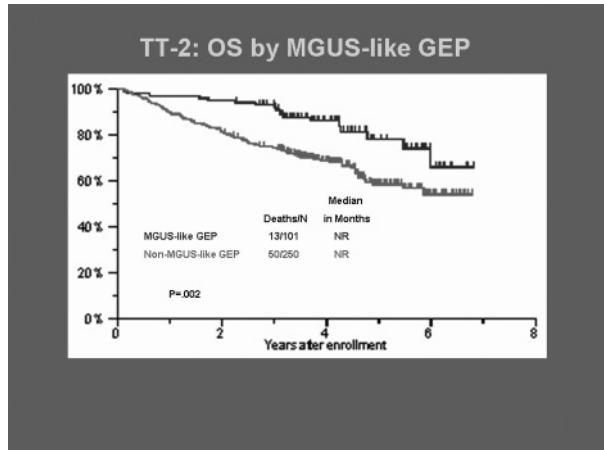
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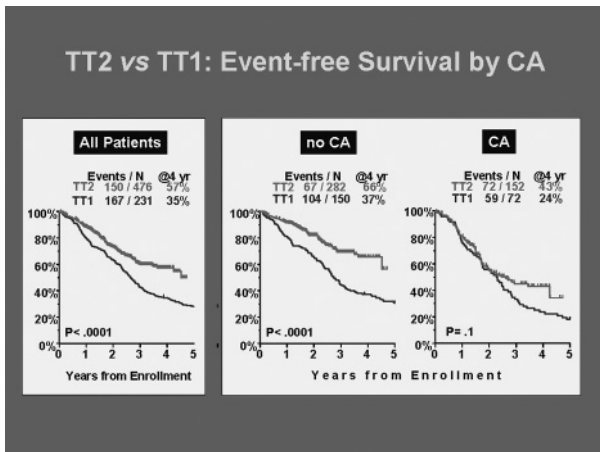
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17



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18

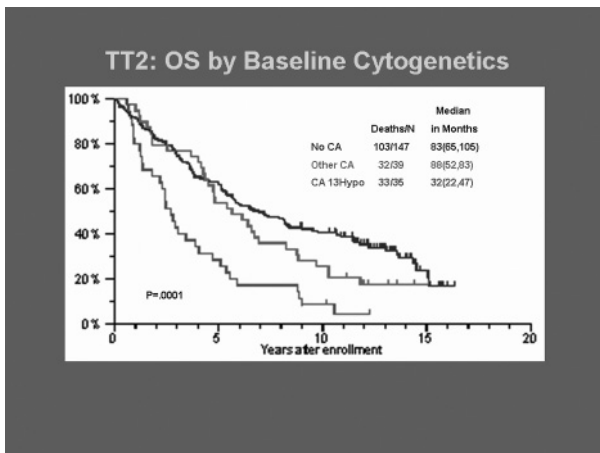
### 10 Gene Model for High Risk MM

Up-regulated		Down-regulated	
CKS1B		AHCYL1	
TMPO		GNG10	
RFC4		EVI5	
TRIP13		MCLC	
FAM72A		C10orf119	

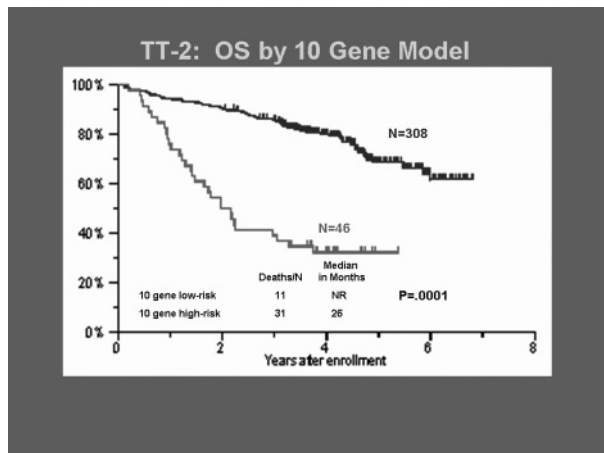
Training Set	Group	N	Low-risk	High-risk
Low-risk	Low-risk	305	283	22
	High-risk	46	3	46
Test Set	Low-risk	159	147	12
	High-risk	22	2	20

92% correctly classified

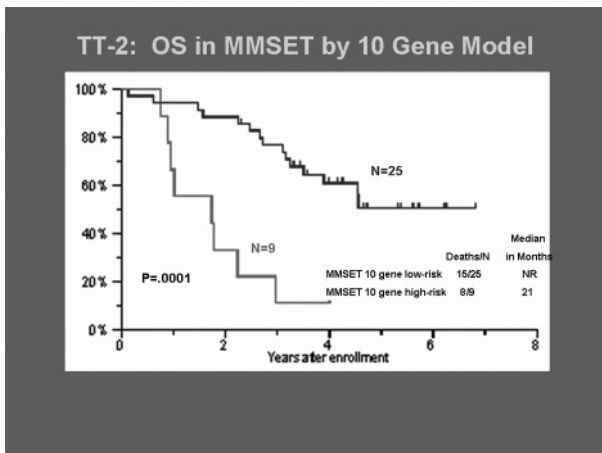
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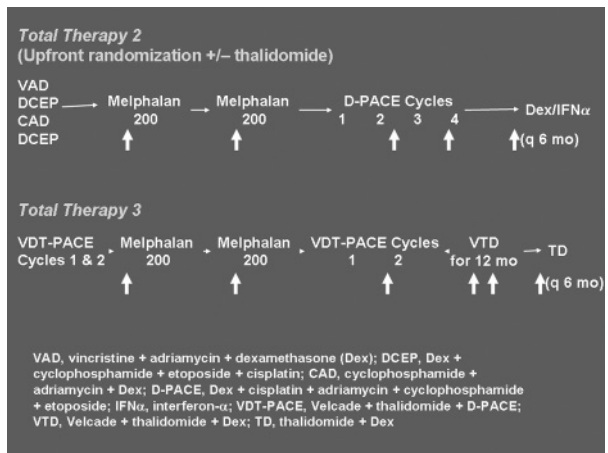
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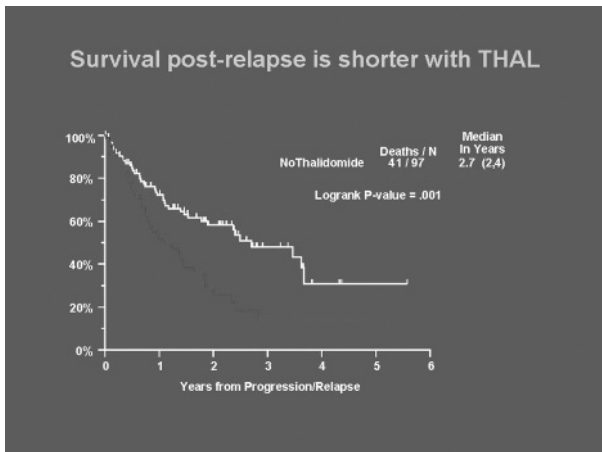
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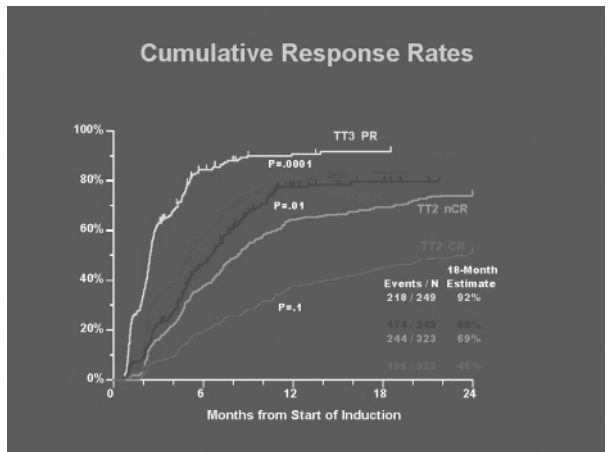
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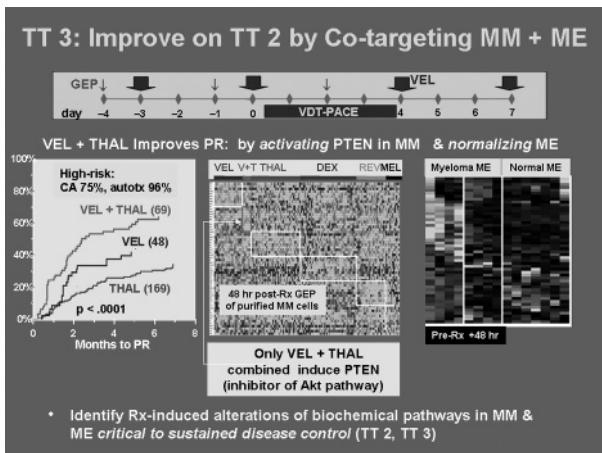
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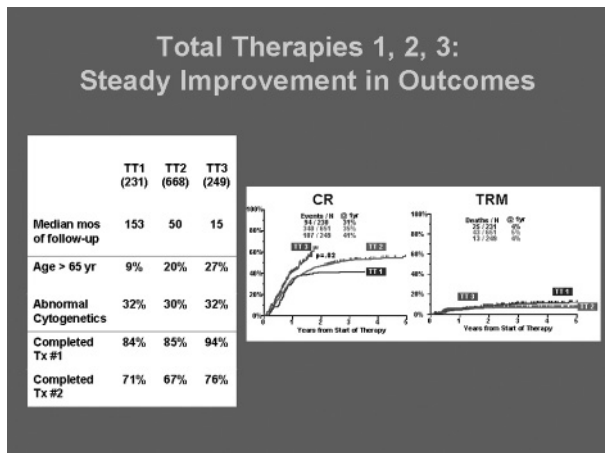
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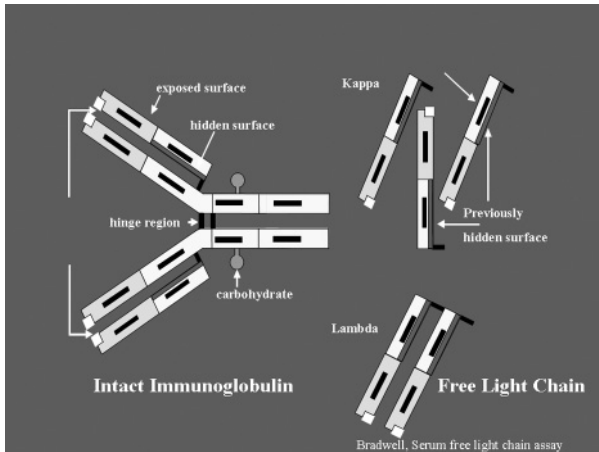
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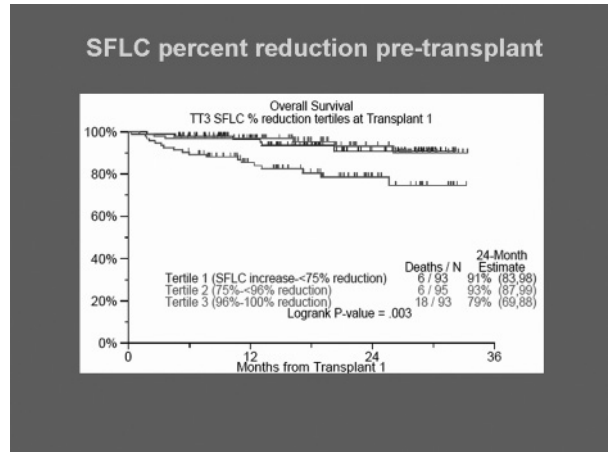
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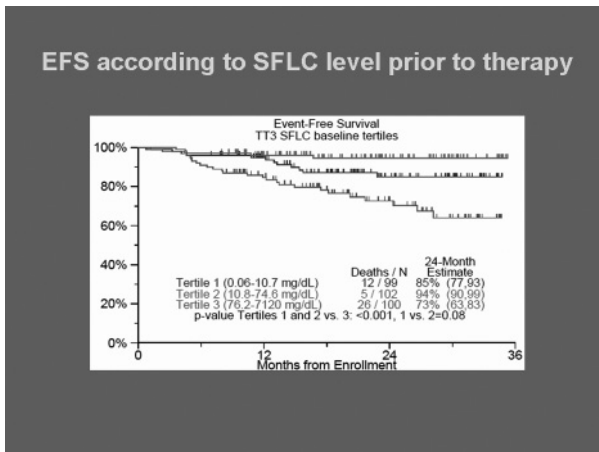
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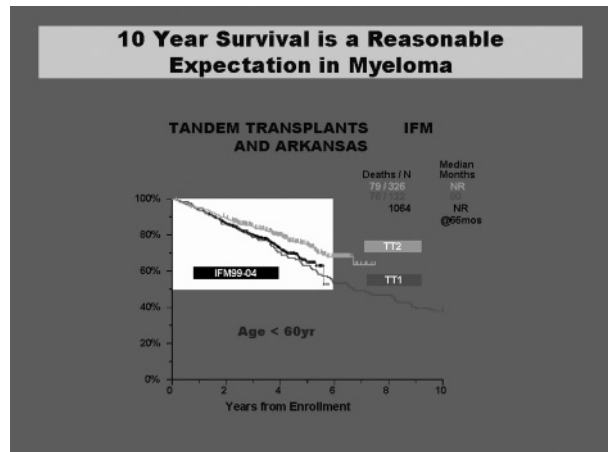
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31



30



32