Graphical presentation of
Clinical Trial Data and Results

Hanumantha Rao Karedla
Cognizant Technology Solutions
18th June 2016
01 | The use of Graphs in Clinical trail reporting
02 | Basic checks to be performed before starting programming of Graphs
03 | Different type of Graphs we produce for CSR, DMC, IA and publications
04 | How to review the Graphs before submitting to customer
05 | Question and Answers
The use of Graphs in Clinical trial reporting

01: Graphical presentation of clinical trial data can quickly and effectively communicate the intended message

02: Emphasis on clear and transparent presentation of data for regulatory review and communications

03: Graphs will help to get your audience’s attention

04: To communicate results, especially to non-statisticians and Management

05: To explore the data before deciding any exploratory or data driven analysis, to check statistical assumptions

06: Easy to detect the outliers
Basic checks before starting programming of Graphs

How many of us go through Statistical analysis Plan (SAP) and Mock shells before start of programming of datasets or TLF’s?
Basic checks before starting programming of Graphs

- Statistical Analysis Plan
- Mock shells
- SDTM/ADAM datasets
- SAS Programs
Basic checks before starting programming of Graphs

01. Mock shells are always a layout and actual graphs should reflect as per the data.

02. Clarify all the ambiguity in mock shells upfront.

03. Ask statistician or colleagues if there are any standard programs in place.

04. Sometimes Statistician might have copied the shells from other studies into mock shells to make it consistent with the project standards.

05. Read all the programming notes given in the mock shells before start of programming.
## Pros and cons

<table>
<thead>
<tr>
<th>Graph</th>
<th>Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better in Presentations</td>
<td>Better in papers</td>
</tr>
<tr>
<td>Can only show summaries</td>
<td>Can often show all the data</td>
</tr>
<tr>
<td>Show only a few variables</td>
<td>Better for multiple variables</td>
</tr>
<tr>
<td>Trend better illustrated</td>
<td>Trend badly illustrated</td>
</tr>
</tbody>
</table>
Different type of Graphs

- Continuous
- Categorical
- Time to event
- Safety
- Statistical graphs
Different type of Graphs

Figure 1: Mean plasma concentrations (unit) of Analyte X for Group A (PK analysis set)
Different type of Graphs

Figure 2

Individual immunology values for Treatment A (Full analysis set)
Different type of Graphs

Figure 3  Geometric mean and 90% CI for ratio of pairs of Groups for parameter (PK analysis set)

- Group A to Group B
- Group B to Group C
- Group A to Group C
- Group A to Group D

0.80  1.20  0.80  1.25  0.80  1.20  0.80  1.25
Different type of Graphs

Box plot by Treatment group (Full analysis set)

A mild outlier is any observation lying between the inner and outer fences on either side, while a serious outlier is an observation that lies beyond the outer fences on either side.

Some definitions:
- Interquartile Range (IQR) = Q3 - Q1
- Inner Fences: Q1 - 1.5 X IQR; Q3 + 1.5 X IQR
- Outer Fences: Q1 - 3 X IQR; Q3 + 3 X IQR

For ALAT, ASAT and ALKPH, the Clinical Concern Level is 2 ULN; for BILTOT, the CCL is 1.5 ULN; where ULN is the Upper Level of Normal Range.
Different type of Graphs

Figure 5
Box plot with mean and median (Full analysis set)

Display Mean and Median Values on a Box Plot

![Box plot with mean and median values](image)
Different type of Graphs

Figure 6

Box plot for two variables (Full analysis set)
Different type of Graphs

Figure 7

Mean change from baseline score over time by treatment (Full analysis set)
Different type of Graphs

Figure 8

% Mean change ((±SD) from baseline score over time by treatment (FAS)
Different type of Graphs

Figure 9  Mean (±SE) on Variable X (Full analysis set)
Different type of Graphs

**Figure 10**
Response rates for all treatment on Variable X (Full analysis set)
Different type of Graphs

Figure 11

Scatter plot of Variable X and Y (Full analysis set)
**Different type of Graphs**

**Figure 12** Statistical analysis of change from baseline score by sub group (Full analysis set)

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Total n</th>
<th>LSM difference (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
</tr>
<tr>
<td>Female</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
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<tr>
<td>18-64</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
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<tr>
<td>&gt;=65</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
</tr>
<tr>
<td>Black or African-American</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
</tr>
<tr>
<td>Other</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
</tr>
<tr>
<td>non-US</td>
<td>xx</td>
<td>(xx,x,xx.x)</td>
</tr>
</tbody>
</table>

LSM difference Relative to Placebo
Different type of Graphs

Figure 13

Forest plot (Full analysis set)

Impact of Treatment on Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio and 95% CL</th>
<th>OR</th>
<th>LCL</th>
<th>UCL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modano (1967)</td>
<td>0.590 0.096 3.634</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Borodan (1981)</td>
<td>0.464 0.201 1.074</td>
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<td></td>
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<tr>
<td>Leighton (1972)</td>
<td>0.394 0.076 2.055</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Novak (1992)</td>
<td>0.490 0.088 2.737</td>
<td></td>
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<tr>
<td>Stawer (1999)</td>
<td>1.250 0.479 3.281</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Truak (2002)</td>
<td>0.129 0.027 0.605</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fayney (2005)</td>
<td>0.313 0.054 1.805</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Modano (1969)</td>
<td>0.429 0.070 2.620</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soloway (2000)</td>
<td>0.718 0.237 2.179</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adams (1999)</td>
<td>0.143 0.082 0.250</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Truak2 (2002)</td>
<td>0.129 0.027 0.605</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fayney2 (2005)</td>
<td>0.313 0.054 1.805</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Modano2 (1989)</td>
<td>0.429 0.070 2.620</td>
<td></td>
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<tr>
<td>Soloway2 (2000)</td>
<td>0.718 0.237 2.179</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adams2 (1999)</td>
<td>0.143 0.082 0.250</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>0.328 0.233 0.462</td>
<td></td>
<td></td>
<td></td>
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</table>
Different type of Graphs

Figure 14
Kaplan-Meier comparison of variable tested between Group A and Group B (FAS set)
Different type of Graphs

Figure 15

Kaplan-Meier comparison of variable tested between Group A and Group B - (FAS set)

Kaplan-Meier Plot

Survival Probability

Disease-Free Survival Time

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Event</th>
<th>Censored</th>
<th>Median Survival</th>
<th>95% CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>38</td>
<td>24</td>
<td>14</td>
<td>192</td>
</tr>
<tr>
<td>AML-Low Risk</td>
<td>54</td>
<td>25</td>
<td>29</td>
<td>641</td>
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<tr>
<td>AML-High Risk</td>
<td>45</td>
<td>34</td>
<td>11</td>
<td>390</td>
</tr>
</tbody>
</table>
Different type of Graphs

Figure 16

AEs for particular patient  (Safety analysis set)
Different type of Graphs

Figure 17

Number (%) of top 20 AE by preferred term (Safety analysis set)

Percent of Top Twenty Adverse Events

- PRURITUS
- APPLICATION SITE PRURITUS
- ERYTHEMA
- APPLICATION SITE ERYTHEMA
- RASH
- APPLICATION SITE IRRITATION
- APPLICATION SITE DERMATITIS
- DIZZINESS
- SKIN IRRITATION
- SINUS BRADYCARDIA
- DIARRHOEA
- HEADACHE
- NASOPHARYNGITIS
- NAUSEA
- COUGH
- UPPER RESPIRATORY TRACT INFECTION
- HYPERHIDROSIS
- MYOCARDIAL INFARCTION
- VOMITING
- APPLICATION SITE VESICLES

Legend:
- ○ Placebo
- + Drug A
- × Drug B
Different type of Graphs

Figure 18

Number (%) of patients reporting AE and SAEs by SOC (Safety analysis set)

Most Frequent On-Therapy Adverse Events
Sorted by Relative Risk

- Arthralgia
- Nausea
- Anorexia
- Hematuria
- Insomnia
- Vomiting
- Dyspepsia
- Weight Decrease
- Respiratory Disorder
- Headache

Percent

Relative Risk with 95% CL

- Drug A
- Drug B
Mean laboratory values over time for laboratory safety variable A (Safety analysis set)
### Different type of Graphs

**Figure 20**

Shift plot comparing baseline to different time points on treatment, for laboratory variables (Safety analysis set)

#### LFT Safety Panel, Baseline vs. Study

<table>
<thead>
<tr>
<th></th>
<th>ALAT</th>
<th>Bilirubin Total</th>
<th>Alk Phosphatase</th>
<th>ASAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Week</td>
<td>![Graph]</td>
<td>![Graph]</td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td>3 Months</td>
<td>![Graph]</td>
<td>![Graph]</td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td>6 Months</td>
<td>![Graph]</td>
<td>![Graph]</td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
</tbody>
</table>

- **Baseline (ULN)**: 0, 1, 2, 3, 4
- **Study (ULN)**: 0, 1, 2, 3, 4

*For ALAT, ASAT and Alkaline Phosphatase, the Clinical Concern Level is 2 ULN; For Bilirubin Total, the CCL is 1.5 ULN: where ULN is the Upper Level of Normal.*
How to review the Graphs before submitting to customer

01. Consistency

Make sure the colors and symbols are clear in Graphs, Maintain consistency of color, Scale and symbol for same treatment across graphs.

02. Compare

Cross check the value, mean, SE, percentage with corresponding table.

03. Reference

Provide a reference table or listing for each graph as a footnote.
Thank You
Looking forward to work with you!
Annexure
Different type of Graphs

Responding Patients

Months after Initial Treatment

- Patient #1: OFF TREATMENT, Follicular, previously treated
- Patient #2: OFF TREATMENT, Follicular, previously treated
- Patient #3: Still On, Follicular, previously treated
- Patient #4: OFF TREATMENT, Follicular, previously treated
- Patient #5: Still On, Follicular, not previously treated
- Patient #6: Still On, Follicular, not previously treated
- Patient #7: Still On, Follicular, previously treated
- Patient #8: Still On, Follicular, previously treated
- Patient #9: Still On, Follicular, previously treated
- Patient #10: Still On, Follicular, not previously treated
- Patient #11: Still On, Follicular, previously treated
- Patient #12: Still On, Marginal Zone B-Cell, not previously treated
- Patient #13: OFF TREATMENT, Mantle Cell, previously treated

SD duration
PR duration
CR duration
Retreatment post-PD
### Table 2.1. Baseline Demographics
(Subjects Exposed to Study Drug)

<table>
<thead>
<tr>
<th></th>
<th>Study XXXX</th>
<th></th>
<th></th>
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<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Drug A</td>
<td>Total</td>
<td>Placebo</td>
<td>Drug A</td>
</tr>
<tr>
<td></td>
<td>(N=165)</td>
<td>(N=164)</td>
<td>(N=329)</td>
<td>(N=165)</td>
<td>(N=164)</td>
</tr>
<tr>
<td>Sex - n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>65 (39.4)</td>
<td>64 (39.0)</td>
<td>129 (39.2)</td>
<td>65 (39.4)</td>
<td>64 (39.0)</td>
</tr>
<tr>
<td>Male</td>
<td>100 (60.6)</td>
<td>100 (61.0)</td>
<td>200 (60.8)</td>
<td>100 (60.6)</td>
<td>100 (61.0)</td>
</tr>
<tr>
<td>Race - n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Caucasian</td>
<td>136 (82)</td>
<td>135 (82)</td>
<td>271 (82)</td>
<td>136 (82)</td>
<td>135 (82)</td>
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<tr>
<td>African American</td>
<td>6 (4)</td>
<td>8 (5)</td>
<td>14 (4)</td>
<td>6 (4)</td>
<td>8 (5)</td>
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<td>10 (6)</td>
<td>23 (7)</td>
<td>13 (8)</td>
<td>10 (6)</td>
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<td>Asian</td>
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<td>13 (4)</td>
<td>6 (4)</td>
<td>7 (4)</td>
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<td>2 (1)</td>
<td>4 (1)</td>
<td>2 (1)</td>
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<td>1 (0)</td>
<td>0 (0)</td>
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<tr>
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<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Other</td>
<td>2 (1)</td>
<td>1 (1)</td>
<td>3 (1)</td>
<td>2 (1)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

### Baseline Demographics

![Different type of Graphs](chart.png)
Different type of Graphs

Histogram with Normal Density Curve

Est. Mean = 23.676470588  Est. Stddev = 8.9872656988
Spec. Mean = 30  Spec. Stddev = 10