

A Brief Survey of Graphs and Tables Often Used During Clinical Data/Regulatory Review : Noting Where Tables are Still Needed

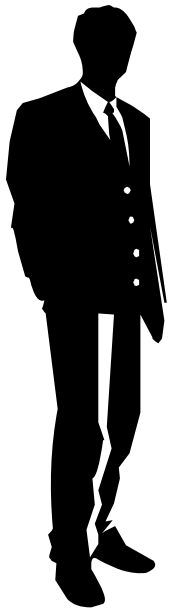
Scott Runyan



JReview Exploring Clinical Data Clinical Safety and Efficacy Reviews

Common Clinical Review Analysis

1. Tables vs Graphs
2. Common Laboratory Shift Tables
3. JReview output interactivity with open analysis
4. Common Adverse Events Tables
5. Multi-Dimensional Graphs for clinical safety review
6. Assessing FDA Standard Analysis Catalog



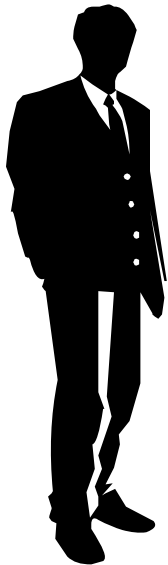
JReview Exploring Clinical Data

Clinical Safety and Efficacy Reviews

Graphs vs Tables

There is no absolute guidance on when to utilize a graph or a table to present data.

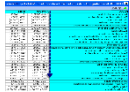
It's all about the data, and what is intended to be reviewed, emphasized, or compared.



JReview Exploring Clinical Data

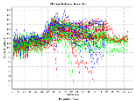
Clinical Safety and Efficacy Reviews

Tables

A small screenshot of a data table from the JReview software. It shows a grid with multiple rows and columns, containing various data points and text, illustrating the multi-dimensional analysis capability of tables.

Tables facilitate multi-dimensional analysis more naturally than graphs with the use of multiple rows, columns, and use of sorting where appropriate. Tables are used to review and compare specific data details.

Graphs



Graphs give data shape and form, to visualize patterns and relationships which is a natural function of our visual system.

Vickey Lozovsky, Information Builders, Spring 2008 Table vs Graph

JReview: Most common clinical safety tables
Tabulation of Lab Test Abnormalities

JReview Exploring Clinical Data

Laboratory Safety Review

Toxicity Grade Shift Tables:

Liver Test Results Baseline Toxicity Grade vs Worsening Post Baseline value

ALT baseline vs max Tox Grade Shift Table - Subset of patients / Output Filter applied						
		Active Arm		Reference		
Parameter	Baseline Toxicity Grade	1	2	1	2	3
Alanine Aminotransferase (U/L)	0	15 (19.23%)	1 (1.28%)	21 (13.64%)	0 (0.00%)	1 (0.65%)
	1	0 (0.00%)	3 (3.85%)	0 (0.00%)	1 (0.65%)	0 (0.00%)
	Subjects(filtered)	15 (19.23%)	4 (5.13%)	21 (13.64%)	1 (0.65%)	1 (0.65%)
	1stColItemSubjects	78 (100.00%)	78 (100.00%)	154 (100.00%)	154 (100.00%)	154 (100.00%)

Key characteristics:

- Shift table includes baseline and degrees of abnormal at baseline vs Degrees of Abnormal post baseline max test result.
- Only including worse post baseline results greater than the baseline toxicity grade

JReview Exploring Clinical Data

Laboratory Safety Review

Toxicity Grade Shift Tables:

Multiple Lab Test Baseline Toxicity Grade vs Worsening Post Baseline value

Tox Grade Shift Table <Lab Tests> Baseline vs max post Baseline toxicity grade row configuration - All I				
Parameter	Baseline Toxicity Grade	max Analysis Toxicity Grade	Active Arm	Reference
Alanine Aminotransferase (U/L)	0	1	15	21
		2	1	
		3		1
	1	2	3	1
		1	21	26
		2		2
Aspartate Aminotransferase (U/L)	0	1		1
		2		2
		3		1
	1	2		2
		3	1	
				1
Bilirubin (umol/L)	0	1	3	8
		2	1	2
		3	1	1
		Subjects(filtered)	32	47

JReview Exploring Clinical Data

Typical Safety Review

New Review focus:

Complex Shift Tables:

Liver Test Results Baseline category vs max Post Baseline value

ALT Shift from Baseline - All Patients / Output Filter applied

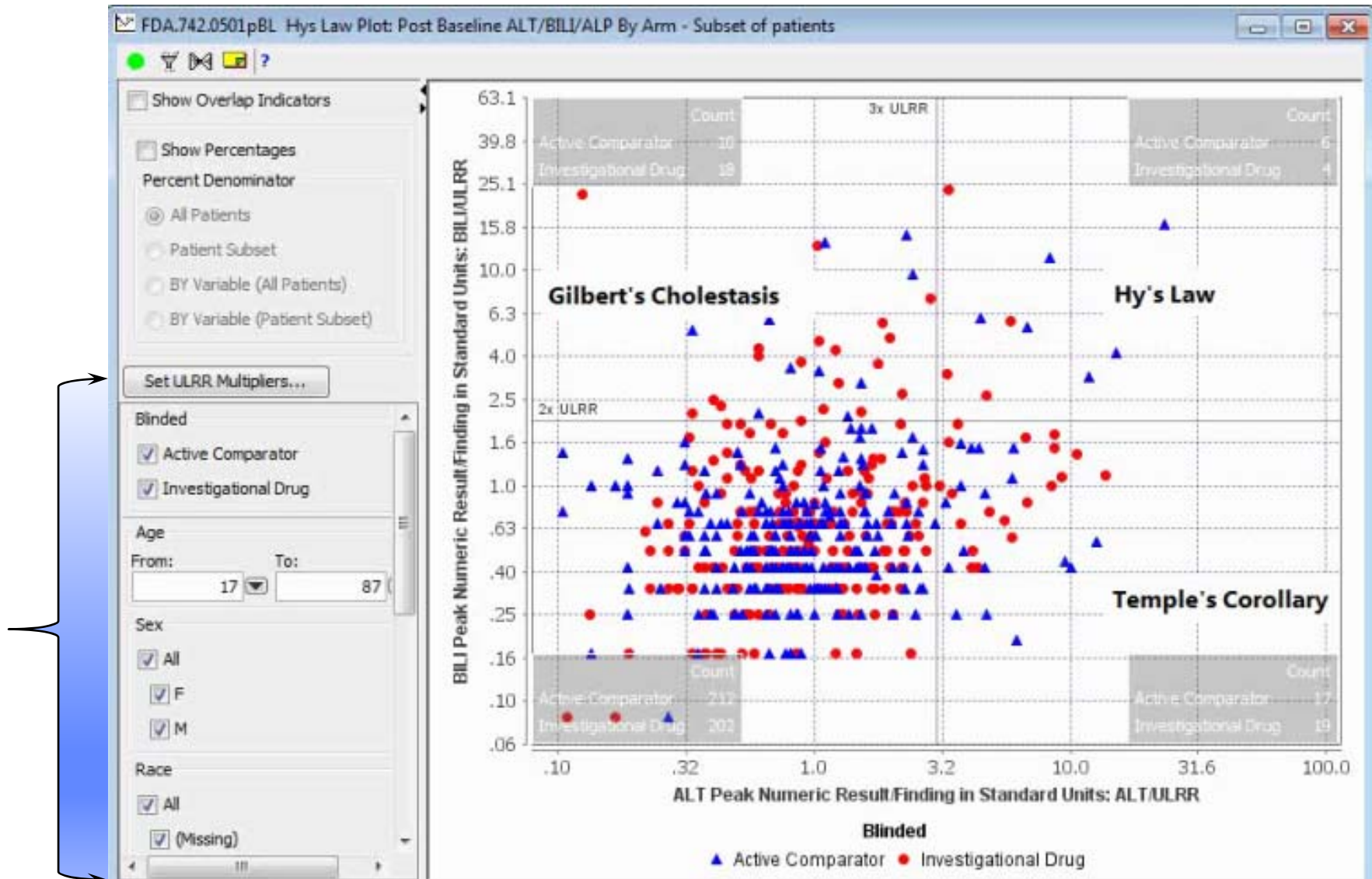
ALT_Shift_from_Baseline	Investigation Drug	BL ALT Normal	BL ALT > ULN <=2xULN	BL ALT > 2xULN <=3xULN	BL ALT > 3xULN <=5xULN
ALT Post Baseline Normal		107 (41.63%)	7 (2.72%)	2 (0.78%)	1 (0.39%)
ALT > ULN <=2xULN		31 (12.06%)	21 (8.17%)	5 (1.95%)	2 (0.78%)
ALT > 2xULN <=3xULN		13 (5.06%)	11 (4.28%)	6 (2.33%)	4 (1.56%)
ALT > 3xULN <=5xULN		5 (1.95%)	4 (1.56%)	4 (1.56%)	3 (1.17%)
ALT > 5xULN <=10xULN		6 (2.33%)	5 (1.95%)	1 (0.39%)	0 (0.00%)
ALT >10xULN <=15xULN		2 (0.78%)	0 (0.00%)	1 (0.39%)	0 (0.00%)
ALT >15xULN <=20xULN		1 (0.39%)	0 (0.00%)	1 (0.39%)	0 (0.00%)
ALT >20xULN		3 (1.17%)	1 (0.39%)	0 (0.00%)	0 (0.00%)
Subjects(filtered)		168 (65.37%)	49 (19.07%)	20 (7.78%)	10 (3.89%)
1stColItemSubjects		257 (100.00%)	257 (100.00%)	257 (100.00%)	257 (100.00%)

This particular output includes subjects that had normal baseline and max post baseline also normal

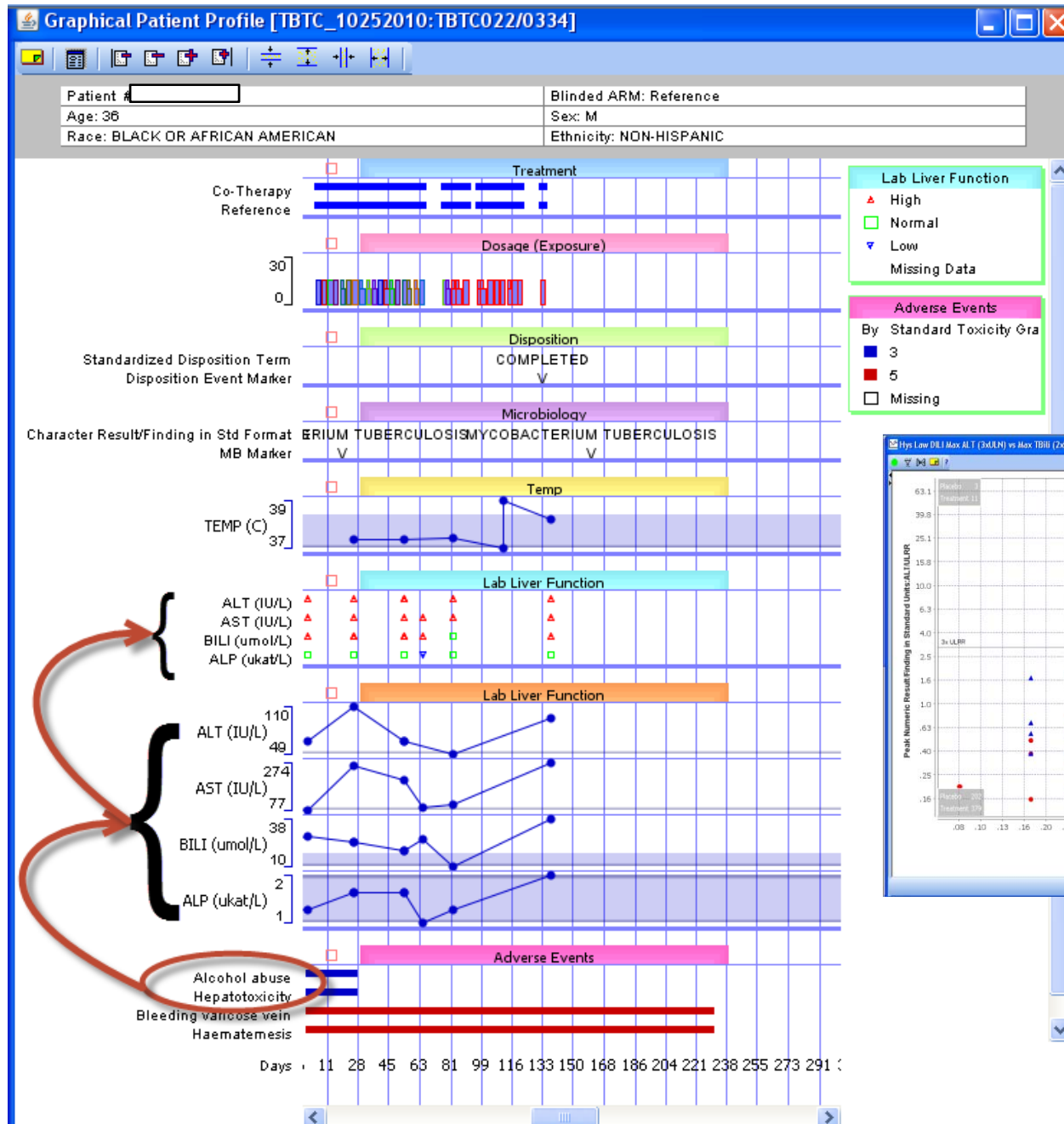
JReview Tables and Graphical outputs interact

JReview: Special Assessments Hepatotoxicity (DILI)

JReview Tables and Graphical outputs interact



JReview Tables and Graphical outputs interact



Hy's Law example –
explore why patients meet
the Hy's Law criteria using
Graphical Patient Profile



JReview: Most common clinical safety tables

Tabulation of Adverse Events

Subject Counts

JReview: Most common clinical safety tables

Subject Counts: Treatment Emergent Adverse Events Body System or Organ Class percent incidence tables

TEAE SOC Descending sort order on Active Treatment Arm : Safety PopulationCrossTab - Subs			
AE SOC	Active Arm	Placebo	Subjects(filtered)
Infections and infestations	1758 (9.64%)	1674 (9.22%)	3432 (8.37%)
Metabolism and nutrition disorders	1680 (9.21%)	1700 (9.36%)	3380 (8.24%)
Cardiac disorders	1322 (7.25%)	1359 (7.48%)	2681 (6.54%)
Gastrointestinal disorders	1321 (7.24%)	1190 (6.55%)	2511 (6.12%)
Musculoskeletal and connective tissue disorders	1250 (6.85%)	1172 (6.45%)	2422 (5.91%)
Nervous system disorders	1008 (5.52%)	1067 (5.87%)	2075 (5.06%)
Investigations	964 (5.28%)	869 (4.78%)	1833 (4.47%)
Renal and urinary disorders	963 (5.28%)	891 (4.91%)	1854 (4.52%)
General disorders and administration site conditions	909 (4.98%)	921 (5.07%)	1830 (4.46%)
Respiratory, thoracic and mediastinal disorders	856 (4.69%)	843 (4.64%)	1699 (4.14%)
Injury, poisoning and procedural complications	725 (3.97%)	724 (3.99%)	1449 (3.53%)
Vascular disorders	697 (3.82%)	699 (3.85%)	1396 (3.40%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	605 (3.32%)	625 (3.44%)	1230 (3.00%)
Skin and subcutaneous tissue disorders	602 (3.30%)	497 (2.74%)	1099 (2.68%)
Blood and lymphatic system disorders	431 (2.36%)	376 (2.07%)	807 (1.97%)
Eye disorders	354 (1.94%)	346 (1.90%)	700 (1.71%)
Psychiatric disorders	251 (1.38%)	314 (1.73%)	565 (1.38%)
Reproductive system and breast disorders	204 (1.12%)	202 (1.11%)	406 (0.99%)
Ear and labyrinth disorders	182 (1.00%)	153 (0.84%)	335 (0.82%)
Hepatobiliary disorders	163 (0.89%)	160 (0.88%)	323 (0.79%)
Endocrine disorders	75 (0.41%)	74 (0.41%)	149 (0.36%)
Surgical and medical procedures	33 (0.18%)	30 (0.17%)	63 (0.15%)
Immune system disorders	32 (0.18%)	46 (0.25%)	78 (0.19%)
Congenital, familial and genetic disorders	12 (0.07%)	14 (0.08%)	26 (0.06%)
Social circumstances	3 (0.02%)	3 (0.02%)	6 (0.01%)
Pregnancy, puerperium and perinatal conditions	0 (0.00%)	1 (0.01%)	1 (0.00%)
Subjects(filtered)	5764 (31.59%)	5626 (30.97%)	41005 (100.00%)
1stColItemSubjects	18245 (100.00%)	18165 (100.00%)	(Denom=1stCol

JReview: Adverse Event Percent Incident Rates

Subject Counts Serious TEAE Cardiac Disorders

Descending Sort by Active Arm

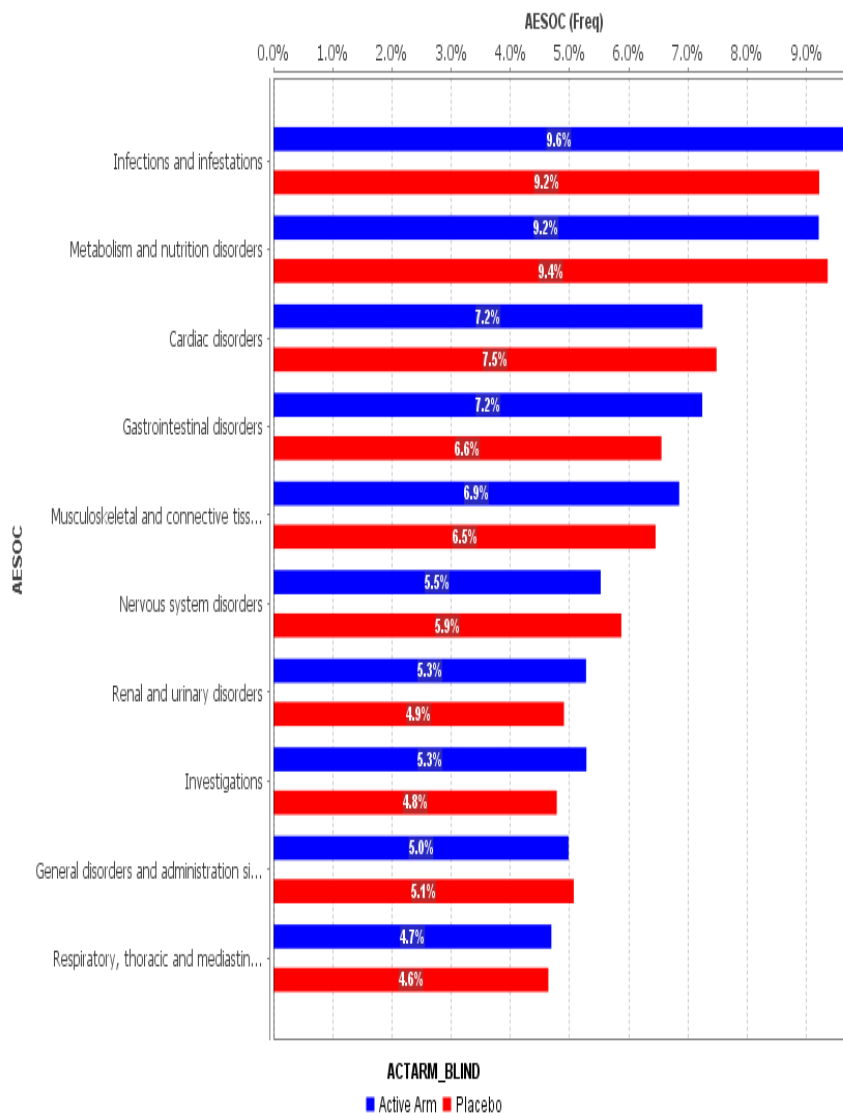
Serious TEAE Cardiac Disorders Descending Sort by Active Arm - Subset of patients / Output File				
AE Type	AESOC	AEHLT	Active Arm	Placebo
Serious Adverse Event	Cardiac disorders	Ischaemic coronary artery disorders	608 (3.33%)	587 (3.23%)
		Heart failures NEC	247 (1.35%)	240 (1.32%)
		Coronary artery disorders NEC	89 (0.49%)	91 (0.50%)
		Supraventricular arrhythmias	80 (0.44%)	94 (0.52%)
		Ventricular arrhythmias and cardiac arrest	49 (0.27%)	61 (0.34%)
		Cardiac conduction disorders	17 (0.09%)	18 (0.10%)
		Cardiomyopathies	16 (0.09%)	9 (0.05%)
		Rate and rhythm disorders NEC	15 (0.08%)	22 (0.12%)
		Left ventricular failures	13 (0.07%)	3 (0.02%)
		Myocardial disorders NEC	4 (0.02%)	3 (0.02%)
		Pericardial disorders NEC	3 (0.02%)	1 (0.01%)
		Cardiac signs and symptoms NEC	3 (0.02%)	6 (0.03%)
		Right ventricular failures	2 (0.01%)	5 (0.03%)
		Aortic valvular disorders	2 (0.01%)	6 (0.03%)
		Cardiac disorders NEC	2 (0.01%)	2 (0.01%)
		Cardiac valve disorders NEC	1 (0.01%)	0 (0.00%)
		Tricuspid valvular disorders	1 (0.01%)	1 (0.01%)
		Cardiac hypertensive complications	1 (0.01%)	1 (0.01%)
		Mitral valvular disorders	1 (0.01%)	4 (0.02%)
		Noninfectious pericarditis	0 (0.00%)	2 (0.01%)
		Heart failure signs and symptoms	0 (0.00%)	2 (0.01%)
		Subjects(filtered)	937 (5.14%)	969 (5.33%)
		1stColItemSubjects	18245 (100.00%)	18165 (100.00%)

JReview: Adverse Event Percent Incident Rates

Cross Tabulation vs Top 10 TEAE SOC Frequency Bar Charts

This comparison highlights Tables can present more data and details when needed

AESOC	Active Arm	Placebo
Infections and infestations	1758 (9.64%)	1674 (9.22%)
Metabolism and nutrition disorders	1680 (9.21%)	1700 (9.36%)
Cardiac disorders	1322 (7.25%)	1359 (7.48%)
Gastrointestinal disorders	1321 (7.24%)	1190 (6.55%)
Musculoskeletal and connective tissue disorders	1250 (6.85%)	1172 (6.45%)
Nervous system disorders	1008 (5.52%)	1067 (5.87%)
Investigations	964 (5.28%)	869 (4.78%)
Renal and urinary disorders	963 (5.28%)	891 (4.91%)
General disorders and administration site conditions	909 (4.98%)	921 (5.07%)
Respiratory, thoracic and mediastinal disorders	856 (4.69%)	843 (4.64%)
Injury, poisoning and procedural complications	725 (3.97%)	724 (3.99%)
Vascular disorders	697 (3.82%)	699 (3.85%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	605 (3.32%)	625 (3.44%)
Skin and subcutaneous tissue disorders	602 (3.30%)	497 (2.74%)
Blood and lymphatic system disorders	431 (2.36%)	376 (2.07%)
Eye disorders	354 (1.94%)	346 (1.90%)
Psychiatric disorders	251 (1.38%)	314 (1.73%)
Reproductive system and breast disorders	204 (1.12%)	202 (1.11%)
Ear and labyrinth disorders	182 (1.00%)	153 (0.84%)
Hepatobiliary disorders	163 (0.89%)	160 (0.88%)
Endocrine disorders	75 (0.41%)	74 (0.41%)
Surgical and medical procedures	33 (0.18%)	30 (0.17%)
Immune system disorders	32 (0.18%)	46 (0.25%)
Congenital, familial and genetic disorders	12 (0.07%)	14 (0.08%)
Social circumstances	3 (0.02%)	3 (0.02%)
Pregnancy, puerperium and perinatal conditions	0 (0.00%)	1 (0.01%)
Subjects(filtered)	5764 (31.59%)	5626 (30.97%)
1stColItemSubjects	18245 (100.00%)	18165 (100.00%)



JReview: Adverse Event Percent Incident Rates

TEAE MedDRA SMQ >5% incidence by active treatment

MedDRA SMQ Treatment Emergent Narrow Search - Subset of patients / Output Filter applied			
Treatment Emergent Flag	SMQ name	Active Arm	Reference
Y	Gastrointestinal nonspecific inflammation and dysfunctional	34 (43.59%)	76 (49.35%)
	Gastrointestinal nonspecific symptoms and therapeutic procedures	33 (42.31%)	72 (46.75%)
	Hypersensitivity (SMQ)	27 (34.62%)	35 (22.73%)
	Haematopoietic cytopenias (SMQ)	25 (32.05%)	56 (36.36%)
	Noninfectious diarrhoea (SMQ)	15 (19.23%)	24 (15.58%)
	Haematopoietic leukopenia (SMQ)	15 (19.23%)	39 (25.32%)
	Oropharyngeal disorders (SMQ)	15 (19.23%)	42 (27.27%)
	Oropharyngeal conditions (excl neoplasms, infections and allergies)	13 (16.67%)	35 (22.73%)
	Haematopoietic thrombocytopenia (SMQ)	13 (16.67%)	29 (18.83%)
	Hypertension (SMQ)	12 (15.38%)	15 (9.74%)
	Acute renal failure (SMQ)	10 (12.82%)	11 (7.14%)
	Peripheral neuropathy (SMQ)	8 (10.26%)	7 (4.55%)
	Haemodynamic oedema, effusions and fluid overload (SMQ)	8 (10.26%)	20 (12.99%)
	Cardiac arrhythmias (SMQ)	7 (8.97%)	3 (1.95%)
	Hyponatraemia/SIADH (SMQ)	7 (8.97%)	8 (5.19%)
	Cardiac arrhythmia terms (incl bradyarrhythmias and	7 (8.97%)	3 (1.95%)
	Drug related hepatic disorders - comprehensive search (SMQ)	6 (7.69%)	10 (6.49%)
	Haemorrhage terms (excl laboratory terms) (SMQ)	6 (7.69%)	22 (14.29%)
	Haemorrhages (SMQ)	6 (7.69%)	22 (14.29%)
	Hepatic disorders (SMQ)	6 (7.69%)	10 (6.49%)
	Bradyarrhythmias (incl conduction defects and disorders of sinus	5 (6.41%)	1 (0.65%)
	Torsade de pointes, shock-associated conditions (SMQ)	5 (6.41%)	1 (0.65%)
	Torsade de pointes/QT prolongation (SMQ)	5 (6.41%)	1 (0.65%)
	Conduction defects (SMQ)	5 (6.41%)	1 (0.65%)
	Shock (SMQ)	5 (6.41%)	1 (0.65%)
	Accidents and injuries (SMQ)	4 (5.13%)	23 (14.94%)
	Liver related investigations, signs and symptoms (SMQ)	4 (5.13%)	7 (4.55%)
	Haemolytic disorders (SMQ)	4 (5.13%)	1 (0.65%)
	Taste and smell disorders (SMQ)	4 (5.13%)	4 (2.60%)
	Hyperglycaemia/new onset diabetes mellitus (SMQ)	4 (5.13%)	14 (9.09%)

JReview: Most common clinical safety tables

MedDRA SMQ Identify Underlying Events

SMQ name	Dictionary Derived Term	Active Arm	Reference
Acute renal failure (SMQ)	Azotaemia	1 (1.28%)	0 (0.00%)
	Proteinuria	13 (16.67%)	3 (1.89%)
	Renal failure	0 (0.00%)	1 (0.63%)
	Renal failure acute	1 (1.28%)	0 (0.00%)
	Renal impairment	9 (11.54%)	11 (6.92%)
	Urine output decreased	0 (0.00%)	1 (0.63%)
	Subjects(filtered)	23 (29.49%)	16 (10.06%)
	1stColItemSubjects	78 (100.00%)	159 (100.00%)
	Jaundice	0 (0.00%)	1 (0.63%)
	Nausea	13 (16.67%)	40 (25.16%)
	Pancreatitis	0 (0.00%)	1 (0.63%)
	Vomiting	9 (11.54%)	21 (13.21%)
	Subjects(filtered)	20 (25.64%)	52 (32.70%)
	1stColItemSubjects	78 (100.00%)	159 (100.00%)

JReview: Adverse Event Incident Rates

Tabulations Treatment Emergent Adverse Events

Multidimensional configuration facilitates deeper reflection,
and consideration of the data details

TEAE Serious and Action Taken by Treatment and Age Category - All Patients					
		ACTIVE		PLACEBO	
		< 40	40-64	< 40	40-64
N	DOSE NOT CHANGED	41 (100.00%)	66 (94.29%)	33 (97.06%)	35 (97.22%)
	DRUG INTERRUPTED	1 (2.44%)	0 (0.00%)	1 (2.94%)	2 (5.56%)
	DRUG WITHDRAWN	2 (4.88%)	7 (10.00%)	1 (2.94%)	2 (5.56%)
Y	DOSE NOT CHANGED	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
	DRUG WITHDRAWN	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.78%)
	Subjects(filtered)	41 (100.00%)	70 (100.00%)	34 (100.00%)	36 (100.00%)

TEAE Serious and Action Taken by Treatment and Sex - All Patients / Output Fi					
		ACTIVE		PLACEBO	
		F	M	F	M
N	DOSE NOT CHANGED	77 (25.58%)	30 (9.97%)	44 (26.51%)	24 (14.46%)
	DRUG INTERRUPTED	1 (0.33%)	0 (0.00%)	1 (0.60%)	2 (1.20%)
	DRUG WITHDRAWN	7 (2.33%)	2 (0.66%)	2 (1.20%)	1 (0.60%)
Y	DOSE NOT CHANGED	1 (0.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	DRUG WITHDRAWN	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.60%)
	Subjects(filtered)	80 (26.58%)	31 (10.30%)	45 (27.11%)	25 (15.06%)
	1stColItemSubjects	301 (100.00%)	301 (100.00%)	166 (100.00%)	166 (100.00%)

JReview: Most common clinical safety tables

Tabulation of Adverse Events

Event Counts

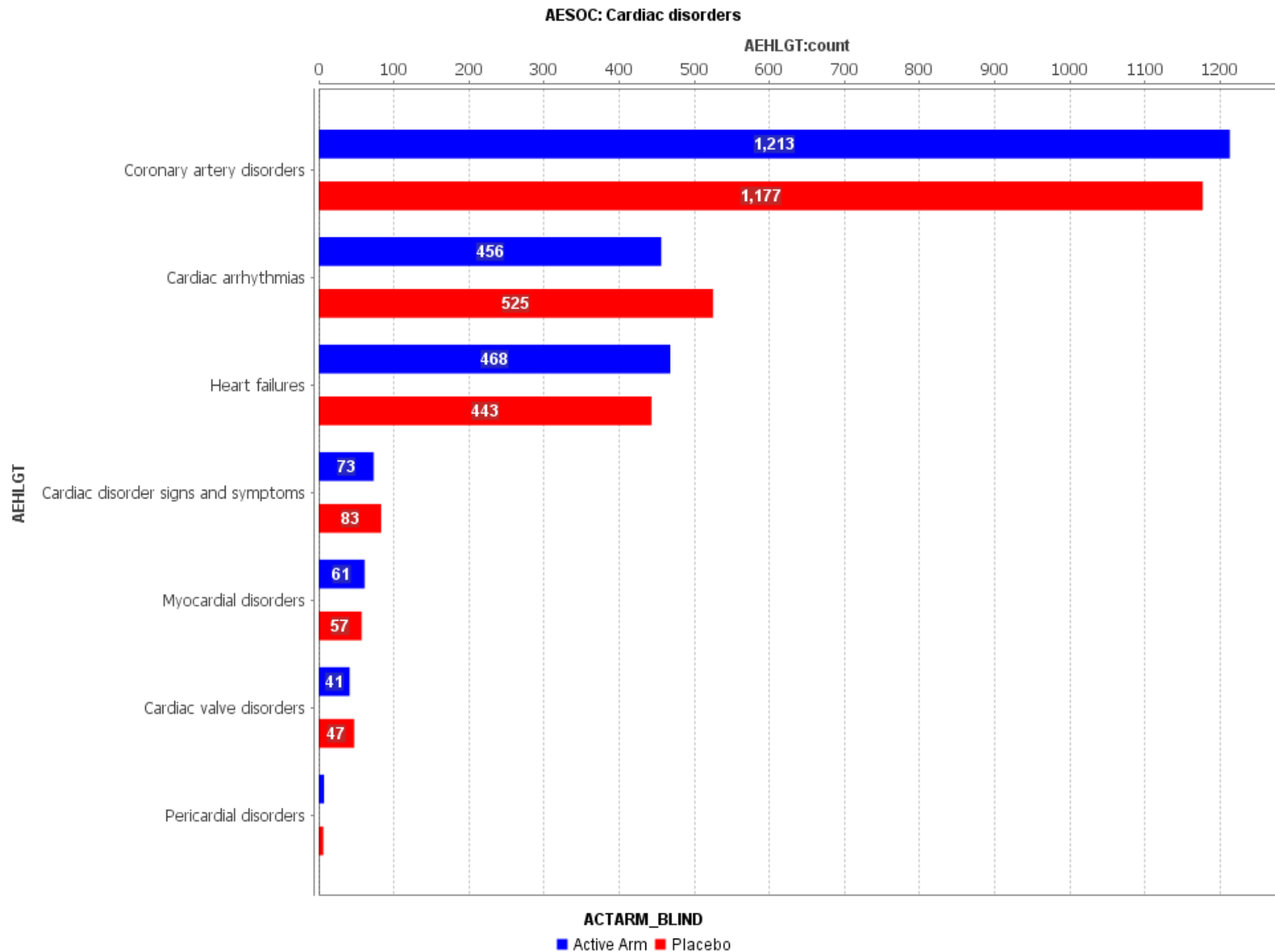
JReview: Adverse Event Incident Rates

Event Counts Treatment Emergent Adverse Events

TEAE SOC Event Counts Percent Incidence by Treatment Descending Sort on Active Arm - Subset			
  			
AESOC	Active Arm	Placebo	Incidence
Metabolism and nutrition disorders	3916 (15.70%)	3911 (16.02%)	7827 (15.86%)
Infections and infestations	2965 (11.89%)	2865 (11.73%)	5830 (11.81%)
Cardiac disorders	2319 (9.30%)	2338 (9.58%)	4657 (9.43%)
Gastrointestinal disorders	2000 (8.02%)	1808 (7.40%)	3808 (7.71%)
Musculoskeletal and connective tissue disorders	1835 (7.36%)	1721 (7.05%)	3556 (7.20%)
Investigations	1550 (6.21%)	1392 (5.70%)	2942 (5.96%)
Nervous system disorders	1377 (5.52%)	1457 (5.97%)	2834 (5.74%)
Renal and urinary disorders	1224 (4.91%)	1160 (4.75%)	2384 (4.83%)
Respiratory, thoracic and mediastinal disorders	1194 (4.79%)	1170 (4.79%)	2364 (4.79%)
General disorders and administration site conditions	1170 (4.69%)	1243 (5.09%)	2413 (4.89%)
Injury, poisoning and procedural complications	947 (3.80%)	979 (4.01%)	1926 (3.90%)
Vascular disorders	878 (3.52%)	883 (3.62%)	1761 (3.57%)
Skin and subcutaneous tissue disorders	807 (3.24%)	672 (2.75%)	1479 (3.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	720 (2.89%)	768 (3.15%)	1488 (3.01%)
Blood and lymphatic system disorders	492 (1.97%)	444 (1.82%)	936 (1.90%)
Eye disorders	446 (1.79%)	468 (1.92%)	914 (1.85%)
Psychiatric disorders	312 (1.25%)	373 (1.53%)	685 (1.39%)
Reproductive system and breast disorders	228 (0.91%)	224 (0.92%)	452 (0.92%)
Ear and labyrinth disorders	219 (0.88%)	173 (0.71%)	392 (0.79%)
Hepatobiliary disorders	184 (0.74%)	191 (0.78%)	375 (0.76%)
Endocrine disorders	76 (0.30%)	79 (0.32%)	155 (0.31%)
Surgical and medical procedures	37 (0.15%)	32 (0.13%)	69 (0.14%)
Immune system disorders	33 (0.13%)	48 (0.20%)	81 (0.16%)
Congenital, familial and genetic disorders	12 (0.05%)	14 (0.06%)	26 (0.05%)
Social circumstances	3 (0.01%)	3 (0.01%)	6 (0.01%)
Pregnancy, puerperium and perinatal conditions	0 (0.00%)	1 (0.00%)	1 (0.00%)
Incidence totals	24944 (100.00%)	24417 (100.00%)	49361 (100.00%)

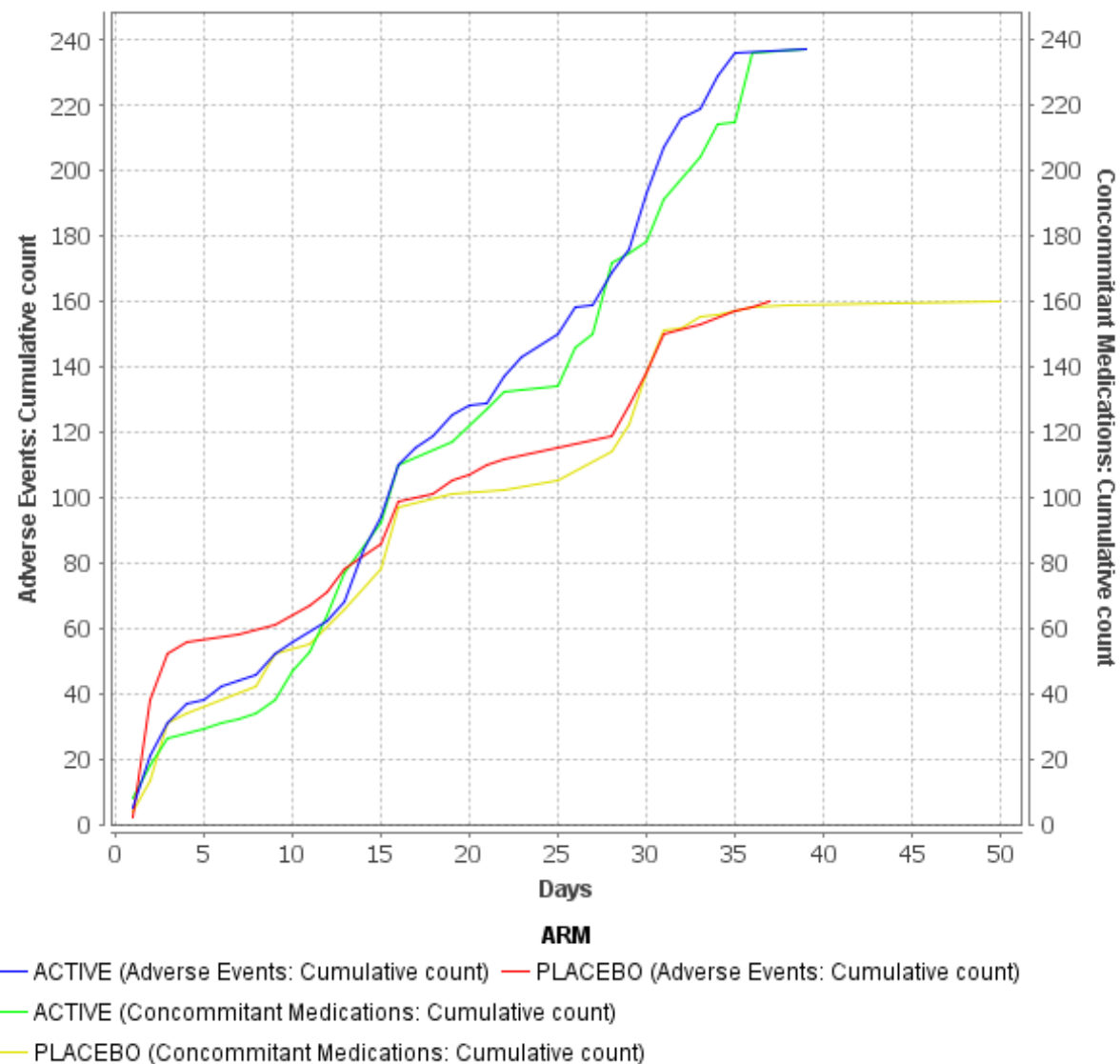
JReview: Adverse Event Incident Rates

Event Counts Treatment Emergent Adverse Events



JReview: Cumulative Plots Treatment Emergent Adverse Events and Concomitant Medications

vs Study Day : Dual Y Axis analysis: by Treatment



JReview: Most common clinical safety tables

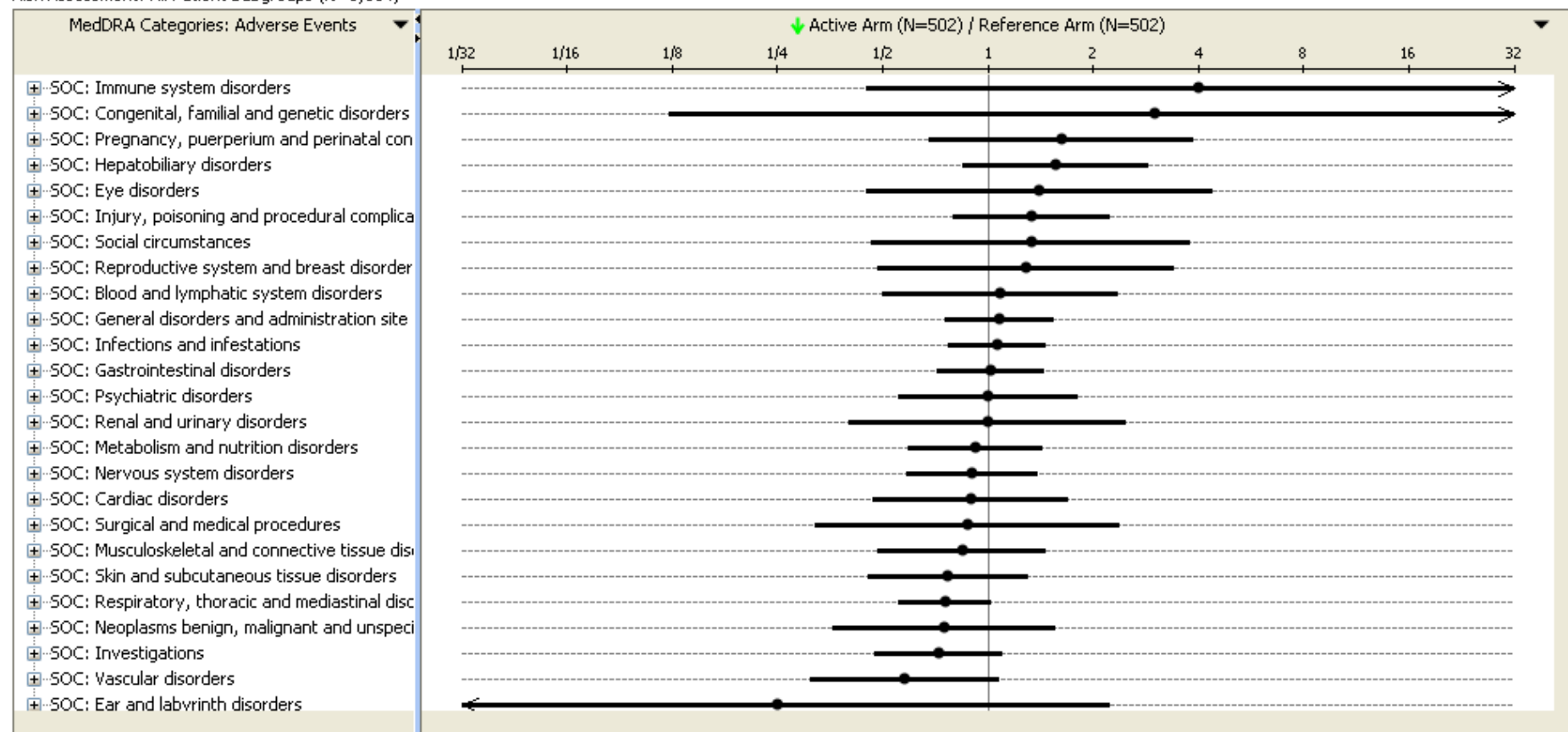
**Multi-Dimensional Graphical
presentations of Adverse Events**

JReview Multi-Dimensional Graphing of Clinical Data

JReview Relative Risk Ratio

Treated Patient Population Risk Profile

Risk Assessment: All Patient Subgroups (N=1,004)



Slide 24

SR1

Add Risk Profiles

Scott Runyan, 8/3/2016

SR2

Animate subgroups and resulting Risk Profile

Scott Runyan, 8/3/2016

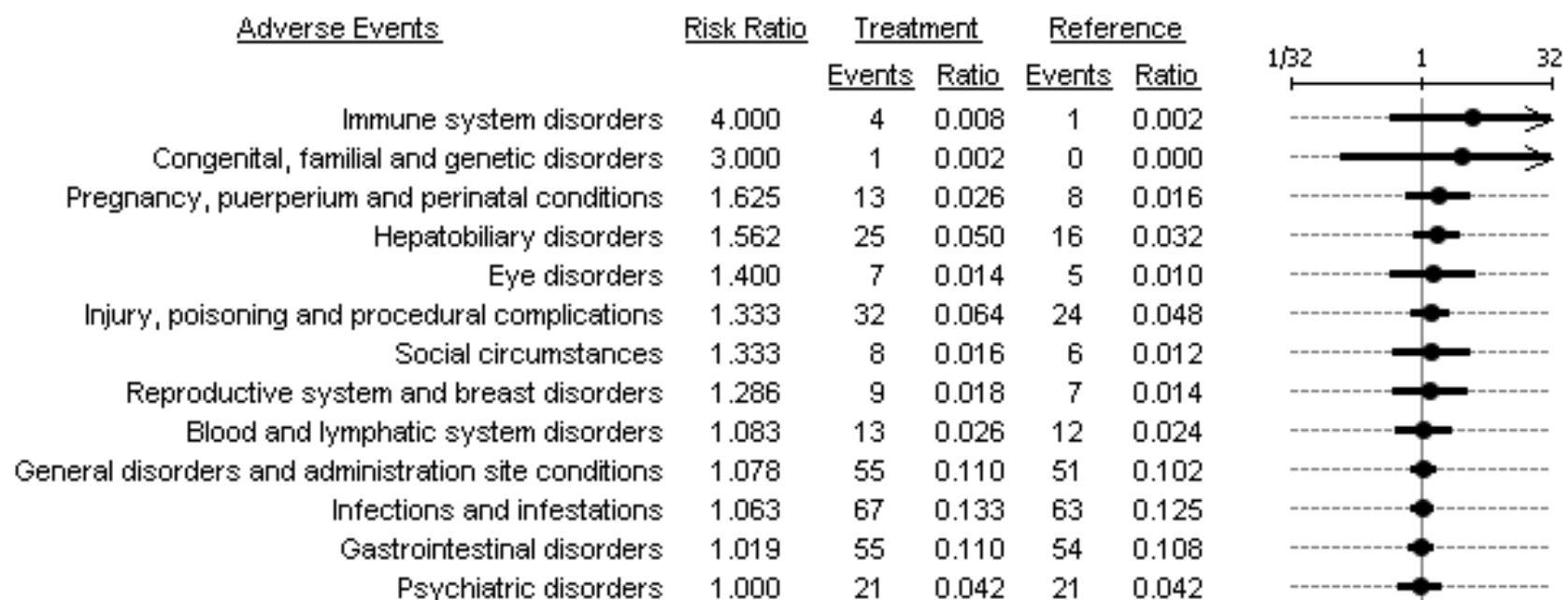
JReview Multi-Dimensional Graphing of Clinical Data

JReview Relative Risk Ratio Plot: Exports out in Tabulation

Relative Risk Ratio

Treatment Group: Active Arm Total Patients: 502

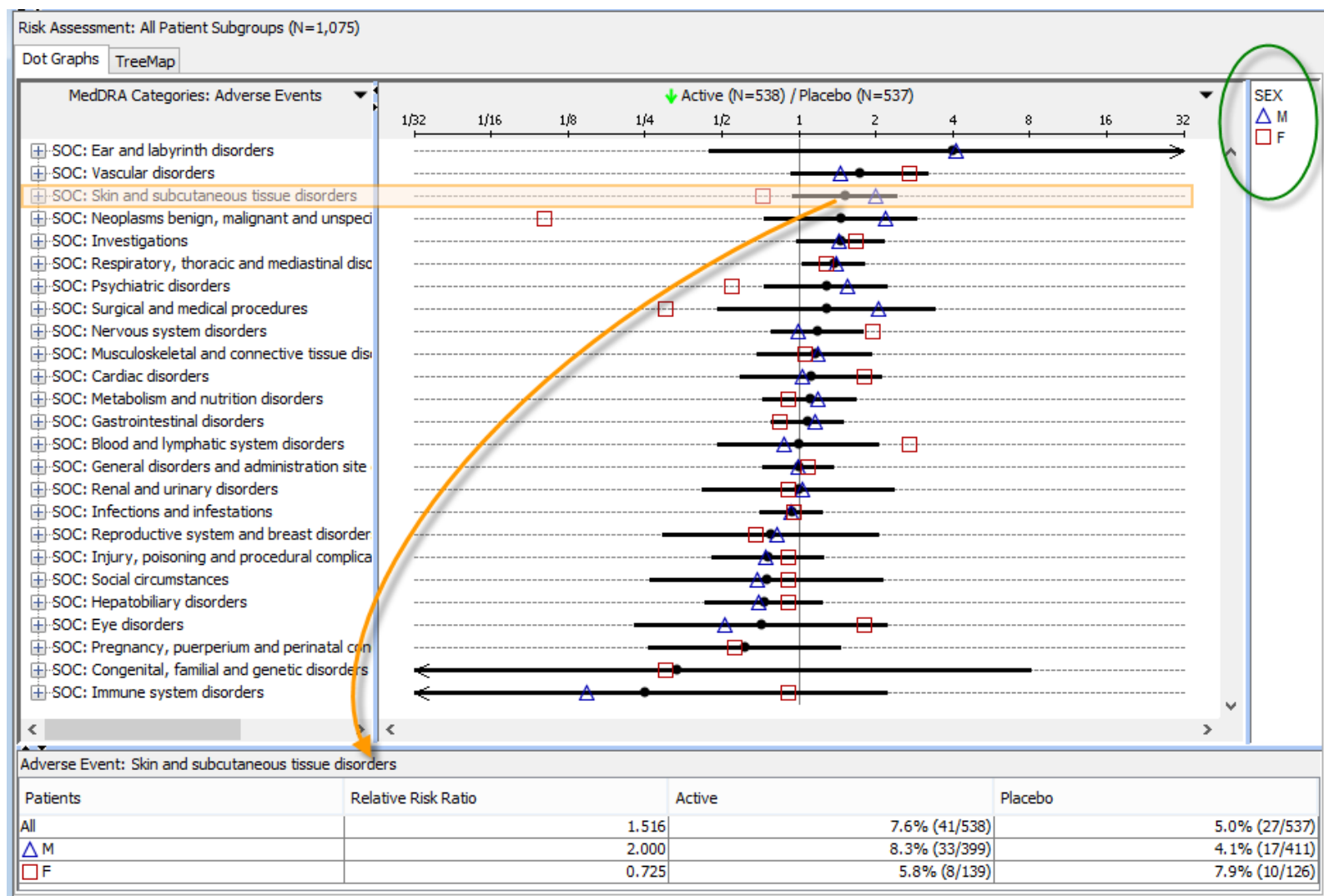
Reference Group: Reference Arm Total Patients: 502



JReview Exploring Clinical Data

JReview Relative Risk Ratio with Subgroup weighting

Sub-Group Contribution



JReview Exploring Clinical Data

JReview Relative Risk Ratio with Subgroup weighting

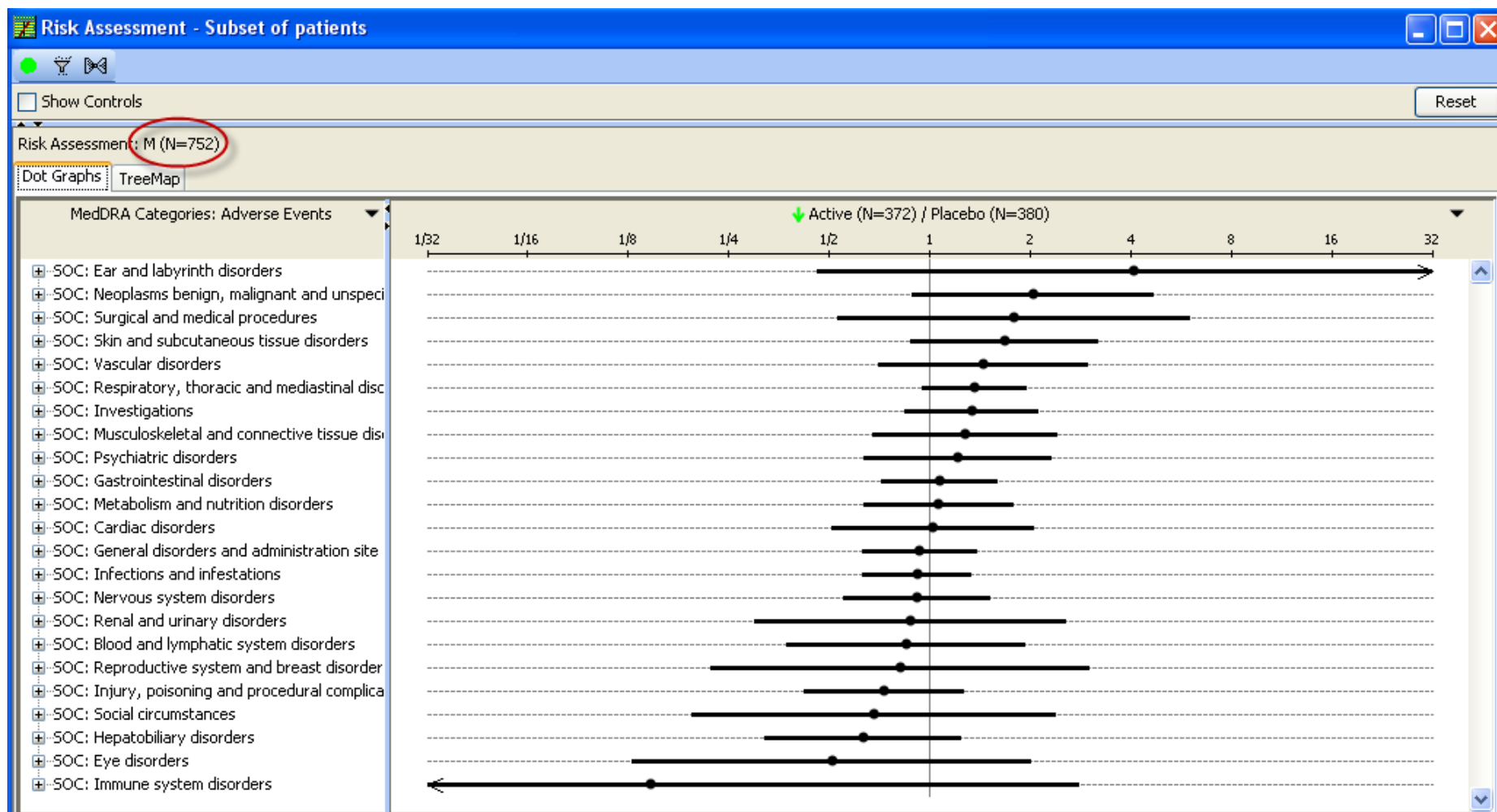
Sub-Group Contribution

Metric: Relative Risk Ratio (zero events corrected to 0.5)						
Treatment Group: Active Arm						
Reference Group: Reference Arm						
Patient Subgroup: All Patient Subgroups (N=1,004)						
MedDRA Level: SOC						
Excluded Range:						
Date: August 2, 2016 6:44:26 AM EDT						
Sex	Treatment	Reference				
M	380	372				
F	122	130				
	M			F		
Adverse Event	Relative Risk Ratio	Occurrences in Treatment	Occurrences in Reference	Relative Risk Ratio	Occurrences in Treatment	Occurrences in Reference
Immune system disorders	6.853	3	0	1.066	1	
Congenital, familial and genetic disorders		0	0	3.196	1	
Pregnancy, puerperium and perinatal conditions		0	0	1.732	13	
Hepatobiliary disorders	1.581	21	13	1.421	4	
Eye disorders	1.958	6	3	0.533	1	
Injury, poisoning and procedural complications	1.371	28	20	1.066	4	
Social circumstances	1.468	6	4	1.066	2	
Reproductive system and breast disorders	1.224	5	4	1.421	4	
Blood and lymphatic system disorders	1.175	12	10	0.533	1	
General disorders and administration site conditions	1.074	45	41	1.066	10	
Infections and infestations	1.088	50	45	1.006	17	
Gastrointestinal disorders	0.933	41	43	1.356	14	
Psychiatric disorders	0.824	16	19	2.664	5	
Renal and urinary disorders	1.142	7	6	0.710	2	
Metabolism and nutrition disorders	0.943	26	27	0.872	9	
Nervous system disorders	1.092	29	26	0.533	7	
Cardiac disorders	0.979	15	15	0.533	2	
Surgical and medical procedures	0.559	4	7	3.197	3	
Musculoskeletal and connective tissue disorders	0.783	16	20	1.066	6	
Skin and subcutaneous tissue disorders	0.596	14	23	1.370	9	
Respiratory, thoracic and mediastinal disorders	0.734	45	60	0.823	17	
Neoplasms benign, malignant and unspecified (incl. dysplasia in situ)	0.489	8	16	9.588	4	

JReview Multi-Dimensional Graphing of Clinical Data

Relative Risk Ratio of Treatment Emergent Adverse Events

Treated Male Patient Population Risk Profile



Slide 28

SR1

Add Risk Profiles

Scott Runyan, 8/3/2016

SR2

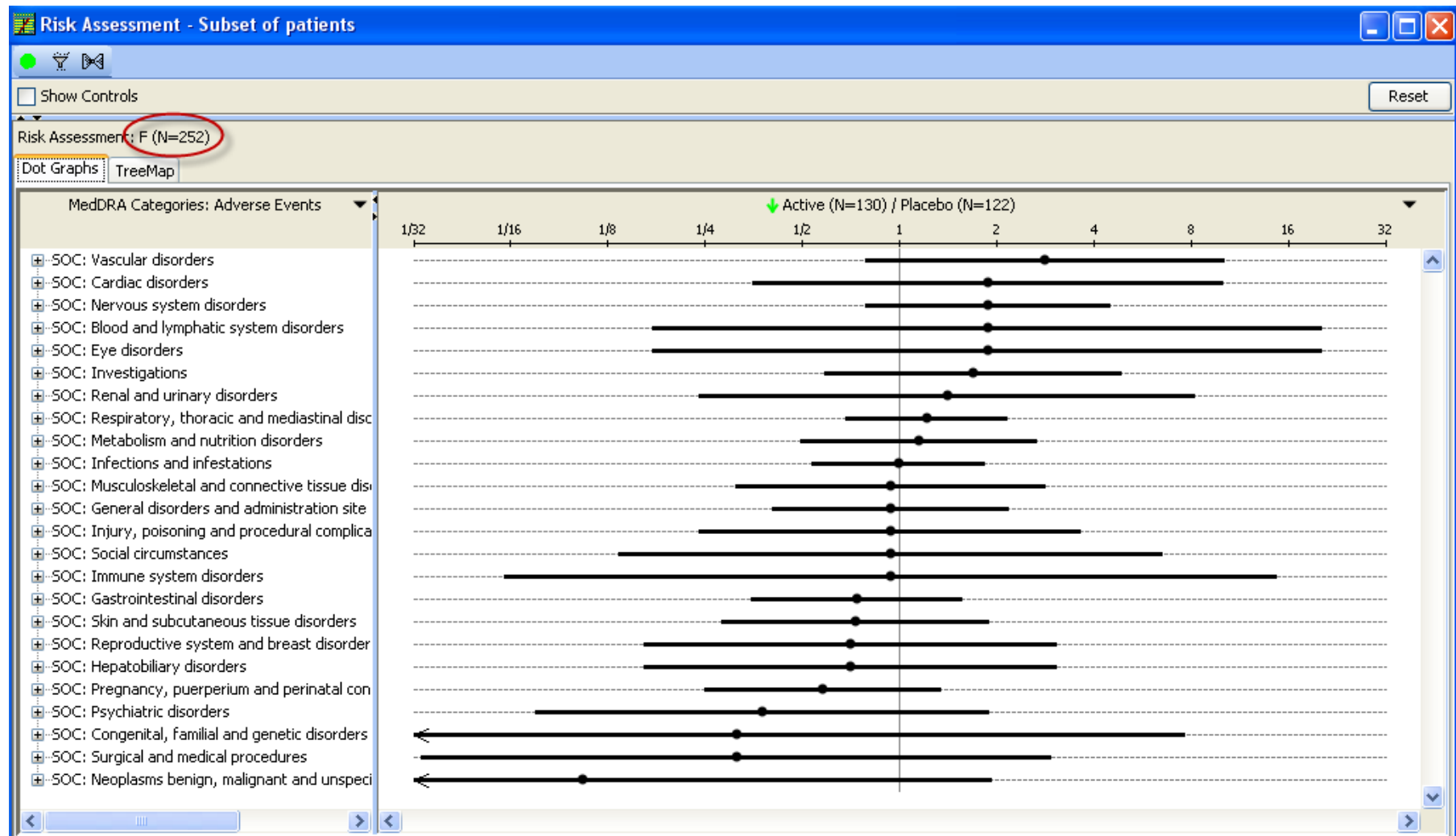
Animate subgroups and resulting Risk Profile

Scott Runyan, 8/3/2016

JReview Multi-Dimensional Graphing of Clinical Data

Relative Risk Ratio of Treatment Emergent Adverse Events

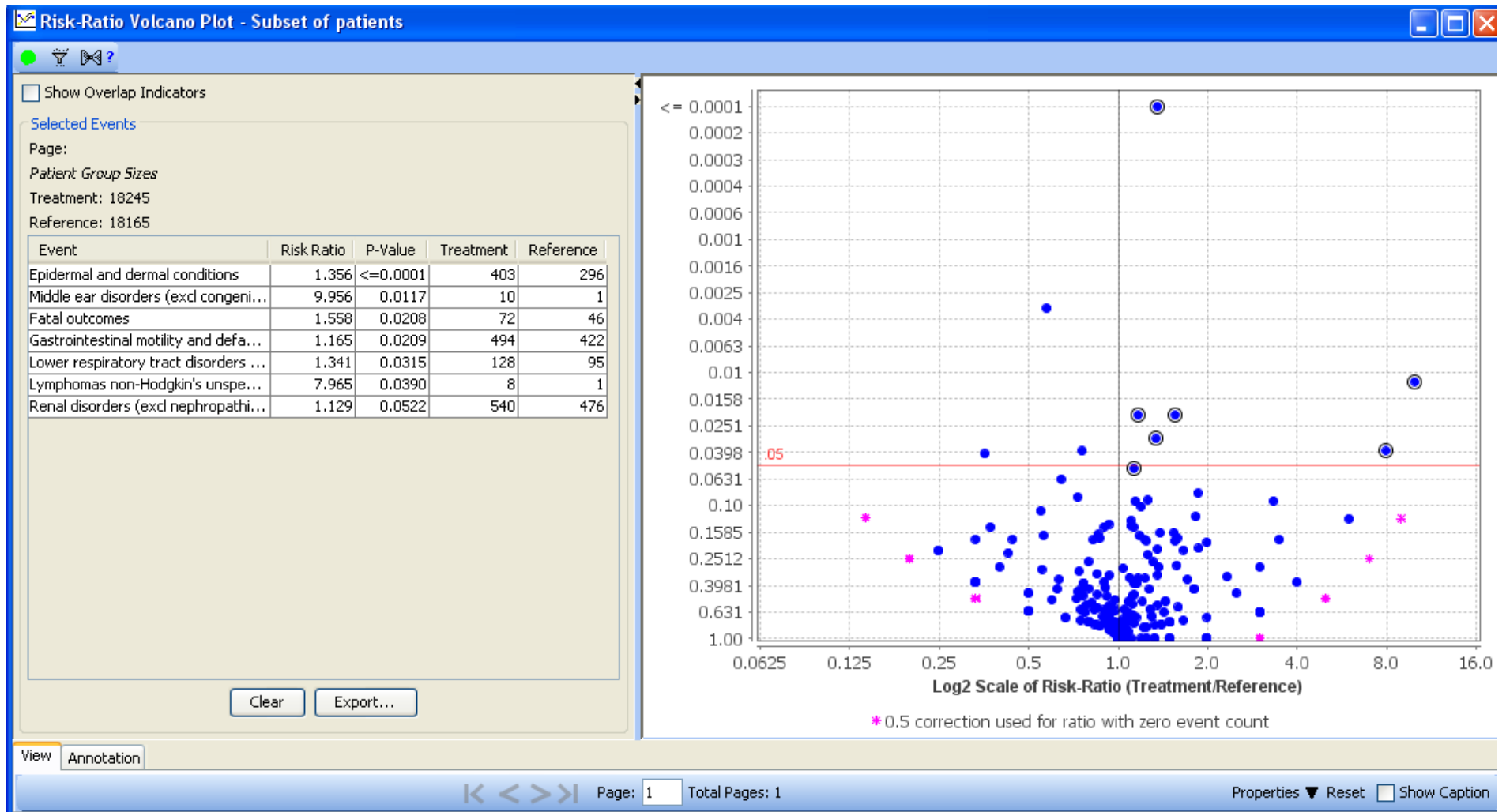
Treated Female Patient Population Risk Profile



JReview Multi-Dimensional Graphing

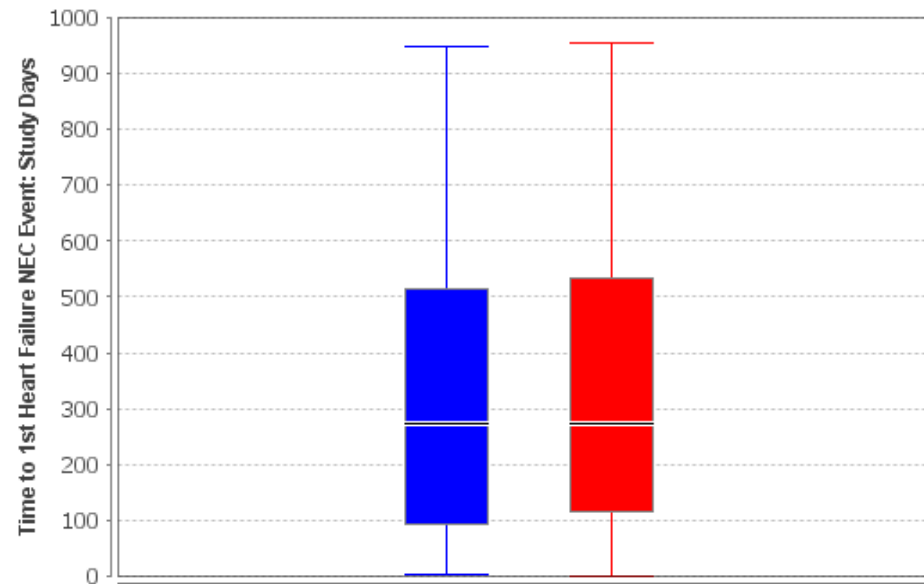
JReview Relative Risk Ratio Volcano Plot

Upper right quadrant is referred to as the label maker



JReview Exploring Clinical Data

Box Whiskers includes additional table data Time to 1st High Level Term Heart Failure NEC Event by Actual Treatment



	Heart failures NEC	
	Active Arm	Placebo
Mean	320.13	333.49
Median	274.50	274.00
Q1	93.00	117.50
Q3	513.00	535.00
Min	4.00	2.00
Max	948.00	953.00
N	244	237

AEHLT

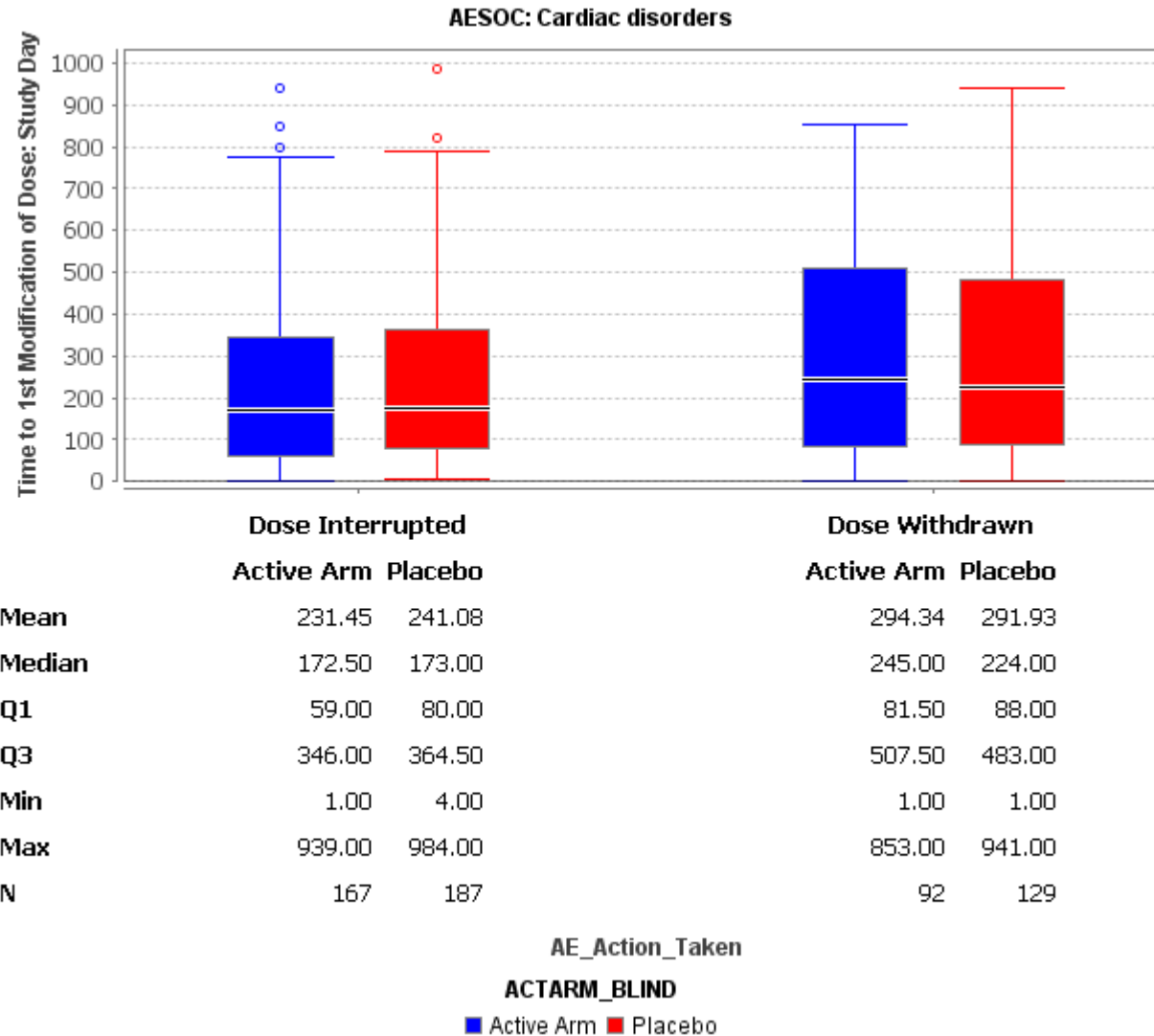
ACTARM_BLIND

■ Active Arm ■ Placebo

Treatment Emergent High Level Term (HLT) Heart Failures NEC:: Time to Event by Actual Treatment

JReview Exploring Clinical Data

Box Whiskers includes additional table data Time to 1st modification of treatment pageBy AE SOC



Cardiac Disorders: Time to 1st Treatment Emergent Adverse Events with Dose Interruption or Dose Withdrawn

JReview Exploring Clinical Data **FDA Standard Analysis Catalog**



JREVIEW Standard Analysis Catalog SDTM Version 3.1.3

CDER Computational Science Center



Better Data, Better Tools, Better Decisions

JReview Exploring Clinical Data

FDA Standard Analysis Catalog

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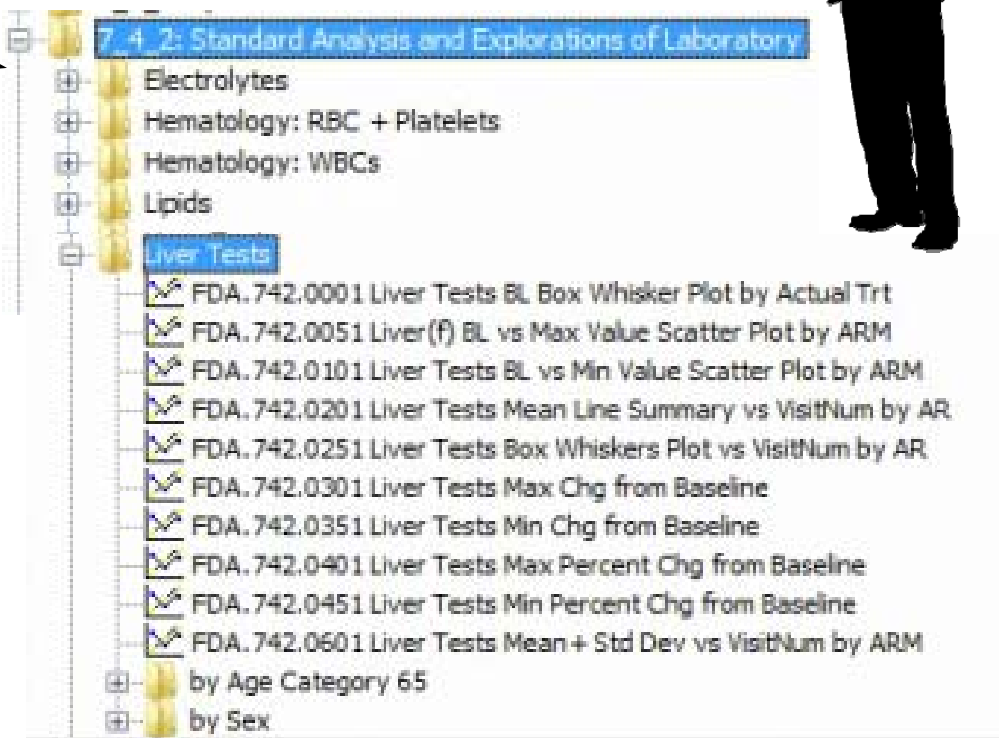
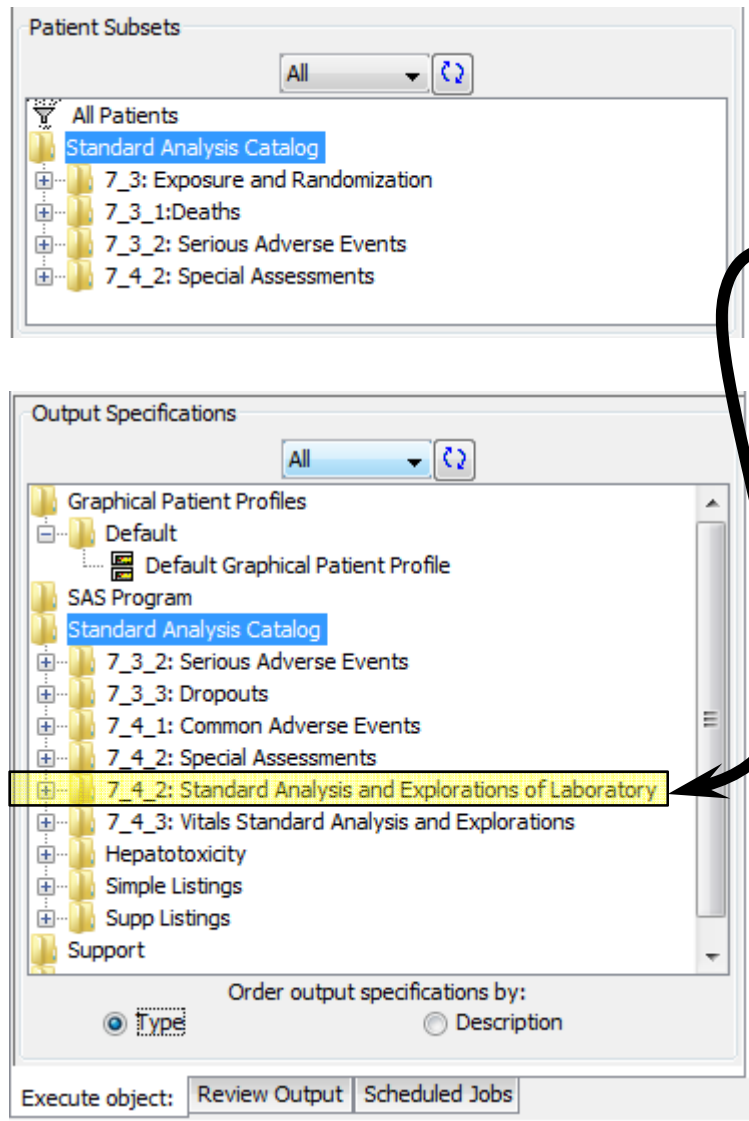
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JReview Exploring Clinical Data

The standard analysis catalog



JReview Exploring Clinical Data

FDA Standard Analysis Catalog



The standard analysis catalog includes a repository of simple domain detail subject listings.

Laboratory Liver function tests Subject Simple Listing - All Patients / Output Filter applied										
Show Filter Refresh										
Description of	Study	Unique	Study Day of	Visit	Visit	Lab	Numeric Result	Std	Ref Range	Baseline
Study ID	Actual Arm	Site ID	Subject ID	Specimen Collection	Number	Name	Test	Std Units	Units	Indicator
			Subject0001	-3	1	SCREENING	ALT	75	U/L	HIGH
				-3	1	SCREENING	ALP	105	U/L	NORMAL
				-3	1	SCREENING	AST	23	U/L	NORMAL
				-3	1	SCREENING	GGT	136	U/L	HIGH
				-3	1	SCREENING	BILI	11.97	umol/L	NORMAL
				3	4	DAY 3	AST	15	U/L	NORMAL
				3	4	DAY 3	BILI	8.55	umol/L	NORMAL
				3	4	DAY 3	ALP	91	U/L	NORMAL
				3	4	DAY 3	ALT	26	U/L	NORMAL
				3	4	DAY 3	GGT	136	U/L	HIGH
				4	11	END OF TREATMENT	BILI	8.55	umol/L	NORMAL
				4	11	END OF TREATMENT	AST	19	U/L	NORMAL
				4	11	END OF TREATMENT	ALT	25	U/L	NORMAL
				4	11	END OF TREATMENT	ALP	90	U/L	NORMAL
				4	11	END OF TREATMENT	GGT	126	U/L	HIGH
			Subject0002	-1	1	SCREENING	AST	12	U/L	NORMAL
				-1	1	SCREENING	GGT	68	U/L	HIGH
				-1	1	SCREENING	ALP	95	U/L	NORMAL
				-1	1	SCREENING	ALT	26	U/L	NORMAL

Simple Listings	
+	AE
+	CE
+	CM
+	CO Comments
+	DA
+	DM
+	DS
+	EG
+	EX
+	FA
+	HO Hospitalization
+	IM Imaging
+	IS Immunogenicity
+	LB
+	<Parameterized> Lab Test
+	Coagulation
+	Electrolyte tests
+	Hematology
+	Lipids
+	Liver Lab tests
+	Renal Lab tests
+	MB
+	MH
+	MS
+	RS Response Assessment
+	SC
+	TS Trial Summary
+	Template
+	VS
+	ZC
+	ZP
+	ZV
+	ZZ
+	Supp Listings

JReview Exploring Clinical Data

FDA Standard Analysis Catalog



Safety Review Analysis

Adverse Events

Tables: 44/76 **58%**

Graphs: 17/76 **22%**

Reports: 12/76 29%

Risk Assessments: 3

Laboratory Analysis

Tables: 34/742 **5%**

Graphs: 688/742 **93%**

Reports: 20/742 3%

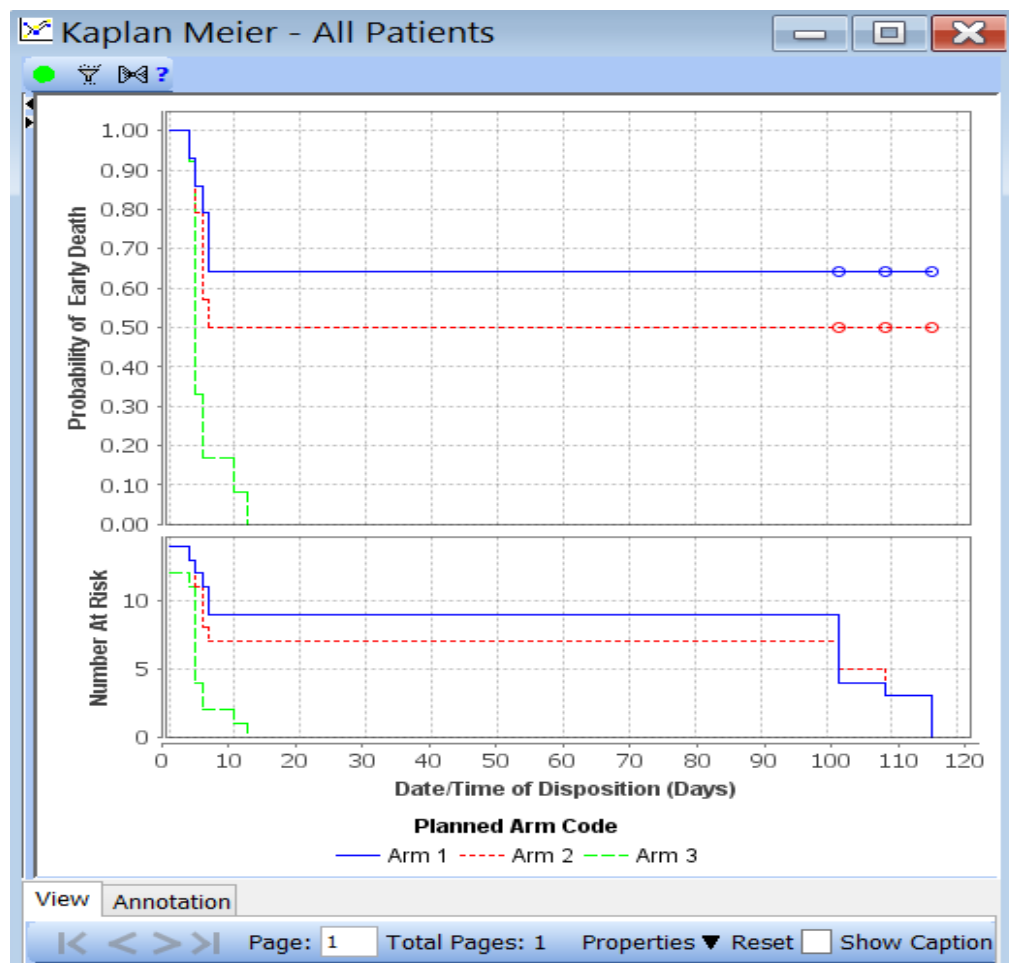
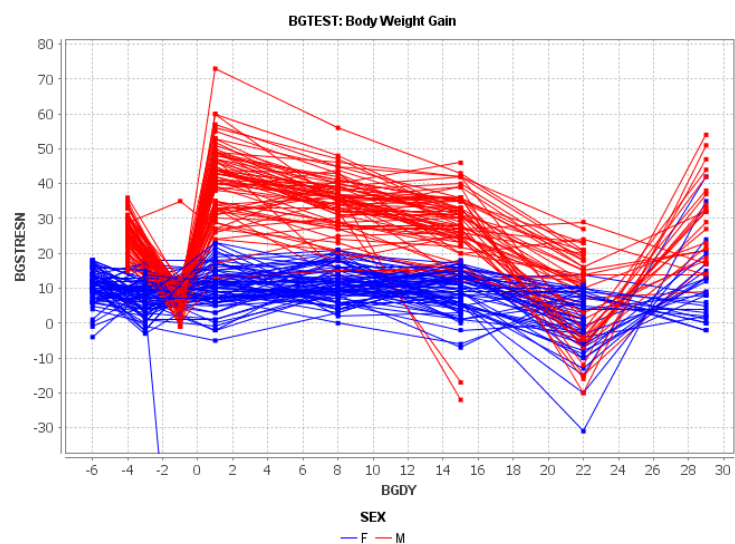
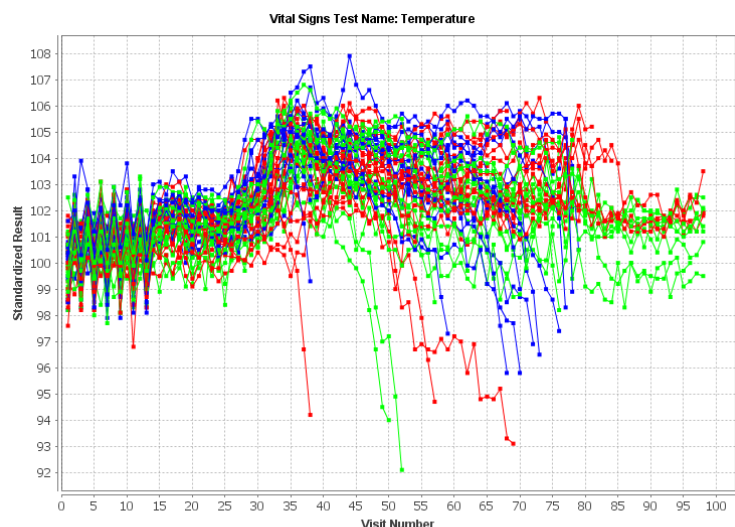
Vitals Analysis

Tables: 8/42 **19%**

Graphs: 34/42 **81%**



JReview Exploring SEND pre-Clinical Data



Standardized Disposition Term	Arm 1	Arm 2	Arm 3	Subjects(filtered)
FOUND DEAD	10 (63%)	5 (31%)	7 (44%)	22 (46%)
MORIBUND SACRIFICE	4 (25%)	10 (63%)	3 (19%)	17 (35%)
TERMINAL SACRIFICE	2 (13%)	1 (6%)	6 (38%)	9 (19%)
Subjects(filtered)	16 (100%)	16 (100%)	16 (100%)	48 (100%)
1stColItemSubjects	16 (100%)	16 (100%)	16 (100%)	(Denom=1stColTot)

Questions

Thank you for taking the time to review our work

For more product information please contact us by email :

info@i-review.com

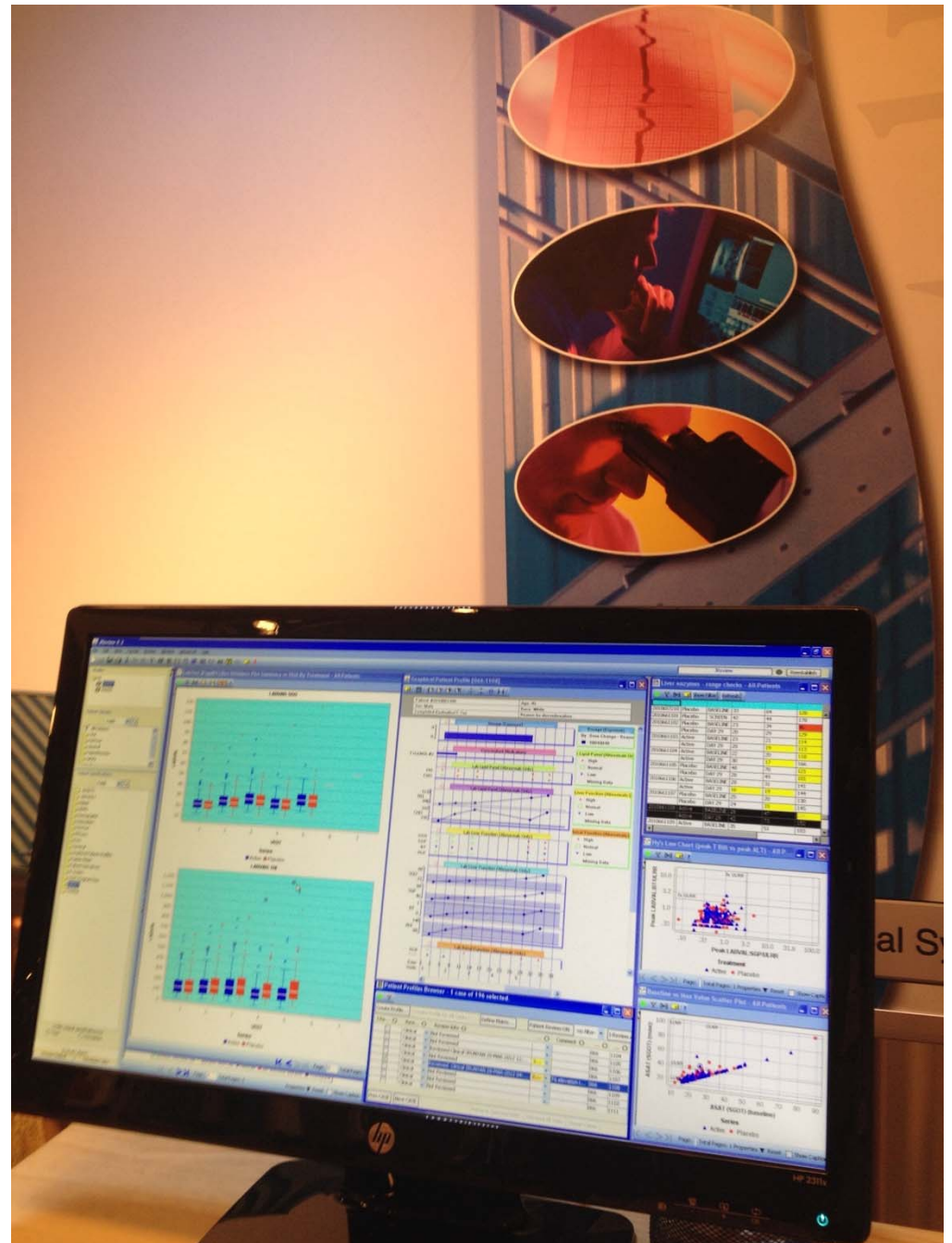
or by phone (908) 996-7881

For more information regarding this presentation please contact:

Scott Runyan by email at

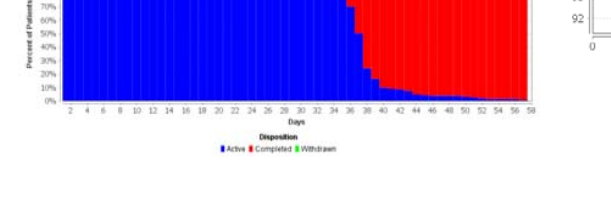
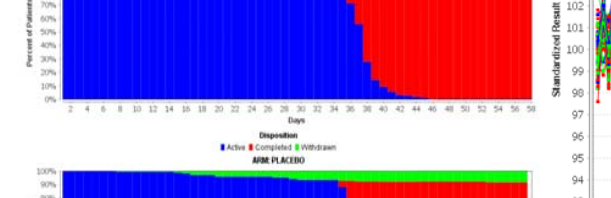
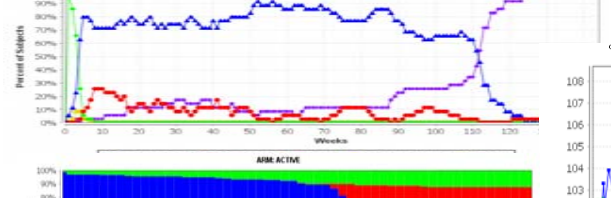
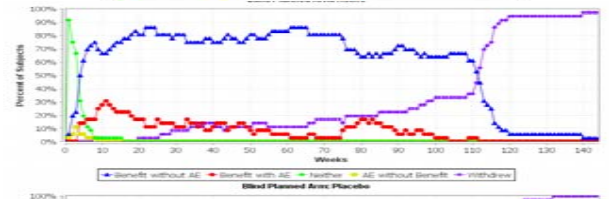
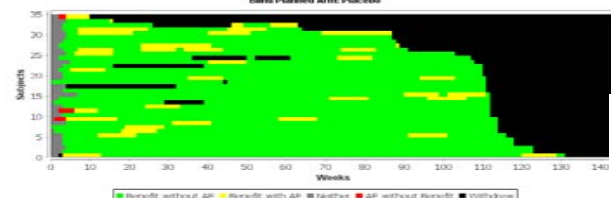
srunyan@i-review.com

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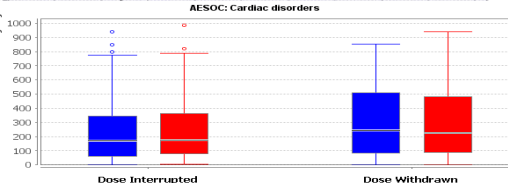


JReview: Getting to know your data

Using a combination of Graphs and Tabulations



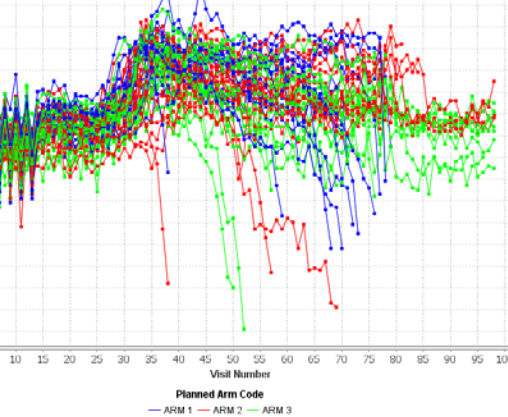
Relative Risk Ratio				
Treatment Group: Active Arm		Total Patients: 502		
Reference Group: Reference Arm		Total Patients: 502		
Adverse Events	Risk Ratio	Treatment Events	Reference Events	Ratio
Immune system disorders	4.000	4	0.008	1
Congenital, familial and genetic disorders	3.000	1	0.002	0
Pregnancy, puerperium and perinatal conditions	1.625	13	0.026	8
Hepatobiliary disorders	1.562	25	0.050	16
Eye disorders	1.400	7	0.014	5
Injury, poisoning and procedural complications	1.333	32	0.064	24
Social circumstances	1.333	8	0.016	6
Reproductive system and breast disorders	1.286	9	0.018	7
Blood and lymphatic system disorders	1.083	13	0.026	12
General disorders and administration site conditions	1.078	55	0.110	51
Infections and infestations	1.063	67	0.133	63
Gastrointestinal disorders	1.019	55	0.110	54
Psychiatric disorders	1.000	21	0.042	21



Dose Interrupted		Dose Withdrawn	
Active Arm	Placebo	Active Arm	Placebo
Mean	231.45	241.08	294.34
Median	172.50	173.00	245.00
Q1	59.00	80.00	81.50
Q3	346.00	364.50	507.50
Min	1.00	4.00	1.00
Max	939.00	984.00	853.00
N	167	187	92

AE_Action_Taken
ACT_ARM_BLIND
Active Arm Placebo

Cardiac Disorders: Time to 1st Treatment Emergent Adverse Events with Dose Interruption or Dose Withdrawn



TEAE SOC Descending sort order on Active Treatment Arm : Safety Population Cro		
Active Arm	Placebo	
1758 (9.64%)	1674 (9.22%)	
1680 (9.21%)	1700 (9.36%)	
1322 (7.25%)	1359 (7.48%)	
1321 (7.24%)	1190 (6.55%)	
1250 (6.85%)	1172 (6.45%)	
1008 (5.52%)	1067 (5.67%)	
964 (5.28%)	869 (4.78%)	
963 (5.28%)	891 (4.91%)	
909 (4.98%)	921 (5.07%)	
856 (4.69%)	843 (4.64%)	
725 (3.97%)	724 (3.99%)	
697 (3.82%)	699 (3.85%)	
605 (3.32%)	625 (3.44%)	
602 (3.30%)	497 (2.74%)	
431 (2.36%)	376 (2.07%)	
354 (1.94%)	346 (1.90%)	
251 (1.38%)	314 (1.73%)	
204 (1.12%)	202 (1.11%)	
182 (1.00%)	153 (0.84%)	
163 (0.89%)	160 (0.88%)	
75 (0.41%)	74 (0.41%)	
33 (0.18%)	30 (0.17%)	
32 (0.18%)	46 (0.25%)	

