```
# Perform univariate and multivariate analysis on GBM Cell 2013 dataset
(Suppl Data 4)

library('survival')
library('openxlsx')

###############
# load dataset and clinical information
###############

data <- read.xlsx('Suppl Table 4.xlsx')

###############
# SURVIVAL STATUS
# Assign 0,1 to overall survival status
# Deceased = 1, Living = 0
###############

data$status2 <- data$OS.Status
data[which(data$OS.Status == "DECEASED"),'status2'] <- 1
data[which(data$OS.Status == "LIVING"),'status2'] <- 0
data$status2 <- as.numeric(data$status2)

###############
# Perform Univariate Analysis - Clinical
###############

# Age
summary(coxph(Surv(data$OS.Months, status2 ) ~ Diagnosis.Age,
              data = data))

# Gender
# male = 1, female = 0
data$Sex2 <- 0
data[which(data$Sex == "Male"),'Sex2'] <- 1
summary(coxph(Surv(OS.Months, status2) ~ Sex2, data = data))

# Subtype Classification
# Make subtypes as factors, with Mesenchymal as reference
data$subtype2 <- data$Gene.Expression.Subtype
data[which(data$Gene.Expression.Subtype == "Classical"),'subtype2'] <- 0
data[which(data$Gene.Expression.Subtype == "G-CIMP"),'subtype2'] <- 1
data[which(data$Gene.Expression.Subtype == "Mesenchymal"),'subtype2'] <-
2
data[which(data$Gene.Expression.Subtype == "Neural"),'subtype2'] <- 3
data[which(data$Gene.Expression.Subtype == "Proneural"),'subtype2'] <- 4
data$subtype2 <- as.numeric(data$subtype2)

subtype_factor <- factor(data$Gene.Expression.Subtype,
                         levels = c("Mesenchymal","Classical","G-
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CIMP","Neural","Proneural"))
summary(coxph(Surv(OS.Months, status2) ~ subtype_factor, data = data))

# IDH mutated
# mutated = 1, WT = 0
data$idh.mutated <- data$IDH1_STATUS
data[which(data$IDH1_STATUS == "R132H"),'idh.mutated'] <- 1
data[which(data$IDH1_STATUS == "WT"),'idh.mutated'] <- 0
class(data$idh.mutated) <- 'numeric'
summary(coxph(Surv(OS.Months, status2) ~ idh.mutated, data = data))

# MGMT Methylation
# methylation = 1, unmethylated = 0
data$methylated <- data$MGMT.Status
data[which(data$MGMT.Status  == "METHYLATED"),'methylated'] <- 1
data[which(data$MGMT.Status == "UNMETHYLATED"),'methylated'] <- 0
class(data$methylated) <- 'numeric'
summary(coxph(Surv(OS.Months, status2) ~ methylated, data = data))

# Treatment (with TMZ)
# Treatment ("Nonstandard Radiation, TMZ Chemo ||
# Standard Radiation, TMZ Chemo || TMZ Chemo, TMZ Chemoradiation
# || TMZ Chemo) = 1
# Others = 0
data$Treatment <- 0
data[which( data$THERAPY_CLASS== "Nonstandard Radiation, TMZ Chemo" |
              data$THERAPY_CLASS =="Standard Radiation, TMZ Chemo" |
              data$THERAPY_CLASS =="TMZ Chemo" |
              data$THERAPY_CLASS =="TMZ Chemoradiation, TMZ
Chemo"),'Treatment'] <- 1
summary(coxph(Surv(OS.Months, status2) ~ Treatment , data = data))

############
# Perform Univariate Analysis - Gene Expression (High vs Low) by median
# High = 1, Low = 0
#############

# AHR
data$AHR_median <- 0
data[which(data$AHR > median(data$AHR, na.rm = T)),'AHR_median'] <- 1
summary(coxph(Surv(OS.Months, status2) ~ AHR_median, data = data))

# ENTPD1
data$ENTPD1_median <- 0
data[which(data$ENTPD1 > median(data$ENTPD1, na.rm =
T)),'ENTPD1_median'] <- 1
summary(coxph(Surv(OS.Months, status2) ~ ENTPD1_median, data = data))

# KLF4
data$KLF4_median <- 0
data[which(data$KLF4 > median(data$KLF4, na.rm = T)),'KLF4_median'] <- 1
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summary(coxph(Surv(OS.Months, status2) ~ KLF4_median, data = data))

# CYP1A1
data$CYP1A1_median <- 0
data[which(data$CYP1A1 > median(data$CYP1A1, na.rm =
T)),'CYP1A1_median'] <- 1
summary(coxph(Surv(OS.Months, status2) ~ CYP1A1_median, data = data))

# STAT1
data$STAT1_median <- 0
data[which(data$STAT1 > median(data$STAT1, na.rm = T)),'STAT1_median']
<- 1
summary(coxph(Surv(OS.Months, status2) ~ STAT1_median, data = data))

# STAT3
data$STAT3_median <- 0
data[which(data$STAT3 > median(data$STAT3, na.rm = T)),'STAT3_median']
<- 1
summary(coxph(Surv(OS.Months, status2) ~ STAT3_median, data = data))

# CCL2
data$CCL2_median <- 0
data[which(data$CCL2 > median(data$CCL2, na.rm = T)),'CCL2_median'] <- 1
summary(coxph(Surv(OS.Months, status2) ~ CCL2_median, data = data))

# CCR2
data$CCR2_median <- 0
data[which(data$CCR2 > median(data$CCR2, na.rm = T) ),'CCR2_median'] <-
1
summary(coxph(Surv(OS.Months, status2) ~ CCR2_median, data = data))



################
# Multivariate Analysis
################

summary(coxph(Surv(OS.Months, status2) ~ Diagnosis.Age  +
                idh.mutated + Treatment + subtype2 + AHR_median, data =
data))
summary(coxph(Surv(OS.Months, status2) ~ Diagnosis.Age + Treatment +
                idh.mutated + subtype2 + ENTPD1_median, data =  data))
summary(coxph(Surv(OS.Months, status2) ~ Diagnosis.Age + idh.mutated +
                Treatment + subtype2 + KLF4_median, data =  data))
summary(coxph(Surv(OS.Months, status2) ~ Diagnosis.Age + idh.mutated +
                Treatment + subtype2 + CYP1A1_median, data =  data))
summary(coxph(Surv(OS.Months, status2) ~ Diagnosis.Age + idh.mutated +
                Treatment + subtype2 + STAT1_median, data =  data))
summary(coxph(Surv(OS.Months, status2) ~ Diagnosis.Age + idh.mutated +
                Treatment + subtype2 + CCL2_median, data =  data))
summary(coxph(Surv(OS.Months, status2) ~ Diagnosis.Age + idh.mutated +
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                Treatment + subtype2 + CCR2_median, data =  data))
summary(coxph(Surv(OS.Months, status2) ~ Diagnosis.Age + idh.mutated +
                Treatment + subtype2 + STAT3_median, data =  data))


# Test the proportionality and goodness of fit for AHR expression
fit <- coxph(Surv(OS.Months, status2) ~ Diagnosis.Age  +
               idh.mutated + Treatment + subtype2 + AHR_median, data =
data)
cox.zph(fit)
```