



Use of Graphics in Clinical Trials

A Discussion

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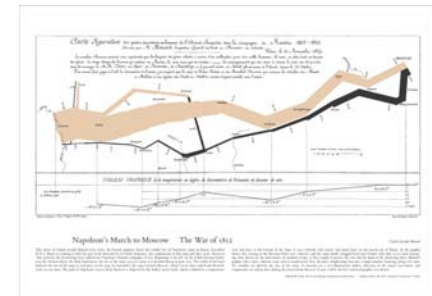


Outline

- Revisiting the Presentations
- Additional Thoughts- A User's Perspective
- Concluding Thoughts

“Well-designed data graphics are usually the simplest and at the same time the most powerful”

Edward Tufte





Use of Graphics in Clinical Trials

- As statisticians we are responsible for presenting the findings of clinical trials. A visually stimulating graphic can capture attention in a way that a table cannot.
- Creating a graph is easy but creating an excellent graph requires care and precision.
- A graph must present the information, illustrate the key points and guard against the potential reader drawing erroneous conclusions.



Revisiting 4 Excellent Presentations

1. Use of graphics in Clinical Trials — [Frank Harrell, Jr.](#)
2. A Case Study of Graphics in Clinical Trials: the Role of Statistical Graphics in Recent Submission/Approval of GSK's Votrient's in US — [Michael Durante](#)
3. Graphics for Exploratory Analysis and Reporting in Clinical Trials — [Michael O'Connell](#)
4. Communicating Clinical Trial Results the Statistical Graphic Way — [Mat Soukup](#)



1. Use of Graphics in Clinical Trials by Frank Harrell

General overview emphasizing graphics as a tool for enhancement of clarity in data presentation.

Key messages:

- Excellent tool to identify patterns.
- To communicate results, especially to non-statisticians.
- Concept of using of micrographics inside tables
- Focus on presenting **safety** data.



A Case Study of Graphics in Clinical Trials by Michael Durante

Case Study for the compound Votrient (pazopanib), approved by the US Food and Drug Administration for the treatment of advanced renal cell carcinoma.

Key Messages:

- Highlights the role of graphics in data presentation.
- A real example/ success story of graphics in effective communication.
- Clear presentation makes the point effectively and aid review process- A win-win situation.
- Main emphasis on **Safety** analysis- to identify signals, summarize safety at patient and study level for LFT, QTc, and general AEs etc.
- **Efficacy** analyses - waterfall and forest plots .

Graphics for Exploratory Analysis and Reporting in Clinical Trials by Michael O'Connell

Presentation on the exploratory, reporting, validation aspect of data using graphics

Key Messages:

- Clinical trials are complex - graphics provides a way to explore/report data.
- Exploratory analysis - medical monitoring, safety assessment, social webs etc.
- Using a palette of graph types report graphics.
- Features of available software.
- Emphasis on **exploratory and safety** analyses.



Communicating Clinical Trial Results the Statistical Graphic Way by Mat Soukup

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



Key Messages:

- Compelling examples of the *good* and the *bad*...
- Incorporate data elements in the graphics.
- Graphics display versus tables for data interpretation.
- Graphical approaches aid in regulatory decision making process.
- Emphasis on both **efficacy & safety** analyses.
- Need for standardization: A joint working group (FDA/Industry/Academia) with a common goal to develop a standard set of graphics for visualizations of clinical trial safety data.



Additional Thoughts – A User's Perspective

Creating a graph requires care and planning.

- Use same scale when data across studies is presented side-by side.
- Appropriate use of tick-marks for both axes - avoid clutter while keeping meaningful information.
- K-M plots with patients at risk information. Think of the appropriate truncation point upfront.
- Plan ahead for consistency- else lots of work when putting together final integrated summary documents.



Additional Thoughts – A User’s Perspective

- Graphics for safety - high on everyone’s list
 - A clear need because important to detect safety signal from large sets of data.
 - Appropriate graphics would help periodic data reviews, e.g., by DMCs, medical monitoring, etc.
- Graphics for efficacy – important
 - for overall summary of treatment efficacy across endpoints, subgroups, studies, etc.
 - Forest plots with sufficient data details – overall summary.
 - Cumulative Distribution Function plots – useful in understanding response.
 - Waterfall plots – examine the point of inflexion (oncology, QTc).

Example - Forest Plot (Lancet 1996)

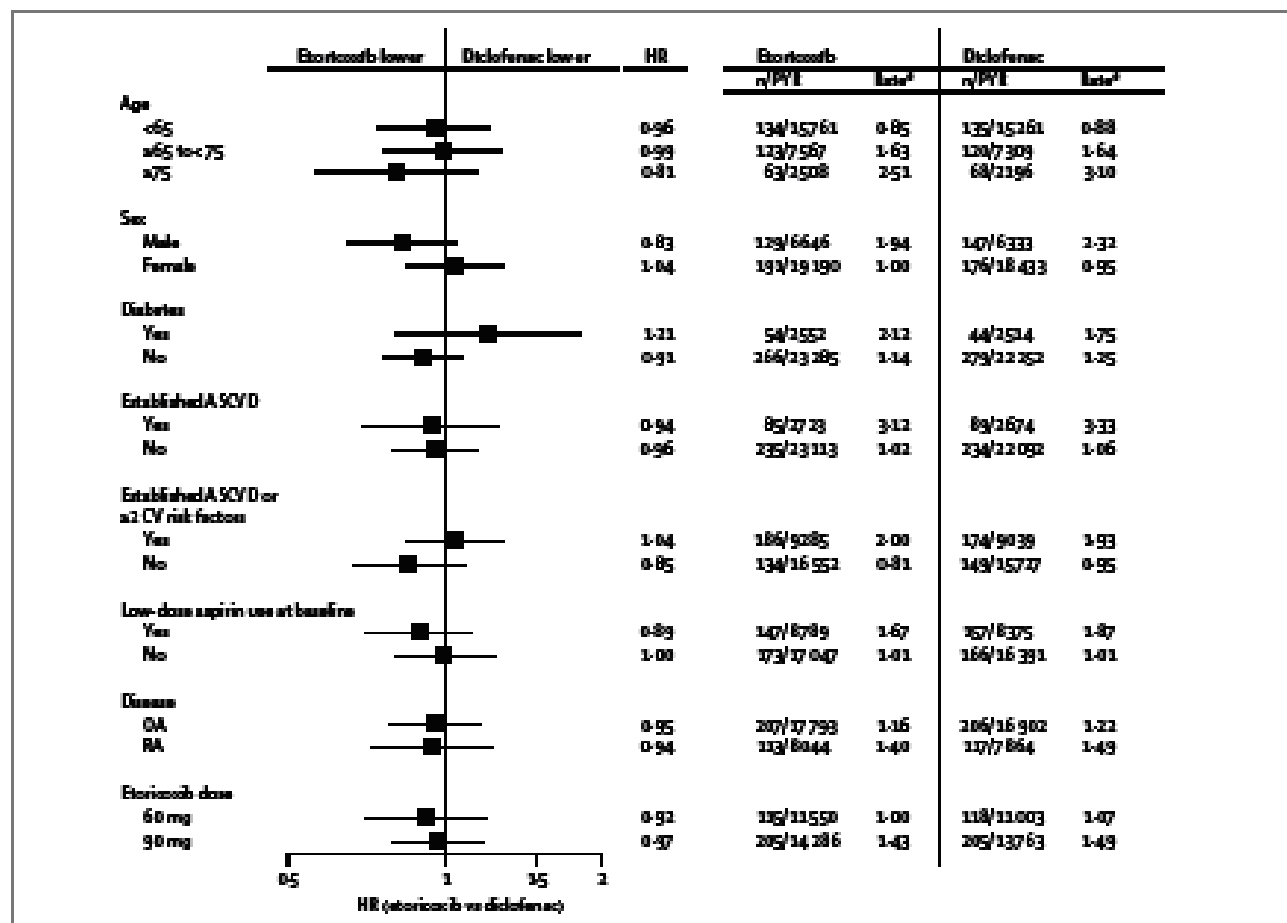
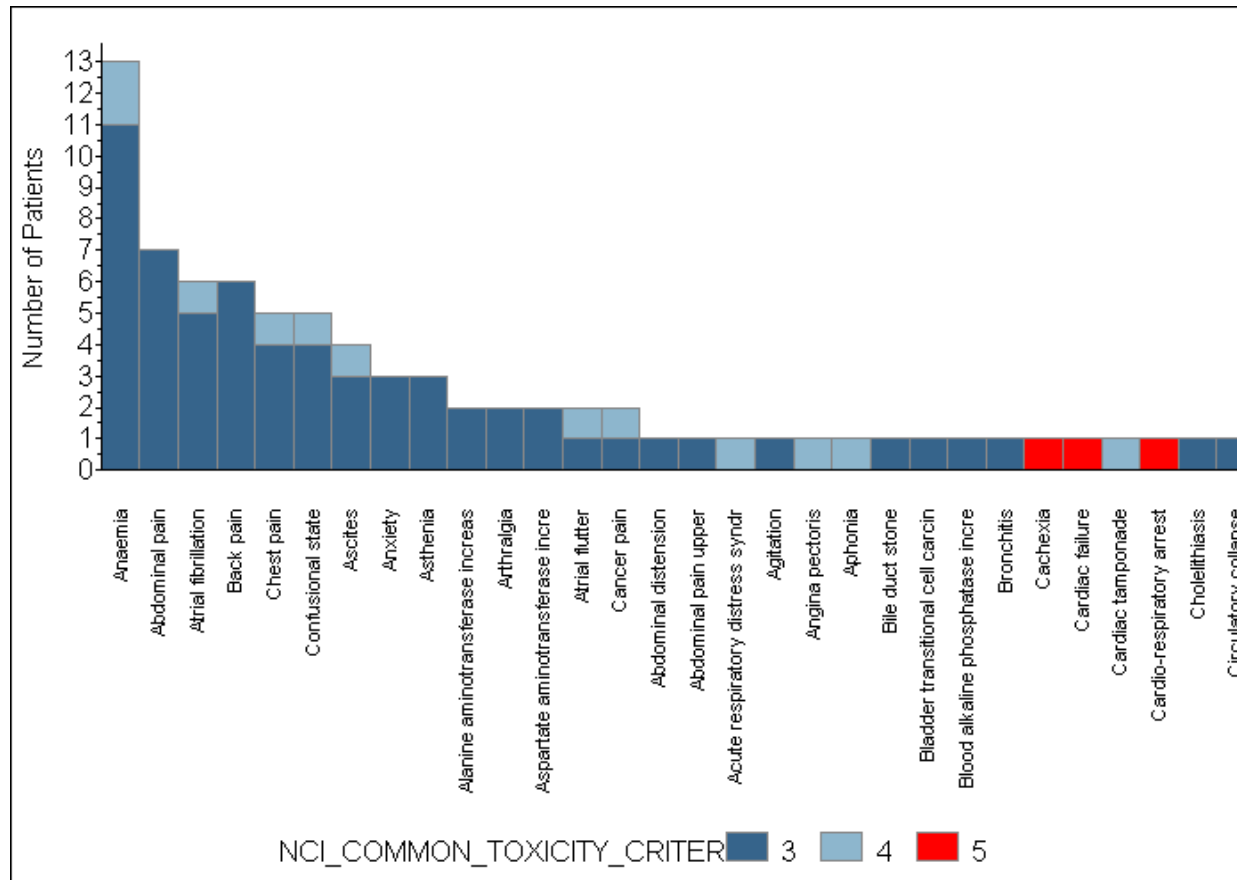
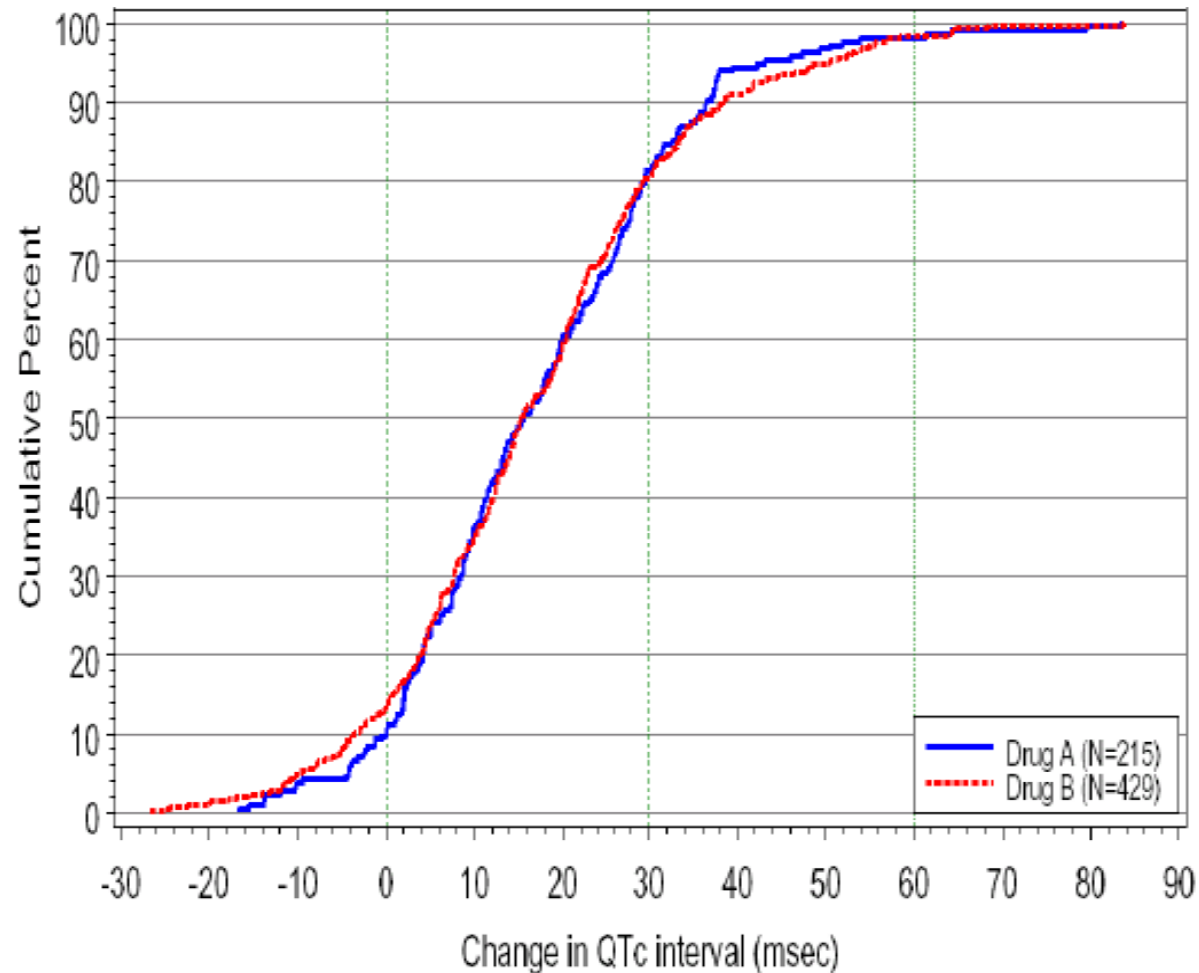


Figure 3: Incidence of thrombotic cardiovascular (CV) events in prespecified subgroups, per-protocol population. ASCVD=atherosclerotic cardiovascular disease. PY=patient-years at risk. *Events per 100 patient-years.

Example- Overall Periodic Safety Monitoring



Example- Cumulative Distribution Plots

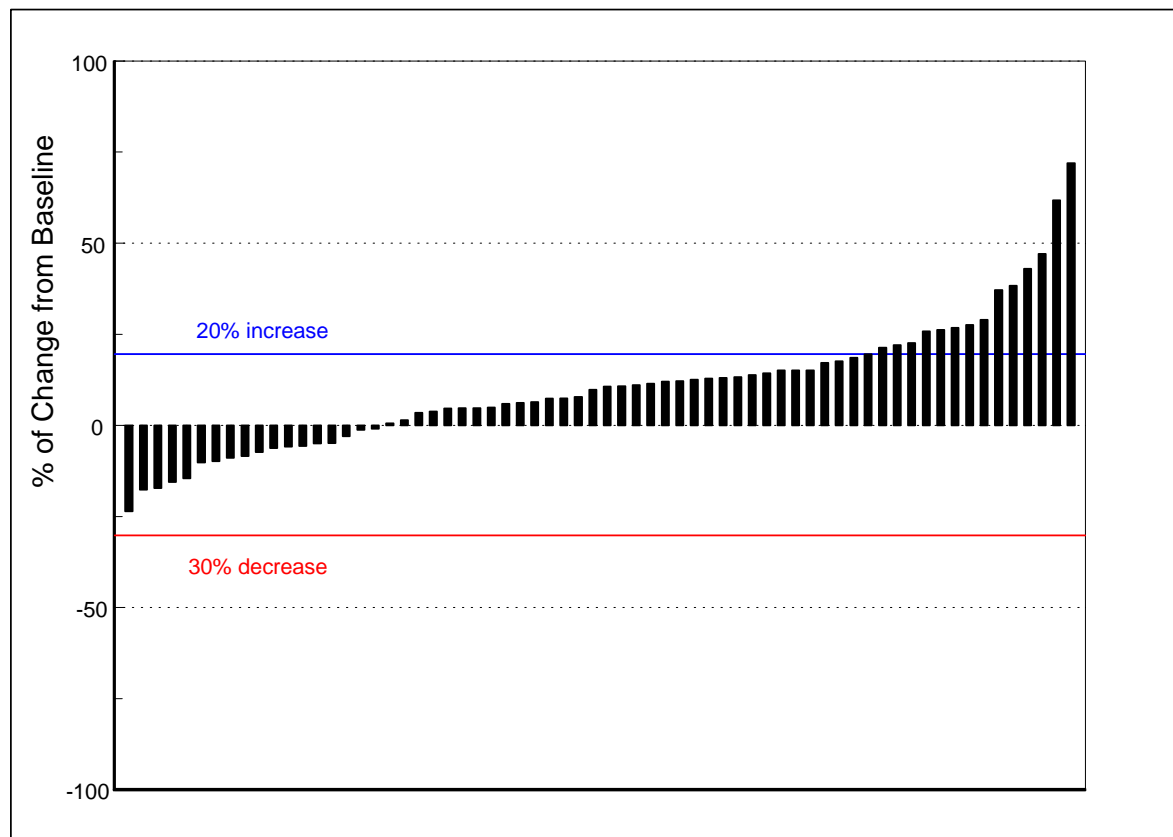


Note: Increase <30msec 'Normal', 30-60msec 'Concern', >60msec 'High'

Source: Ohad Amit, Richard M. Heiberger, Peter W. Lane

Example - Waterfall Plots

Best Percent Change In Target Lesion Assessments by Treatment Arm- examine the point of inflexion



Need to present graphs for treatment groups side-by-side



Concluding Thoughts

- A graphic can stand alone when provided with sufficient data information? Supporting table are provided as backup.
- Should there be FDA/Academic/Pharma focus group for efficacy data as well (similar to safety)?
 - Efficacy data can be more complex and endpoint dependent.
 - Standardization across different data types: continuous, categorical, PRO (diary data), time-to-event data, etc.?
- Implementation of graphics require continued automation of user friendly and easily accessible tools?



Thank You!