

## Evaluation of the Revised International Staging System in an independent cohort of unselected patients with multiple myeloma

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Supplemental table 1: Treatments

Regimen	Number of patients	%
<b>MP</b>	14	2,9
<b>VAD/VADlike</b>	27	5,7
<b>VAD+Thalidomide</b>	3	0,6
<b>MDT:</b> Melphalan Dexamethasone Thalidomide	31	6,5
<b>CTD:</b> Cyclophosphamide Thalidomide Dexamethasone	56	11,8
<b>Thalidomide/Dex</b>	2	0,4
<b>Rd:</b> Lenalidomide/Low Dose Dex	100	21,1
<b>RAD:</b> Lenalidomide Doxorubicin Low Dose Dex	8	1,7
<b>MPR:</b> Melphalan Prednisone Lenalidomide	2	0,4
<b>VD:</b> Bortezomib Dex	24	5,1
<b>VCD:</b> Bortezomib Cyclophosphamide Dex	132	27,8
<b>PAD:</b> Bortezomib Doxorubicin Dex	35	7,4
<b>VMP:</b> Bortezomib Melphalan Prednisone	15	3,2
<b>VTD</b> Bortezomib Thalidomide Dexamethasone	25	5,3
<b>VRD</b> Bortezomib Lenalidomide Dexamethasone	1	0,2

Supplemental table 2: Comparison between the characteristics of the patients in the IMWG<sup>10</sup> and our cohort

	IMWG	5-year OS	Current Cohort	5-year OS
N	3060	NR	475	52%
Median age	62		67	
Age ≤65	65%	NR	47%	66%
Age >65	35%		53%	39%
eGFR < 30 ml/min/1.73 m <sup>2</sup>	NR	NR	20%	30%
eGFR ≥ 30 ml/min/1.73 m <sup>2</sup>			80%	57%
ASCT	65%	NR	36%	73%
No ASCT	35%	NR	64%	40%
ISS-1	38%	77%	24%	79%
ISS-2	38%	62%	34%	54%
ISS-3	24%	47%	44%	33%
High risk cytogenetics	24%	50%	23.5%	35%
Standard Risk cytogenetics	76%	69%	75.5%	57%
Increased LDH (>250 U/L)	13%	47%	15%	33%
Normal LDH (≤250 U/L)	87%	68%	85%	54%
R-ISS-1	28%	82%	18%	77%
R-ISS-2	62%	62%	64%	53%
R-ISS-3	10%	40%	18%	19%

NR: not reported

Figure S1: survival per R-ISS vs ISS in all patients

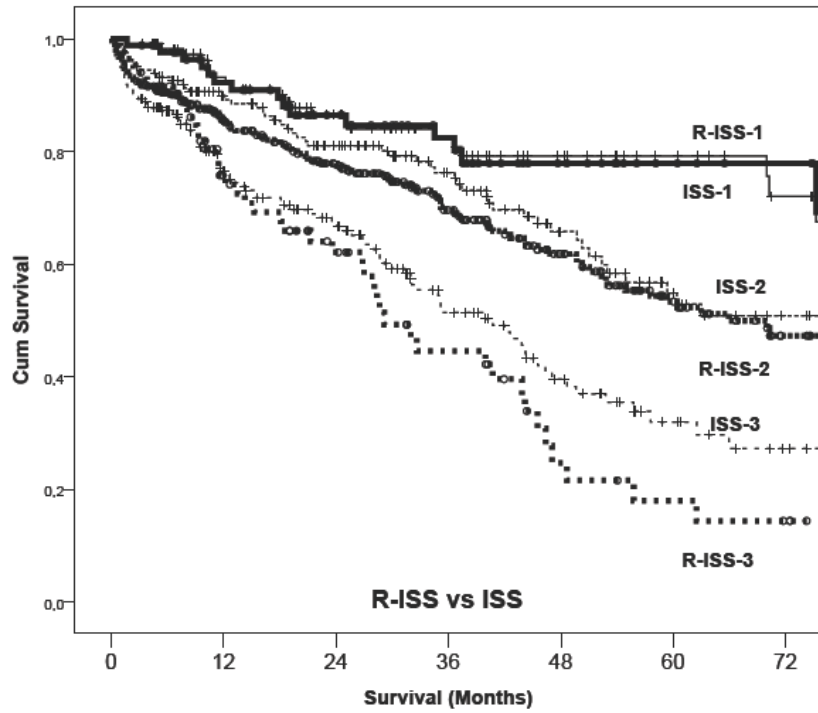


Figure S2: Survival of 495 patients according to Durie Salmon Staging system

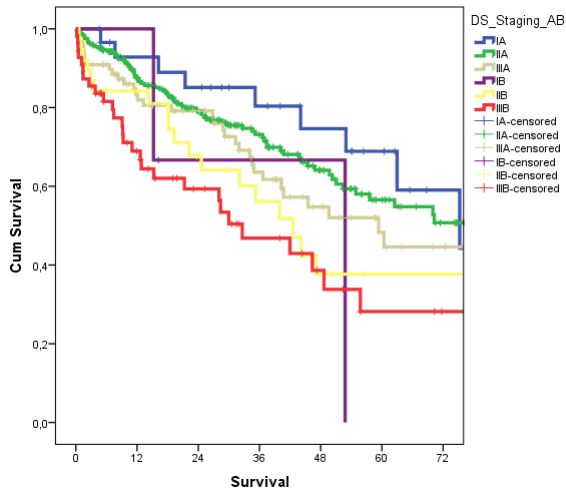


Figure S3: Comparison of ISS and R-ISS in patients that did not receive HDM and those who received HDM

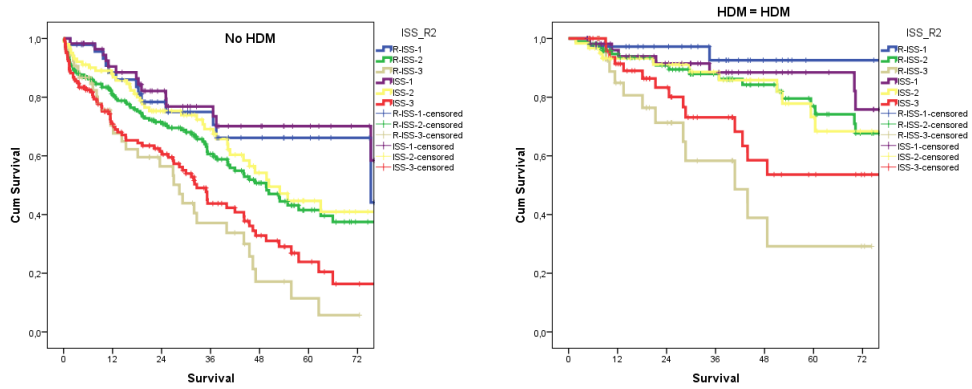


Figure S4: Comparison of R-ISS and ISS in patients who received primary therapy with conventional chemo, thalidomide-based, lenalidomide-based and bortezomib-based therapy

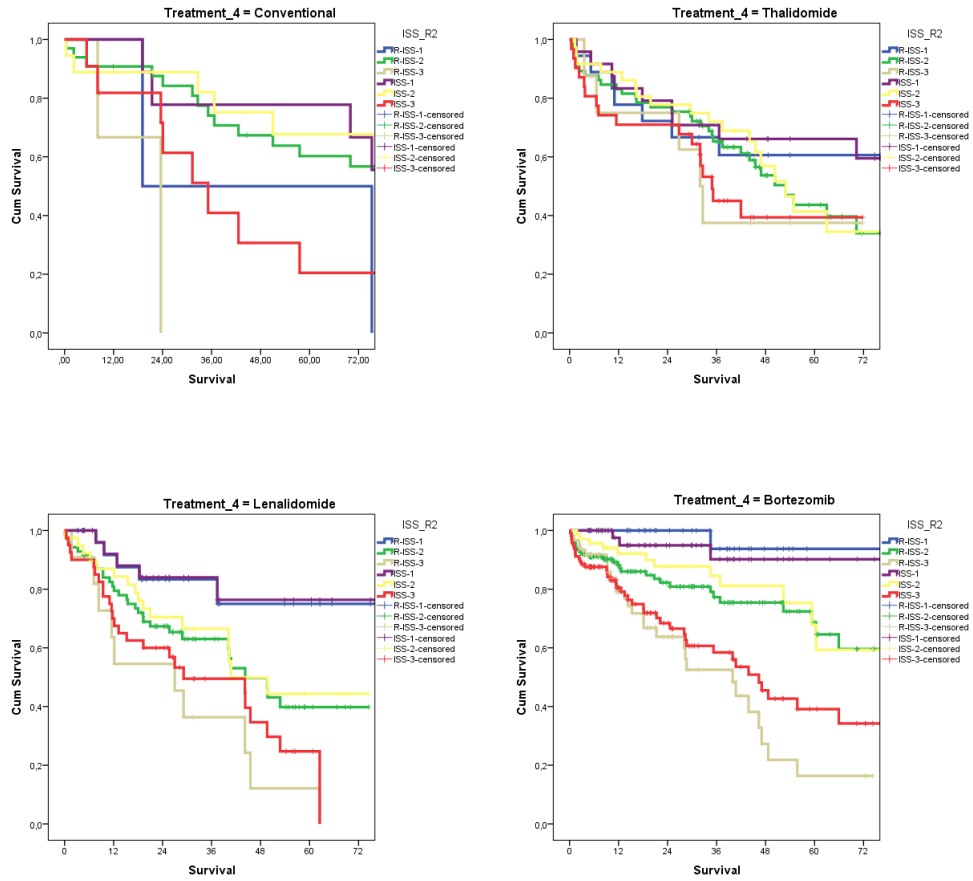


Figure S5: Comparison of R-ISS and ISS in patients <66 and ≥66-75 and ≥76 years of age

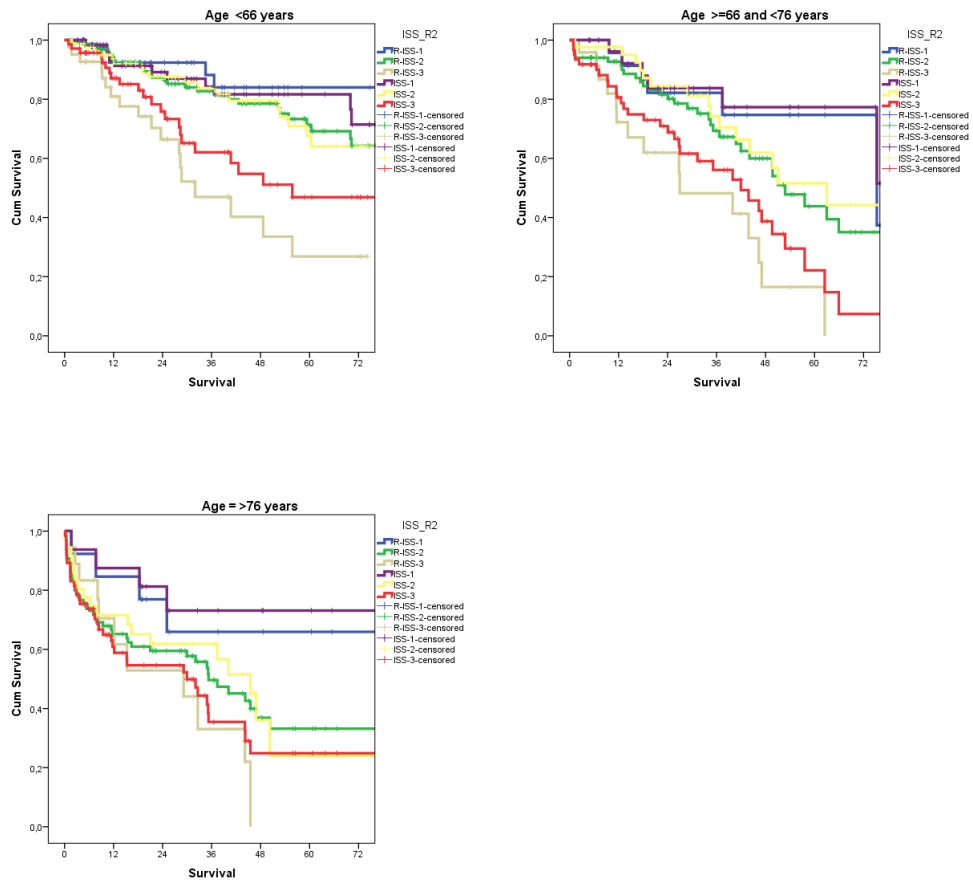
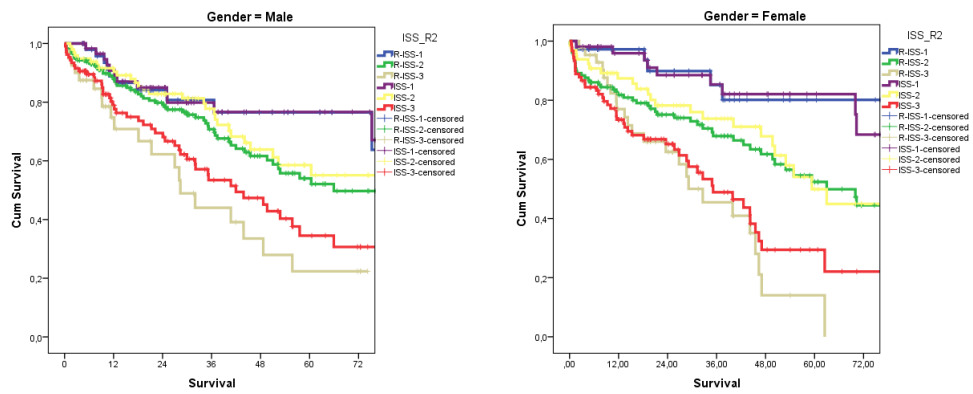


Figure S6: Comparison of R-ISS and ISS in male and female patients



Supplemental Table 3: Multivariate analysis for survival with ISS

	P-value	HR)	95,0% CI for HR	
			Lower	Upper
ISS-1		1		
ISS-2	<b>,022</b>	1,798	1,088	2,973
ISS-3	<b>,002</b>	2,436	1,405	4,223
High Risk Cytogenetics	<b>,000</b>	2,013	1,422	2,851
LDH $\geq$ 250 IU/L	,288	1,242	,833	1,853
Age $\leq$ 65		1		
Age 66-75	,847	1,052	,630	1,757
Age $\geq$ 76	<b>,037</b>	1,783	1,036	3,070
Calcium $\geq$ 11 mg/dl	,575	1,126	,744	1,704
PLT < 130x10 <sup>9</sup> /L	,071	1,485	,966	2,284
Hgb <10 g/dl	,338	1,181	,841	1,659
eGFR < 30 ml/min/1.73 m <sup>2</sup>	,208	1,320	,857	2,036
HDM-ASCT	<b>,025</b>	,538	,313	,927
Conventional Chemo	,694	1		
Thalidomide-based	,840	1,062	,594	1,898
Lenalidomide-based	,565	1,190	,659	2,150
Bortezomib-based	,649	,875	,492	1,556



Supplemental Table 4: Multivariate analysis with Durie-Salmon staging system. Because creatinine, hemoglobin and calcium are included in the D-S are not in the multivariable model

	p-value	HR	95,0% CI for HR	
			Lower	Upper
DS Stage_AB		1		
DS Stage –IIA	,394	1,340	,684	2,623
DS Stage – IIIA	,194	1,615	,783	3,331
DS Stage IB	,131	3,270	,703	15,217
DS Stage IIB	,056	2,225	,980	5,050
DS Stage IIIB	<b>,012</b>	2,739	1,246	6,022
High Risk Cytogenetics	<b>,000</b>	2,158	1,526	3,053
LDH ≥250 IU/L	,207	1,290	,868	1,917
Age < 66				
Age 66-75	,839	1,055	,631	1,764
Age ≥76	<b>,036</b>	1,769	1,037	3,018
PLT <130x 10 <sup>9</sup> /L	,141	1,388	,897	2,150
HDM-ASCT	<b>,002</b>	,426	,247	,735
Conventional Chemo	,838			
Thalidomide-based	,628	,868	,490	1,538
Lenalidomide-based	,979	,992	,553	1,780
Bortezomib-based	,498	,822	,465	1,450