Impact of LEPROTL1, GPR126, WDR74, TBCD12 and PLEKHS1 on survival outcomes for BCPP patients

1 Overview

1.1 Objectives

To assess the effect of age and APOBEC fraction on having wild type or mutated LEPROTL1, GPR126, WDR74, TBCD12 and PLEKHS1 using logistic regression models; and to compute the Kaplan-Meier curves for recurrence-free interval (RFI) [for non-muscle invasive patients only (NMIBC)], disease-specific survival (DSS) and overall survival (OS), individually for non-muscle invasive and muscle invasive patients and the entire population.

1.2 Statistical analysis

Please note that multiple testing has not been accounted for in the analyses.

1.2.1 Outcome measures

Recurrence-free interval (RFI) is defined as the time between the date of trial entry and the date of recurrence. Recurrence is defined as a new occurrence of bladder cancer at the same or different site as the initial index primary cancer. Patients, who have not been observed to have a recurrence by the time of analysis, will be censored at the last date they were known to be recurrence-free.

Disease-specific survival (DSS) is defined as the time from the date of trial entry until the date of death, where the cause of death is attributed to bladder cancer. Patients who died from other causes (i.e. not bladder cancer) will be censored at the date of death. Patients who are alive at the end of the study will be censored at the last date they were known to be alive. Patients for whom the cause of death cannot be clearly classified into disease-specific or other will be excluded from the analysis.

Overall survival (OS) is defined as the time from the date of trial entry until the date of death, from any cause. Patients who are alive at the end of the study will be censored at the last date they were known to be alive.

1.2.2 Logistic regression models

Separate logistic regression models were fitted to determine the effect of age of having a mutation for LEPROTL1, GPR126, WDR74, TBCD12 and PLEKHS1.

Separate logistic regression models were fitted to determine the effect of the APOBEC fraction of having a mutation for LEPROTL1, GPR126, WDR74, TBCD12 and PLEKHS1. For this analysis one unit is considered to be a change in proportion of 0.1. $p<0.05$ has been used as to determine statistical significance.

1.2.3 Survival analysis

Survival outcomes were evaluated using a Kaplan-Meier curve, with a numbers at risk table presented alongside. The number of events for patients for each group (wild type or mutated), and the hazard ratio, 95% confidence interval and p-value estimated using a Cox proportional hazards model were also reported. $p<0.05$ has been used as to determine statistical significance. This analysis is exploratory and as such no adjustment has been made for any confounding variables.

2 Results

2.1 Logistic Regression

2.1.1 Age

302 patients have been included in the analysis.

Table 1: Odds ratio for the individual logistic regression models adjusting for age

	Odds Ratios	**(95% CI)**	
LEPROTL1	1.025	(0.998, 1.053)	p=0.07
GPR126	1.024	(1.002, 1.046)	p=0.03
WDR74	1.022	(0.991, 1.053)	p=0.16
TBCD12	1.044	(1.015, 1.073)	p<0.01
PLEKHS1	1.021	(0.998, 1.044)	p=0.08

The results from the logistic regression models are presented in Table 1, and suggest that GPR126 and TBCD12 are statistically significantly associated with age. The odds of having a mutation increase by 2.6% per year of age for GPR126 and 4.5% per year for TBCD12.

2.1.2 APOBEC Fraction

71 patients have been included in the analysis.

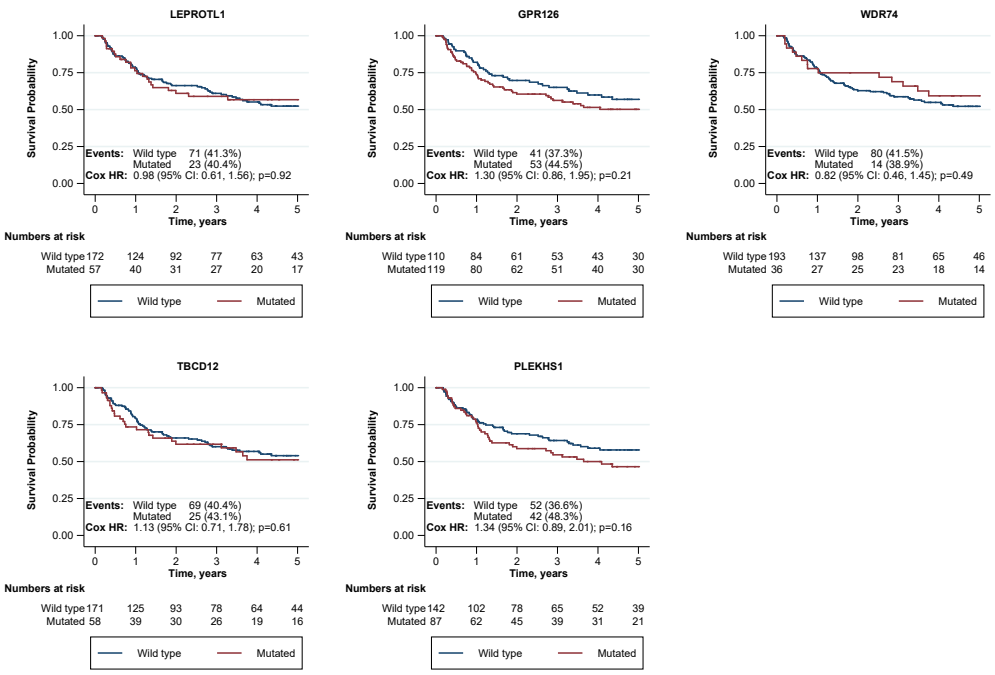
Table 2: Odds ratio for the individual logistic regression models adjusting for APOBEC fraction

	Odds Ratios	**(95% CI)**	
LEPROTL1	1.557	(1.203, 2.014)	p<0.01
GPR126	1.324	(1.075, 1.631)	p<0.01
WDR74	1.056	(0.810, 1.377)	p=0.69
TBCD12	1.712	(1.273, 2.302)	p<0.01
PLEKHS1	1.498	(1.195, 1.877)	p<0.01

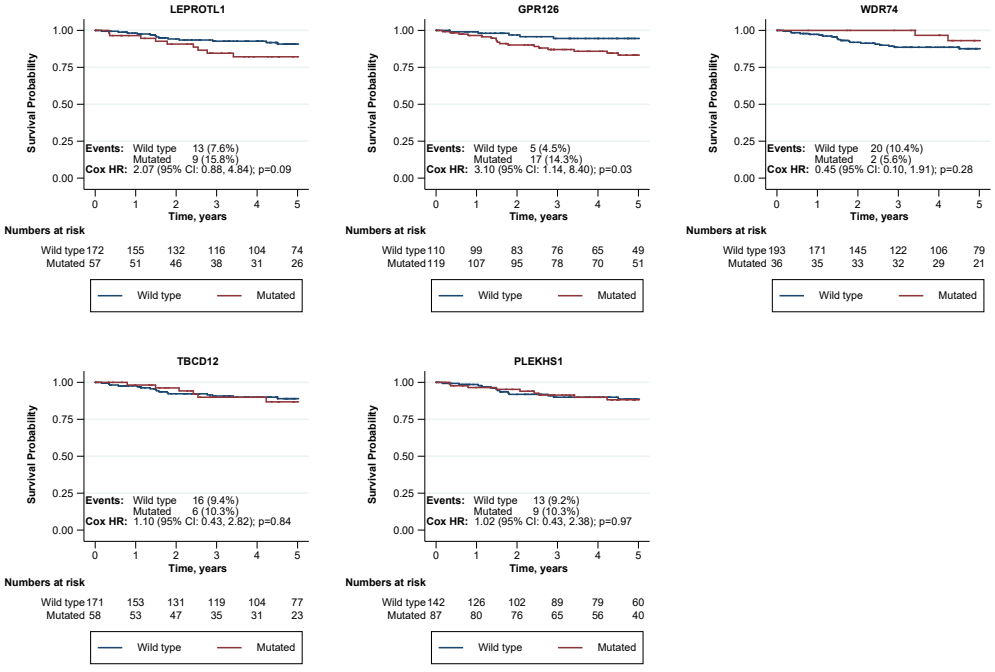
The results from the logistic regression models are presented in Table 2, and suggest that LEPROTL1, GPR126, TBCD12 and PLEKH1 are statistically significantly associated with the APOBEC fraction. The odds of having a mutation increase by 55.7% for LEPROTL1, 32.4% for GPR126, 71.2% for TBCD12 and 49.8% for PLEKHS1 for each 0.1 increase in the APOBEC fraction.

2.2 Survival Analysis

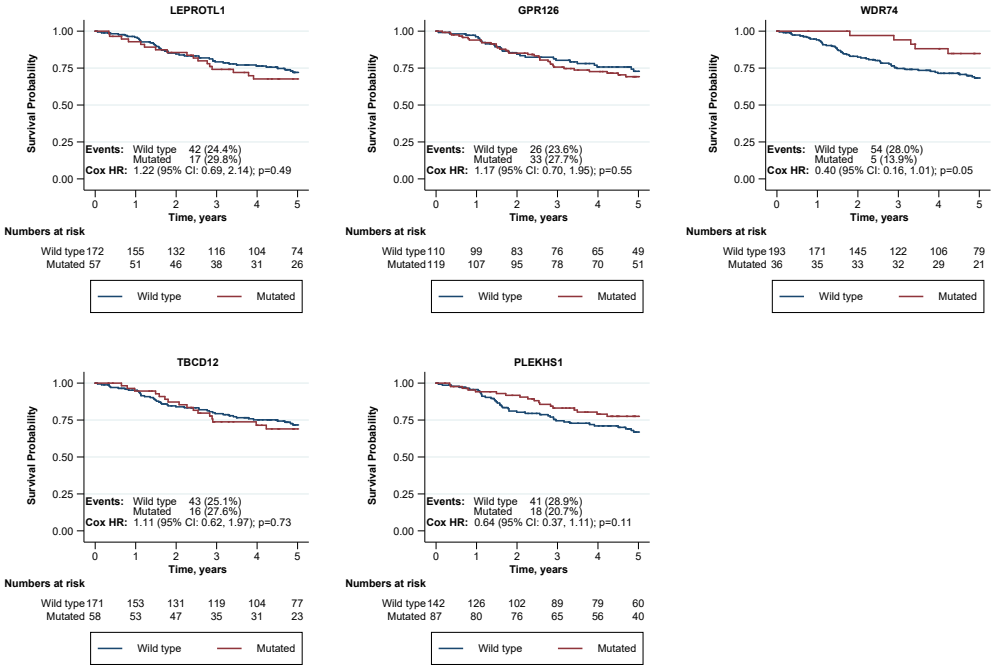
Kaplan-Meier curves for RFI in the NMIBC population



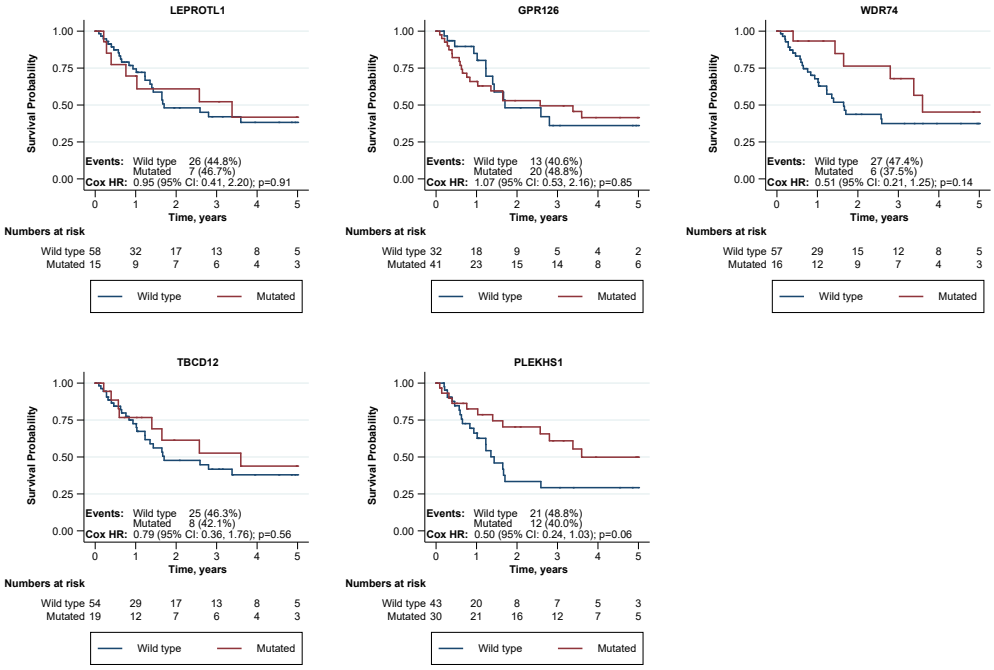
Kaplan-Meier curves for DSS in the NMIBC population



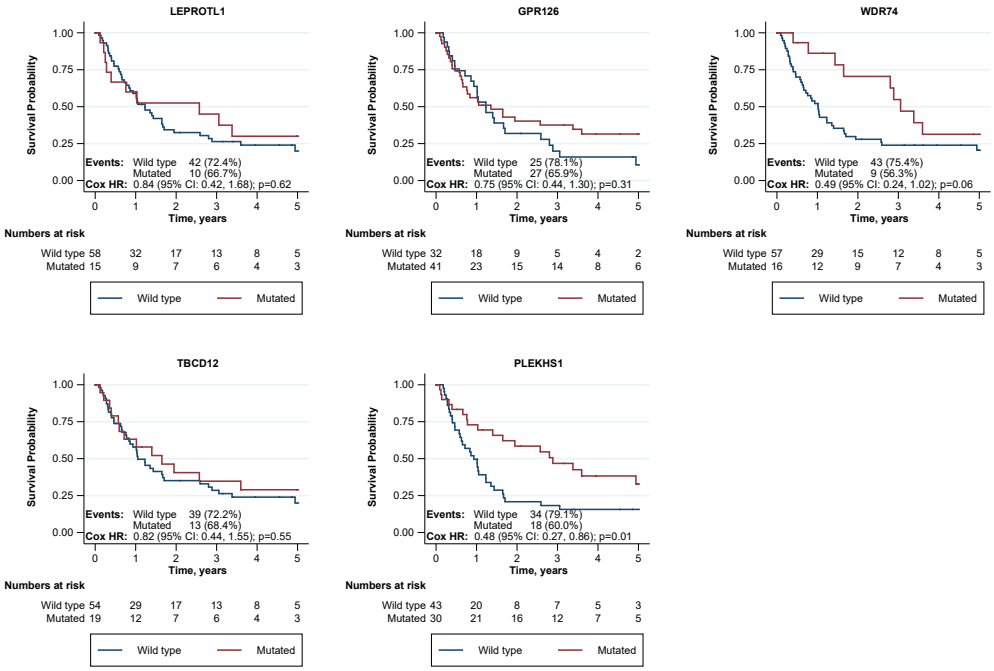
Kaplan-Meier curves for OS in the NMIBC population



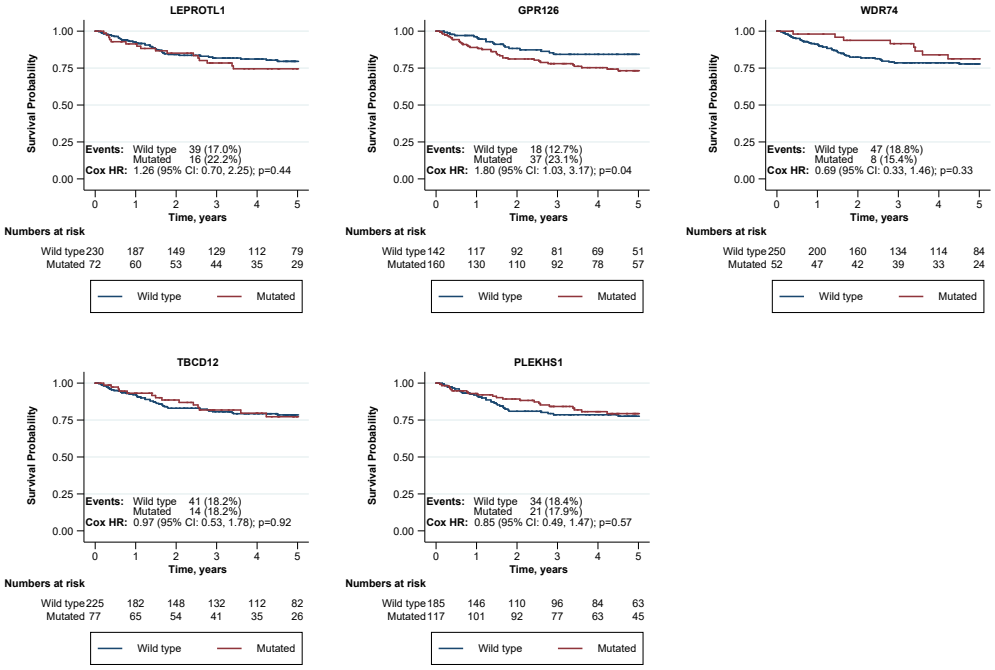
Kaplan-Meier curves for DSS in the MIBC population



Kaplan-Meier curves for OS in the MIBC population



Kaplan-Meier curves for DSS in the overall population



Kaplan-Meier curves for OS in the overall population