

stratification factors for OS analysis

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arm C prognostic effects

```
ds3 <- subset(ds1, ARMCD1 %in% c('C','A') & ITTWTFL %in% 'Y')
ds3$ARMCD1 <- factor(ds3$ARMCD1, levels=c('C','A'))
survfit( Surv(OS, OS.event) ~ ARMCD1, data=ds3)
```

```
## Call: survfit(formula = Surv(OS, OS.event) ~ ARMCD1, data = ds3)
##
##               n events median 0.95LCL 0.95UCL
## ARMCD1=C 338      265   14.7    13.2   17.1
## ARMCD1=A 350      250   19.0    15.9   21.5
```

```
ds3$strata_sex <- factor(ds3$strata_sex, levels=c('M','F'))
```

```
c_sex <- coxph( Surv(OS, OS.event) ~ strata_sex , data = subset(ds3, as.character( ARMCD1 ) %in% 'C')
print(c_sex)
```

```
## Call:
## coxph(formula = Surv(OS, OS.event) ~ strata_sex, data = subset(ds3,
##   as.character(ARMCD1) %in% "C"))
##
##               coef exp(coef) se(coef)      z      p
## strata_sexF -0.2014    0.8176   0.1280 -1.573 0.116
##
## Likelihood ratio test=2.52 on 1 df, p=0.1126
## n= 338, number of events= 265
```

```
ds3$strata_liver <- factor(ds3$strata_liver, levels=c("PRESENT" ,"NOT PRESENT"))
```

```
c_liver <- coxph( Surv(OS, OS.event) ~ strata_liver , data = subset(ds3, as.character( ARMCD1 ) %in%
print(c_liver)
```

```
## Call:
## coxph(formula = Surv(OS, OS.event) ~ strata_liver, data = subset(ds3,
##   as.character(ARMCD1) %in% "C"))
##
##               coef exp(coef) se(coef)      z      p
## strata_liverNOT PRESENT -0.3613    0.6968   0.1599 -2.26 0.0238
##
```

```
## Likelihood ratio test=4.73 on 1 df, p=0.02972
## n= 338, number of events= 265

coxph( Surv(OS, OS.event) ~ strata_IHC , data = subset(ds3, as.character( ARMCD1 ) %in% 'C' ) )

## Call:
## coxph(formula = Surv(OS, OS.event) ~ strata_IHC, data = subset(ds3,
## as.character(ARMCD1) %in% "C"))
##
##               coef exp(coef) se(coef)      z      p
## strata_IHCTC0/1/2_IC2/3 -0.3483   0.7059   0.2017 -1.727 0.0842
## strata_IHCTC3_ANY IC    -0.3758   0.6867   0.1988 -1.890 0.0587
##
## Likelihood ratio test=6.23 on 2 df, p=0.04433
## n= 338, number of events= 265

ds3$strata_IHC <- factor(ifelse(ds3$strata_IHC %in% 'TC0/1/2_IC0/1', 'PDL-', 'PDL+'), levels=c('PDL-', 'PDL+'))

c_ihc <- coxph( Surv(OS, OS.event) ~ strata_IHC , data = subset(ds3, as.character( ARMCD1 ) %in% 'C' ) )

print(c_ihc)

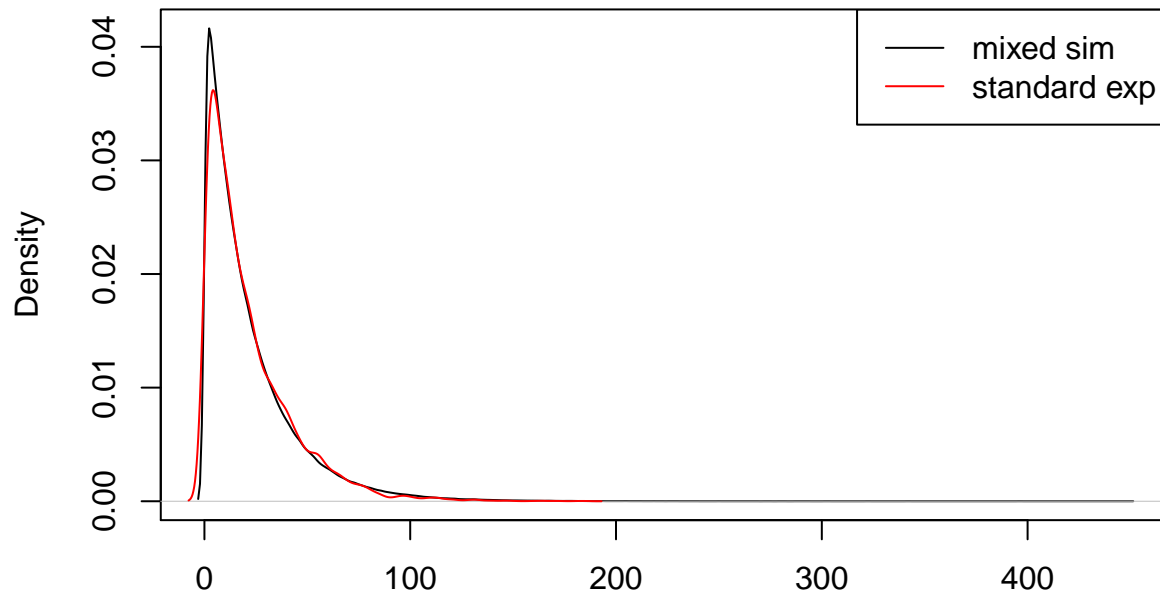
## Call:
## coxph(formula = Surv(OS, OS.event) ~ strata_IHC, data = subset(ds3,
## as.character(ARMCD1) %in% "C"))
##
##               coef exp(coef) se(coef)      z      p
## strata_IHCPDL+ -0.3624   0.6960   0.1501 -2.415 0.0158
##
## Likelihood ratio test=6.22 on 1 df, p=0.01262
## n= 338, number of events= 265

analysis data has 688 patients
```

Table 1: stratification factors

var	referLevel	targetLevel	freq	hr
strata_sex	M	F	0.38	0.82
strata_liver	PRESENT	NOT PRESENT	0.84	0.70
strata_IHC	PDL-	PDL+	0.25	0.70

overall distribution from simulation



N = 1000000 Bandwidth = 1.013

```
## [1] "M1"
## [1] "conditional on M2+,M3+"
## [1] 0.82
## [1] "conditional on M2-,M3+"
## [1] 0.82
## [1] "conditional on M2+,M3-"
## [1] 0.82
## [1] "conditional on M2-,M3-"
## [1] 0.82
## [1] "marginal hr 0.81833198080627"
## [1] "M2"
## [1] "conditional on M1+,M3+"
## [1] 0.7
## [1] "conditional on M1-,M3+"
## [1] 0.7
## [1] "conditional on M1+,M3-"
## [1] 0.7
## [1] "conditional on M1-,M3-"
## [1] 0.7
## [1] "marginal hr 0.698714296875987"
## [1] "M3"
## [1] "conditional on M1+,M2+"
## [1] 0.7
## [1] "conditional on M1-,M2+"
## [1] 0.7
## [1] "conditional on M1+,M2-"
## [1] 0.7
## [1] "conditional on M1-,M2-"
## [1] 0.7
```

```
## [1] "marginal hr 0.695775747918282"
```

Table 2: simulation input

strata_sex	strata_liver	strata_IHC	n	freq_obs	freq_multiply
M	PRESENT	PDL-	57	0.083	0.075
F	PRESENT	PDL-	35	0.051	0.045
M	NOT PRESENT	PDL-	270	0.392	0.392
F	NOT PRESENT	PDL-	152	0.221	0.235
M	PRESENT	PDL+	10	0.015	0.026
F	PRESENT	PDL+	9	0.013	0.015
M	NOT PRESENT	PDL+	93	0.135	0.133
F	NOT PRESENT	PDL+	62	0.090	0.080

	cm.rate	cm.freq
M1+M2+M3+	0.030	0.079
M1-M2+M3+	0.036	0.131
M1+M2-M3+	0.043	0.015
M1-M2-M3+	0.052	0.025
M1+M2+M3-	0.043	0.236
M1-M2+M3-	0.052	0.394
M1+M2-M3-	0.061	0.045
M1-M2-M3-	0.074	0.075

freq_multiply is obtained by multiplying marginal frequency, i.e., assuming independence.

reanalyze outcome with collapsed PDL1 subgroup

Row.names	C_n	A_n	C_event	A_event	O-E	V	log_hr	prob_C_better
F NOT PRESENT PDL-	76	76	61	53	5.704	28.303	-0.201	0.453
F NOT PRESENT PDL+	29	33	16	17	1.918	8.040	-0.236	0.514
F PRESENT PDL-	20	15	16	15	-4.396	6.730	0.616	0.010
F PRESENT PDL+	4	5	3	2	0.852	1.216	-0.694	0.697
M NOT PRESENT PDL-	129	141	106	105	13.366	51.636	-0.257	0.596
M NOT PRESENT PDL+	46	47	34	29	6.030	15.408	-0.388	0.743
M PRESENT PDL-	28	29	25	25	-0.746	12.286	0.064	0.155
M PRESENT PDL+	6	4	4	4	-1.039	1.835	0.541	0.140