Regression II Midterm Project

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Contents

Data Preparation

```
# loading data
midtermdata = read_csv("data/midtermdata.csv")
```

```
## Rows: 1151 Columns: 15
## -- Column specification --------------------------------------------------------
## Delimiter: ","
## dbl (15): id, time, censor, time_d, censor_d, tx, strat2, sex, raceth, ivdru...
##
## i Use `spec()` to retrieve the full column specification for this data.
## i Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

```
# combining categories, creating factor variables, and labelling

# Recode the variables
midtermdata$tx <- factor(
  midtermdata$tx,
  levels = c("0", "1"))

midtermdata$strat2 <- factor(
  midtermdata$strat2,
  levels = c("1", "0"))

midtermdata$sex <- factor(
  midtermdata$sex,
  levels = c("2", "1"))

midtermdata$raceth <- factor(
  ifelse(midtermdata$raceth %in% c(3, 4, 5, 6), 6, midtermdata$raceth),
  levels = c("1", "2", "6"))

midtermdata$ivdrug <- factor(
  ifelse(midtermdata$ivdrug %in% c(2, 3), 2, midtermdata$ivdrug),
  levels = c("2", "1"))

midtermdata$hemophil <-
  factor(midtermdata$hemophil,
         levels = c("0", "1"))

midtermdata$karnof <- factor(
  ifelse(midtermdata$karnof %in% c(80, 70), 70, midtermdata$karnof),
  levels = c("100", "90", "70"))
```

Descriptive statistics

```r
# data exploration
summary(midtermdata)
```

```
##        id              time            censor            time_d     
##  Min.   :   1.0   Min.   :  1.0   Min.   :0.00000   Min.   :  1.0  
##  1st Qu.: 290.5   1st Qu.:174.0   1st Qu.:0.00000   1st Qu.:194.5  
##  Median : 579.0   Median :257.0   Median :0.00000   Median :265.0  
##  Mean   : 579.1   Mean   :230.2   Mean   :0.08341   Mean   :242.3  
##  3rd Qu.: 868.5   3rd Qu.:300.0   3rd Qu.:0.00000   3rd Qu.:306.0  
##  Max.   :1156.0   Max.   :364.0   Max.   :1.00000   Max.   :364.0  
##     censor_d         tx      strat2  sex     raceth  ivdrug  hemophil karnof 
##  Min.   :0.00000   0:577   1:712   2:200   1:596   2:183   0:1116   100:396  
##  1st Qu.:0.00000   1:574   0:439   1:951   2:327   1:968   1:  35   90 :541  
##  Median :0.00000                           6:228                    70 :214  
##  Mean   :0.02259                                                              
##  3rd Qu.:0.00000                                                              
##  Max.   :1.00000                                                              
##       cd4            priorzdv           age       
##  Min.   :  0.00   Min.   :  3.00   Min.   :15.00  
##  1st Qu.: 23.00   1st Qu.: 10.00   1st Qu.:33.00  
##  Median : 74.50   Median : 21.00   Median :38.00  
##  Mean   : 86.46   Mean   : 30.42   Mean   :38.65  
##  3rd Qu.:136.50   3rd Qu.: 42.00   3rd Qu.:44.00  
##  Max.   :392.00   Max.   :312.00   Max.   :73.00  
```

```r
# Summarize Baseline Characteristics
library(table1)

# Define variable labels
table1::label(midtermdata$tx) <- "Treatment"
table1::label(midtermdata$age) <- "Age at Enrollment"
table1::label(midtermdata$cd4) <- "Baseline CD4 Count (cells/mL)"
table1::label(midtermdata$karnof) <- "Karnofsky Performance Scale*"
table1::label(midtermdata$ivdrug) <- "IV Drug Use History*"
table1::label(midtermdata$strat2) <- "CD4 Stratum at Screening"
table1::label(midtermdata$sex) <- "Sex"
table1::label(midtermdata$raceth) <- "Race/Ethnicity*"
table1::label(midtermdata$hemophil) <- "Hemophiliac"
table1::label(midtermdata$priorzdv) <- "Months of prior ZDV use"

# Create a summary table with variable labels
summary_table <- table1(
  ~ age + cd4 + karnof + ivdrug + strat2 + sex + raceth + priorzdv | tx,
  data = midtermdata,
  footnote = "*Race/Ethnicity, Karnofsky Performance Scale, and IV drug use history variables were reco
  caption = "Descriptive Statistics of Baseline Characteristics in HIV Clinical Trial Participants")

print(summary_table)
```

```
## <table class="Rtable1"><caption>Descriptive Statistics of Baseline Characteristics in HIV Clinical T
## 
## <thead>
## <tr>
```

```
## <th class='rowlabel firstrow lastrow'></th>
## <th class='firstrow lastrow'><span class='stratlabel'>0<br><span class='stratn'>(N=577)</span></span
## <th class='firstrow lastrow'><span class='stratlabel'>1<br><span class='stratn'>(N=574)</span></span
## <th class='firstrow lastrow'><span class='stratlabel'>Overall<br><span class='stratn'>(N=1151)</span
## </tr>
## <tfoot><tr><td colspan="4" class="Rtable1-footnote"><p>*Race/Ethnicity, Karnofsky Performance Scale,
## </td></tr></tfoot>
## </thead>
## <tbody>
## <tr>
## <td class='rowlabel firstrow'>Age at Enrollment</td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## </tr>
## <tr>
## <td class='rowlabel'>Mean (SD)</td>
## <td>38.6 (8.82)</td>
## <td>38.7 (8.81)</td>
## <td>38.6 (8.81)</td>
## </tr>
## <tr>
## <td class='rowlabel lastrow'>Median [Min, Max]</td>
## <td class='lastrow'>38.0 [16.0, 73.0]</td>
## <td class='lastrow'>38.0 [15.0, 73.0]</td>
## <td class='lastrow'>38.0 [15.0, 73.0]</td>
## </tr>
## <tr>
## <td class='rowlabel firstrow'>Baseline CD4 Count (cells/mL)</td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## </tr>
## <tr>
## <td class='rowlabel'>Mean (SD)</td>
## <td>84.3 (70.1)</td>
## <td>88.6 (70.0)</td>
## <td>86.5 (70.1)</td>
## </tr>
## <tr>
## <td class='rowlabel lastrow'>Median [Min, Max]</td>
## <td class='lastrow'>69.5 [0, 392]</td>
## <td class='lastrow'>79.5 [0, 348]</td>
## <td class='lastrow'>74.5 [0, 392]</td>
## </tr>
## <tr>
## <td class='rowlabel firstrow'>Karnofsky Performance Scale*</td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## </tr>
## <tr>
## <td class='rowlabel'>100</td>
## <td>202 (35.0%)</td>
```

```
## <td>194 (33.8%)</td>
## <td>396 (34.4%)</td>
## </tr>
## <tr>
## <td class='rowlabel'>90</td>
## <td>267 (46.3%)</td>
## <td>274 (47.7%)</td>
## <td>541 (47.0%)</td>
## </tr>
## <tr>
## <td class='rowlabel lastrow'>70</td>
## <td class='lastrow'>108 (18.7%)</td>
## <td class='lastrow'>106 (18.5%)</td>
## <td class='lastrow'>214 (18.6%)</td>
## </tr>
## <tr>
## <td class='rowlabel firstrow'>IV Drug Use History*</td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## </tr>
## <tr>
## <td class='rowlabel'>2</td>
## <td>93 (16.1%)</td>
## <td>90 (15.7%)</td>
## <td>183 (15.9%)</td>
## </tr>
## <tr>
## <td class='rowlabel lastrow'>1</td>
## <td class='lastrow'>484 (83.9%)</td>
## <td class='lastrow'>484 (84.3%)</td>
## <td class='lastrow'>968 (84.1%)</td>
## </tr>
## <tr>
## <td class='rowlabel firstrow'>CD4 Stratum at Screening</td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## </tr>
## <tr>
## <td class='rowlabel'>1</td>
## <td>357 (61.9%)</td>
## <td>355 (61.8%)</td>
## <td>712 (61.9%)</td>
## </tr>
## <tr>
## <td class='rowlabel lastrow'>0</td>
## <td class='lastrow'>220 (38.1%)</td>
## <td class='lastrow'>219 (38.2%)</td>
## <td class='lastrow'>439 (38.1%)</td>
## </tr>
## <tr>
## <td class='rowlabel firstrow'>Sex</td>
## <td class='firstrow'></td>
```

```
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## </tr>
## <tr>
## <td class='rowlabel'>2</td>
## <td>94 (16.3%)</td>
## <td>106 (18.5%)</td>
## <td>200 (17.4%)</td>
## </tr>
## <tr>
## <td class='rowlabel lastrow'>1</td>
## <td class='lastrow'>483 (83.7%)</td>
## <td class='lastrow'>468 (81.5%)</td>
## <td class='lastrow'>951 (82.6%)</td>
## </tr>
## <tr>
## <td class='rowlabel firstrow'>Race/Ethnicity*</td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## </tr>
## <tr>
## <td class='rowlabel'>1</td>
## <td>294 (51.0%)</td>
## <td>302 (52.6%)</td>
## <td>596 (51.8%)</td>
## </tr>
## <tr>
## <td class='rowlabel'>2</td>
## <td>165 (28.6%)</td>
## <td>162 (28.2%)</td>
## <td>327 (28.4%)</td>
## </tr>
## <tr>
## <td class='rowlabel lastrow'>6</td>
## <td class='lastrow'>118 (20.5%)</td>
## <td class='lastrow'>110 (19.2%)</td>
## <td class='lastrow'>228 (19.8%)</td>
## </tr>
## <tr>
## <td class='rowlabel firstrow'>Months of prior ZDV use</td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## <td class='firstrow'></td>
## </tr>
## <tr>
## <td class='rowlabel'>Mean (SD)</td>
## <td>30.3 (30.9)</td>
## <td>30.5 (27.5)</td>
## <td>30.4 (29.2)</td>
## </tr>
## <tr>
## <td class='rowlabel lastrow'>Median [Min, Max]</td>
## <td class='lastrow'>19.0 [3.00, 312]</td>
```

```
## <td class='lastrow'>22.0 [3.00, 288]</td>
## <td class='lastrow'>21.0 [3.00, 312]</td>
## </tr>
## </tbody>
## </table>
```

Is there sufficient evidence that the three-drug regimen has better PFS compared to the two-drug regimen?

```r
library(survival)

# PFS K-M table
km_pfs = survfit(Surv(time, censor) ~ tx, data = midtermdata, conf.type = "log-log")

summary(km_pfs)
```

```
## Call: survfit(formula = Surv(time, censor) ~ tx, data = midtermdata,
##     conf.type = "log-log")
##
##                 tx=0
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##     1    577       1    0.998 0.00173        0.988        1.000
##     2    575       1    0.997 0.00245        0.986        0.999
##     7    572       2    0.993 0.00346        0.982        0.997
##     9    570       1    0.991 0.00387        0.979        0.996
##    13    567       1    0.990 0.00424        0.977        0.995
##    14    566       1    0.988 0.00458        0.975        0.994
##    15    565       1    0.986 0.00489        0.972        0.993
##    16    564       1    0.984 0.00519        0.970        0.992
##    18    562       1    0.983 0.00547        0.968        0.991
##    20    561       1    0.981 0.00573        0.966        0.989
##    24    560       1    0.979 0.00598        0.963        0.988
##    25    559       1    0.977 0.00622        0.961        0.987
##    26    556       1    0.976 0.00646        0.959        0.985
##    42    551       1    0.974 0.00668        0.957        0.984
##    46    549       1    0.972 0.00690        0.955        0.983
##    52    545       1    0.970 0.00712        0.953        0.981
##    56    539       1    0.968 0.00733        0.950        0.980
##    61    536       1    0.967 0.00753        0.948        0.979
##    64    534       1    0.965 0.00773        0.946        0.977
##    68    530       2    0.961 0.00812        0.942        0.974
##    77    522       1    0.959 0.00831        0.939        0.973
##    82    520       1    0.957 0.00850        0.937        0.971
##    84    517       1    0.956 0.00868        0.935        0.970
##    87    514       1    0.954 0.00886        0.933        0.968
##    90    508       1    0.952 0.00904        0.931        0.967
##    91    506       2    0.948 0.00939        0.926        0.964
##   108    495       1    0.946 0.00956        0.924        0.962
##   112    489       1    0.944 0.00974        0.922        0.960
##   113    486       2    0.940 0.01008        0.917        0.957
##   114    484       1    0.938 0.01024        0.915        0.956
##   115    483       1    0.937 0.01040        0.913        0.954
##   117    482       1    0.935 0.01056        0.910        0.952
##   123    475       1    0.933 0.01072        0.908        0.951
##   126    471       1    0.931 0.01088        0.906        0.949
##   129    470       2    0.927 0.01119        0.901        0.946
##   130    468       1    0.925 0.01134        0.899        0.944
##   135    458       1    0.923 0.01149        0.897        0.942
##   137    456       1    0.921 0.01164        0.894        0.941
```

```
##   149    446       1     0.919 0.01180        0.892        0.939
##   151    444       2     0.914 0.01210        0.887        0.935
##   167    425       1     0.912 0.01226        0.885        0.933
##   169    424       1     0.910 0.01242        0.882        0.932
##   171    422       1     0.908 0.01258        0.880        0.930
##   181    408       1     0.906 0.01274        0.877        0.928
##   184    403       1     0.903 0.01291        0.875        0.926
##   186    401       1     0.901 0.01307        0.872        0.924
##   190    394       1     0.899 0.01324        0.870        0.922
##   194    390       1     0.897 0.01340        0.867        0.920
##   197    382       1     0.894 0.01357        0.864        0.918
##   203    374       1     0.892 0.01374        0.862        0.916
##   206    369       1     0.889 0.01392        0.859        0.914
##   231    329       1     0.887 0.01413        0.856        0.912
##   233    325       2     0.881 0.01456        0.849        0.907
##   245    295       1     0.878 0.01482        0.846        0.904
##   255    279       1     0.875 0.01510        0.842        0.902
##   298    146       1     0.869 0.01614        0.834        0.898
##
##                 tx=1
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##     7    572       1     0.998 0.00175        0.988        1.000
##    13    571       1     0.997 0.00247        0.986        0.999
##    14    570       2     0.993 0.00348        0.981        0.997
##    17    568       1     0.991 0.00389        0.979        0.996
##    18    566       2     0.988 0.00460        0.974        0.994
##    20    563       1     0.986 0.00491        0.972        0.993
##    25    562       1     0.984 0.00521        0.970        0.992
##    35    561       1     0.982 0.00549        0.968        0.991
##    39    559       1     0.981 0.00575        0.965        0.989
##    44    554       1     0.979 0.00601        0.963        0.988
##    46    553       1     0.977 0.00625        0.961        0.987
##    47    550       1     0.975 0.00649        0.959        0.985
##    58    543       1     0.974 0.00672        0.957        0.984
##    65    539       1     0.972 0.00695        0.954        0.983
##    81    528       1     0.970 0.00717        0.952        0.981
##    82    526       1     0.968 0.00739        0.950        0.980
##    85    524       1     0.966 0.00761        0.948        0.978
##    91    519       1     0.964 0.00782        0.945        0.977
##   103    514       1     0.963 0.00802        0.943        0.975
##   105    509       1     0.961 0.00823        0.941        0.974
##   114    504       1     0.959 0.00843        0.939        0.972
##   117    501       1     0.957 0.00863        0.936        0.971
##   127    492       1     0.955 0.00883        0.934        0.969
##   138    482       1     0.953 0.00903        0.932        0.968
##   144    477       1     0.951 0.00923        0.929        0.966
##   174    447       1     0.949 0.00945        0.927        0.964
##   226    375       1     0.946 0.00976        0.923        0.962
##   244    338       1     0.943 0.01012        0.920        0.960
##   248    334       1     0.941 0.01048        0.916        0.958
##   266    272       1     0.937 0.01099        0.912        0.955
##   288    196       1     0.932 0.01193        0.905        0.952
```

```r
# log-rank test
log_rank_PFS <- survdiff(Surv(time, censor) ~ tx, data = midtermdata)

# Extract relevant information
chi_squared <- log_rank_PFS$chisq
degrees_of_freedom <- length(log_rank_PFS$n) - 1
p_value <- pchisq(chi_squared, degrees_of_freedom, lower.tail = FALSE)

# Create a custom table
PFS_logrank <- data.frame(
  "Chi-Squared" = chi_squared,
  "Degrees of Freedom" = degrees_of_freedom,
  "P-Value" = p_value
)

# Display the custom table
knitr::kable(PFS_logrank, caption = "Log-Rank Test Results for PFS", digits = 5)
```

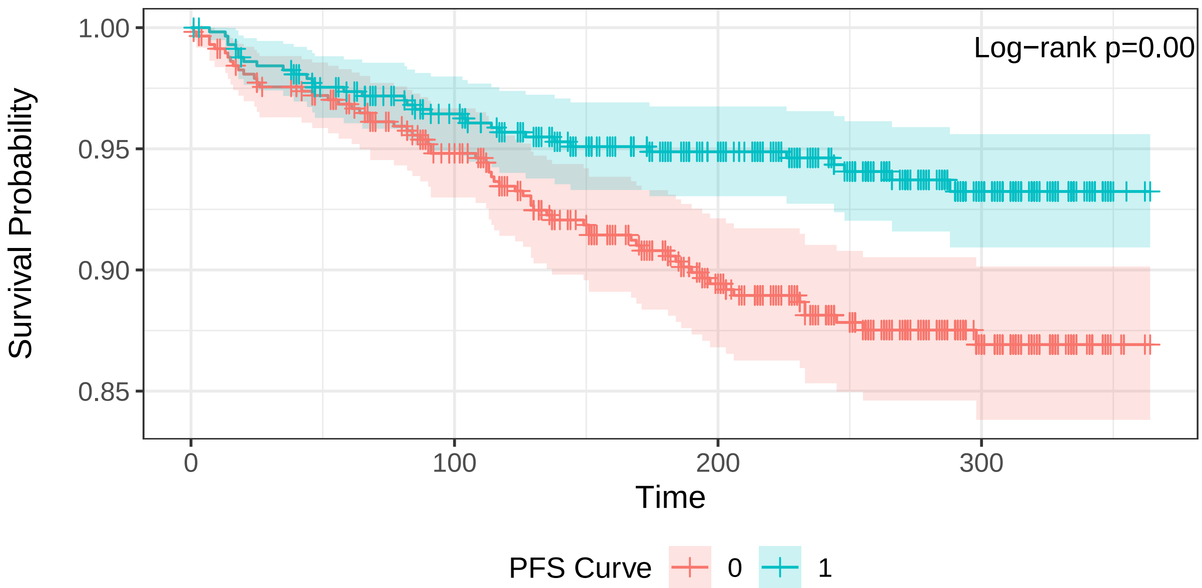
Table 1: Log-Rank Test Results for PFS

Chi.Squared	Degrees.of.Freedom	P.Value
10.54491	1	0.00117

```r
library(ggsurvfit)

# PFS K-M plot
survfit2(Surv(time, censor) ~ tx, data = midtermdata) |>
  ggsurvfit() +
  add_pvalue(location = "annotation",
             caption = "Log-rank {p.value}") +
  add_confidence_interval() +
  add_risktable() +
  add_censor_mark() +
  add_legend_title(title = "PFS Curve")
```

```
## Warning in ggplot2::geom_blank(): All aesthetics have length 1, but the data has 435 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 435 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 435 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 435 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 435 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 435 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 435 rows.
## i Did you mean to use `annotate()`?
```



0				
At Risk	577	500	380	138
Events	0	29	55	63
1				
At Risk	574	515	414	158
Events	0	20	28	33

Our hypotheses: (where s1(t) is tx = 0 and s2(t) is tx = 1) * H0 :S1(t) = S2(t), for all t * H :One of the Sk (t) is different for some t

Test statistic: * Q_log-rank = 10.5

Degree of freedom: * df = 1

P-value: * Pr(21 10.5) = 0.00117 < 0.05

Conclusion: * We reject H0 at the significance level 0.05. The survival curves for patients in two hormone therapy groups are significantly different, and there is sufficient evidence to conclude that the three-drug regimen has better PFS compared to the two-drug regimen.

Wilcoxon Test

```r
# repeat with wilxocon
library(survMisc)

pfs_wilx = ten(survfit(Surv(time, censor) ~ tx, data = midtermdata))
comp(pfs_wilx)
```

```
##                     Q         Var       Z pNorm
## 1           -1.5899e+01  2.3979e+01 -3.2468     2
## n           -1.4882e+04  2.3462e+07 -3.0724     6
## sqrtN       -4.8511e+02  2.3346e+04 -3.1750     5
## S1          -1.5023e+01  2.1892e+01 -3.2109     3
## S2          -1.5007e+01  2.1845e+01 -3.2108     4
## FH_p=1_q=1 -7.9963e-01  5.4297e-02 -3.4316     1
##               maxAbsZ        Var      Q pSupBr
## 1           1.6309e+01 2.3979e+01 3.3304      2
## n           1.5132e+04 2.3462e+07 3.1240      6
## sqrtN       4.9544e+02 2.3346e+04 3.2426      5
## S1          1.5396e+01 2.1892e+01 3.2906      3
## S2          1.5379e+01 2.1845e+01 3.2905      4
## FH_p=1_q=1 8.3262e-01 5.4297e-02 3.5732      1
```

```r
knitr::kable(attributes(pfs_wilx)$lrt[, c(1, 6:8)], "simple", digits = 4)
```

W	chiSq	df	pChisq
1	10.5419	1	0.0012
n	9.4398	1	0.0021
sqrtN	10.0803	1	0.0015
S1	10.3097	1	0.0013
S2	10.3092	1	0.0013
FH_p=1_q=1	11.7761	1	0.0006

```r
# Same conclusion with Wilcoxon Rank Test
```

Are there any other variables significantly associated with PFS?

```r
library(survival)
library(lmtest)
library(gt)

# age
age_pfs = coxph(Surv(time, censor) ~ age,
            data = midtermdata,
            ties = "efron")
summary(age_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ age, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##         coef exp(coef) se(coef)     z Pr(>|z|)
## age 0.02034   1.02055  0.01084 1.877   0.0606 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##     exp(coef) exp(-coef) lower .95 upper .95
## age     1.021     0.9799    0.9991     1.042
##
## Concordance= 0.545  (se = 0.031 )
## Likelihood ratio test= 3.39  on 1 df,   p=0.07
## Wald test            = 3.52  on 1 df,   p=0.06
## Score (logrank) test = 3.52  on 1 df,   p=0.06
```

```r
# cd4
cd4_pfs = coxph(Surv(time, censor) ~ cd4,
            data = midtermdata,
            ties = "efron")
summary(cd4_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ cd4, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##           coef exp(coef)  se(coef)      z Pr(>|z|)
## cd4 -0.016197  0.983933  0.002503 -6.472 9.69e-11 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##     exp(coef) exp(-coef) lower .95 upper .95
## cd4    0.9839      1.016    0.9791    0.9888
##
## Concordance= 0.731  (se = 0.022 )
## Likelihood ratio test= 63.69  on 1 df,   p=1e-15
## Wald test            = 41.88  on 1 df,   p=1e-10
## Score (logrank) test = 48.77  on 1 df,   p=3e-12
```

```r
# hemophil
hemophil_pfs = coxph(Surv(time, censor) ~ hemophil,
            data = midtermdata,
            ties = "efron")
summary(hemophil_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ hemophil, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##              coef exp(coef) se(coef)     z Pr(>|z|)
## hemophil1 0.02027   1.02048  0.58668 0.035    0.972
##
##           exp(coef) exp(-coef) lower .95 upper .95
## hemophil1      1.02     0.9799    0.3232     3.222
##
## Concordance= 0.499  (se = 0.008 )
## Likelihood ratio test= 0  on 1 df,   p=1
## Wald test            = 0  on 1 df,   p=1
## Score (logrank) test = 0  on 1 df,   p=1
```

```r
# ivdrug
ivdrug_pfs = coxph(Surv(time, censor) ~ ivdrug,
            data = midtermdata,
            ties = "efron")
summary(ivdrug_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ ivdrug, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##           coef exp(coef) se(coef)     z Pr(>|z|)
## ivdrug1 0.4025    1.4956   0.3204 1.256    0.209
##
##         exp(coef) exp(-coef) lower .95 upper .95
## ivdrug1     1.496     0.6686    0.7981     2.803
##
## Concordance= 0.524  (se = 0.017 )
## Likelihood ratio test= 1.75  on 1 df,   p=0.2
## Wald test            = 1.58  on 1 df,   p=0.2
## Score (logrank) test = 1.6  on 1 df,   p=0.2
```

```r
# karnof
karnof_pfs = coxph(Surv(time, censor) ~ karnof,
            data = midtermdata,
            ties = "efron")
summary(karnof_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ karnof, data = midtermdata,
##     ties = "efron")
```

```
##
##   n= 1151, number of events= 96
##
##              coef exp(coef) se(coef)     z Pr(>|z|)
## karnof90 0.4782    1.6132   0.2918 1.639    0.101
## karnof70 1.5601    4.7595   0.2885 5.407  6.4e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## karnof90     1.613     0.6199    0.9105     2.858
## karnof70     4.760     0.2101    2.7038     8.378
##
## Concordance= 0.654  (se = 0.028 )
## Likelihood ratio test= 35.8  on 2 df,   p=2e-08
## Wald test            = 38.19  on 2 df,   p=5e-09
## Score (logrank) test = 44.02  on 2 df,   p=3e-10
```

```
# priorzdv
priorzdv_pfs = coxph(Surv(time, censor) ~ priorzdv,
            data = midtermdata,
            ties = "efron")
summary(priorzdv_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ priorzdv, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##                 coef exp(coef)  se(coef)      z Pr(>|z|)
## priorzdv -0.002524  0.997479  0.003842 -0.657    0.511
##
##          exp(coef) exp(-coef) lower .95 upper .95
## priorzdv    0.9975      1.003      0.99     1.005
##
## Concordance= 0.489  (se = 0.027 )
## Likelihood ratio test= 0.46  on 1 df,   p=0.5
## Wald test            = 0.43  on 1 df,   p=0.5
## Score (logrank) test = 0.43  on 1 df,   p=0.5
```

```
# raceth
raceth_pfs = coxph(Surv(time, censor) ~ raceth,
            data = midtermdata,
            ties = "efron")
summary(raceth_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ raceth, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## raceth2 -0.2258    0.7978   0.2594 -0.871    0.384
```

```
## raceth6  0.2608    1.2979   0.2476  1.053    0.292
##
##         exp(coef) exp(-coef) lower .95 upper .95
## raceth2    0.7978     1.2534    0.4799     1.327
## raceth6    1.2979     0.7705    0.7989     2.108
##
## Concordance= 0.547  (se = 0.027 )
## Likelihood ratio test= 2.65  on 2 df,   p=0.3
## Wald test            = 2.68  on 2 df,   p=0.3
## Score (logrank) test = 2.71  on 2 df,   p=0.3
```

```
# sex
sex_pfs = coxph(Surv(time, censor) ~ sex,
            data = midtermdata,
            ties = "efron")
summary(sex_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ sex, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##         coef exp(coef) se(coef)     z Pr(>|z|)
## sex1 0.07916   1.08238  0.28114 0.282    0.778
##
##      exp(coef) exp(-coef) lower .95 upper .95
## sex1     1.082     0.9239    0.6238     1.878
##
## Concordance= 0.502  (se = 0.02 )
## Likelihood ratio test= 0.08  on 1 df,   p=0.8
## Wald test            = 0.08  on 1 df,   p=0.8
## Score (logrank) test = 0.08  on 1 df,   p=0.8
```

```
# strat2
strat2_pfs = coxph(Surv(time, censor) ~ strat2,
            data = midtermdata,
            ties = "efron")
summary(strat2_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ strat2, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##           coef exp(coef) se(coef)     z Pr(>|z|)
## strat20 1.3465    3.8438   0.2223 6.057 1.39e-09 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##         exp(coef) exp(-coef) lower .95 upper .95
## strat20     3.844     0.2602     2.486     5.943
##
## Concordance= 0.665  (se = 0.024 )
```

```
## Likelihood ratio test= 40.95  on 1 df,   p=2e-10
## Wald test            = 36.69  on 1 df,   p=1e-09
## Score (logrank) test = 42.57  on 1 df,   p=7e-11
```

```
# tx
tx_pfs = coxph(Surv(time, censor) ~ tx,
            data = midtermdata,
            ties = "efron")
summary(tx_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ tx, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 96
##
##         coef exp(coef) se(coef)      z Pr(>|z|)
## tx1 -0.6844    0.5044   0.2149 -3.185  0.00145 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##     exp(coef) exp(-coef) lower .95 upper .95
## tx1    0.5044      1.983     0.331    0.7686
##
## Concordance= 0.58  (se = 0.025 )
## Likelihood ratio test= 10.7  on 1 df,   p=0.001
## Wald test            = 10.14  on 1 df,   p=0.001
## Score (logrank) test = 10.54  on 1 df,   p=0.001
```

```
# multivariate Cox model
multivar_pfs = coxph(Surv(time, censor) ~ tx + sex + age + karnof + cd4 + strat2,
            data = midtermdata,
            ties = "efron")

summary(multivar_pfs)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ tx + sex + age + karnof +
##     cd4 + strat2, data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 96
##
##                coef exp(coef)  se(coef)      z Pr(>|z|)
## tx1       -0.659233  0.517248  0.215708 -3.056  0.00224 **
## sex1      -0.089890  0.914031  0.283368 -0.317  0.75108
## age        0.022839  1.023101  0.011432  1.998  0.04575 *
## karnof90   0.435101  1.545119  0.292595  1.487  0.13700
## karnof70   1.175450  3.239600  0.293965  3.999 6.37e-05 ***
## cd4       -0.014943  0.985168  0.003813 -3.919 8.88e-05 ***
## strat20   -0.026813  0.973543  0.343418 -0.078  0.93777
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## tx1         0.5172     1.9333    0.3389    0.7894
```

```
## sex1        0.9140     1.0941    0.5245    1.5928
## age         1.0231     0.9774    1.0004    1.0463
## karnof90    1.5451     0.6472    0.8708    2.7417
## karnof70    3.2396     0.3087    1.8208    5.7639
## cd4         0.9852     1.0151    0.9778    0.9926
## strat20     0.9735     1.0272    0.4966    1.9084
##
## Concordance= 0.778  (se = 0.023 )
## Likelihood ratio test= 98.36  on 7 df,   p=<2e-16
## Wald test            = 78.69  on 7 df,   p=3e-14
## Score (logrank) test = 96.7  on 7 df,   p=<2e-16
```

Partial Likelihood Ratio Test

```
# LRT using lmtest package
library(lmtest)

r_model <- coxph(Surv(time, censor) ~ tx + sex + age + karnof + cd4, data = midtermdata, ties = "efron")

f_model <- coxph(Surv(time, censor) ~ tx + sex + age + karnof + cd4 + strat2 + raceth + ivdrug + hemophi

lrtest(f_model, r_model)
```

```
## Likelihood ratio test
##
## Model 1: Surv(time, censor) ~ tx + sex + age + karnof + cd4 + strat2 +
##     raceth + ivdrug + hemophil + priorzdv
## Model 2: Surv(time, censor) ~ tx + sex + age + karnof + cd4
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1  12 -606.17
## 2   6 -609.26 -6 6.1966     0.4015
```

```
# since there is insufficient evidence to conclude the reduced model is better than the full, I will tr

# selection tests
library(MASS)
stepwise_cox_model <- stepAIC(f_model, direction = "both")
```

```
## Start:  AIC=1236.33
## Surv(time, censor) ~ tx + sex + age + karnof + cd4 + strat2 +
##     raceth + ivdrug + hemophil + priorzdv
##
##            Df    AIC
## - strat2    1 1234.3
## - hemophil  1 1234.3
## - priorzdv  1 1234.3
## - sex       1 1234.7
## - raceth    2 1235.3
## <none>        1236.3
## - ivdrug    1 1237.2
## - age       1 1238.6
## - tx        1 1244.3
## - karnof    2 1251.3
## - cd4       1 1253.2
##
## Step:  AIC=1234.33
## Surv(time, censor) ~ tx + sex + age + karnof + cd4 + raceth +
##     ivdrug + hemophil + priorzdv
##
##            Df    AIC
## - hemophil  1 1232.3
## - priorzdv  1 1232.3
## - sex       1 1232.7
## - raceth    2 1233.3
## <none>        1234.3
## - ivdrug    1 1235.2
## + strat2    1 1236.3
```

```
## - age       1 1236.6
## - tx        1 1242.3
## - karnof    2 1249.4
## - cd4       1 1281.3
##
## Step:  AIC=1232.34
## Surv(time, censor) ~ tx + sex + age + karnof + cd4 + raceth +
##     ivdrug + priorzdv
##
##            Df    AIC
## - priorzdv  1 1230.3
## - sex       1 1230.7
## - raceth    2 1231.4
## <none>        1232.3
## - ivdrug    1 1233.2
## + hemophil  1 1234.3
## + strat2    1 1234.3
## - age       1 1234.7
## - tx        1 1240.4
## - karnof    2 1247.5
## - cd4       1 1279.4
##
## Step:  AIC=1230.35
## Surv(time, censor) ~ tx + sex + age + karnof + cd4 + raceth +
##     ivdrug
##
##            Df    AIC
## - sex       1 1228.7
## - raceth    2 1229.4
## <none>        1230.3
## - ivdrug    1 1231.3
## + priorzdv  1 1232.3
## + hemophil  1 1232.3
## + strat2    1 1232.3
## - age       1 1232.7
## - tx        1 1238.4
## - karnof    2 1245.5
## - cd4       1 1278.2
##
## Step:  AIC=1228.68
## Surv(time, censor) ~ tx + age + karnof + cd4 + raceth + ivdrug
##
##            Df    AIC
## - raceth    2 1227.5
## <none>        1228.7
## - ivdrug    1 1229.6
## + sex       1 1230.3
## + priorzdv  1 1230.7
## + hemophil  1 1230.7
## + strat2    1 1230.7
## - age       1 1230.8
## - tx        1 1236.8
## - karnof    2 1243.9
## - cd4       1 1276.3
```

```
##
## Step:  AIC=1227.49
## Surv(time, censor) ~ tx + age + karnof + cd4 + ivdrug
##
##            Df    AIC
## <none>        1227.5
## - ivdrug    1 1228.6
## + raceth    2 1228.7
## + sex       1 1229.4
## + hemophil  1 1229.5
## + strat2    1 1229.5
## + priorzdv  1 1229.5
## - age       1 1229.5
## - tx        1 1235.8
## - karnof    2 1243.6
## - cd4       1 1274.3
```

```
summary(stepwise_cox_model)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ tx + age + karnof + cd4 +
##     ivdrug, data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 96
##
##                coef exp(coef)  se(coef)      z Pr(>|z|)
## tx1       -0.672031  0.510670  0.215353 -3.121   0.0018 **
## age        0.022923  1.023187  0.011220  2.043   0.0410 *
## karnof90   0.427003  1.532657  0.292413  1.460   0.1442
## karnof70   1.204687  3.335715  0.294216  4.095 4.23e-05 ***
## cd4       -0.014648  0.985459  0.002527 -5.797 6.75e-09 ***
## ivdrug1    0.533927  1.705618  0.321944  1.658   0.0972 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##           exp(coef) exp(-coef) lower .95 upper .95
## tx1          0.5107     1.9582    0.3348    0.7788
## age          1.0232     0.9773    1.0009    1.0459
## karnof90     1.5327     0.6525    0.8641    2.7186
## karnof70     3.3357     0.2998    1.8739    5.9378
## cd4          0.9855     1.0148    0.9806    0.9904
## ivdrug1      1.7056     0.5863    0.9075    3.2057
##
## Concordance= 0.781  (se = 0.023 )
## Likelihood ratio test= 101.4  on 6 df,   p=<2e-16
## Wald test            = 81.9  on 6 df,   p=1e-15
## Score (logrank) test = 95.72  on 6 df,   p=<2e-16
```

```
lrtest(f_model, stepwise_cox_model)
```

```
## Likelihood ratio test
##
## Model 1: Surv(time, censor) ~ tx + sex + age + karnof + cd4 + strat2 +
##     raceth + ivdrug + hemophil + priorzdv
## Model 2: Surv(time, censor) ~ tx + age + karnof + cd4 + ivdrug
```

```
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1  12 -606.17
## 2   6 -607.74 -6 3.1523     0.7895
```

```r
# There is insufficient evidence to conclude that the stepwise model is better than the full model.

lrtest(stepwise_cox_model, r_model)
```

```
## Likelihood ratio test
##
## Model 1: Surv(time, censor) ~ tx + age + karnof + cd4 + ivdrug
## Model 2: Surv(time, censor) ~ tx + sex + age + karnof + cd4
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1   6 -607.74
## 2   6 -609.26  0 3.0442  < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
# Since the step wise model and reduced model are not significantly better than the full model, for the
```

Are there any significant effect modifiers for the relation between the treatment regimens and PFS?

```r
# test interactions (pfs 2)
multivar_pfs2 = coxph(Surv(time, censor) ~ tx + sex + age + karnof + cd4 + cd4*karnof,
                      data = midtermdata,
                      ties = "efron")
summary(multivar_pfs2)
```

```
## Call:
## coxph(formula = Surv(time, censor) ~ tx + sex + age + karnof +
##     cd4 + cd4 * karnof, data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 96
##
##                    coef exp(coef)  se(coef)      z Pr(>|z|)
## tx1          -0.666045  0.513736  0.216025 -3.083 0.002048 **
## sex1         -0.092864  0.911317  0.283423 -0.328 0.743175
## age           0.023516  1.023794  0.011426  2.058 0.039588 *
## karnof90      0.856845  2.355718  0.427700  2.003 0.045137 *
## karnof70      1.572464  4.818508  0.417081  3.770 0.000163 ***
## cd4          -0.008421  0.991614  0.004457 -1.890 0.058822 .
## karnof90:cd4 -0.008516  0.991521  0.005964 -1.428 0.153314
## karnof70:cd4 -0.008751  0.991287  0.006646 -1.317 0.187910
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## tx1             0.5137     1.9465    0.3364    0.7846
## sex1            0.9113     1.0973    0.5229    1.5883
## age             1.0238     0.9768    1.0011    1.0470
## karnof90        2.3557     0.4245    1.0187    5.4473
## karnof70        4.8185     0.2075    2.1276   10.9127
## cd4             0.9916     1.0085    0.9830    1.0003
```

```
## karnof90:cd4    0.9915     1.0086    0.9800    1.0032
## karnof70:cd4    0.9913     1.0088    0.9785    1.0043
##
## Concordance= 0.781  (se = 0.022 )
## Likelihood ratio test= 100.7  on 8 df,   p=<2e-16
## Wald test            = 85.1  on 8 df,   p=5e-15
## Score (logrank) test = 109.9  on 8 df,   p=<2e-16
```

```r
lrtest(r_model, multivar_pfs2)
```

```
## Likelihood ratio test
##
## Model 1: Surv(time, censor) ~ tx + sex + age + karnof + cd4
## Model 2: Surv(time, censor) ~ tx + sex + age + karnof + cd4 + cd4 * karnof
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1   6 -609.26
## 2   8 -608.08  2 2.3597     0.3073
```

There are no significant effect modifiers for the relation between the treatment regimens and PFS.

```r
# final model
final_pfs <- coxph(Surv(time, censor) ~ tx + sex + age + karnof + cd4, data = midtermdata, ties = "efron
```

Is there sufficient evidence that the three-drug regimen has better OS compared to the two-drug regimen?

```r
# OS K-M table
km_os = survfit(Surv(time_d, censor_d) ~ tx, data = midtermdata, conf.type = "log-log")

summary(km_os)
```

```
## Call: survfit(formula = Surv(time_d, censor_d) ~ tx, data = midtermdata,
##     conf.type = "log-log")
##
##                 tx=0
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    15    572       1    0.998 0.00175        0.988        1.000
##    20    570       1    0.997 0.00247        0.986        0.999
##    42    563       1    0.995 0.00303        0.984        0.998
##    50    558       1    0.993 0.00351        0.981        0.997
##    68    546       1    0.991 0.00395        0.979        0.996
##    93    527       1    0.989 0.00437        0.976        0.995
##   107    518       1    0.987 0.00476        0.974        0.994
##   113    509       1    0.985 0.00513        0.971        0.993
##   129    499       1    0.983 0.00549        0.968        0.991
##   155    470       1    0.981 0.00586        0.966        0.990
##   181    445       1    0.979 0.00625        0.963        0.988
##   203    416       2    0.974 0.00705        0.956        0.985
##   231    369       1    0.972 0.00751        0.953        0.983
##   233    365       1    0.969 0.00795        0.949        0.981
##   245    336       1    0.966 0.00843        0.945        0.979
##   268    273       1    0.963 0.00911        0.940        0.977
##   287    209       1    0.958 0.01017        0.933        0.974
##
##                 tx=1
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    59    557       1    0.998 0.00179        0.987        1.000
##    81    543       1    0.996 0.00256        0.986        0.999
##    82    541       1    0.995 0.00315        0.983        0.998
##   107    525       1    0.993 0.00367        0.980        0.997
##   114    522       1    0.991 0.00413        0.978        0.996
##   138    501       1    0.989 0.00457        0.975        0.995
##   144    496       1    0.987 0.00498        0.972        0.994
##   248    352       1    0.984 0.00570        0.968        0.992
```

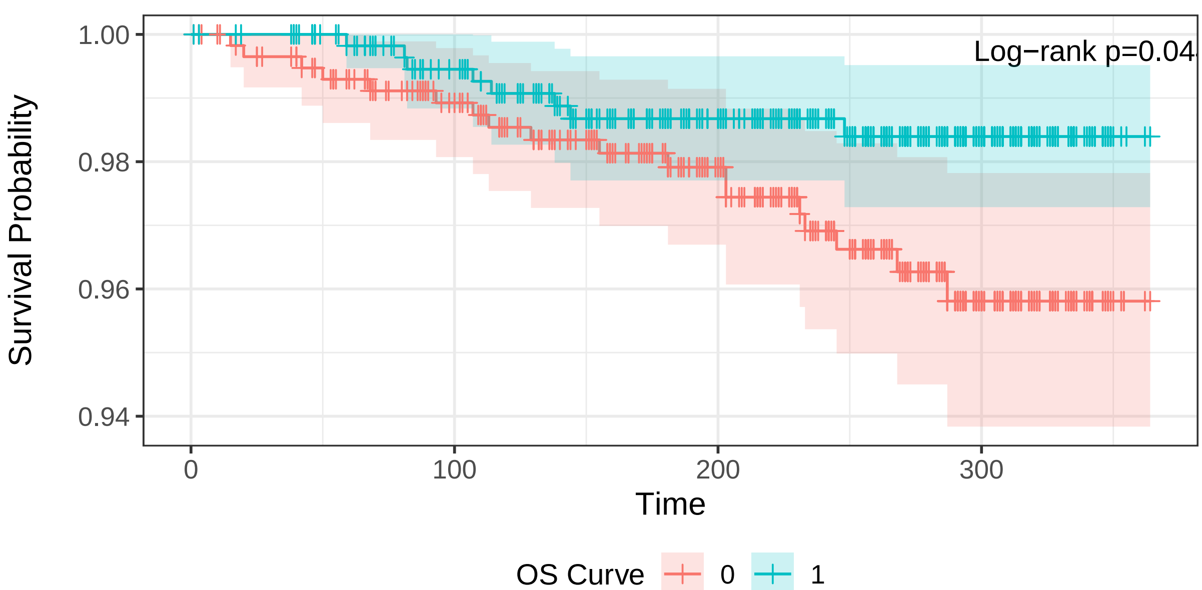
```r
# log-rank test OS
log_rank_OS <- survdiff(Surv(time_d, censor_d) ~ tx, data = midtermdata)

library(ggsurvfit)

# K-M plot
survfit2(Surv(time_d, censor_d) ~ tx, data = midtermdata) |>
  ggsurvfit() +
  add_pvalue(location = "annotation",
             caption = "Log-rank {p.value}") +
  add_risktable() +
  add_confidence_interval() +
```

```r
  add_censor_mark() +
  add_legend_title(title = "OS Curve")
```

```
## Warning in ggplot2::geom_blank(): All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
## All aesthetics have length 1, but the data has 405 rows.
## i Did you mean to use `annotate()`?
```



0					
At Risk	577	523	422	160
Events	0	6	11	18
1					
At Risk	574	532	433	170
Events	0	3	7	8

Our hypotheses: (where s1(t) is tx = 0 and s2(t) is tx = 1) * H0 :S1(t) = S2(t), for all t * H :One of the Sk (t) is different for some t

Test statistic: * Q_log-rank = 4.1

Degree of freedom: * df = 1

P-value: * Pr(21 4.1) = 0.0438 < 0.05

Conclusion: * We reject H0 at the significance level 0.05. The survival curves for patients in two hormone therapy groups are significantly different, and there is sufficient evidence to conclude that the three-drug regimen has better OS compared to the two-drug regimen.

Are there any other variables significantly associated with OS?

```r
# univariate Cox models
# age
age_os = coxph(Surv(time_d, censor_d) ~ age,
            data = midtermdata,
            ties = "efron")
summary(age_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ age, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##        coef exp(coef) se(coef)     z Pr(>|z|)
## age 0.06986   1.07236  0.01842 3.793 0.000149 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##     exp(coef) exp(-coef) lower .95 upper .95
## age     1.072     0.9325     1.034     1.112
##
## Concordance= 0.662  (se = 0.061 )
## Likelihood ratio test= 12.92  on 1 df,   p=3e-04
## Wald test            = 14.38  on 1 df,   p=1e-04
## Score (logrank) test = 14.77  on 1 df,   p=1e-04
```

```r
# cd4
cd4_os = coxph(Surv(time_d, censor_d) ~ cd4,
            data = midtermdata,
            ties = "efron")
summary(cd4_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ cd4, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##         coef exp(coef) se(coef)      z Pr(>|z|)
## cd4 -0.01211   0.98796  0.00424 -2.856  0.00429 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##     exp(coef) exp(-coef) lower .95 upper .95
## cd4     0.988      1.012    0.9798    0.9962
##
```

```
## Concordance= 0.718  (se = 0.051 )
## Likelihood ratio test= 11.09  on 1 df,   p=9e-04
## Wald test            = 8.16  on 1 df,   p=0.004
## Score (logrank) test = 8.95  on 1 df,   p=0.003
```

```
# hemophil
hemophil_os = coxph(Surv(time_d, censor_d) ~ hemophil,
            data = midtermdata,
            ties = "efron")
summary(hemophil_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ hemophil, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##            coef exp(coef) se(coef)     z Pr(>|z|)
## hemophil1 0.253     1.288    1.020 0.248    0.804
##
##           exp(coef) exp(-coef) lower .95 upper .95
## hemophil1     1.288     0.7764    0.1744      9.51
##
## Concordance= 0.5  (se = 0.015 )
## Likelihood ratio test= 0.06  on 1 df,   p=0.8
## Wald test            = 0.06  on 1 df,   p=0.8
## Score (logrank) test = 0.06  on 1 df,   p=0.8
```

```
# ivdrug
ivdrug_os = coxph(Surv(time_d, censor_d) ~ ivdrug,
            data = midtermdata,
            ties = "efron")
summary(ivdrug_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ ivdrug, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##            coef exp(coef) se(coef)      z Pr(>|z|)
## ivdrug1 -0.2243    0.7990   0.4976 -0.451    0.652
##
##         exp(coef) exp(-coef) lower .95 upper .95
## ivdrug1     0.799      1.251    0.3013     2.119
##
## Concordance= 0.515  (se = 0.039 )
## Likelihood ratio test= 0.19  on 1 df,   p=0.7
## Wald test            = 0.2  on 1 df,   p=0.7
## Score (logrank) test = 0.2  on 1 df,   p=0.7
```

```
# karnof
karnof_os = coxph(Surv(time_d, censor_d) ~ karnof,
            data = midtermdata,
            ties = "efron")
summary(karnof_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ karnof, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##             coef exp(coef) se(coef)     z Pr(>|z|)
## karnof90  1.1686    3.2176   0.7818 1.495 0.134968
## karnof70  2.6218   13.7599   0.7528 3.482 0.000497 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## karnof90     3.218    0.31079    0.6951     14.89
## karnof70    13.760    0.07267    3.1463     60.18
##
## Concordance= 0.738  (se = 0.046 )
## Likelihood ratio test= 22.45  on 2 df,   p=1e-05
## Wald test            = 19.84  on 2 df,   p=5e-05
## Score (logrank) test = 27.73  on 2 df,   p=9e-07
```

```r
# priorzdv
priorzdv_os = coxph(Surv(time_d, censor_d) ~ priorzdv,
            data = midtermdata,
            ties = "efron")
summary(priorzdv_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ priorzdv, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##               coef exp(coef)  se(coef)     z Pr(>|z|)
## priorzdv -0.011925  0.988146  0.009538 -1.25    0.211
##
##          exp(coef) exp(-coef) lower .95 upper .95
## priorzdv    0.9881      1.012    0.9698     1.007
##
## Concordance= 0.537  (se = 0.047 )
## Likelihood ratio test= 1.91  on 1 df,   p=0.2
## Wald test            = 1.56  on 1 df,   p=0.2
## Score (logrank) test = 1.47  on 1 df,   p=0.2
```

```r
# raceth
raceth_os = coxph(Surv(time_d, censor_d) ~ raceth,
            data = midtermdata,
            ties = "efron")
summary(raceth_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ raceth, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
```

```
##
##           coef exp(coef) se(coef)     z Pr(>|z|)
## raceth2 0.5108    1.6667   0.4499 1.136    0.256
## raceth6 0.4018    1.4945   0.5075 0.792    0.429
##
##         exp(coef) exp(-coef) lower .95 upper .95
## raceth2     1.667     0.6000    0.6901     4.025
## raceth6     1.494     0.6691    0.5527     4.041
##
## Concordance= 0.533  (se = 0.051 )
## Likelihood ratio test= 1.44  on 2 df,   p=0.5
## Wald test            = 1.43  on 2 df,   p=0.5
## Score (logrank) test = 1.45  on 2 df,   p=0.5
```

```
# sex
sex_os = coxph(Surv(time_d, censor_d) ~ sex,
            data = midtermdata,
            ties = "efron")
summary(sex_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ sex, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##         coef exp(coef) se(coef)      z Pr(>|z|)
## sex1 -0.2011    0.8179   0.4977 -0.404    0.686
##
##      exp(coef) exp(-coef) lower .95 upper .95
## sex1    0.8179      1.223    0.3083     2.169
##
## Concordance= 0.526  (se = 0.042 )
## Likelihood ratio test= 0.16  on 1 df,   p=0.7
## Wald test            = 0.16  on 1 df,   p=0.7
## Score (logrank) test = 0.16  on 1 df,   p=0.7
```

```
# strat2
strat2_os = coxph(Surv(time_d, censor_d) ~ strat2,
            data = midtermdata,
            ties = "efron")
summary(strat2_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ strat2, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##           coef exp(coef) se(coef)     z Pr(>|z|)
## strat20 1.2502    3.4910   0.4251 2.941  0.00327 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##         exp(coef) exp(-coef) lower .95 upper .95
```

```
## strat20     3.491     0.2865     1.517     8.031
##
## Concordance= 0.665  (se = 0.044 )
## Likelihood ratio test= 9.57  on 1 df,   p=0.002
## Wald test            = 8.65  on 1 df,   p=0.003
## Score (logrank) test = 9.83  on 1 df,   p=0.002
```

```
# tx
tx_os = coxph(Surv(time_d, censor_d) ~ tx,
            data = midtermdata,
            ties = "efron")
summary(tx_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ tx, data = midtermdata,
##     ties = "efron")
##
##   n= 1151, number of events= 26
##
##         coef exp(coef) se(coef)      z Pr(>|z|)
## tx1 -0.8325    0.4350   0.4249 -1.959   0.0501 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##     exp(coef) exp(-coef) lower .95 upper .95
## tx1     0.435      2.299    0.1891         1
##
## Concordance= 0.589  (se = 0.047 )
## Likelihood ratio test= 4.17  on 1 df,   p=0.04
## Wald test            = 3.84  on 1 df,   p=0.05
## Score (logrank) test = 4.06  on 1 df,   p=0.04
```

```
# multivariate Cox model
multivar_os = coxph(Surv(time_d, censor_d) ~ tx + sex + age + karnof + cd4 + strat2,
            data = midtermdata,
            ties = "efron")

summary(multivar_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ tx + sex + age + karnof +
##     cd4 + strat2, data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 26
##
##                coef  exp(coef)  se(coef)      z Pr(>|z|)
## tx1       -0.837280  0.432886  0.427025 -1.961 0.049911 *
## sex1      -0.479337  0.619194  0.500800 -0.957 0.338495
## age        0.075964  1.078923  0.020166  3.767 0.000165 ***
## karnof90   1.068820  2.911941  0.782957  1.365 0.172219
## karnof70   2.115247  8.291637  0.760643  2.781 0.005421 **
## cd4       -0.006521  0.993500  0.006101 -1.069 0.285116
## strat20    0.640907  1.898201  0.666967  0.961 0.336589
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
##          exp(coef) exp(-coef) lower .95 upper .95
## tx1         0.4329     2.3101    0.1875    0.9997
## sex1        0.6192     1.6150    0.2320    1.6524
## age         1.0789     0.9268    1.0371    1.1224
## karnof90    2.9119     0.3434    0.6277   13.5094
## karnof70    8.2916     0.1206    1.8672   36.8215
## cd4         0.9935     1.0065    0.9817    1.0055
## strat20     1.8982     0.5268    0.5136    7.0156
##
## Concordance= 0.855  (se = 0.032 )
## Likelihood ratio test= 46.15  on 7 df,   p=8e-08
## Wald test            = 40.53  on 7 df,   p=1e-06
## Score (logrank) test = 51.07  on 7 df,   p=9e-09
```

Partial LRT Test

```
#
full_model <- coxph(Surv(time_d, censor_d) ~ tx + age + sex + cd4 + strat2 + karnof + raceth + ivdrug +

reduced_model <- coxph(Surv(time_d, censor_d) ~ tx + sex + age + karnof, data = midtermdata, ties = "ef
summary(reduced_model)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ tx + sex + age + karnof,
##     data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 26
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## tx1      -0.82813   0.43686  0.42587 -1.945  0.05183 .
## sex1     -0.44035   0.64381  0.50012 -0.881  0.37859
## age       0.05947   1.06128  0.01855  3.206  0.00135 **
## karnof90  1.10123   3.00785  0.78271  1.407  0.15945
## karnof70  2.43823  11.45277  0.75679  3.222  0.00127 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## tx1         0.4369    2.28904    0.1896     1.007
## sex1        0.6438    1.55326    0.2416     1.716
## age         1.0613    0.94226    1.0234     1.101
## karnof90    3.0079    0.33246    0.6486    13.948
## karnof70   11.4528    0.08732    2.5985    50.477
##
## Concordance= 0.821  (se = 0.037 )
## Likelihood ratio test= 36.66  on 5 df,   p=7e-07
## Wald test            = 35.88  on 5 df,   p=1e-06
## Score (logrank) test = 44.02  on 5 df,   p=2e-08
```

```
# LRT using lmtest package
lrtest(full_model, reduced_model)
```

```
## Likelihood ratio test
##
## Model 1: Surv(time_d, censor_d) ~ tx + age + sex + cd4 + strat2 + karnof +
##     raceth + ivdrug + hemophil + priorzdv
## Model 2: Surv(time_d, censor_d) ~ tx + sex + age + karnof
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1  12 -152.79
## 2   5 -159.02 -7 12.462    0.08634 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
# since there is insufficient evidence to conclude the reduced model is better than the full, I will tr

# selection tests
library(MASS)
stepwise_cox_model2 <- stepAIC(full_model, direction = "both")
```

```
## Start:  AIC=329.58
```

```
## Surv(time_d, censor_d) ~ tx + age + sex + cd4 + strat2 + karnof +
##     raceth + ivdrug + hemophil + priorzdv
##
##            Df    AIC
## - raceth    2 325.95
## - ivdrug    1 327.63
## - hemophil  1 328.28
## - sex       1 328.39
## - cd4       1 328.42
## - strat2    1 328.50
## - priorzdv  1 329.47
## <none>        329.58
## - tx        1 331.19
## - karnof    2 338.94
## - age       1 341.25
##
## Step:  AIC=325.95
## Surv(time_d, censor_d) ~ tx + age + sex + cd4 + strat2 + karnof +
##     ivdrug + hemophil + priorzdv
##
##            Df    AIC
## - ivdrug    1 324.05
## - hemophil  1 324.64
## - cd4       1 324.82
## - sex       1 324.85
## - strat2    1 324.97
## <none>        325.95
## - priorzdv  1 326.06
## - tx        1 327.84
## + raceth    2 329.58
## - karnof    2 335.28
## - age       1 337.79
##
## Step:  AIC=324.05
## Surv(time_d, censor_d) ~ tx + age + sex + cd4 + strat2 + karnof +
##     hemophil + priorzdv
##
##            Df    AIC
## - hemophil  1 322.72
## - cd4       1 322.87
## - sex       1 322.94
## - strat2    1 323.12
## <none>        324.05
## - priorzdv  1 324.11
## + ivdrug    1 325.95
## - tx        1 325.98
## + raceth    2 327.63
## - karnof    2 333.41
## - age       1 335.81
##
## Step:  AIC=322.72
## Surv(time_d, censor_d) ~ tx + age + sex + cd4 + strat2 + karnof +
##     priorzdv
##
```

```
##            Df    AIC
## - sex       1 321.52
## - cd4       1 321.59
## - strat2    1 321.77
## - priorzdv  1 322.56
## <none>        322.72
## + hemophil  1 324.05
## + ivdrug    1 324.64
## - tx        1 324.93
## + raceth    2 326.33
## - karnof    2 331.64
## - age       1 334.15
##
## Step:  AIC=321.52
## Surv(time_d, censor_d) ~ tx + age + cd4 + strat2 + karnof + priorzdv
##
##            Df    AIC
## - cd4       1 320.44
## - strat2    1 320.50
## - priorzdv  1 321.39
## <none>        321.52
## + sex       1 322.72
## + hemophil  1 322.94
## + ivdrug    1 323.44
## - tx        1 323.91
## + raceth    2 325.04
## - karnof    2 330.90
## - age       1 332.45
##
## Step:  AIC=320.44
## Surv(time_d, censor_d) ~ tx + age + strat2 + karnof + priorzdv
##
##            Df    AIC
## <none>        320.44
## - priorzdv  1 320.68
## + cd4       1 321.52
## + sex       1 321.59
## + hemophil  1 321.82
## + ivdrug    1 322.40
## - tx        1 322.99
## + raceth    2 323.92
## - strat2    1 325.20
## - karnof    2 330.81
## - age       1 331.43
```

```r
summary(stepwise_cox_model2)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ tx + age + strat2 +
##     karnof + priorzdv, data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 26
##
##                coef  exp(coef)  se(coef)      z Pr(>|z|)
## tx1       -0.870740  0.418642  0.425814 -2.045  0.04087 *
```

```
## age       0.073224  1.075972  0.019398  3.775  0.00016 ***
## strat20   1.109687  3.033408  0.446465  2.485  0.01294 *
## karnof90  1.113312  3.044425  0.783030  1.422  0.15508
## karnof70  2.205802  9.077529  0.760295  2.901  0.00372 **
## priorzdv -0.013098  0.986988  0.009572 -1.368  0.17120
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## tx1         0.4186     2.3887    0.1817    0.9645
## age         1.0760     0.9294    1.0358    1.1177
## strat20     3.0334     0.3297    1.2644    7.2772
## karnof90    3.0444     0.3285    0.6561   14.1261
## karnof70    9.0775     0.1102    2.0455   40.2840
## priorzdv    0.9870     1.0132    0.9686    1.0057
##
## Concordance= 0.864  (se = 0.029 )
## Likelihood ratio test= 46.27  on 6 df,   p=3e-08
## Wald test            = 42.75  on 6 df,   p=1e-07
## Score (logrank) test = 51.63  on 6 df,   p=2e-09
```

```
lrtest(full_model, stepwise_cox_model2)
```

```
## Likelihood ratio test
##
## Model 1: Surv(time_d, censor_d) ~ tx + age + sex + cd4 + strat2 + karnof +
##     raceth + ivdrug + hemophil + priorzdv
## Model 2: Surv(time_d, censor_d) ~ tx + age + strat2 + karnof + priorzdv
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1  12 -152.79
## 2   6 -154.22 -6 2.8539      0.827
```

```
# There is insufficient evidence to conclude that the stepwise model is better than the full model.

# is the stepwise model better than the reduced model?
lrtest(reduced_model, stepwise_cox_model2)
```

```
## Likelihood ratio test
##
## Model 1: Surv(time_d, censor_d) ~ tx + sex + age + karnof
## Model 2: Surv(time_d, censor_d) ~ tx + age + strat2 + karnof + priorzdv
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1   5 -159.02
## 2   6 -154.22  1 9.6085   0.001937 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

For the sake of parsimony, I will choose my initial reduced model over the stepwise model.

Are there any significant effect modifiers for the relation between the treatment regimens and OS?

```r
# test interactions (OS 2)
multivar_os2 = coxph(Surv(time_d, censor_d) ~ tx + sex + age + karnof + karnof*tx,
                     data = midtermdata,
                     ties = "efron")
```

```
## Warning in coxph.fit(X, Y, istrat, offset, init, control, weights = weights, :
## Loglik converged before variable 1,6,7 ; coefficient may be infinite.
```

```r
summary(multivar_os2)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ tx + sex + age + karnof +
##     karnof * tx, data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 26
##
##                    coef  exp(coef)   se(coef)      z Pr(>|z|)
## tx1           -1.780e+01  1.859e-08  5.180e+03 -0.003  0.99726
## sex1          -4.298e-01  6.506e-01  5.023e-01 -0.856  0.39221
## age            5.958e-02  1.061e+00  1.866e-02  3.192  0.00141 **
## karnof90       5.305e-01  1.700e+00  8.382e-01  0.633  0.52676
## karnof70       2.126e+00  8.379e+00  7.750e-01  2.743  0.00609 **
## tx1:karnof90   1.752e+01  4.067e+07  5.180e+03  0.003  0.99730
## tx1:karnof70   1.679e+01  1.965e+07  5.180e+03  0.003  0.99741
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## tx1          1.859e-08  5.380e+07    0.0000       Inf
## sex1         6.506e-01  1.537e+00    0.2431     1.741
## age          1.061e+00  9.422e-01    1.0233     1.101
## karnof90     1.700e+00  5.883e-01    0.3288     8.787
## karnof70     8.379e+00  1.193e-01    1.8344    38.274
## tx1:karnof90 4.067e+07  2.459e-08    0.0000       Inf
## tx1:karnof70 1.965e+07  5.090e-08    0.0000       Inf
##
## Concordance= 0.83  (se = 0.034 )
## Likelihood ratio test= 38.86  on 7 df,   p=2e-06
## Wald test            = 33.13  on 7 df,   p=3e-05
## Score (logrank) test = 51.44  on 7 df,   p=8e-09
```

```r
summary(multivar_os)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ tx + sex + age + karnof +
##     cd4 + strat2, data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 26
##
##               coef exp(coef)  se(coef)      z Pr(>|z|)
## tx1      -0.837280  0.432886  0.427025 -1.961 0.049911 *
## sex1     -0.479337  0.619194  0.500800 -0.957 0.338495
```

```
## age       0.075964  1.078923  0.020166  3.767 0.000165 ***
## karnof90  1.068820  2.911941  0.782957  1.365 0.172219
## karnof70  2.115247  8.291637  0.760643  2.781 0.005421 **
## cd4      -0.006521  0.993500  0.006101 -1.069 0.285116
## strat20   0.640907  1.898201  0.666967  0.961 0.336589
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## tx1         0.4329     2.3101    0.1875    0.9997
## sex1        0.6192     1.6150    0.2320    1.6524
## age         1.0789     0.9268    1.0371    1.1224
## karnof90    2.9119     0.3434    0.6277   13.5094
## karnof70    8.2916     0.1206    1.8672   36.8215
## cd4         0.9935     1.0065    0.9817    1.0055
## strat20     1.8982     0.5268    0.5136    7.0156
##
## Concordance= 0.855  (se = 0.032 )
## Likelihood ratio test= 46.15  on 7 df,   p=8e-08
## Wald test            = 40.53  on 7 df,   p=1e-06
## Score (logrank) test = 51.07  on 7 df,   p=9e-09
```

There are no significant effect modifiers for the relation between the treatment regimens and OS.

Final Model Display

```r
#final model
final_os <- coxph(Surv(time_d, censor_d) ~ tx + sex + age + karnof, data = midtermdata, ties = "efron")
summary(reduced_model)
```

```
## Call:
## coxph(formula = Surv(time_d, censor_d) ~ tx + sex + age + karnof,
##     data = midtermdata, ties = "efron")
##
##   n= 1151, number of events= 26
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## tx1      -0.82813   0.43686  0.42587 -1.945  0.05183 .
## sex1     -0.44035   0.64381  0.50012 -0.881  0.37859
## age       0.05947   1.06128  0.01855  3.206  0.00135 **
## karnof90  1.10123   3.00785  0.78271  1.407  0.15945
## karnof70  2.43823  11.45277  0.75679  3.222  0.00127 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## tx1         0.4369    2.28904    0.1896     1.007
## sex1        0.6438    1.55326    0.2416     1.716
## age         1.0613    0.94226    1.0234     1.101
## karnof90    3.0079    0.33246    0.6486    13.948
## karnof70   11.4528    0.08732    2.5985    50.477
##
## Concordance= 0.821  (se = 0.037 )
## Likelihood ratio test= 36.66  on 5 df,   p=7e-07
## Wald test            = 35.88  on 5 df,   p=1e-06
## Score (logrank) test = 44.02  on 5 df,   p=2e-08
```