RESEARCH ARTICLE

Clinical profiles of multiple myeloma in Asia—An Asian Myeloma Network study

Kihyun Kim,[1] Jae Hoon Lee,[2]* Jin Seok Kim,[3] Chang Ki Min,[4] Sung Soo Yoon,[5] Kazuyuki Shimizu,[6] Takaaki Chou,[7] Hiroshi Kosugi,[8] Kenshi Suzuki,[9] Wenming Chen,[10] Jian Hou,[11] Jin Lu,[12] Xiao-Jun Huang,[12] Shang-Yi Huang,[13] Wee Joo Chng,[14] Daryl Tan,[15,16] Gerrard Teoh,[17] Chor Sang Chim,[18] Weerasak Nawarawong,[19] Noppadol Siritanaratkul,[20] and Brian G. Durie[21]*

The incidence of multiple myeloma (MM) is known to be variable according to ethnicity. However, the differences in clinical characteristics between ethnic groups are not well-defined. In Asian countries, although the incidence of MM has been lower than that of Western countries, there is growing evidence that MM is increasing rapidly. The Asian Myeloma Network decided to initiate the first multinational project to describe the clinical characteristics of MM and the clinical practices in Asia. Data were retrospectively collected from 23 centers in 7 countries and regions. The clinical characteristics at diagnosis, survival rates and initial treatment of 3,405 symptomatic MM patients were described. Median age was 62 years (range, 19–106), with 55.6% of being male. Median overall survival (OS) was 47 months (95% CI 44.0–50.0). Stem cell transplantation was performed in 666 patients who showed better survival rates (79 vs. 41 months, $P < 0.001$). The first-line treatments of 2,970 patients were analyzed. The overall response rate was 71% including very good partial response or better in 31% of the 2,660 patients those were able to be evaluated. New drugs including bortezomib, thalidomide, and lenalidomide were used in 36% of 2,970 patients and affected OS when used as a first-line treatment.
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Introduction

Multiple myeloma (MM) is one of the most common hematologic malignancies, with 103,826 new cases and 72,453 deaths annually, comprising 0.8% and 1% of all cancers, respectively [1]. Its incidence is known to vary by ethnicity, with Asians showing a relatively lower incidence than Caucasians [1]. However, recent reports have suggested that the incidence of MM is increasing in some Asian countries [2,3]. There have been reports describing the clinical profiles [4–6] as well as the cytogenetic characteristics [7–9] of MM in Asia, with some studies revealing unique findings in their national cohorts. There have also been reports describing unique drug toxicity profiles such as interstitial pneumonitis among Japanese bortezomib users [10,11], as well as lower incidence of thromboembolism among thalidomide users in some Asian countries, even without antithrombotic prophylaxis, strongly suggesting differences in pharmacogenomics [12,13]. Although several studies on the clinical features of MM in Asian countries have been published, all of them were nationwide studies that did not include a variety of Asian ethnicities and did not incorporate recent changes in epidemiology and medical practices. Recognizing the need for Asian multi-national studies, the Asian Myeloma Network (AMN) was launched in March 2011 under the auspices of the International Myeloma Foundation (IMF) with the participation of 7 countries and regions which already had national myeloma study groups at the time: China, Hong Kong, Japan, Korea, Singapore, Taiwan, and Thailand. For our first project, we conducted a multinational study to define the clinical characteristics of MM in Asian countries. Our key question was whether MM in Asia has characteristics that differ from its presentation in Western countries.

[1]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [2]Division of Hematology-Oncology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, South Korea; [3]Division of Hematology, Department of Internal Medicine, Yonsei University College of Medicine, Severance Hospital, Seoul, South Korea; [4]Hematology, Department of Internal Medicine, Seoul St. Mary's Hospital, the Catholic University of Korea, Seoul, Korea; [5]Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea; [6]Department of Hematology, Tokai Central Hospital, Japan; [7]Hematology, Department of Internal Medicine, Niigata Cancer Center Hospital, Niigata, Japan; [8]Department of Hematology, Ogaki Municipal Hospital, Ogaki, Japan; [9]Department of Hematology, Japanese Red Cross Medical Center, Tokyo, Japan; [10]Department of Hematology, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China; [11]Myeloma and Lymphoma Center, Department of Hematology, Chang Zheng Hospital, Shanghai, China; [12]Department of Hematology, Peking University People's Hospital Peking University Institute of Hematology, Beijing, China; [13]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; [14]Department of Haematology-Oncology, National University Cancer Institute of Singapore, National University Health System, Singapore, Singapore; [15]Department of Internal Medicine, Raffles Cancer Center, Raffles Hospital, Singapore; [16]Department of Medicine, Department of Hematology Singapore General Hospital, Singapore, Singapore; [17]Gerrard Teoh Hematology & Medical Clinic, Novena Medical Center, Singapore, Singapore; [18]Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong, China; [19]Department of Medicine, Chiang Mai Medical School, Maung, Thailand; [20]Division of Hematology, Department of Medicine, Siriraj Hospital, Bangkok, Thailand; [21]Department of Hematology, Cedars-Sinai Comprehensive Cancer Center, Los Angeles, CA, USA

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***Correspondence to:** Jae Hoon Lee, Division of Hematology-Oncology, Department of Internal Medicine, Gachon University Gil Medical Center, 1198 Guwol-dong, Namdong-gu, Incheon 405-220, South Korea. E-mail: jhlee@gilhospital.com or Brian G. Durie, Department of Hematology, Cedars-Sinai Comprehensive Cancer Center, Los Angeles, CA USA. E-mail: BDurie@myeloma.org
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Methods

Patients. Data from 3,405 symptomatic myeloma patients was collected from tertiary centers of seven countries/regions: China, Hong Kong, Japan, Korea, Singapore, Taiwan, and Thailand. The number of patients was not distributed according to the population or size of respective countries or regions as the study was designed to include about 500 cases from each country or region. The year of diagnosis ranged from 1986 to 2011. Clinical and laboratory data at the time of diagnosis and data on treatment were retrospectively collected from medical records and existing databases. The data were sent to the principal investigators as written case record forms or electronic data forms. Each patient's data was labeled with a unique identification number to minimize the risk of exposing private medical information. The study protocol was approved by institutional review boards in accordance with the declaration of Helsinki.

Statistical analysis. The Chi-square test was used to test the correlation of categorical variables, with the Fisher's exact test applied when appropriate. The distribution of continuous variables across different groups was compared using the Student's *t* test or the Mann-Whitney U test. Overall survival (OS) was estimated from the date of the diagnosis until the date of death or the last follow-up for living patients. Patients who were lost to follow-up were censored at the date of last contact. Cumulative survival curves were plotted according to the Kaplan and Meier method. The log-rank test was used to compare survival differences among categorical variables. The Cox proportional hazard model was used for multivariate analysis of OS. Due to missing data, three different multivariate analyses were conducted with different sets of variables: baseline characteristics in combination with treatment variables, cytogenetics or FISH results. All p values were 2-sided, with 0.05 chosen as the level of statistical significance. All statistical analyses were performed using a statistical software package (SPSS, Version 20.0, and Chicago, IL).

Results

Clinical characteristics

The median age of all patients was 62 years (range, 19–106), and 55.6% were male. The most common heavy chain type was IgG (55.2%), followed by IgA (22.0%). Light chain disease (17.9%) was the third common myeloma subtype. Bone lesions were documented in 60.2% of the patients and extramedullary plasmacytoma in 15.4% of the patients. Hypercalcemia, significant azotemia, significant anemia, and thrombocytopenia were presented in 16.7%, 23.4%, 60.7%, and 8.8% of patients, respectively. The International Stage System

TABLE I. Clinical Characteristics of the Patients

		Total	China	Hong Kong	Japan	Korea	Singapore	Taiwan	Thailand
	No of centers	23	3	1	3	3	2	1	10
	N	3405	798	109	601	587	493	414	403
	%	100	23.4	3.2	17.7	17.2	14.5	12.2	11.8
Age	median	62	59	65	66	61	62	63	59
	range	19–106	23–106	35–93	29–90	23–93	25–93	24–90	19–95
	< 65	58.5%	68.4%	48.6%	42.1%	63.7%	55.6%	53.1%	67.5%
	≥ 65	41.5%	31.6%	51.4%	57.9%	36.3%	44.4%	46.9%	32.5%
Gender	Female	44.4%	38.6%	32.1%	49.4%	46.7%	48.7%	35.0%	53.1%
	Male	55.6%	61.4%	67.9%	50.6%	53.3%	51.3%	65.0%	46.9%
Heavy Chain Type	N	3129	736	99	594	587	481	406	226
	IgG	55.2%	50.4%	48.5%	58.8%	48.6%	63.4%	50.2%	65.5%
	IgA	22.0%	23.2%	18.2%	19.7%	24.2%	20.8%	23.9%	19.5%
	IgD	3.1%	6.0%	7.1%	3.4%	1.5%	1.0%	3.2%	0.0%
	LCD	17.9%	17.8%	23.2%	17.3%	20.6%	13.3%	20.9%	15.0%
	Non-secretory	1.9%	2.3%	0.0%	0.7%	4.3%	1.2%	1.5%	0.0%
Hemoglobin	N	3271	759	104	572	587	470	377	402
	≥10.0 g/dl	39.3%	37.4%	44.2%	46.2%	41.9%	40.2%	37.4%	29.1%
	<10.0 g/dl	60.7%	62.6%	55.8%	53.8%	58.1%	59.8%	62.6%	70.9%
Platelets	N	3157	734	15	574	587	468	376	403
	<70 X 109/l	8.8%	10.1%	6.7%	12.9%	5.6%	5.3%	10.1%	7.9%
	≥70 X 109/l	91.2%	89.9%	93.3%	87.1%	94.4%	94.7%	89.9%	92.1%
Bone lesion	N	2661	201	88	570	581	404	414	403
	yes	60.2%	74.6%	73.9%	80.0%	67.3%	46.3%	57.2%	28.5%
	no	39.8%	25.4%	26.1%	20.0%	32.7%	53.7%	42.8%	71.5%
Extramedullary plasmacytoma	N	3093	797	99	580	585	353	414	265
	presence	15.4%	15.6%	20.2%	5.2%	23.9%	14.2%	12.6%	22.6%
	absence	84.6%	84.4%	79.8%	94.8%	76.1%	85.8%	87.4%	77.4%
Serum creatinine	N	3173	709	71	571	587	462	373	400
	<2.0 mg/dl	76.6%	76.0%	80.3%	83.9%	82.8%	75.1%	69.2%	66.5%
	≥2.0 mg/dl	23.4%	24.0%	19.7%	16.1%	17.2%	24.9%	30.8%	33.5%
Serum albumin	N	3030	686	93	588	587	454	235	387
	<3.5 g/dl	52.0%	51.6%	52.7%	40.6%	52.0%	63.9%	39.6%	63.3%
	≥3.5 g/dl	48.0%	48.4%	47.3%	59.4%	48.0%	36.1%	60.4%	36.7%
Serum beta 2-microglobulin	N	2857	660	62	507	587	403	324	314
	<3.5 mg/l	34.5%	29.1%	37.1%	41.6%	35.6%	39.7%	37.3%	22.6%
	3.5–5.5 mg/l	23.4%	22.0%	35.5%	26.0%	25.9%	24.3%	18.8%	18.5%
	>5.5 mg/l	42.1%	48.9%	27.4%	32.3%	38.5%	36.0%	43.8%	58.9%
ISS	N	2984	775	59	532	587	446	273	312
	I	19.9%	16.5%	25.4%	30.8%	22.1%	15.5%	18.3%	12.2%
	II	36.1%	32.8%	45.8%	36.8%	39.4%	44.4%	29.7%	28.5%
	III	44.0%	50.7%	28.8%	32.3%	38.5%	40.1%	52.0%	59.3%
Serum calcium	N	3063	670	69	570	587	408	367	392
	≥10.5 mg/dl	16.7%	13.1%	40.6%	13.5%	11.9%	13.5%	19.6%	31.1%
	<10.5 mg/dl	83.3%	86.9%	59.4%	86.5%	88.1%	86.5%	80.4%	68.9%
Plasma cells of BM	N	3042	723	64	529	587	385	382	372
	<30%	41.1%	51.6%	42.2%	55.6%	35.9%	36.4%	30.9%	23.1%
	30–70%	40.5%	36.8%	35.9%	35.9%	45.3%	48.1%	41.9%	38.2%
	>70%	18.4%	11.6%	21.9%	8.5%	18.7%	15.6%	27.2%	38.7%

LCD, light chain disease; ISS, international staging system; BM, bone marrow.

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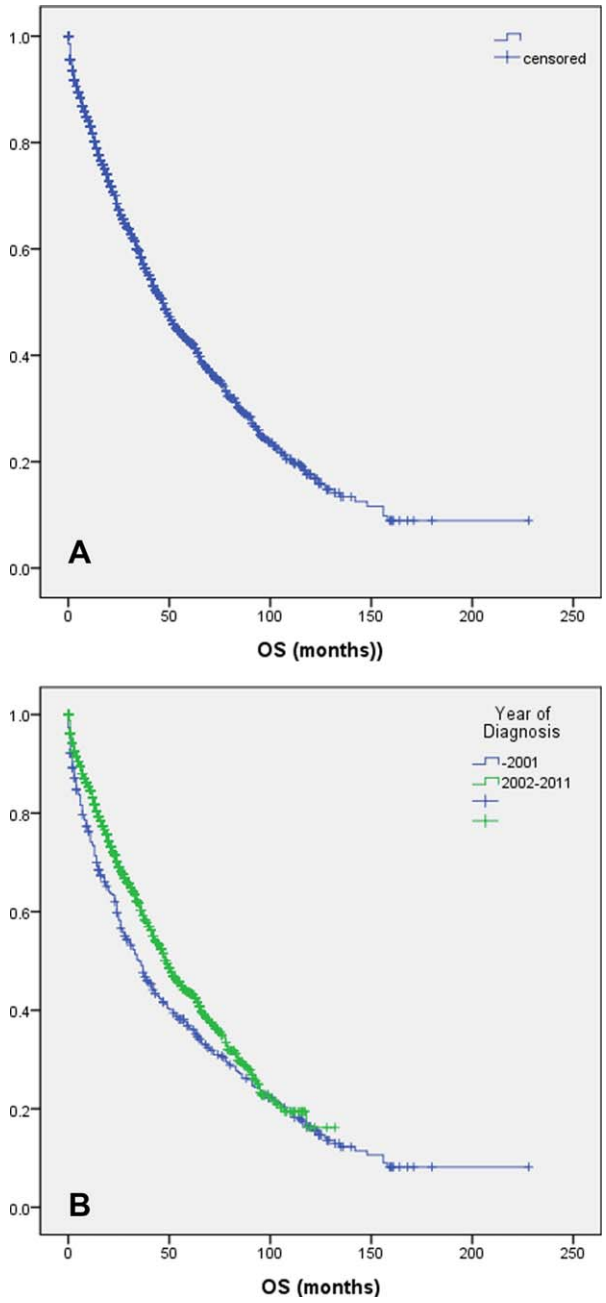

Figure 1. Overall survival of Asian myeloma patients. A: Overall survival of 3405 Asian myeloma patients. Median OS was 47 months. B: OS according to the year of diagnosis. [1986–2001 ($n = 486$) vs. 2002–2011 ($n = 2,919$), 35 vs. 49 months, $P < 0.001$]. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

(ISS) was 19.9%/36.1%/44.0% for stages I/II/III, respectively. Detailed baseline characteristics are summarized in Table I. The median overall survival (OS) was 47 months (95% CI 44.0–50.0) (Fig. 1A).

Cytogenetics

Conventional cytogenetic results were available in 1,681 patients and FISH results were available in a smaller subset of patients due to the variable capabilities of the study centers over various time periods. We could gather the results of FISH for t(11;14)/ t(4;14)/ t(14;16)/ 17p deletions from 683/637/498/854 patients, respectively. The proportion of each genetic abnormality observed and overall survival are summarized in Table II. Abnormal cytogenetics was observed in 32.5% of the patients. The rates of diploidy/hyperdiploidy/nonhyperdiploidy were 70.1%/14.8%/15.1%, respectively. 13q deletions were detected in 12.2%

TABLE II. Cytogenetics of the Patients

		N (%)	OS (months)	*P* value
Conventional cytogenetics	Total	1681	47	
	Normal	1135 (67.5%)	53	<0.001
	Abnormal	546 (32.5%)	34	
Cytogenetic ploidy	Total	1660	47	
	Diploidy	1164 (70.1%)	53	<0.001
	Hyperdiploidy	245 (14.8%)	37	
	Nonhyperdiploidy	251 (14.8%)	28	
Cytogenetic 13q deletion	Total	1647	48	
	Yes	201 (12.7%)	24	<0.001
	No	1446 (87.8%)	52	
FISH t(11;14)	Total	683	54	
	Yes	119 (17.4%)	47	0.936
	No	564 (82.6%)	54	
FISH t(4;14)	Total	637	53	
	Yes	67 (10.5%)	34	0.02
	No	570 (89.5%)	60	
FISH t(14;16)	Total	498	66	
	Yes	22 (4.4%)	NR	0.365
	No	476 (95.6%)	66	
FISH 17p deletion	Total	854	51	
	Yes	114 (13.3%)	38	0.061
	No	740 (87.7%)	54	

of the patients by conventional cytogenetics. By FISH study, the rates of t(11;14)/t(4;14)/t(14;16)/17p deletions were 17.4%/10.5%/4.4%/13.3%, respectively. The Chinese data showed a higher incidence of 17p deletions. On univariate analyses the presence of abnormal conventional cytogenetics, non-ploidy karyotype, 13q deletion, and t(4;14) were associated with significant negative impact on overall survival ($P < 0.05$), while the 17p deletion by FISH was associated with a nonsignificant trend towards an inferior survival outcome ($P = 0.061$).

Treatment

Treatment characteristics and response outcomes are summarized in Table III. Autologous transplantation was conducted in 19.8% (666 patients).The first-line treatment of 2,970 patients was analyzed. The overall response rate was 71%, with a very good partial response (VGPR) or better observed in 31% of the 2660 evaluable patients. New drugs including bortezomib, thalidomide, and lenalidomide were administered to 36% of 2,970 patients and they impacted on the overall survival on multivariate analysis.

Survival and prognostic factors

The clinical parameters affecting overall survival by univariate analysis were age, hemoglobin, platelets, extramedullary plasmacytoma, bone marrow plasma cells, serum calcium, serum albumin, serum creatinine, serum beta-2 microglobulin, heavy chain type, and ISS (Table IV). OS of patients who were diagnosed in recent 10 years was better than those who were diagnosed before (Fig. 1B). Autologous stem cell transplantation (ASCT) and response to first-line treatment were found to be prognostic variables by univariate analysis (Table III). On multivariate analyses heavy chain type, ISS, BMPC, extramedullary plasmacytoma, and serum creatinine were identified as significant prognostic factors. In addition, novel drug exposure as a first-line treatment, transplantation, 13q deletion by conventional cytogenetics, and the presence of any adverse FISH abnormality including t(4;14), t(14;16), and 17p deletions were also identified as important prognostic factors (Table V).

Discussion

MM is characterized by its unique clinical characteristics of bone lesions and the presence of M-protein. The ethnic difference in the incidence of MM has been shown in US SEER data and IARC data, with Asians having a relatively lower incidence of MM [1]. Although

TABLE III. Treatment and Prognostic Significance

		N	OS (months)	*P* value		*N*	OS (months)	*P* value
ASCT (*N* = 3,371)	Yes	666 (19.8%)	79	<0.001				
	No	2705 (80.2%)	41					
First-line treatment (*N* = 2,970)	New drugs	1067 (35.9%)	49	0.098	IMiDs-based	502 (16.9%)	49	0.286
					Bortezomib-based	447 (15.1%)	51	
					Bortzomib andIMiDs	118 (4.0%)	53	
	conventional	1903 (64.1%)	48		conventional	1903 (64.1%)	48	
Response to first-line treatment (*N* = 2,660)	≥ VGPR	821 (30.9%)	69	<0.001	CR	450 (16.9%)	68	<0.001
					nCR	124 (4.7%)	64	
					VGPR	247 (9.3%)	77	
	PR	1053 (39.6%)	50		PR	1053 (39.6%)	50	
	< PR	786 (29.5%)	34		MR	102 (3.8%)	42	
					SD	481 (18.1%)	34	
					PD	203 (7.6%)	22	

ASCT, autologous stem cell transplantation; IMiDs, immune modulating drugs; CR, complete response; VGPR, very good partial response; PR, partial response; MR, minor response; SD, stable disease; PD, progressive disease.

this lower genetic susceptibility has been partly attributed to genetic polymorphisms [14,15], the exact reason has not been elucidated. Recently, there is growing evidence that MM incidence rates are increasing in some Asian countries such as South Korea and Taiwan [2,3]. The South Korean experience is particularly interesting. The incidence of MM in South Korea has doubled over a 10-year period, and based on recent national cancer registry data increase was 10 times compared with MM incidence of 20 years ago. The difference

TABLE IV. Univariate Analysis for Overall Survival

		Total	Median OS (months)	*P* value
Age	*N*	3,405		
	<65	1,992 (58.5%)	55	<0.001
	≥65	1,413 (41.5%)	37	
Gender	Female	1,513 (44.4%)	50	0.262
	Male	1,892 (55.6%)	45	
Type	*N*	3,129		
	IgG	55.2%	52	0.002
	IgA	22.0%	43	
	IgD	3.1%	33	
	LCD	17.9%	43	
	Nonsecretory	1.9%	67	
	other	0.5%		
Hemoglobin	*N*	3271		
	≥10.0 g/dL	1,287 (39.3%)	64	<0.001
	<10.0 g/dL	1,984 (60.7%)	40	
Platelets	N	3157		
	<70 × 109/L	277 (8.8%)	34	0.001
	≥70 × 109/L	2,880 (91.2%)	48	
Bone lesion	N	2661		
	Yes	1,601 (60.2%)	48	0.554
	No	1,969 (39.8%)	52	
Extramedullary plasmacytoma	*N*	3,093		
	presence	476 (15.4%)	40	0.01
	absence	2,617 (84.6%)	49	
Serum creatinine	*N*	3173		
	<2.0 mg/dL	2,430 (76.6%)	52	<0.001
	≥2.0 mg/dL	741 (23.4%)	31	
Serum albumin	*N*	3,030		
	<3.5 g/dL	1,575 (52%)	40	<0.001
	≥3.5 g/dL	1,455 (48%)	58	
Serum beta 2-microglobulin	*N*	2,857		
	<3.5 mg/L	987 (34.5%)	68	<0.001
	3.5–5.5 mg/L	668 (23.4%)	52	
	>5.5 mg/L	1,202 (42.1%)	33	
ISS	*N*	2,984		
	I	594 (19.9%)	80	<0.001
	II	1,076 (36.1%)	53	
	III	1,314 (44%)	33	
Serum calcium		3,063		
	≥10.5 mg/dL	512 (16.7%)	33	<0.001
	<10.5 mg/dL	2,551 (83.3%)	50	
Plasma cells of BM	*N*	3,042		
	<30%	1,249 (41.1%)	59	<0.001
	30–70%	1,232 (40.5%)	45	
	>70%	561 (18.4%)	34	

LCD, light chain disease; ISS, international staging system; BM, bone marrow.

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TABLE V. Multivariate Analysis for Overall Survival

		HR	95% CI	p value
Baseline characteristicswith treatment ($N = 1,580$)	Heavy chain type others vs. IgG	1.228	1.049–1.437	0.01
	ISS II vs. I	1.299	1.029–1.64	0.028
	ISS III vs. I	1.847	1.43–2.385	<0.001
	Plasma cells in BM >70% vs. <30%	1.332	1.06–1.675	0.014
	Plasmacytoma presence vs. absence	1.528	1.228–1.902	<0.001
	Scr ≥2.0 vs. <2.0 mg/dl	1.25	1.009–1.548	0.042
	First-line Treatment New drug vs. chemotherapy	0.675	0.544–0.826	<0.001
	Transplantation yes vs. no	0.456	0.372–0.56	<0.001
Baseline characteristics with conventional cytogenetics ($N = 1,239$)	age ≥ 65 vs. <65	1.531	1.295–1.809	<0.001
	heavy chain type others vs. IgG	1.255	1.063–1.481	0.007
	ISS II vs. I	1.449	1.133–1.854	0.003
	ISS III vs. I	1.751	1.326–2.312	<0.001
	Plasmacytoma presence vs. absence	1.372	1.081–1.741	0.009
	Scr≥2.0 vs. <2.0 mg/dl	1.459	1.143–1.862	0.002
	13q deletion yes vs. no	1.873	1.421–2.469	<0.001
Baseline characteristics with FISH ($N = 441$)	age ≥ 65 vs. <65	1.546	1.109–2.154	0.01
	ISS II vs. I	1.86	1.049–3.3	0.034
	ISS III vs. I	3.096	1.704–5.626	<0.001
	platelets $<70 \times 10^9$ vs. $\geq 70 \times 10^9$/L	1.665	1.06–20616	0.027
	Plasmacytoma presence vs. absence	2.025	1.333–3.076	0.001
	t(4;14), t(14;16) or 17p deletion yes vs. no	1.488	1.027–2.155	0.035

ISS, international staging system; BM, bone marrow; Scr, serum creatinine.

is even more striking when reference is made to the national mortality data and incidence survey by their society of hematology [2]. The incidence of total cancers in South Korea increased two times during last 10 years, while, the incidence of acute leukemias was almost static during the same period. As a result, MM is currently ranked as the third most common hematologic malignancy, surpassing acute lymphoblastic leukemia (ALL) in 2007 and approaching the incidence of acute myeloid leukemia (AML) [16]. Exactly the same observation, doubling of MM incidence in last 10 years, has been reported in Taiwan, which has a similar socioeconomic development status as South Korea, but different ethnic groups [3]. Other countries in Asia have also reported an increasing incidence of MM, although the degree of increase has varied. The exact reasons for this increase have yet to be explored. Of course increased detection may have played an important role, especially in early period. The other two speculated factors are industrialization and aging. Industrialization is associated with increased exposure to chemical carcinogens, ionizing radiation, air pollution, Westernized diets, and obesity, which are known predisposing factors for developing MM [17]. Aging is suspected to be another important contributing factor. MM is considered a disease of the elderly and its incidence increases sharply with age, as shown in the SEER as well as the South Korean data [16]. Japan is a good example for this observation. Although Japan has a moderate age-adjusted incidence rate of MM, its crude incidence is the highest among Asian countries because the country has a larger elderly population. In the same vein, South Koreans have been witnessing an 18-year increase in the median life expectancy over a 37-year observation period, an unprecedented change that is suspected to be strongly associated with the increased rates of MM. One more thing we should consider is the incidence of monoclonal gammopathy of undetermined significance (MGUS) among Asian countries. Surprisingly, the incidence of MGUS is almost equivalent or only slightly lower than what has been reported in Western countries, although the number of studies is very limited [18–20]. Considering that MM is almost always preceded by MGUS,[21] the reported incidence of MGUS in Asian countries would lead us to expect that the incidence of MM will further increase in the near future. When we consider the enormous population of Asia, with 4 billion people in 47 countries, and its growing economy, the impact of MM on health care systems is expected to increase dramatically.

We sought to identify the characteristics of MM in Asian regions and compare them with the published data on Western counterparts [22]. As patients included in our study come from major tertiary centers in Asia, our data may not representative of the true characteristics of MM in Asia due to selection bias. Nonetheless, this is the very first pooled analysis of MM in Asian countries and our survival data may reflect the possible outcomes of MM patients who are able to receive proper MM care in tertiary centers where resources are not limited. The median age of this cohort was 62, which is slightly lower than that in Western reports [22]. Japan showed the highest median age, which seems to reflect their larger elderly population. The median age of MM seems to be closely related to the median life expectancy of the population. In Korea, for example, the median age of MM was only 54 years in the 1960s, which had increased to 67 years in 2010. During the same period, the median life span of the Korean population increased from 64 years to 81years, which seems to be related with the median age of MM. Since South Korea is rapidly moving from an aging society to an aged society, this trend is expected to continue. Most countries showed a greater number of males affected by MM. Although Thailand's cohort showed an interesting female predominance, this could be related to the small size of the cohort. In fact, female predominance has not been reported in other studies from Thailand. Bone lesions were detected in 60.2% of the patients. Japan reported the highest rates of bone lesions while Thailand reported the lowest. These trends could be related to the availability of imaging facilities for MRI or PET scans, as well as reimbursement issues. Significant anemia and thrombocytopenia were observed in 60.7% and 8.8%, respectively, of the patients, and extramedullary plasmacytoma was observed in 15.5% of the patients, with South Korea and Thailand reporting slightly higher incidences. The incidence of hypercalcemia, hypoalbuminemia, significant azotemia, and M-protein were not significantly different from the Western literature [22]. The rates of patients with ISS stages I/II/III were 19.9%/36.1%/44%, respectively, which represented a higher incidence of advanced disease compared to the original ISS reports which showed incidences of ISS stages I/II/III of 28%/33%/39%, respectively. This might be due to the relatively later diagnosis of MM in Asia compared to Western countries or a later presentation of patients to the tertiary centers involved in this study. Cytogenetic profiles of our patients also showed trends similar to the Western literature [23]. Singapore reported the highest incidences of abnormal cytogenetics and 13q deletions, and this might reflect their higher quality of laboratories. FISH data was available in only a minority of the patients

because of differences in the facilities of the participating centers. FISH abnormalities such as t(11;14), t(4;14), t(14;16) and 17p deletions were also found at similar rates when compared with Western literature. However, the rate of 17p deletions in the Chinese cohort was 29.2%, which is unusually high. This may reflect later diagnosis or presentation of patients since P53 deletion is a late genetic event in myeloma development. This observation needs further confirmation to determine if there could be an ethnic variation. However, data from Hong Kong and Singapore, 2 regions with a predominant Chinese ethnic population do not show a higher incidence of 17p deletion. Conventional therapy was performed in 64.1% of the patients while novel drugs were given in 36%. Conventional therapy consisted of various combinations with alkylating agents such as melphalan or cyclophosphamide, vincristine, doxorubicin and steroids. The Chinese cohort had more populations exposed to novel drugs because of patients receiving care in tertiary hospitals with many clinical trials. Although the median age of our cohort was 62, only 19.8 % of the patients underwent stem cell transplantation (SCT), mainly ASCT. These rates seemed to be related to the availability and experience of transplantation facilities. South Korea had the highest rate of SCT among the countries studied. The overall survival of SCT was 79 months, which is better than that of conventional therapy (41 months). Although the impact of novel agents in the first-line treatment was not significant in univariate analysis (49 vs. 48 months, $P = 0.098$), it was significant in multivariate analysis ($P < 0.001$). We also observed survival improvement in patients who were diagnosed in recent 10 years as the report from Mayo clinic [24].

The clinical parameters affecting overall survival were not different from the Western data. Our study corroborates Western data with regard to the prognostic significance of baseline characteristics like heavy chain type, ISS, BMPC, presence of extramedullary plasmacytoma, and serum creatinine. Novel drug exposure as a first-line treatment, transplantation, 13q deletion by conventional cytogenetics, and the presence of t(4;14), t(14;16), or 17p deletion were also identified as important prognostic markers among Asians. In fact, some of the Asian cytogenetics data were already incorporated in a recent global trial and did not differ from Western data [25].

In summary, there are no unique clinical characteristics of MM that are peculiar to Asian patients. Although some country-specific characteristics were observed, these need to be further verified in future studies. Notwithstanding the selection bias and the limitation of the study population in representing true Asian MM characteristics, this project highlights that by availing proper MM care to Asian MM patients, a reasonable clinical outcome can be achieved and this will provide a platform for the design of future studies and clinical trials involving Asian MM patients.

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Author Contributions

Contribution: K.K. and J.H.L designed the study, collected and analyzed the data, and wrote the manuscript; and J.S.K., C.K.M., S.S.Y., K.S., T.C., H.K., K.S., W.C., J.H., J.L., S-Y.H., W. J.C., D.T., G.T., J.C., W.N., N.S., B.G.D. contributed to collecting the data, writing and reviewing the manuscript.

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