Machine Learning Approaches to Predict Infection Risk in Multiple Myeloma Patients Receiving Bispecific Antibody Therapy

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Background: Treatment of Multiple Myeloma (MM) with bispecific antibodies (bsAb) results in an increased risk of infection, and predicting this risk is a significant unmet need. Aim: Develop machine learning (ML) models to predict risk of infection in MM patients receiving bsAb therapy. Methods: Clinical data was retrospectively collected in a multi-institutional cohort study (n=353), enrolling patients treated with at least one full dose of teclistamab or talquetamab. Using Python, AutoGluon-Tabular and PyTorch, ML models were developed considering infection and severe infection (= CTCAE Grade 3) as binary problems. To avoid overfitting and address imbalanced data, k-fold bagging, automatic sample weighting, and out-of-fold predictions were used. Feature importance was assessed using SHapley Additive exPlanations. Results: Patients treated with teclistamab were more likely to develop infection as compared to talquetamab (p=0.0001). Cumulative dose of bsAbs, number of prior ASCT, and absolute lymphocyte count had the largest impact on predicted risk. A neural network identified patients at risk of developing severe infection within 365 days of bsAb therapy with AUC of 0.78; a LightGBM identified patients at risk of developing severe infection within 90 days of bsAb therapy with AUC of 0.86; AUC was improved to 0.88 for predicting severe infections within 90 days with a stacked ensemble model, at risk of overfitting given cohort size. Conclusions: To our knowledge, this is the first ML model that predicts infection risk within 90 days of initiating bsAb for MM, and will be validated in larger patient cohorts.

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