Original Post-hoc Analysis

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Post-hoc analysis suggests there is more benefit for the addition of cetuximab for patients with KRAS wild-type tumors, who are treated with infusional 5-FU (OxMdg) rather than capecitabine (XELOX), had zero or one metastatic site, or liver only metastatic disease (N=96, HR=0.55, 95% CI 0.35-0.87, p=0.011).

Load data.

```
load(file = "COIN_Final.Rdata")
```

Filter patients.

```
data <- patient_data

data <- data[data$KRAS=="Wild-type",]
data <- data[data$CHEMO=="OxMdG",]
data <- data[data$metsites<2 | data$mlivonly=="Yes",]
```

How many left in each treatment arm?

```
table(data$TRT)
```

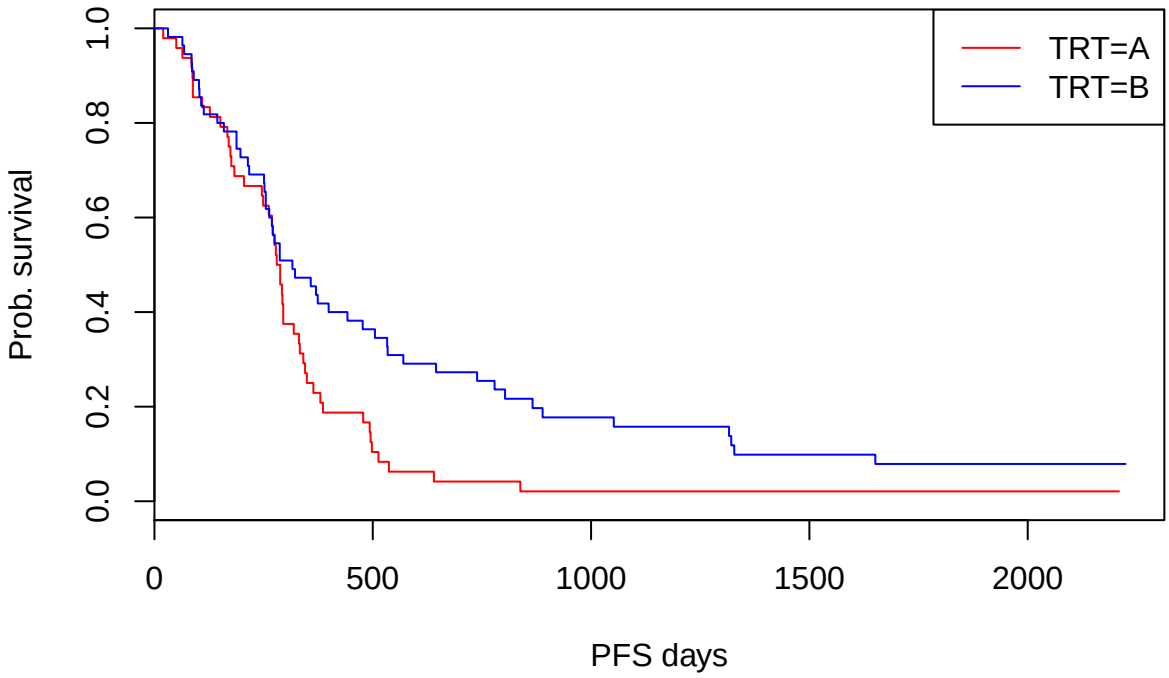
```
##
##  A  B
## 48 55
```

Plot KM etc.

```
library(survival)
#library("survminer")

data$SurvObj.pfs <- with(data, Surv(pfstime, pfsevent))
data$SurvObj.os <- with(data, Surv(ostime, osevent))
col=c("red", "blue")
lty=c(1,1)

km <- survfit(SurvObj.pfs ~ TRT, data=data)
plot(km, col=col, xlab="PFS days", ylab="Prob. survival", lty = lty)
legend("topright", col=col, legend = names(km$strata), lty = lty)
```




```
print(km)
```

```
## Call: survfit(formula = SurvObj.pfs ~ TRT, data = data)
##
##    316 observations deleted due to missingness
##         n events median 0.95LCL 0.95UCL
## TRT=A 48     47    284     262     331
## TRT=B 55     50    316     263     505
```

```
survdiff(SurvObj.pfs ~ TRT, data=data)
```

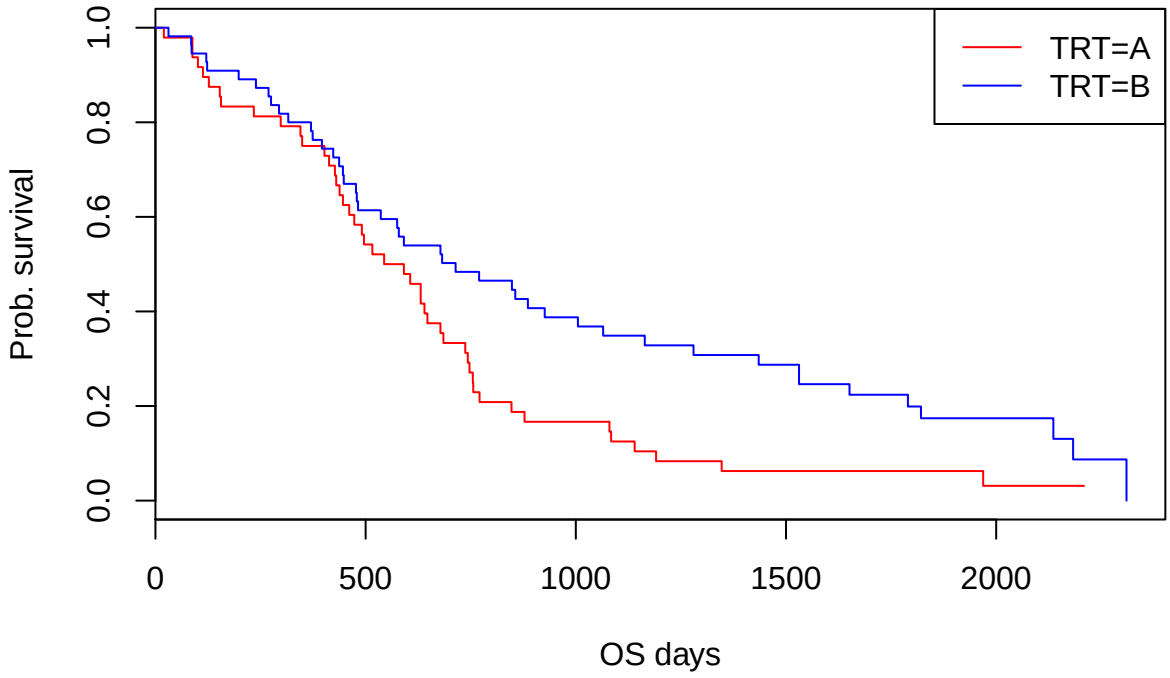
```
## Call:
## survdiff(formula = SurvObj.pfs ~ TRT, data = data)
##
## n=103, 316 observations deleted due to missingness.
##
##         N Observed Expected (O-E)^2/E (O-E)^2/V
## TRT=A 48       47     35.6      3.67      6.23
## TRT=B 55       50     61.4      2.12      6.23
##
##  Chisq= 6.2  on 1 degrees of freedom, p= 0.01
```

```
cox <- coxph(SurvObj.pfs ~ TRT, data=data)
summary(cox)
```

```
## Call:
## coxph(formula = SurvObj.pfs ~ TRT, data = data)
##
```

```
##   n= 103, number of events= 97
##    (316 observations deleted due to missingness)
##
##         coef exp(coef) se(coef)     z Pr(>|z|)
## TRTB -0.5246    0.5918   0.2124 -2.47   0.0135 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##      exp(coef) exp(-coef) lower .95 upper .95
## TRTB    0.5918       1.69    0.3903    0.8973
##
## Concordance= 0.546  (se = 0.029 )
## Rsquare= 0.057   (max possible= 0.999 )
## Likelihood ratio test= 6.05  on 1 df,   p=0.01
## Wald test            = 6.1  on 1 df,   p=0.01
## Score (logrank) test = 6.22  on 1 df,   p=0.01
```

```
km <- survfit(SurvObj.os ~ TRT, data=data)
plot(km, col=col, xlab="OS days", ylab="Prob. survival", lty = lty)
legend("topright", col=col, legend = names(km$strata), lty=lty)
```




```
print(km)
```

```
## Call: survfit(formula = SurvObj.os ~ TRT, data = data)
##
##    316 observations deleted due to missingness
##        n events median 0.95LCL 0.95UCL
```

```
## TRT=A 48     46    568     461     685
## TRT=B 55     46    714     482    1164
```

```
survdiff(SurvObj.os ~ TRT, data=data)
```

```
## Call:
## survdiff(formula = SurvObj.os ~ TRT, data = data)
##
## n=103, 316 observations deleted due to missingness.
##
##        N Observed Expected (O-E)^2/E (O-E)^2/V
## TRT=A 48       46     34.7      3.66      6.19
## TRT=B 55       46     57.3      2.22      6.19
##
##  Chisq= 6.2  on 1 degrees of freedom, p= 0.01
```

```
cox <- coxph(SurvObj.os ~ TRT, data=data)
summary(cox)
```

```
## Call:
## coxph(formula = SurvObj.os ~ TRT, data = data)
##
##   n= 103, number of events= 92
##    (316 observations deleted due to missingness)
##
##         coef exp(coef) se(coef)      z Pr(>|z|)
## TRTB -0.5292    0.5890   0.2150 -2.461   0.0138 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##      exp(coef) exp(-coef) lower .95 upper .95
## TRTB     0.589      1.698    0.3865    0.8978
##
## Concordance= 0.553  (se = 0.029 )
## Rsquare= 0.057   (max possible= 0.999 )
## Likelihood ratio test= 6.02  on 1 df,   p=0.01
## Wald test            = 6.06  on 1 df,   p=0.01
## Score (logrank) test = 6.18  on 1 df,   p=0.01
```

Session Information

```
sessionInfo()
```

```
## R version 3.5.1 (2018-07-02)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows 10 x64 (build 17134)
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=English_United Kingdom.1252
## [2] LC_CTYPE=English_United Kingdom.1252
## [3] LC_MONETARY=English_United Kingdom.1252
## [4] LC_NUMERIC=C
```

```
## [5] LC_TIME=English_United Kingdom.1252
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
## [1] survival_2.42-6
##
## loaded via a namespace (and not attached):
##  [1] Rcpp_1.0.1      lattice_0.20-35 digest_0.6.18   rprojroot_1.3-2
##  [5] grid_3.5.1      backports_1.1.2 magrittr_1.5    evaluate_0.12
##  [9] stringi_1.1.7   Matrix_1.2-14   rmarkdown_1.10  splines_3.5.1
## [13] tools_3.5.1     stringr_1.3.1   yaml_2.2.0      compiler_3.5.1
## [17] htmltools_0.3.6 knitr_1.20
```