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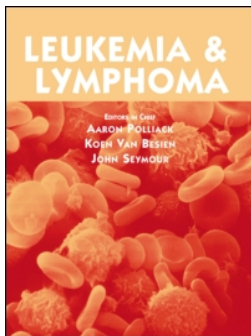
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Different outcomes for transplant-eligible newly diagnosed multiple myeloma patients in Latin America according to the public versus private management: a GELAMM study



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Different outcomes for transplant-eligible newly diagnosed multiple myeloma patients in Latin America according to the public versus private management: a GELAMM study

Camila Peña^a , Eloisa Riva^{b*}, Natalia Schutz^{c*}, Luz Tarín-Arzaga^d, Humberto Martínez-Cordero^e, Virginia Bove^f, Rocío Osorio^g, Mauricio Chandía^h, Cecilia Beltránⁱ, Javier Schulz^j, Daniela Cardemil^j, Carolina Contreras^k, Carmen Gloria Vergara^k, Javiera Donoso^l, Marcela Espinoza^m, Gabriel La Roccaⁿ, Hernán López-Vidal^o, Pilar León^p, Christine Rojas Hopkins^q, Pablo Soto^r, Sandra Aranda^s, Vivianne Torres^t, Macarena Roa^u, Paola Ochoa^u, Patricio Jose Duarte^v, Guillermina Remaggi^w, Sebastián Yantorno^x, Ariel Corzo^y, Soledad Zabaljauregui^z, Claudia Shanley^{aa}, Sergio Lopresti^{ab}, Sergio Orlando^{ac}, Verónica Verri^{ad}, Luis Quiroga^{ae}, Carlos García^{af}, Vanesa Fernández^{ag}, Jhoanna Ramirez^{ah}, Alicia Molina^{ai}, María Pacheco^{ai}, Alex Mite^{ai}, Inés Reyes^{aj}, Brenner Sabando^{ak}, Francisca Ramírez^{ak}, Claudia Sossa^{al}, Virginia Abello^{am}, Henry Idrobo^{an}, Kenny Mauricio Galvez Cardenas^{ao}, Domingo Saavedra^{ap}, Guillermo Quintero^{aq}, Raimundo Gazitúa^{ar}, Lina Gaviria^{as}, Rigoberto Gomez^{at}, Mónica Osuna^{au}, Alicia Henao-Uribe^{av}, Omar Cantú-Martínez^d, David Gómez-Almaguer^d , Yarely Itzayana García-Navarrete^{aw,ax}, Antonio Cruz-Mora^{aw,ay}, Yahveth Cantero-Fortiz^{aw,az} , Guillermo J Ruiz-Argüelles^{aw,ax}  and Dorotea Fantl^c

^aHospital Del Salvador, Santiago, Chile; ^bDepartment of Hematology, Hospital de Clínicas, Montevideo, Uruguay; ^cHospital Italiano de Buenos Aires, Buenos Aires, Argentina; ^dHospital Universitario Dr José Eleuterio González, Monterrey, Mexico; ^eHematology and Bone Marrow Transplantation Department - Instituto Nacional de Cancerología ESE de Colombia, Bogotá, Colombia; ^fHospital Central de las FFAA, Montevideo, Uruguay; ^gHospital de Arica, Arica, Chile; ^hHospital Regional de Concepción, Concepción, Chile; ⁱHospital Regional de Temuco, Temuco, Chile; ^jHospital Clínico Magallanes, Punta Arenas, Chile; ^kHospital Regional de Rancagua, Rancagua, Chile; ^lHospital Sótero del Río, Santiago, Chile; ^mHospital San José, Santiago, Chile; ⁿHospital de Coyhaique, Santiago, Chile; ^oHospital Barros Luco Trudeau, Santiago de Chile, Chile; ^pHospital Carlos Van Buren, Valparaíso, Chile; ^qHospital Dr Gustavo Fricke, Vina del Mar, Chile; ^rHospital Regional de Puerto Montt, Santiago, Chile; ^sHospital San Juan de Dios, Santiago, Chile; ^tHospital base de Valdivia, Valdivia, Chile; ^uInstituto Alexander Fleming, Buenos Aires, Argentina; ^vDepartment of Hematology, CEMIC, Buenos Aires, Argentina; ^wFundaleu, Buenos Aires, Argentina; ^xHospital Italiano de la Plata, La Plata, Chile; ^yHospital de Clínicas, Buenos Aires, Argentina; ^zAcademia Nacional de Medicina - IIHEMA, Buenos Aires, Argentina; ^{aa}Hospital Británico de Buenos Aires, Buenos Aires, Argentina; ^{ab}Hospital Posadas, El Palomar, Argentina; ^{ac}Hospital Rossi, La Plata, Argentina; ^{ad}IDIM, Buenos Aires, Argentina; ^{ae}Department of Medicine, Hospital Churrucá, Buenos Aires, Argentina; ^{af}Clínica, 25 de Mayo, Buenos Aires, Argentina; ^{ag}Hospital Méndez, Buenos Aires, Argentina; ^{ah}Institución Hospital IESS, Guayaquil, Ecuador; ^{ai}Hospital IESS, Guayaquil, Ecuador; ^{aj}IDYTES, Guayaquil, Ecuador; ^{ak}IESS, Guayaquil, Ecuador; ^{al}Clínica FOSCAL, Floridablanca, Colombia; ^{am}Hospital de San José. Fundación Universitaria de Ciencias de la Salud (FUCS), Bogotá, Colombia; ^{an}Hospital Universitario Del Valle Evaristo Garcia E.S.E, Cali, Colombia; ^{ao}Hospital Pablo Tobón Uribe, Medellín, Colombia; ^{ap}Fundación Colombiana de Cancerología, Colombia Medellín; ^{aq}Hospital Universitario de la Fundación Santa Fe de Bogotá, Bogotá, Colombia; ^{ar}Instituto Oncológico Fundación Arturo López Pérez, Santiago, Chile; ^{as}Hospital Universitario San Vicente de Paul, Medellín, Colombia; ^{at}Instituto Catalán de Oncología, Cali, Colombia; ^{au}Clínica Los Nogales, Bogotá, Colombia; ^{av}Clínica De Oncología Astorga, Medellín, Colombia; ^{aw}Clínica Ruiz, Centro de Hematología y Medicina Interna de Puebla, Puebla, Mexico; ^{ax}Universidad Popular Autónoma del Estado de Puebla, Puebla, Mexico; ^{ay}Benemérita Universidad Autónoma de Puebla, Puebla, Mexico; ^{az}Universidad de las Américas Puebla, Puebla, Mexico

ABSTRACT

The aim of this study was to describe clinical and survival characteristics of transplant-eligible multiple myeloma (MM) patients in Latin America (LA), with a special focus on differences between public and private healthcare facilities. We included 1293 patients diagnosed between 2010 and 2018. A great disparity in outcomes and survival between both groups was observed. Late diagnosis and low access to adequate frontline therapy and ASCT in public institutions probably explain these differences. Patients treated with novel drug induction protocols, followed by autologous stem cell transplantation (ASCT) and maintenance, have similar overall survival compared to that published internationally.

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Multiple myeloma; Latin America; autologous stem cell transplantation; proteasome inhibitor

Introduction

Multiple myeloma (MM) represents 1% of all cancers and 10–15% of all hematologic malignancies [1–3]. MM is, therefore, one of the most frequent hematologic neoplasms. In the Western world, the age-standardized incidence of MM has been reported to be approximately 5 cases per 100,000 [4,5]. Due to the lack of registries, the real incidence of MM in Latin America (LA) is unknown.

Despite advances in treatment strategies in recent decades, the gold standard therapy for fit/young, newly diagnosed MM patients continues to be induction regimen based on proteasome inhibitors (PI) followed by high dose chemotherapy with autologous hematopoietic stem cell transplantation (ASCT) [6].

The rationale for frontline PI-based combination was assessed in a meta-analysis performed by Sonneveld et al. [7]. This resulted in the recommendation of PI-based induction regimen in different international guidelines (ESMO, NCCN and ASCO). Currently, the standard of care is VRd (bortezomib, lenalidomide and dexamethasone) regimen, although VTd (bortezomib, thalidomide and dexamethasone) or CyBorD (cyclophosphamide, bortezomib and dexamethasone) are also commonly used.

In LA, the access to currently recommended standard of care is very heterogeneous. Lack of access to drugs and/or their financing mainly affects countries where the public health system provides treatment to the majority of the population.

There is scarce data on the baseline characteristics and outcomes of transplant-eligible MM patients in LA. The aim of this study was to make a clinical and survival characterization of transplant-eligible MM patients in different countries of LA, with a special focus on differences between outcomes in public and private healthcare facilities.

Patients and methods

An international multicenter retrospective cohort study was conducted. All members of the Grupo de Estudio Latinoamericano de Mieloma Múltiple (GELAMM) were invited to participate. Demographic, clinical and laboratory data were collected through a standardized form that was sent to all participating centers. Potential patients were identified from each center's databases. Data were obtained from their medical records and were included consecutively in code form. Approvals were obtained from the Ethics committees of all participating institutions.

Consecutive transplant-eligible patients with active MM diagnosed between 2010 and 2018 from Chile, Argentina, Ecuador, Mexico, Colombia, and Uruguay were included.

Baseline characteristics at diagnosis and frontline therapy outcomes, including outcomes of ASCT, were analyzed. Transplant-eligible patients were defined as patients ≤ 65 years old, fit to undergo the transplant procedure. The diagnosis of MM was defined according to the International Myeloma Working Group (IMWG) 2014 criteria [8] and staging was performed in adherence to the International Staging System (ISS) recommendations [9]. Induction therapy, defined as frontline treatment planned at diagnosis and before proceeding to ASCT was evaluated. The 2016 IMWG criteria for evaluating response and progression/relapse were used [10]. Public health in LA is referring to that system that provides health care from the state (from the health or labor Ministry).

Exclusion criteria were lack of minimum information in medical records, a diagnosis of plasma cell leukemia, light-chain (AL) amyloidosis or solitary plasmacytoma, and HIV infection.

Statistical analysis

The baseline characteristics of the patients were planned to be presented descriptively and comparisons between private and public management were made using Student's *t* test, Chi-square (χ^2) or ANOVA, as appropriate. Overall survival was calculated using the Kaplan–Meier curves method. Progression-free survival (PFS) was not calculated. The main reason is that in one of the participating countries (Chile), patients of the public health system can only be transplanted if they achieve a complete remission or very good partial response after first-line treatment. This sometimes leads to the initiation of a second line without progression of the disease, resulting in erroneous data in PFS. Also, second-line options were heterogeneous in the different countries. Comparisons of survival between groups were made by the log-rank test, and Cox regression analysis was utilized to identify baseline characteristics with prognostic value in terms of outcomes. Statistical analysis was performed by using STATA 13 software (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP).

Results

We included 1293 transplant-eligible MM patients in the study, 363 from Chile, 395 from Argentina, 209 from

Colombia, 45 from Ecuador, 151 from Mexico, and 130 from Uruguay. The baseline characteristics of the patients at diagnosis and therapeutic strategies undertaken are shown in Table 1. Median age was 54 years (range 22–65) and male-to-female patient ratio was 1:0.9. IgG was the most frequent isotype (57%), followed by light chains (LC) (19%); 74% were classified as ISS II or III. Bone disease was the most frequent myeloma-defining event (64%), followed by anemia (56%), renal failure (24%), and hypercalcemia (16%). Fluorescence *in situ* hybridization (FISH) analysis was performed in only 32% of patients, with del17p being the most frequent anomaly found (10%).

The most frequently used induction regimen was cyclophosphamide, bortezomib, and dexamethasone (CyBorD) (40%), followed by cyclophosphamide-thalidomide-dexamethasone (CTD) (19%), and bortezomib-thalidomide-dexamethasone (VTD) (17%) (Table 1). Median hemoglobin (g/dL), Calcium (mg/dL), and creatinine (mg/dL) was 9.7 in public vs 10.5 in private

setting ($p < .001$), 10.3 vs 9.6 ($p < .001$), and 2.4 vs 1.6 ($p = .021$), respectively.

Optimal response (\geq very good partial response: VGPR) was achieved in 37% of patients in the CyBorD group, 46% in the VTD group, and 36% in the CTD group.

Only 53% of patients actually received ASCT. Ecuador has the lowest rate of transplanted patients (6%), followed by Chile (26%). The higher rate was found in Argentina, with 87% (Table 2).

Maintenance therapy was administered in 62% of patients, in 57% lenalidomide-based, and in 33% thalidomide-based.

Among study participants, 592 patients (46%) received treatment in public institutions. The proportion of patients treated in the public setting by country is shown in Table 2. Significant differences were found between both groups. Patients treated in the public institutions were more symptomatic at diagnosis, had more advanced disease ($p = .01$), received less

Table 1. Characteristics of the patients at diagnosis according to institution of origin (public or private).

Characteristics	Total $n = 1293$		Public setting $n = 592$ (46%)		Private setting $n = 701$ (54%)		p value
	N°	%	N°	%	N°	%	
Age (median, range)	54 (22–65)		54 (22–65)		54 (23–65)		.903
Sex	$n = 1293$	100	$n = 592$	100	$n = 701$	100	
Female	606	47	287	49	318	45	.286
Male	687	53	305	51	383	55	.286
ISS	$n = 1095$	87	$n = 475$	80	$n = 620$	88	
I	290	26	114	24	176	28	.103
II	340	31	136	29	204	33	.130
III	465	43	225	47	240	39	.004
Laboratory findings	$n = 1189$	92	$n = 496$	84	$n = 693$	99	
Anemia	665	56	302	61	363	52	.004
Renal failure	288	24	151	30	137	20	<.001
Hypercalcemia	194	16	127	26	67	10	<.001
Bone disease	759	64	386	78	373	54	.009
FISH performed	$n = 410$	32	$n = 103$	17	$n = 307$	44	
TP53 (+)	42	10	12	12	30	10	.902
t(14;16) (+)	4	1	2	2	2	0.5	.708
t(4;14) (+)	21	5	6	2	15	5	.284
Induction regimen	$n = 1269$	98	$n = 581$	98	$n = 688$	98	
CyborD	510	40	125	22	385	56	<.001
VTD	215	17	71	12	144	21	<.001
RVD	31	2	0	0	31	4	<.001
CTD	238	19	204	35	34	5	<.001
TalDex	110	9	74	13	36	5	<.001
Other with novel agents	104	8	58	10	46	7	<.001
Others without novel agents	61	5	49	8	12	2	<.001
Induction	$n = 1104$	85	$n = 474$	43	$n = 630$	57	
Bortezomib-based	756	68	196	41	560	88	<.001
Transplant	$n = 1293$	97	$n = 588$	98	$n = 669$	85	
Performed	669	53	206	35	463	69	<.001
Maintenance	$n = 823$	64	$n = 317$	54	$n = 506$	72	
Performed	518	62	170	54	348	77	<.001
Thalidomide-based	179	33	117	69	51	14	<.001
Lenalidomide-based	290	57	37	22	251	74	<.001
Bortezomib-based	43	8	15	8	28	8	.985
Other	11	2	1	1	10	4	.097

ASCT: autologous stem cell transplantation; CyBorD: cyclophosphamide, bortezomib, and dexamethasone; CTD: cyclophosphamide, thalidomide and dexamethasone; RVD, lenalidomide, bortezomib and dexamethasone; TalDex: thalidomide and dexamethasone; VTD: bortezomib, thalidomide and dexamethasone.

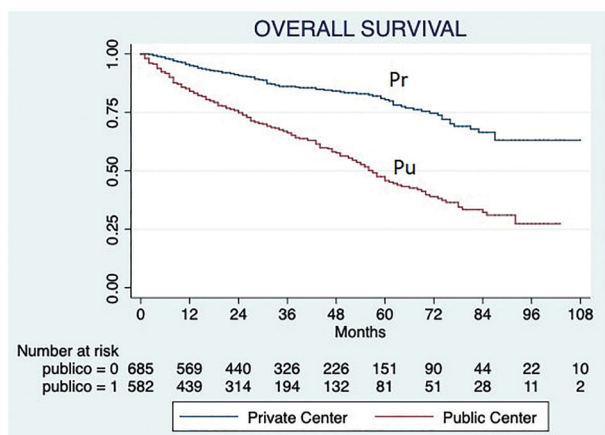
Bold values are statistically significant.

frequently bortezomib-based induction therapy (<0.001), ASCT (<0.001) and maintenance therapy, and received more thalidomide-based maintenance therapy ($p < .001$) (Table 1).

With a median follow-up of 32 months (range 1–113), the 5-year OS was 64% (IC 95% 60–67). When comparing public versus private settings, 5-year OS was 46% vs 80%, with a median OS of 56 months vs not reached, respectively ($p < .0001$) (Figure 1). However, in a multivariate analysis, being treated in the public setting was no associated with worse outcome ($p = .052$), when adjusted by ISS, induction treatment, access to ASCT and maintenance. Hypercalcemia (<0.0001), achieving response less than VGPR ($p < .0001$), not undergoing ASCT ($p = .001$), and not receiving maintenance therapy ($p < .0001$) were independent factors associated with worse outcome (Table 3).

Table 2. Characteristics among different countries cohorts.

Characteristic	Country					
	Argentina	Chile	Colombia	Mexico	Uruguay	Ecuador
Total	395	363	209	151	130	45
Centers	12	20	13	2	28	1
Public setting	18%	97%	0%	44%	42%	100%
Private setting	82%	3%	100%	56%	58%	0%
ISS						
I	34%	22%	19%	26%	26%	37%
II	39%	31%	22%	29%	27%	22%
III	27%	47%	59%	45%	47%	41%
Induction						
Bortezomib-based	97%	11%	96%	41%	45%	82%
Maintenance						
Total	71%	52%	76%	67%	22%	72%
Lenalidomide-based	61%	6%	77%	9%	11%	19%
Thalidomide based	8%	91%	5%	70%	70%	74%
Bortezomib-based	7%	0%	16%	9%	16%	3%
Transplant						
Performed	87%	26%	42%	44%	53%	6%



A subgroup analysis regarding patients who get ASCT was performed (Tables 4 and 5). In this subgroup analysis, for the patients who had ASCT, the 5 years OS was 85% for the private group versus 70% for the public group ($p = .007$). For the patients who did not had ASCT, the 5 years OS was 67 vs 30%, respectively ($p < .0001$) (Figure 2).

Table 3. Multivariate analysis of clinical and laboratory factors at diagnosis associated with worse overall survival.

Variables	Multivariate analysis		
	HR (95% CI)	IC	p value
Public center	1.46	0.99–2.16	.05
ISS III	1.24	0.85–1.81	.25
Renal failure	1.04	0.67–1.60	.85
Hypercalcemia	2.49	1.57–3.95	<.0001
No Bortezomib-based induction	1.43	0.96–2.13	.07
No transplant	0.37	0.25–0.54	.001
No VGPR or better	0.55	0.32–0.64	<.0001
No maintenance	0.45	0.32–0.64	<.0001

VGPR: very good partial response.

Bold values are statistically significant.

Table 4. Characteristics of patients with and without ASCT.

Characteristics	ASCT	NO ASCT	p value
	n = 1293	n = 624 (48%)	
Total patients	n = 669 (52%)	n = 624 (48%)	
	N° (%)	N° (%)	
Age (median, IQR)	55 (49–59)	56 (51–60)	<.001
Sex male	359 (54)	310 (46)	.693
Private setting	463 (70)	206 (38)	<.001
ISS III	212 (32)	246 (39)	<.001
Renal failure	105 / 636 (16)	183 / 538 (34)	<.001
Bortezomib-based induction	513 (77)	279 (46)	<.001
Induction response \geq PR	572 (89)	286 (66)	<.001
Induction response \geq VGPR	328 (51)	130 (30)	<.001
Maintenance	428 (70)	90 (39)	<.001

PR: partial response; VGPR: very good partial response.

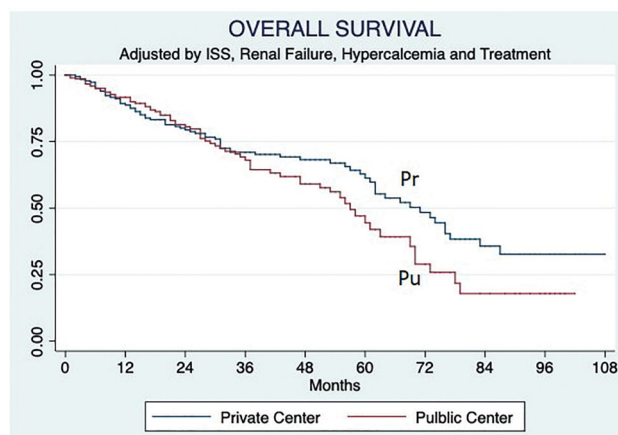


Figure 1. Left: OS between both groups, from patients treated in the public vs private setting. Right: OS adjusted by ISS score, renal failure, hypercalcemia and treatment.

Discussion

We present data that suggest strong differences in clinical presentation and outcomes in MM patients whether they have been treated in the public or private system in LA countries.

Nevertheless, the multivariate model indicates that this covariate is not significant for OS survival per se, while better OS was associated with earlier diagnosis, adequate induction regimen and ASCT. As shown here, only 35% of the public patients had ASCT vs a 69% in the private patients, and bortezomib-based induction was lower in the public setting.

Studies regarding MM outcomes in LA are limited. The first report was published by Hungria et al. in 2017, including 852 Latin American patients from 23 institutions from Argentina, Peru, Chile, Mexico, and Brazil [11]. More recently, Hungria et al. [12] reported treatment patterns and outcomes of 1103 MM patients diagnosed

between 2008 and 2015 from seven LA countries. Other data for MM patients in LA come from local efforts, such as the Colombian, Chilean and Uruguayan registries, and from some Mexican centers [13–16].

LA comprises a vast territory with varying gross domestic product among different countries and great heterogeneity in health care facilities [17–22]. An interesting prior study from GELAMM reported the results of a survey that showed a great disparity in treatment availability for MM across different countries in LA, especially between public and private healthcare systems [23].

Our results showed significant differences in NDMM patients, candidates for ASCT treated at private and public health institutions, particularly in the severity of symptoms at diagnosis, ISS staging, access to PI-based induction, access to ASCT and maintenance therapy.

This topic was also discussed by Pessoa de Magalhaes et al. [24], who described that first-line MM chemotherapy regimens in LA for young and elderly patients in public institutions were triplets based on thalidomide, whereas in private institutions, bortezomib based regimens were used. They reported sub-optimal treatment (including ASCT) in the public system in 30% of the participating countries. Another example of this was reported by Tarín-Arzaga et al. They compared the results of treatment between the public and private healthcare systems in northeastern Mexico [25]. This study showed that MM was diagnosed at a more advanced stage in the public system, and was usually treated with thalidomide-based

Table 5. Subgroup multivariate analysis: patients that underwent ASCT.

Variables	Multivariate analysis		
	HR (95% CI)	IC	p value
Private center	1.8	1.02–3.20	.04
ISS III	1.18	0.70–1.98	.53
Renal failure	0.79	0.38–1.67	.55
Hypercalcemia	2.02	0.86–4.77	.1
Bortezomib-based induction	1.53	0.78–2.99	.2
Complete response	0.44	0.26–0.75	.002
Maintenance	0.58	0.35–0.95	.03

Bold values are statistically significant.

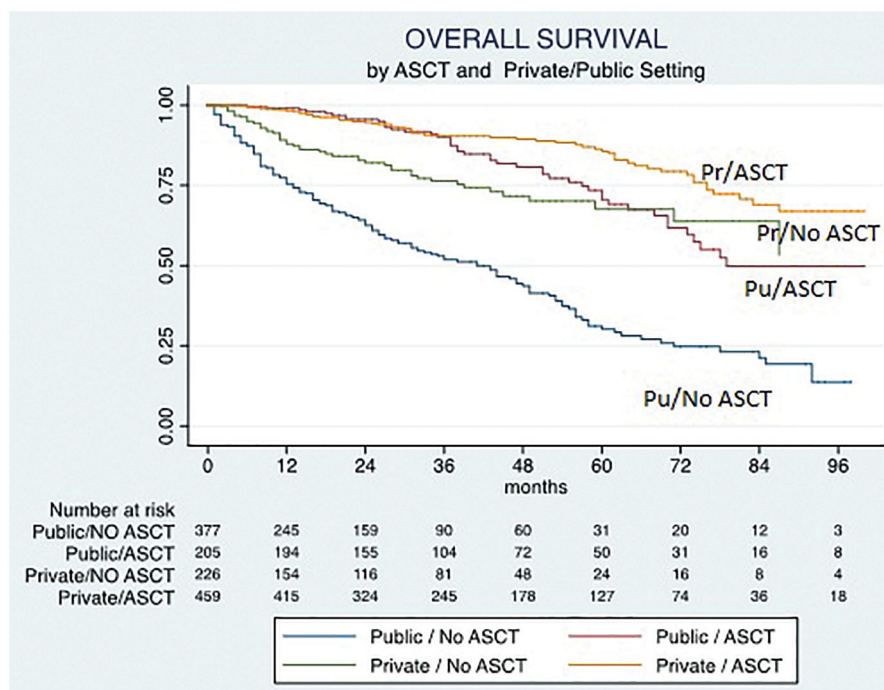


Figure 2. Overall survival by autologous stem cell transplantation (ASCT) and public or private setting.

regimens instead of triplets that include a PI. The outcomes were far better for patients treated in private centers with a very good partial response or a complete response rate of 65 vs. 41% in the public system ($p = .005$) and a median overall survival of 79 versus 41 months, respectively ($p < .001$). Hungria et al. [12] also reported differences in outcomes between both systems, with patients from private centers receiving more bortezomib-based induction (54.3 vs 15.2%) and ASCT (49.4 vs 21.6%) than public centers. Nowadays, the recommended induction regimen is a PI (mostly bortezomib) based induction [7,26]. Our data suggest that this regimen is more likely to be administered in private facilities. Chile was the country with lowest rates of bortezomib-based induction regimen. In this country, CTD was the only treatment approved for these patients in the public system at the time of the study. Although CTD regimen is considered suboptimal, it is still used in LA, especially in the public health system. In the HOLA trial [12], it was the most commonly used treatment. In this study, 19% of the whole cohort was treated with CTD, and 35% of patients from public institutions. CTD use in transplant-eligible patients was also evaluated in Brazil by Crusoe et al. [27] and it was associated with lower survival.

One of the major concerns was the difference between access to ASCT (35 versus 69%). Patients who received ASCT were relatively younger, were more likely to be treated in the private setting, had more bortezomib-based induction regimens, and better responses. They also received more maintenance therapy. On the other hand, patients who did not receive ASCT were more likely to be from the public system, had more advanced disease and renal failure.

ASCT in MM patients in LA is still a very good therapeutic option regarding cost-benefit analysis. Gale et al. showed that about one-half of autologous transplants in LA between 2003 and 2012 were in patients with MM [28]. Nevertheless, access to ASCT in LA is heterogeneous, and many patients do not receive transplantation despite having been considered suitable candidates, particularly in the public setting. We found that only half of ASCT candidates finally underwent the procedure. This is consistent with the results reported by Hungria et al. [11] that reported that 51.2% of eligible patients received ASCT. In our analysis, Ecuador and Chile had the lowest rates of ASCT. In particular, Ecuador has only one transplantation center with five beds for the entire public health system. Chile has two centers in the public setting, but very strict indications for ASCT in MM patients (<60 years old and in \geq VGPR).

OS in this young cohort was lower than expected, mainly due to poor OS in patients from the public system. On the other hand, OS in patients from private centers is comparable with international reports [29].

Maintenance entails better outcomes [30–33]. Two-thirds of our cohort received maintenance therapy. This was associated with better outcomes, regardless of the used drug. In the public setting, 69% was based on thalidomide, whereas in the private setting 74% was lenalidomide-based. Thalidomide is known to cause significant peripheral neuropathy, often leading to treatment discontinuation. Moreover, it has been reported ineffective in patients with high-risk cytogenetics [34,35]. Thus, this strategy (mostly used in public centers) has to be considered suboptimal.

We acknowledge several limitations of our study, particularly due to its retrospective nature. Although several centers were included, public services are underrepresented in some countries (Colombia and Argentina) which may have an impact on the differences reported. These results should be verified including more LA countries to assess the generalizability of our findings

Conclusion

This is the largest study on transplant-eligible patients with MM in LA. A great disparity was seen between public and private healthcare systems regarding burden of the disease at diagnosis, access to novel drugs and outcomes. OS in patients treated with adequate induction regimens, ASCT and maintenance are similar to that reported internationally. Reasons for approximately half of the potential candidates not being transplanted clearly merit further analysis.

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Disclosure Statement

The authors report no conflict of interest.

ORCID

Camila Peña  <https://orcid.org/0000-0002-8076-2077>

David Gómez-Almaguer  <http://orcid.org/0000-0002-0460-6427>

Yahveth Cantero-Fortiz  <http://orcid.org/0000-0003-0329-6487>

Guillermo J Ruiz-Argüelles  <https://orcid.org/0000-0002-9335-0653>

References

- [1] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin.* 2017;67(1):7–30.
- [2] Bladé J, Cibeira MT, Fernández de Larrea C, et al. Multiple myeloma. *Ann Oncol.* 2010;21 Suppl 7: vii313–9.
- [3] Dimopoulos MA, Terpos E. Multiple myeloma. *Ann Oncol.* 2010;21(Suppl 7):vii143–50.
- [4] Phekoo KJ, Schey SA, Richards MA, et al.; on behalf of Consultant Haematologists, South Thames Haematology Specialist Committee. A population study to define the incidence and survival of multiple myeloma in a National Health Service Region in the UK, Consultant Haematologists, South Thames Haematology Specialist Committee. *Br J Haematol.* 2004;127(3):299–304.
- [5] Sant M, Allemani C, Tereanu C, et al.; HAEMACARE Working Group. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood.* 2010;116(19):3724–3734.
- [6] Gay F, Engelhardt M, Terpos E, et al. From transplant to novel cellular therapies in multiple myeloma: European Myeloma Network guidelines and future perspectives. *Haematologica.* 2018;103(2):197–211.
- [7] Sonneveld P, Goldschmidt H, Rosiñol L, et al. Bortezomib-based versus non bortezomib-based induction treatment before autologous stem-cell transplantation in patients with previously untreated multiple myeloma: a meta-analysis of phase III randomized, controlled trials. *J Clin Oncol.* 2013;31(26): 3279–3287.
- [8] Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol.* 2014;15(12):e538–48–e548.
- [9] Greipp PR, San Miguel J, Durie BG, et al. International staging system for multiple myeloma. *J Clin Oncol.* 2005;23(15):3412–3420.
- [10] Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. *Lancet Oncol.* 2016;17(8): e328–e346.
- [11] Hungria VT, Maiolino A, Martinez G, et al.; International Myeloma Working Group Latin America. Observational study of multiple myeloma in Latin America. *Ann Hematol.* 2017;96(1):65–72.
- [12] Hungria VT, Martínez-Baños DM, Peñafiel CR, et al. Multiple myeloma treatment patterns and clinical outcomes in Latin America: Haemato-Oncology (HOLA) Observational Study, 2008–2016. *Br J Haematol.* 2020; 188(3):383–393.
- [13] Peña C, Rojas C, Rojas H, et al. Survival of 1,103 Chilean patients with multiple myeloma receiving different therapeutic protocols from 2000 to 2016. *Rev Méd Chile.* 2018;146(7):869–875.
- [14] Riva E, Bove V, Villano F, et al. From guidelines to real-world: results from the National Multiple Myeloma Registry in Uruguay on 222 newly diagnosed multiple myeloma patients from 2012 to 2015. *Curr Med Res Opin.* 2019;8:1–7.
- [15] Abello V, Idrobo H, Sossa CL, et al. The Status of Multiple Myeloma in Colombia: First Report of the Colombian Registry for Hemato-Oncological Diseases (RENEHOC). *Asociación Colombiana de Hematología y Oncología (ACHO). Blood.* 2018;132(Supplement 1): 5597–5597.
- [16] Ruiz-Argüelles GJ, Gómez-Rangel JD, Ruiz-Delgado GJ, et al. Multiple myeloma in Mexico: a 20-year experience at a single institution. *Arch Med Res.* 2004;35(2): 163–167.
- [17] Belizán JM, Cafferata ML, Belizán M, et al. Health inequality in Latin America. *Lancet.* 2007;370(9599): 1599–1600.
- [18] Belló M, Becerril-Montekio VM. Sistema de salud de Argentina. *Salud Publica Mex.* 2011;53(2):S96–S108.
- [19] Aran D, Laca H. Sistema de salud de Uruguay. *Salud Publica Mex.* 2013;53(2):S265–S274.
- [20] Guerrero R, Gallego AI, Becerril-Montekio V, et al. Sistema de salud de Colombia. *Salud Publica Mex.* 2011;53 (supl 2):S144–S155.
- [21] Lucio R, Villacrés N, Henríquez R. Sistema de salud de Ecuador. *Salud Publica Mex.* 2011;53 (Suppl 2): S177–S187.
- [22] Gómez-Dantés O, Sesma S, Becerril VM, et al. Sistema de Salud de México. *Salud Publica Mex* 2011. 53(Suppl 2):S220–S223.
- [23] Riva E, Schutz N, Peña C, et al. Significant differences in access to tests and treatments for multiple myeloma between public and private systems in Latin America. Results from a Latin American survey. *GELAMM (Grupo de Estudio Latino Americano de Mieloma Múltiple). Ann Hematol.* 2020;99(5): 1025–1030.
- [24] Pessoa de Magalhães Filho RJ, Crusoe E, Riva E, et al. Analysis of availability and access of anti-myeloma drugs and impact on the management of multiple myeloma in Latin American Countries. *Clin Lymphoma Myeloma Leuk.* 2019;19(1):e43–e50.
- [25] Tarín-Arzaga L, Arredondo-Campos D, Martínez-Pacheco V, et al. Impact of the affordability of new agents in patients with multiple myeloma: Real-world data of current clinical practice in Mexico. *Cancer.* 2018;124(9):1946–1953.
- [26] Nooka AK, Kaufman JL, Behera M, et al. Bortezomib-containing induction regimens in transplant-eligible myeloma patients: a meta-analysis of phase 3 randomized clinical trials. *Cancer.* 2013;119(23): 4119–4128.
- [27] de Queiroz Crusoe E, Higashi F, Padilha MP, et al. Outcomes of autologous transplantation for multiple myeloma according to different induction regimens. *Rev Bras Hematol Hemoter.* 2014;36(1): 19–24.
- [28] Gale RP, Seber A, Bonfim C, et al. Haematopoietic cell transplants in Latin America. *Bone Marrow Transplant.* 2016;51(7):898–905.
- [29] Paquin AR, Kumar SK, Buadi FK, et al. Overall survival of transplant eligible patients with newly diagnosed multiple myeloma: comparative effectiveness analysis of modern induction regimens on outcome. *Blood Cancer J.* 2018;8(12):125.

- [30] Palumbo A, Cavallo F, Gay F, et al. Autologous transplantation and maintenance therapy in multiple myeloma. *N Engl J Med.* 2014;371(10):895–905.
- [31] Attal M, Lauwers-Cances V, Marit G, et al. Lenalidomide maintenance after stem-cell transplantation for multiple myeloma. *N Engl J Med.* 2012; 366(19):1782–1791.
- [32] McCarthy PL, Owzar K, Hofmeister CC, et al. Lenalidomide after stem-cell transplantation for multiple myeloma. *N Engl J Med.* 2012;366(19): 1770–1781.
- [33] Jackson GH, Davies FE, Pawlyn C, et al. Lenalidomide is a highly effective maintenance therapy in myeloma patients of all ages; results of the phase III myeloma XI study. *Blood.* 2016;128(22):1143–1143.
- [34] Attal M, Harousseau J-L, Leyvraz S, for the Inter-Groupe Francophone du Myelome (IFM), et al. Maintenance therapy with thalidomide improves survival in patients with multiple myeloma. *Blood.* 2006; 108(10):3289–3294.
- [35] Morgan GJ, Gregory WM, Davies FE, et al.; on behalf of the National Cancer Research Institute Haematological Oncology Clinical Studies Group. The role of maintenance thalidomide therapy in multiple myeloma: MRC Myeloma IX results and meta-analysis. *Blood.* 2012; 119(1):7–15.