## Todays Session

### Statistical Graphics for Analysis of Drug Safety and Efficacy

**Section on Statistical Graphics,** Section on Risk Analysis, WNAR

*Organizer(s): Michael O'Connell, Insightful Corporation*

*Chair(s): Stephen Kaluzny, Insightful Corporation*

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>2:05 PM</td>
<td>Statistical Graphics for Analysis and Reporting of Clinical Trials</td>
</tr>
<tr>
<td>2:25 PM</td>
<td>Using Graphics To Discover and Explore</td>
</tr>
<tr>
<td>2:45 PM</td>
<td>Statistical Graphics for the Analysis of Safety and Efficacy Data from Clinical Trials</td>
</tr>
<tr>
<td>3:05 PM</td>
<td>Graphical Analyses of Clinical Trial Safety Data</td>
</tr>
<tr>
<td>3:25 PM</td>
<td>Design of Statistical Graphics for Clinical Data</td>
</tr>
<tr>
<td>3:45 PM</td>
<td>Floor Discussion</td>
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</table>
Todays Session

Michael O’Connell
  + Statistical Graphics Principles – Functional Areas, Software

Julia Wang
  + Graphs for Exploratory Data Analysis

William Bushnell
  + Graphs for Safety - Labs, AEs, patient profile, ...

Haijun Ma
  + Graphs for Safety - Labs, AEs, patient profile, ...

Rich Heiberger
  + Graphs / Design for Vitals, Labs, AEs, ...
Statistical Graphics for Analysis and Reporting of Clinical Data

Michael O’Connell

July, 2007
My Outline

Business Problem
  + Clinical Drug Development – Use of Graphics

Statistical Graphics
  + Graphics Principles, Elements, Types and Patterns

Graphics in Functional Areas
  + Design, Review, Report

Software
  + Graphics breakdown and mashup
Clinical Drug Development

Need to go faster, better/safer and cheaper!!  [$1B/yr drug = $3M/day]
Statistical Graphics drive faster and better decisions

Speed the analysis and reporting process
  + Faster registrational documents

Improve the quality of decisions
  + Rapid and clear information from data

Increase likelihood of discerning safety and efficacy signals
  + Comparative graphical analysis on all safety and efficacy data

Provide consistent form of communication across organization, cultures and functional areas

Improve interactions between sponsors and FDA
  + FDA wants transparency and clear analysis / presentation
Excellence in statistical graphics consists of complex ideas communicated with clarity, precision and efficiency

+ Show all the data when possible
  - Multivariate data and metadata
+ Induce the viewer to think about the substance rather than the graphic design – maximize the data-to-ink ratio
+ Encourage the eye to compare different pieces of data – leverage reader’s investment by showing multiple plots of same type
+ Reveal the data at several levels of detail, from a broad overview to the fine structure
+ Serve a clear purpose: description, exploration, tabulation
+ Be closely integrated with the statistical and verbal descriptions of a data set
+ Use gray scale and color sparingly
Variable Grouping
+ Symbols, colors for groups – compare pieces of data
+ Treatment v Placebo

Trellis Plots and Conditioning
+ Panels for subjects, sub-groups – principle of small multiples
+ Adverse Event groups

Matrix Plots
+ Plots for individual variables together – multivariate data
+ Lab panels

Metadata – Margins and Axes
+ Use of ticks, color-regions, margins around plots – multivariate metadata
+ Safety and Efficacy combination graphics

Brushing, Drilldown
+ Data browsing – levels of detail
+ Population Lab -> Subject Lab -> AE -> demographics
Summary stats – univariate categorical
+ Dotplot
+ Barchart [low data-to-ink ratio]
+ Pie chart [poor perception]

Distributions – univariate continuous
+ Boxplot
+ Empirical CDF
+ Density Plot
+ Histogram

Relations and trends
+ Line plot
+ Scatter plot
+ Scatter plot matrix
+ Surface, contour and image (heatmap) plots
+ Kaplan Meier Plot
+ Forest Plot
Figures convey trial designs and expected trial behavior

- Data analyst produces for clinician and management
- Multiple trial options are compared – operations (e.g. accrual) and potential outcomes for variety of scenarios

Examples

- Protocol
- SAP

Color and Format

- Needs to be clear and easy to interpret and compare designs
- Statistical (e.g. # events) and calendar information need to be clearly communicated

Illustrate today with survival trials
Trial Design Graphic: Sequential HR Design

- **H_0:** HR > 1
- **H_1:** HR < 0.7

**Futility boundary (Pocock)**

**Efficacy boundary (O’Brien-Fleming)**

**Inferiority of Treatment**

**Superiority of Treatment**
Trial Design Graphic: Sequential HR Design

NAccrual = 700  Accrual Rate = 25.6  Accrual Time = 27.3  Study Time = 48.3

HR = 0.7
HR = 1

Accrual
Events
At Risk
Interim Analyses

Calendar Time (Months)
Sample Size

Distribution of Efficacy Boundary Crossing

Z (Efficient Score)

Superiority
Futility
Inferiority

Fixed-Sample Size

Design Parameters:
Simulation runs = 100000
α = 0.05
Power = 0.8

Simulation Results:
P(cross upper boundary) = 0.93712
P(cross lower boundary) = 0.06288
Mean sample size = 54.62555
Median sample size = 50

Line Plot | Matrix

Courtesy Kye Gilder, Biogen
Figure not necessarily self-contained

+ Data analyst produces for detailed review with clinician
+ Data analyst produces for the data analyst

Examples

+ Clinical data review by/with clinician
+ Viewing all data – data cleaning
+ Residual diagnostics - identification of functional form of relationship, assessing model assumptions

Color and Format

+ Few pre-defined rules
+ Just make it clear and easy to interpret
**Adverse Events - Interpretive Goals**

Which adverse events are elevated in treatment vs. placebo?

How rapid is onset in treatment vs. placebo?

*Population level analysis is important*

**Labs - Interpretive Goals**

Which subjects have elevated (liver) labs?

Are there subjects with elevation on multiple labs?

*Subject Level analysis is important*
## Adverse Events with Severity and Time

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<th></th>
<th>Baseline</th>
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<th>Baseline</th>
<th></th>
<th>Week 12</th>
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<th>Week 12</th>
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<td>Vehicle</td>
<td>Active</td>
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<td>Active</td>
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<td>Active</td>
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<td>((N = 400))</td>
<td>((N = 900))</td>
<td>((N = 400))</td>
<td>((N = 900))</td>
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<td><strong>Erythema</strong></td>
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<tr>
<td>Absent (0)</td>
<td>550 (55)</td>
<td>250 (50)</td>
<td>600 (67)</td>
<td>375 (94)</td>
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<tr>
<td>Mild (1)</td>
<td>350 (35)</td>
<td>220 (44)</td>
<td>250 (29)</td>
<td>20 (5)</td>
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<tr>
<td>Moderate (2)</td>
<td>80 (8)</td>
<td>25 (5)</td>
<td>45 (5)</td>
<td>5 (1)</td>
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<td></td>
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<tr>
<td>Severe (3)</td>
<td>20 (2)</td>
<td>5 (1)</td>
<td>5 (1)</td>
<td>0 (0)</td>
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<tr>
<td><strong>Burning</strong></td>
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<td></td>
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<tr>
<td>Absent (0)</td>
<td>800 (80)</td>
<td>380 (76)</td>
<td>750 (83)</td>
<td>325 (82)</td>
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<td>Mild (1)</td>
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Data Courtesy Mat Soukup, FDA
Local Topical Safety

<table>
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<th>Itching</th>
<th>Scaling</th>
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<tbody>
<tr>
<td>Treatment</td>
<td>Vehicle (●)</td>
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</table>

- Itching: Lower values at Base, increasing to peak at wk 4, then decreasing.
- Scaling: Highest values at wk 4, then decreasing.
- Burning: No significant changes.
- Dryness: No significant changes.
- Erythema: No significant changes.

Time:
- Base, wk 2, wk 4, wk 8, wk 12

Mean Value:
- Itching: Peak at wk 4.
- Scaling: Peak at wk 4.
- Burning: No peak.
- Dryness: No peak.
- Erythema: No peak.
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<th>TRT.B/428</th>
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<td>Skin and subcutaneous tis</td>
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<td>Ageusia</td>
<td>Nervous system disorders</td>
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<td>1</td>
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<td>Blood and lymphatic system</td>
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<td>Anxiety</td>
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<td>Arthralgia</td>
<td>Musculoskeletal and connective tissue</td>
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<td>8</td>
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<td>Aspartate aminotransferase</td>
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<td>3</td>
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<tr>
<td>Asthenia</td>
<td>General disorders and adm</td>
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<td>Back pain</td>
<td>Musculoskeletal and connective tissue</td>
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<tr>
<td>Chills</td>
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</table>

Data Courtesy Mike Durante, GSK
Adverse Event Review Graphic: B&B Model

Scatter / pRisk Plot | Brush, Drill

B&B Model: \( \theta_{ij} \sim \pi_i I\{0\} + (1-\pi_i) N(\mu_{\theta_i}, \sigma_{\theta_i}^2) \)
## Analyze Selected Patients

### By Demographics

### Demographics

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Treatment Group</th>
<th>Treatment Start Date</th>
<th>Age</th>
<th>Sex</th>
<th>Ethnicity</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>BMI (kg/m²)</th>
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<td>01/20/2005</td>
<td>61</td>
<td>M</td>
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<td>M</td>
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<tr>
<td>31-358-2268</td>
<td>Prostinal High Dose</td>
<td>06/30/2005</td>
<td>77</td>
<td>F</td>
<td>AFRICAN DESCENT (NEGRO, BLACK)</td>
<td>166.1</td>
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<td>83.01</td>
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</table>
# Insightful Clinical Review

## Patient 31-353-2188: Adverse Events

<table>
<thead>
<tr>
<th>Dictionary-Derived Term</th>
<th>Body System or Organ Class</th>
<th>Serious Event</th>
<th>Severity</th>
<th>Assessed Causality</th>
<th>Adverse Event Start Date</th>
<th>Adverse Event End Date</th>
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<tr>
<td>DIZZINESS</td>
<td>NERVOUS SYSTEM DISORDERS</td>
<td>N</td>
<td>MODERATE</td>
<td>NONE</td>
<td>06/02/1992</td>
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<td>MILD</td>
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<td>UPPER RESPIRATORY TRACT INFECTION</td>
<td>INFECTIONS AND INFESTATIONS</td>
<td>N</td>
<td>MILD</td>
<td>NONE</td>
<td>01/11/2004</td>
<td>01/19/2004</td>
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<td>UPPER RESPIRATORY TRACT INFECTION</td>
<td>INFECTIONS AND INFESTATIONS</td>
<td>N</td>
<td>MILD</td>
<td>NONE</td>
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<tr>
<td>NAUSEA</td>
<td>GASTROINTESTINAL DISORDERS</td>
<td>N</td>
<td>MILD</td>
<td>PROBABLE</td>
<td>02/04/2004</td>
<td>06/25/2004</td>
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<td>MILD</td>
<td>PROBABLE</td>
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## Patient 31-353-2188: Liver Function Tests

<table>
<thead>
<tr>
<th>Visit</th>
<th>Date</th>
<th>Alanine Aminotransferase</th>
<th>Alkaline Phosphatase</th>
<th>Aspartate Aminotransferase</th>
<th>Gamma Glutamyl Transferase</th>
<th>Albumin</th>
<th>Bilirubin</th>
<th>Protein</th>
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<td>12.57</td>
<td>73.07</td>
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</table>

**Key:** Lab Data
- **Above Upper Limit of Normal**
- **Below Lower Limit of Normal**
Figure must be self-contained
  + In-text figures should have an explanation in the caption

Figure must be documented
  + Log file
  + Time stamp
  + Source data and output file references

Examples
  + NDA Submission
  + Scientific Publication
  + Clinical Study Report and Presentation

Color / Format
  + Must be interpretable when copied in black and white
  + Compatible with Microsoft Word
  + Resizable
Depression
Dyspnoea.exertional
Hepatic.function.abnormal
Pain.in.jaw
Pyrexia
Skin.hypopigmentation
Anaemia
Paraesthesia
Hair.texture.abnormal
Hypotrichosis
Pharyngolaryngeal.pain
Dry.mouth
Hyperbilirubinaemia
Dysphonia
Cystitis
Urine.tract.infection
Visual.acuity.reduction
Pain.in.extremity
Dysgeusia
Hyperbilirubinaemia
Dysphonia
Cystitis
Pharyngolaryngeal.pain
Hypotrichosis
Hair.texture.abnormal
Paraesthesia
Anaemia
Skin.hypopigmentation
Pyrexia
Pain.in.jaw
Hepatic.function.abnormal
Dysphonia.exertional
Depression
Adverse Event Report Graphic

Dot Plot | Group

Protocol: 38-316
Candidate: Oncology 38-316-001

Dotplot of Variable Importance
Random Forest Inside-Out Model

Fatigue
Hypokalaemia
Nausea
Dry.mouth
Hypertension
Abdominal.distension
Hyperbilirubinaemia
Skin.depigmentation
Pain.in.jaw
Aspartate.aminotransferase.increased
Dysgeusia
Confusional.state
Headache
Chills
Paraesthesia
Constipation
Skin.hypopigmentation
Oedema.peripheral
Urinary.tract.infection
Dysphonia
Mouth.ulceration
Pain.in.extremity
Gastrooesophageal.reflux.disease
Epistaxis

Variable Importance

Trt$_{ij}$ = f (PT$_j$) + e$_{ij}$

i = 1, ..., 642 subjects, j = 1, ..., 111 AEs
Easy creation of (information-rich) statistical graphics for clinical data analysis
  + Dot plot, box plot, line plot, etc...

Easy re-purposing of graphs across studies and functional areas
  + Graph standards – layering on (CDISC) data standards

Use of same graphs in exploratory and validated areas
  + Windows/UNIX exploratory and UNIX compliant

Consistent use of graphs across organization
  + Graphic language for effective communication
Graphics System Mashup

**Design**

- Statistics
  - Specify Graph From Type Palette
  - Create/Add Graph Pattern to Store
  - Select Graph Pattern from Store
  - Add Type to Palette

- Monitors Data Mgt
  - Apply Pattern to Data

- Clinical Statistics
  - Apply Pattern to Bound Data

**Review**

- Statistics Programming
  - Run Bound Pattern for NDA

**Report**

- Publishing
  - Apply CSS Style to Bound Pattern

**Clinical Graphics Store**

- Persisted Graph Types, Patterns, Styles & Metadata (WEBDAV)
- S-PLUS Script Files (SSC)

**Instream**

**Unblinded**
# Graph Types and Patterns

## Graph Types

### Summary stats – univariate categorical
- Dotplot
- Barchart [low data-to-ink ratio]
- Pie chart [poor perception]

### Distributions – univariate continuous
- Boxplot
- Empirical CDF
- Density Plot
- Histogram

### Relations and trends
- Line plot
- Scatter plot
- Scatter plot matrix
- Surface, contour and image plots

## Graph Patterns

- Forest Plot
- My AE Dotplot with Intervals
- My Boxplot
- Kaplan Meier Plot
- My Patient Profile Liver Plot
- My Liver Lab Shift Plot
- My Liver Lab Scatter Plot Matrix
Diarrhoea
Dyspepsia
Nausea
Stomatitis
Gastrointestinal pain
Vomiting
Haemorrhoidal haemorrhage
Large intestine perforation
Proctitis
Flatulence
Abdominal pain
Abdominal pain upper
Gastroesophageal reflux disease
Gastric disorder
Toothache
Abdominal pain lower
Abdominal pain
Flatulence
Proctitis
Large intestine perforation
Haemorrhoidal haemorrhage
Vomiting
Gastrointestinal pain
Stomatitis
Nausea
Dyspepsia
Diarrhoea

log-10 Empirical RR

Bayes Posterior Mean of Log Relative Risk with 99% BCI
Combined Graphical and Tabular Reports

Body Plot

Treatment Minus Placebo Stain at Week 4
### Patient 31-351-2207: Adverse Events

<table>
<thead>
<tr>
<th>Dictionary-Derived Term</th>
<th>Body System or Organ Class</th>
<th>Serious Event</th>
<th>Severity</th>
<th>Assessed Causality</th>
<th>Adverse Event Start Date</th>
<th>Adverse Event End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIARRHOEA</td>
<td>GASTROINTESTINAL DISORDERS</td>
<td>N</td>
<td>MILD</td>
<td>POSSIBLE</td>
<td>06/13/2005</td>
<td>NA</td>
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<tr>
<td>DIARRHOEA</td>
<td>GASTROINTESTINAL DISORDERS</td>
<td>N</td>
<td>MILD</td>
<td>REMOTE</td>
<td>06/13/2005</td>
<td>NA</td>
</tr>
<tr>
<td>SKIN ODOR ABNORMAL</td>
<td>SKIN AND SUBCUTANEOUS TISSUE DISORDERS</td>
<td>N</td>
<td>MILD</td>
<td>REMOTE</td>
<td>06/13/2005</td>
<td>NA</td>
</tr>
<tr>
<td>PRURITUS</td>
<td>SKIN AND SUBCUTANEOUS TISSUE DISORDERS</td>
<td>N</td>
<td>MILD</td>
<td>REMOTE</td>
<td>06/14/2005</td>
<td>NA</td>
</tr>
<tr>
<td>ABDOMINAL PAIN</td>
<td>GASTROINTESTINAL DISORDERS</td>
<td>N</td>
<td>MILD</td>
<td>PROBABLE</td>
<td>06/21/2005</td>
<td>07/10/2005</td>
</tr>
<tr>
<td>ABDOMINAL PAIN</td>
<td>GASTROINTESTINAL DISORDERS</td>
<td>N</td>
<td>MILD</td>
<td>PROBABLE</td>
<td>06/21/2005</td>
<td>07/10/2005</td>
</tr>
<tr>
<td>UPPER RESPIRATORY TRACT INFECTION</td>
<td>INFECTIONS AND INFESTATIONS</td>
<td>N</td>
<td>MILD</td>
<td>REMOTE</td>
<td>07/22/2005</td>
<td>08/11/2005</td>
</tr>
<tr>
<td>UPPER RESPIRATORY TRACT INFECTION</td>
<td>INFECTIONS AND INFESTATIONS</td>
<td>N</td>
<td>MILD</td>
<td>REMOTE</td>
<td>07/22/2005</td>
<td>08/11/2005</td>
</tr>
<tr>
<td>FATIGUE</td>
<td>GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS</td>
<td>N</td>
<td>MILD</td>
<td>REMOTE</td>
<td>07/31/2005</td>
<td>NA</td>
</tr>
<tr>
<td>HORDEOLUM</td>
<td>INFECTIONS AND INFESTATIONS</td>
<td>N</td>
<td>MILD</td>
<td>REMOTE</td>
<td>08/01/2005</td>
<td>NA</td>
</tr>
</tbody>
</table>

### Patient 31-351-2207: Liver Function Tests

<table>
<thead>
<tr>
<th>Visit</th>
<th>Date</th>
<th>Alanine Aminotransferase</th>
<th>Aspartate Aminotransferase</th>
<th>Gamma Glutamyl Transferase</th>
<th>Albumin</th>
<th>Bilirubin</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAB BASELINE</td>
<td>05/29/2005</td>
<td>63.94</td>
<td>81.97</td>
<td>37.98</td>
<td>67.95</td>
<td>41</td>
<td>39.27</td>
</tr>
<tr>
<td>UNsched</td>
<td>09/07/2005</td>
<td>66.94</td>
<td>79.98</td>
<td>35.98</td>
<td>69.96</td>
<td>42</td>
<td>34.15</td>
</tr>
<tr>
<td>WEEK 2</td>
<td>06/26/2005</td>
<td>47.12</td>
<td>95.05</td>
<td>26.05</td>
<td>66.1</td>
<td>40.01</td>
<td>18.83</td>
</tr>
<tr>
<td>WEEK 4</td>
<td>07/10/2005</td>
<td>51.18</td>
<td>89.08</td>
<td>43.07</td>
<td>59.15</td>
<td>42.01</td>
<td>34.38</td>
</tr>
<tr>
<td>WEEK 6</td>
<td>07/21/2005</td>
<td>60.31</td>
<td>89.13</td>
<td>32.11</td>
<td>51.26</td>
<td>41.02</td>
<td>25.95</td>
</tr>
<tr>
<td>WEEK 8</td>
<td>08/06/2005</td>
<td>71.37</td>
<td>77.15</td>
<td>35.14</td>
<td>71.31</td>
<td>38</td>
<td>21.3</td>
</tr>
<tr>
<td>WEEK 12</td>
<td>09/01/2005</td>
<td>70.43</td>
<td>90.18</td>
<td>36.16</td>
<td>60.36</td>
<td>40.03</td>
<td>15.81</td>
</tr>
<tr>
<td>WEEK 16</td>
<td>10/01/2005</td>
<td>36.49</td>
<td>75.2</td>
<td>26.18</td>
<td>47.41</td>
<td>38.04</td>
<td>24.42</td>
</tr>
<tr>
<td>WEEK 20</td>
<td>10/27/2005</td>
<td>36.56</td>
<td>83.23</td>
<td>23.2</td>
<td>49.46</td>
<td>43.04</td>
<td>26.19</td>
</tr>
<tr>
<td>WEEK 24</td>
<td>11/26/2005</td>
<td>43.82</td>
<td>71.25</td>
<td>28.23</td>
<td>53.51</td>
<td>41.05</td>
<td>31.38</td>
</tr>
<tr>
<td>WEEK 26</td>
<td>12/10/2005</td>
<td>38.68</td>
<td>73.28</td>
<td>23.25</td>
<td>48.56</td>
<td>41.05</td>
<td>19.47</td>
</tr>
</tbody>
</table>
## Futures: Interactive Clinical Review on the iPhone

### Top 24 AEs

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Placebo</th>
<th>Placebo Low Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>DYSPEPSIA</td>
<td>16 (21%)</td>
<td>44 (56%)</td>
</tr>
<tr>
<td>ABDOMINAL PAIN</td>
<td>8 (11%)</td>
<td>24 (31%)</td>
</tr>
<tr>
<td>PRURITUS</td>
<td>7 (9%)</td>
<td>14 (18%)</td>
</tr>
<tr>
<td>NAUSEA</td>
<td>7 (9%)</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>RASH</td>
<td>5 (7%)</td>
<td>11 (14%)</td>
</tr>
<tr>
<td>DIZZINESS</td>
<td>5 (7%)</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>VOMITING</td>
<td>4 (5%)</td>
<td>9 (12%)</td>
</tr>
<tr>
<td>SKIN IRITATION</td>
<td>4 (5%)</td>
<td>9 (12%)</td>
</tr>
<tr>
<td>SINUS BRADYCARDIA</td>
<td>4 (5%)</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>FATIGUE</td>
<td>3 (4%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>COUGH</td>
<td>3 (4%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>UPPER RESPIRATORY TRACT INFECTION</td>
<td>3 (4%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>UROPHARYNGITIS</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>HEPATOBILIARY INFECTION</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>BRAHMOHYDROMYTAL</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>HEADACHE</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>MYOCARDIAL INFARCTION</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>SYNCOPE</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>NASAL CONGESTION</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>DERMAL PERIPHERAL PAIN</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>ELECTROCARDIOGRAMAL ST SEGMENTAL DEPRESSION</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>ATRIOVENTRICULAR BLOCK SECOND DEGREE</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>ATRIAL TACHYCARDIA</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>UROMICROSOMATION</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>SALIVARY HYPERSECRETION</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>
Interactive Clinical Review on the iPhone
Interactive Clinical Review on the iPhone
Key Clinical Graphics Use Cases – Mashups

Point-click specification of statistical graphics (stats, programming)
  + Easy to create informative statistical graphics (point-click)
  + Comprehensive palette of graph types: dot plot, box plot, line plot, ...

Create / save a graph pattern for re-use on bound or new data
  + Instream clinical data review / cleaning (data refresh)
  + Analysis of different trial/endpoint by different person/TA (CDISC helps)

System creation of script to be run in validated environment
  + Oracle / SAS and submission reporting

Graph styling and presentation with bound data (publishing)
  + Graph in to company power point style e.g. b&w <-> color
  + Graph in to journal style
  + No change to scientific graph content

Create / add new graph type (stats)
  + New statistical graphics added by statistics for use throughout

Permissioned re-purposing of complex statistical graphics
Insightful Services Oriented Architecture

- XML Protocol Define.xml
- XML Graph Definition
- Graph View File (SPJ)
- Persisted Graph Patterns, Styles & Metadata (WEBDAV)
- Create/Edit Graph Publish Pattern Retrieve Pattern
- Graph View - UI Hooks - CSS
- S-PLUS Enterprise Server

Clinical Data
- SAS
- Oracle
- CDISC
- EDC
- Safety

Libraries
- TOM
- XSL
- GOM
- SPJ
- WMF
- PDF
- LOG

Insightful Clinical Graphics
Statistical Graphics are at the core in the analysis and interpretation of clinical / safety data

+ Comparative analysis of treatment effects
+ Exploratory – understand the data, cleaning and outliers
+ Review – all components of population and patient level data
+ Submission – clinical study reports
+ Presentation – scientific and marketing applications

Consistency in statistical graphics principles/standards is key

+ S-PLUS Trellis™ and S-PLUS Graphlets™ provide consistency across graph types and environments
+ Same graphs in reports and exploratory data browsing
+ Graphical language across organizations and industry

This is widely recognized by industry and the FDA
In the not too distant future…… I see a world where

Statistical Graphics are widely used to anchor the messaging from clinical studies
  + Group and Trellis / Metadata / Drill-down

Statistical Graphics are mashed up within pharma companies for rapid design, analysis, review, submission, publication and presentation
  + Using the clinical graphics taxonomy – types and patterns

A standard Statistical Graphics palette with rich APIs for repurposing is used across industry and the FDA
  + Simple interactions between industry and the FDA

Safety and the critical path are making this reality
Michael O’Connell
moconnell@insightful.com

Today’s presentation will be available on our website soon
http://www.insightful.com/news_events

Insightful’s 10th User Conference in Atlantic City
Insightful Impact 2007
October 10-11, 2007, Tropicana Hotel, Atlantic City