

**Table S7. Performances of marker and clinical variable combinations using machine learning (TEST set)**

Global population (7 days – 36 months; n=240)								TRAIN Cohort
Models	AUC [95% CI]	Sensitivity	Specificity	PPV	NPV	LR+	LR-	AUC [95% CI]
<b>gbm_5CV + TRAIL + MxA</b>	0.826[0.770;0.880]	74%	80%	66%	85%	<b>3.621</b>	0.329	0.854[0.815;0.893]
gamLoess_5CV + PCT + MxA	0.819[0.762;0.874]	67%	80%	64%	82%	3.376	0.415	0.849[0.806;0.891]
glmboost_5CV + PCT + TRAIL	0.827[0.772;0.882]	74%	78%	64%	85%	3.311	0.337	0.833[0.792;0.873]
gam_5CV + CRP + MxA	0.807[0.747;0.866]	74%	75%	61%	84%	2.897	0.351	0.851[0.809;0.893]
gbm_5CV + TRAIL	0.819[0.762;0.875]	80%	72%	60%	87%	2.846	0.281	0.849[0.809;0.889]
glmboost_5CV + CRP + TRAIL	0.818[0.761;0.874]	75%	73%	60%	85%	2.804	0.341	0.844[0.804;0.884]
gamLoess_CRP + TRAIL	0.820[0.765;0.875]	80%	67%	56%	86%	2.408	0.303	0.825[0.784;0.866]
gamLoess_PCT + TRAIL	0.831[0.776;0.884]	85%	62%	55%	88%	2.249	0.248	0.800[0.755;0.845]
gamLoess_CRP + MxA	0.797[0.735;0.859]	76%	65%	54%	84%	2.175	0.366	0.840[0.797;0.884]
ctree_5CV + CRP	0.791[0.732;0.850]	82%	62%	54%	87%	2.149	0.289	0.818[0.777;0.860]
gamLoess_5CV + PCT	0.775[0.711;0.838]	85%	55%	50%	87%	1.869	0.283	0.792[0.744;0.841]
gamLoess_5CV + MxA	0.773[0.710;0.834]	87%	52%	49%	88%	1.819	0.251	0.807[0.759;0.855]
glm_TRAIL	0.813[0.756;0.869]	87%	52%	49%	88%	1.795	0.254	0.785[0.739;0.832]
pls_PCT + MxA	0.798[0.732;0.862]	83%	51%	48%	85%	1.699	0.327	0.805[0.757;0.852]
glm_MxA	0.711[0.639;0.782]	87%	28%	39%	80%	1.207	0.467	0.761[0.708;0.815]
glm_CRP	0.773[0.709;0.835]	95%	18%	38%	88%	1.159	0.267	0.783[0.735;0.832]
slda_5CV	0.641[0.567;0.714]	96%	8%	36%	81%	1.051	0.431	0.691[0.635;0.746]
glm_PCT	0.789[0.725;0.851]	95%	7%	35%	73%	1.024	0.68	0.714[0.659;0.768]
≤ 3 months (7 – 91 days; n=77)								
Models	AUC [95% CI]	Sensitivity	Specificity	PPV	NPV	LR+	LR-	
multinom_5CV + MxA + CRP	0.866[0.754;0.977]	50%	98%	89%	88%	<b>31.000</b>	0.508	
gam_5CV + MxA + PCT	0.919[0.836;1.000]	69%	97%	85%	92%	21.313	0.323	
knn_PCT + MxA	0.903[0.828;0.978]	69%	97%	85%	92%	21.313	0.323	
knn_CRP + MxA	0.903[0.816;0.989]	69%	95%	79%	92%	14.208	0.328	
<b>slda_5CV + MxA + TRAIL</b>	<b>0.893[0.800;0.986]</b>	<b>75%</b>	<b>92%</b>	<b>71%</b>	<b>93%</b>	<b>9.300</b>	<b>0.272</b>	
ctree_5CV + TRAIL	0.857[0.752;0.962]	69%	89%	61%	92%	6.089	0.352	
ctree_5CV + CRP + TRAIL	0.846[0.725;0.967]	69%	89%	61%	92%	6.089	0.352	
knn_CRP + TRAIL	0.850[0.743;0.956]	69%	87%	58%	92%	5.328	0.359	
gam_5CV + PCT + TRAIL	0.865[0.775;0.864]	56%	87%	53%	89%	4.359	0.502	
pls_PCT + TRAIL	0.848[0.743;0.951]	56%	86%	50%	88%	3.875	0.512	
glm_TRAIL	0.840[0.731;0.947]	75%	81%	50%	93%	3.875	0.31	
glm_CRP	0.743[0.586;0.899]	50%	87%	50%	87%	3.875	0.574	
lda_5CV + CRP	0.760[0.609;0.910]	69%	79%	46%	91%	3.279	0.395	
glm_MxA	0.824[0.691;0.955]	75%	74%	43%	92%	2.906	0.337	
dwdLinear_5CV + PCT	0.811[0.690;0.932]	56%	81%	43%	88%	2.906	0.543	
glm_PCT	0.793[0.654;0.931]	88%	69%	42%	96%	2.855	0.18	
glm_5CV + MxA	0.855[0.752;0.957]	81%	66%	38%	93%	2.399	0.284	
knn_5CV	0.622[0.478;0.765]	100%	13%	23%	100%	1.148	0	
> 3 months (92 days – 36 months; n=163)								
Models	AUC [95% CI]	Sensitivity	Specificity	PPV	NPV	LR+	LR-	
gamLoess_5CV + CRP + TRAIL	0.800[0.731;0.869]	69%	75%	66%	77%	<b>2.736</b>	0.413	
glmboost_5CV + PCT + TRAIL	0.793[0.722;0.864]	78%	67%	63%	81%	2.389	0.327	
knn_CRP + TRAIL	0.792[0.721;0.863]	85%	60%	60%	85%	2.132	0.245	
knn_PCT + MxA	0.753[0.679;0.827]	77%	63%	60%	79%	2.076	0.373	
<b>gbm_5CV + MxA + TRAIL</b>	<b>0.782[0.711;0.853]</b>	<b>82%</b>	<b>60%</b>	<b>60%</b>	<b>83%</b>	<b>2.059</b>	<b>0.294</b>	
gamLoess_5CV + MxA + CRP	0.754[0.678;0.829]	82%	60%	60%	83%	2.059	0.294	
gbm_5CV + PCT	0.752[0.675;0.828]	56%	73%	59%	70%	2.042	0.607	
gbm_5CV + TRAIL	0.798[0.727;0.868]	85%	58%	59%	85%	2.026	0.254	
slda_5CV + MxA + PCT	0.770[0.696;0.842]	78%	59%	58%	79%	1.899	0.374	
gbm_5CV + MxA	0.710[0.629;0.790]	81%	57%	57%	81%	1.874	0.336	
gamLoess_5CV + CRP	0.757[0.682;0.831]	75%	58%	56%	76%	1.781	0.432	
gamLoess_PCT + TRAIL	0.809[0.740;0.877]	88%	48%	55%	85%	1.711	0.243	
gbm_5CV	0.663[0.576;0.750]	68%	58%	54%	71%	1.607	0.559	
glm_CRP	0.738[0.660;0.814]	90%	39%	51%	84%	1.469	0.264	
glm_TRAIL	0.782[0.708;0.855]	96%	25%	48%	89%	1.279	0.175	
knn_CRP + MxA	0.740[0.660;0.819]	93%	19%	45%	78%	1.143	0.388	
glm_MxA	0.673[0.587;0.759]	94%	13%	44%	75%	1.077	0.466	
glm_PCT	0.774[0.698;0.848]	96%	7%	43%	70%	1.032	0.599	

Models achieving the targeted performance criteria are highlighted in green (light green: LR+ ≥ 5.67 but < 8.5 and/or LR- ≤ 0.5 but > 0.3; dark green: LR+ ≥ 8.5 and LR- ≤ 0.3).

The best performing model in the global population is in bold.

Abbreviations: AUC, area under the curve; CI, confidence interval; LR-, negative likelihood ratio; LR+, positive likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.