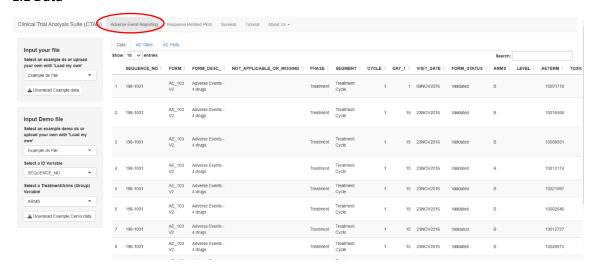
CTAS: Clinical Trial Analyses Suite Tutorial

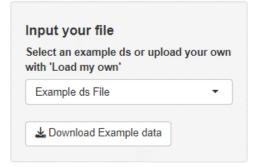
Table of Contents

- I. CTAS Tutorial
- II. Troubleshooting Guide

TAB 1. ADVERSE EVENT (AE) REPORTING

1.1 Data



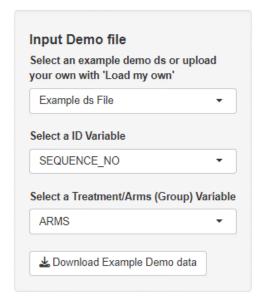




Step 1:

Select the example dataset or upload your own.

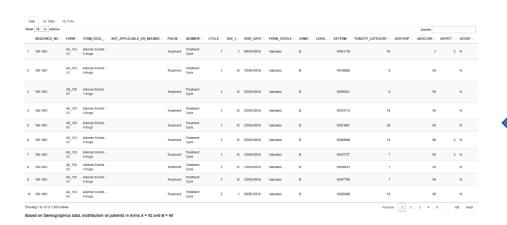
To view example data and format, use download button to view .csv file.



Step 2:

Select the example demo dataset or upload your own. The distribution of patients within each Arm (select variable from dropdown) will be calculated based on this dataset. Also, select the ID variable.

To view example demo data and format, use download button to view .csv file.



1.2 AE Table Reporting

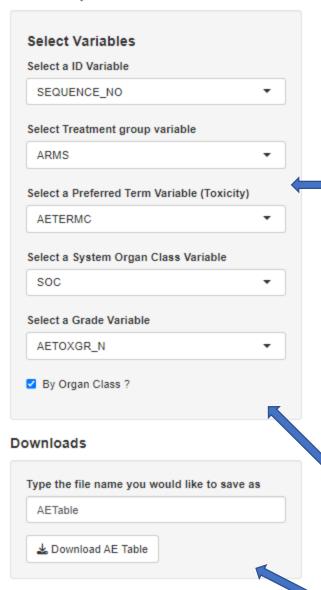


Step 3:

AE data is displayed. Any erroneous data entries can be identified here.

Specific variables of interest or patients of interest can be shortlisted by entering in the search bar on the top right.

AE table specifications



Step 4:

Select the variables in the dataset:

ID = Unique identifier common to both demographic and AE dataset.

Treatment group = Ex. Arms. This could be a single Arm study or a 2 Arm study. The two Arms need to be hardcoded as A and B in the dataset.

Preferred Term = Toxicity variable. This should be a character variable and not a numerical variable with factors in SAS. Please convert numerical variable into character using the put statement in SAS.

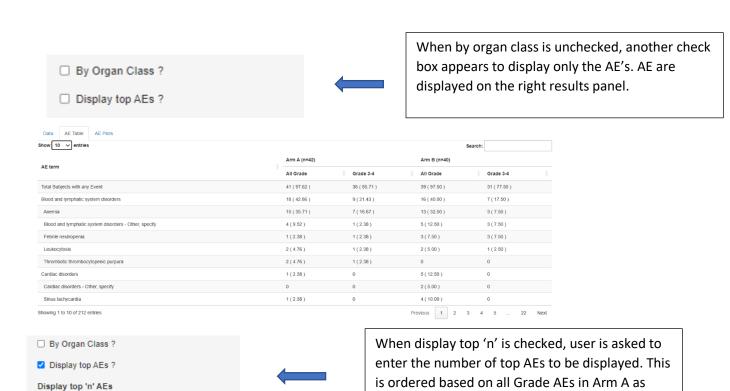
System Organ Class (SOC) = This represents the class of the AEs. Ex. Heart diseases, Vascular disorders, etc.

Grade = This should be a numerical variable representing the grade of the AE.

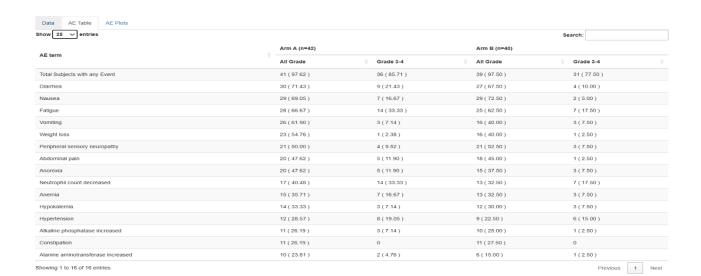
After selecting the variables in both dataset, if IDs in both datasets are different, an error message will appear "The AE data patients are different from Demographics dataset. Please ensure same patients are included".

Results are displayed by System Organ Class. To display AEs not grouped by Organ class, uncheck this box. Once unchecked, another option appears to ask users to display top AE's. See next page for options.

Download Result tables as a .csv file. This table is on the same format as the results.



seen below.

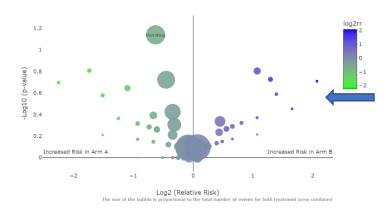


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1.3 AE plots



Volcano plot for AEs with 2 Arms



Volcano plot is displayed comparing the AEs in the two Arms. When a single arm dataset is uploaded, Volcano and Dot plots will not be created.

The x-axis represents the log2 relative risk and y-axis represents the log10 p-values computed using the fisher exact test. Each bubble represents an adverse event, with bubble size indicative of the total number of adverse events that occur for both treatment Arms combined. Specifically, the bubble area is proportional to the total number of events.

Based on AE results, Nausea is the most commonly occurring adverse event during this trial. Log2 (Relative Risk) of 0 represents no difference in risk between the 2 Arms, while bubbles to the right indicate a higher risk for subjects in Arm B (i.e. – If Log2 (RR) = 1, that is the same as an RR=2), and bubbles to the left indicate a higher risk for subjects in Arm A. Color, green and blue helps to emphasize adverse events that are more common in Arms A or B, respectively. The size of the bubble represents the total number of occurrences of the AE of interest. Names of events with total number of occurrences with Fisher's exact test p <0.1 are displayed.

Hovering over the plots displays the corresponding AE while using the CTAS shiny app.

Volcano plot specifications

Annotate AEs that are significant at alpha (default <= 0.1)

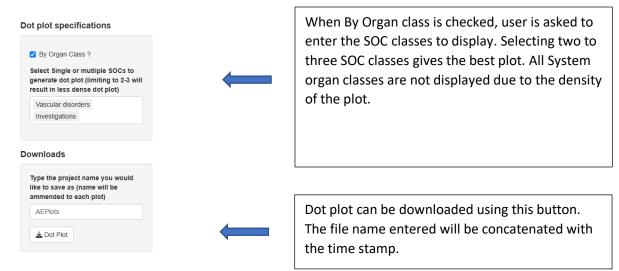
0.1

0.99

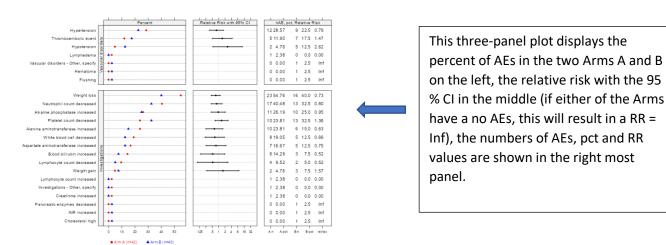
0 0.2 0.4 0.6 0.8 0.99



AEs are annotated based on the user defined cut off (default is 0.1).

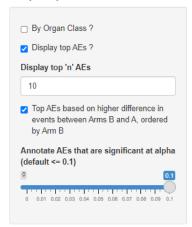


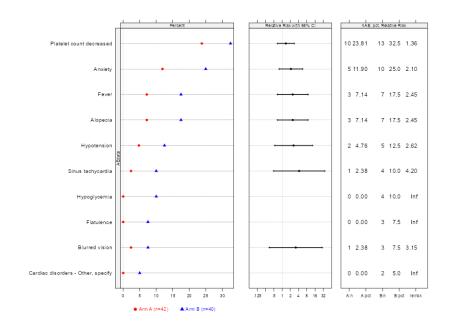
Dot plot for AEs with 2 Arms



Dot plot for AEs with 2 Arms

Dot plot specifications

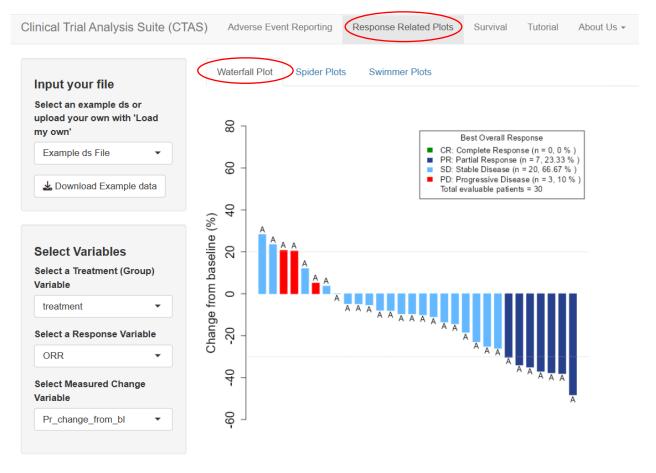


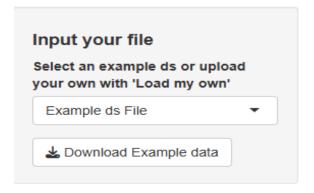


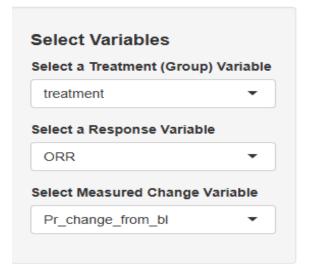
When Organ Class is unchecked, another checkbox appears with display top AEs. If unchecked, all AEs are displayed and might result in a dense plot. If display top AEs are checked, user is requested to enter the number of top AEs to display, e.g., 10. Dot plot is plotted based on higher difference between Arms B and A and ordering based on descending order in B. When unchecked the plot is ordered by Arm A.

TAB 2. RESPONSE RELATED PLOTS

2.1 Water Fall plot







Step 1:

Select the example dataset or upload your own.

To view example data and format, use download button to view .csv file.

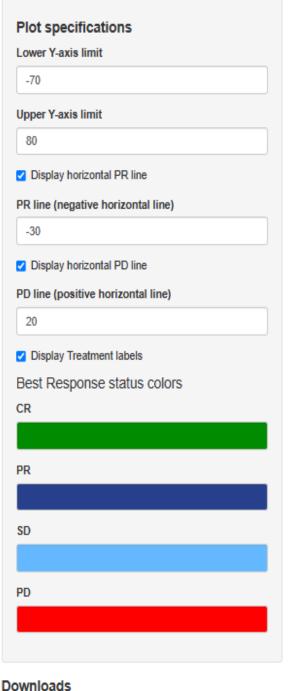
Step 2:

Select the variables in the dataset. This ds should we in wide format i.e. one patient per row.

<u>Treatment group</u> = Ex. Arms. This could be a single Arm study or a 2 Arm study. The two Arms need to be hardcoded as A and B in the dataset.

<u>Response variable</u> = Variable for the Best overall response (bor).

Measure of Change variable = This variable represents the change from baseline or change from nadir to be plotted on y-axis.



Step 3:

Select waterfall plot specifications.

Y limits: Lower and Upper y-axis limits if needed to be adjusted to fit the data.

Horizontal lines: PR and PD PR is the grey dashed line on the negative side of the y-axis PD is the grey dashed line on the positive side of the y-axis

User can choose to display either one or both horizontal lines. User enters the location (value for each PR and PD line)

Treatment labels: User can choose to display treatment Arm labels above or below each bar of the waterfall plot.

<u>Colors:</u> Choose colors for each response status.

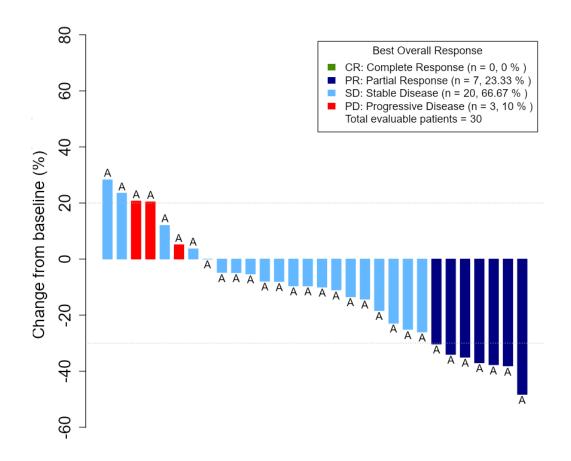
Type the file name you would like to save as (name will be ammended to each plot)

WaterfallPlot



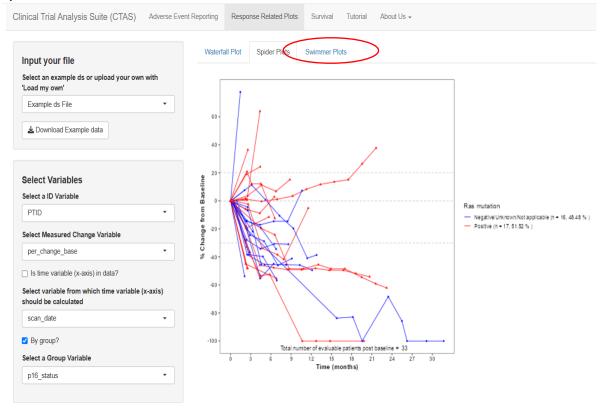
Step 4:

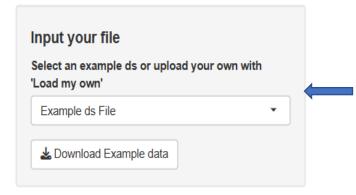
Download waterfall plot using the button. Name of the waterfall plot entered by the user will be amended with the time stamp at time of download.

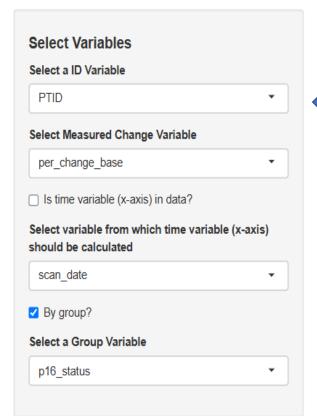


Waterfall plot data is ordered based on BOR status from left to right. Legend includes the total number of evaluable patients in the dataset and the numbers in each Response category.

2.2 Spider Plot







Step 1:

Select the example long dataset or upload your own.

To view example data and format, use download button to view .csv file.

Step 2:

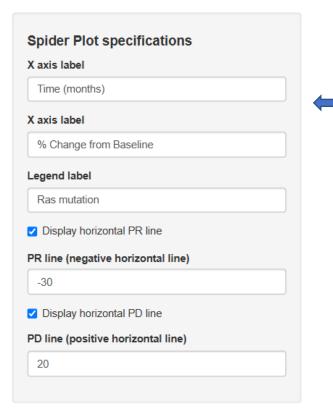
Select data variables for plotting.

<u>ID variable</u>: Select unique Patient Identifier variable

<u>Measure of Change variable</u> = This variable represents the change from baseline or change from nadir to be plotted on y-axis.

If time variable e.g. Months or weeks (x-axis), is in the available in the data, we can check box which will reveal dropdown to select that time variable. If not, a date variable for each time point can be chosen based on which time points will be calculated.

Group: If plot should be displayed by group, then check "by Group?" option and select the variable from the dataset. If "by Group?" is not checked, plot will not be color coded.



Step 3:

User can update x- axis and y-axis label based on the dataset used.

Further choose to display the PR and PD lines and at what position.

Downloads

Type the file name you would like to save as (name will be ammended to each plot)

SpiderPlot

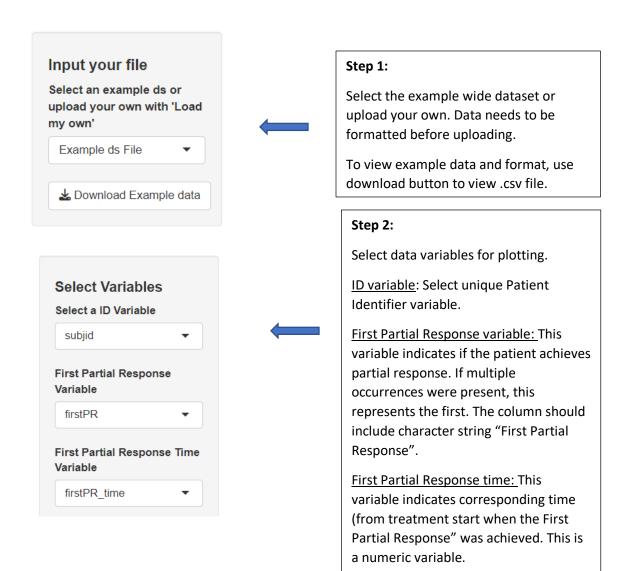
▲ Download Spider Plot

Step 4:

Download Spider plot using the button. Name of the spider plot entered by the user will be amended with the time stamp at time of download.

2.3 Swimmer Plot

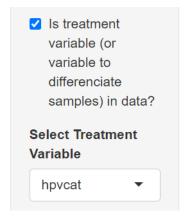




See table below for each of the

variables required.

Variable	Definition
subjid	one line per patient- only those that have at least one CR/PR
	Enter "First Progressive Response" if patient has occurrence of first PR, NA
firstPR	otherwise
firstPR_time	time (days/months/years) from treatment start to first PR occurrence
	Enter "First Complete Response" if patient has occurrence of first CR, NA
firstCR	otherwise
firstCR_time	time (days/months/years) from treatment start to first CR occurrence
	Enter "First Progressive Disease" if patient has occurrence of first PD, NA
firstPD	otherwise
firstPD_time	time (days/months/years) from treatment start to first PD occurrence
	Enter "First Stable Disease" if patient has occurrence of first SD, NA
firstSD	otherwise
firstSD_time	time (days/months/years) from treatment start to first SD occurrence
OS	Time (days/months/years) from treatment start to death or last contact
OS_censor	Death for those who died and NA otherwise
trtstart	0 for patients on treatment
	time (days/months/years) to end of treatment (or last scan date) from
trtend	treatment initiation
trtcap	Treatment Stop if patient stopped treatment, NA otherwise
Group	Group variable, if available e. g. HPV status or Response status
Fustart	Follow up Start – is the same as treatment end
Fuend	Follow up End - time from treatment start to off study date
Durable Responder	Time between first CR/PR to progression or death (whichever comes first) or
(DR)	last scan date otherwise. If >6 months then patient is a DR
	Continued response - 1 for those who have continued response (did not died
Continued_Resp	or progressed), NA otherwise



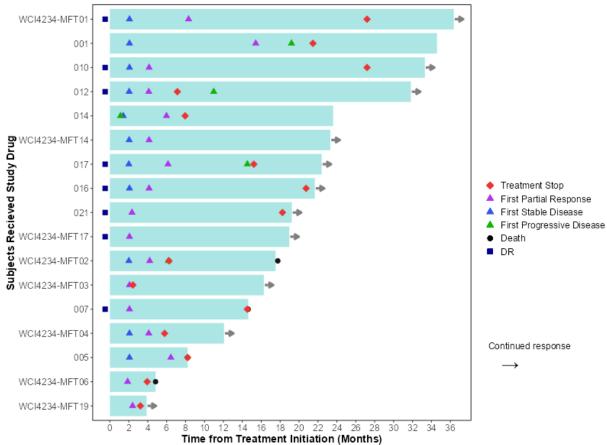


Step 3:

Select whether swimmer plot should be display by group or not. If it is to be displayed by group, a treatment variable should be made available in the dataset.

If box is unchecked, the selection of treatment variable option disappears.

Swimmer plot example without group



A Durable Responder (DR) is a subject who has confirmed response for at least 6 months

Swimmer Plot specifications

Display subject ID in swimmer plot?

X axis label

Time from Treatment Initiation (Mo

Y axis label

Subjects Recieved Study Drug

Legend label

HPV status

- Display Treatment Stop status
- ✓ Display Partial response status
- Display Stable disease status
- Display Progressive disease status
- Display Complete response status
- Display Death status
- Display Durable Responder status
- Display Continued Response status

Step 4: Display options

Select if subject ID is to be displayed on the y axis of swimmer's plot. If unchecked, only dashes will appear.

X and Y axis labels can be updated using the text box

Legend label can be updated when 2 or more groups are present (treatment available option is checked).

User can choose whether they would like to display each of these status (Treatment Stop. PR, SD, PD, CR, DR, and continued response).

Downloads

Type the file name you would like to save as (name will be ammended to each plot)

SwimmerPlot

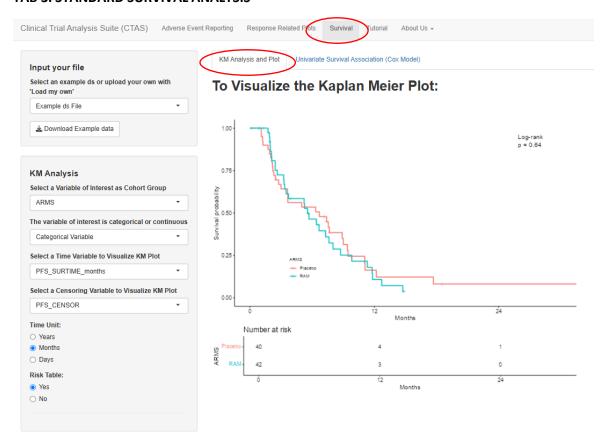


▲ Download Swimmer Plot

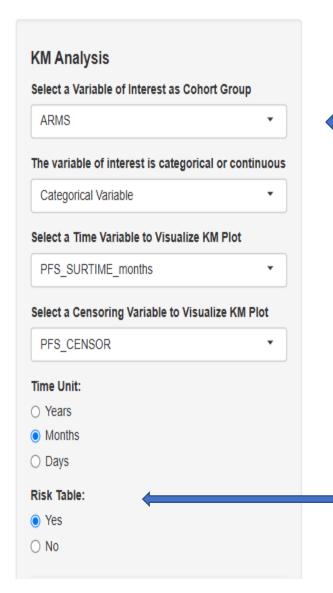
Step 5:

Download Swimmer plot using the button. Name of the Swimmer plot entered by the user will be amended with the time stamp at time of download.

TAB 3. STANDARD SURVIVAL ANALYSIS



Input your file Select an example ds or upload your own with 'Load my own' Example ds File Download Example data



Step 1:

Select the example long dataset or upload your own.

To view example data and format, use download button to view .csv file.

Step 2:

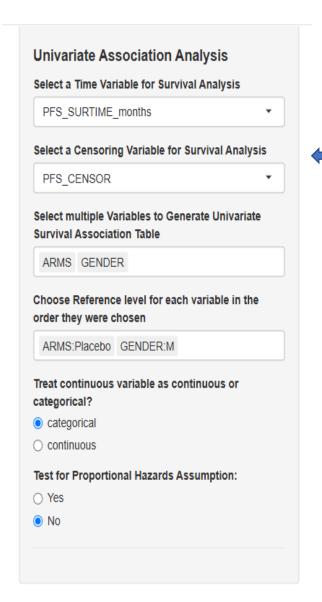
The variables from the input file will be available as drop down for selection. Choose variable of interest to divide the cohort. If continuous, a new set of parameters appear to dichotomize the continuous variable. The user can select an optimal cut-off based on the data, or either subset it by 25th or 50th or 75th percentile. Any sample with values above 25th percentile will be considered as "High" and remaining "Low". Similarly for the other groupings.

If this variable is categorical, change drop down to categorical and the cutoff choice will disappear.

Also, choose appropriate variable for survival time, censor status (0- Censor, 1- Event) variables from your uploaded dataset to carry out Kaplan Meir analysis. User can also select the appropriate time unit (Years, Months or Days). Years being the default here.

Step 3:

User can opt to display the number at risk table under the KM curve in each categorical group.



Step 4:

Choose appropriate survival time, censor status (0- Censor, 1- Event) variables from your uploaded dataset for conducting the Univariate analysis.

Enter variable(s) to generate the univariate analysis table to test association between variable and survival using the Cox PH Model.

User can also test for PH assumption. An additional column will be added with the PH assumption p-value.

Downloads



Step 5:

User can download the results from the univariate analysis association for the variable(s) of his/her interest.

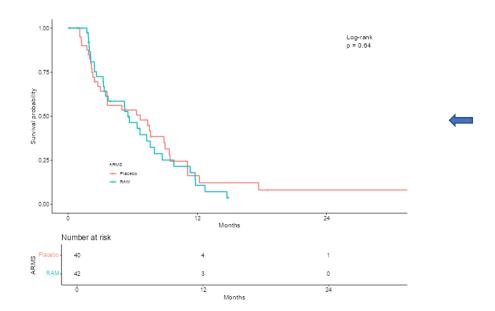
Similar, download is available on the KM Analysis and Plot tab.



Univariate Survival
Association analysis table is
displayed for the single or
multiple variables selected
by the user. For example,
here categorical variable
Group and dichotomized
continuous variable (based
on 25th percentile cut point)
are being tested.

KM Analysis and Plot Univariate Survival Association (Cox Model)

To Visualize the Kaplan Meier Plot:



KM plot stratified by the categorical variable Arms. An at risk table is displayed under the KM plot. The time unit is years but can be changed using the options mentioned previously.