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ISS Versus R-ISS for Risk Stratification of Multiple Myeloma Patients undergoing Autologous Stem Cell Transplant

Rafael Ríos-Tamayo[1,2,3,4], **Antonio Romero**[2], **José Manuel Puerta**[2], **Pedro Antonio González**[2], **Elisa López-Fernández**[2], **Lucía Moratalla**[2], **Juan Sáinz**[1,2,3,4], **Manuel Jurado**[1,2,3,4]

[1]*Monoclonal Gammopathies Unit, University Hospital Virgen de las Nieves, Granada, Spain*

[2]*Department of Hematology, University Hospital Virgen de las Nieves, Granada, Spain*

[3]*Genomic Oncology Area, GENYO, Centre for Genomics and Oncological Research: Pfizer /University of Granada/Andalusian Regional Government, PTS, Granada, Spain*

[4]*Instituto de Investigación Biosanitaria de Granada (Ibs.GRANADA), Hospitales Universitarios de Granada/Universidad de Granada, Granada, Spain*

[*]**Corresponding author**: Rafael Ríos-Tamayo, Monoclonal Gammopathies Unit, University Hospital Virgen de las Nieves, Avda Fuerzas Armadas, 2, 18014 Granada, Spain, Tel: +34 671592298; Email: rriost33@gmail.com

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Introduction

Multiple myeloma (MM) is a very heterogeneous disease that remains incurable for most patients. Everything is changing quickly in MM, including diagnosis, prognosis and therapy. The prognosis of newly diagnosed MM (NDMM) is currently based on the International Staging System (ISS) [1] and the interphase fluorescence in situ hybridization (FISH) [2]. However, a growing body of evidence supports the inclusion of new prognostic factors whose contribution may help to define the outcome of each patient in a more accurate way. Thereby, a revised ISS (R-ISS) has just been launched [3], combining ISS with FISH (after CD 138 plasma cell purification) and serum lactate dehydrogenase (LDH). Del(17p), translocation t(4;14) and t(4;16) were considered chromosomal abnormalities with high risk. LDH was recorded as normal or high.

From the beginning, in the nineties, autologous stem cell transplant (ASCT) has shown a positive impact in a selected group of patients, the so-called candidates. Despite some controversial aspects and the widespread use of the novel agents, nowadays ASCT is still considered a standard of care for candidate patients. We have just reported that ASCT is an independent prognostic factor along with ISS, LDH, the renal impairment (RI) and the presence of concomitant amyloidosis [4]. Here we report a single institution series of MM patients who had ASCT to evaluate the prognostic impact of both systems. ISS was based on data from clinical trial and non-clinical trial patients; whereas R-ISS has been derived only from patients enrolled onto clinical trial (data were available in 3060 of 4445 patients). Therefore, its performance in real-life patients is not known.

Patients and methods

All NDMM symptomatic patients included in the Granada population-based MM registry from 1995 to July 2015 who had a first ASCT as initial treatment were the basis of the study. Patients with smoldering MM as well as plasma cell leukemia were excluded. Common baseline prognostic factors were recorded as previously reported [5]. We analyzed two calendar periods: 1995-2005 and 2006-2015.

Median overall survival (OS) was calculated in months (m) from the date of diagnosis (first bone marrow aspirate or biopsy) until the date of death, loss to follow-up, or end of study (August 12, 2015), whichever occurred first. The log-rank test was used to estimate differences in survival curves. Comparisons for categorical variables among different groups were made with the $\chi 2$-test, whereas comparisons of means of quantitative continuous variables between two groups were made with the t-test. All p-values were two-sided. Data were analyzed with SPSS v20 software.

Results

One hundred and twenty four patients (25,9%) in a series of 479 consecutive symptomatic NDMM patients included in our population-based registry during the period of study, underwent early ASCT. Most of these patients were not enrolled onto clinical trials. There were 67 men (54%) and 46 women which median age was 56 years (21-70), 54 in men and 56.3 in women (p=0.088). Median time from diagnosis to ASCT was 10.5 m (3.4-114). 42 patients were transplanted during the first calendar period and 82 in the last decade. OS for the two periods (Figure1) was 50.1 m; 95% confidence interval (95% CI), 29.2-70.9 versus 104.1 m; 95% CI, 63.4-144.8;p=0.111.

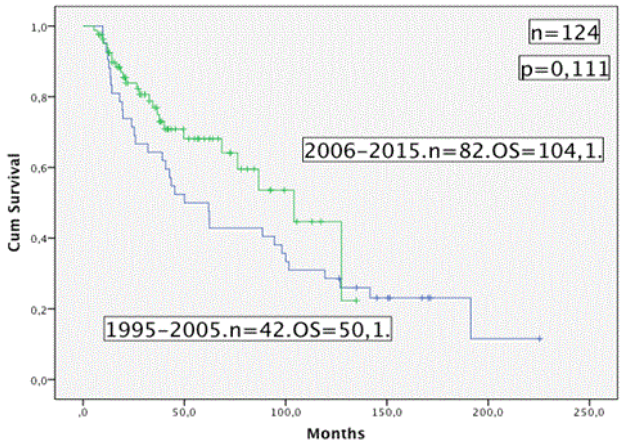

Figure 1: Overall survival according to the two periods of time

22 (17.7%) of these 124 patients underwent a second transplant: 5 ASCT (1 tandem auto-auto, 4 as salvage therapy) and 17 reduced-intensity conditioning allogeneic (RICAllo, 12 tandem auto-RICAllo, 5 as salvage therapy). OS for patients with only first ASCT (ASCT1), ASCT1+2, and ASCT1+AlloRIC was 76.3 m, 100.1 and not reached

(p=0.219), respectively. A plateau can be observed for patients who had a second transplant (Figure 2).

We could use ISS in 83 patients (Figure 3) demonstrating a good discriminative power (p=0.034). On the other hand, the necessary information to calculate R-ISS was available in 46 patients (Figure 4), showing a better performance (p= 0.008), being superb the outcome for patients with R-ISS 1.

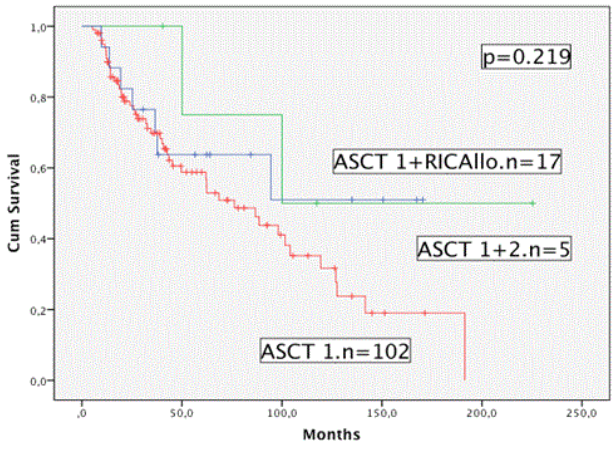

Figure 2: Overall survival according to second transplant

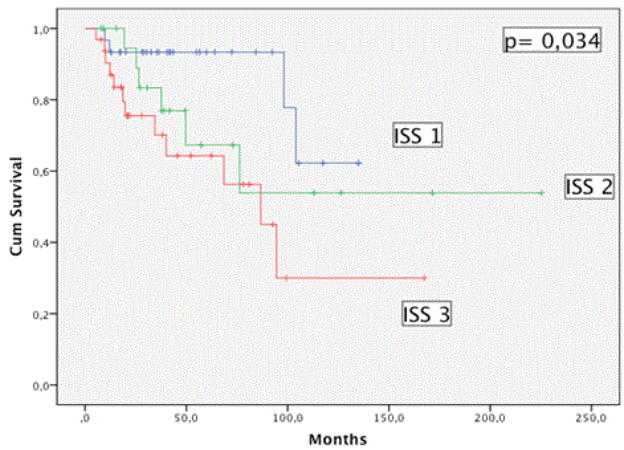

Figure 3: Overall survival according to ISS

Discussion

ASCT as part of first line therapy in NDMM candidate patients remains a standard of care. Moreover, its frequency is increasing over time. OS have improved in the last decade, but did not reach statistical significance between the two periods of the study. The optimal therapy for patients relapsing after first ASCT remains controversial.

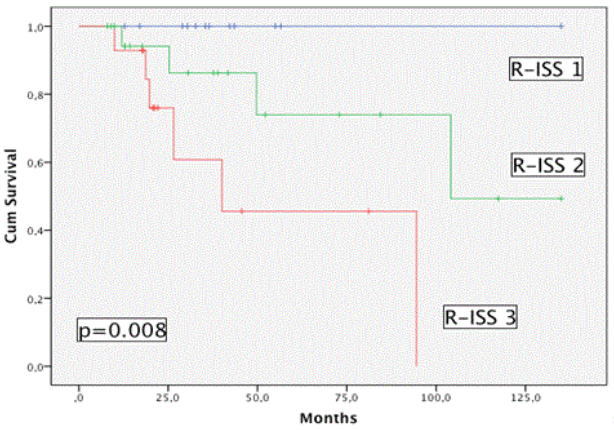

Figure 4: Overall survival according to R-ISS

Performing a second transplant in selected patients demonstrates a trend to better OS. We do not find statistically significant differences in OS between a second ASCT and a second RICAllo. A tandem ASCT-RICAllo shows encouraging outcomes in selected patients.

In short, the ISS remains a powerful prognostic factor in NDMM undergoing ASCT. Despite the small sample size of this preliminary report, as expected, the R-ISS seems to be an even better prognostic tool that works fine in real-life patients. Current FISH-based high-risk classification could be probably improved, including abnormalities of chromosome 1 [6-8]. An accurate prognostic evaluation is needed to face the personalized medicine. R-ISS should be used widely to help us to apply an evidence-based risk-adapted therapy to NDMM patients.

References

1. Greipp PR, San Miguel J, Durie BG, Crowley JJ, Barlogie B, et al. (2005) International staging system for multiple myeloma. J Clin Oncol 23: 3412-3420.
2. Chng WJ, Dispenzieri A, Chim CS, Fonseca R, Goldschmidt H, et al. (2014) IMWG consensus on risk stratification in multiple myeloma. Leukemia 28: 269-277.
3. Palumbo A, Avet-Loiseau H, Oliva S, Lokhorst HM, Goldschmidt H, et al. (2015) Revised International Staging System for Multiple Myeloma: A Report From International Myeloma Working Group. J Clin Oncol .
4. Ríos-Tamayo R, Sánchez MJ, Puerta JM, Sáinz J, Chang DY, et al. (2015) Trends in survival of multiple myeloma: A thirty-year population-based study in a single institution. Cancer Epidemiol .
5. Ríos-Tamayo R, Sánchez MJ, de Veas JLG, Rodríguez T, Puerta JM, et al. (2015) Light Chain Multiple Myeloma: A Single Institution Series. J Leuk 3:184.
6. Hebraud B, Leleu X, Lauwers-Cances V, Roussel M, Caillot D, et al. (2014) Deletion of the 1p32 region is a major independent prognostic factor in young patients with myeloma: the IFM experience on 1195 patients. Leukemia 28: 675-679.
7. Biran N, Malhotra J, Bagiella E, Cho HJ, Jagannath S, et al. (2014) Patients with newly diagnosed multiple myeloma and chromosome 1 amplification have poor outcomes despite the use of novel triplet regimens. Am J Hematol 89: 616-620.
8. Nahi H, Vâtsveen TK, Lund J, Heeg BM, et al. (2015) Proteasome inhibitors and IMiDs can overcome some high-risk cytogenetics in multiple myeloma but not gain 1q21. Eur J Haematol .