

# Prognostic factors and outcome of Multiple Myeloma patients enrolled in European clinical trials after a long-term follow-up

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**HARMONY is a European Network of Excellence that captures, integrates, analyzes and harmonizes Big Data from multi-disciplinary sources. HARMONY focuses on Hematologic Malignancies with unmet clinical needs such as multiple myeloma.**

**HARMONY has developed a Data Platform to register outcome measures that are relevant to different groups of stakeholders, such as physicians, patients, data scientists, drug developers, policy makers and regulators.**

## Hematologic Malignancies (HM) – Multiple Myeloma (MM)

The first steps to be taken in each HM and particularly in MM:

- to rapidly capture the current status of treatment
- to define the areas of utmost need
- to redefine treatment goals based on individualized risk assessments and outcome measures

## Synergy and collaborations

HARMONY builds on pre-existing long-term collaborations to accelerate this process. In the MM field the synergy with existing structures - European and national co-operative groups - is particularly relevant.

## Revised-ISS

The clinical outcome of MM patients is heterogeneous. International staging system (ISS), chromosomal abnormalities (CA) detected by interphase fluorescent in situ hybridization (FISH) and serum lactate dehydrogenase (LDH) predict prognosis in newly diagnosed MM (NDMM).

In 2015, taking advantage of the analysis of 4,445 NDMM patients enrolled into 11 European clinical trials, these prognostic factors were combined to produce a simple and powerful risk stratification algorithm with an improved prognostic power, called "revised ISS" (R-ISS) (Palumbo et al JCO 2015, Fig 1).

However, a better definition of patients' prognosis has only partially guided therapeutic choices and influenced the outcome of high risk patients that still remains unsatisfactory. This patients' population represents an unmet clinical need even in the novel agent era.

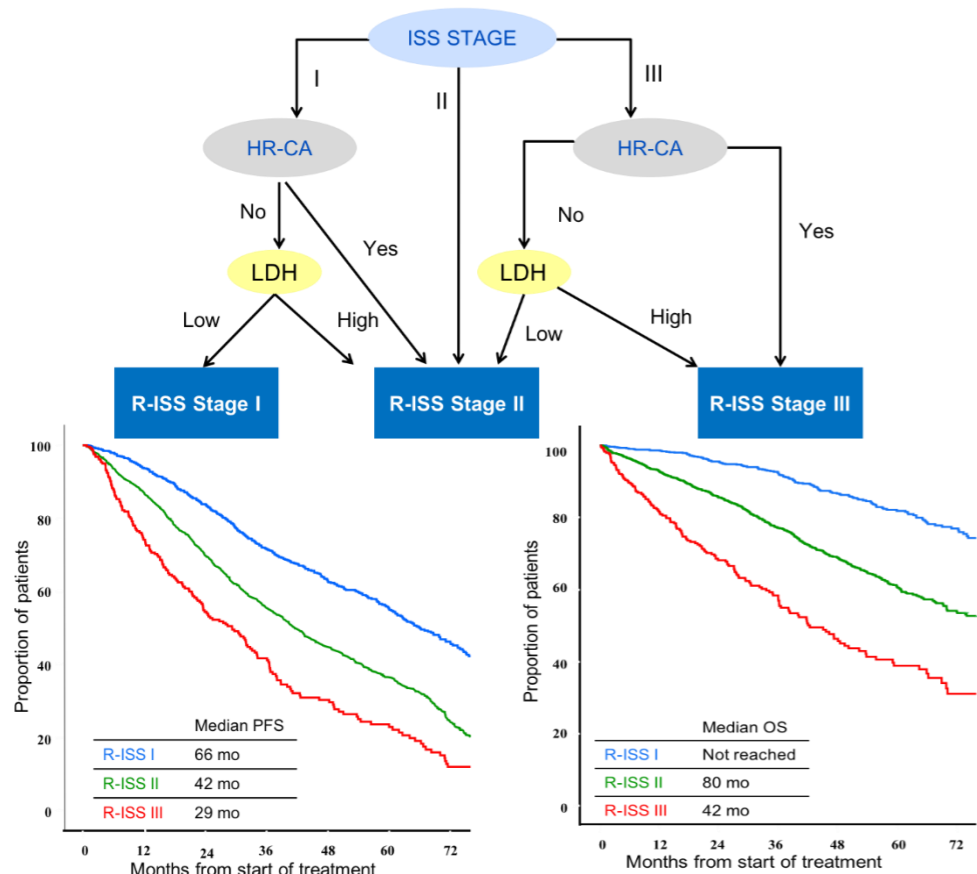
## MM-specific pilot project

European cooperative groups are working together to provide an extended follow-up of the original trials included in the R-ISS project adding other relevant datasets with mature data from clinical trials enrolling NDMM patients treated with novel agents (Fig 2).

The primary endpoint of the project is to validate R-ISS comparing it with ISS, CA and LDH levels alone after an extended follow-up.

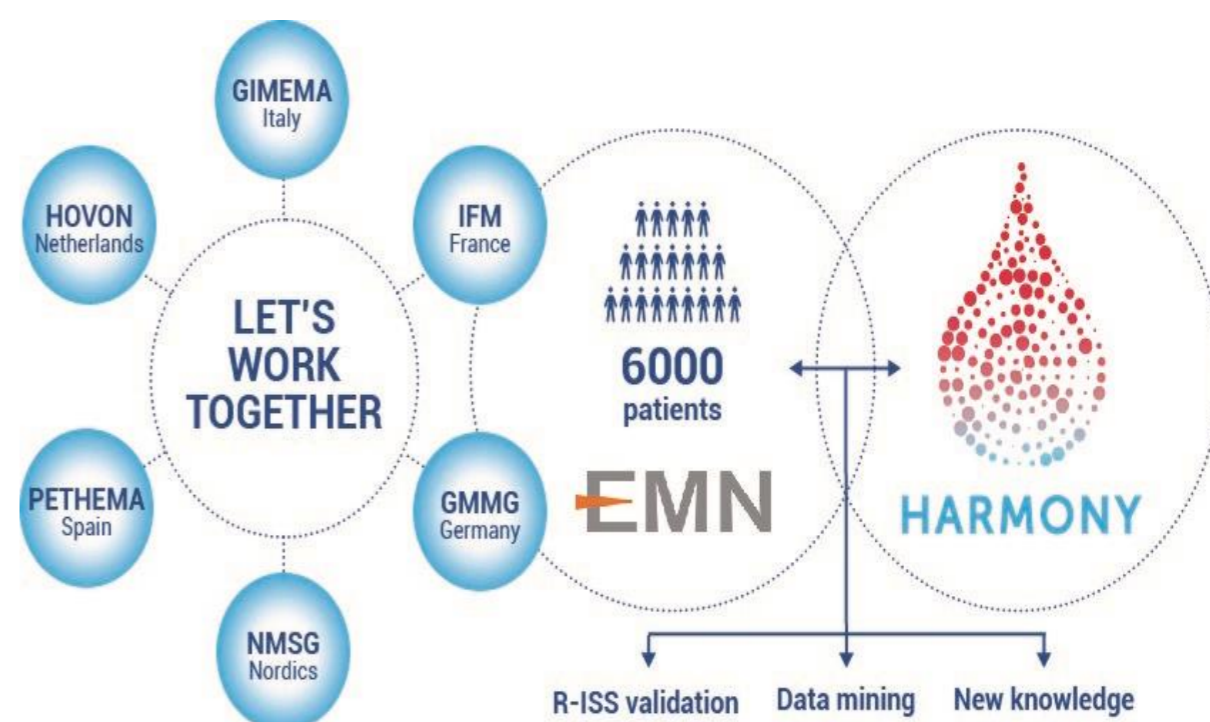
Secondary endpoints will include the analysis of the outcome of patients with low and high-risk features (defined according to R-ISS, ISS alone, CA alone, LDH alone, baseline creatinine clearance, best response to therapy) treated with different novel agents i.e. thalidomide, bortezomib, lenalidomide and different treatment approaches i.e. autologous stem cell transplantation (ASCT) vs no ASCT, fixed duration of therapy (FDT) vs continuous therapy (CT).

Fig.1



Palumbo A. et al J Clin Oncol 2015 33(26):2863-9

Fig.2



R-ISS: revised International Staging System.

## EMN-Harmony partnership

This project will test data sharing between European cooperative groups in the context of the HARMONY project. A collaboration between HARMONY and an important European MM trialist group, namely the European Myeloma Network (EMN), is ongoing in order to accelerate this process.

## Conclusion

Prognosis prediction is still an open issue in MM, the outcome of high risk patients is still unsatisfactory and a risk-adapted therapy is not a standard therapeutic approach. The HARMONY project is a unique opportunity to collect data from different European cooperative groups trying to shed light on this important issue and to improve patient management.