

# EORTC HNSCC Honore et al\_06052024 Final Analysis

Code ▼

```
library(swimplot) library(grid) library(gtable) library(readr) library(mosaic) library(dplyr) library(survival)
library(survminer) library(ggplot2) library(scales) library(coxphf) library(ggthemes) library(tidyverse)
library(gtsummary) library(flextable) library(parameters) library(car) library(ComplexHeatmap) library(tidyverse)
library(readxl) library(janitor) library(DT) library(rms)
```

#ctDNA positivity by stage and window

Hide

```
#Number of Pts at Baseline - percentage positivity by stage
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.Base!="",]
circ_datadf <- as.data.frame(circ_data)

total_base <- sum(!is.na(circ_data$ctDNA.Base))
print(total_base)
```

```
[1] 42
```

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```
circ_data$ctDNA.Base <- as.factor(circ_data$ctDNA.Base)
cont_table_base <- table(circ_data$Stage, circ_data$ctDNA.Base)
print(cont_table_base)
```

	NEGATIVE	POSITIVE
III	0	16
IVA	0	20
IVB	1	5

Hide

```
#Number of Pts at post-treatment time point - percentage positivity by stage
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("0P-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
circ_datadf <- as.data.frame(circ_data)

total_mrd <- sum(!is.na(circ_data$ctDNA.postTx))
print(total_mrd)
```

```
[1] 42
```

[Hide](#)

```
circ_data$ctDNA.postTx <- as.factor(circ_data$ctDNA.postTx)
cont_table_mrd <- table(circ_data$Stage, circ_data$ctDNA.postTx)
print(cont_table_mrd)
```

	NEGATIVE	POSITIVE
III	13	2
IVA	21	0
IVB	4	2

#Summary Table

[Hide](#)

```

rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]

circ_data_subset <- circ_data %>%
  select(
    Gender,
    Age,
    Smoking.Assumption,
    Alcohol.Assumption,
    Prim.Location,
    ECOG,
    Stage,
    Stage.TNM,
    p16,
    NAC,
    Treatment.Type,
    RFS.Event,
    OS.Event,
    FU.Biopsy.months) %>%
  mutate(
    Gender = factor(Gender),
    Age = as.numeric(Age),
    Smoking.Assumption = factor(Smoking.Assumption),
    Alcohol.Assumption = factor(Alcohol.Assumption),
    Prim.Location = factor(Prim.Location),
    ECOG = factor(ECOG),
    Stage = factor(Stage),
    Stage.TNM = factor(Stage.TNM),
    p16 = factor(p16),
    NAC = factor(NAC, levels = c("FALSE", "TRUE"), labels = c("No treatment", "Neoadjuvant Treatment")),
    Treatment.Type = factor(Treatment.Type),
    RFS.Event = factor(RFS.Event, levels = c("FALSE", "TRUE"), labels = c("No Recurrence", "Recurrence")),
    OS.Event = factor(OS.Event, levels = c("FALSE", "TRUE"), labels = c("Alive", "Deceased")),
    FU.Biopsy.months = as.numeric(FU.Biopsy.months))
table1 <- circ_data_subset %>%
  tbl_summary(
    statistic = list(
      all_continuous() ~ "{median} ({min} - {max})",
      all_categorical() ~ "{n} ({p}%)" ) %>%
    bold_labels()
  )
table1

```

Characteristic	N = 43 <sup>1</sup>
<b>Gender</b>	
Female	10 (23%)
Male	33 (77%)
<b>Age</b>	67 (28 - 102)
<b>Smoking.Assumption</b>	35 (81%)
<b>Alcohol.Assumption</b>	27 (63%)
<b>Prim.Location</b>	
Hypopharynx	5 (12%)
Larynx	6 (14%)
Oral cavity	5 (12%)
Oropharynx	27 (63%)
<b>ECOG</b>	
0	27 (63%)
1	14 (33%)
2	2 (4.7%)
<b>Stage</b>	
III	16 (37%)
IVA	21 (49%)
IVB	6 (14%)
<b>Stage.TNM</b>	
T1-T3N1M0	12 (28%)
T1-T4N2M0	13 (30%)
T1-T4N3M0	6 (14%)
T3N0M0	4 (9.3%)
T4aN0-N1M0	8 (19%)
<sup>1</sup> n (%); Median (Range)	

Characteristic	N = 43 <sup>1</sup>
<b>p16</b>	
Negative	26 (60%)
Positive	17 (40%)
<b>NAC</b>	
No treatment	37 (86%)
Neoadjuvant Treatment	6 (14%)
<b>Treatment.Type</b>	
Chemotherapy	1 (2.3%)
Radiochemotherapy	29 (67%)
Radiochemotherapy, Surgery	5 (12%)
Radioimmunotherapy	2 (4.7%)
Radiotherapy	3 (7.0%)
Radiotherapy, Surgery	2 (4.7%)
Surgery	1 (2.3%)
<b>RFS.Event</b>	
No Recurrence	32 (74%)
Recurrence	11 (26%)
<b>OS.Event</b>	
Alive	33 (77%)
Deceased	10 (23%)
<b>FU.Biopsy.months</b>	20 (4 - 45)
<sup>1</sup> n (%); Median (Range)	

Hide

```
fit1 <- as_flex_table(  
  table1,  
  include = everything(),  
  return_calls = FALSE,  
  strip_md_bold = TRUE)
```

Warning: The ``strip_md_bold`` argument of ``as_flex_table()`` is deprecated as of gtsummary 1.6.0.  
This warning is displayed once every 8 hours.  
Call ``lifecycle::last_lifecycle_warnings()`` to see where this warning was generated.

Hide

fit1

Characteristic	N = 43 <sup>1</sup>
<b>Gender</b>	
Female	10 (23%)
Male	33 (77%)
<b>Age</b>	67 (28 - 102)
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<b>Alcohol.Assumption</b>	27 (63%)
<b>Prim.Location</b>	
Hypopharynx	5 (12%)
Larynx	6 (14%)
Oral cavity	5 (12%)
Oropharynx	27 (63%)
<b>ECOG</b>	
0	27 (63%)
1	14 (33%)
2	2 (4.7%)
<b>Stage</b>	
III	16 (37%)
IVA	21 (49%)
IVB	6 (14%)
<b>Stage.TNM</b>	
T1-T3N1M0	12 (28%)
T1-T4N2M0	13 (30%)
T1-T4N3M0	6 (14%)
T3N0M0	4 (9.3%)

<sup>1</sup>n (%); Median (Range)

Characteristic	N = 43 <sup>1</sup>
T4aN0-N1M0	8 (19%)
p16	
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RFS.Event	
No Recurrence	32 (74%)
Recurrence	11 (26%)
OS.Event	
Alive	33 (77%)
Deceased	10 (23%)
FU.Biopsy.months	20 (4 - 45)

<sup>1</sup>n (%); Median (Range)

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```
save_as_docx(fit1, path= "~/Downloads/table1.docx")
```

#Heatmap for the clinical factors

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```

rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data %>% arrange(Stage)
circ_datadf <- as.data.frame(circ_data)

ha <- HeatmapAnnotation(
  Stage = circ_data$Stage,
  Gender = circ_data$Gender,
  Prim.Location = circ_data$Prim.Location,
  p16 = circ_data$p16,
  NAC = circ_data$NAC,
  ctDNA.Base = circ_data$ctDNA.Base,
  ctDNA.postTx = circ_data$ctDNA.postTx,
  RFS.Event = circ_data$RFS.Event,
  OS.Event = circ_data$OS.Event,

  col = list(Stage = c("III" = "seagreen1", "IVA" = "khaki", "IVB" = "orange"),
    Gender = c("Female" = "goldenrod", "Male" = "blue4"),
    Prim.Location = c("Hypopharynx" = "purple", "Oropharynx" = "lightblue", "Larynx" = "brown2", "Oral cavity" = "lightgrey"),
    p16 = c("Negative" = "yellow", "Positive" = "brown"),
    NAC = c("TRUE" = "darkmagenta", "FALSE" = "grey"),
    ctDNA.Base = c("POSITIVE" = "red3", "NEGATIVE" = "blue"),
    ctDNA.postTx = c("POSITIVE" = "red3", "NEGATIVE" = "blue"),
    RFS.Event = c("TRUE" = "red3", "FALSE" = "blue"),
    OS.Event = c("TRUE" = "black", "FALSE" = "grey")
  )
)
ht <- Heatmap(matrix(nrow = 0, ncol = length(circ_data$Stage)), show_row_names = FALSE, cluster_rows = F, cluster_columns = FALSE, top_annotation = ha)
pdf("heatmap.pdf", width = 7, height = 7)
draw(ht, annotation_legend_side = "bottom")
dev.off()

```

#Overview plot

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```
setwd("~/Downloads")
clinstage <- read.csv("OP-16933_ HNSCC OP.csv")
clinstage_df <- as.data.frame(clinstage)

# Creating the basic swimmer plot
oplot <- swimmer_plot(df=clinstage_df,
                      id='PatientName',
                      end='fu.diff.months',
                      fill='gray',
                      width=.01)

# Adding themes and scales
oplot <- oplot + theme(panel.border = element_blank())
oplot <- oplot + scale_y_continuous(breaks = seq(0, 48, by = 3))
oplot <- oplot + labs(x = "Patients", y = "Months from Diagnosis")

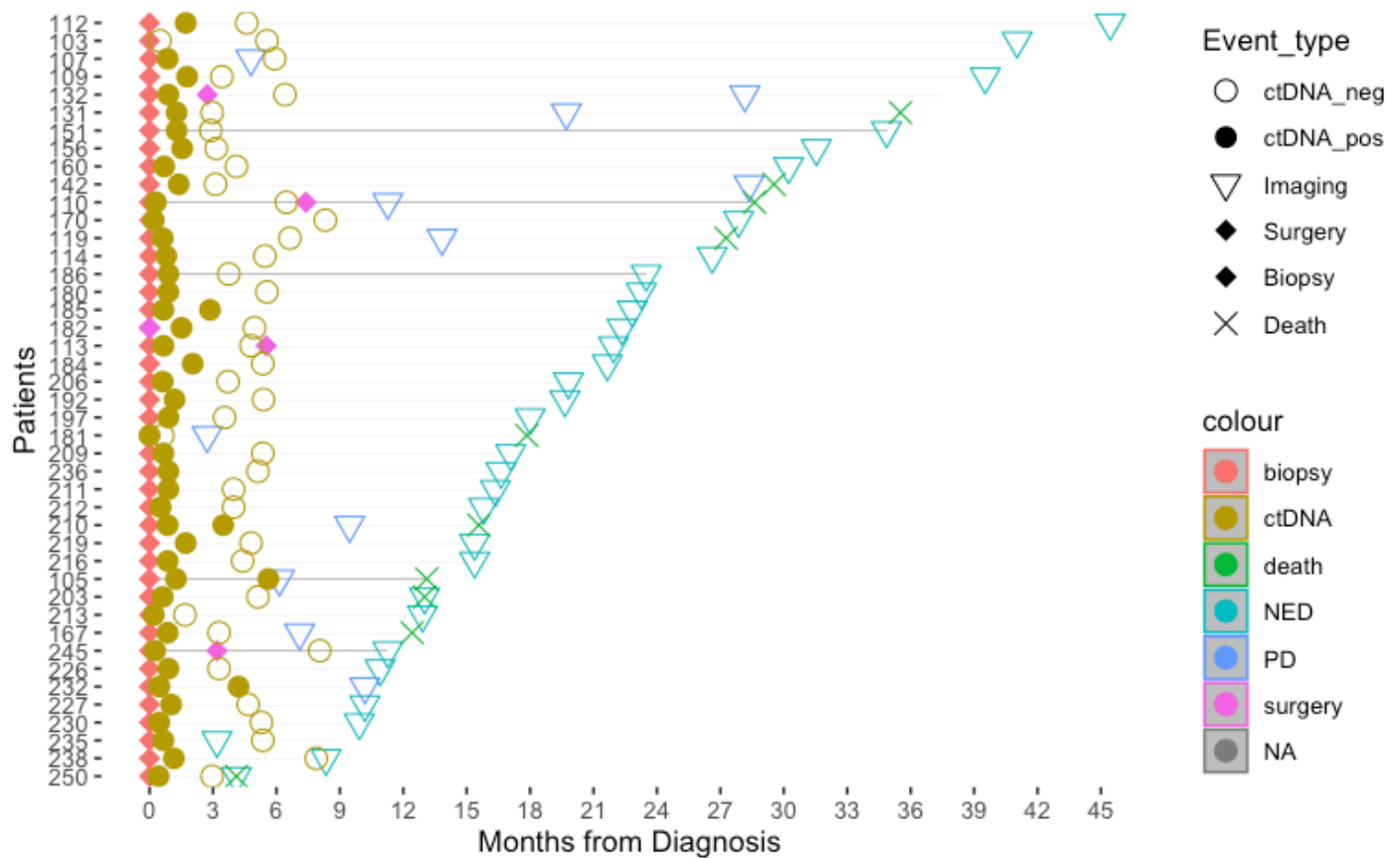
# Adding swimmer points
oplot_ev1 <- oplot + swimmer_points(df_points=clinstage_df,
                                    id='PatientName',
                                    time='date.diff.months',
                                    name_shape = 'Event_type',
                                    name_col = 'Event',
                                    size=3.5, fill='black')

# Optionally uncomment and use col='darkgreen' if needed

# Adding shape manual scale
oplot_ev1.1 <- oplot_ev1 + ggplot2::scale_shape_manual(name="Event_type",
                                                         values=c(1,16,6,18,18,4),
                                                         breaks=c('ctDNA_neg', 'ctDNA_pos',
                                                                    'Imaging', 'Surgery', 'Biopsy', 'Death'))

# Display the plot
oplot_ev1.1
```

Warning: Removed 43 rows containing missing values (`geom\_point()`).


[Hide](#)

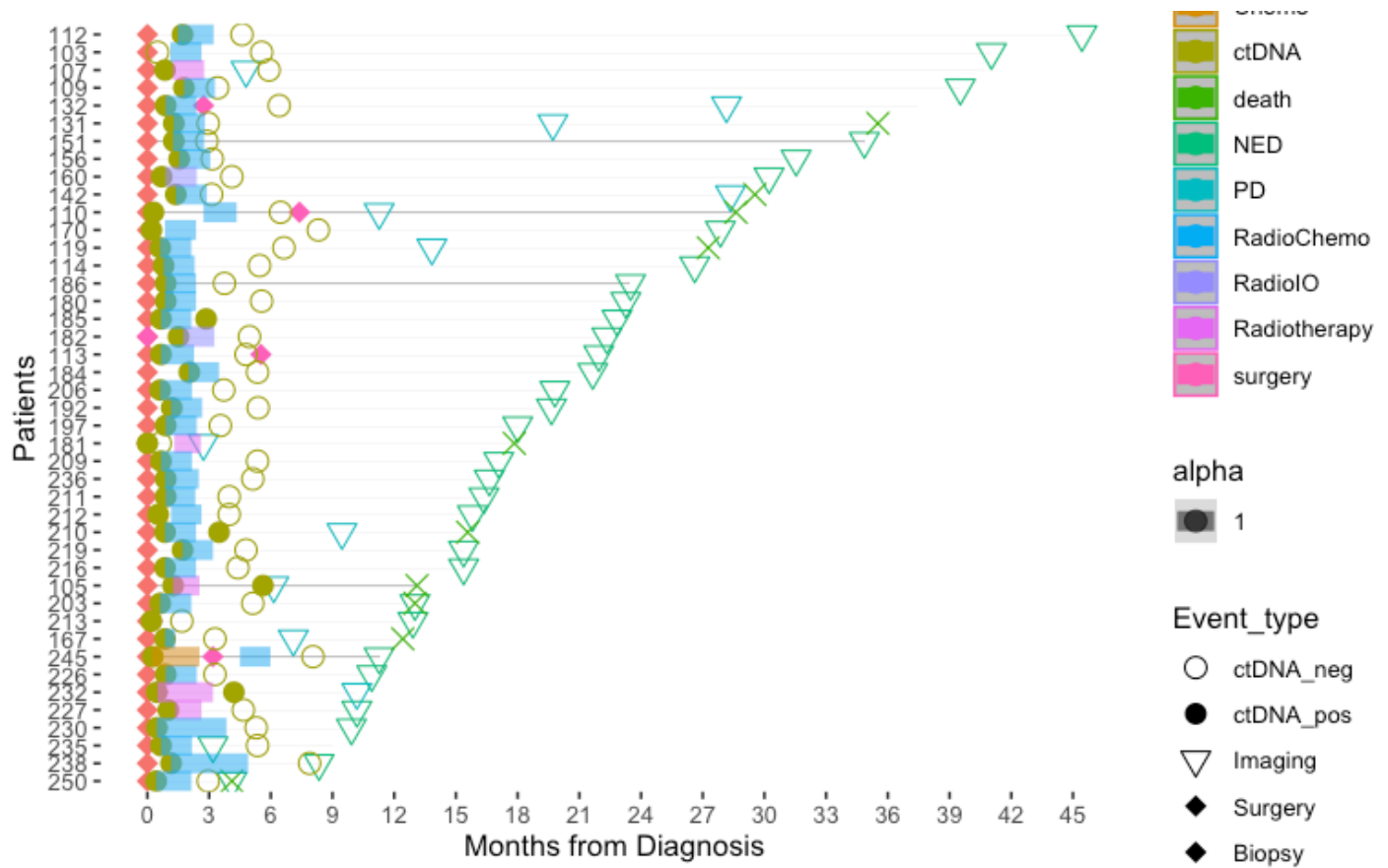
```

oplot_ev2 <- oplot_ev1.1 + swimmer_lines(df_lines=cl
instage_df,
Name',
tart.months',
d.months',
x_type',
= 1.0)
oplot_ev2 <- oplot_ev2 + guides(linetype = guide_leg
end(override.aes = list(size = 5, color = "black")))
oplot_ev2

```

Warning: Removed 43 rows containing missing values (`geom\_point()`).

Warning: Removed 191 rows containing missing values (`geom\_segment()`).


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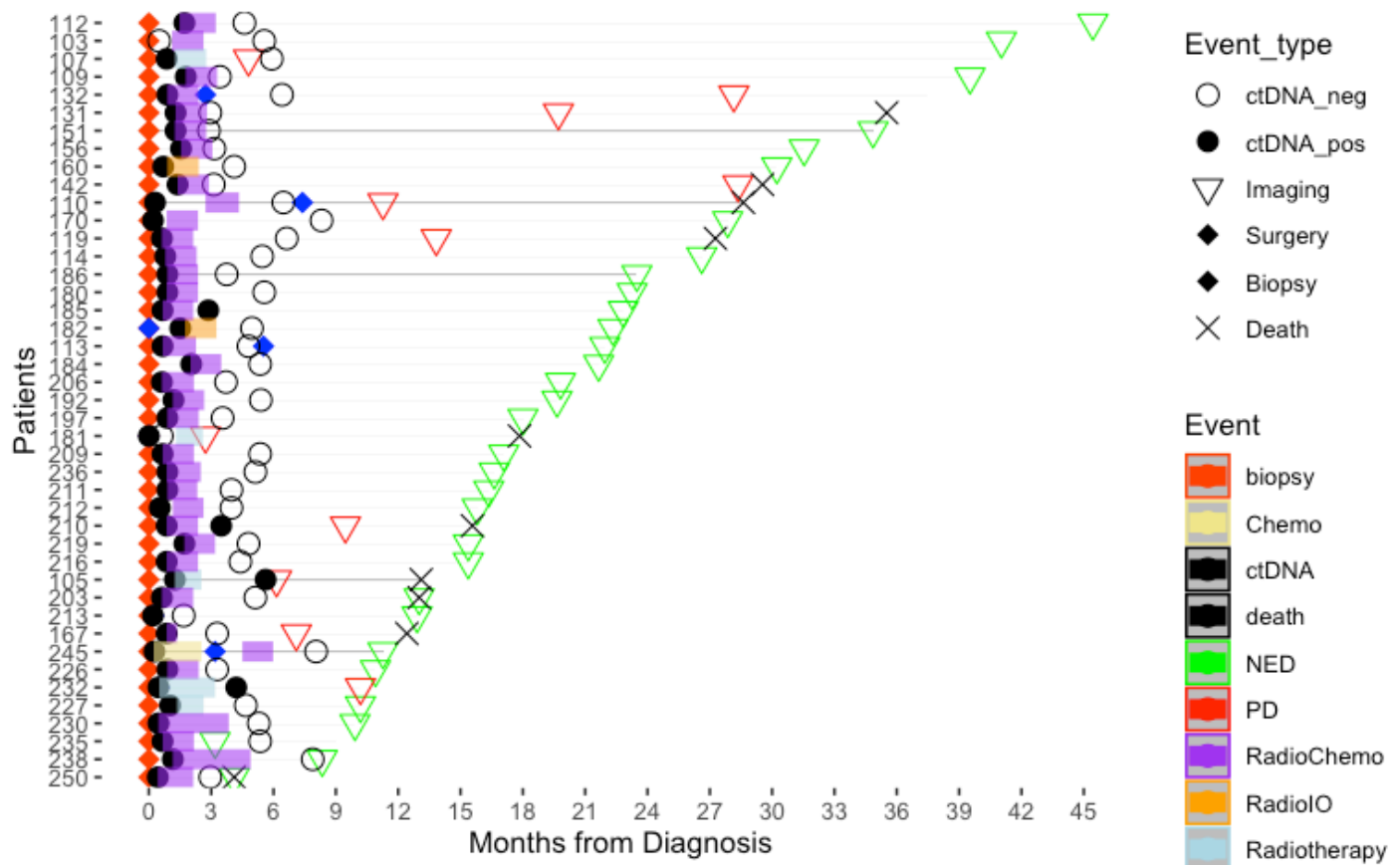
```

      oplot_ev2.2 <- oplot_ev2 + ggplot2::scale_color_manual(
        name="Event",values=c( "orangered", "khaki", "black", "black", "green", "red", "purple",
        "orange", "lightblue", "blue"))
      oplot_ev2.2

```

Warning: Removed 43 rows containing missing values (`geom\_point()`).

Warning: Removed 191 rows containing missing values (`geom\_segment()`).



#RFS in Complete Cohort (N=50)

Hide

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_datadf <- as.data.frame(circ_data)

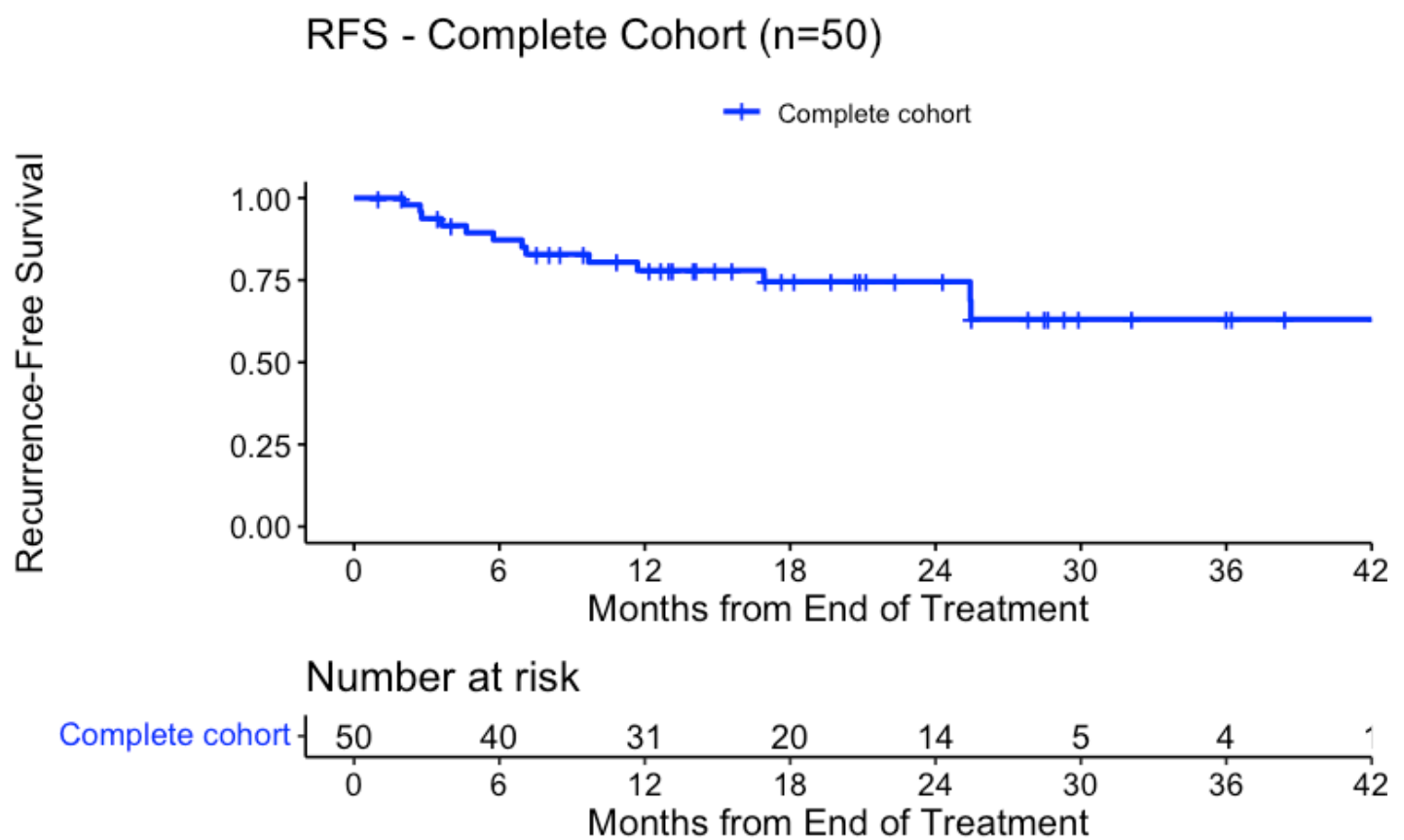
survfit(Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)~HNSCC.Cohort, data = circ_data)
```

Call: survfit(formula = Surv(time = circ\_data\$RFS.months, event = circ\_data\$RFS.Event) ~ HNSCC.Cohort, data = circ\_data)

	n	events	median	0.95LCL	0.95UCL
[1,]	50	13	NA	25.5	NA

Hide

```
surv_object <- Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)
KM_curve <- survfit(surv_object ~ HNSCC.Cohort, data = circ_data, conf.int=0.95, conf.type="log-log")
ggsurvplot(KM_curve, data = circ_data, pval = FALSE, conf.int = FALSE, risk.table = TRUE, break.time.by=6, palette=c("blue"), title="RFS - Complete Cohort (n=50)", ylab="Recurrence-Free Survival", xlab="Months from End of Treatment", legend.labs=c("Complete cohort"), legend.title="")
```

[Hide](#)

```
summary(KM_curve, times= c(18, 24, 36))
```

```
Call: survfit(formula = surv_object ~ HNSCC.Cohort, data = circ_data,
  conf.int = 0.95, conf.type = "log-log")
```

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
18	20	11	0.746	0.0679	0.583	0.852
24	14	0	0.746	0.0679	0.583	0.852
36	4	2	0.631	0.0942	0.419	0.783

#OS in Complete Cohort (N=50)

Hide

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_datadf <- as.data.frame(circ_data)

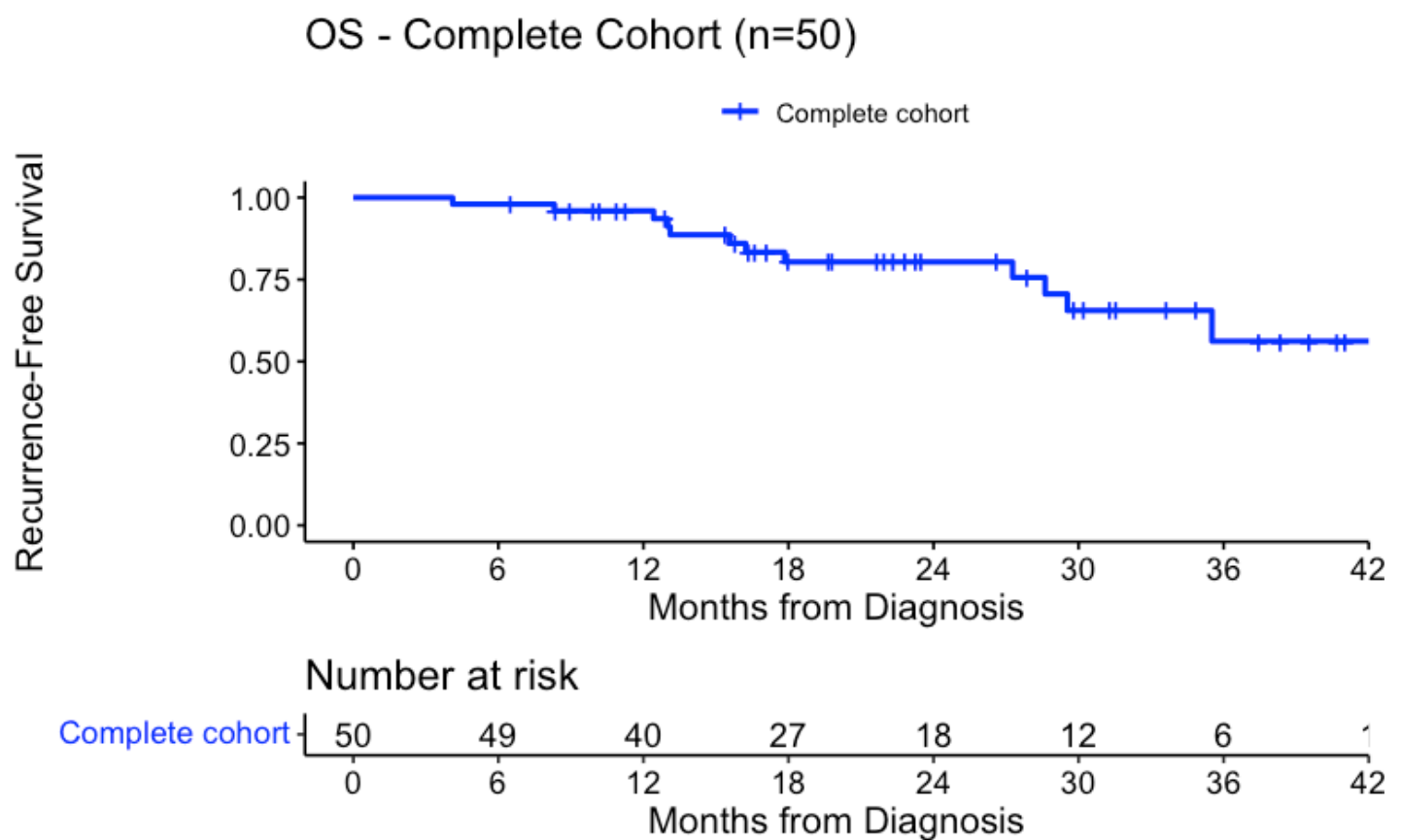
survfit(Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)~HNSCC.Cohor
t, data = circ_data)
```

```
Call: survfit(formula = Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Eve
nt) ~
  HNSCC.Cohort, data = circ_data)
```

	n	events	median	0.95LCL	0.95UCL
[1,]	50	12	NA	29.5	NA

Hide

```
surv_object <-Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)
KM_curve <- survfit(surv_object ~ HNSCC.Cohort, data = circ_data,conf.int=0.95,conf.type
="log-log")
ggsurvplot(KM_curve, data = circ_data, pval = FALSE, conf.int = FALSE, risk.table = TRU
E, break.time.by=6, palette=c("blue"), title="OS - Complete Cohort (n=50)", ylab= "Recur
rence-Free Survival", xlab="Months from Diagnosis", legend.labs=c("Complete cohort"), le
gend.title="")
```

[Hide](#)

```
summary(KM_curve, times= c(18, 24, 36))
```

```
Call: survfit(formula = surv_object ~ HNSCC.Cohort, data = circ_data,
  conf.int = 0.95, conf.type = "log-log")
```

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
18	27	8	0.804	0.0632	0.643	0.898
24	18	0	0.804	0.0632	0.643	0.898
36	6	4	0.562	0.1177	0.309	0.754

## #Association of Baseline ctDNA MTM levels with clinicopathological factors

[Hide](#)

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.Base!="",]
circ_datadf <- as.data.frame(circ_data)

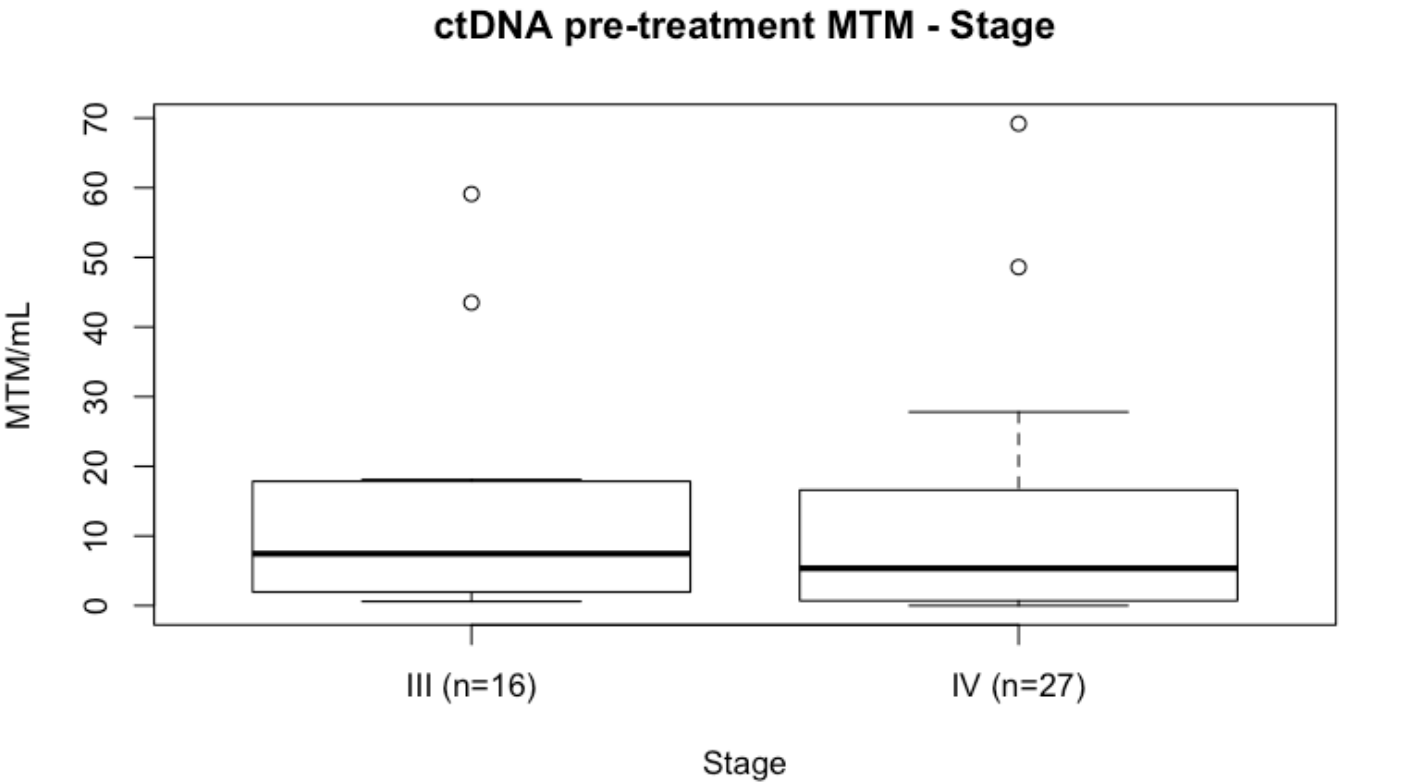
tally(~cStage, data=circ_data, margins = TRUE)
```

cStage		
III	IV	Total
16	26	42

[Hide](#)

```
circ_data$cStage <- factor(circ_data$cStage, levels = c("III","IV"), labels = c("III (n=
16)","IV (n=27)"))
boxplot(ctDNA.Base.MTM~cStage, data=circ_data, main="ctDNA pre-treatment MTM - Stage", x
lab="Stage", ylab="MTM/mL", col="white",border="black")
```





Hide

```
m1<-wilcox.test(ctDNA.Base.MTM ~ cStage, data=circ_data, na.rm=TRUE, paired=FALSE, exact
=FALSE, conf.int=TRUE)
print(m1)
```

Wilcoxon rank sum test with continuity correction

```
data: ctDNA.Base.MTM by cStage
W = 228, p-value = 0.6135
alternative hypothesis: true location shift is not equal to 0
95 percent confidence interval:
 -5.400007  6.100017
sample estimates:
difference in location
      1.0637
```

Hide

```
tally(~cT.Status, data=circ_data, margins = TRUE)
```

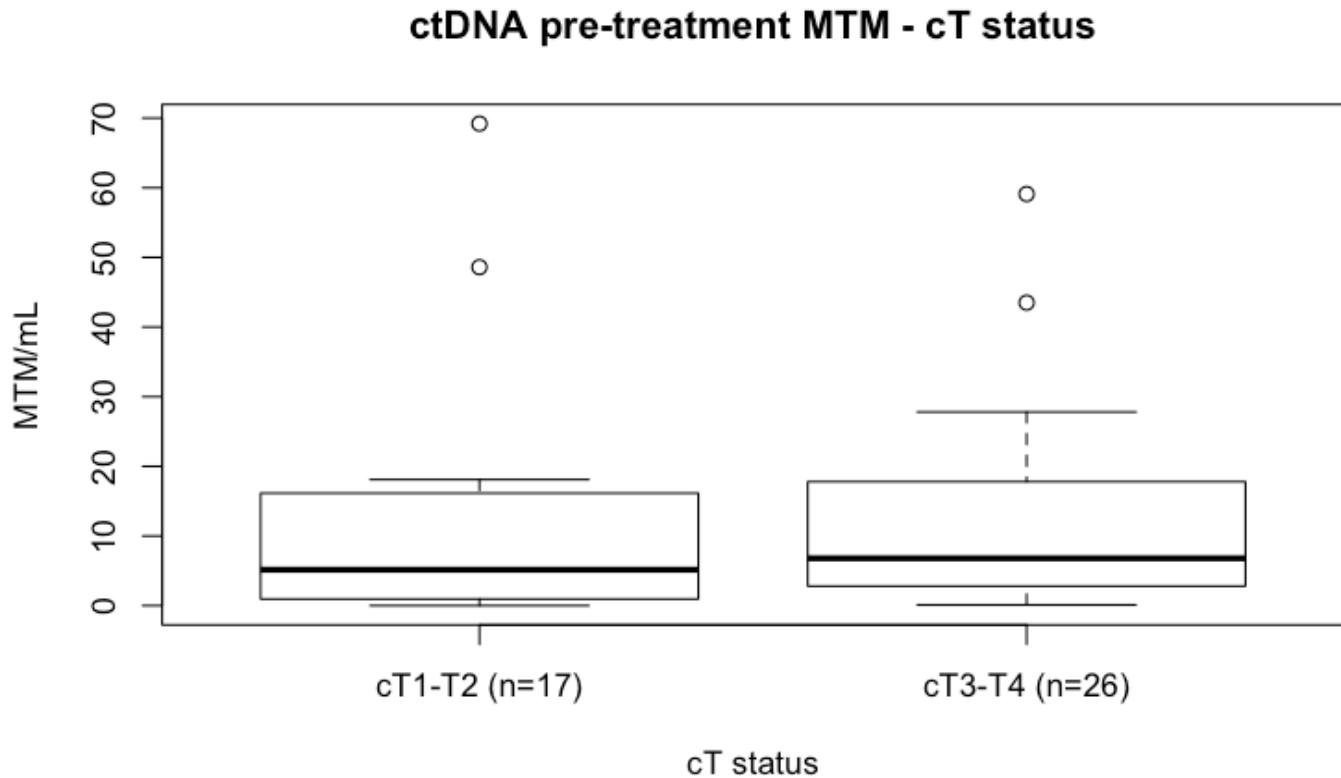
cT.Status		
cT1-T2	cT3-T4	Total
16	26	42

Hide

```

circ_data$cT.Status <- factor(circ_data$cT.Status, levels = c("cT1-T2","cT3-T4"), labels =
= c("cT1-T2 (n=17)","cT3-T4 (n=26)"))
boxplot(ctDNA.Base.MTM~cT.Status, data=circ_data, main="ctDNA pre-treatment MTM - cT sta
tus", xlab="cT status", ylab="MTM/mL", col="white",border="black")

```



Hide

```

m2<-wilcox.test(ctDNA.Base.MTM ~ cT.Status, data=circ_data, na.rm=TRUE, paired=FALSE, ex
act=FALSE, conf.int=TRUE)
print(m2)

```

Wilcoxon rank sum test with continuity correction

```

data: ctDNA.Base.MTM by cT.Status
W = 179, p-value = 0.4603
alternative hypothesis: true location shift is not equal to 0
95 percent confidence interval:
 -8.499967  3.599946
sample estimates:
difference in location
 -1.59994

```

Hide

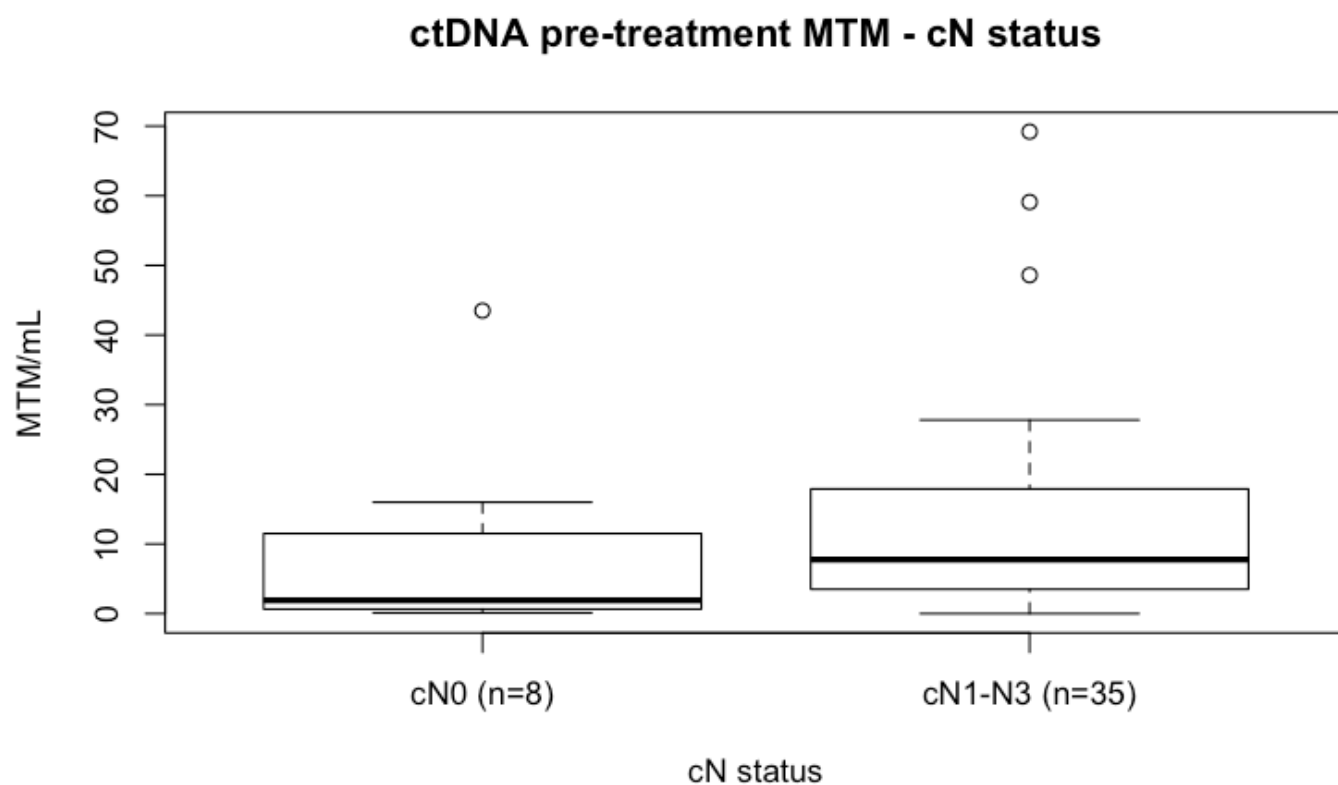
```
tally(~cN.Status, data=circ_data, margins = TRUE)
```

cN.Status

cN0	cN1-N3	Total
8	34	42

[Hide](#)

```
circ_data$cN.Status <- factor(circ_data$cN.Status, levels = c("cN0","cN1-N3"), labels =
c("cN0 (n=8)","cN1-N3 (n=35)"))
boxplot(ctDNA.Base.MTM~cN.Status, data=circ_data, main="ctDNA pre-treatment MTM - cN sta
tus", xlab="cN status", ylab="MTM/mL", col="white",border="black")
```


[Hide](#)

```
m3<-wilcox.test(ctDNA.Base.MTM ~ cN.Status, data=circ_data, na.rm=TRUE, paired=FALSE, ex
act=FALSE, conf.int=TRUE)
print(m3)
```

Wilcoxon rank sum test with continuity correction

data: ctDNA.Base.MTM by cN.Status

W = 93, p-value = 0.1733

alternative hypothesis: true location shift is not equal to 0

95 percent confidence interval:

-12.900026 1.300003

sample estimates:

difference in location

-3.227956

[Hide](#)

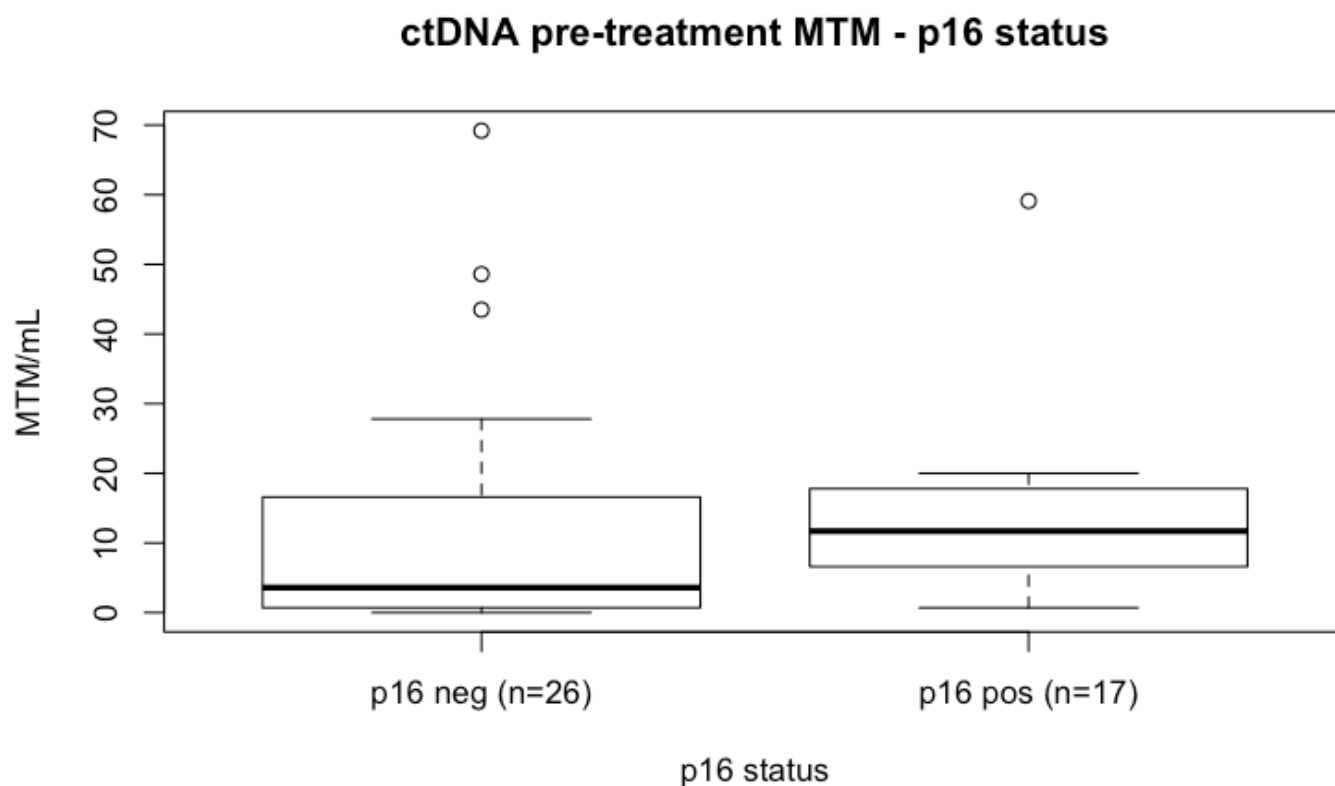
```
tally(~p16, data=circ_data, margins = TRUE)
```

p16

Negative	Positive	Total
25	17	42

[Hide](#)

```
circ_data$p16 <- factor(circ_data$p16, levels = c("Negative","Positive"), labels = c("p16 neg (n=26)","p16 pos (n=17)"))  
boxplot(ctDNA.Base.MTM~p16, data=circ_data, main="ctDNA pre-treatment MTM - p16 status",  
xlab="p16 status", ylab="MTM/mL", col="white",border="black")
```



Hide

```
m4<-wilcox.test(ctDNA.Base.MTM ~ p16, data=circ_data, na.rm=TRUE, paired=FALSE, exact=FALSE, conf.int=TRUE)
print(m4)
```

Wilcoxon rank sum test with continuity correction

```
data: ctDNA.Base.MTM by p16
W = 142.5, p-value = 0.07488
alternative hypothesis: true location shift is not equal to 0
95 percent confidence interval:
 -10.79993  1.59996
sample estimates:
difference in location
      -5.100049
```

#RFS by ctDNA post-treatment

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```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("0P-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
circ_datadf <- as.data.frame(circ_data)

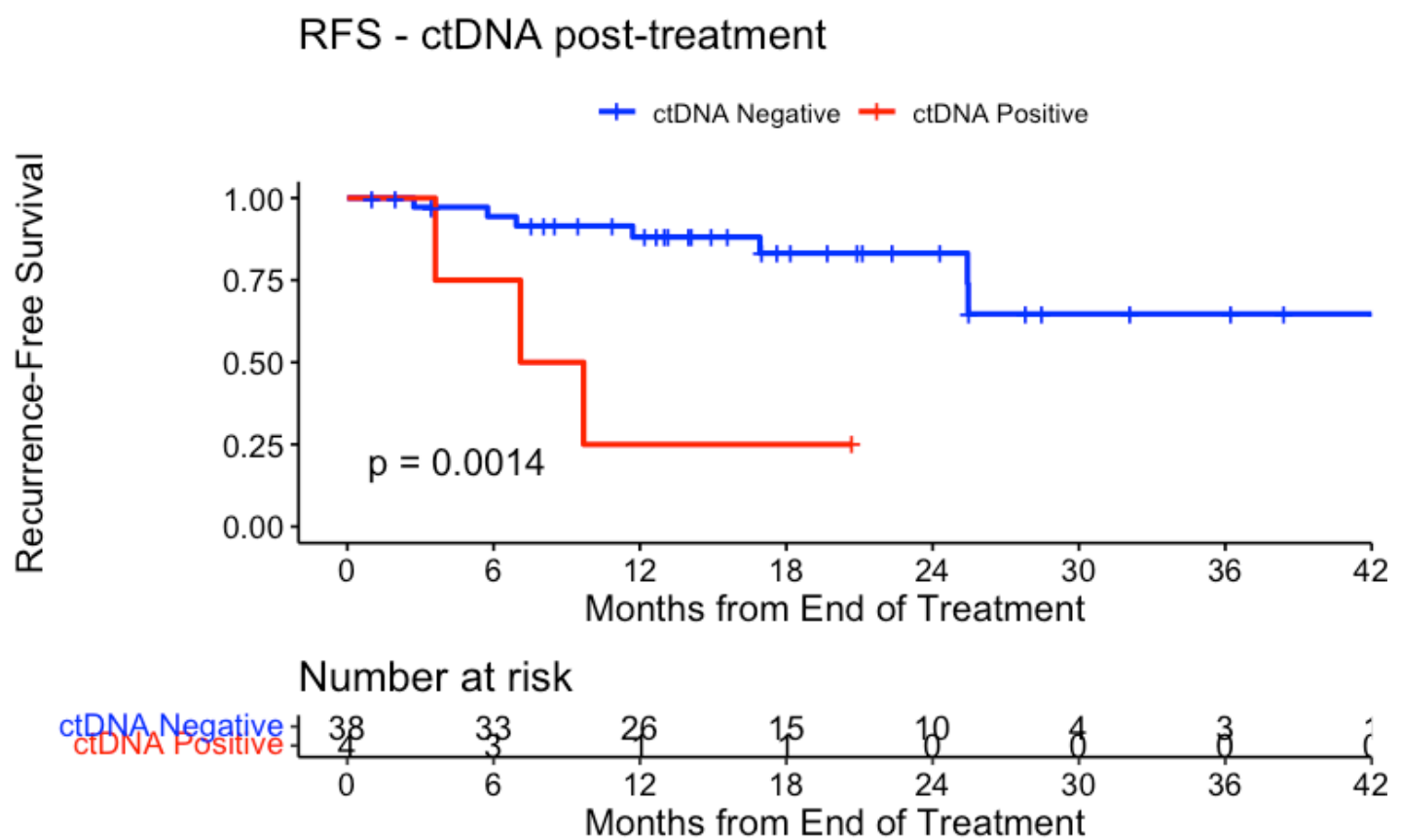
survfit(Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)~ctDNA.postTx, data = circ_data)
```

```
Call: survfit(formula = Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event) ~ ctDNA.postTx, data = circ_data)
```

	n	events	median	0.95LCL	0.95UCL
ctDNA.postTx=NEGATIVE	38	7	NA	25.46	NA
ctDNA.postTx=POSITIVE	4	3	8.39	3.61	NA

Hide

```
surv_object <- Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)
KM_curve <- survfit(surv_object ~ ctDNA.postTx, data = circ_data, conf.int=0.95, conf.type="log-log")
ggsurvplot(KM_curve, data = circ_data, pval = TRUE, conf.int = FALSE, risk.table = TRUE, break.time.by=6, palette=c("blue","red"), title="RFS - ctDNA post-treatment", ylab= "Recurrence-Free Survival", xlab="Months from End of Treatment", legend.labs=c("ctDNA Negative", "ctDNA Positive"), legend.title="")
```

[Hide](#)

```
summary(KM_curve, times= c(0, 24, 36))
```

```
Call: survfit(formula = surv_object ~ ctDNA.postTx, data = circ_data,
  conf.int = 0.95, conf.type = "log-log")
```

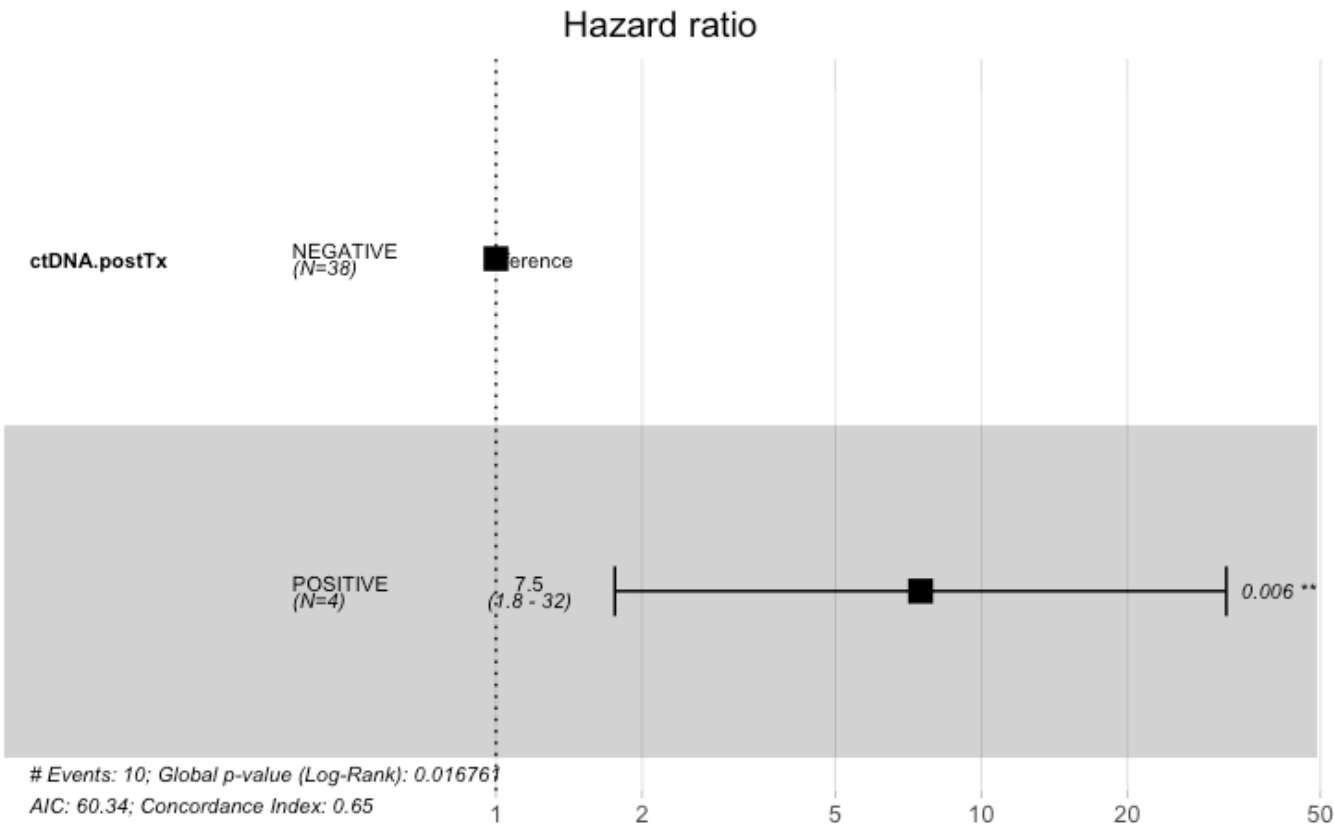
ctDNA.postTx=NEGATIVE							
time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI	
0	38	0	1.000	0.0000	1.000	1.000	
24	10	5	0.832	0.0712	0.633	0.929	
36	3	2	0.647	0.1279	0.346	0.836	

ctDNA.postTx=POSITIVE							
CI	time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
1	0	4	0	1	0	1	

Hide

```
circ_data$ctDNA.postTx <- factor(circ_data$ctDNA.postTx, levels=c("NEGATIVE","POSITIVE"))
cox_fit <- coxph(surv_object ~ ctDNA.postTx, data=circ_data)
ggforest(cox_fit,data = circ_data)
```



Hide

```
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ ctDNA.postTx, data = circ_data)
```

```
n= 42, number of events= 10
```

```

              coef exp(coef) se(coef)      z Pr(>|z|)
ctDNA.postTxPOSITIVE 2.0148    7.4995  0.7402 2.722  0.00649 **
---

```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```

              exp(coef) exp(-coef) lower .95 upper .95
ctDNA.postTxPOSITIVE    7.5      0.1333    1.758      32

```

```
Concordance= 0.652 (se = 0.078 )
```

```
Likelihood ratio test= 5.72 on 1 df,  p=0.02
```

```
Wald test = 7.41 on 1 df,  p=0.006
```

```
Score (logrank) test = 10.2 on 1 df,  p=0.001
```

[Hide](#)

```
cox_fit_summary <- summary(cox_fit)
```

```
#Extract values for HR, 95% CI, and p-value
```

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_C  
I, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 7.5 (1.76-32); p = 0.006"
```

#OS by ctDNA post-treatment

[Hide](#)

```
rm(list=ls())
```

```
setwd("~/Downloads")
```

```
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
```

```
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
```

```
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
```

```
circ_datadf <- as.data.frame(circ_data)
```

```
survfit(Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)~ctDNA.postT  
x, data = circ_data)
```



```
Call: survfit(formula = Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event) ~
```

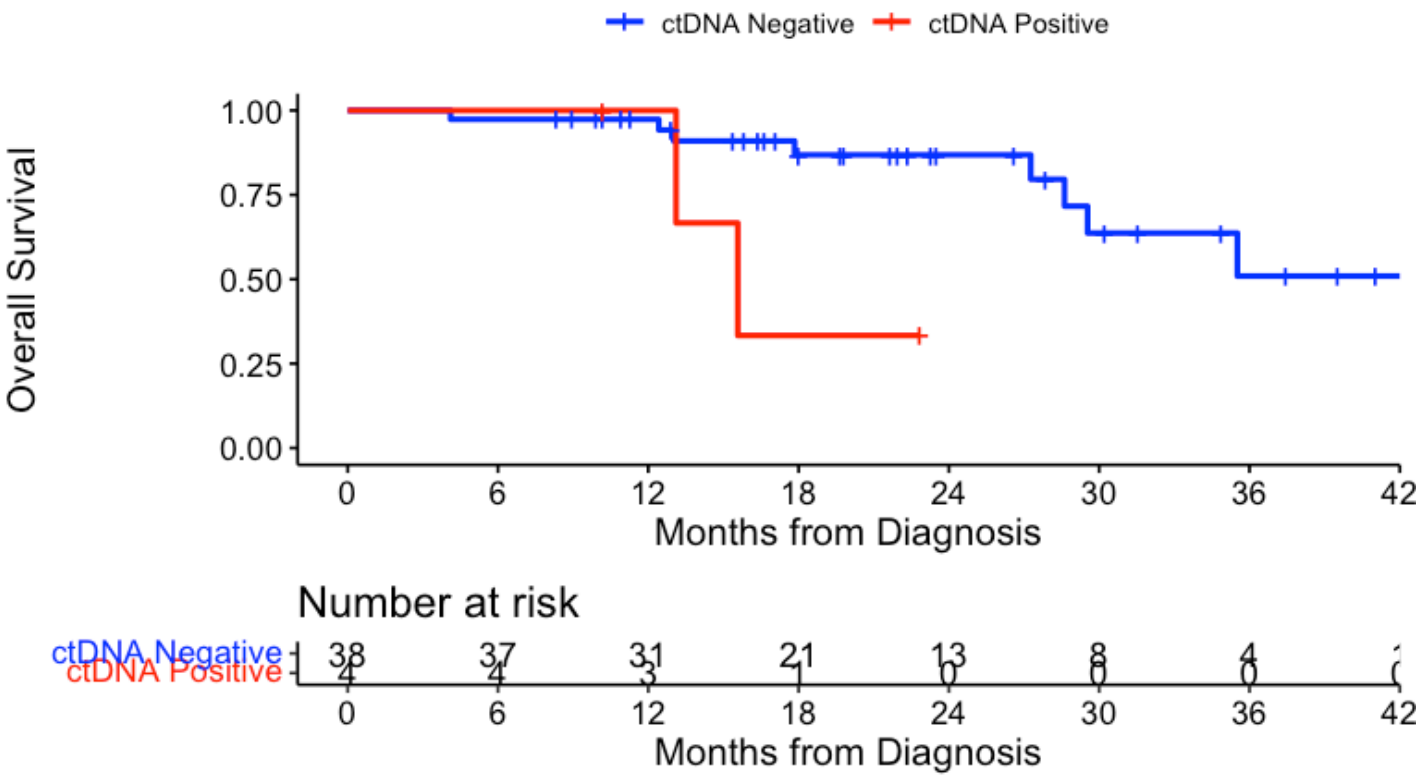
```
ctDNA.postTx, data = circ_data)
```

	n	events	median	0.95LCL	0.95UCL
ctDNA.postTx=NEGATIVE	38	8	NA	29.5	NA
ctDNA.postTx=POSITIVE	4	2	15.6	13.1	NA

[Hide](#)

```
surv_object <-Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)
KM_curve <- survfit(surv_object ~ ctDNA.postTx, data = circ_data,conf.int=0.95,conf.type
="log-log")
ggsurvplot(KM_curve, data = circ_data, pval = FALSE, conf.int = FALSE, risk.table = TRUE,
break.time.by=6, palette=c("blue","red"), title="OS - ctDNA post-treatment", ylab= "Overall Survival",
xlab="Months from Diagnosis", legend.labs=c("ctDNA Negative", "ctDNA Positive"), legend.title="")
```

OS - ctDNA post-treatment



Hide

```
summary(KM_curve, times= c(0, 24, 36))
```

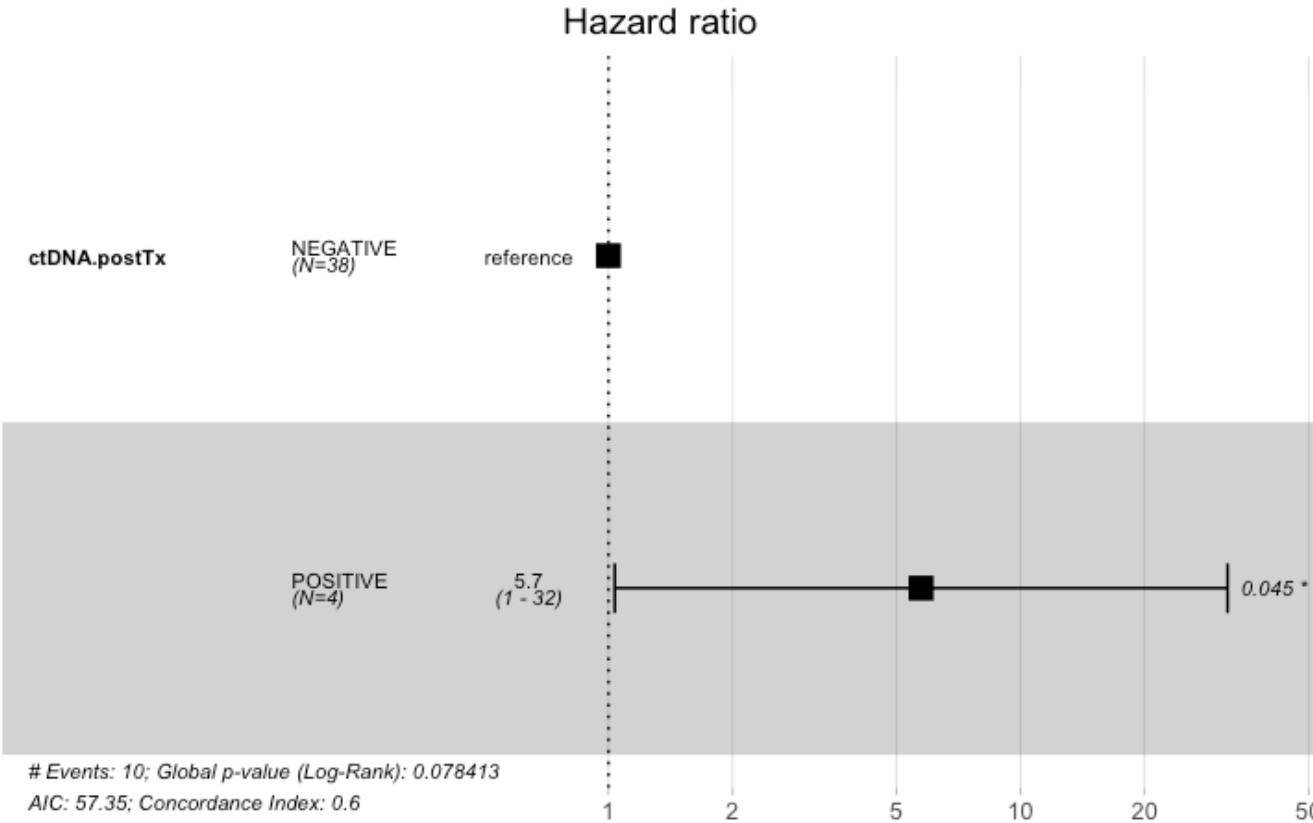
```
Call: survfit(formula = surv_object ~ ctDNA.postTx, data = circ_data,
  conf.int = 0.95, conf.type = "log-log")
```

ctDNA.postTx=NEGATIVE							
time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI	
0	38	0	1.000	0.0000	1.000	1.000	
24	13	4	0.868	0.0625	0.681	0.949	
36	4	4	0.509	0.1509	0.203	0.752	

ctDNA.postTx=POSITIVE							
CI	time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
1	0	4	0	1	0	1	

Hide

```
circ_data$ctDNA.postTx <- factor(circ_data$ctDNA.postTx, levels=c("NEGATIVE", "POSITIVE"))
cox_fit <- coxph(surv_object ~ ctDNA.postTx, data=circ_data)
ggforest(cox_fit, data = circ_data)
```



Hide

```
summary(cox_fit)
```

```
Call:
coxph(formula = surv_object ~ ctDNA.postTx, data = circ_data)

n= 42, number of events= 10

              coef exp(coef) se(coef) z Pr(>|z|)
ctDNA.postTxPOSITIVE 1.7472    5.7385  0.8736 2  0.0455 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

              exp(coef) exp(-coef) lower .95 upper .95
ctDNA.postTxPOSITIVE    5.738    0.1743    1.036    31.8

Concordance= 0.6 (se = 0.074 )
Likelihood ratio test= 3.1 on 1 df,  p=0.08
Wald test              = 4 on 1 df,  p=0.05
Score (logrank) test = 5.11 on 1 df,  p=0.02
```

Hide

```

cox_fit_summary <- summary(cox_fit)

#Extract values for HR, 95% CI, and p-value
HR <- cox_fit_summary$coefficients[2]
lower_CI <- cox_fit_summary$conf.int[3]
upper_CI <- cox_fit_summary$conf.int[4]
p_value <- cox_fit_summary$coefficients[5]
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
print(label_text)

```

```
[1] "HR = 5.74 (1.04-31.8); p = 0.045"
```

### #Multivariate cox regression for RFS

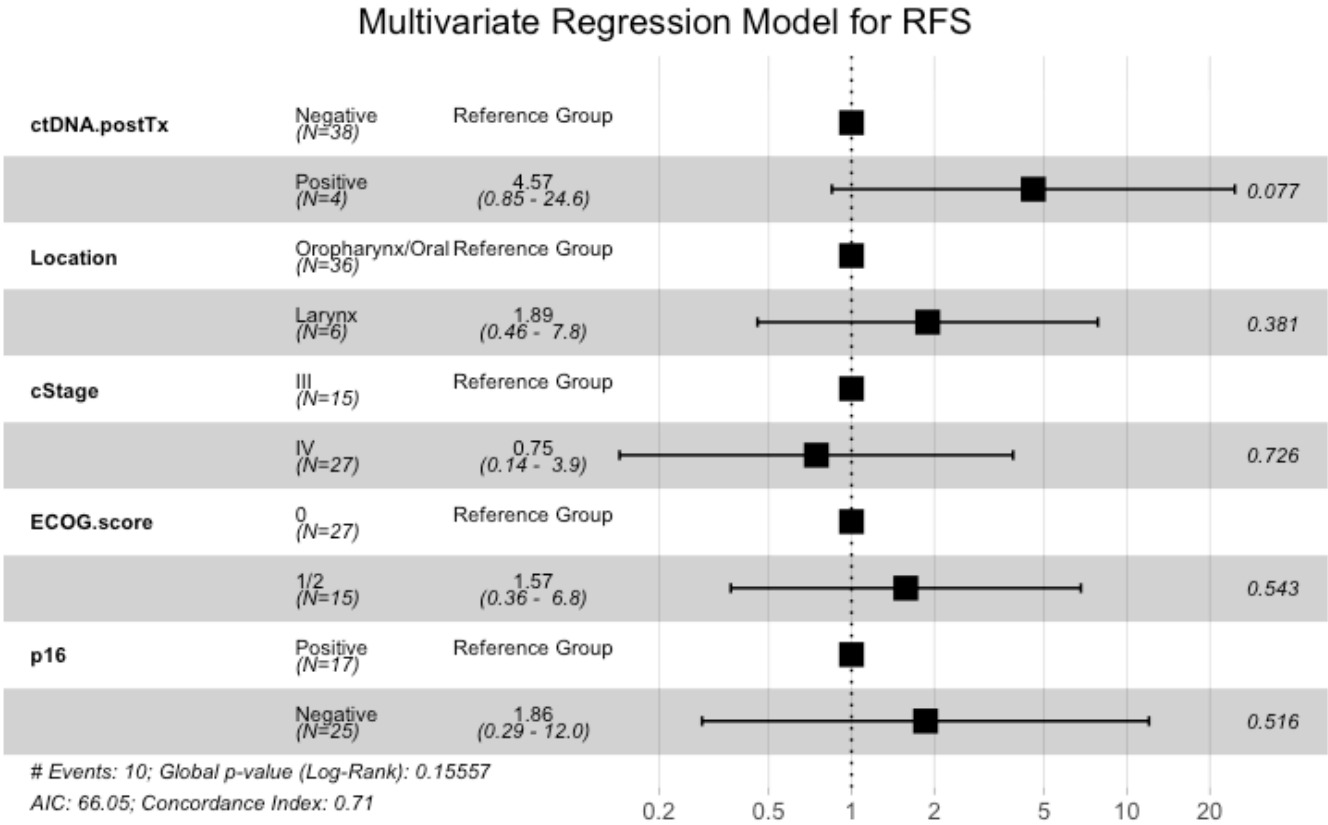
[Hide](#)

```

rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
circ_datadf <- as.data.frame(circ_data)

circ_data$ctDNA.postTx <- factor(circ_data$ctDNA.postTx, levels=c("NEGATIVE","POSITIVE"), labels = c("Negative", "Positive"))
circ_data$Gender <- factor(circ_data$Gender, levels = c("Female", "Male"), labels = c("Female", "Male"))
circ_data$Location <- factor(circ_data$Location, levels = c("Oropharynx/Oral", "Larynx"))
circ_data$ECOG.score <- factor(circ_data$ECOG.score, levels = c("0", "1"), labels = c("0", "1/2"))
circ_data$cStage <- factor(circ_data$cStage, levels = c("III", "IV"))
circ_data$NAC <- factor(circ_data$NAC, levels = c("TRUE", "FALSE"))
circ_data$p16 <- factor(circ_data$p16, levels = c("Positive", "Negative"))
surv_object <- Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)
cox_fit <- coxph(surv_object ~ ctDNA.postTx + Location + cStage + ECOG.score + p16, data=circ_data)
ggforest(cox_fit, data = circ_data, main = "Multivariate Regression Model for RFS", refLabel = "Reference Group")

```



Hide

```
test.ph <- cox.zph(cox_fit)
```

## #Univariate RFS cox regression for variables included in MVA

Hide

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
surv_object <- Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)
circ_data$ctDNA.postTx <- factor(circ_data$ctDNA.postTx, levels=c("NEGATIVE","POSITIVE"), labels = c("Negative", "Positive")) #univariate for ctDNA post-treatment
cox_fit <- coxph(surv_object ~ ctDNA.postTx, data=circ_data)
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ ctDNA.postTx, data = circ_data)
```

```
n= 42, number of events= 10
```

```
              coef exp(coef) se(coef)      z Pr(>|z|)
ctDNA.postTxPositive 2.0148    7.4995  0.7402 2.722  0.00649 **
```

```
----
```

```
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
              exp(coef) exp(-coef) lower .95 upper .95
ctDNA.postTxPositive    7.5      0.1333    1.758      32
```

```
Concordance= 0.652 (se = 0.078 )
```

```
Likelihood ratio test= 5.72 on 1 df,  p=0.02
```

```
Wald test            = 7.41 on 1 df,  p=0.006
```

```
Score (logrank) test = 10.2 on 1 df,  p=0.001
```

Hide

```
cox_fit_summary <- summary(cox_fit)
```

```
#Extract values for HR, 95% CI, and p-value
```

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 7.5 (1.76-32); p = 0.006"
```

Hide

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
surv_object <- Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)
circ_data$Location <- factor(circ_data$Location, levels = c("Oropharynx/Oral", "Larynx")) #univariate for Primary location
cox_fit <- coxph(surv_object ~ Location, data=circ_data)
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ Location, data = circ_data)
```

n= 42, number of events= 10

	coef	exp(coef)	se(coef)	z	Pr(> z )
LocationLarynx	0.8617	2.3671	0.6970	1.236	0.216

	exp(coef)	exp(-coef)	lower .95	upper .95
LocationLarynx	2.367	0.4225	0.6038	9.28

Concordance= 0.58 (se = 0.079 )

Likelihood ratio test= 1.34 on 1 df, p=0.2

Wald test = 1.53 on 1 df, p=0.2

Score (logrank) test = 1.62 on 1 df, p=0.2

Hide

```
cox_fit_summary <- summary(cox_fit)
```

#Extract values for HR, 95% CI, and p-value

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 2.37 (0.6-9.28); p = 0.216"
```

Hide

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
surv_object <- Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)
circ_data$cStage <- factor(circ_data$cStage, levels = c("III", "IV")) #univariate for St
age
cox_fit <- coxph(surv_object ~ cStage, data=circ_data)
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ cStage, data = circ_data)
```

n= 42, number of events= 10

	coef	exp(coef)	se(coef)	z	Pr(> z )
cStageIV	-0.3674	0.6925	0.6669	-0.551	0.582

	exp(coef)	exp(-coef)	lower .95	upper .95
cStageIV	0.6925	1.444	0.1874	2.559

Concordance= 0.537 (se = 0.085 )

Likelihood ratio test= 0.3 on 1 df, p=0.6

Wald test = 0.3 on 1 df, p=0.6

Score (logrank) test = 0.31 on 1 df, p=0.6

Hide

```
cox_fit_summary <- summary(cox_fit)
```

#Extract values for HR, 95% CI, and p-value

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_C
I, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 0.69 (0.19-2.56); p = 0.582"
```

Hide



```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
surv_object <- Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)
circ_data$ECOG.score <- factor(circ_data$ECOG.score, levels = c("0", "1"), labels = c("0", "1/2")) #univariate for ECOG
cox_fit <- coxph(surv_object ~ ECOG.score, data=circ_data)
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ ECOG.score, data = circ_data)
```

n= 42, number of events= 10

	coef	exp(coef)	se(coef)	z	Pr(> z )
ECOG.score1/2	0.8908	2.4370	0.6357	1.401	0.161

	exp(coef)	exp(-coef)	lower .95	upper .95
ECOG.score1/2	2.437	0.4103	0.701	8.472

Concordance= 0.626 (se = 0.083 )

Likelihood ratio test= 1.9 on 1 df, p=0.2

Wald test = 1.96 on 1 df, p=0.2

Score (logrank) test = 2.09 on 1 df, p=0.1

Hide

```
cox_fit_summary <- summary(cox_fit)
```

#Extract values for HR, 95% CI, and p-value

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 2.44 (0.7-8.47); p = 0.161"
```

Hide

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
surv_object <- Surv(time = circ_data$RFS.months, event = circ_data$RFS.Event)
circ_data$p16 <- factor(circ_data$p16, levels = c("Positive", "Negative")) #univariate for p16
cox_fit <- coxph(surv_object ~ p16, data=circ_data)
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ p16, data = circ_data)
```

n= 42, number of events= 10

	coef	exp(coef)	se(coef)	z	Pr(> z )
p16Negative	1.0538	2.8686	0.7935	1.328	0.184

	exp(coef)	exp(-coef)	lower .95	upper .95
p16Negative	2.869	0.3486	0.6056	13.59

Concordance= 0.63 (se = 0.058 )

Likelihood ratio test= 2.11 on 1 df, p=0.1

Wald test = 1.76 on 1 df, p=0.2

Score (logrank) test = 1.93 on 1 df, p=0.2

Hide

```
cox_fit_summary <- summary(cox_fit)
```

#Extract values for HR, 95% CI, and p-value

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 2.87 (0.61-13.59); p = 0.184"
```

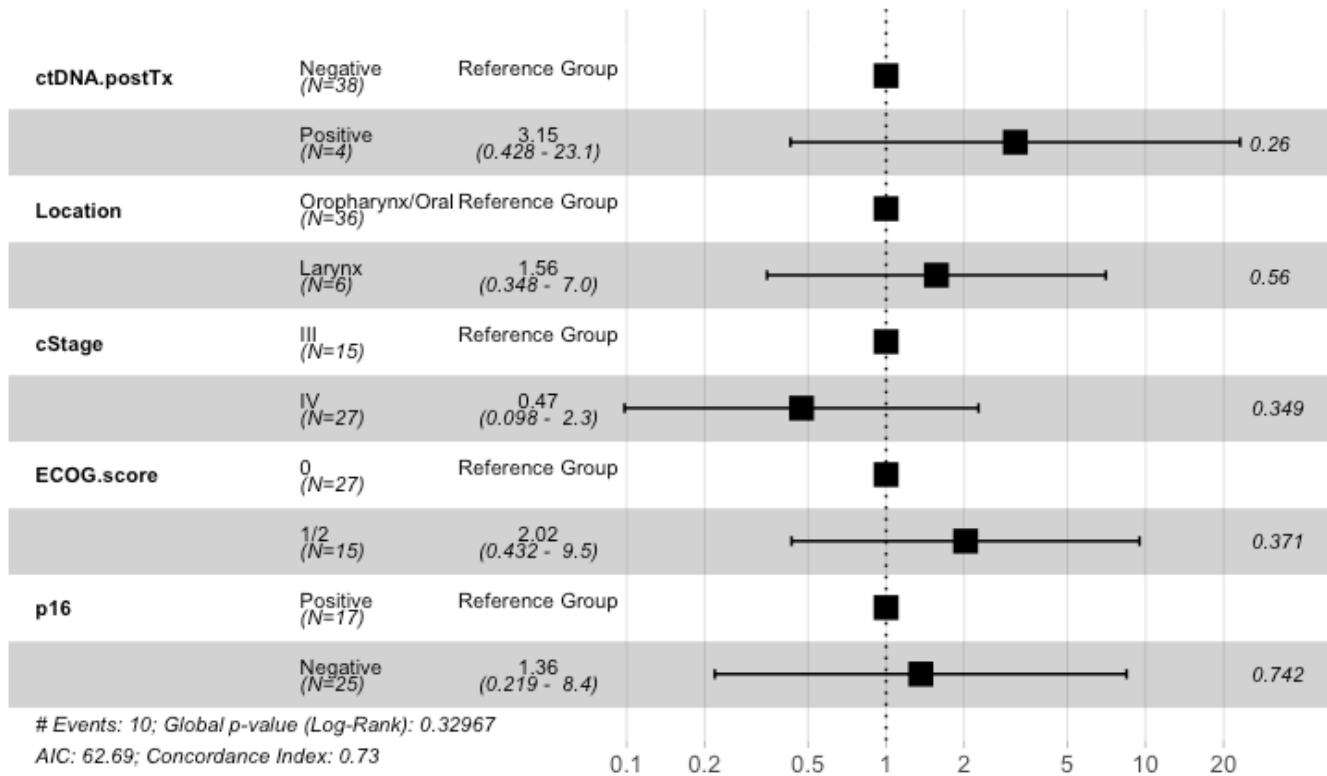
#Multivariate cox regression for OS

Hide

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
circ_datadf <- as.data.frame(circ_data)

circ_data$ctDNA.postTx <- factor(circ_data$ctDNA.postTx, levels=c("NEGATIVE","POSITIVE"), labels = c("Negative", "Positive"))
circ_data$Gender <- factor(circ_data$Gender, levels = c("Female", "Male"), labels = c("Female", "Male"))
circ_data$Location <- factor(circ_data$Location, levels = c("Oropharynx/Oral", "Larynx"))
circ_data$ECOG.score <- factor(circ_data$ECOG.score, levels = c("0", "1"), labels = c("0", "1/2"))
circ_data$cStage <- factor(circ_data$cStage, levels = c("III", "IV"))
circ_data$NAC <- factor(circ_data$NAC, levels = c("TRUE", "FALSE"))
circ_data$p16 <- factor(circ_data$p16, levels = c("Positive", "Negative"))
surv_object <- Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)
cox_fit <- coxph(surv_object ~ ctDNA.postTx + Location + cStage + ECOG.score + p16, data=circ_data)
ggforest(cox_fit, data = circ_data, main = "Multivariate Regression Model for OS", refLabel = "Reference Group")
```

## Multivariate Regression Model for OS


[Hide](#)

```
test.ph <- cox.zph(cox_fit)
```

#Univariate OS cox regression for variables included in MVA

[Hide](#)

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
surv_object <- Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)
circ_data$ctDNA.postTx <- factor(circ_data$ctDNA.postTx, levels=c("NEGATIVE","POSITIVE"), labels = c("Negative", "Positive")) #univariate for ctDNA post-treatment
cox_fit <- coxph(surv_object ~ ctDNA.postTx, data=circ_data)
summary(cox_fit)
```

```
Call:
coxph(formula = surv_object ~ ctDNA.postTx, data = circ_data)

n= 42, number of events= 10

              coef exp(coef) se(coef) z Pr(>|z|)
ctDNA.postTxPositive 1.7472    5.7385  0.8736 2  0.0455 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

              exp(coef) exp(-coef) lower .95 upper .95
ctDNA.postTxPositive    5.738    0.1743    1.036    31.8

Concordance= 0.6 (se = 0.074 )
Likelihood ratio test= 3.1 on 1 df,  p=0.08
Wald test               = 4 on 1 df,  p=0.05
Score (logrank) test = 5.11 on 1 df,  p=0.02
```

Hide

```
cox_fit_summary <- summary(cox_fit)

#Extract values for HR, 95% CI, and p-value
HR <- cox_fit_summary$coefficients[2]
lower_CI <- cox_fit_summary$conf.int[3]
upper_CI <- cox_fit_summary$conf.int[4]
p_value <- cox_fit_summary$coefficients[5]
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
print(label_text)
```

```
[1] "HR = 5.74 (1.04-31.8); p = 0.045"
```

Hide

```
rm(list=ls())
setwd("~/Downloads")
circ_data <- read.csv("OP-16933_HNSCC Clinical data.csv")
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
surv_object <- Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)
circ_data$Location <- factor(circ_data$Location, levels = c("Oropharynx/Oral", "Larynx")) #univariate for Primary location
cox_fit <- coxph(surv_object ~ Location, data=circ_data)
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ Location, data = circ_data)
```

n= 42, number of events= 10

	coef	exp(coef)	se(coef)	z	Pr(> z )
LocationLarynx	0.7183	2.0509	0.6926	1.037	0.3

	exp(coef)	exp(-coef)	lower .95	upper .95
LocationLarynx	2.051	0.4876	0.5277	7.97

Concordance= 0.553 (se = 0.07 )

Likelihood ratio test= 0.97 on 1 df, p=0.3

Wald test = 1.08 on 1 df, p=0.3

Score (logrank) test = 1.12 on 1 df, p=0.3

[Hide](#)

```
cox_fit_summary <- summary(cox_fit)
```

#Extract values for HR, 95% CI, and p-value

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 2.05 (0.53-7.97); p = 0.3"
```

[Hide](#)

```
rm(list=ls())
```

```
setwd("~/Downloads")
```

```
circ_data <- read.csv("0P-16933_HNSCC Clinical data.csv")
```

```
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
```

```
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
```

```
surv_object <- Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)
```

```
circ_data$cStage <- factor(circ_data$cStage, levels = c("III", "IV")) #univariate for Stage
```

```
cox_fit <- coxph(surv_object ~ cStage, data=circ_data)
```

```
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ cStage, data = circ_data)
```

```
n= 42, number of events= 10
```

	coef	exp(coef)	se(coef)	z	Pr(> z )
cStageIV	-0.5638	0.5690	0.6561	-0.859	0.39

	exp(coef)	exp(-coef)	lower .95	upper .95
cStageIV	0.569	1.757	0.1573	2.059

Concordance= 0.565 (se = 0.09 )

Likelihood ratio test= 0.71 on 1 df, p=0.4

Wald test = 0.74 on 1 df, p=0.4

Score (logrank) test = 0.76 on 1 df, p=0.4

[Hide](#)

```
cox_fit_summary <- summary(cox_fit)
```

```
#Extract values for HR, 95% CI, and p-value
```

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 0.57 (0.16-2.06); p = 0.39"
```

[Hide](#)

```
rm(list=ls())
```

```
setwd("~/Downloads")
```

```
circ_data <- read.csv("0P-16933_HNSCC Clinical data.csv")
```

```
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
```

```
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
```

```
surv_object <- Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)
```

```
circ_data$ECOG.score <- factor(circ_data$ECOG.score, levels = c("0", "1"), labels = c("0", "1/2")) #univariate for ECOG
```

```
cox_fit <- coxph(surv_object ~ ECOG.score, data=circ_data)
```

```
summary(cox_fit)
```

Call:

```
coxph(formula = surv_object ~ ECOG.score, data = circ_data)
```

n= 42, number of events= 10

	coef	exp(coef)	se(coef)	z	Pr(> z )
ECOG.score1/2	0.9052	2.4724	0.6403	1.414	0.157

	exp(coef)	exp(-coef)	lower .95	upper .95
ECOG.score1/2	2.472	0.4045	0.7048	8.673

Concordance= 0.701 (se = 0.08 )

Likelihood ratio test= 1.94 on 1 df, p=0.2

Wald test = 2 on 1 df, p=0.2

Score (logrank) test = 2.13 on 1 df, p=0.1

[Hide](#)

```
cox_fit_summary <- summary(cox_fit)
```

#Extract values for HR, 95% CI, and p-value

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 2.47 (0.7-8.67); p = 0.157"
```

[Hide](#)

```
rm(list=ls())
```

```
setwd("~/Downloads")
```

```
circ_data <- read.csv("0P-16933_HNSCC Clinical data.csv")
```

```
circ_data <- circ_data[circ_data$ctDNA.available=="TRUE",]
```

```
circ_data <- circ_data[circ_data$ctDNA.postTx!="",]
```

```
surv_object <- Surv(time = circ_data$FU.Biopsy.months, event = circ_data$OS.Event)
```

```
circ_data$p16 <- factor(circ_data$p16, levels = c("Positive", "Negative")) #univariate for p16
```

```
cox_fit <- coxph(surv_object ~ p16, data=circ_data)
```

```
summary(cox_fit)
```



Call:

```
coxph(formula = surv_object ~ p16, data = circ_data)
```

```
n= 42, number of events= 10
```

	coef	exp(coef)	se(coef)	z	Pr(> z )
p16Negative	0.5330	1.7041	0.6911	0.771	0.441

	exp(coef)	exp(-coef)	lower .95	upper .95
p16Negative	1.704	0.5868	0.4397	6.604

Concordance= 0.583 (se = 0.092 )

Likelihood ratio test= 0.63 on 1 df, p=0.4

Wald test = 0.59 on 1 df, p=0.4

Score (logrank) test = 0.61 on 1 df, p=0.4

[Hide](#)

```
cox_fit_summary <- summary(cox_fit)
```

```
#Extract values for HR, 95% CI, and p-value
```

```
HR <- cox_fit_summary$coefficients[2]
```

```
lower_CI <- cox_fit_summary$conf.int[3]
```

```
upper_CI <- cox_fit_summary$conf.int[4]
```

```
p_value <- cox_fit_summary$coefficients[5]
```

```
label_text <- paste0("HR = ", round(HR, 2), " (", round(lower_CI, 2), "-", round(upper_CI, 2), "); p = ", round(p_value, 3))
```

```
print(label_text)
```

```
[1] "HR = 1.7 (0.44-6.6); p = 0.441"
```