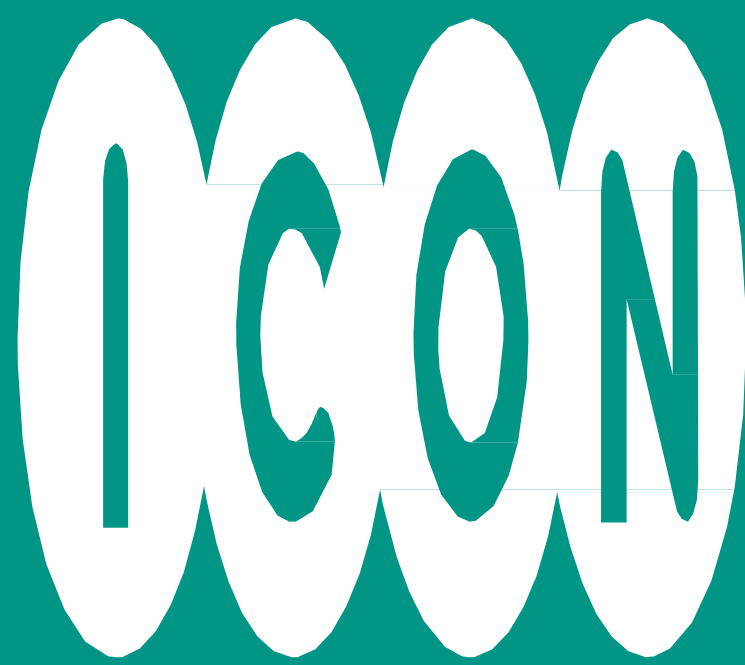




PP12: Oncology Data through Customized Graphics



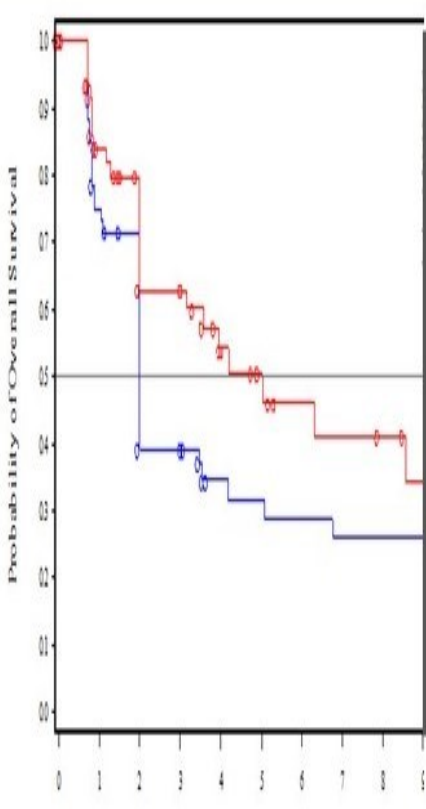
Introduction

- Easy to recognize patterns and find exemptions
- Different colors, patterns, symbols can translate the message clearly
- Easy to understand complex clinical data
- Effectively translate the data to non-clinicians
- Commonly used plots for potential safety and efficacy endpoint
 - Waterfall Plot
 - Swimmer Plot
 - Kaplan-Meier Plot
 - Forest Plot
 - Boxplot
- SAS ODS Graphics (SG Procedures/GTL) and SAS/GRAPH Annotate provide great flexibility for generating these customized graphics.

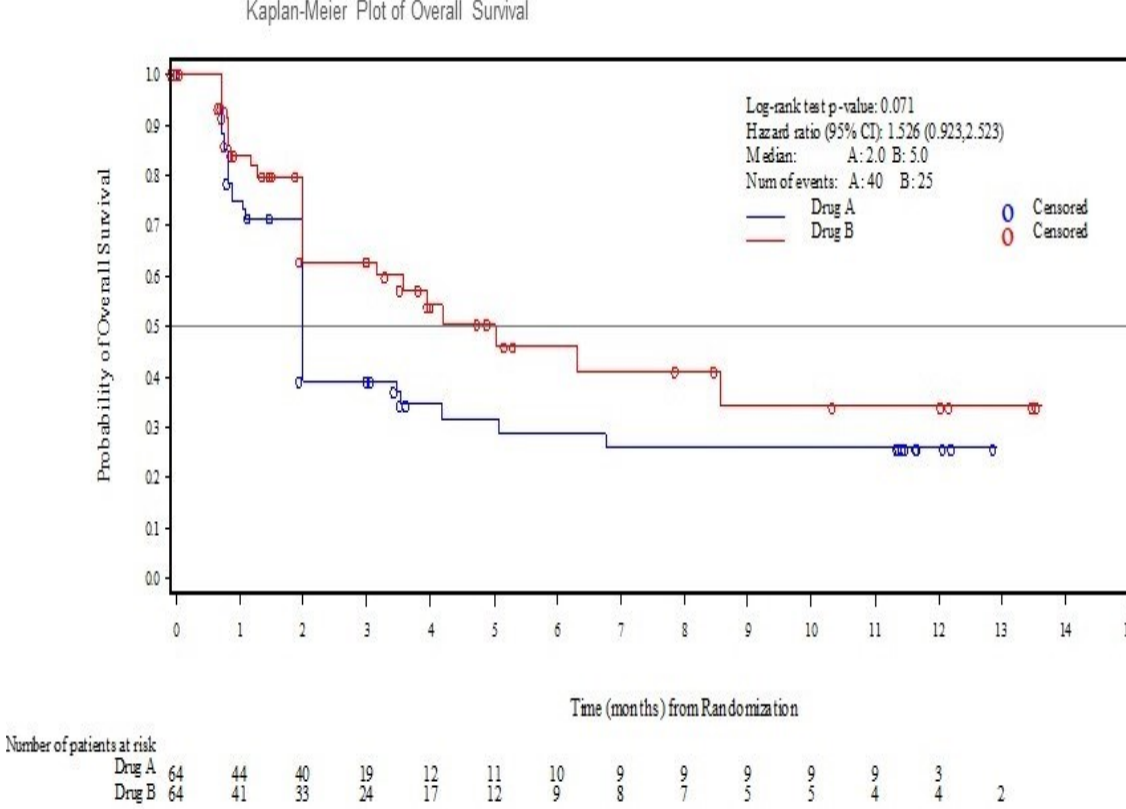
Oncology Efficacy Endpoints at a Glance

Kaplan-Meier Plot (K-M)

- K-M is the most frequent method used overall for survival analysis or efficacy.
- KM is a visual presentation of censored survival/failure or time to event curves, e.g. PFS, OS.
 - OS is the "gold standard" among primary endpoints. Time from randomization until death from any cause. Usually presented as Median OS, or percentage of subjects alive at specified timepoints.
 - PFS is the time from randomization to disease progression or death.
- In order to generate a K-M plot, at least two pieces of data are required for each subject:
 - the status at last observation (event or censored defined as per analysis plan)
 - the time to event (or time to censoring)
- If the survival functions between two or more groups are to be compared, then a third piece of data is required: the group assignment of each subject
- For each interval, probability of survival is calculated as number of subjects surviving divided by number of subjects at risk.
- Subjects who have died, dropped out, or not reached the time yet are not counted as at risk.
- Negative events (e.g., PFS, OS) result in a left to right descending pattern as subjects no longer "survive" the event: They experience disease progression or death.



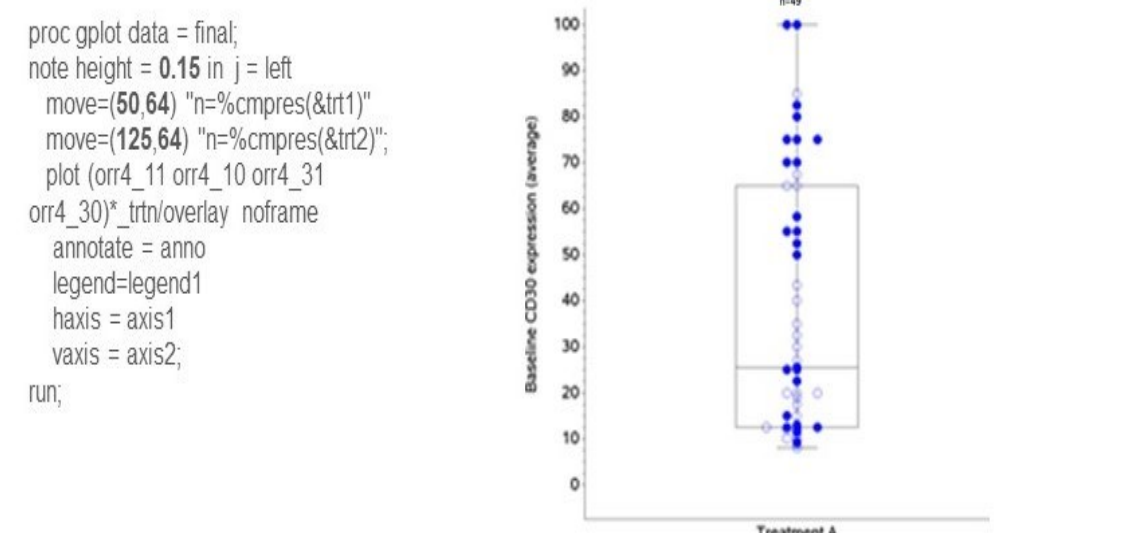
- The first step in this process is to refer to ODS graphics to output the PROC LIFETEST survival dataset.
- Cox Proportional hazards model to estimate hazard ratio between treatment arms adjusted for covariates and log-rank test p-value.
- Annotation dataset is needed to place various elements on the graph.
- The graphical approaches to produce plot can vary significantly e.g. SGPLOT or GPLOT.
- In our example, SAS/GRAPH PROC GPLOT is used.



BOX Plot

- Boxplot is a popular and useful tool for exploring continuous oncology endpoints, e.g. baseline or change from baseline value for endpoints of interest.
- Boxplots are simple visualizations that are powerful to convey variation in data without making any assumptions about the underlying statistical distribution.
- A boxplot can provide treatment comparison of the mean, median, 25th and 75th percentile, minimum, and maximum.
- shows distributions of data is particularly useful for understanding the shape of the distribution and whether there are outliers
- In addition to the continuous endpoint, investigators may also be interested in information of a categorical endpoint displayed on the same graph.
- This can be achieved by using SAS/GRAPH PROC GPLOT and the ANNOTATE facility to create a box plot superimposed by a scatter plot.

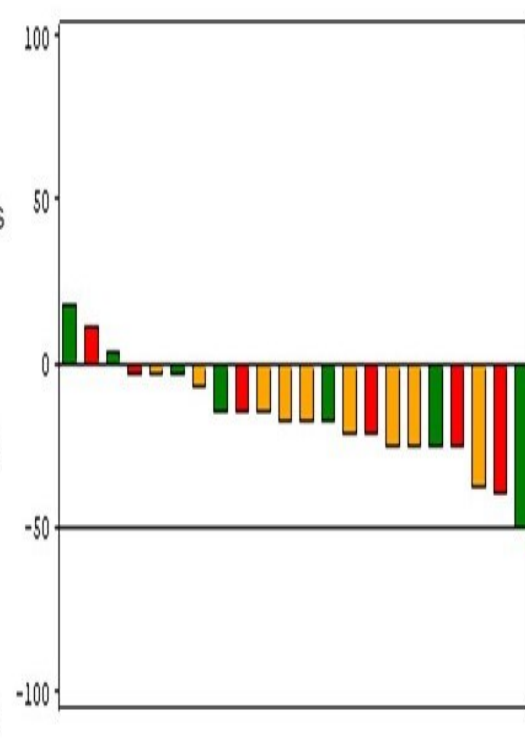
- In our example, continuous endpoint is baseline CD30 expression and categorical endpoint is objective response rate (ORR). ORR will be superimposed on a box plot of a continuous endpoint, baseline CD30 expression.
- The response values for ORR are 0 (non-responder) or 1 (responder).
- "jittering" will be implemented to offset the identical X and Y values by manipulating the horizontal X values used for the scatter plot. The "jittering" technique manipulates the X values based on the counts of each response value for each treatment group. The Y value (ORR) will be shifted to the right by adding the count value multiplied by a factor of 0.5. If the count value is small, it will be shifted to the left by subtracting the count value multiplied by the same factor for odd count values.
- The SAS ANNOTATE macros %NAME and %LINE will be utilized to create ANNOTATE observations to draw lines for the box plot for the continuous endpoint baseline CD30 expression.
- The mean, median, 25th and 75th percentile, and minimum and maximum cross-tab from SAS PROC UNIVARIATE.



Waterfall Plot

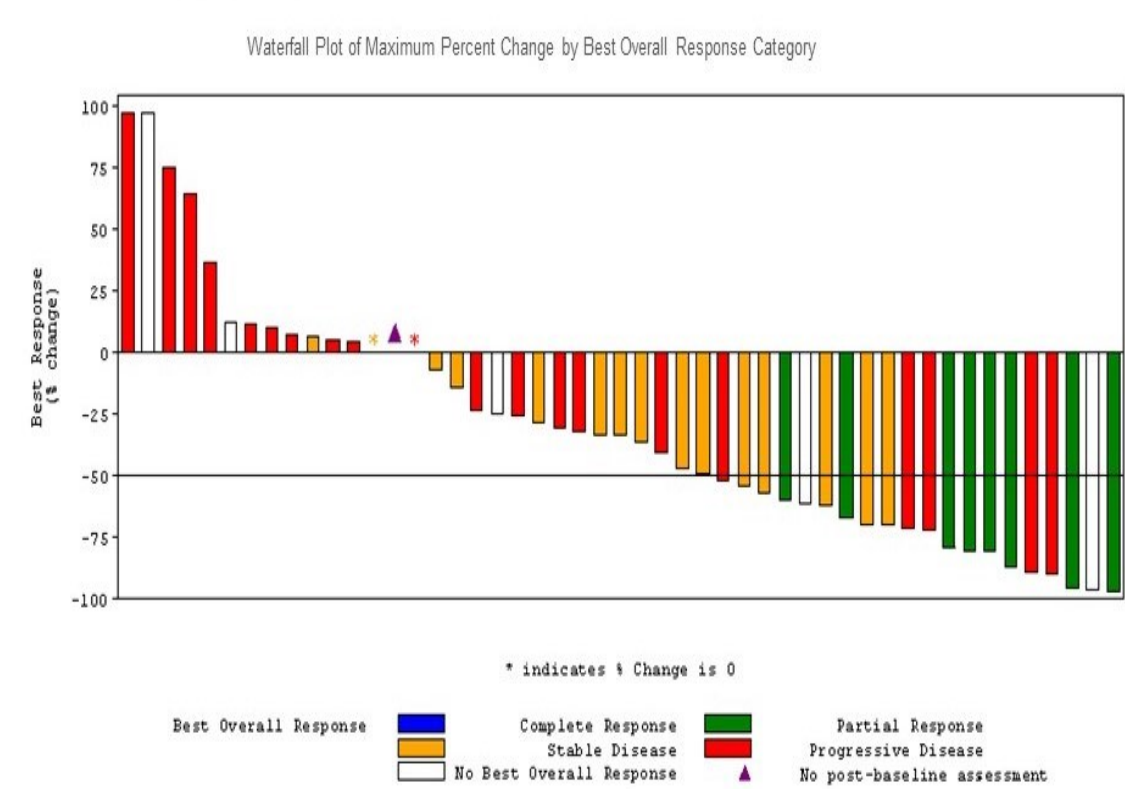
- Widely used in oncology clinical trials to present the variability of outcomes.
- A waterfall plot is used to present each individual subject's response to a particular drug based on a parameter, such as tumor burden.
- Best way to display the improvement (reduction) in tumor size seen in each of the participating subjects
- Work best in a study with a smaller cohort of subjects.
- Provide clear picture of study results from worst to best, based on the parameters included.

- Each of the bars in the plot refer to the percentage of change in the target lesions as compared to the baseline measurements for each subject.
- This baseline change usually corresponds to as the "best response" to the treatment for each subject.
- Waterfall plot go from the worst value from the left to the best value to the right side of the plot i.e., improvement (reduction) in tumor.
- Vertical bars above the line represent worst response described as positive percent.
- Vertical bars below x-axis represent achieved tumor reduction, described as negative percent.



Data from PR10 study

SUBJ	AGE	SEX
201	75	M
202	75	F
203	68	M
204	67	M
205	67	M
206	67	M
207	67	M
208	67	M
209	67	M
210	67	M
211	67	M
212	67	M
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292	67	M
293	67	M
294	67	M
295	67	M
296	67	M
297	67	M
298	67	M
299	67	M
300	67	M



Forest Plot

- The plot visually shows whether a treatment does or does not provide a positive outcome
- Great visual tool for subgroup analysis
- One of the best ways to visualize data as table and graph on one page
- Best used for displaying point estimates and their associated confidence intervals for treatment comparison in subgroup analysis.
- The confidence intervals for subgroups are represented by horizontal lines on the graph with their point estimates annotated on the lines.
- These statistics as well as the median survival time and frequencies by treatment are often added to the graph to provide a complete picture of the efficacy data.



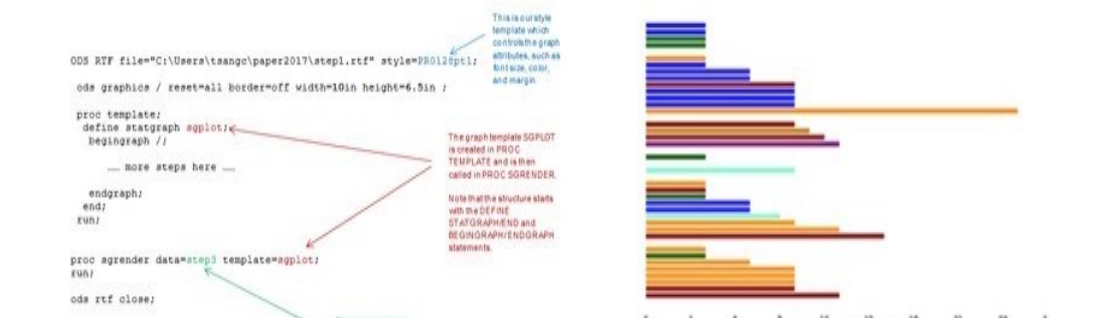
Using SAS/GRAPH PROC GPLOT and ANNOTATE data set (ANNOPLOT), with frequency of events, median PFS, and hazard ratio with 95% confidence intervals, will be referenced using the ANNO= option.

```
proc gplot data=final ANNO = ANNOPLOT;
note height = 0.15 in j = left
move=(75.2) "Favors Drug A <"
move=(84.27) "_____";
plot y=x=block / axis=axis1
href=1
vaxis=axis2 nologend noframe;
run;
```

Swimmer Plot

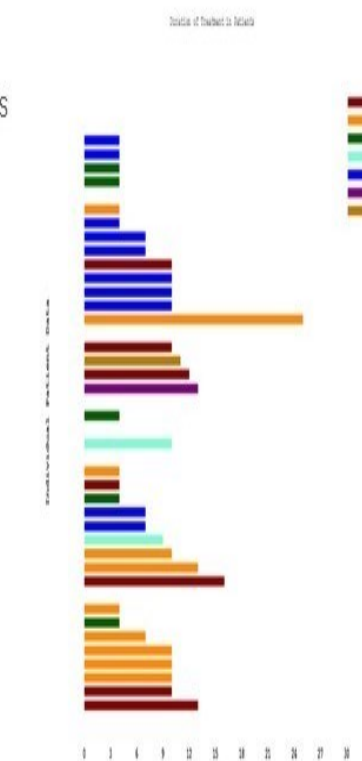
- Another useful visual tool to assess treatment efficacy endpoints for individual subjects
- It is a graphical way to display subject's response story
- Each bar looks like a swim lane and hence called swimmer plot
- Efficacy endpoints may include tumor response evaluation over time as measured by Response Evaluation Criteria in Solid Tumors (RECIST), or percent change from baseline in target lesions for measurable disease as defined by the presence of at least one measurable lesion.
- These endpoints are always juxtaposed with other valuable information, such as treatment doses, duration of treatment, primary tumor type, and treatment status to create a compelling visual presentation.

- A swimmer plot may display individual subject data by dose group and primary tumor type.
- The bars represent the duration of treatment in weeks.
- Primary tumor types are differentiated by colors of the bars.
- Annotation can be added for the following information: tumor response assessment (such as CR, PR, SD, PD) over time, percent change at maximum reduction from baseline in target lesions, and treatment status (ongoing).
- SAS GTL is used for creating the swimmer plot. PROCTEMPLATE is used for creating the graph template.



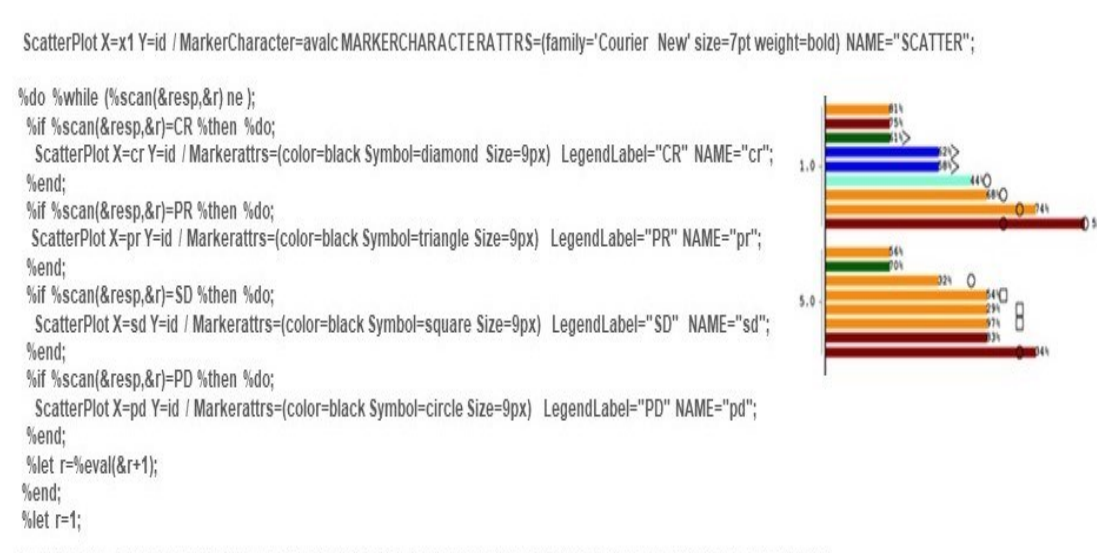
VECTORPLOT and DISCRETELEGEND

- In PROC TEMPLATE, the VECTORPLOT statement can be used for creating bars or lines by adjusting the thickness option (THICKNESS).
- For example, VECTORPLOT can be used to create the horizontal bars based on treatment duration (TREATDUR) for the X axis and the record identifier (ID) for the Y axis. These values are also grouped to primary tumor type (PRIMTYP). Note that the top right legend for the grouped variable is created by the DISCRETELEGEND statement.



SCATTERPLOT

- In PROC TEMPLATE, the SCATTERPLOT statements can be used to annotate symbols or text.
- For example, SCATTERPLOT is used to create annotation for the tumor response over time (CR, PR, SD and PD), treatment status (AE), and the percent change at maximum reduction from baseline (X1).



- The DISCRETELEGEND statement can be used to create the legend for these endpoints.

DISCRETELEGEND

```
%do while (%scan(&resp,&1) ne );
%let %scan(&resp,&1)=CR %then %do;
%let %scan(&resp,&1)=PR %then %do;
%let %scan(&resp,&1)=SD %then %do;
%let %scan(&resp,&1)=PD %then %do;
%let %scan(&resp,&1)=AE %then %do;
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