MultipleMyelomaHub

General MM, Patients eligible for transplant

Comparison of three staging systems for newly diagnosed MM patients undergoing ASCT

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Multiple myeloma (MM) is a complicated cancer where no two patients (pts) are alike. In 2005, the need for a stratification system of the disease led to the introduction of the International Staging System (ISS). The ISS includes three risk stages (I–III) of low, standard, and high risk, respectively, according to measurements of baseline serum levels of β2-microglobulin (β2M) and albumin. The median overall survival (OS) for each of the stages I, II, and III was calculated to be 62, 44, and 29 months, respectively.

The International Myeloma Working Group (IMWG) 2014 and the revised- (R-) ISS staging systems were introduced in 2014 and 2015, respectively. The IMWG 2014 system included cytogenetic abnormalities (CA) and it is made up of three stages of low, intermediate, and high risk. The revised- (R-) ISS staging system expanded on the ISS system by including an assessment of CA as well as serum lactate dehydrogenase (LDH) levels - a marker of cell proliferation and disease burden. Currently, all three systems (ISS, IMWG-2014, and R-ISS) are used to stage pts with MM.

Emma C. Scott, from the Knight Cancer Institute, Oregon Health and Science University, Portland, US, and colleagues, used data from 2008 to 2014 from the Centre for International Blood and Marrow Transplant Research to compare the prognostic value of the above three staging systems. The comparison was performed among newly diagnosed (ND) MM pts who were eligible to receive autologous stem cell transplantation (ASCT). The reliability of each of the three systems was evaluated by calculating the separation score (SEP), where a larger SEP represents a greater outcome difference between pt groups.

The results of this study were published in Biology of Blood and Marrow Transplantation in August 2018.

Study Design:

- Number of pts = 628
- Number of pts per staging system:
  - ISS I: N = 244; ISS II: N =214; ISS III: N = 170
  - R-ISS I: N = 199; R-ISS II: N = 360; R-ISS III: N = 69
  - IMWG-2014 Low: N = 130; Standard: N = 451; High: N = 47
- Median follow-up = 48 months (range, 3–99)

Key Data:

- Cumulative incidence of relapse/progression at three years: R-ISS I = 35% (range, 28–42); R-ISS II = 50% (range, 44–55); R-ISS III = 65% (range, 51–78) ($P < 0.001$)

- Progression-free survival (PFS) at three years: R-ISS I = 64% (range, 57–71); R-ISS II = 47% (range, 41–53); R-ISS III = 32% (range, 20–45) ($P < 0.001$)
- Overall survival (OS) at three years: R-ISS I = 88% (range, 83–93); R-ISS II = 75% (range, 70–80); R-ISS III= 56% (range, 43–69) ($P < 0.001$)
- SEP between ISS I-III = 1.4 for relapse/progression; 1.42 for PFS; 1.58 for OS
- SEP between R-ISS I-III = 1.53 for relapse/progression; 1.59 for PFS; 1.74 for OS
- SEP between IMWG-2014 low–high = 1.24 for relapse/progression; 1.24 for PFS; 1.6 for OS
- The SEP values reveal that the R-ISS provides the greatest degree of differentiation between the survival curves for each stage
- There is good agreement between ISS and R-ISS, but poor agreement between ISS/R-ISS and IMWG-2014

Conclusions

Comparison of the three contemporary staging systems reveals that the R-ISS is the most reliable tool for staging young and/or fit NDMM pts. A caveat of the R-ISS is that it relies on the measurement of serum LDH at diagnosis, which is not routinely performed. This study supports the wide use of the R-ISS as a prognostic tool in myeloma.

References

Scott E.C. *et al.* Staging Systems for Newly Diagnosed Myeloma Patients Undergoing Autologous Hematopoietic Cell Transplant: The Revised International Staging System shows the most Differentiation between Groups. Biology of Blood and Marrow Transplantation. 2018 Aug 21. pii:S1083-8791(18)30478-6. DOI: 10.1016/j.bbmt.2018.08.013. [Epub ahead of print].