

points and 17 patients were stable. We have developed a 2-level procedure. In the first level, a 65-gene predictor achieved a classification accuracy of  $78.3 \pm 8.6\%$  in identifying improved patients. In the second level, the rest of patients analyzed by 136 genes classifier that distinguished between worsened and stable patients, achieving  $70.0 \pm 11.6\%$  accuracy. The ITGB4, KLK8, IGA1 and LGALS14 genes known to be associated with MS pathogenesis were presented in both classifiers.

**Conclusion:** Early stage blood transcriptional patterns could predict 2 years clinical outcome in DMD-free RRMS patients.

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#### P1577/791

##### Machine learning approach to identify early predictors of MS progression: the NeuroArtP3 project

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**Introduction:** The NeuroArtP3 (NET-2018-12366666) is a multi-site project co-funded by the Italian Ministry of Health, involving clinical and computational centers, which aims to develop a predictive, preventive and personalized approach in neurological diseases. Given its heterogeneity and largely unpredictable clinical outcomes and disability progression from disease onset, in Multiple Sclerosis (MS) the identification of reliable progression markers is of paramount importance. Most available studies are performed on small sample sizes, therefore machine learning (ML) approaches on large cohorts of patients can help to overcome this limitation.

**Objectives/Aims:** To develop predictive models of disease progression through ML approaches, analyzing a retrospectively evaluated multicentric large cohort of MS patients.

**Methods:** **Data.** A total of 722 newly-diagnosed SM patients were retrospectively enrolled in three Italian MS centres (Trento,

Firenze, Genova). Dataset included demographic, clinical, MRI and biochemical data collected during routine clinical practice at baseline and in four follow-up visits (6, 12, 24 and 36 months). **Machine Learning Pipeline.** The implemented pipeline compared different ML models (Random Forest, Extra Trees and XGBoost) through the use of a Nested Randomized Grid Search Cross Validation strategy to maximize the Matthews Correlation Coefficient (MCC). The best model was selected and trained using a randomized grid search on an unseen train/test split of the entire dataset. Finally, different performance metrics were computed: AUC-ROC, MCC, PRC and F1-score. To understand how clinical features impacted the selected model's output we computed attributes importances and performed a ML explainability analysis.

**Results:** Random Forest achieved the highest score, with a test set AUC of 0.78. Features with highest predictive impact were EDSS (24,12 and 6 months), time interval between symptoms onset and first clinical evaluation, age at symptoms onset, diagnosis and treatment start, number of relapses at 6 months, brainstem onset and MS phenotype.

**Conclusion:** Machine learning analysis showed a robust performance, strengthening evidence in literature. Higher EDSS, age at onset, number of early relapses, and brainstem involvement were confirmed as significant predictors of MS progression. Notably, time interval between onset and first clinical evaluation emerged in the analysis, underlying the impact of early treatment on the disease course.

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##### Fall prediction model in people with multiple sclerosis based on patient reported outcomes and gait metrics

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