

ABC Study: ABC-NIS-01

A prospective, multicenter, non-interventional, observational study to evaluate safety and effectiveness of WonderDrug™ in subjects with XYZ

Full Analysis Set (FAS)

ALEA Study No.:

ALEA01

Sponsor Name:

ABC

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Statistical Analysis:

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1 List of Abbreviations and Definition of Terms

Abbreviation or specialist term	Explanation
ADaM	Analysis Data Model
BL	Baseline
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
FAS	Full Analysis Set
HGB	Hemoglobin
KM	Kaplan-Meier
knitr	knitr: A General-Purpose Package for Dynamic Report Generation in R, Yihui Xie, 2017
LOCF	Last Observation Carried Forward
N	Number of observations
NA	Not Available
OS	Overall Survival
Q1	Lower quartile
Q3	Upper quartile
R	R Foundation for Statistical Computing, Vienna, Austria
RStudio	RStudio: Integrated Development Environment for R. RStudio, Inc., Boston, MA
SAP	Statistical Analysis Plan
SAS	SAS Institute Inc., Cary, NC, USA.
SD	Standard Deviation
SS	Sums of Squares
Tex Live	Tex Live, Tex Users Group, Portland, OR, USA
USUBJID	Unique Subject Identifier
WBC	White Blood Cell

2 Statistical Methods

Statistical analyses of this non-interventional study were descriptive and exploratory in nature. For continuous variables, summary statistics, e.g., the mean, standard deviation (SD), median, lower (Q1) and upper quartiles (Q3) and minimum and maximum values were calculated. For dichotomous and categorical variables, the number and percentage of participants in each category were reported. 95% confidence intervals (CIs) for categorical variables were calculated according to the Wilson score method, without continuity correction. 95% CIs for approximately normally distributed continuous variables were calculated using the *t*-distribution. For the body weight, the geometric mean was presented together with 95% CIs. The geometric mean was calculated as the anti-logarithm of the mean of the log-transformed values.

The Fisher's exact test or Pearson's χ^2 test was used to compare categorical variables, the Wilcoxon test or Kruskal-Wallis test was used to compare differences in continuous variables between two or more groups.

Shift tables from Baseline to week 24 were presented for HGB and WBC based on changes in the normal ranges and tested with the McNemar's test/Bowker's symmetry test.

Log body weight was analyzed in a multiple linear regression model with sex, age and height as independent variables. An ANOVA table was constructed with Type I, II and III sum of squares.

Overall survival (time from baseline to death or censoring) was estimated by the univariate Kaplan-Meier method and the median time to event was presented together with 95% CIs, overall and stratified by age group <65 years vs \geq 65 years. Survival curves were compared by the log-rank test.

All p-values were descriptive and no adjustments for multiplicity were made.


All analyses were based on the Full Analysis Set (FAS), consisting of all subjects that received at least one dose of Wonder-Drug™. Analysis was based on available data at each timepoint (i.e. missing data were not imputed), with exception of the analysis of WBC over time: the last observation carried forward (LOCF) method was used to input missing data and was presented - as sensitivity analysis - in addition to the analysis of the non-imputed data.

Subgroup analyses were performed by age group (<65 years, \geq 65 years).

R version 3.4.2 (The R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis.

All data were *fictitious* and the statistical methods that were applied served mainly as examples to show the usage of *R* code within different *R* packages. Data were generated with SAS v. 9.4 (SAS Institute Inc., Cary, NC, USA) using e.g. following functions: `rand("BINOMIAL", p, n)`, `rand("NORMAL", mu, sigma)`, `exp(rand("NORMAL", mu, sigma))` and `-log(ranuni(x))`. CDISC ADaM standards were partly applied. [clindocu/sasxpt-r](#) was used to generate the data definition table and to import SAS .xpt files into R with associated user-defined formats (i.e. R *factor(s)*, *levels* and *label(s)*).

This report was generated with [Tex Live 2017](#), [RStudio](#), [R](#) and [knitr](#).

The data definition table (DDT) of all analysis datasets can be found here:  (double click to open)

Following *R* packages were used:

- `library(knitr)`
- `library(foreign)`
- `library(tidyverse)`
- `library(Hmisc)`
- `library(xtable)`
- `library(gridExtra)`
- `library(survminer)`
- `library(ggthemes)`
- `library(reporttools)`
- `library(texreg)`
- `library(car)`

All code for generating this report can be found in appendix [A](#).

3 Data Sets Analysed

Data were collected from 180 subjects from 9 study sites, all meeting the criteria for the FAS. 139 subjects were younger than 65 years, 41 subjects were older than or equal 65 years.










The disposition of subjects is shown in figure 1 and is tabulated in table 4. Baseline characteristics (Age, Sex, Race, Weight, Height, BMI, ECOG, HGB) are summarized in table 7.

3.1 Study Sites, by Age Category

Table 2: Study Sites by Age Category - Hmisc::summary.formula

	<65	≥65	Combined
	N = 139	N = 41	N = 180
Study Site Identifier			
01	6% $\frac{9}{139}$	5% $\frac{2}{41}$	6% $\frac{11}{180}$
02	6% $\frac{8}{139}$	10% $\frac{4}{41}$	7% $\frac{12}{180}$
03	12% $\frac{17}{139}$	10% $\frac{4}{41}$	12% $\frac{21}{180}$
04	19% $\frac{26}{139}$	22% $\frac{9}{41}$	19% $\frac{35}{180}$
05	6% $\frac{9}{139}$	15% $\frac{6}{41}$	8% $\frac{15}{180}$
06	14% $\frac{20}{139}$	12% $\frac{5}{41}$	14% $\frac{25}{180}$
07	7% $\frac{10}{139}$	5% $\frac{2}{41}$	7% $\frac{12}{180}$
08	19% $\frac{26}{139}$	7% $\frac{3}{41}$	16% $\frac{29}{180}$
09	10% $\frac{14}{139}$	15% $\frac{6}{41}$	11% $\frac{20}{180}$

Table 3: Study Sites by Age Category - Hmisc.summary with dotchart

	<65	≥65	Combined
	N = 139	N = 41	N = 180
Study Site Identifier			
01	6% $\frac{9}{139}$	5% $\frac{2}{41}$	
02	6% $\frac{8}{139}$	10% $\frac{4}{41}$	
03	12% $\frac{17}{139}$	10% $\frac{4}{41}$	
04	19% $\frac{26}{139}$	22% $\frac{9}{41}$	
05	6% $\frac{9}{139}$	15% $\frac{6}{41}$	
06	14% $\frac{20}{139}$	12% $\frac{5}{41}$	
07	7% $\frac{10}{139}$	5% $\frac{2}{41}$	
08	19% $\frac{26}{139}$	7% $\frac{3}{41}$	
09	10% $\frac{14}{139}$	15% $\frac{6}{41}$	

3.2 Disposition of Subjects

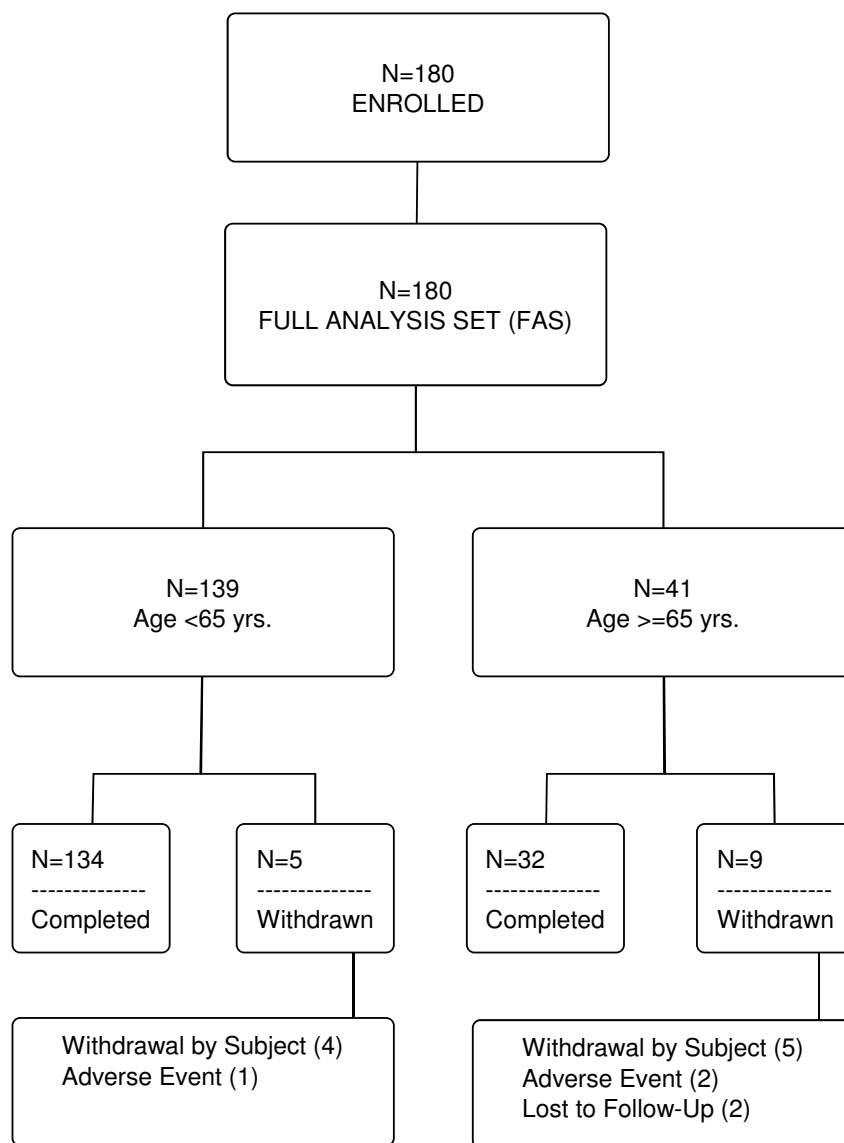


Figure 1: Disposition of Subjects

3.3 Disposition of Subjects, by Age Category

```
s6 <- summary(AGEGR1 ~ EOSSTT + DCSREAS, data = ADSL, method = 'reverse',
              overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)

latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,
      prtest = "P", dotchart = FALSE,
      caption = "Disposition of Subjects - Hmisc.summary with na.include = F",
      caption.loc = "top",
      middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "Dispos")
```

Table 4: Disposition of Subjects - Hmisc.summary with na.include = F

	N	<65		≥65		Combined
		N = 139		N = 41		N = 180
End of Study Status	180					
Completed		96%	$\frac{134}{139}$	78%	$\frac{32}{41}$	92% $\frac{166}{180}$
Discontinued		4%	$\frac{5}{139}$	22%	$\frac{9}{41}$	8% $\frac{14}{180}$
Ongoing		0%	$\frac{0}{139}$	0%	$\frac{0}{41}$	0% $\frac{0}{180}$
Reason for Discontinuation from Study	14					
Adverse Event		20%	$\frac{1}{5}$	22%	$\frac{2}{9}$	21% $\frac{3}{14}$
Lost to Follow-Up		0%	$\frac{0}{5}$	22%	$\frac{2}{9}$	14% $\frac{2}{14}$
Withdrawal by Subject		80%	$\frac{4}{5}$	56%	$\frac{5}{9}$	64% $\frac{9}{14}$

N is the number of non-missing values.

3.3.1 Listing Reason for Non-Completion

```
df1 <- ADSL %>%
  select(USUBJID, SEX, AGE, DCSREAS, DSTERM) %>%
  filter(DCSREAS != "") %>%
  arrange(DCSREAS)

my_table <- xtable(df1, caption = "Listing Reason for Non-Completion - xtable",
                  align = "lrrrlp{6cm}", caption.placement = "top")

digits(my_table)[4] <- 0 # Age (column 4 with 0 digits);
print(my_table, caption.placement = "top", size = "small", include.rownames = TRUE,
      table.placement = "htb", tabular.environment = "longtable", floating = FALSE)
```

Table 5: Listing Reason for Non-Completion - xtable

	USUBJID	SEX	AGE	DCSREAS	DSTERM
1	ALEA01-02-022	Female	75	Adverse Event	Severe Nausea
2	ALEA01-04-064	Male	77	Adverse Event	Vomiting
3	ALEA01-05-082	Female	43	Adverse Event	Severe Skin rash
4	ALEA01-02-016	Male	74	Lost to Follow-Up	Subject moved
5	ALEA01-04-054	Female	80	Lost to Follow-Up	Subject was lost to follow-up
6	ALEA01-01-008	Female	51	Withdrawal by Subject	Withdrew consent
7	ALEA01-03-033	Female	66	Withdrawal by Subject	Withdrew consent
8	ALEA01-03-043	Male	65	Withdrawal by Subject	Withdrew consent
9	ALEA01-03-044	Male	65	Withdrawal by Subject	Consent withdrawn by subject
10	ALEA01-04-048	Male	78	Withdrawal by Subject	Withdrew consent
11	ALEA01-07-127	Female	76	Withdrawal by Subject	Withdrew consent
12	ALEA01-08-132	Female	61	Withdrawal by Subject	Withdrew consent
13	ALEA01-08-145	Female	48	Withdrawal by Subject	Withdrew consent
14	ALEA01-09-175	Male	64	Withdrawal by Subject	Withdrew consent

4 Demographic and Other Baseline Characteristics

4.1 Demographic and Other Baseline Characteristics - Hmisc

Table 6: Demographic and Other Baseline Characteristics - Hmisc.summary

	N	<65 N = 139		≥65 N = 41		Combined N = 180	
Age	180	42.5	51.0 58.0	(49.2 ±10.7)	68.0	72.0 78.0	(73.1 ± 6.3)
Sex	179						
Female			43%	$\frac{60}{138}$		54%	$\frac{22}{41}$
Male			57%	$\frac{78}{138}$		46%	$\frac{19}{41}$
Race	180						
White			99%	$\frac{137}{139}$		100%	$\frac{41}{41}$
Black or African American			1%	$\frac{2}{139}$		0%	$\frac{0}{41}$
American Indian or Alaska Native			0%	$\frac{0}{139}$		0%	$\frac{0}{41}$
Asian			0%	$\frac{0}{139}$		0%	$\frac{0}{41}$
Weight at Baseline (kg)	177	57	66 81	(69 ±16)	59	67 76	(69 ±18)
Height (cm)	180	166.0	170.0 173.0	(170.0 ± 5.4)	166.0	171.0 173.0	(170.0 ± 4.6)
Body Mass Index (kg/m2)	177	20.1	22.9 27.1	(23.9 ± 5.2)	20.4	22.9 26.2	(23.7 ± 5.7)
ECOG at Baseline	174						
0			54%	$\frac{73}{135}$		49%	$\frac{19}{39}$
1			39%	$\frac{53}{135}$		33%	$\frac{13}{39}$
2			7%	$\frac{9}{135}$		13%	$\frac{5}{39}$
3			0%	$\frac{0}{135}$		5%	$\frac{2}{39}$
4			0%	$\frac{0}{135}$		0%	$\frac{0}{39}$
Hemoglobin at Baseline (g/dL)	180	8.50	8.90 9.40	(8.92 ±0.68)	8.50	9.00 9.80	(9.09 ±0.94)
		8.50	8.90 9.50	(8.96 ±0.75)			

a b c represent the lower quartile a , the median b , and the upper quartile c for continuous variables. $x \pm s$ represents $\bar{X} \pm 1$ SD. N is the number of non-missing values.

Table 7: Demographic and Other Baseline Characteristics - Hmisc.summary with units and P-value

		N	<65			≥65			Combined			P-value			
			N = 139			N = 41			N = 180						
Age	years	180	42.5	51.0	58.0	(49.2 ±10.7)	68.0	72.0	78.0	(73.1 ± 6.3)	45.0	55.0	63.2	(54.6 ±14.1)	<0.001 ¹
Sex		179													0.25 ²
Female				43%	$\frac{60}{138}$		54%	$\frac{22}{41}$			46%	$\frac{82}{179}$			
Male				57%	$\frac{78}{138}$		46%	$\frac{19}{41}$			54%	$\frac{97}{179}$			
Race		180													0.44 ²
White				99%	$\frac{137}{139}$		100%	$\frac{41}{41}$			99%	$\frac{178}{180}$			
Black or African American				1%	$\frac{2}{139}$		0%	$\frac{0}{41}$			1%	$\frac{2}{180}$			
American Indian or Alaska Native				0%	$\frac{0}{139}$		0%	$\frac{0}{41}$			0%	$\frac{0}{180}$			
Asian				0%	$\frac{0}{139}$		0%	$\frac{0}{41}$			0%	$\frac{0}{180}$			
Weight at Baseline	kg	177	57	66	81	(69 ±16)	59	67	76	(69 ±18)	57	66	80	(69 ±17)	0.74 ¹
Height	cm	180	166.0	170.0	173.0	(170.0 ± 5.4)	166.0	171.0	173.0	(170.0 ± 4.6)	166.0	170.0	173.0	(170.0 ± 5.2)	0.9 ¹
Body Mass Index	kg/m2	177	20.1	22.9	27.1	(23.9 ± 5.2)	20.4	22.9	26.2	(23.7 ± 5.7)	20.2	22.9	27.1	(23.9 ± 5.3)	0.84 ¹
ECOG at Baseline		174													0.032 ²
0				54%	$\frac{73}{135}$		49%	$\frac{19}{39}$			53%	$\frac{92}{174}$			
1				39%	$\frac{53}{135}$		33%	$\frac{13}{39}$			38%	$\frac{66}{174}$			
2				7%	$\frac{9}{135}$		13%	$\frac{5}{39}$			8%	$\frac{14}{174}$			
3				0%	$\frac{0}{135}$		5%	$\frac{2}{39}$			1%	$\frac{2}{174}$			
4				0%	$\frac{0}{135}$		0%	$\frac{0}{39}$			0%	$\frac{0}{174}$			
Hemoglobin at Baseline	g/dL	180	8.50	8.90	9.40	(8.92 ±0.68)	8.50	9.00	9.80	(9.09 ±0.94)	8.50	8.90	9.50	(8.96 ±0.75)	0.31 ¹

a b c represent the lower quartile a , the median b , and the upper quartile c for continuous variables. $x \pm s$ represents $\bar{X} \pm 1$ SD. N is the number of non-missing values. Tests used:¹Wilcoxon test; ²Pearson test

4.2 Demographic and Other Baseline Characteristics - reporttools:::tableContinuous

```
# Generate dataframe with variables;
vars <- with(ADSL, data.frame(
  "Age years" = AGE,
  "Weight kg" = WEIGHTBL,
  "Height cm" = HEIGHT,
  "BMI kg.m2" = BMI,
  "Hemoglobin g.dL" = HGBBL))

cap <- "Baseline Characteristics - reporttools:::tableContinuous - Wilcoxon test"
lab <- "tab:BaseChar"
bye <- ADSL$AGEGR1

tableContinuous(vars = vars, cap = cap, caption.placement = "top", group = bye, lab = lab,
  prec = c(0, 1, 1, 1, 1, 1, 1, 2, 1, 0), longtable = TRUE, print.pval = "kruskal")
```

Table 8: Baseline Characteristics - reporttools:::tableContinuous - Wilcoxon test

Variable	Levels	n	Min	q ₁	\tilde{x}	\bar{x}	q ₃	Max	s	IQR	#NA
Age.years	<65	139	18.0	42.5	51.0	49.2	58.0	64.0	10.74	15.5	0
	>=65	41	65.0	68.0	72.0	73.1	78.0	88.0	6.32	10.0	0
<i>p</i> < 0.0001	all	180	18.0	45.0	55.0	54.6	63.2	88.0	14.12	18.2	0
Weight.kg	<65	137	40.4	56.8	66.3	69.3	80.6	117.1	16.47	23.8	2
	>=65	40	42.4	58.8	66.6	68.6	76.5	126.9	17.53	17.6	1
<i>p</i> = 0.74	all	177	40.4	57.4	66.4	69.2	79.7	126.9	16.67	22.3	3
Height.cm	<65	139	159.0	166.0	170.0	170.0	173.0	184.0	5.38	7.0	0
	>=65	41	162.0	166.0	171.0	170.0	173.0	180.0	4.63	7.0	0
<i>p</i> = 0.90	all	180	159.0	166.0	170.0	170.0	173.0	184.0	5.21	7.0	0
BMI.kg.m2	<65	137	14.5	20.1	22.9	23.9	27.1	41.5	5.24	7.0	2
	>=65	40	14.2	20.4	22.9	23.7	26.2	41.0	5.72	5.8	1
<i>p</i> = 0.84	all	177	14.2	20.2	22.9	23.9	27.1	41.5	5.34	6.9	3
Hemoglobin.g.dL	<65	139	6.8	8.5	8.9	8.9	9.4	10.8	0.68	0.9	0
	>=65	41	7.2	8.5	9.0	9.1	9.8	12.0	0.94	1.3	0
<i>p</i> = 0.31	all	180	6.8	8.5	8.9	9.0	9.5	12.0	0.75	1.0	0

4.3 Demographic and Other Baseline Characteristics - reporttools::tableNominal

```
vars <- with(ADSL, data.frame(
  "Sex" = SEX,
  "Race" = RACE,
  "ECOG" = ECOGBL))
```

```
cap <- "Baseline Char. - tableNominal - NAs excluded - Fisher's exact test"
lab <- "tab:01_BaseCategor"
bye <- ADSL$AGEGR1
```

```
tableNominal(vars = vars, cap = cap, caption.placement = "top", group = bye, vertical = FALSE,
  lab = lab, longtable = TRUE, cumsum = FALSE,
  miss.cat = NA, print.pval = "fisher", fisher.B = Inf)
```

Table 9: Baseline Char. - tableNominal - NAs excluded - Fisher's exact test

Variable	Levels	n<65	%<65	n>=65	%>=65	n _{all}	% _{all}
Sex	Female	60	43.5	22	53.7	82	45.8
	Male	78	56.5	19	46.3	97	54.2
p = 0.29	all	138	100.0	41	100.0	179	100.0
Race	White	137	98.6	41	100.0	178	98.9
	Black or African American	2	1.4	0	0.0	2	1.1
	American Indian or Alaska Native	0	0.0	0	0.0	0	0.0
	Asian	0	0.0	0	0.0	0	0.0
p = 1.00	all	139	100.0	41	100.0	180	100.0
ECOG	0	73	54.1	19	48.7	92	52.9
	1	53	39.3	13	33.3	66	37.9
	2	9	6.7	5	12.8	14	8.1
	3	0	0.0	2	5.1	2	1.1
	4	0	0.0	0	0.0	0	0.0
p = 0.06	all	135	100.0	39	100.0	174	100.0

```
tableNominal(vars = vars, cap = cap, caption.placement = "top", group = bye, vertical = FALSE,
  lab = lab, longtable = TRUE, cumsum = FALSE,
  miss.cat = c(1:ncol(vars)))
```

Table 10: Baseline Characteristics - tableNominal - NAs as category

Variable	Levels	n<65	%<65	n>=65	%>=65	n _{all}	% _{all}
Sex	Female	60	43.2	22	53.7	82	45.6
	Male	78	56.1	19	46.3	97	53.9
	missing	1	0.7	0	0.0	1	0.6
	all	139	100.0	41	100.0	180	100.0
Race	White	137	98.6	41	100.0	178	98.9
	Black or African American	2	1.4	0	0.0	2	1.1
	American Indian or Alaska Native	0	0.0	0	0.0	0	0.0
	Asian	0	0.0	0	0.0	0	0.0
	all	139	100.0	41	100.0	180	100.0
ECOG	0	73	52.5	19	46.3	92	51.1
	1	53	38.1	13	31.7	66	36.7
	2	9	6.5	5	12.2	14	7.8
	3	0	0.0	2	4.9	2	1.1
	4	0	0.0	0	0.0	0	0.0
	missing	4	2.9	2	4.9	6	3.3
	all	139	100.0	41	100.0	180	100.0

4.4 Histogram Age

```
df_hist <- ADSL %>% select(AGE) %>%
  mutate(Param = AGE) %>%
  filter(!is.na(Param))

myLabel <- "Age (yrs.)"
myWidth <- 3
cap <- "Histogram Age (yrs.)"

# Create histogram with;;
# ref.label="HistPlot"
```

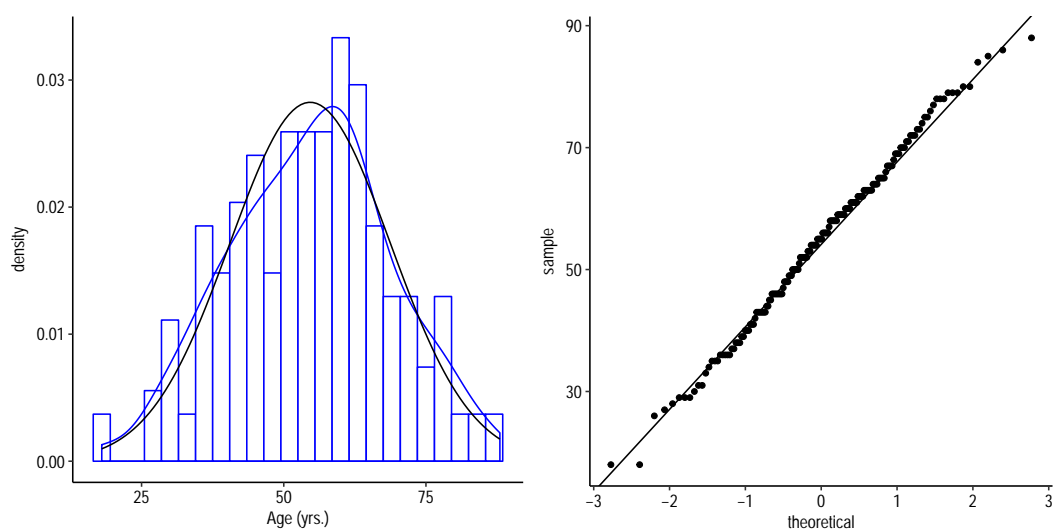


Figure 2: Histogram Age (yrs.)

Variable	Test	P.value
Age (yrs.)	Shapiro-Wilk normality test	0.714500

4.5 Histogram Weight at Baseline

```
# Histogram, density, normal distr., saphiro wilk;
p1 <- ggplot(df_hist, aes(x = Param)) +
  geom_histogram(aes(y = ..density..), binwidth = myWidth, colour = "blue", fill = "white") +
  geom_density(colour = "blue") +
  stat_function(fun = dnorm, colour = "black",
               args = list(mean = mean(df_hist$Param), sd = sd(df_hist$Param))) +
  xlab(myLabel) +
  theme_pubr()

# from https://stackoverflow.com/questions/4357031/qnorm-and-qqline-in-ggplot2/:
qqplot_data <- function(vec) {
  # argument: vector of numbers
  # following four lines from base R's qqline()
  y <- quantile(vec[!is.na(vec)], c(0.25, 0.75))
  x <- qnorm(c(0.25, 0.75))
  slope <- diff(y)/diff(x)
  int <- y[1L] - slope * x[1L]
  d <- data.frame(resids = vec)
  ggplot(d, aes(sample = resids)) + stat_qq() + geom_abline(slope = slope, intercept = int)
}

p2 <- qqplot_data(df_hist$Param) + theme_pubr()

grid.arrange(p1, p2, ncol = 2)
```

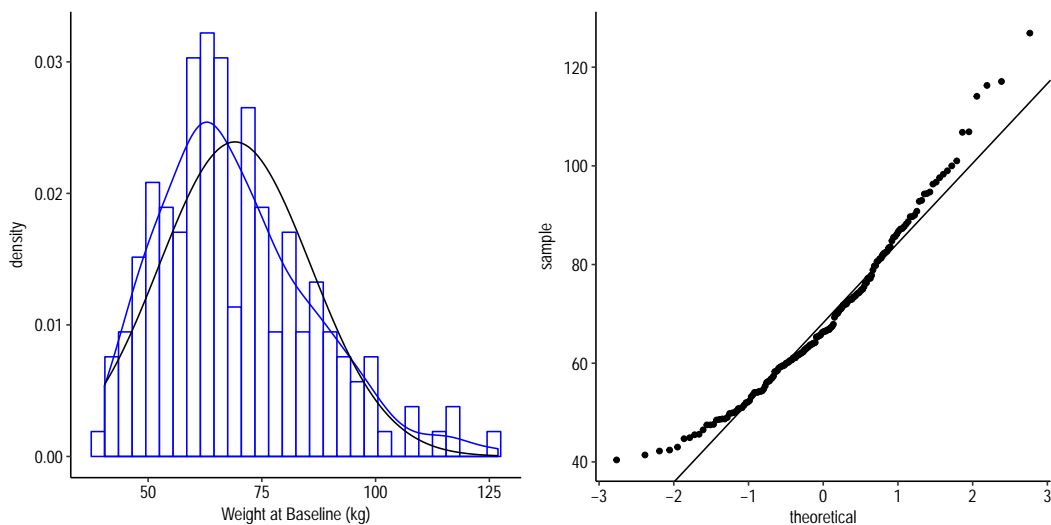


Figure 3: Histogram Weight (kg) at Baseline

```
# Normality Test;
m1 <- shapiro.test(df_hist$Param)
d1 <- data.frame(Variable = myLabel, Test = m1$method, P.value = m1$p.value)
my_table <- xtable(d1, digits = 6)
print(my_table, caption.placement = "top", size = "small", include.rownames = FALSE,
      table.placement = "htb", digits = 6, tabular.environment = "longtable", floating = FALSE)
```

Variable	Test	P.value
Weight at Baseline (kg)	Shapiro-Wilk normality test	0.000075

4.6 Weight at Baseline - Boxplot, Density Plot, QQ-Plot

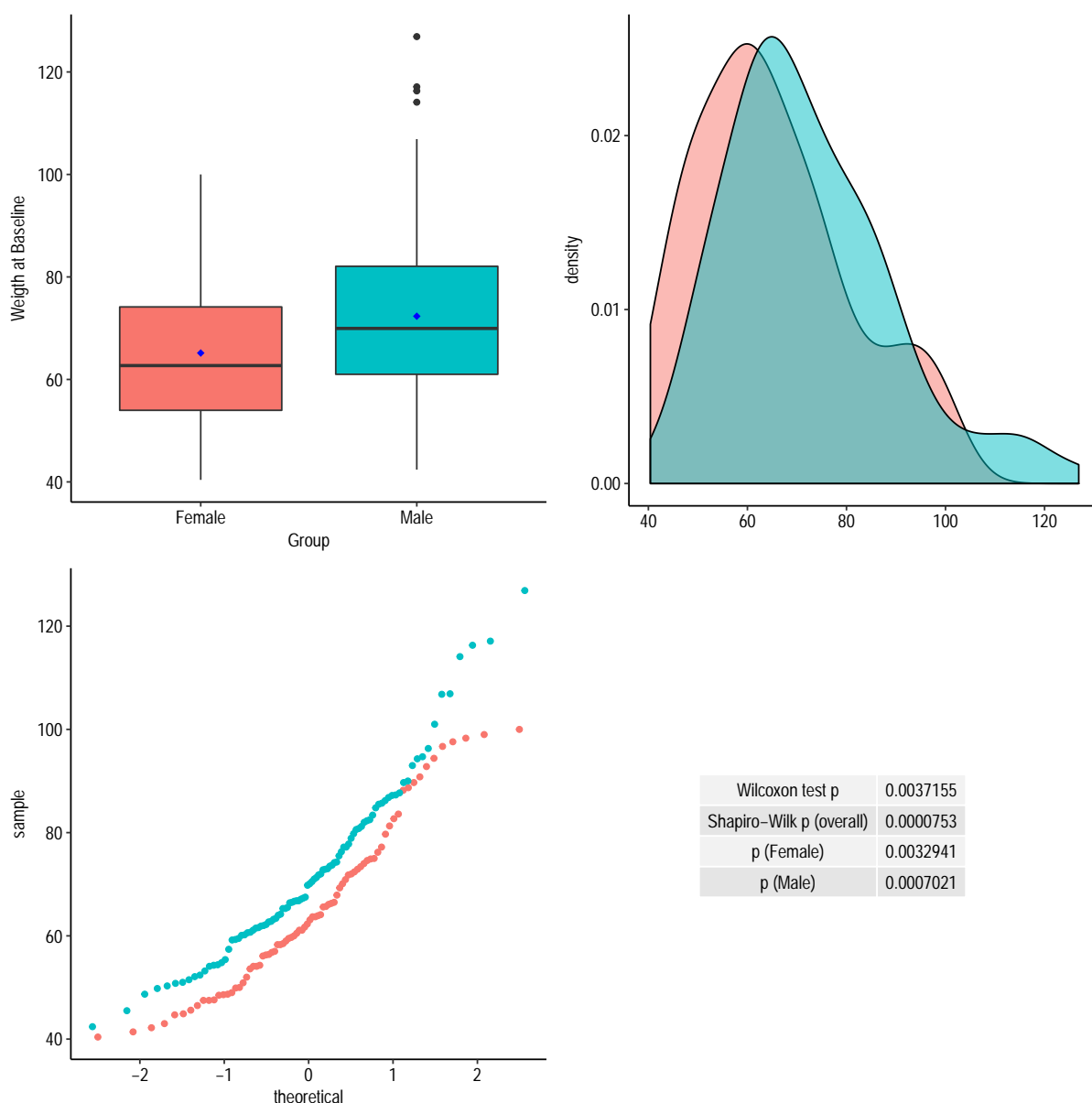


Figure 4: Weight (kg) at Baseline, by Sex

```
myCaption <- "Summary Statistics: Weight (kg) at Baseline"

# Enter not transformed Variable Name here;
LbyQUART(mydata$WEIGHTBL, mydata$SEX)
```

Table 13: Summary Statistics: Weight (kg) at Baseline

	N	Mean	Median	SD	Q1	Q3	Min	Max
Female	80	65.2	62.7	15.67	54.0	74.2	40.4	100.0
Male	96	72.3	69.9	16.87	61.0	82.1	42.4	126.9
ALL	176	69.1	66.3	16.68	57.3	79.1	40.4	126.9

4.7 Log10 Weight at Baseline - Boxplot, Density Plot, QQ-Plot

```
mydata <- ADSL %>% select(WEIGHTBL, L10WTBL, SEX) %>%
  mutate(Param = L10WTBL) %>%
  filter(!is.na(Param)) %>%
  filter(!is.na(SEX))

myLab <- "Log10 Weighth"
cap <- "Log10 Weight (kg) at Baseline, by Sex"

# Please adapt code, when you use other and/or more Groups than SEX Female/Male;
# Boxplot, density plot, qqplot, kruskall wallis, sphiro wilk;

# Boxplot 2 Groups of SEX;
p1 <- ggplot(mydata, aes(SEX, Param, fill = SEX)) +
  geom_boxplot() +
  labs(x = "Group", y = myLab) +
  stat_summary(fun.y = mean, colour = "blue", geom = "point", shape = 18, size = 2) +
  guides(fill = FALSE) +
  theme_pubr()

# Histogramme Density Plots by SEX;
p2 <- ggplot(mydata, aes(x = Param, fill = SEX)) +
  geom_density(alpha = .5) + guides(fill = FALSE) +
  xlab("") +
  theme_pubr()

# QQ-Plot 2 Groups of SEX;
p3 <- ggplot(mydata) +
  stat_qq(aes(sample = Param, colour = factor(SEX))) +
  guides(colour = "none") +
  theme_pubr()

mydata1 <- subset(mydata, SEX == "Female")
mydata2 <- subset(mydata, SEX == "Male")
pNORM <- shapiro.test(mydata$Param)
pNORM1 <- shapiro.test(mydata1$Param)
pNORM2 <- shapiro.test(mydata2$Param)

# Kruskal test;
p_All <- kruskal.test(Param ~ SEX, data = mydata)

test_res_mat <- matrix(c("Wilcoxon test p",
  "Shapiro-Wilk p (overall)",
  "p (Female)",
  "p (Male)",
  round(p_All$p.value, digits = 7),
  round(pNORM$p.value, digits = 7),
  round(pNORM1$p.value, digits = 7),
  round(pNORM2$p.value, digits = 7)), byrow = FALSE, nrow = 4)

# Print matrix;
p4 <- tableGrob(test_res_mat)

# Grid;
grid.arrange(p1, p2, p3, p4, ncol = 2, nrow = 2)
```

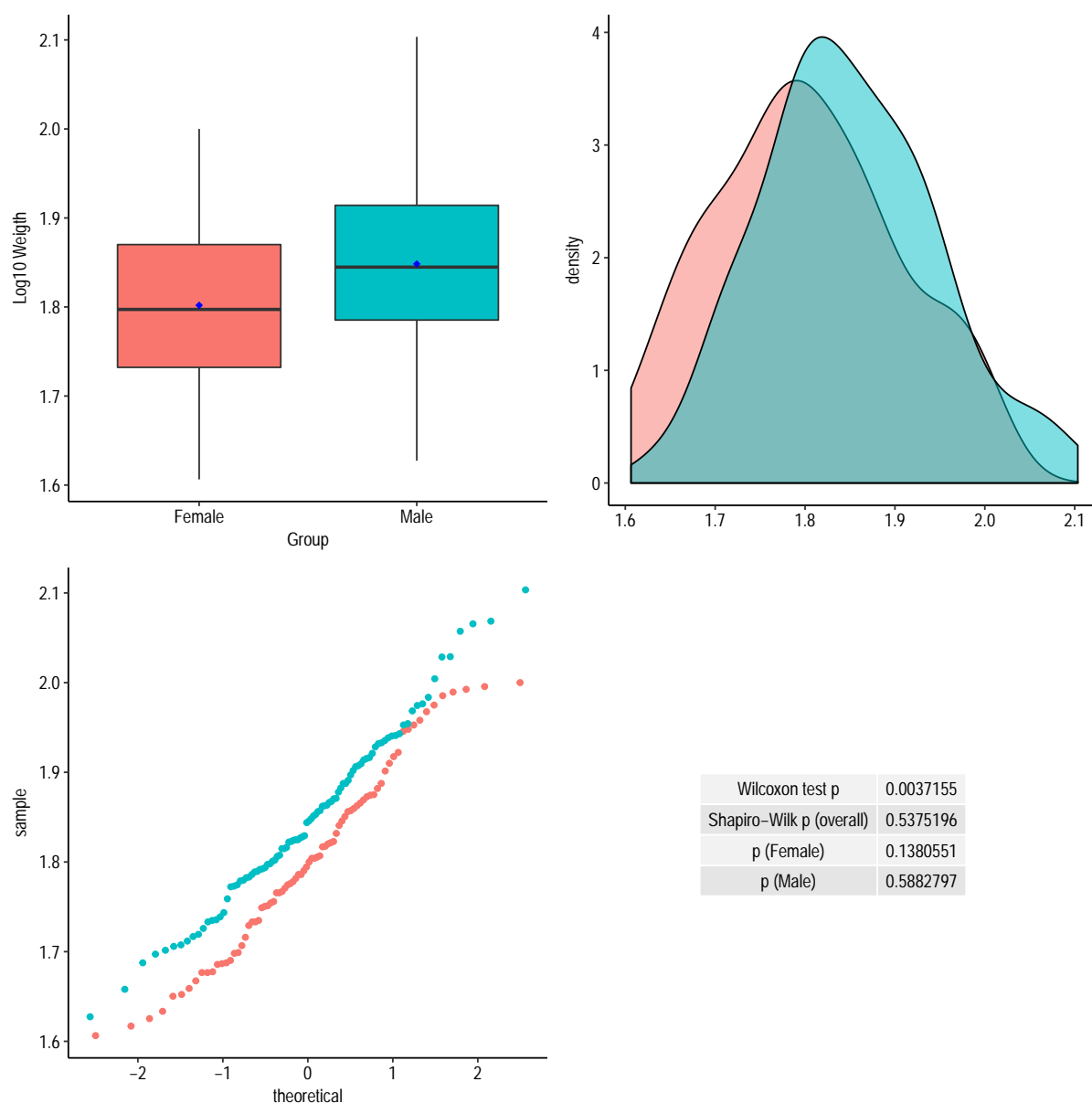


Figure 5: Log10 Weight (kg) at Baseline, by Sex

```
myCaption <- "Geometric Mean +/- 95 CIs: Weight (kg) at Baseline"
```

```
# Enter not transformed Variable Name here;
```

```
LbyGEO(mydata$WEIGHTBL, mydata$SEX)
```

Table 14: Geometric Mean +/- 95 CIs: Weight (kg) at Baseline

	N	Geo.Mean	Median	Min	Max	95LowerCI	95UpperCI
Female	80	63.4	62.7	40	100	60.1	66.8
Male	96	70.5	69.9	42	127	67.4	73.8
ALL	176	67.2	66.3	40	127	64.9	69.6

4.8 Sex at Baseline

```
df_cat <- select(ADSL, SEX) %>%
  mutate(Level = SEX) %>%
  filter(Level != "")
```

```
cap <- "SEX at Baseline - polar chart, bar chart, pie chart"
```

```
# polar chart;
p1 <- ggplot(df_cat, aes(x = Level, fill = Level)) +
  geom_bar() +
  coord_polar() +
  theme_bw() +
  theme(legend.position = "none")

# bar chart;
p2 <- ggplot(df_cat, aes(x = Level, fill = Level)) +
  geom_bar(aes(y = (..count..)/sum(..count..))) +
  scale_y_continuous(labels = scales::percent) +
  labs(y = "Percent") +
  theme_bw() +
  theme(axis.title.x = element_blank(), axis.text.x = element_text(angle = 45, hjust = 1)) +
  theme(legend.position = "none")

# pie chart;
p3 <- ggplot(df_cat, aes(x = factor(1), fill = Level)) +
  geom_bar(width = 1, colour = "black") +
  coord_polar(theta = "y") +
  scale_x_discrete(name = "") +
  scale_y_continuous(name = "") +
  guides(fill = guide_legend(title = NULL)) +
  theme_pubr() +
  theme(legend.text = element_text(angle = 45)) +
  theme(legend.position = "top")

grid.arrange(p1, p2, p3, ncol = 3)
```

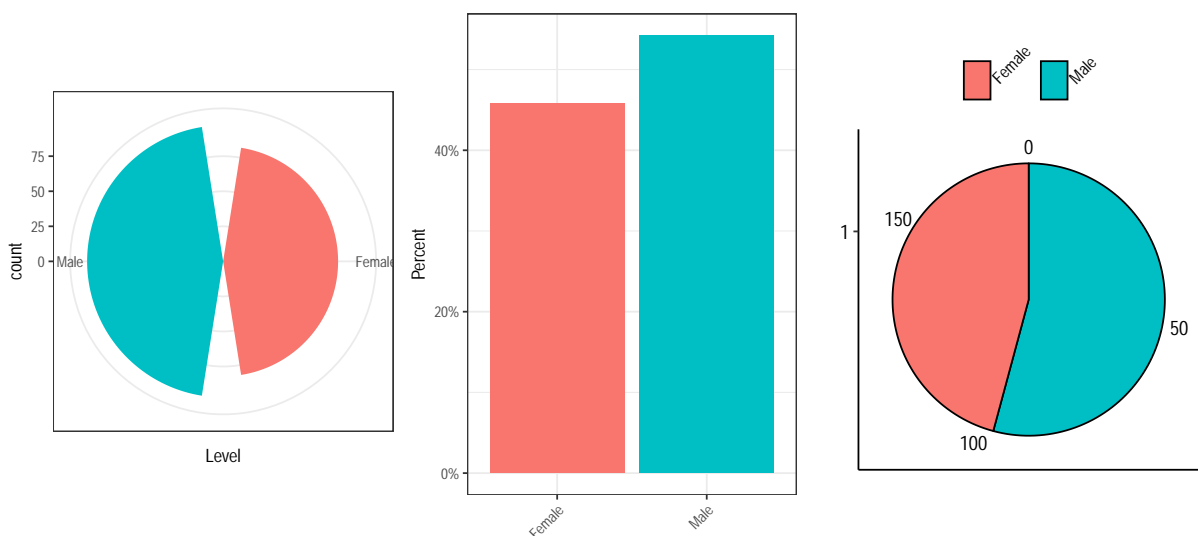


Figure 6: SEX at Baseline - polar chart, bar chart, pie chart

4.9 ECOG at Baseline

```
df_cat <- select(ADSL, ECOGBL) %>%
  mutate(Level = ECOGBL) %>%
  filter(Level != "")
```

```
cap <- "ECOG at Baseline - polar chart, bar chart, pie chart"
```

```
# polar chart;
p1 <- ggplot(df_cat, aes(x = Level, fill = Level)) +
  geom_bar() +
  coord_polar() +
  theme_bw() +
  theme(legend.position = "none")

# bar chart;
p2 <- ggplot(df_cat, aes(x = Level, fill = Level)) +
  geom_bar(aes(y = (..count..)/sum(..count..))) +
  scale_y_continuous(labels = scales::percent) +
  labs(y = "Percent") +
  theme_bw() +
  theme(axis.title.x = element_blank(), axis.text.x = element_text(angle = 45, hjust = 1)) +
  theme(legend.position = "none")

# pie chart;
p3 <- ggplot(df_cat, aes(x = factor(1), fill = Level)) +
  geom_bar(width = 1, colour = "black") +
  coord_polar(theta = "y") +
  scale_x_discrete(name = "") +
  scale_y_continuous(name = "") +
  guides(fill = guide_legend(title = NULL)) +
  theme_pubr() +
  theme(legend.text = element_text(angle = 45)) +
  theme(legend.position = "top")

grid.arrange(p1, p2, p3, ncol = 3)
```

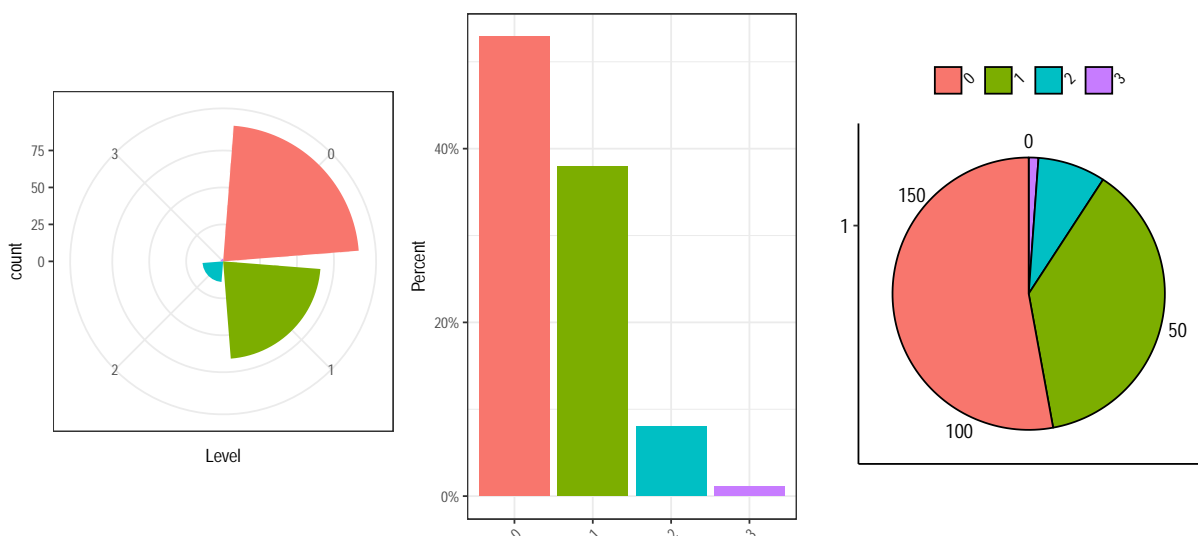


Figure 7: ECOG at Baseline - polar chart, bar chart, pie chart

4.10 ECOG at Baseline, by Age Group (1)

```
cap <- "ECOG Status at Baseline, by Age Group (up to 100\\%) - stacked bar chart"
df1 <- ADSL %>% select(AGEGR1, ECOGBL) %>%
  filter(!is.na(ECOGBL))

df1$ECOG <- factor(df1$ECOG, c("5", "4", "3", "2", "1", "0"), exclude = "")
levels(df1$ECOG) <- c("5", "4", "3", "2", "1", "0")

ggplot(data = df1, aes(x = AGEGR1, y = 1, fill = ECOG)) +
  geom_bar(stat = "identity", position = "fill") +
  labs(x = "Age Group (yrs.)", y = "100 %") +
  theme_pubr()
```

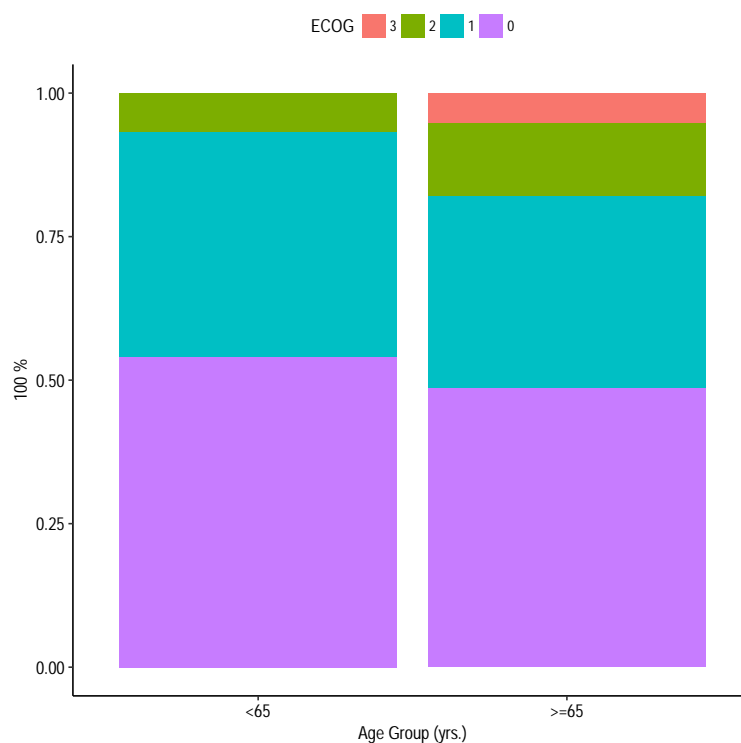


Figure 8: ECOG Status at Baseline, by Age Group (up to 100%) - stacked bar chart

4.11 ECOG at Baseline, by Age Group (2)

```
# Using latex Method \includegraphics{};
pdf("ECOG_STAT_2.pdf")

ggplot(data = df1, aes(x = AGEGR1, fill = ECOG)) +
  geom_bar(position = position_dodge(0.92)) +
  labs(x = "Age Group (yrs.)") +
  theme_pubr()
```

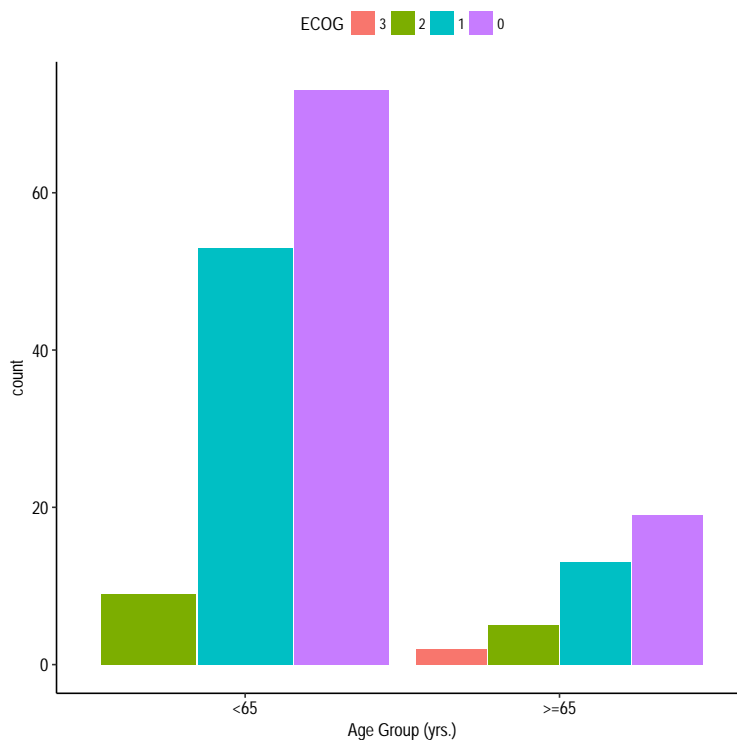
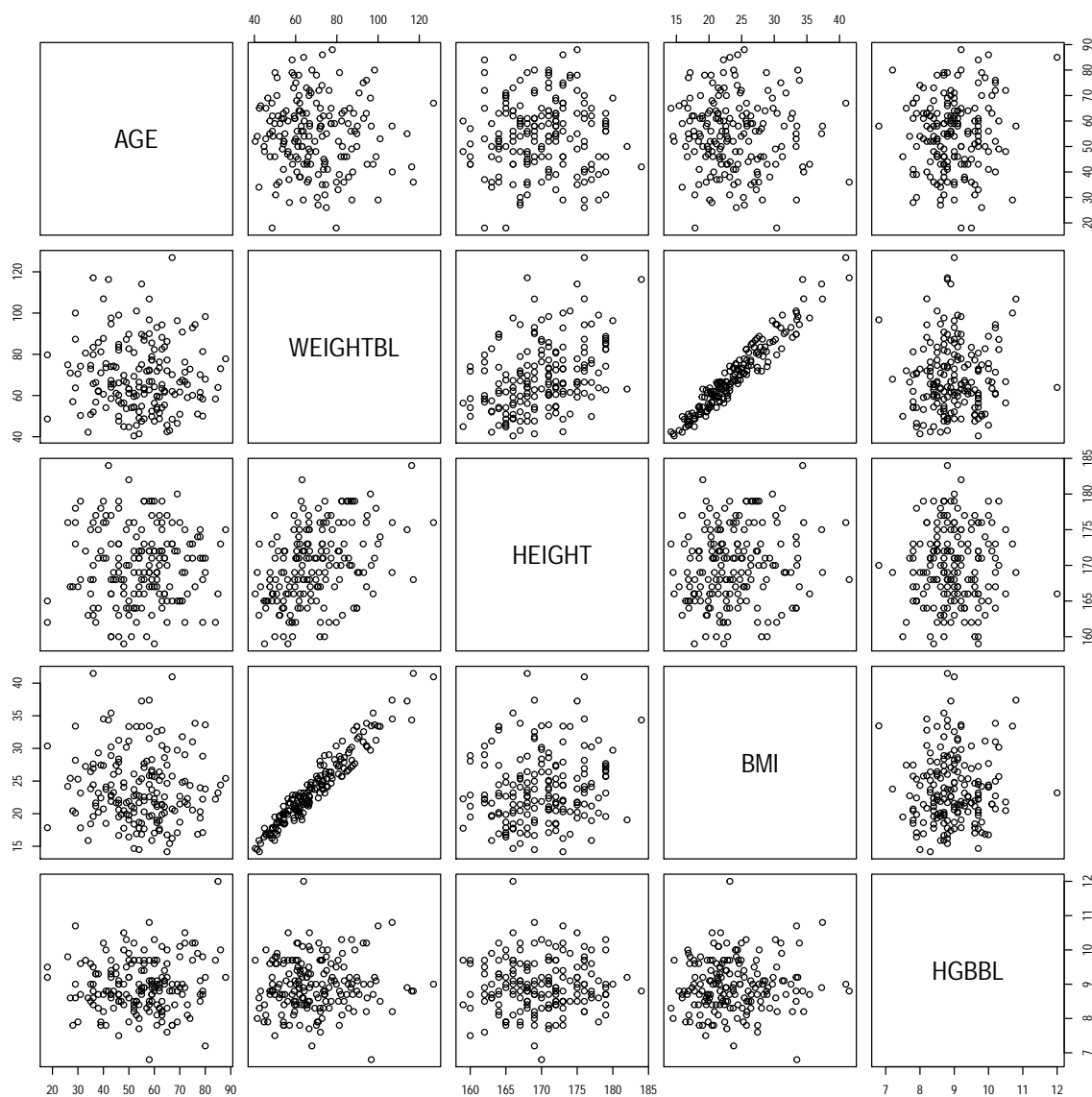


Figure 9: ECOG Status at Baseline, by Age Group - side by side bar chart

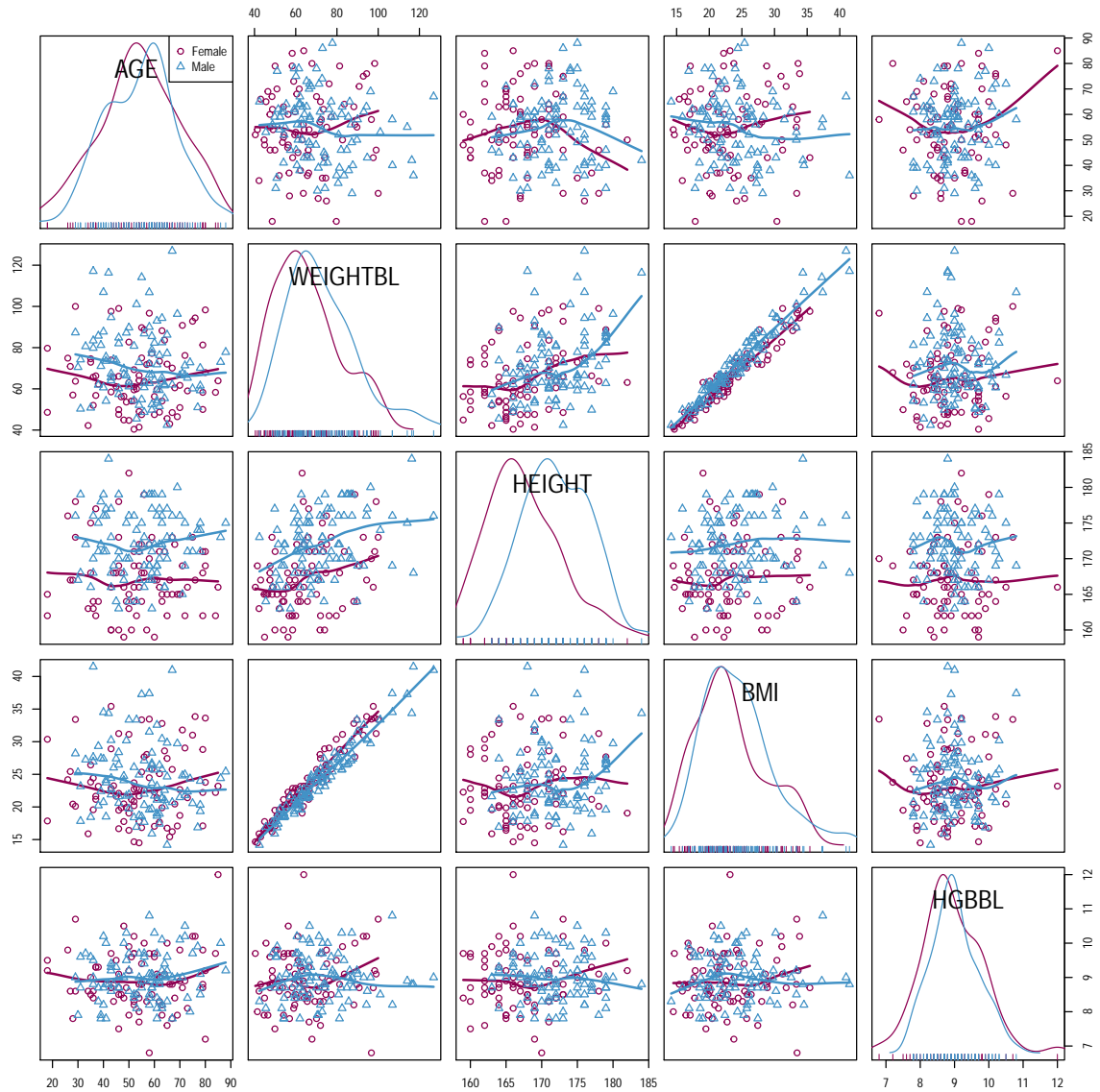
4.12 Scatterplot Matrix, graphics::pairs

```
df1 <- ADSL %>% select(AGE, WEIGHTBL, HEIGHT, BMI, HGBBL)
# Very simple: Scatter plot matrix of all variables in dataframe;
pairs(df1)
```



4.13 Scatterplot Matrix, by Sex, car::scatterplotMatrix

```
df1 <- ADL %>% select(AGE, WEIGHTBL, HEIGHT, BMI, HGBBL, SEX)
scatterplotMatrix(~ AGE + WEIGHTBL + HEIGHT + BMI + HGBBL | SEX,
  by.group = TRUE, reg.line = TRUE, col = c("#8E0152", "#4292C6"), data = df1)
```



4.14 Scatterplot, Weight as a function of Height, by Sex

```
# Using latex Method \includegraphics{};
pdf("HEIGHT_WEIGHT.pdf")

df2 <- ADSL %>% select(SEX, HEIGHT, WEIGHTBL) %>%
  filter(!is.na(HEIGHT) & !is.na(WEIGHTBL) & !is.na(SEX))

ggplot(df2, aes(x = HEIGHT, y = WEIGHTBL, col = SEX)) +
  geom_point(alpha = 0.8) +
  labs(x = "Height cm", y = "Weight kg") +
  stat_smooth(aes(group = SEX), method = "lm", se = T, level = 0.95) +
  scale_color_manual(values = c("#8E0152", "#4292C6")) +
  theme_pubr()
```

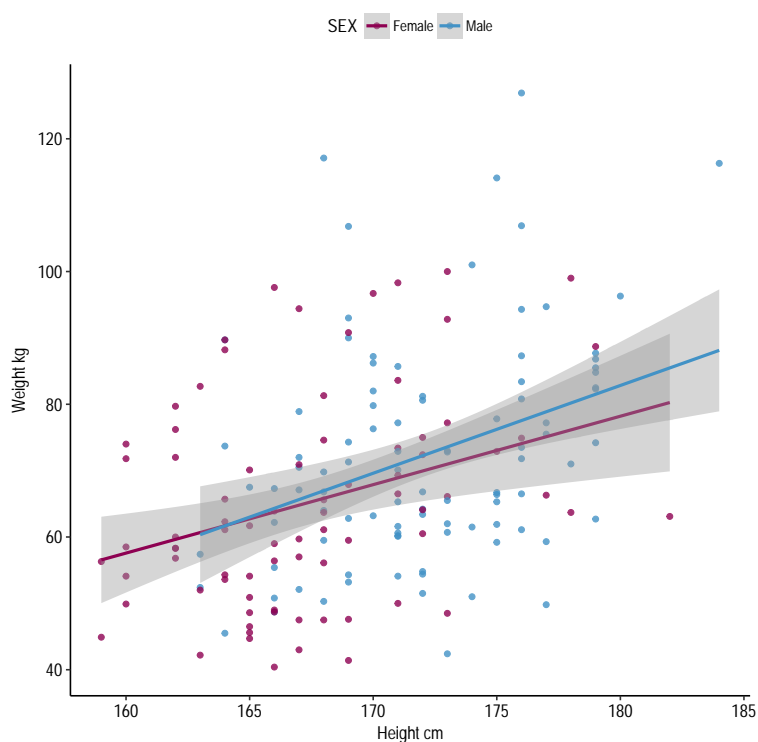


Figure 10: Scatter Plot Height, Weight, by Sex with confid. interval

4.15 Example: Linear Model Log10 Weight - Sex + Age + Height

```
model <- lm(L10WTBL ~ SEX + AGE + HEIGHT, data = ADSL)
cap <- "Linear model Log10 Weight: Sex + Age + Height - latex::xtable(lm)"
```

```
latex(xtable(model), digits = 2, file = "", title = "", here = TRUE, caption = cap,
      label = runif(1))
```

Table 15: Linear model Log10 Weight: Sex + Age + Height - latex::xtable(lm)

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	0.61418	0.2548	2.41	0.0170031
SEXMale	0.01275	0.0159	0.80	0.4243560
AGE	-0.00034	0.0005	-0.69	0.4932872
HEIGHT	0.00721	0.0015	4.77	0.0000039

```
cap <- "Linear model Log10 Weight: Sex + Age + Height - texreg::texreg(lm)"
```

```
texreg(model, caption.above = T, digits = 3, caption = cap, float.pos = "!htpb",
      label = runif(1))
```

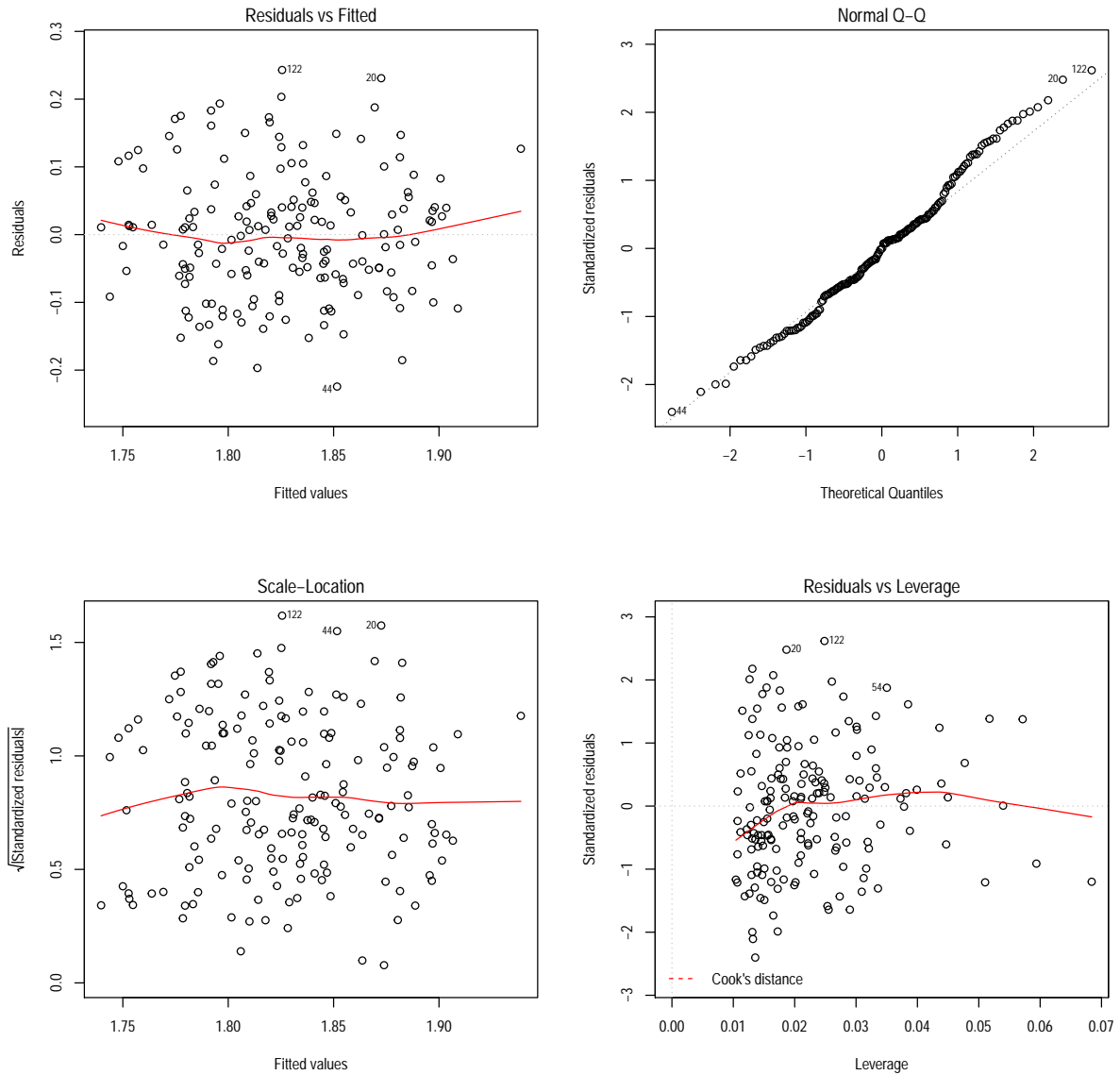
Table 16: Linear model Log10 Weight: Sex + Age + Height - texreg::texreg(lm)

	Model 1
(Intercept)	0.614*
	(0.255)
SEXMale	0.013
	(0.016)
AGE	-0.000
	(0.001)
HEIGHT	0.007***
	(0.002)
R ²	0.165
Adj. R ²	0.150
Num. obs.	176
RMSE	0.094

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

4.16 Example: Linear Model - Diagnostic Plots

```
model <- lm(as.numeric(L10WTBTL) ~ SEX + AGE + HEIGHT, data = ADSL)
par(mfrow = c(2, 2))
plot(model)
```



4.17 Example: ANOVA model with Type I, II, III SS

```
cap <- "ANOVA Type I SS - stats::anova"
aov_1 <- anova(model)

latex(xtable(aov_1), digits = 2, file = "", title = "", here = TRUE, caption = cap,
      label = runif(1))
```

Table 17: ANOVA Type I SS - stats::anova

	Df	Sum Sq	Mean Sq	F value	Pr(>F)
SEX	1	0.0942	0.0942	10.66	0.0013189
AGE	1	0.0046	0.0046	0.52	0.4712297
HEIGHT	1	0.2010	0.2010	22.74	0.0000039
Residuals	172	1.5201	0.0088		

```
cap <- "ANOVA Type II SS - car::Anova"
aov_2 <- Anova(model, type = "II")

latex(xtable(aov_2), digits = 2, file = "", title = "", here = TRUE, caption = cap,
      label = runif(1))
```

Table 18: ANOVA Type II SS - car::Anova

	Sum Sq	Df	F value	Pr(>F)
SEX	0.0057	1	0.64	0.4243560
AGE	0.0042	1	0.47	0.4932872
HEIGHT	0.2010	1	22.74	0.0000039
Residuals	1.5201	172		

```
cap <- "ANOVA Type III SS - car::Anova"
# options(contrasts=c("contr.helmert", "contr.poly")) # like SAS and SPSS (?);
options(contrasts = c("contr.sum", "contr.poly"))
aov_3 <- Anova(model, type = "III")
options(contrasts = c("contr.treatment", "contr.poly")) # default;

latex(xtable(aov_3), digits = 2, file = "", title = "", here = TRUE, caption = cap,
      label = runif(1))
```

Table 19: ANOVA Type III SS - car::Anova

	Sum Sq	Df	F value	Pr(>F)
(Intercept)	0.0513	1	5.81	0.0170031
SEX	0.0057	1	0.64	0.4243560
AGE	0.0042	1	0.47	0.4932872
HEIGHT	0.2010	1	22.74	0.0000039
Residuals	1.5201	172		

5 Overall Survival

5.1 OS Kaplan-Meier Curves +/- 95% CIs

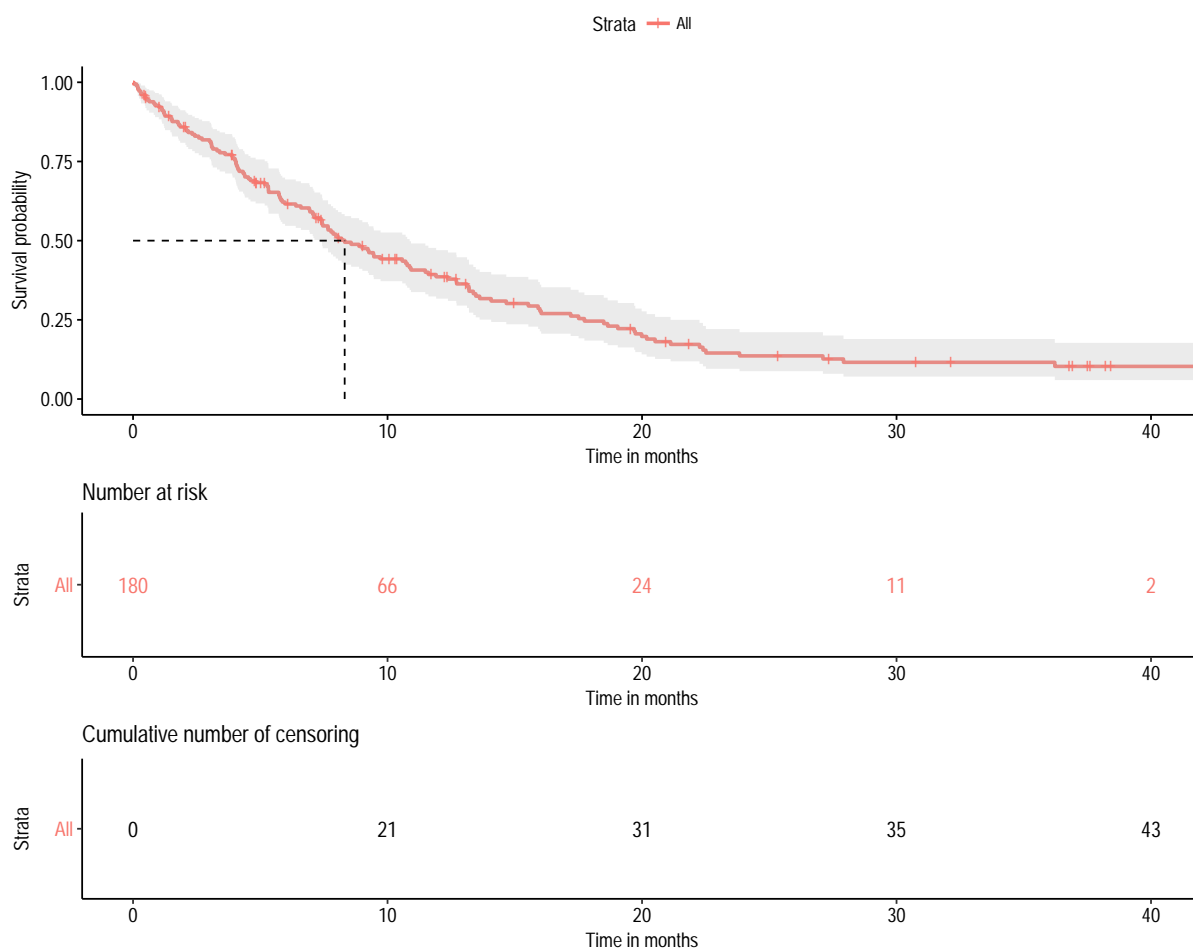


Figure 11: Overall Survival (overall)

```
## Call: survfit(formula = Surv(Time, Status == 0) ~ 1, data = df_KM)
##
##      n events median 0.95LCL 0.95UCL
## 180.00 135.00   8.32   7.36  10.87
## [1] "Kaplan-Meier Estimates"
```

Table 20: Overall Survival KM Quartiles +/- 95% CIs

Category	quantile	lower	upper
25	4.03	3.08	5.28
50	8.32	7.36	10.87
75	17.74	14.07	21.12

5.2 OS Kaplan-Meier Curves, Strata Age 65 yrs.

```
# Generate KM dataset;
df_KM <- ADTTE %>%
  mutate(AGE = AGEGR1, Time = AVAL, Status = CNSR) %>%
  filter(!is.na(AGE))

fit <- survfit(Surv(Time, Status == 0) ~ AGE, data = df_KM)
fit2 <- survdiff(Surv(Time, Status == 0) ~ AGE, rho = 0, data = df_KM)
cap <- "Overall Survival (Strata Age 65 yrs. at Baseline)"
```

```
ggsurvplot(fit, data = df_KM,
  pval = TRUE,
  conf.int = TRUE,
  xlab = "Time in months",
  risk.table = TRUE, # Add risk table
  risk.table.col = "strata", # Change risk table color by groups
  linetype = "strata", # Change line type by groups
  surv.median.line = "hv", # Specify median survival
  cumcensor = TRUE,
  ggtheme = theme_pubr() # Change ggplot2 theme
)
```

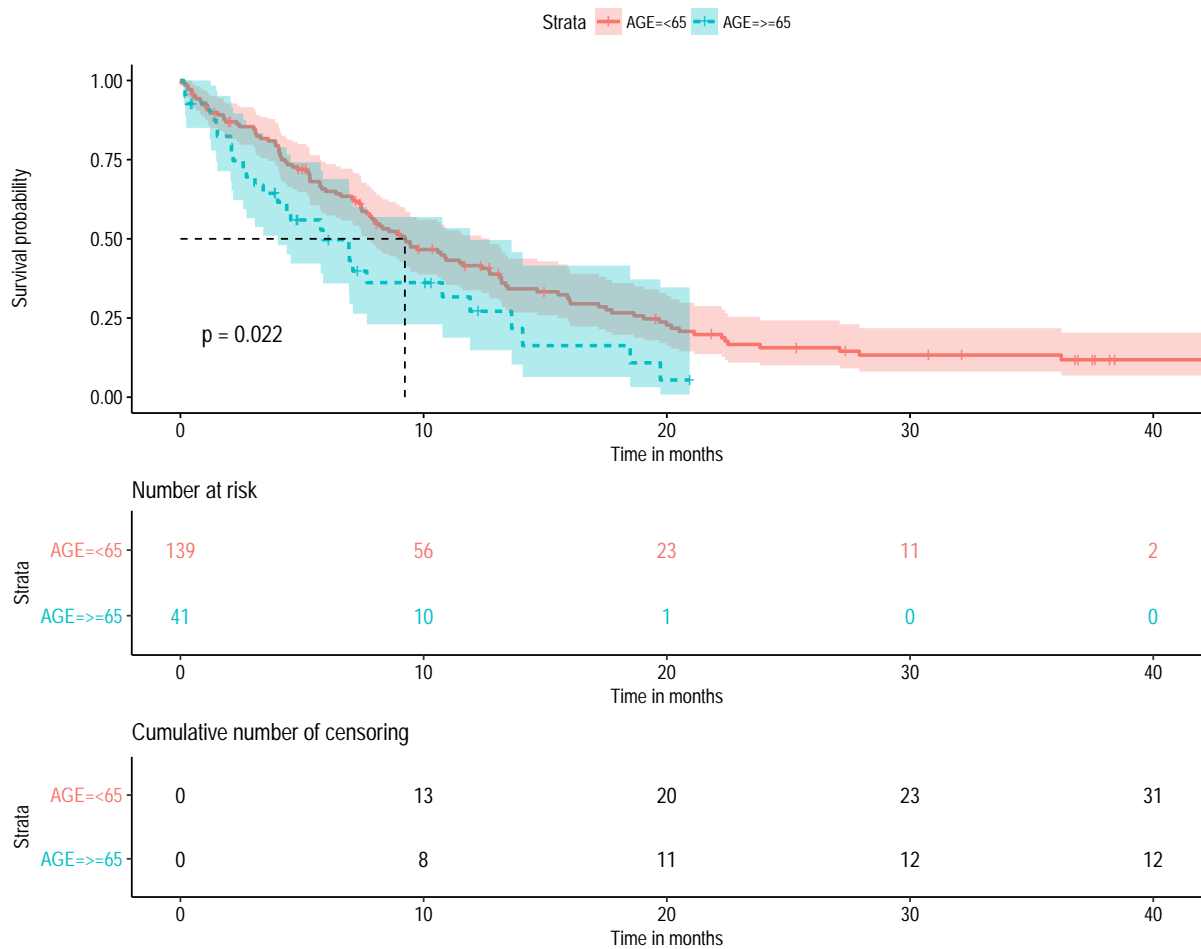


Figure 12: Overall Survival (Strata Age 65 yrs. at Baseline)

```
fit

## Call: survfit(formula = Surv(Time, Status == 0) ~ AGE, data = df_KM)
##
##           n events median 0.95LCL 0.95UCL
## AGE=<65  139    106   9.23    7.78    12.7
## AGE=>=65   41     29   5.86    4.00    11.9

fit2

## Call:
## survdiff(formula = Surv(Time, Status == 0) ~ AGE, data = df_KM,
##          rho = 0)
##
##           N Observed Expected (O-E)^2/E (O-E)^2/V
## AGE=<65  139      106    115.3    0.743    5.23
## AGE=>=65   41       29    19.7    4.336    5.23
##
## Chisq= 5.2 on 1 degrees of freedom, p= 0.0223
```

```
KMquart(fit, "Overall Survival KM Quartiles +/- 95%% CIs (Strata Age 65 yrs.)")
```

Table 21: Overall Survival KM Quartiles +/- 95% CIs (Strata Age 65 yrs.)

Category	quantile.25	quantile.50	quantile.75	lower.25	lower.50	lower.75	upper.25	upper.50	upper.75
AGE=<65	4.17	9.23	19.0	3.62	7.78	15.53	5.80	12.7	23.8
AGE=>=65	2.17	5.86	13.6	1.47	4.00	7.66	4.53	11.9	

6 Laboratory Data

6.1 Hemoglobin over Time

```
df_BOX <- ADLB %>% select(PARAM, PARAMCD, AVISIT, AVISITN, AVAL) %>%
  mutate(Xaxis = AVISIT, Yaxis = AVAL) %>%
  filter(PARAMCD == "HGB")

xLab <- "Visit"
yLab <- "g/dL"
cap <- "Hemoglobin over Time - Boxplot"
```

```
myCaption <- "Summary of Hemoglobin over Time, mean +/- 95\% CIs"
LbyCI(df_BOX$AVAL, df_BOX$AVISIT, size = "small")
```

Table 22: Summary of Hemoglobin over Time, mean +/- 95% CIs

	N	Mean	Median	SD	95LowerCI	95UpperCI	Min	Max
Baseline	180	9.0	8.9	0.75	8.9	9.1	6.8	12.0
Week 8	180	10.8	10.8	1.32	10.6	11.0	6.9	13.5
Week 16	180	11.0	11.0	1.28	10.8	11.2	7.7	14.4
Week 24	180	11.3	11.3	1.10	11.1	11.4	8.2	15.5
ALL	720	10.5	10.5	1.45	10.4	10.6	6.8	15.5

```
myCaption <- "Summary of Hemoglobin over Time, Q1, Q3"
LbyQUART(df_BOX$AVAL, df_BOX$AVISIT, size = "small")
```

Table 23: Summary of Hemoglobin over Time, Q1, Q3

	N	Mean	Median	SD	Q1	Q3	Min	Max
Baseline	180	9.0	8.9	0.75	8.5	9.5	6.8	12.0
Week 8	180	10.8	10.8	1.32	9.8	11.8	6.9	13.5
Week 16	180	11.0	11.0	1.28	10.3	11.9	7.7	14.4
Week 24	180	11.3	11.3	1.10	10.6	11.9	8.2	15.5
ALL	720	10.5	10.5	1.45	9.4	11.5	6.8	15.5

6.2 Hemoglobin over Time, boxplot

```
ggplot(df_BOX, aes(Xaxis, Yaxis, fill = Xaxis)) +  
  geom_boxplot() +  
  labs(x = xLab, y = yLab) +  
  stat_summary(fun.y = mean, colour = "blue", geom = "point", shape = 8, size = 2) +  
  guides(fill = FALSE) +  
  theme_pubr()
```

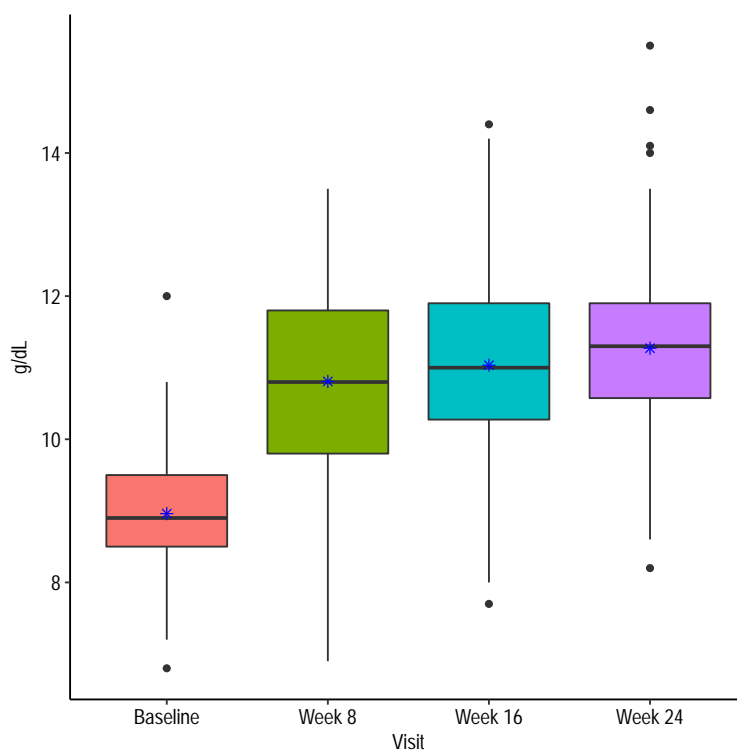


Figure 13: Hemoglobin over Time - Boxplot

6.3 Hemoglobin over Time, jitter

```
cap <- "Hemoglobin over Time, mean +/- SD - jitter"
df1 <- ADLB %>% select(PARAM, PARAMCD, AVISIT, AVISITN, AVAL) %>%
  mutate(Xaxis = AVISIT, Yaxis = AVAL) %>%
  filter(PARAMCD == "HGB")

ggplot(df1, aes(x = Xaxis, y = Yaxis)) +
  stat_summary(fun.y = mean, geom = "point", col = "red", size = 3) +
  geom_point(alpha = 0.2, position = position_jitter(width = 0.12, height = 0.01)) +
  stat_summary(fun.data = mean_sdl, fun.args = list(mult = 1),
    geom = "errorbar", width = 0.2, col = "red") +
  labs(x = "Visit", y = "g/dL") +
  theme_pubr()
```

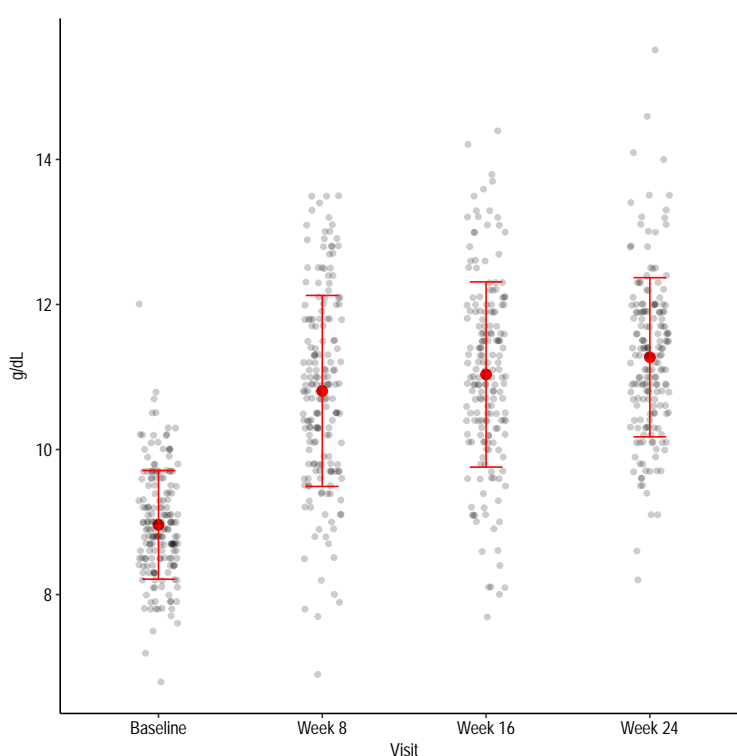


Figure 14: Hemoglobin over Time, mean +/- SD - jitter

6.4 Hemoglobin, Shift Table Baseline vs. Week 24

```
# Subset HGB at W24
df_W24 <- ADLB %>% select(AGEGR1, AVISIT, PARAMCD, BNRIND2, ANRIND2, SHIFT2) %>%
  filter(PARAMCD == "HGB" & AVISIT == "Week 24")
label(df_W24$SHIFT2) <- "Shift BL to Week 24"

s6 <- summary(AGEGR1 ~ SHIFT2, data = df_W24, method = 'reverse',
  overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)

latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,
  prtest = "P", dotchart = FALSE,
  caption = "Hemoglobin, Shift Table Baseline to Week 24", caption.loc = "top",
  middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "HGB_SH24")
```

Table 24: Hemoglobin, Shift Table Baseline to Week 24

	<65		≥65		Combined	
	N = 139		N = 41		N = 180	
Shift BL to Week 24						
Abnormal to Abnormal	90%	$\frac{125}{139}$	78%	$\frac{32}{41}$	87%	$\frac{157}{180}$
Abnormal to Normal	10%	$\frac{14}{139}$	20%	$\frac{8}{41}$	12%	$\frac{22}{180}$
Normal to Normal	0%	$\frac{0}{139}$	2%	$\frac{1}{41}$	1%	$\frac{1}{180}$
Normal to Abnormal	0%	$\frac{0}{139}$	0%	$\frac{0}{41}$	0%	$\frac{0}{180}$

```
tab1 <- table(df_W24$BNRIND2, df_W24$ANRIND2)
tab2 <- as.data.frame(tab1)
tab_sum <- addmargins(tab1)

cap <- "Hemoglobin, Shift Table Baseline to Week 24 (overall)"
latex(tab_sum, file = "", here = TRUE, title = "Baseline/W24",
  caption = cap, label = runif(1))
```

Table 25: Hemoglobin, Shift Table Baseline to Week 24 (overall)

Baseline/W24	Abnormal	Normal	Sum
Abnormal	157	22	179
Normal	0	1	1
Sum	157	23	180

```
mcnemar.test(tab1)
```

McNemar's Chi-squared test with continuity correction

data: tab1 McNemar's chi-squared = 20, df = 1, p-value = 0.000008

6.5 Hemoglobin, Shift Table Baseline vs. Week 24

```
p1 <- ggplot(tab2, aes(Var1, Var2)) +  
  geom_point(aes(size = Freq), colour = "#9999FF") +  
  scale_x_discrete() +  
  geom_text(aes(label = Freq)) +  
  labs(x = "Baseline", y = "Week 24") +  
  # scale_size_continuous(range = c(5, 20), guide = FALSE) + # hide legend;  
  scale_size_continuous(range = c(5, 20)) +  
  theme_bw()
```

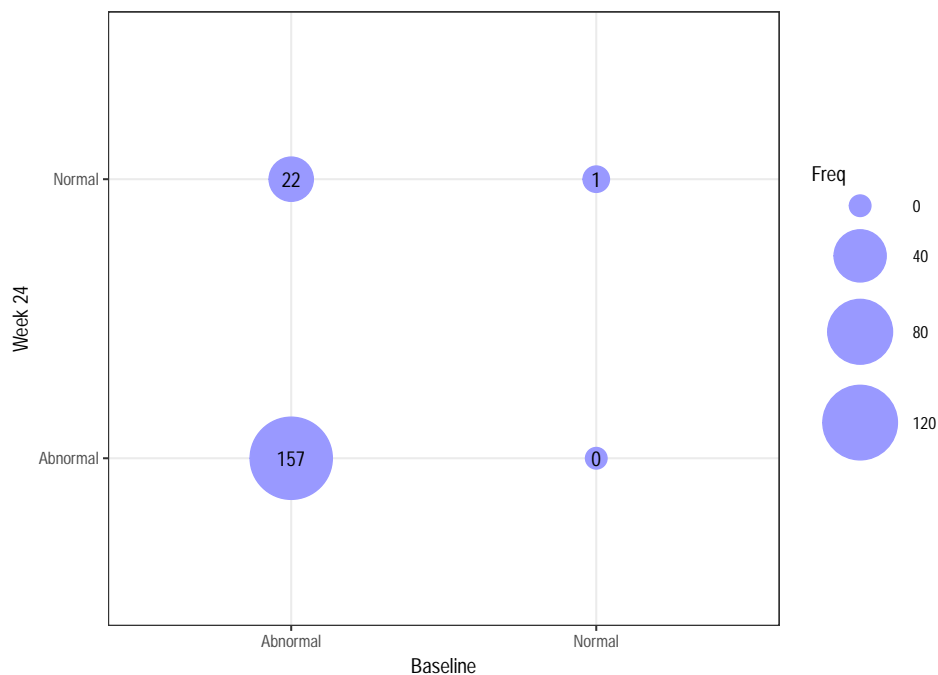


Figure 15: Hemoglobin, Shift Table Baseline to Week 24

6.6 WBC over Time (no data imputation, LOCF)

Table 26: Summary of WBC over Time, mean +/- 95% CIs (no data imputation)

	N	Mean	Median	SD	95LowerCI	95UpperCI	Min	Max
Baseline	180	5.0	4.9	2.77	4.6	5.4	0.1	13.2
Week 8	145	6.2	6.2	2.93	5.7	6.6	0.2	13.1
Week 16	148	6.2	6.4	2.98	5.7	6.7	0.2	13.3
Week 24	140	6.9	7.0	2.59	6.4	7.3	0.2	14.1
ALL	613	6.0	6.0	2.90	5.7	6.2	0.1	14.1

Table 27: Summary of WBC over Time, mean +/- 95% CIs (LOCF)

	N	Mean	Median	SD	95LowerCI	95UpperCI	Min	Max
Baseline	180	5.0	4.9	2.77	4.6	5.4	0.1	13.2
Week 8	180	5.8	5.8	3.01	5.4	6.3	0.1	13.2
Week 16	180	6.1	6.3	2.96	5.6	6.5	0.2	13.3
Week 24	180	6.6	6.7	2.77	6.2	7.0	0.2	14.1
ALL	720	5.9	5.9	2.94	5.6	6.1	0.1	14.1

Table 28: Summary of WBC over Time, Q1, Q3 (no data imputation)

	N	Mean	Median	SD	Q1	Q3	Min	Max
Baseline	180	5.0	4.9	2.77	3.0	7.0	0.1	13.2
Week 8	145	6.2	6.2	2.93	4.0	8.4	0.2	13.1
Week 16	148	6.2	6.4	2.98	4.1	8.1	0.2	13.3
Week 24	140	6.9	7.0	2.59	5.1	8.7	0.2	14.1
ALL	613	6.0	6.0	2.90	4.0	8.1	0.1	14.1

Table 29: Summary of WBC over Time, Q1, Q3 (LOCF)

	N	Mean	Median	SD	Q1	Q3	Min	Max
Baseline	180	5.0	4.9	2.77	3.0	7.0	0.1	13.2
Week 8	180	5.8	5.8	3.01	3.6	8.1	0.1	13.2
Week 16	180	6.1	6.3	2.96	4.0	8.0	0.2	13.3
Week 24	180	6.6	6.7	2.77	4.7	8.6	0.2	14.1
ALL	720	5.9	5.9	2.94	3.8	8.0	0.1	14.1

6.7 WBC over Time, boxplots

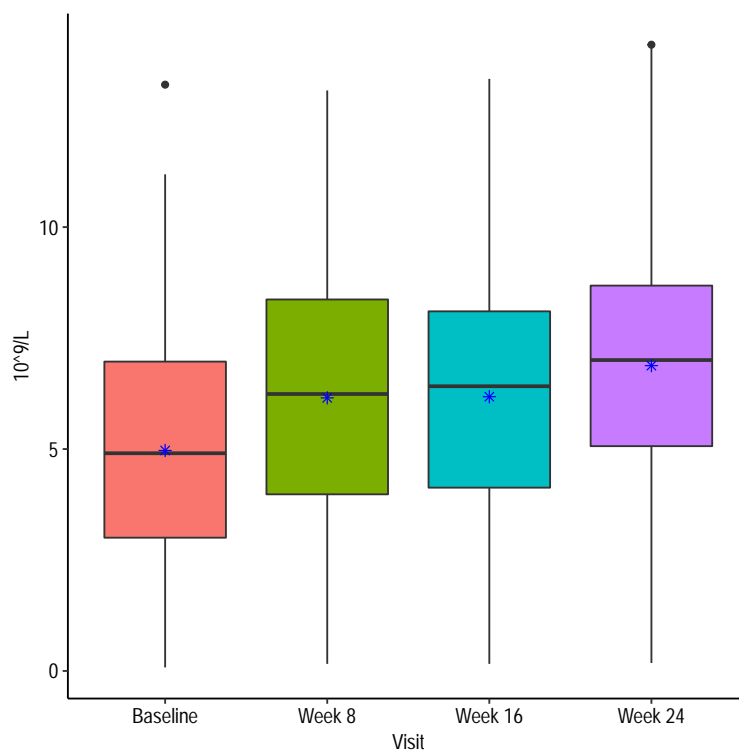


Figure 16: WBC over Time - Boxplot (no data imputation)

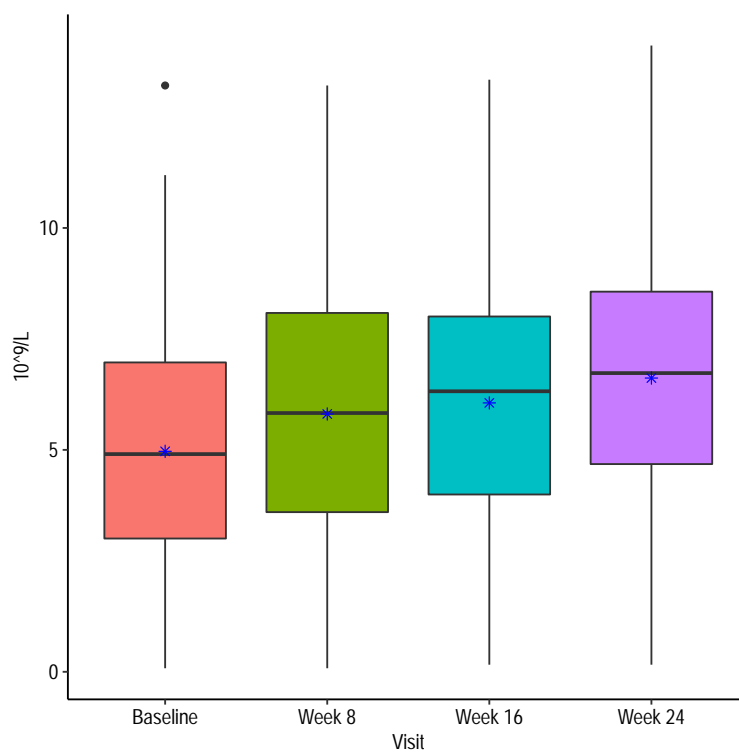


Figure 17: WBC over Time - Boxplot (LOCF)

6.8 WBC, Shift Table Baseline vs. Week 24 (no data imputation)

Table 30: WBC, Shift Table Baseline to Week 24 (no data imputation)

	<65		≥65		Combined	
	N = 106		N = 34		N = 140	
Shift BL to Week 24						
Low to Low	8%	$\frac{8}{106}$	3%	$\frac{1}{34}$	6%	$\frac{9}{140}$
Low to Normal	28%	$\frac{30}{106}$	21%	$\frac{7}{34}$	26%	$\frac{37}{140}$
Low to High	2%	$\frac{2}{106}$	3%	$\frac{1}{34}$	2%	$\frac{3}{140}$
Normal to Low	8%	$\frac{8}{106}$	0%	$\frac{0}{34}$	6%	$\frac{8}{140}$
Normal to Normal	45%	$\frac{48}{106}$	62%	$\frac{21}{34}$	49%	$\frac{69}{140}$
Normal to High	6%	$\frac{6}{106}$	6%	$\frac{2}{34}$	6%	$\frac{8}{140}$
High to Low	1%	$\frac{1}{106}$	0%	$\frac{0}{34}$	1%	$\frac{1}{140}$
High to Normal	2%	$\frac{2}{106}$	6%	$\frac{2}{34}$	3%	$\frac{4}{140}$
High to High	1%	$\frac{1}{106}$	0%	$\frac{0}{34}$	1%	$\frac{1}{140}$

Table 31: WBC, Shift Table Baseline to Week 24 (no data imputation)

Baseline/W24	Low	Normal	High
Low	9	37	3
Normal	8	69	8
High	1	4	1

McNemar's Chi-squared test

data: tab1 McNemar's chi-squared = 20, df = 3, p-value = 0.0001

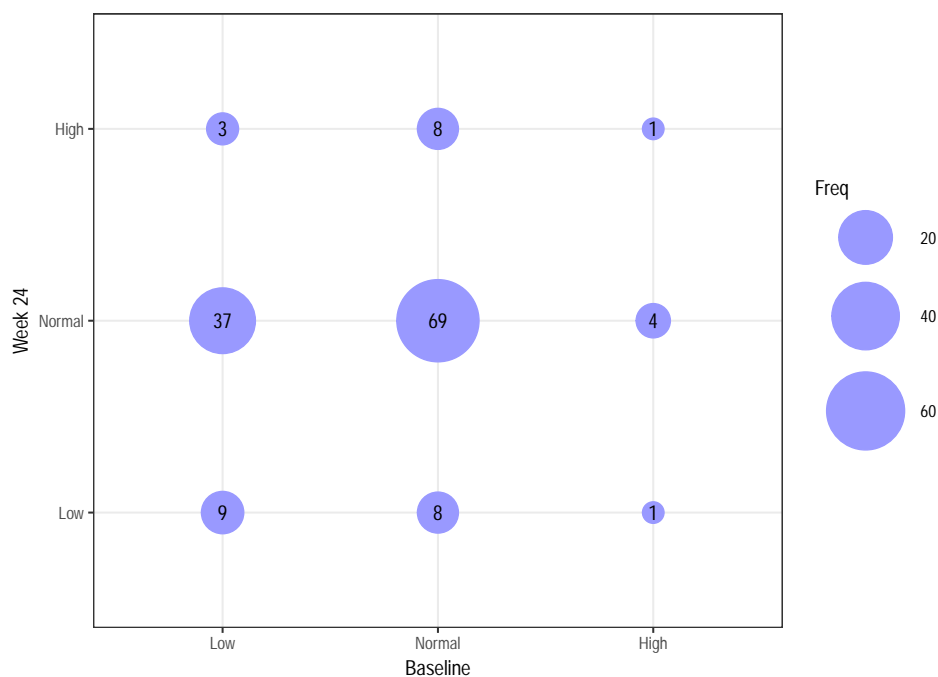


Figure 18: WBC, Shift Table Baseline to Week 24 (no data imputation)

7 Tumor Response

Table 32: Objective Tumor Response Rate - (SD, PD, Missing counted as Non Responder)

	<65		≥65		Combined	P-value
	N = 139		N = 41		N = 180	
Objective Tumor Response Rate						0.012
Responder	54%	$\frac{75}{139}$	32%	$\frac{13}{41}$	49%	$\frac{88}{180}$
Non Responder	46%	$\frac{64}{139}$	68%	$\frac{28}{41}$	51%	$\frac{92}{180}$

Test used:Pearson test

```
ADRS1$AVALC2 <- ADRS1$AVALC
label(ADRS1$AVALC2) <- "Best Overall Response"

s6 <- summary(AGEGR1 ~ AVALC2, data = ADRS1, method = 'reverse',
              overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)

latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,
      prtest = "P", dotchart = FALSE,
      caption = "Best Overall Response", caption.loc = "top",
      middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "RESP2")
```

Table 33: Best Overall Response

	<65		≥65		Combined	
	N = 139		N = 41		N = 180	
Best Overall Response						
Complete Response	14%	$\frac{20}{139}$	5%	$\frac{2}{41}$	12%	$\frac{22}{180}$
Partial Response	40%	$\frac{55}{139}$	27%	$\frac{11}{41}$	37%	$\frac{66}{180}$
Stable Disease	33%	$\frac{46}{139}$	44%	$\frac{18}{41}$	36%	$\frac{64}{180}$
Progressive Disease	10%	$\frac{14}{139}$	20%	$\frac{8}{41}$	12%	$\frac{22}{180}$
Missing	3%	$\frac{4}{139}$	5%	$\frac{2}{41}$	3%	$\frac{6}{180}$

```
BiFreqCI(ADRS2$AVALC2, cap = "Objective Tumor Response Rate (95%% Wilson Score CIs w/o cont. corr.)")
```

Table 34: Objective Tumor Response Rate (95% Wilson Score CIs w/o cont. corr.)

95% Wilson CIs	EVENT	N	PointEst	Lower	Upper
Responder	88	180	48.9	41.7	56.1
Non Responder	92	180	51.1	43.9	58.3

```
BiFreqCI(ADRS1$AVALC2, cap = "Best Overall Response (95%% Wilson Score Interval w/o cont. corr.)")
```

Table 35: Best Overall Response (95% Wilson Score Interval w/o cont. corr.)

95% Wilson CIs	EVENT	N	PointEst	Lower	Upper
Complete Response	22	180	12.2	8.2	17.8
Partial Response	66	180	36.7	30.0	43.9
Stable Disease	64	180	35.6	28.9	42.8
Progressive Disease	22	180	12.2	8.2	17.8
Missing	6	180	3.3	1.5	7.1


```
# Example: VAR_myset will not printed because results="hide";
VAR_myset
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% CREATE TITLE PAGE;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

<<TITEL, child='00_TITLE_PAGE.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% CREATE TABLE OF CONTENTS;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

\setcounter{page}{2}

\tableofcontents

\listoftables

\listoffigures

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% ABBREVIATIONS;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

<<ABBREVIATIONS, child='00_ABBREVIATIONS.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% GLOBAL OPTIONS;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

<<set-options, echo=FALSE>>=
# Options
options(replace.assign = TRUE, width = 80)

# disabling scientific notation in R;
options(scipen = 999)

# Set digit option;
options(digits = 2)

pdf.options(family = "Helvetica-Narrow")

# Define knitr chunk options;
opts_chunk$set(fig.width = 7,
               fig.height = 7,
               out.width = '10cm',
               fig.pos = 'H',
               fig.align = 'center',
               fig.path = './figure/Plot-',
               fig.keep = 'all',
               cache = FALSE,
               echo = FALSE,           # FALSE: no output of R code;
               message = FALSE,       # FALSE: no output of R messages;
               warning = FALSE,       # FALSE: no output of warnings;
               dev = 'pdf')
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% READ SAS XPT FILES WITH USER-DEFINED FORMATS;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

<<external-code>>=
```

```
source("impsas_xpt.R")
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
Read R Chunks and user defined R Functions;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

<<read-external, warning=TRUE>>=
### Read chunks;
read_chunk("00_chunks.R")

### Read R functions;
source("00_r_functions.R")
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
ANALYSIS PROGRAMS - BEGIN;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Include R program 01_DEMOG.Rnw;

<<DEMOG, child='01_DEMOG.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Include R program 01_DEMO_FIG.Rnw;

<<DEMOG_FIG, child='01_DEMOG_FIG.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Include R program 01_LINEAR_MODEL.Rnw;

<<LINEAR_MODEL, child='01_LINEAR_MODEL.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Include R program 02_KAPLAN.Rnw;

<<KAPLAN, child='02_KAPLAN.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Include R program 03_LAB_HGB.Rnw;

<<LABEXHGB, child='03_LAB_HGB.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Include R program 03_LAB_WBC.Rnw;

<<LABEXWBC, child='03_LAB_WBC.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%% Include R program 04_RESPONSE.Rnw;

<<RESPONSE, child='04_RESPONSE.Rnw'>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
ANALYSIS PROGRAMS - END;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
APPENDIX INCLUDE ALL KNITR CODE;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage

\begin{appendix}
```

```
\section{All Code for Generating this Report} \label{AllCode}
\subsection{Master Rnw File ALEA01.Rnw}
\fvset{fontsize=\small} % fancyvrb option;
\VerbatimInput{ALEA01.Rnw}

\clearpage
\newpage
\subsection{File 00\_TITLE\_PAGE.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{00\_TITLE\_PAGE.Rnw}

\clearpage
\newpage
\subsection{File 00\_ABBREVIATIONS.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{00\_ABBREVIATIONS.Rnw}

\clearpage
\newpage
\subsection{File impsas\_xpt.R}
Following \emph{.R script file} was generated automatically
with \href{https://github.com/clindocu/sasxpt-r}{clindocu/sasxpt-r:}

\lstinputlisting{impsas_xpt.R} % input file with autom. line breaks;

\clearpage
\newpage
\subsection{File 00\_chunks.R}
\fvset{fontsize=\small}
\VerbatimInput{00\_chunks.R}

\clearpage
\newpage
\subsection{File 00\_r\_functions.R}
\fvset{fontsize=\small}
\VerbatimInput{00\_r\_functions.R}

\clearpage
\newpage
\subsection{File 01\_DEMOG.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{01\_DEMOG.Rnw}

\clearpage
\newpage
\subsection{File 01\_DEMOG\_FIG.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{01\_DEMOG\_FIG.Rnw}

\clearpage
\newpage
\subsection{File 01\_LINEAR\_MODEL.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{01\_LINEAR\_MODEL.Rnw}

\clearpage
\newpage
\subsection{File 02\_KAPLAN.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{02\_KAPLAN.Rnw}

\clearpage
\newpage
\subsection{File 03\_LAB\_HGB.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{03\_LAB\_HGB.Rnw}
```

```
\clearpage
\newpage
\subsection{File 03\_LAB\_WBC.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{03_LAB_WBC.Rnw}
```

```
\clearpage
\newpage
\subsection{File 04\_RESPONSE.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{04_RESPONSE.Rnw}
```

```
\clearpage
\newpage
\subsection{File 99\_HISTORY.Rnw}
\fvset{fontsize=\small}
\VerbatimInput{99_HISTORY.Rnw}
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%% APPENDIX VERSION HISTORY;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
<<HISTORY, child='99_HISTORY.Rnw'>=
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%% APPENDIX TECHNICAL DETAILS;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage
\newpage
```

```
\section{Technical Details}
```

```
\tiny{
% \subsection{System Details}
% <<echo=TRUE>>=
% Sys.info()
% @
\subsection{R Version}
<<echo=TRUE>>=
  R.Version()
@
\subsection{Active R packages}
<<echo=TRUE>>=
  sessionInfo()
@
\subsection{PDF \LaTeX{}}
<<echo=TRUE>>=
  Sys.which("pdflatex")
@
\subsection{System Time}
<<echo=TRUE>>=
  Sys.time()
@
}
```

```
\end{appendix}
```

```
\end{document}
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%% END DOCUMENT;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

A.2 File 00_TITLE_PAGE.Rnw

```
\begin{titlepage}
%%%% HEADER - BEGIN
\fancyhead[L]{\tiny{ALEA Study No.: ALEA01 \\\n
Sponsor Study No.: ABC-NIS-01 \\\n
Version 1 from: \today \\\n
Generated by: Alea Iacta}}
\fancyhead[C]{Non-Interventional Study ABC-NIS-01 \\\n
Statistical Tables, Listings and Figures \\\n
\tiny{\Sexpr{VAR_myset}}}

\fancyhead[R]{\includegraphics[scale=0.5]{logo.jpg}}
\thispagestyle{fancy}
\cfoot{}
%%%% HEADER - END
\vspace*{2cm}
%%%% CENTER - BEGIN;
\begin{center}\large

{\huge
ABC Study: ABC-NIS-01}

\vspace*{0.5cm}

{\huge
A prospective, multicenter, non-interventional, observational study to evaluate
safety and effectiveness of WonderDrug\texttrademark $ $ in subjects with XYZ}

\vspace*{2cm}

%%% POPULATION;
{\LARGE \Sexpr{VAR_myset}} \\\n
\vspace*{1cm}

%%% ALEA STUDY NO, SPONSOR;
\begin{flushleft}
\textbf{ALEA Study No.:} \\\n
ALEA01 \\\n [.3cm]

\textbf{Sponsor Name:} \\\n
ABC \\\n [.3cm]

\textbf{Sponsor Study No:} \\\n
ABC-NIS-01 \\\n
\end{flushleft}

%%% BELOW;
\vfill

%%% ON LEFT SIDE;
\begin{flushleft}
\textbf{Statistical Analysis:} \\\n
alea iacta \\\n
Version 1 from: \today

\vspace*{.5cm}
\small
E-mail: clindocu@aleaiacta.eu \\\n
\end{flushleft}

\end{center}
%%%% CENTER - END;
\end{titlepage}
```

A.3 File 00_ABBREVIATIONS.Rnw

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% ABBREVIATIONS - BEGIN  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
  
\clearpage  
\newpage  
\section[List of Abbreviations and Definition of Terms]  
  
\begin{longtable}[ht]{p{2.5cm} p {11.8cm}}  
  \toprule \\  
  \textbf{Abbreviation or specialist term} & \textbf{Explanation} \\  
  \bottomrule \\  
ADaM & Analysis Data Model \\  
BL & Baseline \\  
CDISC & \href{https://www.cdisc.org}{Clinical Data Interchange Standards Consortium} \\  
CI & Confidence Interval \\  
FAS & Full Analysis Set \\  
HGB & Hemoglobin \\  
KM & Kaplan-Meier \\  
knitr & \href{https://github.com/yihui/knitr}{knitr: A General-Purpose Package for Dynamic Report Generation in R, Yihui Xie, 2017} \\  
LOCF & Last Observation Carried Forward \\  
N & Number of observations \\  
NA & Not Available \\  
OS & Overall Survival \\  
Q1 & Lower quartile \\  
Q3 & Upper quartile \\  
R & \href{https://www.r-project.org/}{R Foundation for Statistical Computing, Vienna, Austria} \\  
RStudio & \href{https://github.com/rstudio/rstudio}{RStudio: Integrated Development Environment for R. RStudio, Inc., Boston, MA} \\  
SAP & Statistical Analysis Plan \\  
SAS & \href{https://www.sas.com}{SAS Institute Inc., Cary, NC, USA.} \\  
SD & Standard Deviation \\  
SS & Sums of Squares \\  
Tex Live & \href{http://www.tug.org/texlive}{Tex Live, Tex Users Group, Portland, OR, USA} \\  
USUBJID & Unique Subject Identifier \\  
WBC & White Blood Cell \\  
\hline  
  
\end{longtable}  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% ABBREVIATIONS - END  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```


A.4 File impsas_xpt.R

Following *.R script* file was generated automatically with [clindocu/sasxpt-r](#):

```
##### Set R working directory
setwd("C:/Temp/ALEA01/")
##### Use install.packages("knitr"), install.packages("foreign"), etc. if necessary
library(knitr)
library(foreign)
##### tidyverse: ggplot2, tibble, tidyr, readr, purrr, dplyr
library(tidyverse)
library(Hmisc)
library(xtable)
library(gridExtra)
library(survminer)
library(ggthemes)
library(reporttools)
library(texreg)
library(car)
##### Read all .xpt files from working directory. Derive date/times. Set factor, levels, labels.
ADLB <- read.xport("ADLB.xpt")
ADRS1 <- read.xport("ADRS1.xpt")
ADRS2 <- read.xport("ADRS2.xpt")
ADSL <- read.xport("ADSL.xpt")
ADTTE <- read.xport("ADTTE.xpt")
label(ADLB$STUDYID) <- "Study Identifier"
label(ADLB$USUBJID) <- "Unique Subject Identifier"
label(ADLB$ASEQ) <- "Sequence Number"
ADLB$SEX <- factor(ADLB$SEX, c("F", "M"), exclude = "")
levels(ADLB$SEX) <- c("Female", "Male")
label(ADLB$SEX) <- "Sex"
label(ADLB$PARAM) <- "Parameter"
label(ADLB$PARAMCD) <- "Parameter Code"
ADLB$AVISIT <- factor(ADLB$AVISIT, c("BASELINE", "WEEK 8", "WEEK 16", "WEEK 24"), exclude = "")
levels(ADLB$AVISIT) <- c("Baseline", "Week 8", "Week 16", "Week 24")
label(ADLB$AVISIT) <- "Analysis Visit"
label(ADLB$AVISITN) <- "Analysis Visit (N)"
label(ADLB$AVAL) <- "Analysis value"
label(ADLB$BASE) <- "Baseline Value"
label(ADLB$CHG) <- "Change from Baseline"
label(ADLB$PCHG) <- "Percent Change from Baseline"
label(ADLB$DTYPE) <- "Derivation Type"
label(ADLB$ANRLO) <- "Analysis Normal Range Lower Limit"
label(ADLB$ANRHI) <- "Analysis Normal Range Upper Limit"
ADLB$ANRIND <- factor(ADLB$ANRIND, c("LOW", "NORMAL", "HIGH"), exclude = "")
levels(ADLB$ANRIND) <- c("Low", "Normal", "High")
label(ADLB$ANRIND) <- "Analysis Reference Range Indicator"
ADLB$ABLFL <- factor(ADLB$ABLFL, c("Y"), exclude = "")
levels(ADLB$ABLFL) <- c("Yes")
label(ADLB$ABLFL) <- "Baseline Record Flag"
ADLB$BNRIND <- factor(ADLB$BNRIND, c("LOW", "NORMAL", "HIGH"), exclude = "")
levels(ADLB$BNRIND) <- c("Low", "Normal", "High")
label(ADLB$BNRIND) <- "Baseline Reference Range Indicator"
ADLB$SHIFT1 <- factor(ADLB$SHIFT1, c("LOW to LOW", "LOW to NORMAL", "LOW to HIGH", "NORMAL to LOW", "NORMAL to NORMAL", "NORMAL to HIGH", "HIGH to LOW", "HIGH to NORMAL", "HIGH to HIGH"), exclude = "")
levels(ADLB$SHIFT1) <- c("Low to Low", "Low to Normal", "Low to High", "Normal to Low", "Normal to Normal", "Normal to High", "High to Low", "High to Normal", "High to High")
label(ADLB$SHIFT1) <- "Shift 1"
ADLB$ANRIND2 <- factor(ADLB$ANRIND2, c("ABNORMAL", "NORMAL"), exclude = "")
levels(ADLB$ANRIND2) <- c("Abnormal", "Normal")
label(ADLB$ANRIND2) <- "Analysis Reference Range Indicator 2"
```

```
ADLB$BNRIND2 <- factor(ADLB$BNRIND2, c("ABNORMAL", "NORMAL"), exclude = "")
levels(ADLB$BNRIND2) <- c("Abnormal", "Normal")
label(ADLB$BNRIND2) <- "Baseline Reference Range Indicator 2"
ADLB$SHIFT2 <- factor(ADLB$SHIFT2, c("ABNORMAL to ABNORMAL", "ABNORMAL to NORMAL", "NORMAL
to NORMAL", "NORMAL to ABNORMAL"), exclude = "")
levels(ADLB$SHIFT2) <- c("Abnormal to Abnormal", "Abnormal to Normal", "Normal to Normal", "Normal to
Abnormal")
label(ADLB$SHIFT2) <- "Shift 2"
label(ADLB$AGEGR1) <- "Pooled Age Group 1"
label(ADRS1$STUDYID) <- "Study Identifier"
label(ADRS1$USUBJID) <- "Unique Subject Identifier"
label(ADRS1$PARAMCD) <- "Parameter Code"
label(ADRS1$PARAM) <- "Parameter"
label(ADRS1$AVAL) <- "Analysis Value"
ADRS1$AVALC <- factor(ADRS1$AVALC, c("COMPLETE RESPONSE", "PARTIAL RESPONSE", "STABLE DISEASE
", "PROGRESSIVE DISEASE", "MISSING"), exclude = "")
levels(ADRS1$AVALC) <- c("Complete Response", "Partial Response", "Stable Disease", "Progressive Disease", "
Missing")
label(ADRS1$AVALC) <- "Analysis Value (C)"
label(ADRS1$RSEVALN) <- "Assessor type (N)"
label(ADRS1$RSEVAL) <- "Assessor type"
label(ADRS1$PARCAT1) <- "Parameter Category 1"
label(ADRS1$AGEGR1) <- "Pooled Age Group 1"
label(ADRS2$STUDYID) <- "Study Identifier"
label(ADRS2$USUBJID) <- "Unique Subject Identifier"
label(ADRS2$PARAMCD) <- "Parameter Code"
label(ADRS2$PARAM) <- "Parameter"
label(ADRS2$AVAL) <- "Analysis Value"
ADRS2$AVALC <- factor(ADRS2$AVALC, c("RESPONDER", "NON RESPONDER"), exclude = "")
levels(ADRS2$AVALC) <- c("Responder", "Non Responder")
label(ADRS2$AVALC) <- "Analysis Value (C)"
label(ADRS2$RSEVALN) <- "Assessor type (N)"
label(ADRS2$RSEVAL) <- "Assessor type"
label(ADRS2$PARCAT1) <- "Parameter Category 1"
label(ADRS2$AGEGR1) <- "Pooled Age Group 1"
label(ADSL$STUDYID) <- "Study Identifier"
label(ADSL$USUBJID) <- "Unique Subject Identifier"
label(ADSL$SUBJID) <- "Subject Identifier for the Study"
label(ADSL$SITEID) <- "Study Site Identifier"
label(ADSL$AGE) <- "Age"
label(ADSL$AGEU) <- "Age Units"
label(ADSL$AGEGR1) <- "Pooled Age Group 1"
label(ADSL$AGEGR1N) <- "Pooled Age Group 1 (N)"
ADSL$SEX <- factor(ADSL$SEX, c("F", "M"), exclude = "")
levels(ADSL$SEX) <- c("Female", "Male")
label(ADSL$SEX) <- "Sex"
ADSL$SEXN <- factor(ADSL$SEXN, c(0, 1), exclude = "")
levels(ADSL$SEXN) <- c("Female", "Male")
label(ADSL$SEXN) <- "Sex (N)"
ADSL$RACE <- factor(ADSL$RACE, c("WHITE", "BLACK OR AFRICAN AMERICAN", "AMERICAN INDIAN OR
ALASKA NATIVE", "ASIAN"), exclude = "")
levels(ADSL$RACE) <- c("White", "Black or African American", "American Indian or Alaska Native", "Asian")
label(ADSL$RACE) <- "Race"
ADSL$RACEN <- factor(ADSL$RACEN, c(1, 2, 3, 4), exclude = "")
levels(ADSL$RACEN) <- c("White", "Black or African American", "American Indian or Alaska Native", "Asian")
label(ADSL$RACEN) <- "Race (N)"
label(ADSL$WEIGHTBL) <- "Weight at Baseline (kg)"
label(ADSL$L10WTBL) <- "Log10(Weight (kg))"
label(ADSL$HEIGHT) <- "Height (cm)"
label(ADSL$BMI) <- "Body Mass Index (kg/m2)"
label(ADSL$ARM) <- "Description of Planned Arm"
```

```
label(ADSL$TRT01P) <- "Description of Actual Arm"
ADSL$FASFL <- factor(ADSL$FASFL, c("Y", "N"), exclude = "")
levels(ADSL$FASFL) <- c("Yes", "No")
label(ADSL$FASFL) <- "Full Analysis Set Population Flag"
label(ADSL$HGBBL) <- "Hemoglobin at Baseline (g/dL)"
ADSL$ECOGBL <- factor(ADSL$ECOGBL, c(0, 1, 2, 3, 4), exclude = "")
levels(ADSL$ECOGBL) <- c("0", "1", "2", "3", "4")
label(ADSL$ECOGBL) <- "ECOG at Baseline"
label(ADSL$DSTERM) <- "Reported Term for the Disposition Event"
ADSL$EOSSTT <- factor(ADSL$EOSSTT, c("COMPLETED", "DISCONTINUED", "ONGOING"), exclude = "")
levels(ADSL$EOSSTT) <- c("Completed", "Discontinued", "Ongoing")
label(ADSL$EOSSTT) <- "End of Study Status"
ADSL$DCSREAS <- factor(ADSL$DCSREAS, c("ADVERSE EVENT", "LOST TO FOLLOW-UP", "WITHDRAWAL
  BY SUBJECT"), exclude = "")
levels(ADSL$DCSREAS) <- c("Adverse Event", "Lost to Follow-Up", "Withdrawal by Subject")
label(ADSL$DCSREAS) <- "Reason for Discontinuation from Study"
label(ADTTE$STUDYID) <- "Study Identifier"
label(ADTTE$USUBJID) <- "Unique Subject Identifier"
label(ADTTE$ASEQ) <- "Analysis Sequence Number"
label(ADTTE$PARAM) <- "Parameter"
label(ADTTE$PARAMCD) <- "Parameter Code"
label(ADTTE$AVAL) <- "Analysis Value"
label(ADTTE$CNSR) <- "Censor (1=censored)"
label(ADTTE$EVNTDESC) <- "Event or Censoring Description"
label(ADTTE$AGEGR1) <- "Pooled Age Group 1"
label(ADTTE$AGEGR1N) <- "Pooled Age Group 1 (N)"
```

A.5 File 00_chunks.R

```
## ---- tabCont ----
# SD has one decimal place more than other statistics;
tableContinuous(vars = vars, cap = cap, caption.placement = "top", lab = lab,
  prec = c(0, 1, 1, 1, 1, 1, 1, 2, 1, 0), longtable = TRUE)

## ---- tabContBy ----
tableContinuous(vars = vars, cap = cap, caption.placement = "top", group = bye, lab = lab,
  prec = c(0, 1, 1, 1, 1, 1, 1, 2, 1, 0), longtable = TRUE, print.pval = "kruskal")

## ---- tabNom ----
tableNominal(vars = vars, cap = cap, caption.placement = "top", vertical = FALSE,
  lab = lab, longtable = TRUE, cumsum = FALSE, miss.cat = c(1:ncol(vars)))

## ---- tabNomBy ----
tableNominal(vars = vars, cap = cap, caption.placement = "top", group = bye, vertical = FALSE,
  lab = lab, longtable = TRUE, cumsum = FALSE,
  miss.cat = NA, print.pval = "fisher", fisher.B = Inf)

## ---- tabNomBy2 ----
tableNominal(vars = vars, cap = cap, caption.placement = "top", group = bye, vertical = FALSE,
  lab = lab, longtable = TRUE, cumsum = FALSE,
  miss.cat = c(1:ncol(vars)))

## ---- texreglm ----
texreg(model, caption.above = T, digits = 3, caption = cap, float.pos = "!htpb",
  label = runif(1))

## ---- reglm ----
latex(xtable(model), digits = 2, file = "", title = "", here = TRUE, caption = cap,
  label = runif(1))

## ---- HistPlot ----
# Histogram, density, normal distr., saphiro wilk;
p1 <- ggplot(df_hist, aes(x = Param)) +
  geom_histogram(aes(y = ..density..), binwidth = myWidth, colour = "blue", fill = "white") +
  geom_density(colour = "blue") +
  stat_function(fun = dnorm, colour = "black",
    args = list(mean = mean(df_hist$Param), sd = sd(df_hist$Param))) +
  xlab(myLabel) +
  theme_pubr()

# from https://stackoverflow.com/questions/4357031/qnorm-and-qqline-in-ggplot2/:
qqplot_data <- function(vec) {
  # argument: vector of numbers
  # following four lines from base R's qqline()
  y <- quantile(vec[!is.na(vec)], c(0.25, 0.75))
  x <- qnorm(c(0.25, 0.75))
  slope <- diff(y)/diff(x)
  int <- y[1L] - slope * x[1L]
  d <- data.frame(resids = vec)
  ggplot(d, aes(sample = resids)) + stat_qq() + geom_abline(slope = slope, intercept = int)
}

p2 <- qqplot_data(df_hist$Param) + theme_pubr()

grid.arrange(p1, p2, ncol = 2)

# Normality Test;
m1 <- shapiro.test(df_hist$Param)
d1 <- data.frame(Variable = myLabel, Test = m1$method, P.value = m1$p.value)
my_table <- xtable(d1, digits = 6)
print(my_table, caption.placement = "top", size = "small", include.rownames = FALSE,
  table.placement = "htb", digits = 6, tabular.environment = "longtable", floating = FALSE)
```

```
## ---- CatPlot ----
# polar chart;
p1 <- ggplot(df_cat, aes(x = Level, fill = Level)) +
  geom_bar() +
  coord_polar() +
  theme_bw() +
  theme(legend.position = "none")

# bar chart;
p2 <- ggplot(df_cat, aes(x = Level, fill = Level)) +
  geom_bar(aes(y = (..count..)/sum(..count..))) +
  scale_y_continuous(labels = scales::percent) +
  labs(y = "Percent") +
  theme_bw() +
  theme(axis.title.x = element_blank(), axis.text.x = element_text(angle = 45, hjust = 1)) +
  theme(legend.position = "none")

# pie chart;
p3 <- ggplot(df_cat, aes(x = factor(1), fill = Level)) +
  geom_bar(width = 1, colour = "black") +
  coord_polar(theta = "y") +
  scale_x_discrete(name = "") +
  scale_y_continuous(name = "") +
  guides(fill = guide_legend(title = NULL)) +
  theme_pubr() +
  theme(legend.text = element_text(angle = 45)) +
  theme(legend.position = "top")

grid.arrange(p1, p2, p3, ncol = 3)

## ---- KmPlot ----
ggsurvplot(fit, data          = df_KM,
            pval              = TRUE,
            conf.int          = TRUE,
            xlab              = "Time in months",
            risk.table        = TRUE,                # Add risk table
            risk.table.col    = "strata",            # Change risk table color by groups
            linetype          = "strata",            # Change line type by groups
            surv.median.line = "hv",                # Specify median survival
            ggtheme           = theme_pubr()         # Change ggplot2 theme
)
fit
fit2

## ---- KmPlotCens ----
ggsurvplot(fit, data = df_KM,
            pval              = TRUE,
            conf.int          = TRUE,
            xlab              = "Time in months",
            risk.table        = TRUE,                # Add risk table
            risk.table.col    = "strata",            # Change risk table color by groups
            linetype          = "strata",            # Change line type by groups
            surv.median.line = "hv",                # Specify median survival
            cumcensor         = TRUE,
            ggtheme           = theme_pubr()         # Change ggplot2 theme
)
fit
fit2

## ---- BoxPlotNoColor ----
ggplot(df_BOX, aes(Xaxis, Yaxis)) +
  geom_boxplot() +
  labs(x = xLab, y = yLab) +
  stat_summary(fun.y = mean, colour = "blue", geom = "point", shape = 18, size = 2) +
  theme_pubr()
```

```
## ---- BoxPlot ----
ggplot(df_BOX, aes(Xaxis, Yaxis, fill = Xaxis)) +
  geom_boxplot() +
  labs(x = xLab, y = yLab) +
  stat_summary(fun.y = mean, colour = "blue", geom = "point", shape = 8, size = 2) +
  guides(fill = FALSE) +
  theme_pubr()

## ---- HistSex ----
# Please adapt code, when you use other and/or more Groups than SEX Female/Male;
# Boxplot, density plot, qqplot, kruskall wallis, sphiro wilk;

# Boxplot 2 Groups of SEX;
p1 <- ggplot(mydata, aes(SEX, Param, fill = SEX)) +
  geom_boxplot() +
  labs(x = "Group", y = myLab) +
  stat_summary(fun.y = mean, colour = "blue", geom = "point", shape = 18, size = 2) +
  guides(fill = FALSE) +
  theme_pubr()

# Histogramme Density Plots by SEX;
p2 <- ggplot(mydata, aes(x = Param, fill = SEX)) +
  geom_density(alpha = .5) + guides(fill = FALSE) +
  xlab("") +
  theme_pubr()

# QQ-Plot 2 Groups of SEX;
p3 <- ggplot(mydata) +
  stat_qq(aes(sample = Param, colour = factor(SEX))) +
  guides(colour = "none") +
  theme_pubr()

mydata1 <- subset(mydata, SEX == "Female")
mydata2 <- subset(mydata, SEX == "Male")
pNORM <- shapiro.test(mydata$Param)
pNORM1 <- shapiro.test(mydata1$Param)
pNORM2 <- shapiro.test(mydata2$Param)

# Kruskal test;
p_All <- kruskal.test(Param ~ SEX, data = mydata)

test_res_mat <- matrix(c("Wilcoxon test p",
                        "Shapiro-Wilk p (overall)",
                        "p (Female)",
                        "p (Male)",
                        round(p_All$p.value, digits = 7),
                        round(pNORM$p.value, digits = 7),
                        round(pNORM1$p.value, digits = 7),
                        round(pNORM2$p.value, digits = 7)), byrow = FALSE, nrow = 4)

# Print matrix;
p4 <- tableGrob(test_res_mat)

# Grid;
grid.arrange(p1, p2, p3, p4, ncol = 2, nrow = 2)
```

A.6 File 00_r_functions.R

```
# Function NoObs: number of non-missing values;
NoObs <- function(x) {
  sum(!is.na(x))
}

# Function LbyCI: Confidence Intervals;
LbyCI <- function(x, y, ...) {
  latex(
    bystats(x, y,
      fun = function(x) c("Mean" = mean(x),
        "Median" = median(x),
        "SD" = apply(x, 2, sd),
        "95LowerCI" = (mean(x) - qt(.975, NoObs(x) - 1) * apply(x, 2, sd) / sqrt(NoObs(x))),
        "95UpperCI" = (mean(x) + qt(.975, NoObs(x) - 1) * apply(x, 2, sd) / sqrt(NoObs(x))),
        "Min" = min(x),
        "Max" = max(x)), nmiss = FALSE),
    file = "",
    caption.loc = "top",
    caption = myCaption,
    cdec = c(0, 1, 1, 2, 1, 1, 1, 1), # decimal places;
    label = runif(1), # to avoid error: There were multiply-defined labels;
    rowlabel = "",
    here = T, ...)
}

# Function LbyGEO: Geometric Mean, CIs;
# If x = 0 then e.g. converted to one (1) so that log will be set to zero (0) for the calculation (t.b.d.)
LbyGEO <- function(x, y, ...) {
  latex(
    bystats(x, y,
      fun = function(x) c('Geo.Mean' = exp(mean(log(x))),
        'Median' = median(x),
        'Min' = min(x),
        'Max' = max(x),
        "95LowerCI" = exp(mean(log(x))
          - qt(0.975, NoObs(x) - 1) * sd(log(x) / sqrt(NoObs(x)))),
        "95UpperCI" = exp(mean(log(x))
          + qt(0.975, NoObs(x) - 1) * sd(log(x) / sqrt(NoObs(x))))),
        nmiss = FALSE),
    file = "",
    caption.loc = 'top',
    caption = myCaption,
    cdec = c(0, 1, 1, 0, 0, 1, 1), # decimal places;
    label = runif(1),
    rowlabel = "",
    here = T, ...)
}

# Function LbyQUART: Mean, Median, Quartils;
LbyQUART <- function(x, y, ...){
  latex(
    bystats(x, y,
      fun = function(x) c("Mean" = mean(x),
        "Median" = median(x),
        "SD" = apply(x, 2, sd),
        "Q1" = apply(x, 2, quantile, c(.25)),
        "Q3" = apply(x, 2, quantile, c(.75)),
        "Min" = min(x),
        "Max" = max(x)), nmiss = FALSE),
    file = "",
    caption.loc = "top",
    caption = myCaption,
    cdec = c(0, 1, 1, 2, 1, 1, 1, 1), # decimal places;
    label = runif(1),
```

```
    rowlabel    = "",
    here        = T, ... )
}

# Function BiFreqCI: Wilson score CIs;
BiFreqCI <- function(x, cap) {
  a <- table(x)
  b <- cbind(a, "all" = sum(a))
  erg <- binconf(b[, "a"], b[, "all"], method = "wilson")
  erg2 <- cbind("EVENT" = b[, "a"], "N" = b[, "all"], round(erg * 100, 1))
  latex(as.data.frame(erg2), file = "", here = TRUE, title = "95\\% Wilson CIs",
        caption = cap, label = runif(1))
}

# Function KMquart: Kaplan Meier quartiles;
KMquart <- function(fit, cap){
  Category <- as.data.frame(quantile(fit))
  latex(Category, file = "", digits = 3, landscape = FALSE, here = T, size = "small",
        long = TRUE, caption = cap, label = runif(1))
}
```


A.7 File 01_DEMOG.Rnw

```

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%% DEMOGRAPHICS - BEGIN
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

\clearpage
\newpage
\section{Statistical Methods}
Statistical analyses of this non-interventional study were descriptive and exploratory in nature.
For continuous variables, summary statistics, e.g., the mean, standard deviation (SD), median,
lower (Q1) and upper quartiles (Q3) and minimum and maximum values were calculated.
For dichotomous and categorical variables, the number and percentage of participants in each
category were reported. 95% confidence intervals (CIs) for categorical variables were
calculated according to the Wilson score method, without continuity correction. 95% CIs for
approximately normally distributed continuous variables were calculated using
the \textit{t}-distribution. For the body weight, the geometric mean was presented
together with 95% CIs. The geometric mean was calculated as the anti-logarithm of the
mean of the log-transformed values. \\
The Fisher's exact test or Pearson's  $\chi^2$  test was used to compare categorical
variables, the Wilcoxon test or Kruskal-Wallis test was used to compare differences in continuous
variables between two or more groups. \\
Shift tables from Baseline to week 24 were presented for HGB and WBC based on changes in the
normal ranges and tested with the McNemar's test/Bowker's symmetry test. \\
Log body weight was analyzed in a multiple linear regression model with sex, age and
height as independent variables. An ANOVA table was constructed with Type I, II and III
sum of squares.

Overall survival (time from baseline to death or censoring) was estimated
by the univariate Kaplan-Meier method and the median time to event was presented
together with 95% CIs, overall and stratified by age group <65 years vs  $\geq$  65 years
Survival curves were compared by the log-rank test. \\

All p-values were descriptive and no adjustments for multiplicity were made. \\

All analyses were based on the Full Analysis Set (FAS), consisting of all
subjects that received at least on dose of WonderDrug®. Analysis was based
on available data at each timepoint (i.e. missing data were not imputed), with exception
of the analysis of WBC over time: the last observation carried
forward (LOCF) method was used to input missing data and was presented - as sensitivity
analysis - in addition to the analysis of the non-imputed data. \\
Subgroup analyses were performed by age group (<65 years,  $\geq$  65 years). \\

R version 3.4.2 (The R Foundation for Statistical Computing, Vienna, Austria) was
used for statistical analysis. \\

All data were \textit{fictitious} and the statistical methods that were applied served mainly
as examples to show the usage of \emph{R code} within different \emph{R packages}.
Data were generated with \href{https://www.sas.com}{SAS} v. 9.4
(SAS Institute Inc., Cary, NC, USA) using e.g. following functions:
\textit{rand("BINOMIAL", p, n)}, \textit{rand("NORMAL", mu, sigma)},
\textit{exp(rand("NORMAL", mu, sigma))} and \textit{-log(ranuni(x))}. \emph{CDISC ADaM}
standards were partly applied.
\href{https://github.com/clindocu/sasxpt-r}{clindocu/sasxpt-r} was used to
generate the data definition table and to import SAS .xpt files into R with associated
user-defined formats (i.e. R \emph{factor(s)},
levels and label(s)). \\
This report was generated with \href{http://www.tug.org/texlive}{Tex Live 2017},
\href{https://github.com/rstudio/rstudio}{RStudio},
\href{https://www.r-project.org}{R} and \href{https://github.com/yihui/knitr}{knitr}. \\

The data definition table (DDT) of all analysis datasets can be found here:
\attachfile[appearance=true, icon=Tag, description=Data Definition Table Analysis Datasets,
color=0.254902 0.411765 0.882353, mimetype=application/pdf,subject=DDT]{DDT.pdf}
\tiny (double click to open) \\
\normalsize

```

Following `\emph{R packages}` were used:

```
\begin{itemize}
\item library(knitr)
\item library(foreign)
\item library(tidyverse)
\item library(Hmisc)
\item library(xtable)
\item library(gridExtra)
\item library(survminer)
\item library(ggthemes)
\item library(reporttools)
\item library(texreg)
\item library(car)
\end{itemize}
```

All code for generating this report can be found in appendix `\ref{AllCode}`.

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% Text with \Sexpr{}
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage
\newpage
\section{Data Sets Analysed}
Data were collected from \Sexpr{length(which(ADSL[["FASFL"]] == "Yes"))} subjects
from \Sexpr{sum(table(table(ADSL$SITEID)))} study sites, all meeting the criteria for
the FAS. \Sexpr{length(which(ADSL[["AGEGR1"]] == "<65"))} subjects were younger
than 65 years, \Sexpr{length(which(ADSL[["AGEGR1"]] == ">=65"))} subjects were older
than or equal 65 years. \\
```

The disposition of subjects is shown in figure `\ref{SubjDis}` and is tabulated in
table `\ref{Dispos}`. Baseline characteristics (Age, Sex, Race, Weight, Height, BMI,
ECOG, HGB) are summarized in table `\ref{ADemo2}`.

`\subsection{Study Sites, by Age Category}`

```
<<results='asis'>>=
# Hmisc:::summary.formula options;
# overall= TRUE      - column with overall statistics;
# test = FALSE       - no test statistics;
# na.include = FALSE - if TRUE, exclude missing values from being counted as category;
# continuous = 8     - threshold for when a numeric variable is considered to be continuous;
s6 <- summary(AGEGR1 ~ SITEID, data = ADSL, method = 'reverse',
              overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)

# Hmisc:::latex() options;;
# npct = "both"      - numerator and denominator;
# landscape = FALSE   - portrait;
# long = TRUE         - print the results for the first category on its own line;
# prmsd = TRUE        - print mean and SD after the three quantiles;
# here = TRUE         - table will appear here;
# prtest = 'P'        - P value when test = TRUE (can be c('P','stat','df','name'));
# dotchart = FALSE    - no dotcharts in output;
# longtable = FALSE:  - does not allow multiple pages;
# caption = ""        - text string to use as a caption;
# caption.loc = "top" - top or bottom;
# middle.bold = TRUE  - bold face for the middle quantile;
# file = ""           - LaTeX code will just printed to standard output;
# digits = 2          - digits for printing (continuous variables);
# exclude1 = FALSE    - e.g. prints Female/Male, when TRUE: Female only;
# label = ""          - unique label, can be referenced with \ref{myLabel};
latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,
      prtest = "P", dotchart = FALSE, longtable = FALSE,
      caption = "Study Sites by Age Category - Hmisc:::summary.formula",
```

```
caption.loc = "top",
middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "Site01")
@
```

```
<<results='asis'>>=
s6 <- summary(AGEGR1 ~ SITEID, data = ADSL, method = 'reverse',
              overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)
```

```
latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,
      prtest = "P", dotchart = TRUE, longtable = FALSE,
      caption = "Study Sites by Age Category - Hmisc.summary with dotchart",
      caption.loc = "top",
      middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "Site02")
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% Include a PDF File
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{Disposition of Subjects}
\begin{figure}[htp!]
  \centering
  \includegraphics[width=15cm]{Disposition.pdf}
  \caption{Disposition of Subjects}
  \label{SubjDis}
\end{figure}
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{Disposition of Subjects, by Age Category}
<<results='asis', echo=TRUE>>=
s6 <- summary(AGEGR1 ~ EOSSTT + DCSREAS, data = ADSL, method = 'reverse',
              overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)

latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,
      prtest = "P", dotchart = FALSE,
      caption = "Disposition of Subjects - Hmisc.summary with na.include = F",
      caption.loc = "top",
      middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "Dispos")
@
```

```
\subsubsection{Listing Reason for Non-Completion}
```

```
<<results='asis', echo=TRUE>>=
df1 <- ADSL %>%
  select(USUBJID, SEX, AGE, DCSREAS, DSTERM) %>%
  filter(DCSREAS != "") %>%
  arrange(DCSREAS)

my_table <- xtable(df1, caption = "Listing Reason for Non-Completion - xtable",
                  align = "lrrrlp{6cm}", caption.placement = "top")

digits(my_table)[4] <- 0 # Age (column 4 with 0 digits);
print(my_table, caption.placement = "top", size = "small", include.rownames = TRUE,
      table.placement = "htb", tabular.environment = "longtable", floating = FALSE)
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\section{Demographic and Other Baseline Characteristics}
\subsection{Demographic and Other Baseline Characteristics - Hmisc}
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
%\clearpage
%\newpage

<<results='asis'>>=
# Add unit to Age in ADSL;
units(ADSL$AGE) <- "years"

s6 <- summary(AGEGR1 ~ AGE + SEX + RACE + WEIGHTBL + HEIGHT + BMI + ECOGBL + HGBBL,
              data = ADSL, method = 'reverse', overall = TRUE, test = FALSE,
              na.include = FALSE, na.rm = TRUE, continuous = 8)

latex(s6, npct = "both", landscape = TRUE, long = TRUE, prmsd = TRUE, here = T,
      prtest = "P", dotchart = FALSE,
      caption = "Demographic and Other Baseline Characteristics - Hmisc.summary",
      caption.loc = "top",
      middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "ADemo1")
@

<<results='asis'>>=
# Create new variables;
ADSL$WBL <- ADSL$WEIGHTBL
ADSL$HBL <- ADSL$HEIGHT
ADSL$BML <- ADSL$BMI
ADSL$HML <- ADSL$HGBBL

# Add Labels;
label(ADSL$WBL) <- "Weight at Baseline"
label(ADSL$HBL) <- "Height"
label(ADSL$BML) <- "Body Mass Index"
label(ADSL$HML) <- "Hemoglobin at Baseline"

### Add uniits;
units(ADSL$WBL) <- "kg"
units(ADSL$HBL) <- "cm"
units(ADSL$BML) <- "kg/m2"
units(ADSL$HML) <- "g/dL"

s6 <- summary(AGEGR1 ~ AGE + SEX + RACE + WBL + HBL + BML + ECOGBL + HML, data = ADSL,
              method = 'reverse', overall = TRUE, test = TRUE,
              na.include = FALSE, na.rm = TRUE, continuous = 8)

latex(s6, npct = "both", landscape = TRUE, long = TRUE, prmsd = TRUE, here = T,
      prtest = "P", dotchart = FALSE,
      caption = "Demographic and Other Baseline Characteristics - Hmisc.summary with units and P-value",
      caption.loc = "top", middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "ADemo2")
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%\clearpage
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\subsection{Demographic and Other Baseline Characteristics - reporttools::tableContinuous}

<<01_BaseChar, results='asis', echo=TRUE>>=
# Generate dataframe with variables;
vars <- with(ADSL, data.frame(
  "Age years" = AGE,
  "Weight kg" = WEIGHTBL,
  "Height cm" = HEIGHT,
  "BMI kg.m2" = BMI,
  "Hemoglobin g.dL" = HGBBL))

cap <- "Baseline Characteristics - reporttools::tableContinuous - Wilcoxon test"
lab <- "tab:BaseChar"
bye <- ADSL$AGEGR1
@
```

```
<<ref.label="tabContBy", results='asis', echo=TRUE>>=  
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
\clearpage  
\newpage  
\subsection{Demographic and Other Baseline Characteristics - reporttools::tableNominal}
```

```
<<O1_BaseCategor, results='asis', echo=TRUE>>=  
vars <- with(ADSL, data.frame(  
  "Sex" = SEX,  
  "Race" = RACE,  
  "ECOG" = ECOGBL))
```

```
cap <- "Baseline Char. - tableNominal - NAs excluded - Fisher's exact test"  
lab <- "tab:O1_BaseCategor"  
bye <- ADSL$AGEGR1  
@
```

```
<<ref.label="tabNomBy", results='asis', echo=TRUE>>=  
@
```

```
<<O1_BaseCatMiss, results='asis'>>=  
cap <- "Baseline Characteristics - tableNominal - NAs as category"  
lab <- "tab:O1_BaseCatMiss"  
bye <- ADSL$AGEGR1  
@
```

```
<<ref.label="tabNomBy2", results='asis', echo=TRUE>>=  
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% DEMOGRAPHICS - END  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

A.8 File 01_DEMOG_FIG.Rnw

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% DEMOGRAPHICS FIGURES - BEGIN  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
\clearpage  
\newpage  
\subsection{Histogram Age}  
  
<<demo3, echo=TRUE>>=  
df_hist <- ADSL %>% select(AGE) %>%  
  mutate(Param = AGE) %>%  
  filter(!is.na(Param))  
  
myLabel <- "Age (yrs.)"  
myWidth <- 3  
cap <- "Histogram Age (yrs.)"  
  
# Create histogram with::  
# ref.label="HistPlot"  
@  
  
<<Age, ref.label="HistPlot", results='asis', fig.width=10, fig.height=5, out.width='14cm', fig.cap=cap>>=  
@  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
\clearpage  
\newpage  
\subsection{Histogram Weight at Baseline}  
  
<<demo4>>=  
# NOTE: Subjects with missing SEX were excluded (consistency with next table);  
df_hist <- ADSL %>% select(WEIGHTBL, SEX) %>%  
  mutate(Param = WEIGHTBL) %>%  
  filter(!is.na(Param) & !is.na(SEX))  
  
myLabel <- "Weight at Baseline (kg)"  
myWidth <- 3  
cap <- "Histogram Weight (kg) at Baseline"  
@  
  
<<Wght, ref.label="HistPlot", results='asis', fig.width=10, fig.height=5, out.width='14cm', echo=T, fig.cap=cap>>=  
@  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
\clearpage  
\newpage  
\subsection{Weight at Baseline - Boxplot, Density Plot, QQ-Plot}  
<<demo5>>=  
mydata <- ADSL %>% select(WEIGHTBL, SEX) %>%  
  mutate(Param = WEIGHTBL) %>%  
  filter(!is.na(Param)) %>%  
  filter(!is.na(SEX))  
  
myLab <- "Weigth at Baseline"  
cap <- "Weight (kg) at Baseline, by Sex"  
@  
  
<<Wght2, ref.label="HistSex", fig.width=10, fig.height=10, out.width='16cm', fig.cap=cap>>=  
@  
  
<<demo6, results='asis', echo=TRUE>>=  
myCaption <- "Summary Statistics: Weight (kg) at Baseline"
```

```
# Enter not transformed Variable Name here;
LbyQUART(mydata$WEIGHTBL, mydata$SEX)
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{Log10 Weight at Baseline - Boxplot, Density Plot, QQ-Plot}
<<echo=TRUE>>=
mydata <- ADSL %>% select(WEIGHTBL, L10WTBL, SEX) %>%
  mutate(Param = L10WTBL) %>%
  filter(!is.na(Param)) %>%
  filter(!is.na(SEX))

myLab <- "Log10 Weigth"
cap <- "Log10 Weight (kg) at Baseline, by Sex"
@

<<LgWeight, ref.label="HistSex", fig.width=10, fig.height=10, out.width='16cm', echo=TRUE, fig.cap=cap>>=
@

<<results='asis', echo=TRUE>>=
myCaption <- "Geometric Mean +/- 95 CIs: Weight (kg) at Baseline"

# Enter not transformed Variable Name here;
LbyGEO(mydata$WEIGHTBL, mydata$SEX)
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{Sex at Baseline}

<<01_SEX, echo=TRUE>>=
df_cat <- select(ADSL, SEX) %>%
  mutate(Level = SEX) %>%
  filter(Level != "")

cap <- "SEX at Baseline - polar chart, bar chart, pie chart"
@

<<SEX, ref.label="CatPlot", fig.width=10, fig.height=4.5, out.width='16cm', echo=TRUE, fig.cap=cap>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{ECOG at Baseline}

<<01_ECOG, echo=TRUE>>=
df_cat <- select(ADSL, ECOGBL) %>%
  mutate(Level = ECOGBL) %>%
  filter(Level != "")

cap <- "ECOG at Baseline - polar chart, bar chart, pie chart"
@

<<ECOG_CAT, ref.label="CatPlot", fig.width=10, fig.height=4.5, out.width='16cm', echo=TRUE, fig.cap=cap>>=
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{ECOG at Baseline, by Age Group (1)}
```

```
<<ECOG_STACKED, echo=TRUE, fig.cap=cap, out.width='10cm'>>=
cap <- "ECOG Status at Baseline, by Age Group (up to 100\\%) - stacked bar chart"
df1 <- ADSL %>% select(AGEGR1, ECOGBL) %>%
  filter(!is.na(ECOGBL))
```

```
df1$ECOG <- factor(df1$ECOG, c("5", "4", "3", "2", "1", "0"), exclude = "")
levels(df1$ECOG) <- c("5", "4", "3", "2", "1", "0")
```

```
ggplot(data = df1, aes(x = AGEGR1, y = 1, fill = ECOG)) +
  geom_bar(stat = "identity", position = "fill") +
  labs(x = "Age Group (yrs.)", y = "100 %") +
  theme_pubr()
```

@

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage
\newpage
\subsection{ECOG at Baseline, by Age Group (2)}
```

```
<<echo=TRUE>>=
# Using latex Method \includegraphics{};
pdf("ECOG_STAT_2.pdf")
```

```
ggplot(data = df1, aes(x = AGEGR1, fill = ECOG)) +
  geom_bar(position = position_dodge(0.92)) +
  labs(x = "Age Group (yrs.)") +
  theme_pubr()
```

@

```
\begin{figure}[H]
\centering
\includegraphics[width=10cm, height=10cm]{ECOG_STAT_2.pdf}
\caption{ECOG Status at Baseline, by Age Group - side by side bar chart}
\end{figure}
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage
\newpage
\subsection{Scatterplot Matrix, graphics::pairs}
```

```
<<echo=TRUE, fig.width=10, fig.height=10, out.width='16cm'>>=
df1 <- ADSL %>% select(AGE, WEIGHTBL, HEIGHT, BMI, HGBBL)
# Very simple: Scatter plot matrix of all variables in dataframe;
pairs(df1)
```

@

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage
\newpage
\subsection{Scatterplot Matrix, by Sex, car::scatterplotMatrix}
```

```
<<echo=TRUE, fig.width=10, fig.height=10, out.width='16cm'>>=
df1 <- ADSL %>% select(AGE, WEIGHTBL, HEIGHT, BMI, HGBBL, SEX)
scatterplotMatrix(~ AGE + WEIGHTBL + HEIGHT + BMI + HGBBL | SEX,
  by.group = TRUE, reg.line = TRUE, col = c("#8E0152", "#4292C6"), data = df1)
```

@

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage
\newpage
\subsection{Scatterplot, Weight as a function of Height, by Sex}
<<echo=TRUE, fig.width=5, fig.height=5, out.width='10cm'>>=
# Using latex Method \includegraphics{};
pdf("HEIGHT_WEIGHT.pdf")
```



```
df2 <- ADSL %>% select(SEX, HEIGHT, WEIGHTBL) %>%  
  filter(!is.na(HEIGHT) & !is.na(WEIGHTBL) & !is.na(SEX))  
  
ggplot(df2, aes(x = HEIGHT, y = WEIGHTBL, col = SEX)) +  
  geom_point(alpha = 0.8) +  
  labs(x = "Height cm", y = "Weight kg") +  
  stat_smooth(aes(group = SEX), method = "lm", se = T, level = 0.95) +  
  scale_color_manual(values = c("#8E0152", "#4292C6")) +  
  theme_pubr()  
@
```

```
\begin{figure}[H]  
  \centering  
  \includegraphics[width=10cm, height=10cm]{HEIGHT_WEIGHT.pdf}  
  \caption{Scatter Plot Height, Weight, by Sex with confid. interval}  
\end{figure}
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% DEMOGRAPHICS FIGURES - END  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

A.9 File 01_LINEAR_MODEL.Rnw

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%%% LINEAR MODEL - BEGIN  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
  
\clearpage  
\newpage  
\subsection{Example: Linear Model Log10 Weight - Sex + Age + Height}  
  
<<01_ModelWeight, results='asis', echo=TRUE>>=  
model <- lm(L10WTBL ~ SEX + AGE + HEIGHT, data = ADSL)  
cap <- "Linear model Log10 Weight: Sex + Age + Height - latex::xtable(lm)"  
@  
  
<<ref.label="reglm", results='asis', echo=TRUE>>=  
@  
  
<<01_ModelWeight2, results='asis', echo=TRUE>>=  
cap <- "Linear model Log10 Weight: Sex + Age + Height - texreg::texreg(lm)"  
@  
  
<<ref.label="texreglm", results='asis', echo=TRUE>>=  
@  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
\clearpage  
\newpage  
\subsection{Example: Linear Model - Diagnostic Plots}  
  
<<echo=TRUE, fig.width=10, fig.height=10, out.width='16cm'>>=  
model <- lm(as.numeric(L10WTBL) ~ SEX + AGE + HEIGHT, data = ADSL)  
par(mfrow = c(2, 2))  
plot(model)  
@  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%%% LINEAR MODEL - END  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%%% ANOVA MODEL - BEGIN  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
  
\clearpage  
\newpage  
\subsection{Example: ANOVA model with Type I, II, III SS}  
  
<<results='asis', echo=TRUE>>=  
cap <- "ANOVA Type I SS - stats::anova"  
aov_1 <- anova(model)  
  
latex(xtable(aov_1), digits = 2, file = "", title = "", here = TRUE, caption = cap,  
      label = runif(1))  
@  
  
<<results='asis', echo=TRUE>>=  
cap <- "ANOVA Type II SS - car::Anova"  
aov_2 <- Anova(model, type = "II")  
  
latex(xtable(aov_2), digits = 2, file = "", title = "", here = TRUE, caption = cap,  
      label = runif(1))  
@  
  
<<results='asis', echo=TRUE>>=
```

```
cap <- "ANOVA Type III SS - car::Anova"
# options(contrasts=c("contr.helmert", "contr.poly")) # like SAS and SPSS (?);
options(contrasts = c("contr.sum", "contr.poly"))
aov_3 <- Anova(model, type = "III")
options(contrasts = c("contr.treatment", "contr.poly")) # default;

latex(xtable(aov_3), digits = 2, file = "", title = "", here = TRUE, caption = cap,
      label = runif(1))
```

```
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% ANOVA MODEL - BEGIN
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

A.10 File 02_KAPLAN.Rnw

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% KAPLAN MEIER CURVES - BEGIN
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

\clearpage
\newpage
\section{Overall Survival}
\subsection{OS Kaplan-Meier Curves +/- 95\% CIs}

<<01_OS>>=
df_KM <- ADTTE %>%
  mutate(Time = AVAL, Status = CNSR)

fit <- survfit(Surv(Time, Status == 0) ~ 1, data = df_KM)
fit2 <- "Kaplan-Meier Estimates"
cap <- "Overall Survival (overall)"
@

<<OS, ref.label="KmPlotCens", fig.width=10, fig.height=8, out.width='16cm', fig.cap=cap>>=
@

<<results='asis'>>=
KMquart(fit, "Overall Survival KM Quartiles +/- 95\% CIs")
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{OS Kaplan-Meier Curves, Strata Age 65 yrs.}

<<01_KMAG1, echo=TRUE>>=
# Generate KM dataset;
df_KM <- ADTTE %>%
  mutate(AGE = AGEGR1, Time = AVAL, Status = CNSR) %>%
  filter(!is.na(AGE))

fit <- survfit(Surv(Time, Status == 0) ~ AGE, data = df_KM)
fit2 <- survdiff(Surv(Time, Status == 0) ~ AGE, rho = 0, data = df_KM)
cap <- "Overall Survival (Strata Age 65 yrs. at Baseline)"
@

<<KMAG1, ref.label="KmPlotCens", fig.width=10, fig.height=8, out.width='16cm', echo=TRUE, fig.cap=cap>>=
@

<<results='asis', echo=TRUE>>=
KMquart(fit, "Overall Survival KM Quartiles +/- 95\% CIs (Strata Age 65 yrs.)")
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% KAPLAN MEIER CURVES - END
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

A.11 File 03_LAB_HGB.Rnw

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% LABORATORY PARAMETER HGB - BEGIN  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage  
\newpage  
\section{Laboratory Data}  
\subsection{Hemoglobin over Time}
```

```
<<03_HGBBOX, echo=TRUE>>=  
df_BOX <- ADLB %>% select(PARAM, PARAMCD, AVISIT, AVISITN, AVAL) %>%  
  mutate(Xaxis = AVISIT, Yaxis = AVAL) %>%  
  filter(PARAMCD == "HGB")
```

```
xLab <- "Visit"  
yLab <- "g/dL"  
cap <- "Hemoglobin over Time - Boxplot"  
@
```

```
<<03_HGBCI, results='asis', echo=TRUE>>=  
myCaption <- "Summary of Hemoglobin over Time, mean +/- 95%% CIs"  
LbyCI(df_BOX$AVAL, df_BOX$AVISIT, size = "small")  
@
```

```
<<03_HGBQUART, results='asis', echo=TRUE>>=  
myCaption <- "Summary of Hemoglobin over Time, Q1, Q3"  
LbyQUART(df_BOX$AVAL, df_BOX$AVISIT, size = "small")  
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage  
\newpage  
\subsection{Hemoglobin over Time, boxplot}  
<<HGB_Box, ref.label="BoxPlot", fig.width=6, fig.height=6, out.width='10cm', echo=TRUE, fig.cap=cap>>=  
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage  
\newpage  
\subsection{Hemoglobin over Time, jitter}  
<<HGB_jitter, fig.width=7, fig.height=7, out.width='10cm', echo=TRUE, fig.cap=cap>>=  
cap <- "Hemoglobin over Time, mean +/- SD - jitter"  
df1 <- ADLB %>% select(PARAM, PARAMCD, AVISIT, AVISITN, AVAL) %>%  
  mutate(Xaxis = AVISIT, Yaxis = AVAL) %>%  
  filter(PARAMCD == "HGB")
```

```
ggplot(df1, aes(x = Xaxis, y = Yaxis)) +  
  stat_summary(fun.y = mean, geom = "point", col = "red", size = 3) +  
  geom_point(alpha = 0.2, position = position_jitter(width = 0.12, height = 0.01)) +  
  stat_summary(fun.data = mean_sdl, fun.args = list(mult = 1),  
    geom = "errorbar", width = 0.2, col = "red") +  
  labs(x = "Visit", y = "g/dL") +  
  theme_pubr()  
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

```
\clearpage  
\newpage  
\subsection{Hemoglobin, Shift Table Baseline vs. Week 24}
```

```
<<results='asis', echo=TRUE>>=
# Subset HGB at W24
df_W24 <- ADLB %>% select(AGEGR1, AVISIT, PARAMCD, BNRIND2, ANRIND2, SHIFT2) %>%
  filter(PARAMCD == "HGB" & AVISIT == "Week 24")
label(df_W24$SHIFT2) <- "Shift BL to Week 24"

s6 <- summary(AGEGR1 ~ SHIFT2, data = df_W24, method = 'reverse',
  overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)

latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,
  prtest = "P", dotchart = FALSE,
  caption = "Hemoglobin, Shift Table Baseline to Week 24", caption.loc = "top",
  middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "HGB_SH24")
@
```

```
<<results='asis', echo=TRUE>>=
tab1 <- table(df_W24$BNRIND2, df_W24$ANRIND2)
tab2 <- as.data.frame(tab1)
tab_sum <- addmargins(tab1)

cap <- "Hemoglobin, Shift Table Baseline to Week 24 (overall)"
latex(tab_sum, file = "", here = TRUE, title = "Baseline/W24",
  caption = cap, label = runif(1))
mcnemar.test(tab1)
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{Hemoglobin, Shift Table Baseline vs. Week 24}
```

```
<<echo=TRUE, fig.width=7, fig.height=5>>=
p1 <- ggplot(tab2, aes(Var1, Var2)) +
  geom_point(aes(size = Freq), colour = "#9999FF") +
  scale_x_discrete() +
  geom_text(aes(label = Freq)) +
  labs(x = "Baseline", y = "Week 24") +
  # scale_size_continuous(range = c(5, 20), guide = FALSE) + # hide legend;
  scale_size_continuous(range = c(5, 20)) +
  theme_bw()
@
```

```
<<shifHGB, fig.width=7, fig.height=5>>=
# Example: ggsave() function for saving plot;
ggsave("HGB_Shift24.pdf", p1)
@
```

```
\begin{figure}[H]
  \centering
  \includegraphics[width=0.7\textwidth]{HGB_Shift24.pdf}
  \caption{Hemoglobin, Shift Table Baseline to Week 24}
\end{figure}
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% LABORATORY PARAMETER HGB - END
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

A.12 File 03_LAB_WBC.Rnw

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%%% LABORATORY PARAMETER WBC - BEGIN  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
  
\clearpage  
\newpage  
\subsection{WBC over Time (no data imputation, LOCF)}  
  
<<03_WBCBOX>>=  
df_aval <- ADLB %>% select(PARAM, PARAMCD, AVISIT, AVISITN, AVAL, DTYPE) %>%  
  mutate(Xaxis = AVISIT, Yaxis = AVAL) %>%  
  filter(PARAMCD == "WBC" & DTYPE == "")  
  
df_LOCF <- ADLB %>% select(PARAM, PARAMCD, AVISIT, AVISITN, AVAL, DTYPE) %>%  
  mutate(Xaxis = AVISIT, Yaxis = AVAL) %>%  
  filter(PARAMCD == "WBC" & (DTYPE == "" | DTYPE == "LOCF"))  
@  
  
<<03_WBCCI, results='asis'>>=  
myCaption <- "Summary of WBC over Time, mean +/- 95%% CIs (no data imputation)"  
LbyCI(df_aval$AVAL, df_aval$AVISIT, size = "small")  
@  
  
<<03_WBCCI2, results='asis'>>=  
myCaption <- "Summary of WBC over Time, mean +/- 95%% CIs (LOCF)"  
LbyCI(df_LOCF$AVAL, df_LOCF$AVISIT, size = "small")  
@  
  
<<03_WBCQUART, results='asis'>>=  
myCaption <- "Summary of WBC over Time, Q1, Q3 (no data imputation)"  
LbyQUART(df_aval$AVAL, df_aval$AVISIT, size = "small")  
@  
  
<<03_WBCQUART2, results='asis'>>=  
myCaption <- "Summary of WBC over Time, Q1, Q3 (LOCF)"  
LbyQUART(df_LOCF$AVAL, df_LOCF$AVISIT, size = "small")  
@  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
\clearpage  
\newpage  
\subsection{WBC over Time, boxplots}  
  
<<03_WBCBOX1>>=  
df_BOX <- df_aval  
xLab <- "Visit"  
yLab <- "109/L"  
cap <- "WBC over Time - Boxplot (no data imputation)"  
@  
  
<<WBC_Box_Aval, ref.label="BoxPlot", fig.width=6, fig.height=6, out.width='10cm', fig.cap=cap>>=  
@  
  
<<03_WBCBOX2>>=  
df_BOX <- df_LOCF  
xLab <- "Visit"  
yLab <- "109/L"  
cap <- "WBC over Time - Boxplot (LOCF)"  
@  
  
<<WBC_Box_LOCF, ref.label="BoxPlot", fig.width=6, fig.height=6, out.width='10cm', fig.cap=cap>>=  
@
```

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
\clearpage
\newpage
\subsection{WBC, Shift Table Baseline vs. Week 24 (no data imputation)}

<<results='asis'>>=
#### Subset WBC at W24
df_W24 <- ADLB %>% select(AGEGR1, AVISIT, PARAMCD, BNRIND, ANRIND, SHIFT1, DTYPE) %>%
  filter(PARAMCD == "WBC" & AVISIT == "Week 24" & DTYPE == "")
label(df_W24$SHIFT1) <- "Shift BL to Week 24"

s6 <- summary(AGEGR1 ~ SHIFT1, data = df_W24, method = 'reverse',
  overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)

latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,
  prtest = "P", dotchart = FALSE,
  caption = "WBC, Shift Table Baseline to Week 24 (no data imputation)", caption.loc = "top",
  middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "WBC_SH24")
@

<<results='asis'>>=
#print(CrossTable(tab1))
tab1 <- table(df_W24$BNRIND, df_W24$ANRIND)
tab2 <- as.data.frame(tab1)
#tab_sum <- addmargins(tab1)

cap <- "WBC, Shift Table Baseline to Week 24 (no data imputation)"
latex(tab1, file = "", here = TRUE, title = "Baseline/W24", caption = cap, label = runif(1))
mcnemar.test(tab1)
@

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

<<fig.width=7, fig.height=5>>=
p1 <- ggplot(tab2, aes(Var1, Var2)) +
  geom_point(aes(size = Freq), colour = "#9999FF") +
  scale_x_discrete() +
  geom_text(aes(label = Freq)) +
  labs(x = "Baseline", y = "Week 24") +
  scale_size_continuous(range = c(5, 20)) +
  theme_bw()
@

<<shiftWBC, fig.width=7, fig.height=5>>=
# Example: ggsave() function for saving plot;
ggsave("WBC_Shift24.pdf", p1)
@

\begin{figure}[H]
  \centering
  \includegraphics[width=0.7\textwidth]{WBC_Shift24.pdf}
  \caption{WBC, Shift Table Baseline to Week 24 (no data imputation)}
\end{figure}

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%% LABORATORY PARAMETER WBC - END
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```


A.13 File 04_RESPONSE.Rnw

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% TUMOR RESPONSE - BEGIN  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
  
\clearpage  
\newpage  
\section{Tumor Response}  
  
<<results='asis'>>=  
ADRS2$AVALC2 <- ADRS2$AVALC  
label(ADRS2$AVALC2) <- "Objective Tumor Response Rate"  
  
s6 <- summary(AGEGR1 ~ AVALC2, data = ADRS2, method = 'reverse',  
              overall = TRUE, test = TRUE, na.include = FALSE, continuous = 8)  
  
latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,  
      prtest = "P", dotchart = FALSE,  
      caption = "Objective Tumor Response Rate - (SD, PD, Missing counted as Non Responder)", caption.loc = "top",  
      middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "RESP1")  
@  
  
<<results='asis', echo=TRUE>>=  
ADRS1$AVALC2 <- ADRS1$AVALC  
label(ADRS1$AVALC2) <- "Best Overall Response"  
  
s6 <- summary(AGEGR1 ~ AVALC2, data = ADRS1, method = 'reverse',  
              overall = TRUE, test = FALSE, na.include = FALSE, continuous = 8)  
  
latex(s6, npct = "both", landscape = FALSE, long = TRUE, prmsd = TRUE, here = TRUE,  
      prtest = "P", dotchart = FALSE,  
      caption = "Best Overall Response", caption.loc = "top",  
      middle.bold = TRUE, file = "", digits = 2, exclude1 = FALSE, label = "RESP2")  
@  
  
<<results='asis', echo=TRUE>>=  
BiFreqCI(ADRS2$AVALC2, cap = "Objective Tumor Response Rate (95\\% Wilson Score CIs w/o cont. corr.)")  
BiFreqCI(ADRS1$AVALC2, cap = "Best Overall Response (95\\% Wilson Score Interval w/o cont. corr.)")  
@  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% TUMOR RESPONSE - END  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```

A.14 File 99_HISTORY.Rnw

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% VERSION HISTORY - BEGIN  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
  
\clearpage  
\newpage  
\section{Version History}  
  
\begin{longtable}[ht]{p{3cm} p{4cm} p{6.7cm} }  
  \toprule \\  
  \textbf{Version} & \textbf{Date} & \textbf{Summary of Changes} \\  
  \bottomrule \\  
  \endhead  
01 & October 24, 2017 & New Document \\  
  
\hline  
\end{longtable}  
  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%  
%% VERSION HISTORY - END  
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
```


C Technical Details

C.1 R Version

```
R.Version()

## $platform
## [1] "x86_64-w64-mingw32"
##
## $arch
## [1] "x86_64"
##
## $os
## [1] "mingw32"
##
## $system
## [1] "x86_64, mingw32"
##
## $status
## [1] ""
##
## $major
## [1] "3"
##
## $minor
## [1] "4.2"
##
## $year
## [1] "2017"
##
## $month
## [1] "09"
##
## $day
## [1] "28"
##
## $`svn rev`
## [1] "73368"
##
## $language
## [1] "R"
##
## $version.string
## [1] "R version 3.4.2 (2017-09-28)"
##
## $nickname
## [1] "Short Summer"
```

C.2 Active R packages

```
sessionInfo()

## R version 3.4.2 (2017-09-28)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows 7 x64 (build 7601) Service Pack 1
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=German_Austria.1252 LC_CTYPE=German_Austria.1252
## [3] LC_MONETARY=German_Austria.1252 LC_NUMERIC=C
## [6] LC_TIME=German_Austria.1252
##
## attached base packages:
## [1] stats      graphics  grDevices  utils      datasets  methods   base
##
## other attached packages:
## [1] bindrcpp_0.2      car_2.1-5      texreg_1.36.23  reporttools_1.1.2
## [5] ggthemes_3.4.0    survminer_0.4.0 ggpubr_0.1.5    magrittr_1.5
## [9] gridExtra_2.3     xtable_1.8-2   Hmisc_4.0-3     Formula_1.2-2
## [13] survival_2.41-3   lattice_0.20-35 dplyr_0.7.4     purrr_0.2.3
## [17] readr_1.1.1       tidyr_0.7.1    tibble_1.3.4    ggplot2_2.2.1
## [21] tidyverse_1.1.1   foreign_0.8-69 knitr_1.17
##
## loaded via a namespace (and not attached):
## [1] httr_1.3.1        jsonlite_1.5    splines_3.4.2
## [4] modelr_0.1.1      assertthat_0.2.0 highr_0.6
## [7] latticeExtra_0.6-28 cellranger_1.1.0 backports_1.1.1
## [10] quantreg_5.33     glue_1.1.1      digest_0.6.12
## [13] RColorBrewer_1.1-2 checkmate_1.8.4 minqa_1.2.4
## [16] rvest_0.3.2       colorspace_1.3-2 cmprsk_2.2-7
## [19] htmltools_0.3.6   Matrix_1.2-11   plyr_1.8.4
## [22] psych_1.7.8       pkgconfig_2.0.1 broom_0.4.2
## [25] SparseM_1.77      haven_1.1.0     scales_0.5.0
## [28] km.ci_0.5-2       MatrixModels_0.4-1 lme4_1.1-14
## [31] KMSurv_0.1-5      htmlTable_1.9   mgcv_1.8-22
## [34] nnet_7.3-12       lazyeval_0.2.0  pbkrtest_0.4-7
## [37] mnormt_1.5-5      readxl_1.0.0    evaluate_0.10.1
## [40] nlme_3.1-131      MASS_7.3-47     forcats_0.2.0
## [43] xml2_1.1.1        tools_3.4.2     data.table_1.10.4-2
## [46] hms_0.3           stringr_1.2.0   munsell_0.4.3
## [49] cluster_2.0.6     compiler_3.4.2  rlang_0.1.2
## [52] nloptr_1.0.4       grid_3.4.2      htmlwidgets_0.9
## [55] labeling_0.3       base64enc_0.1-3 gtable_0.2.0
## [58] reshape2_1.4.2    R6_2.2.2        zoo_1.8-0
## [61] lubridate_1.6.0    survMisc_0.5.4  bindr_0.1
## [64] stringi_1.1.5     parallel_3.4.2 Rcpp_0.12.13
## [67] rpart_4.1-11      acepack_1.4.1
```

C.3 PDF \LaTeX

```
Sys.which("pdflatex")

##
## "C:\\texlive\\2017\\bin\\win32\\pdflatex.exe"
```

C.4 System Time

```
Sys.time()
```

```
## [1] "2017-10-24 15:59:11 CEST"
```