

Patient Similarity Network of Multiple Myeloma Identifies Patient Sub-groups with Distinct Genetic and Clinical Features

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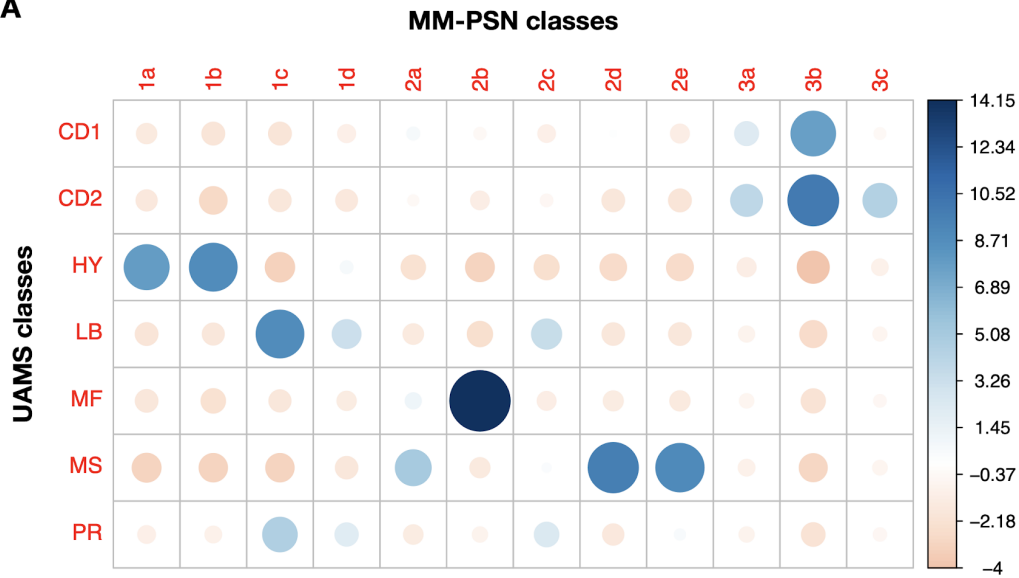
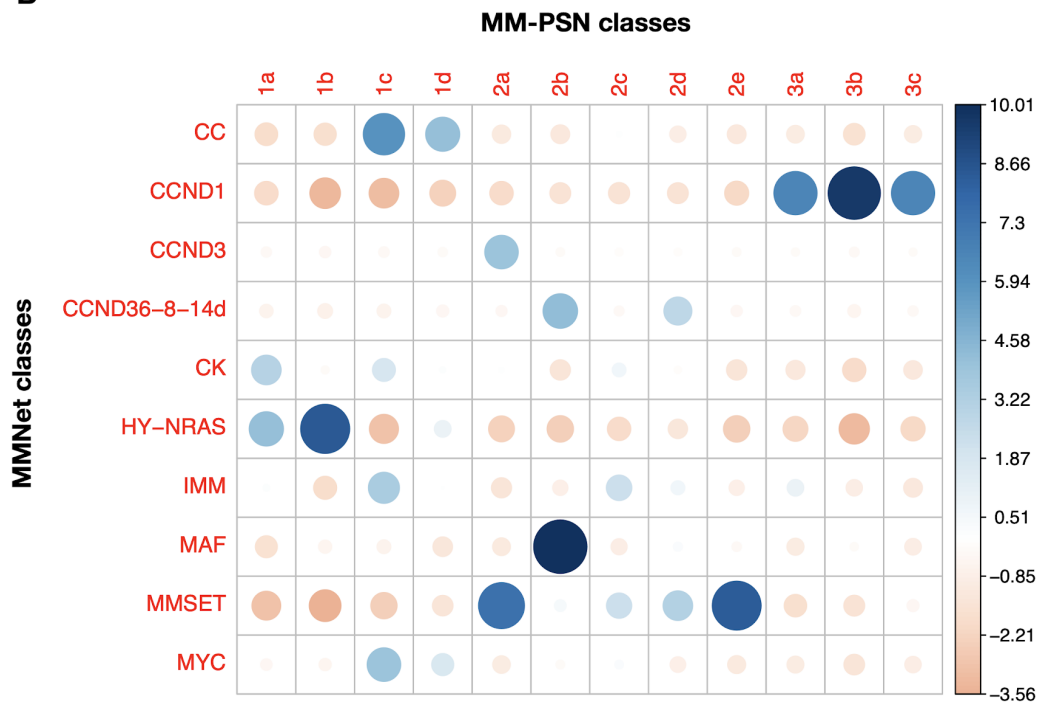
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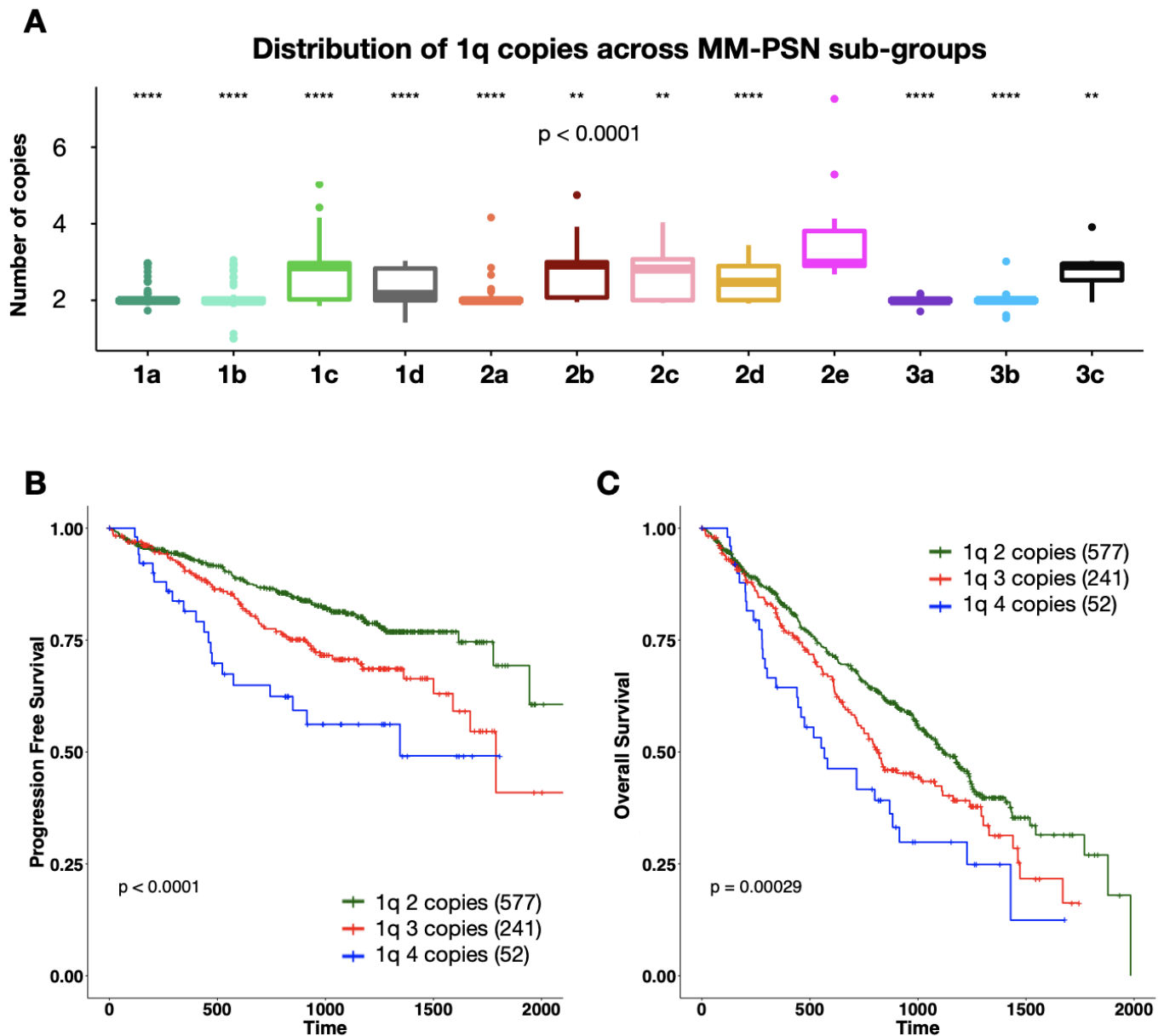
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SUPPLEMENTARY FIGURES

A**B**

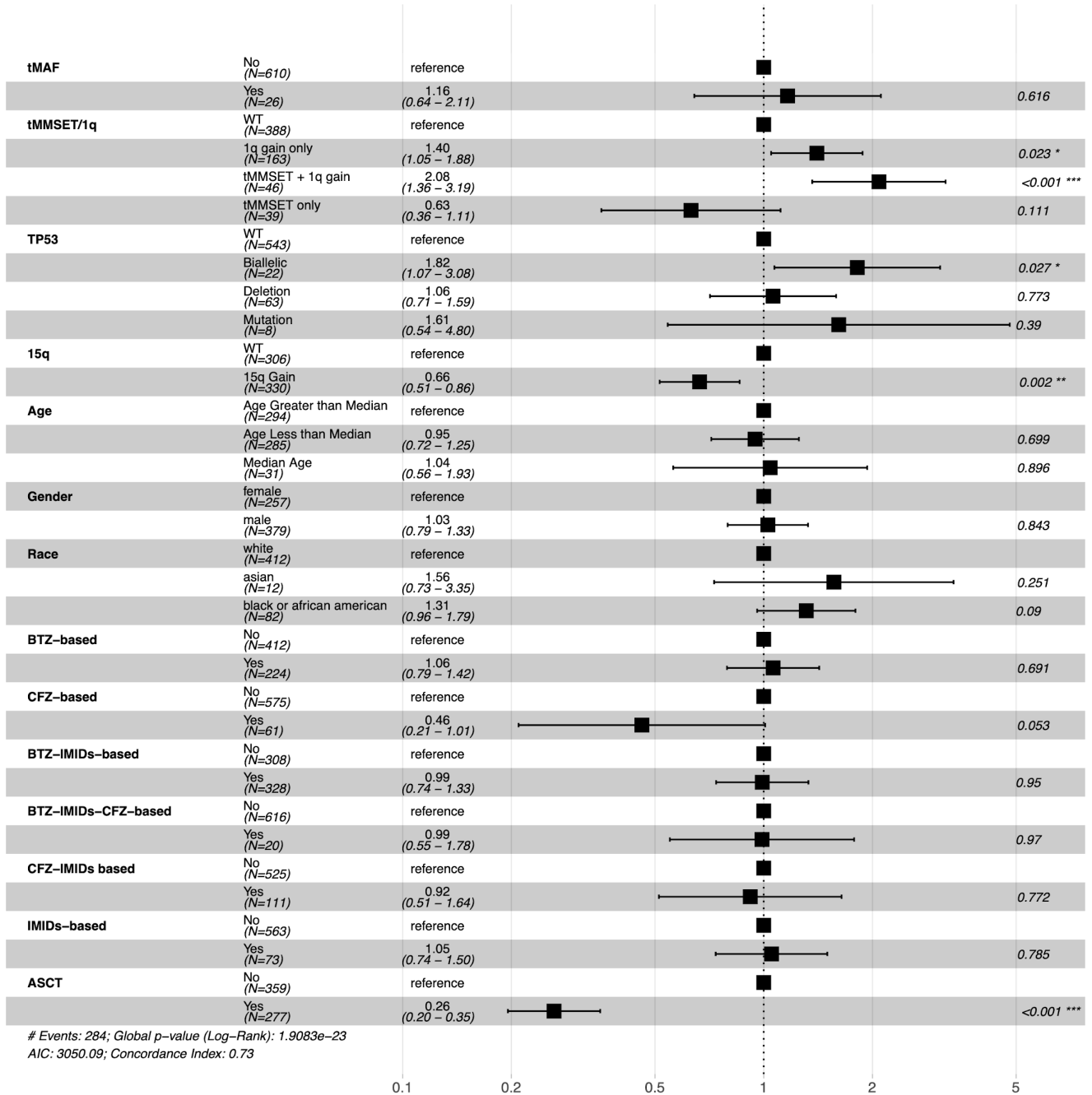
Supp Fig. 1. Comparison of MM-PSN sub-groups with UAMS and MMNet classes. The comparison was performed using Pearson residuals. Positive residuals are in blue and specify a positive association between the corresponding classes. Negative residuals are in red and imply a negative association between the corresponding classes. **A.** Comparison between the MM-PSN sub-groups and the UAMS classes (CD1/CD2: CCND1; HY: hyperdiploid; LB: low bone disease; MF: MAF; MS: MMSET; PR: proliferative). **B.** Comparison between the MM-PSN sub-groups and the MMNet classes (CC: cell cycle; CK: cytokines; IMM: immune).



Supp Fig. 2. Prognostic implications of 1q gain and amplification. **A.** The distribution of the number of copies of 1q across MM-PSN sub-groups show a significantly higher number of copies in patients in 2e. The stars on top of each bar indicate significance compared to 2e (ns: $P > 0.05$, *: $P \leq 0.05$, **: $P \leq 0.01$, ***: $P \leq 0.001$, ****, $P \leq 0.0001$). **B-C.** Number of 1q copies significantly stratify PFS and OS. Amplification of 1q (4 or more copies) confers much worse prognosis than gain (3 copies).

Progression-Free Survival

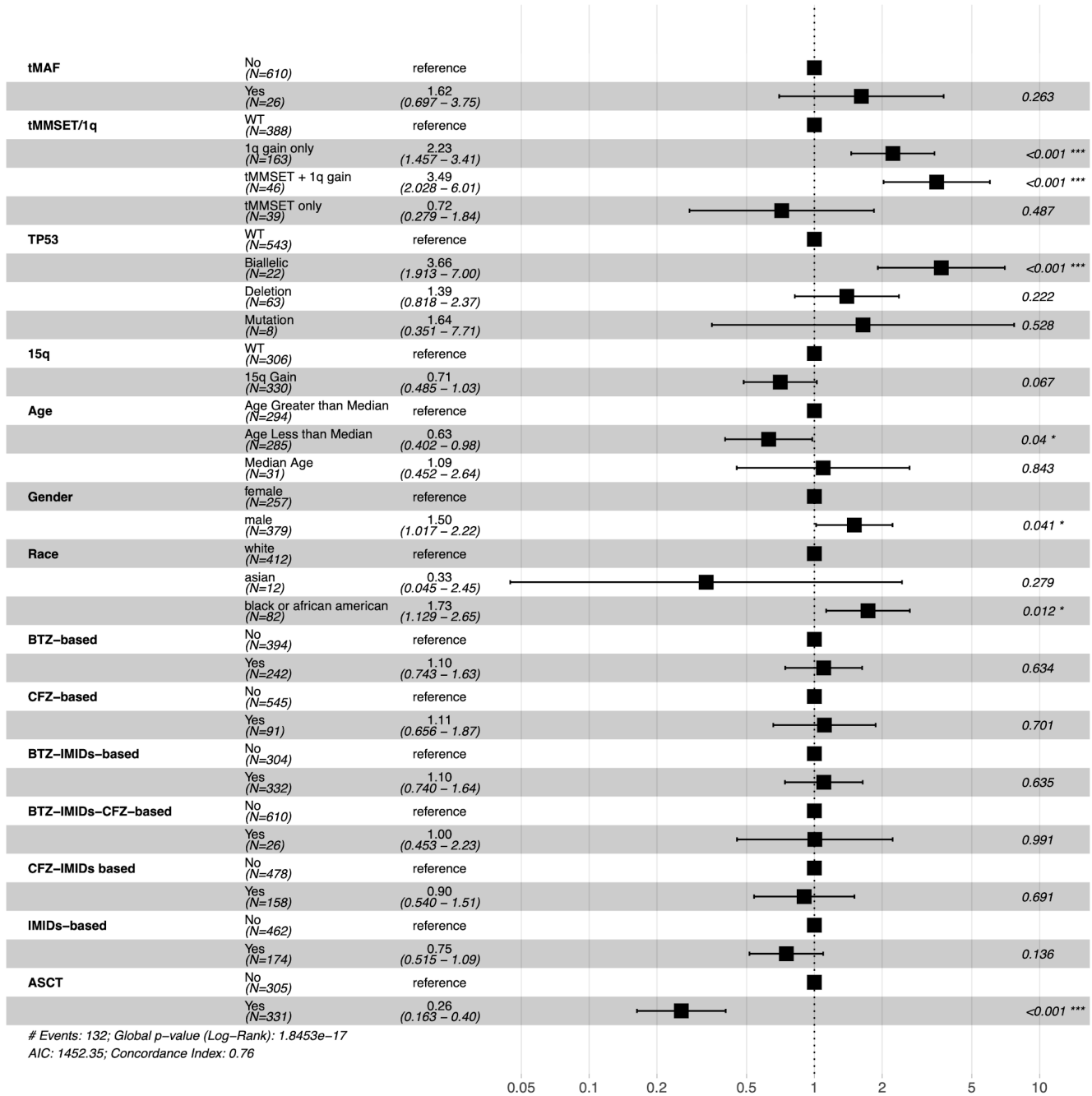
Hazard ratio



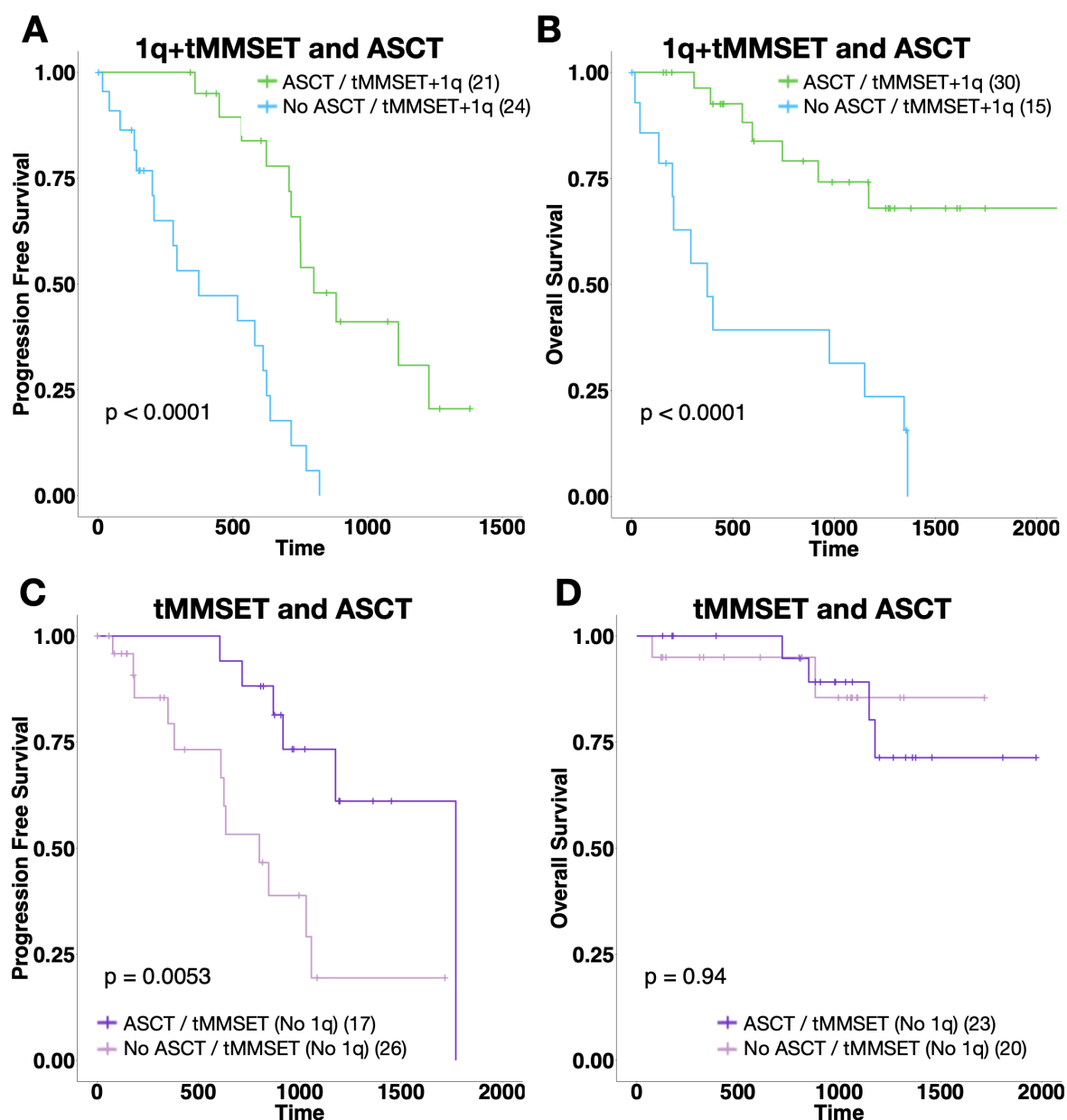
Supp Fig. 3. Multivariate cox-regression analysis of progression free survival. The analysis reveals that 1q gain, its combination with tMMSET and biallelic inactivation of TP53 are significantly associated with shorter PFS, while gain of 15q is associated with better PFS. Among treatments, autologous Stem Cell Transplant (ASCT) is significantly associated with better survival in the context of all the high-risk factors included in the model. Carfilzomib-based treatments have borderline significant benefits.

Overall Survival

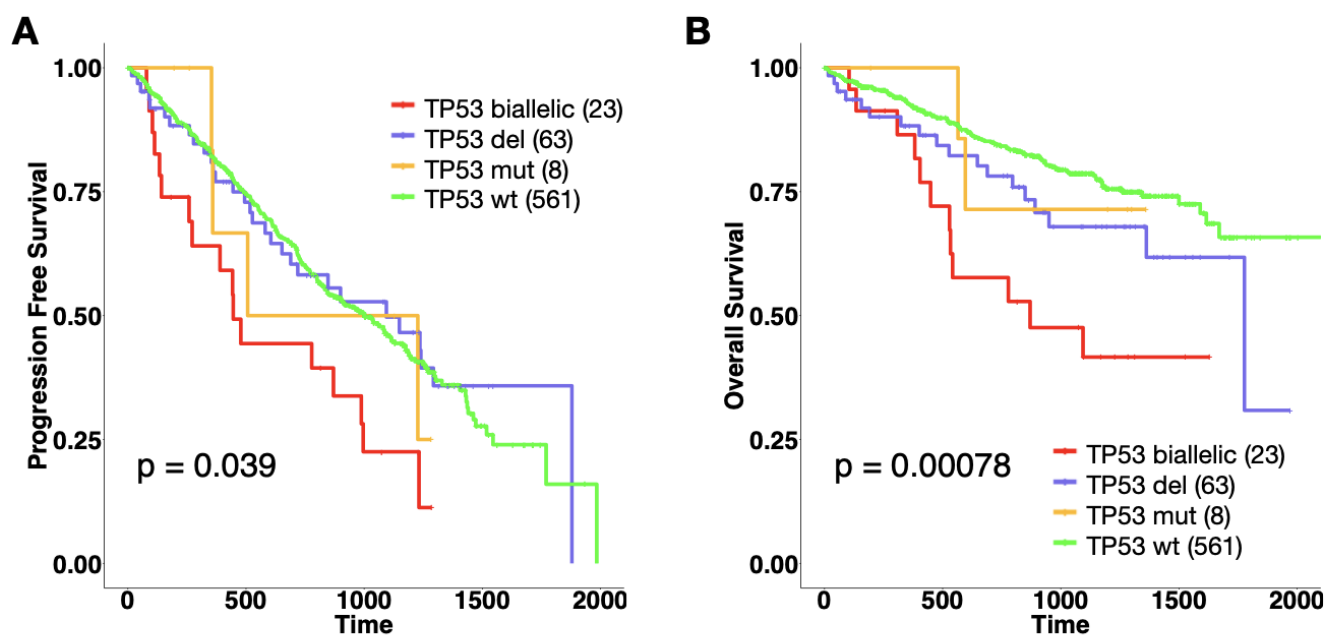
Hazard ratio



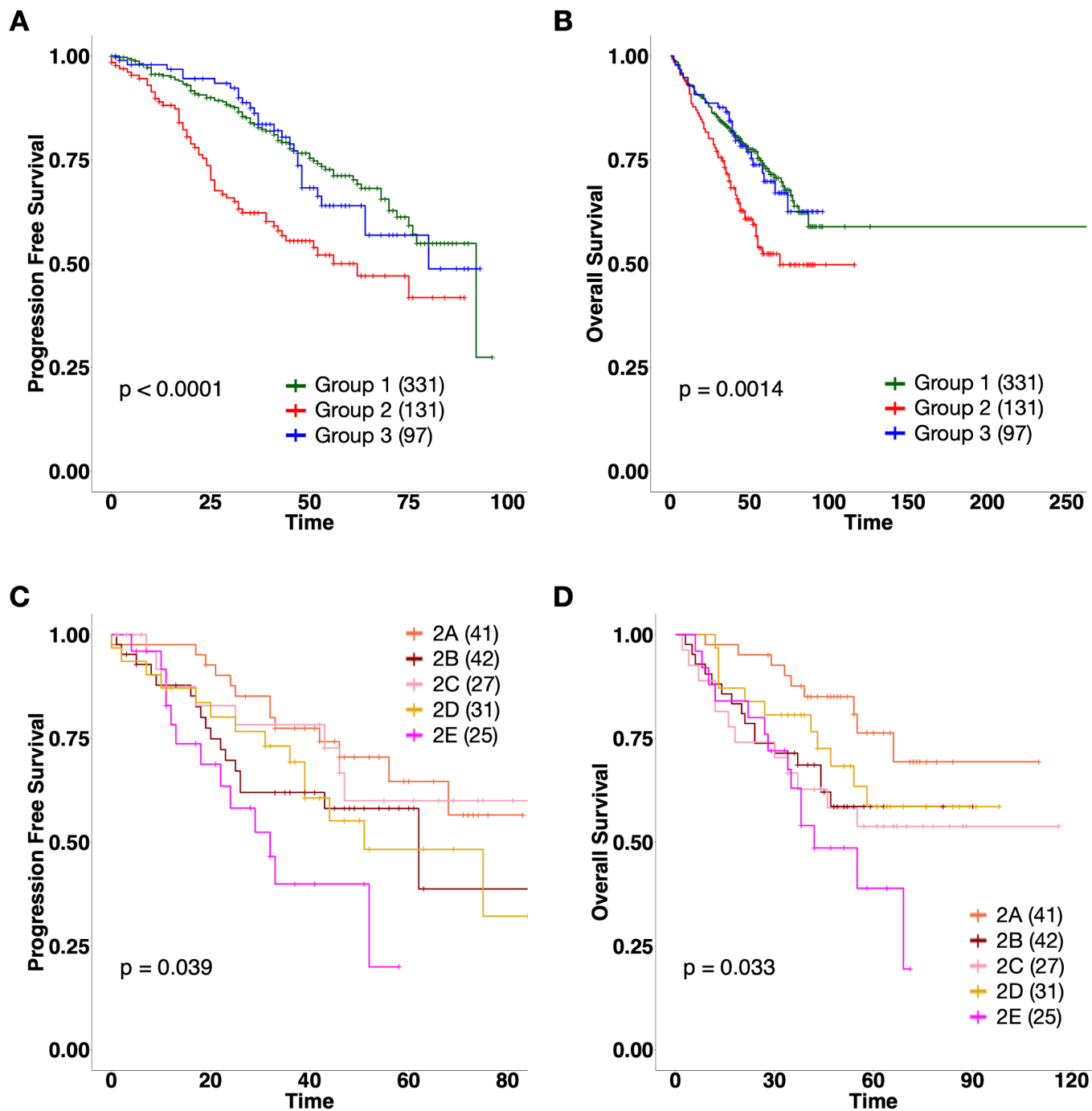
Supp Fig. 4. Multivariate cox-regression analysis of overall survival. The analysis reveals that 1q gain, its combination with tMMSET and biallelic inactivation of TP53 are significantly associated with shorter OS. Gain of 15q has borderline significant benefit in terms of OS. Younger patients (age < median = 65 yo) have also significantly longer OS. Male and black african-american patients have significantly shorter OS. Among the treatments, only ASCT is significantly associated with better OS.



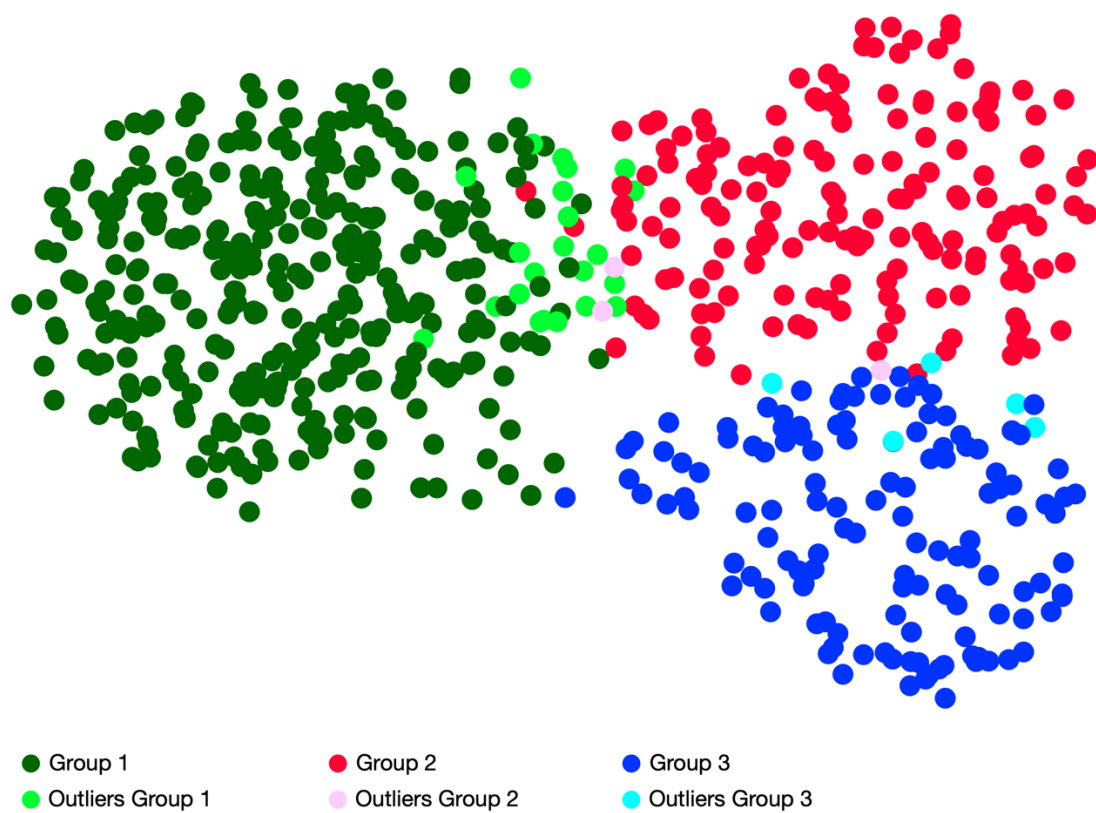
Supp Fig. 5. Multivariate cox-regression analysis of overall survival. A, B. Survival plots show that patients with 1q gain and tMMSET who received ASCT have significantly better PFS and OS compared to patients that didn't receive ASCT. C, D. Survival plots show that patients with 1q gain and tMMSET who received ASCT have significantly better PFS but no significant difference in OS.



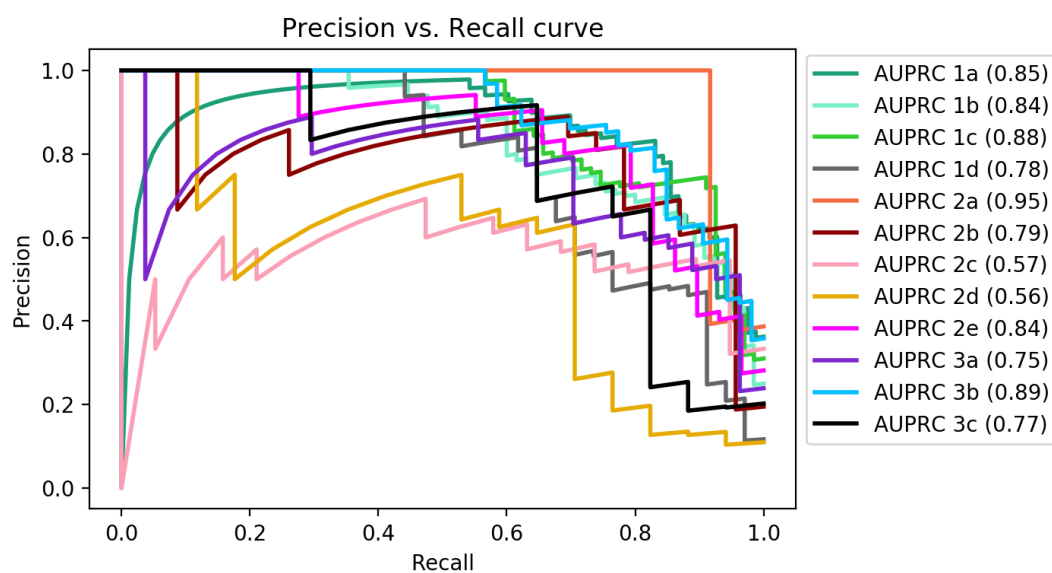
Supp Fig. 6. Biallelic inactivation of TP53. The plots show that biallelic inactivation of TP53, i.e. both deletion and mutation, is significantly associated with worse PFS and OS.



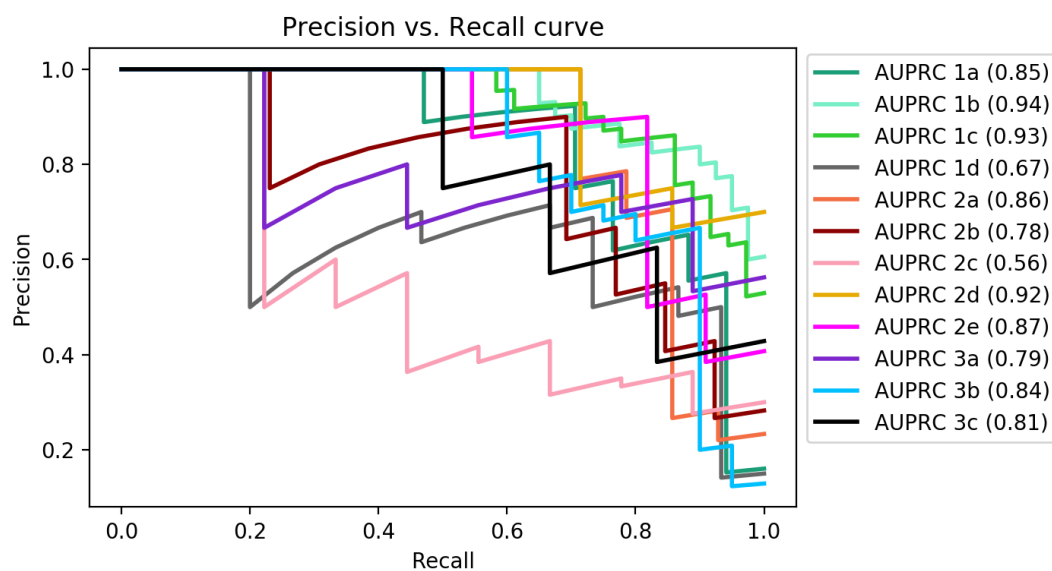
Supp Fig. 7. Validation of MM-PSN sub-groups in an independent dataset. A gene expression classifier was generated based on the 12 MM-PSN sub-groups and used to predict sub-groups in a cohort of newly diagnosed MM patients pre-TT2 and pre-TT3 treatment. **A, B.** Survival plots of the predicted three main groups show significantly worse PFS and OS of group 2, concordantly with MM-PSN findings. **C, D.** Survival plots of the predicted sub-groups in group 2 indicate worse PFS and OS of sub-group 2e, concordantly with MM-PSN findings.



Supp Fig. 8. Outliers in MM-PSN. The three main groups and their outliers, which were identified by re-applying spectral clustering increasing the number of groups.



(A)



(B)

Supp Fig. 9. Performance of the MM-PSN classifier. Precision vs Recall curves for (A) training set and (B) test set.