Clinical Classifier Challenge: Improving Risk Stratification in TaLG Bladder Cancer Objective

Ewan Gibb, PhD

Using the datasets provided, your goal is to develop a classifier/model that improves the clinical stratification of recurrence-free survival (RFS) in low-grade, stage Ta bladder cancer patients. The classifier should effectively separate patients into at least two groups with prognostic value beyond the current EAU risk stratification for recurrence risk, ensuring meaningful clinical impact. Consider exploring ways your classifier can refine risk stratification by identifying patients with lower or higher genomic risk within existing clinical risk groups.

Note: Progression data is available in the UROMOL dataset, but it is not required for the final report.

Datasets & Cohorts

- **UROMOL cohort**: Use this dataset for model training, testing, and internal validation.
- **Knowles cohort**: Strictly for external validation. Note that this cohort has slightly lower risk and limited clinical data, making it useful for assessing model generalizability.

Key Considerations

- **Clinical Relevance:** Does your classifier provide new, actionable insights, or is it reiterating known clinical factors? It should add new prognostic information to be useful.
- **Model Evaluation:** How will you assess the performance of your classifier? What metrics (e.g., AUC, accuracy, sensitivity/specificity, Kaplan-Meier analysis) will you use?
- **Feature Selection:** Which variables contribute most to stratifying patients effectively? Consider both clinical* and molecular factors.
- **Interpretability:** How would you explain your classifier's results to a clinician?

*For this exercise, it is valid to include clinical variables.

Available Variables

Your dataset includes a mix of clinical and molecular variables. Consider which ones may be relevant for predicting recurrence risk:

- Patient demographics (Age, Sex, Smoking)
- Tumor characteristics (Stage, Grade, Size, Concomitant CIS, Incident tumor)
- Risk factors (EAU risk, BCG treatment)
- Molecular classification (UROMOL2021); previous classification scheme from
- Recurrence & progression data (RFS time, PFS time, Follow-up time)
- Gene expression data (exprs); this is RNA-seq data for UROMOL and microarray data in the Knowles cohort – this may impact your model design

Deliverables

1. **Classifier Development:** A well-structured model trained and tested on UROMOL, with validation on the Knowles cohort. Please provide model or source code using a GitHub URL.

2. **Performance Metrics:** A report on how well your classifier stratifies patients, including visualizations. In addition to Kaplan-Meier curves, please include at least one or two additional performance metrics to evaluate your classifier:
    - AUC
    - C-index
    - Calibration Plot
    - Decision Curve Analysis
    - Confusion Matrix

    Please include whichever metrics are most relevant to your classifier, but the above options should provide a comprehensive evaluation. Alternative analyses are welcomed, if appropriate for your model.
3. **Clinical Interpretation:** A brief explanation of how your classifier could be used in practice, keeping in mind what clinicians need to know. How should a clinician interpret the test results and suggested changes to patient management are appropriate here.

Hints & Tips

- Keep the clinician's perspective in mind - what would make your model useful in decision-making?
- Think critically about the variables: are all features necessary, or can some be removed to improve model simplicity?
- Aim for transparency - black-box models may be powerful but difficult to apply in clinical settings.

Submission Format

Your submission should be no more than 2 single-spaced pages (excluding references), Times New Roman 12 pt font and minimum 2.54cm (1 inch) margins. References (Nature format) must be included. The font for captions cannot be smaller than 10pt.