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A Web-Based Risk Calculator for Machine Learning-Derived Risk Scores in Multiple Myeloma

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BACKGROUND

Risk stratification in multiple myeloma (MM) has traditionally relied on clinical and cytogenetic parameters, often with limited predictive accuracy. Machine learning enables more precise risk models by analyzing large datasets and complex variable interactions. A machine learning—based classifier was recently developed using data from the Harmony project.

METHODS

The calculator, developed as a Shiny web application, includes three models—Baseline Risk, Treatment-related, and Dynamic—plus a Help window. The server processes inputs, runs calculations, and generates percentile-based risk graphs.

Risk scores for Overall Survival (OS) and Progression-Free Survival (PFS) are derived from:

- Baseline Risk Model (with/without Cytogenetics): Uses age, hemoglobin, β2-microglobulin, and albumin, with optional inputs for 1q Gain and 17p Deletion.
- Treatment-related Model (with/without Cytogenetics): Adds treatment type (PI-based, IMID-based, PI-IMID-based).
- Dynamic Risk Model: Includes all previous variables (except treatment) plus Best Response to Treatment (Complete Response, Very Good Partial Response, Partial Response, Stable Disease, Progressive Disease).

Scores are further stratified by transplant eligibility, comparing patient risk percentiles within eligible and non-eligible cohorts.



Figure 1. Workflow of model development and validation using the HARMONY cohort (N = 14,345). The dataset was split into a training set (N = 7,072) for model development—including baseline-risk, treatment-based, and dynamic-risk models (OS and PFS)—and a test set (N = 3,771) for validation. The QR code links to the Risk Calculator.

RESULTS

Users select a model and enter values for age, hemoglobin, β2-microglobulin, and albumin, optionally adding cytogenetic data in the Baseline and Treatment-related models. The calculator generates percentile-based risk scores for OS and PFS.

Results appear as intuitive risk graphs (0–100), showing the patient's relative risk within the training cohort. The tool also stratifies OS and PFS by transplant eligibility, refining risk assessment and supporting clinical decision-making.

HARMONY

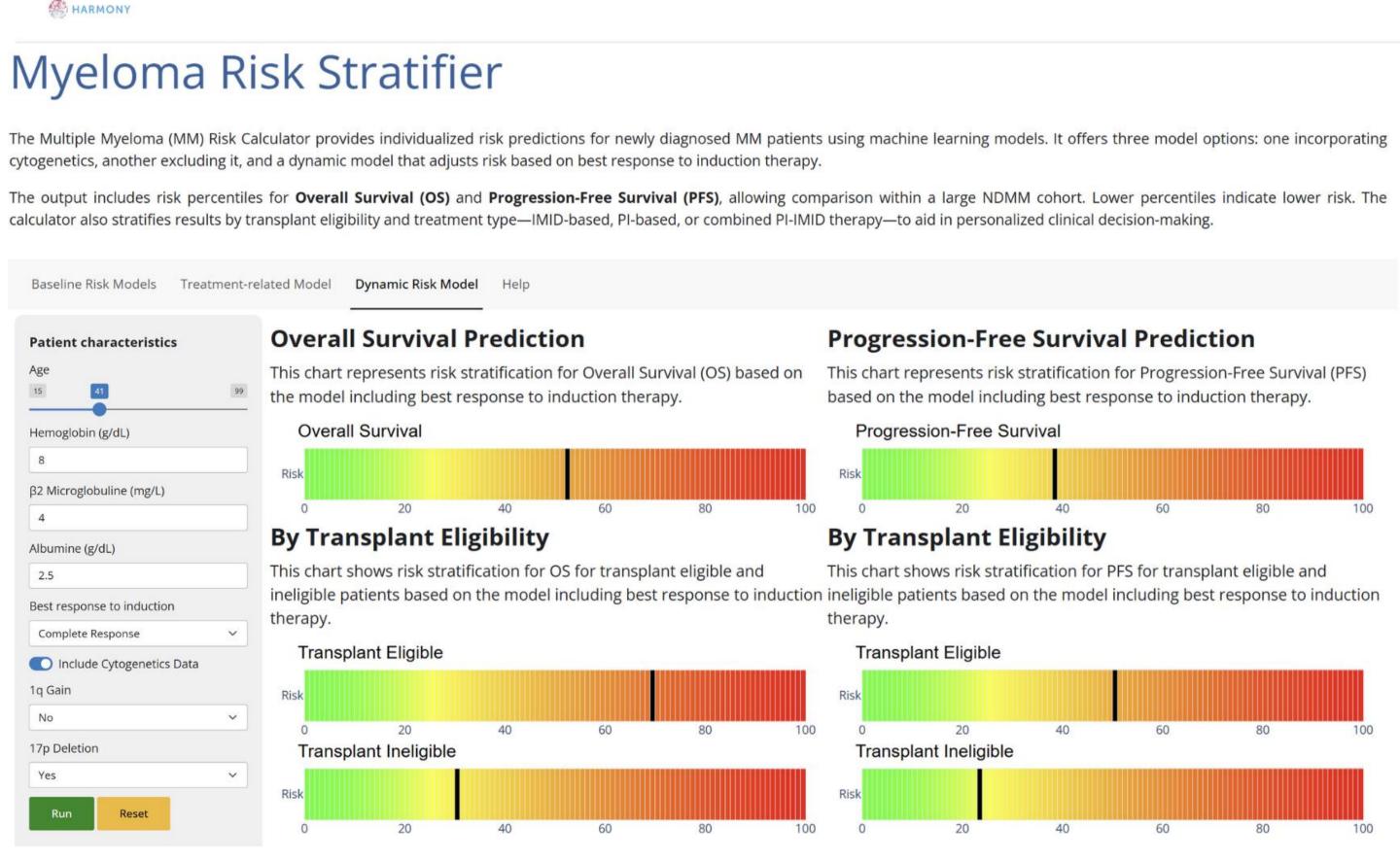


Figure 2A. Interface of the Dynamic Risk Model in the Myeloma Risk Stratifier. The tool allows input of patient-specific characteristics to generate individualized risk predictions for Overall Survival (OS) and Progression-Free Survival (PFS), including stratification by transplant eligibility. Results are displayed as percentiles, with lower values indicating lower risk.

Myeloma Risk Stratifier The Multiple Myeloma (MM) Risk Calculator provides individualized risk predictions for newly diagnosed MM patients using machine learning models. It offers three model options: one incorporating cytogenetics, another excluding it, and a dynamic model that adjusts risk based on best response to induction therapy. The output includes risk percentiles for Overall Survival (OS) and Progression-Free Survival (PFS), allowing comparison within a large NDMM cohort. Lower percentiles indicate lower risk. The calculator also stratifies results by transplant eligibility and treatment type—IMID-based, PI-based, or combined PI-IMID therapy—to aid in personalized clinical decision-making. Baseline Risk Models Treatment-related Model Dynamic Risk Model Help **Progression-Free Survival Prediction Overall Survival Prediction Patient characteristics** This chart represents risk stratification for Overall Survival (OS) based on This chart represents risk stratification for Progression-Free Survival (PFS) the model including best response to induction therapy. based on the model including best response to induction therapy. Overall Survival Progression-Free Survival Hemoglobin (g/dL) β2 Microglobuline (mg/L) By Transplant Eligibility By Transplant Eligibility Albumine (g/dL) This chart shows risk stratification for PFS for transplant eligible and This chart shows risk stratification for OS for transplant eligible and ineligible patients based on the model including best response to induction ineligible patients based on the model including best response to induction Best response to induction Partial Response Transplant Eligible Transplant Eligible Include Cytogenetics Data

Figure 2B. Example output of the Dynamic Risk Model in the Myeloma Risk Stratifier with updated patient inputs. Risk percentiles for Overall Survival (OS) and Progression-Free Survival (PFS) are displayed, including subgroup stratification by transplant eligibility. Higher percentiles indicate greater risk, assisting in individualized treatment planning.

CONCLUSIONS

This web-based calculator provides automated risk assessment integrating clinical, cytogenetic, and treatment response data. Its intuitive design supports personalized decision-making.

Access: https://taxonomy.harmony-platform.eu/riskcalculator/

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