CD138+ spectra and disease course

Test for associations between spectrum and overall survival (OS) and time to first-line treatment failure (TTF) in the MMRF CoMMpass data.

0. Setup   Define data directory

```r
data_dir = "/path/to/data" # exclude ending "/"
```

Load packages

```r
# Install and load required R packages
library(dplyr)
library(data.table)
library(ggplot2)
library(MASS)
library(survivalAnalysis)
```

Load spectra (PC1-PC39) and clinical data

```r
dt.all = read.csv(paste0(data_dir,"/baseline-clinical-spectra-sd.csv"))
```

```r
dt.os = dt.all %>% dplyr::select("SEQ_ID","ttcos","censos",starts_with("PC"))
dt.os$censos = as.integer(dt.os$censos) # set variable type
os = analyse_multivariate(data = dt.os,
                          time_status = vars(ttcos,censos),
                          covariates = colnames(dplyr::select(dt.os,
                                                             ends_with("_SD"))))
summary(os$coxph)
```

1. Overall Surival (OS)

```
## Call:
## coxph(formula = Surv(ttcos, censos) ~ PC1_SD + PC2_SD + PC3_SD +
##      PC4_SD + PC5_SD + PC6_SD + PC7_SD + PC8_SD + PC9_SD + PC10_SD +
##      PC11_SD + PC12_SD + PC13_SD + PC14_SD + PC15_SD + PC16_SD +
##      PC17_SD + PC18_SD + PC19_SD + PC20_SD + PC21_SD + PC22_SD +
##      PC23_SD + PC24_SD + PC25_SD + PC26_SD + PC27_SD + PC28_SD +
##      PC29_SD + PC30_SD + PC31_SD + PC32_SD + PC33_SD + PC34_SD +
##      PC35_SD + PC36_SD + PC37_SD + PC38_SD + PC39_SD, data = data)
##
##   n= 767, number of events= 179
```

```
##
##            coef exp(coef) se(coef)      z Pr(>|z|)
## PC1_SD   0.026871  1.027235 0.080787  0.333 0.739428
## PC2_SD  -0.291561  0.747096 0.076402 -3.816 0.000136 ***
## PC3_SD   0.210978  1.234885 0.078732  2.680 0.007369 **
## PC4_SD   0.381052  1.463823 0.073818  5.162 2.44e-07 ***
## PC5_SD  -0.374155  0.687870 0.075677 -4.944 7.65e-07 ***
## PC6_SD  -0.125065  0.882439 0.072257 -1.731 0.083482 .
## PC7_SD   0.112293  1.118841 0.076481  1.468 0.142035
## PC8_SD  -0.027304  0.973065 0.074522 -0.366 0.714074
## PC9_SD  -0.358321  0.698849 0.077383 -4.630 3.65e-06 ***
## PC10_SD -0.001629  0.998373 0.077594 -0.021 0.983254
## PC11_SD  0.153255  1.165622 0.074084  2.069 0.038576 *
## PC12_SD -0.171030  0.842796 0.074222 -2.304 0.021205 *
## PC13_SD  0.169723  1.184976 0.078155  2.172 0.029884 *
## PC14_SD  0.107841  1.113870 0.074179  1.454 0.146006
## PC15_SD -0.036570  0.964091 0.077588 -0.471 0.637402
## PC16_SD  0.020997  1.021219 0.074219  0.283 0.777248
## PC17_SD  0.086638  1.090502 0.074737  1.159 0.246358
## PC18_SD  0.033310  1.033871 0.074791  0.445 0.656050
## PC19_SD  0.140862  1.151265 0.071093  1.981 0.047549 *
## PC20_SD -0.187049  0.829403 0.077904 -2.401 0.016350 *
## PC21_SD  0.052896  1.054320 0.076280  0.693 0.488027
## PC22_SD  0.104868  1.110564 0.079765  1.315 0.188605
## PC23_SD  0.172993  1.188858 0.078498  2.204 0.027539 *
## PC24_SD -0.080973  0.922219 0.076618 -1.057 0.290588
## PC25_SD  0.048022  1.049194 0.074227  0.647 0.517656
## PC26_SD  0.189426  1.208556 0.080589  2.351 0.018747 *
## PC27_SD -0.122069  0.885087 0.077833 -1.568 0.116800
## PC28_SD  0.044954  1.045980 0.077150  0.583 0.560105
## PC29_SD -0.029837  0.970604 0.074425 -0.401 0.688495
## PC30_SD  0.023348  1.023622 0.075695  0.308 0.757744
## PC31_SD -0.053809  0.947613 0.076769 -0.701 0.483348
## PC32_SD  0.033643  1.034215 0.075940  0.443 0.657755
## PC33_SD -0.102449  0.902624 0.077248 -1.326 0.184762
## PC34_SD -0.126208  0.881431 0.074846 -1.686 0.091750 .
## PC35_SD  0.047805  1.048966 0.076960  0.621 0.534490
## PC36_SD  0.041790  1.042675 0.079192  0.528 0.597706
## PC37_SD  0.031977  1.032494 0.076800  0.416 0.677142
## PC38_SD -0.122550  0.884662 0.074906 -1.636 0.101832
## PC39_SD  0.062319  1.064302 0.073272  0.851 0.395038
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##         exp(coef) exp(-coef) lower .95 upper .95
## PC1_SD     1.0272     0.9735    0.8768    1.2035
## PC2_SD     0.7471     1.3385    0.6432    0.8678
## PC3_SD     1.2349     0.8098    1.0583    1.4409
## PC4_SD     1.4638     0.6831    1.2666    1.6917
## PC5_SD     0.6879     1.4538    0.5930    0.7979
## PC6_SD     0.8824     1.1332    0.7659    1.0167
## PC7_SD     1.1188     0.8938    0.9631    1.2998
## PC8_SD     0.9731     1.0277    0.8408    1.1261
## PC9_SD     0.6988     1.4309    0.6005    0.8133
```

```
## PC10_SD    0.9984    1.0016    0.8575    1.1624
## PC11_SD    1.1656    0.8579    1.0081    1.3478
## PC12_SD    0.8428    1.1865    0.7287    0.9748
## PC13_SD    1.1850    0.8439    1.0167    1.3811
## PC14_SD    1.1139    0.8978    0.9631    1.2882
## PC15_SD    0.9641    1.0372    0.8281    1.1224
## PC16_SD    1.0212    0.9792    0.8830    1.1811
## PC17_SD    1.0905    0.9170    0.9419    1.2625
## PC18_SD    1.0339    0.9672    0.8929    1.1971
## PC19_SD    1.1513    0.8686    1.0015    1.3234
## PC20_SD    0.8294    1.2057    0.7120    0.9662
## PC21_SD    1.0543    0.9485    0.9079    1.2243
## PC22_SD    1.1106    0.9004    0.9498    1.2985
## PC23_SD    1.1889    0.8411    1.0193    1.3866
## PC24_SD    0.9222    1.0843    0.7936    1.0716
## PC25_SD    1.0492    0.9531    0.9071    1.2135
## PC26_SD    1.2086    0.8274    1.0320    1.4154
## PC27_SD    0.8851    1.1298    0.7599    1.0310
## PC28_SD    1.0460    0.9560    0.8992    1.2167
## PC29_SD    0.9706    1.0303    0.8389    1.1230
## PC30_SD    1.0236    0.9769    0.8825    1.1873
## PC31_SD    0.9476    1.0553    0.8152    1.1015
## PC32_SD    1.0342    0.9669    0.8912    1.2002
## PC33_SD    0.9026    1.1079    0.7758    1.0502
## PC34_SD    0.8814    1.1345    0.7612    1.0207
## PC35_SD    1.0490    0.9533    0.9021    1.2197
## PC36_SD    1.0427    0.9591    0.8928    1.2177
## PC37_SD    1.0325    0.9685    0.8882    1.2002
## PC38_SD    0.8847    1.1304    0.7639    1.0246
## PC39_SD    1.0643    0.9396    0.9219    1.2287
##
## Concordance= 0.737  (se = 0.021 )
## Likelihood ratio test= 163.8  on 39 df,   p=<2e-16
## Wald test            = 188.7  on 39 df,   p=<2e-16
## Score (logrank) test = 205.5  on 39 df,   p=<2e-16
```

```r
summary(os$coxph)$logtest
```

```
##         test          df        pvalue
## 1.638210e+02 3.900000e+01 3.089567e-17
```

```r
# count spectrum in model with p < .05
nsig = data.table(summary(os$coxph)$coeff[,"Pr(>|z|)"]) %>%
  subset(V1<0.05) %>% nrow()
print(paste0(nsig," spectra significant at p<.05"))
```

```
## [1] "12 spectra significant at p<.05"
```

```r
dt.tf = dt.all %>% dplyr::select("SEQ_ID","ttctf1","censtf1",starts_with("PC"))
dt.tf$censtf1 = as.integer(dt.tf$censtf1) # set variable type
```

```
tf <- analyse_multivariate(data = dt.tf,
                           time_status = vars(ttctf1,censtf1),
                           covariates = colnames(dplyr::select(dt.tf,
                                                             ends_with("_SD"))))
summary(tf$coxph)
```

2. Time to first-line treatment failure (TTF)

```
## Call:
## coxph(formula = Surv(ttctf1, censtf1) ~ PC1_SD + PC2_SD + PC3_SD +
##     PC4_SD + PC5_SD + PC6_SD + PC7_SD + PC8_SD + PC9_SD + PC10_SD +
##     PC11_SD + PC12_SD + PC13_SD + PC14_SD + PC15_SD + PC16_SD +
##     PC17_SD + PC18_SD + PC19_SD + PC20_SD + PC21_SD + PC22_SD +
##     PC23_SD + PC24_SD + PC25_SD + PC26_SD + PC27_SD + PC28_SD +
##     PC29_SD + PC30_SD + PC31_SD + PC32_SD + PC33_SD + PC34_SD +
##     PC35_SD + PC36_SD + PC37_SD + PC38_SD + PC39_SD, data = data)
##
##   n= 767, number of events= 369
##
##                 coef exp(coef)  se(coef)      z Pr(>|z|)
## PC1_SD  -0.169700  0.843918  0.056585 -2.999  0.00271 **
## PC2_SD  -0.243463  0.783909  0.053377 -4.561 5.09e-06 ***
## PC3_SD  -0.003402  0.996604  0.057277 -0.059  0.95264
## PC4_SD   0.124410  1.132480  0.053027  2.346  0.01897 *
## PC5_SD  -0.279147  0.756428  0.053785 -5.190 2.10e-07 ***
## PC6_SD  -0.083910  0.919514  0.052134 -1.609  0.10751
## PC7_SD  -0.019812  0.980383  0.053169 -0.373  0.70943
## PC8_SD  -0.010502  0.989553  0.050509 -0.208  0.83529
## PC9_SD  -0.213329  0.807890  0.054249 -3.932 8.41e-05 ***
## PC10_SD -0.155342  0.856122  0.054626 -2.844  0.00446 **
## PC11_SD  0.087709  1.091670  0.052224  1.679  0.09306 .
## PC12_SD  0.027697  1.028084  0.054241  0.511  0.60962
## PC13_SD  0.078915  1.082113  0.055786  1.415  0.15718
## PC14_SD  0.092643  1.097070  0.053538  1.730  0.08356 .
## PC15_SD -0.037856  0.962851  0.053873 -0.703  0.48225
## PC16_SD  0.086059  1.089871  0.053540  1.607  0.10797
## PC17_SD -0.017507  0.982646  0.052520 -0.333  0.73889
## PC18_SD  0.134659  1.144146  0.052261  2.577  0.00998 **
## PC19_SD  0.084478  1.088149  0.052247  1.617  0.10590
## PC20_SD -0.082134  0.921149  0.054126 -1.517  0.12915
## PC21_SD  0.029130  1.029558  0.053586  0.544  0.58671
## PC22_SD  0.084510  1.088184  0.052768  1.602  0.10926
## PC23_SD  0.065259  1.067436  0.053486  1.220  0.22242
## PC24_SD -0.092220  0.911904  0.053038 -1.739  0.08208 .
## PC25_SD  0.098895  1.103951  0.053992  1.832  0.06700 .
## PC26_SD  0.051742  1.053104  0.055259  0.936  0.34909
## PC27_SD -0.036259  0.964391  0.052727 -0.688  0.49166
## PC28_SD -0.011260  0.988803  0.053589 -0.210  0.83357
## PC29_SD  0.019423  1.019613  0.053059  0.366  0.71431
## PC30_SD -0.005187  0.994827  0.053607 -0.097  0.92292
## PC31_SD  0.103178  1.108689  0.052972  1.948  0.05144 .
## PC32_SD  0.109329  1.115529  0.054053  2.023  0.04311 *
## PC33_SD -0.019192  0.980991  0.052378 -0.366  0.71406
```

```
## PC34_SD -0.004758  0.995253  0.052640 -0.090  0.92798
## PC35_SD -0.017176  0.982971  0.054046 -0.318  0.75063
## PC36_SD -0.063563  0.938415  0.053972 -1.178  0.23891
## PC37_SD -0.018140  0.982024  0.054375 -0.334  0.73868
## PC38_SD -0.005895  0.994122  0.051273 -0.115  0.90846
## PC39_SD -0.067569  0.934664  0.053909 -1.253  0.21007
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## PC1_SD     0.8439     1.1849    0.7553    0.9429
## PC2_SD     0.7839     1.2757    0.7060    0.8704
## PC3_SD     0.9966     1.0034    0.8908    1.1150
## PC4_SD     1.1325     0.8830    1.0207    1.2565
## PC5_SD     0.7564     1.3220    0.6807    0.8405
## PC6_SD     0.9195     1.0875    0.8302    1.0184
## PC7_SD     0.9804     1.0200    0.8834    1.0881
## PC8_SD     0.9896     1.0106    0.8963    1.0925
## PC9_SD     0.8079     1.2378    0.7264    0.8985
## PC10_SD    0.8561     1.1681    0.7692    0.9529
## PC11_SD    1.0917     0.9160    0.9855    1.2093
## PC12_SD    1.0281     0.9727    0.9244    1.1434
## PC13_SD    1.0821     0.9241    0.9700    1.2071
## PC14_SD    1.0971     0.9115    0.9878    1.2184
## PC15_SD    0.9629     1.0386    0.8664    1.0701
## PC16_SD    1.0899     0.9175    0.9813    1.2105
## PC17_SD    0.9826     1.0177    0.8865    1.0892
## PC18_SD    1.1441     0.8740    1.0328    1.2676
## PC19_SD    1.0881     0.9190    0.9822    1.2055
## PC20_SD    0.9211     1.0856    0.8284    1.0242
## PC21_SD    1.0296     0.9713    0.9269    1.1436
## PC22_SD    1.0882     0.9190    0.9813    1.2068
## PC23_SD    1.0674     0.9368    0.9612    1.1854
## PC24_SD    0.9119     1.0966    0.8219    1.0118
## PC25_SD    1.1040     0.9058    0.9931    1.2272
## PC26_SD    1.0531     0.9496    0.9450    1.1736
## PC27_SD    0.9644     1.0369    0.8697    1.0694
## PC28_SD    0.9888     1.0113    0.8902    1.0983
## PC29_SD    1.0196     0.9808    0.9189    1.1314
## PC30_SD    0.9948     1.0052    0.8956    1.1050
## PC31_SD    1.1087     0.9020    0.9994    1.2300
## PC32_SD    1.1155     0.8964    1.0034    1.2402
## PC33_SD    0.9810     1.0194    0.8853    1.0871
## PC34_SD    0.9953     1.0048    0.8977    1.1034
## PC35_SD    0.9830     1.0173    0.8842    1.0928
## PC36_SD    0.9384     1.0656    0.8442    1.0431
## PC37_SD    0.9820     1.0183    0.8828    1.0925
## PC38_SD    0.9941     1.0059    0.8991    1.0992
## PC39_SD    0.9347     1.0699    0.8409    1.0388
##
## Concordance= 0.657  (se = 0.014 )
## Likelihood ratio test= 117.7  on 39 df,   p=8e-10
## Wald test            = 122.3  on 39 df,   p=2e-10
## Score (logrank) test = 126.1  on 39 df,   p=4e-11
```

```r
summary(tf$coxph)$logtest
```

```
##         test           df       pvalue
## 1.177001e+02 3.900000e+01 7.916211e-10
```

```r
# count spectrum in model with p < .05
nsig = data.table(summary(tf$coxph)$coeff[,"Pr(>|z|)"]) %>%
  subset(V1<0.05) %>% nrow()
print(paste0(nsig," spectra significant at p<.05"))
```

```
## [1] "8 spectra significant at p<.05"
```

Save model results

```r
save(tf,os,file = "rdata/mod.disease-course.rdata")
```