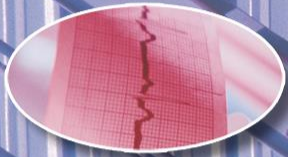


Integrated Clinical Systems, Inc.

Exploring Clinical Data using JReview®



JReview Exploring Clinical Data

PhUSE presentation September 2012

Clinical Data Review Tasks

- A. Baseline analysis
- B. Safety Review
- C. Efficacy Review
- D. Surveillance

JReview Exploring Clinical Data

PhUSE presentation September 2012

A. Getting to know your data

1. Risk Assessments
2. AE Incident Rates
3. Baseline characteristics of Patient Populations
4. Summary Line Charts- Mean / Mean Chg from BL
5. Summary Box Whiskers – Baseline/ Chg from BL at Visits
6. Summary Bar Chart Mean Chg from Baseline

B. Identify patients that Died/SAE/Discontinued

1. Kaplan Meier – Rate/Time to death analysis

C. Shifts from Baseline – Laboratory Analysis

1. Identify patients with abnormal lab results and shift from Baseline
 - a) Scatter Plot Baseline vs Max, Baseline vs Min for example
 - b) Report Listings: Highlighting abnormal results

JReview Exploring Clinical Data

PhUSE presentation September 2012

D. Getting to Know Your Patients

1. Graphical Patient Profiles
2. Patient Visit Data Reports
3. Patient Narratives

E. Special Assessments:

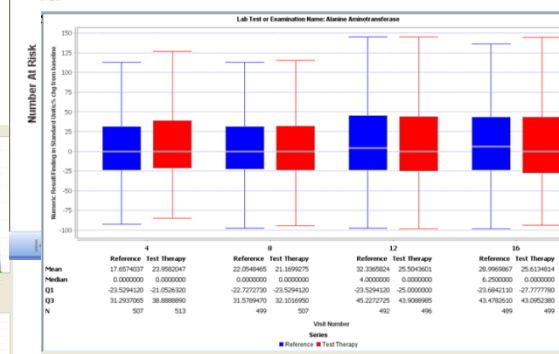
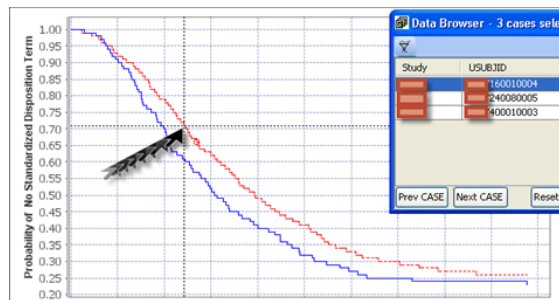
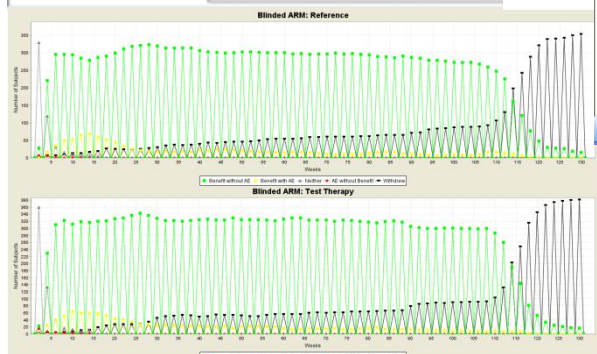
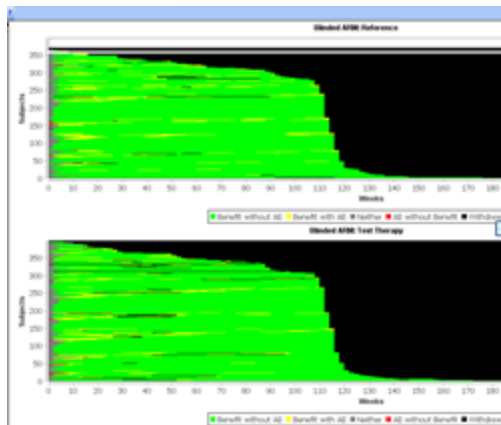
- a) Hy's Law example – explore why patients meet the criteria
 - (AST/ALT > 3xULN
 - andSelect Bilirubin >2xULN
 - andSelect Alkaline Phosphatase < 2xULN
- b) Elevated Amylase and Lypase -Asymptomatic/Symptomatic pancreatitis

F. Driven by submission protocol and findings

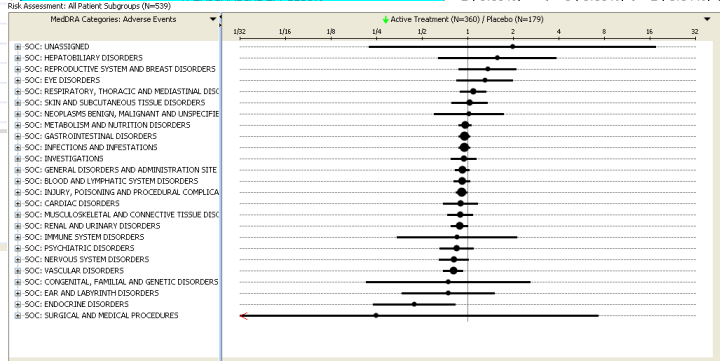
4. AE results in Therapy interrupted –
 - a) was patient rechallenged? What was the outcome?
 - b) What was the cause of interruption? Labeling issue?

G. Benefit Risk Assessment

JReview: Getting to know your data



MedDRA SOC or equivalent	MedDRA PT or equivalent	Active Treatment	Placebo	Subjects
CARDIAC DISORDERS	TACHYCARDIA	32 (8.89%)	11 (6.15%)	43 (7.23%)
	ATRIAL FIBRILLATION	22 (6.11%)	9 (5.03%)	31 (5.21%)
	BRADYCARDIA	11 (3.06%)	7 (3.91%)	18 (3.03%)
	CARDIAC FAILURE	10 (2.78%)	2 (1.12%)	12 (2.02%)
	CARDIAC FAILURE CONGESTIVE	9 (2.50%)	4 (2.23%)	13 (2.18%)
	LEFT VENTRICULAR HYPERTROPHY	7 (1.94%)	2 (1.12%)	9 (1.51%)
	SINUS BRADYCARDIA	7 (1.94%)	4 (2.23%)	11 (1.85%)
	PALPITATIONS	5 (1.39%)	5 (2.79%)	10 (1.68%)
	MYOCARDIAL INFARCTION	5 (1.39%)	2 (1.12%)	7 (1.18%)
	ANGINA PECTORIS	4 (1.11%)	6 (3.35%)	10 (1.68%)
	ARRHYTHMIA	4 (1.11%)	4 (2.23%)	8 (1.34%)
	VENTRICULAR TACHYCARDIA	3 (0.83%)	1 (0.56%)	4 (0.67%)
	ACUTE CORONARY SYNDROME	3 (0.83%)	0 (0.00%)	3 (0.50%)
	ATRIOVENTRICULAR BLOCK FIRST DEGREE	3 (0.83%)	2 (1.12%)	5 (0.84%)
	SINUS TACHYCARDIA	3 (0.83%)	2 (1.12%)	5 (0.84%)
	VENTRICULAR EXTRASYSTOLES	3 (0.83%)	0 (0.00%)	3 (0.50%)
	MYOCARDIAL ISCHAEMIA	2 (0.56%)	1 (0.56%)	3 (0.50%)
	PERICARDIAL EFFUSION	2 (0.56%)	0 (0.00%)	2 (0.34%)

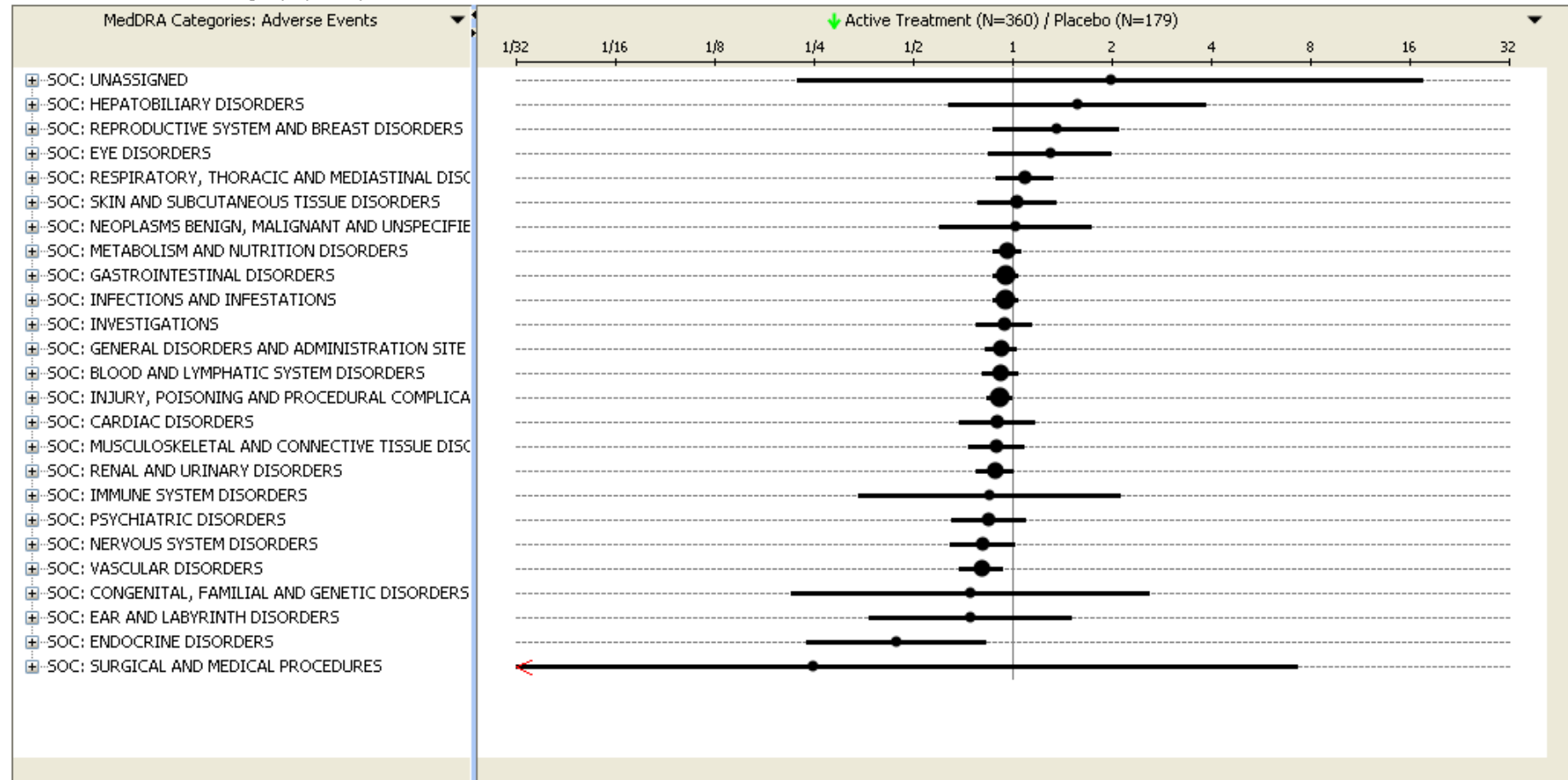


GETTING TO KNOW YOUR DATA USING JREVIEW

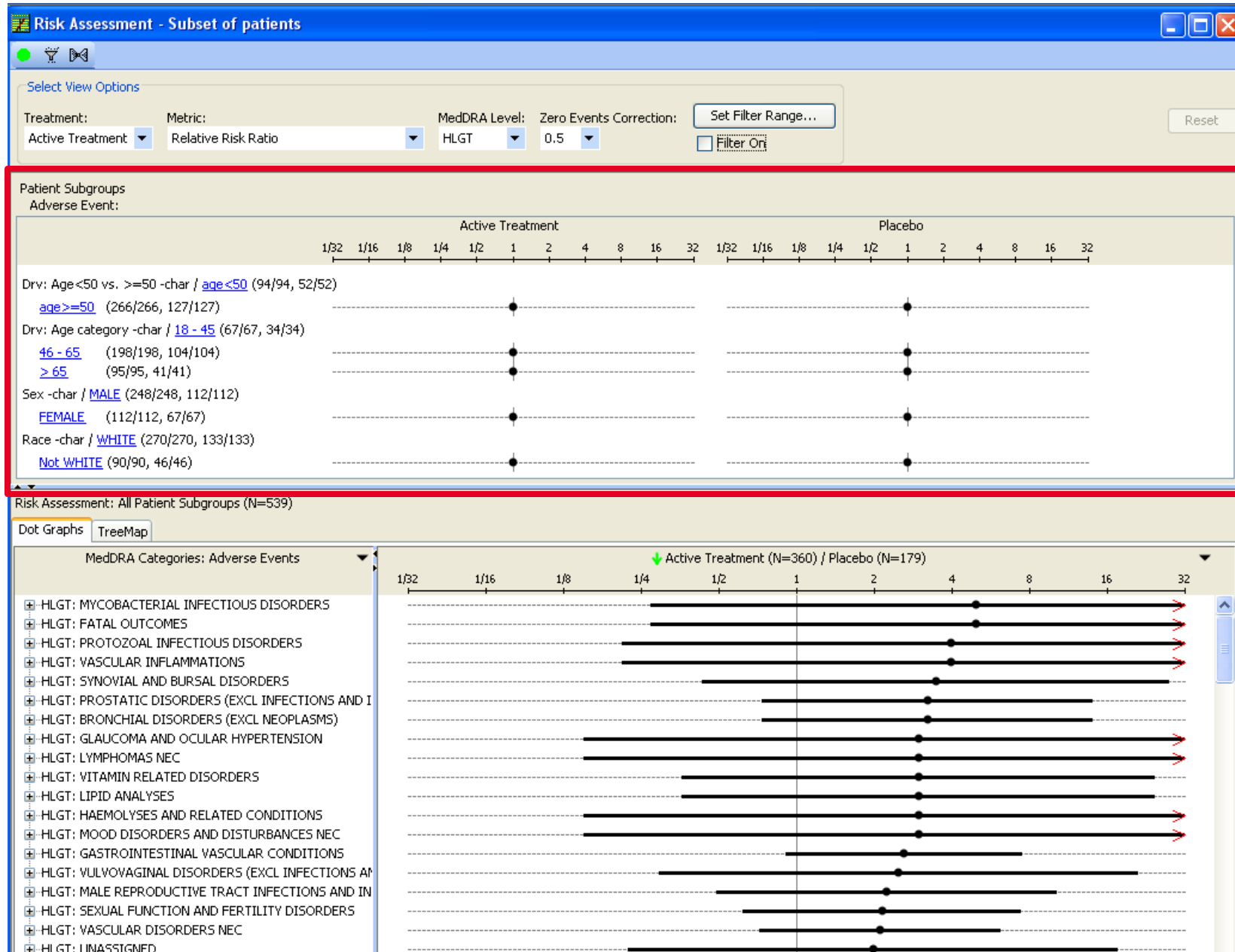
1. Risk Assessments
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6. Summary Bar Chart Mean Chg from Baseline

JReview: Risk Assessments: SOC

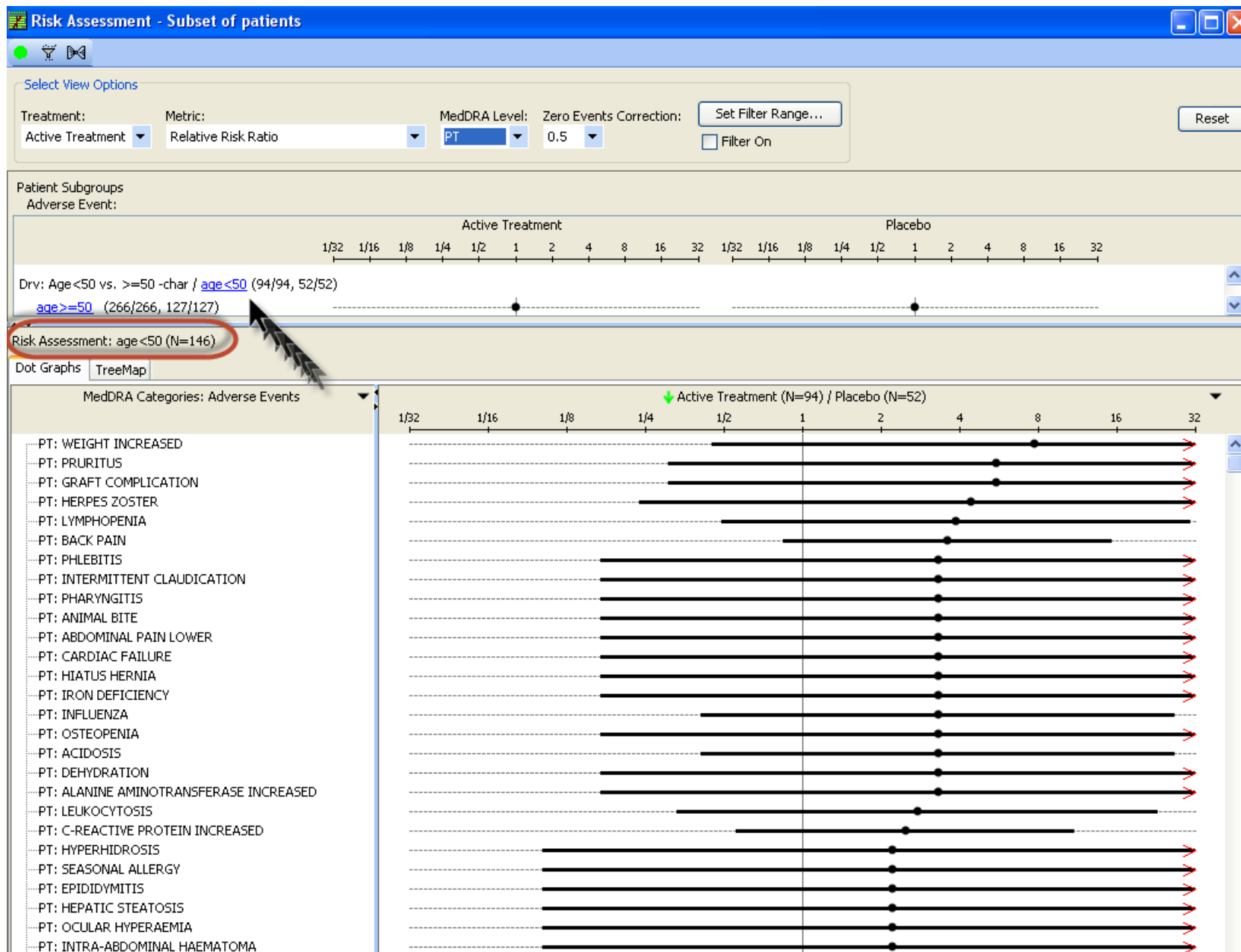
Risk Assessment: All Patient Subgroups (N=539)



JReview: Risk Assessments RR: HLGTT Patient Subsets



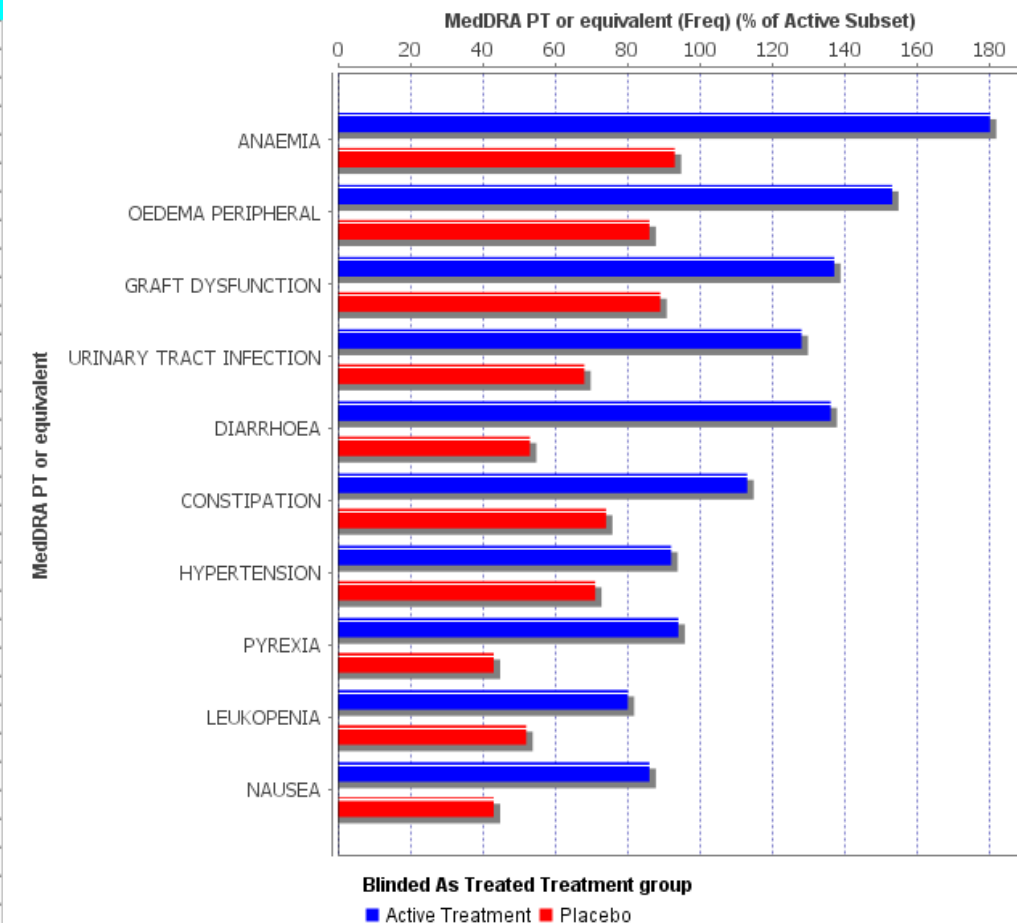
JReview: Risk Assessments RR Profiles: Patient Subsets



JReview: Adverse Event Incident Rates

Cross Tabulations Whole Body and Top N Frequency Bar Charts

MedDRA PT or equivalent	Active Treatment	Placebo	Subjects
ANAEMIA	180 (50.00%)	93 (51.96%)	273 (45.88%)
OEDEMA PERIPHERAL	153 (42.50%)	86 (48.04%)	239 (40.17%)
GRAFT DYSFUNCTION	137 (38.06%)	89 (49.72%)	226 (37.98%)
DIARRHOEA	136 (37.78%)	53 (29.61%)	189 (31.76%)
URINARY TRACT INFECTION	128 (35.56%)	68 (37.99%)	196 (32.94%)
CONSTIPATION	113 (31.39%)	74 (41.34%)	187 (31.43%)
PYREXIA	94 (26.11%)	43 (24.02%)	137 (23.03%)
HYPERTENSION	92 (25.56%)	71 (39.66%)	163 (27.39%)
NAUSEA	86 (23.89%)	43 (24.02%)	129 (21.68%)
HYPERKALAEMIA	83 (23.06%)	36 (20.11%)	119 (20.00%)
LEUKOPENIA	80 (22.22%)	52 (29.05%)	132 (22.18%)
PROCEDURAL PAIN	73 (20.28%)	31 (17.32%)	104 (17.48%)
HYPOKALAEMIA	69 (19.17%)	33 (18.44%)	102 (17.14%)
VOMITING	68 (18.89%)	33 (18.44%)	101 (16.97%)
HAEMATURIA	67 (18.61%)	34 (18.99%)	101 (16.97%)
COUGH	67 (18.61%)	24 (13.41%)	91 (15.29%)
PROTEINURIA	63 (17.50%)	22 (12.29%)	85 (14.29%)
HYPOPHOSPHATAEMIA	63 (17.50%)	20 (11.17%)	83 (13.95%)
HYPOTENSION	62 (17.22%)	21 (11.73%)	83 (13.95%)
HYPERGLYCAEMIA	60 (16.67%)	28 (15.64%)	88 (14.79%)
HYPOCALCAEMIA	60 (16.67%)	18 (10.06%)	78 (13.11%)
ABDOMINAL PAIN	57 (15.83%)	27 (15.08%)	84 (14.12%)
BLOOD CREATININE INCREASED	54 (15.00%)	32 (17.88%)	86 (14.45%)
DYSPNOEA	54 (15.00%)	30 (16.76%)	84 (14.12%)
INSOMNIA	52 (14.44%)	36 (20.11%)	88 (14.79%)
BACK PAIN	51 (14.17%)	26 (14.53%)	77 (12.94%)
CYTOMEGALOVIRUS INFECTION	50 (13.89%)	26 (14.53%)	76 (12.77%)
HEADACHE	49 (13.61%)	34 (18.99%)	83 (13.95%)
INCISION SITE PAIN	47 (13.06%)	35 (19.55%)	82 (13.78%)
NASOPHARYNGITIS	45 (12.50%)	18 (10.06%)	63 (10.59%)
OEDEMA	44 (12.22%)	19 (10.61%)	63 (10.59%)
DYSLIPIDAEMIA	43 (11.94%)	32 (17.88%)	75 (12.61%)
RENAL TUBULAR NECROSIS	41 (11.39%)	32 (17.88%)	73 (12.27%)
ANXIETY	40 (11.11%)	25 (13.97%)	65 (10.92%)
BRONCHITIS	38 (10.56%)	15 (8.38%)	53 (8.91%)
DYSURIA	37 (10.28%)	12 (6.70%)	49 (8.24%)
PAIN IN EXTREMITY	36 (10.00%)	25 (13.97%)	61 (10.25%)
HYPERCHOLESTEROLAEMIA	36 (10.00%)	21 (11.73%)	57 (9.58%)

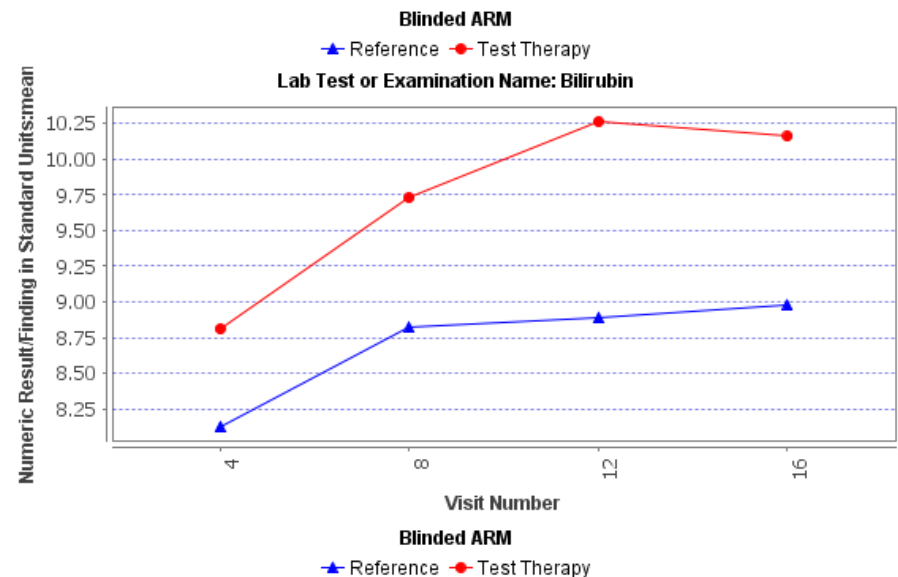
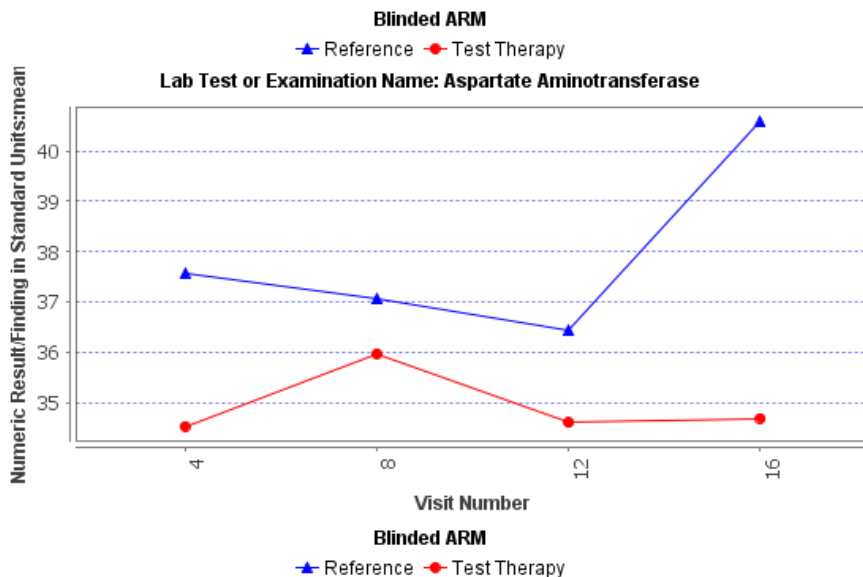
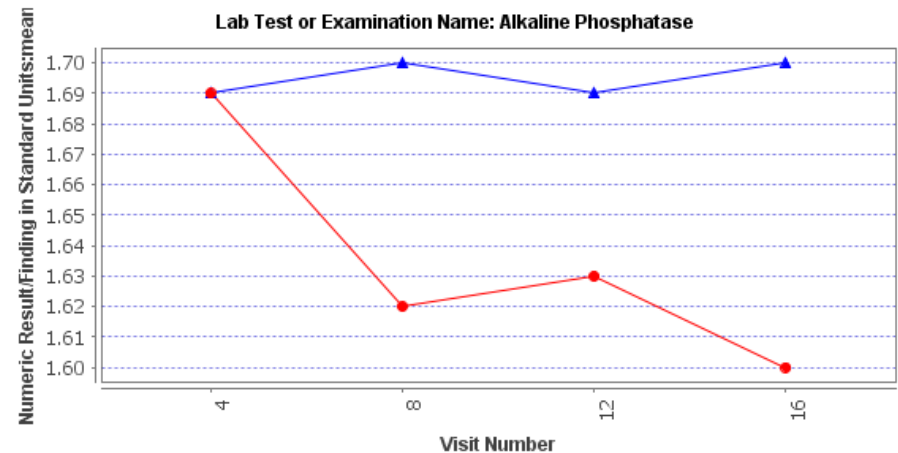
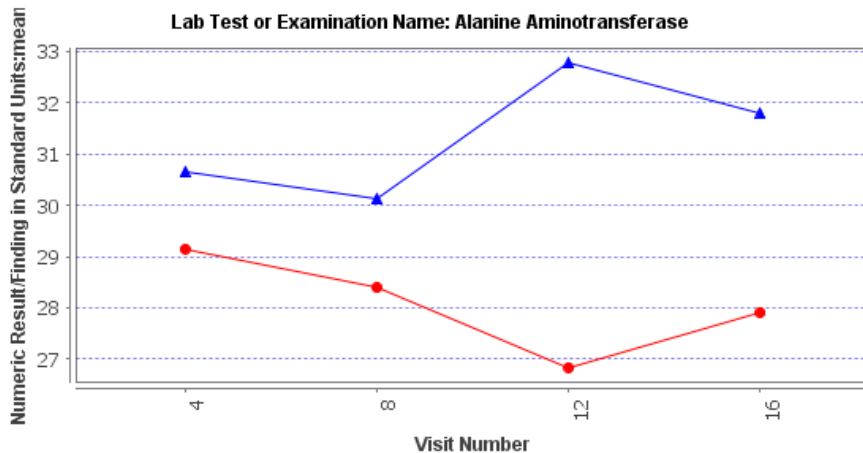


Top 10 MedDRA Preferred Term AE's 2D BarChart Frequency Distribution By Treatment ARM

JReview: Line Chart Summaries

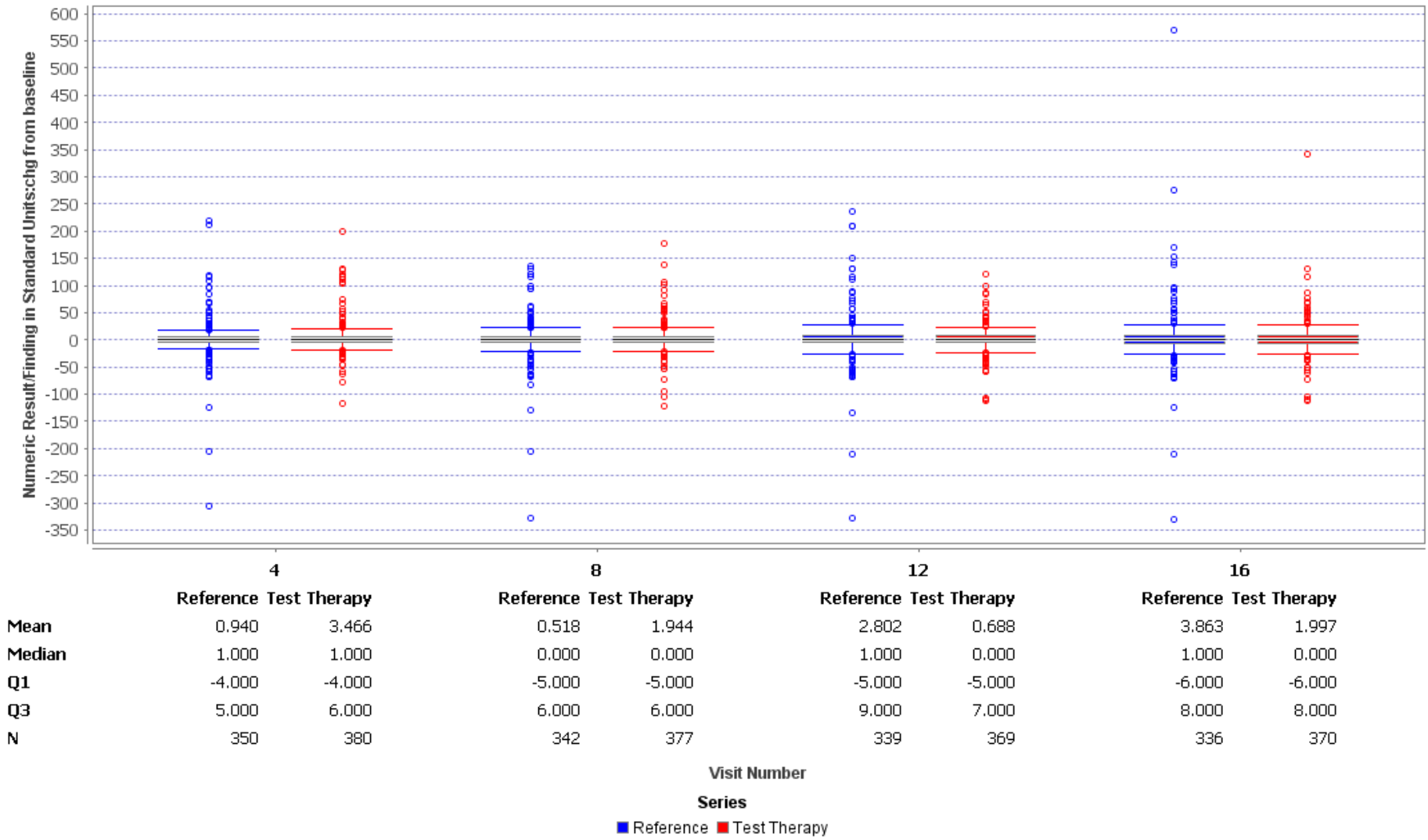
Laboratory Examples: Liver f lab tests

Power of Page By variables



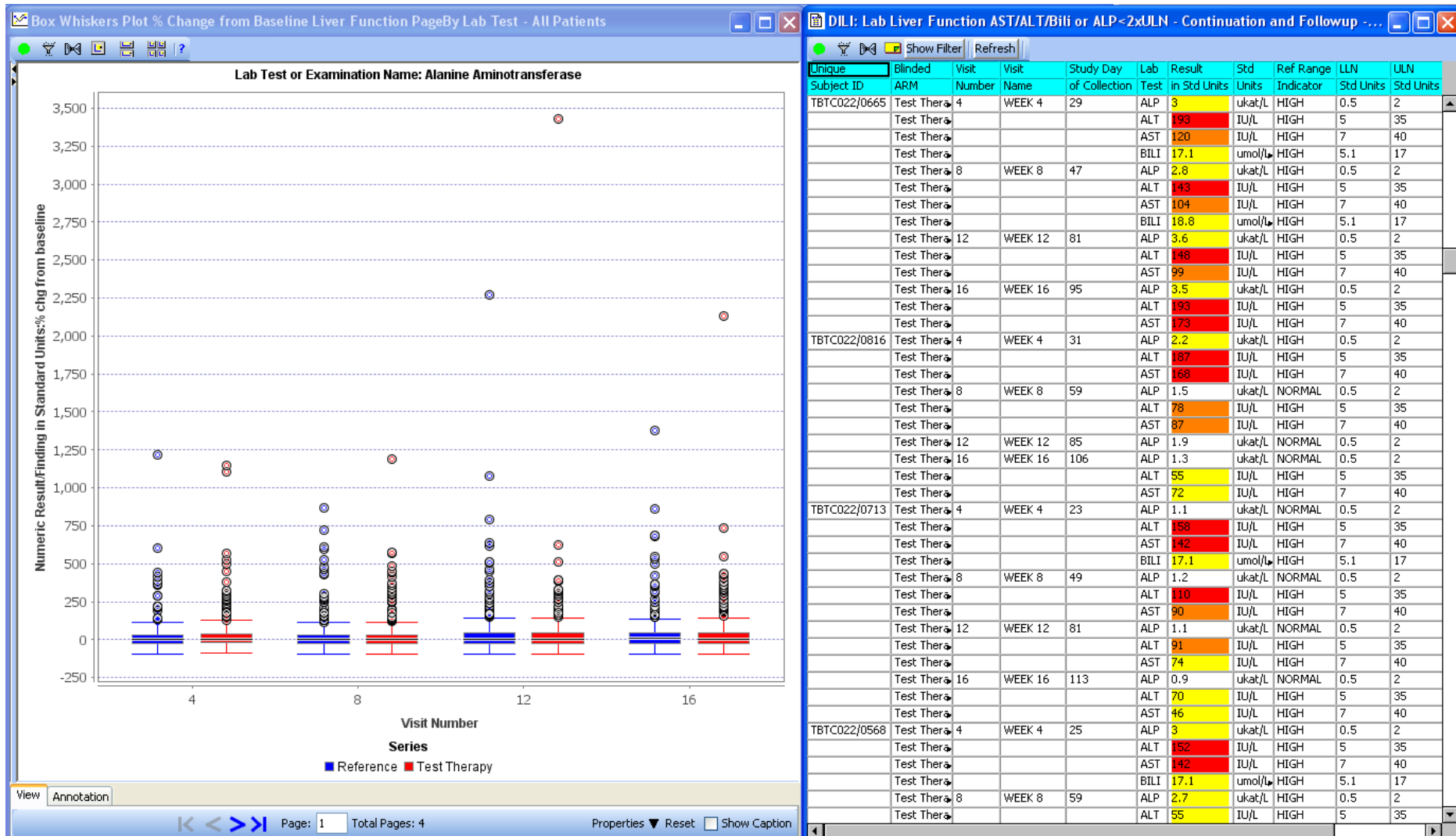
JReview: Chg from Baseline Box Whiskers

Lab Test or Examination Name: Alanine Aminotransferase



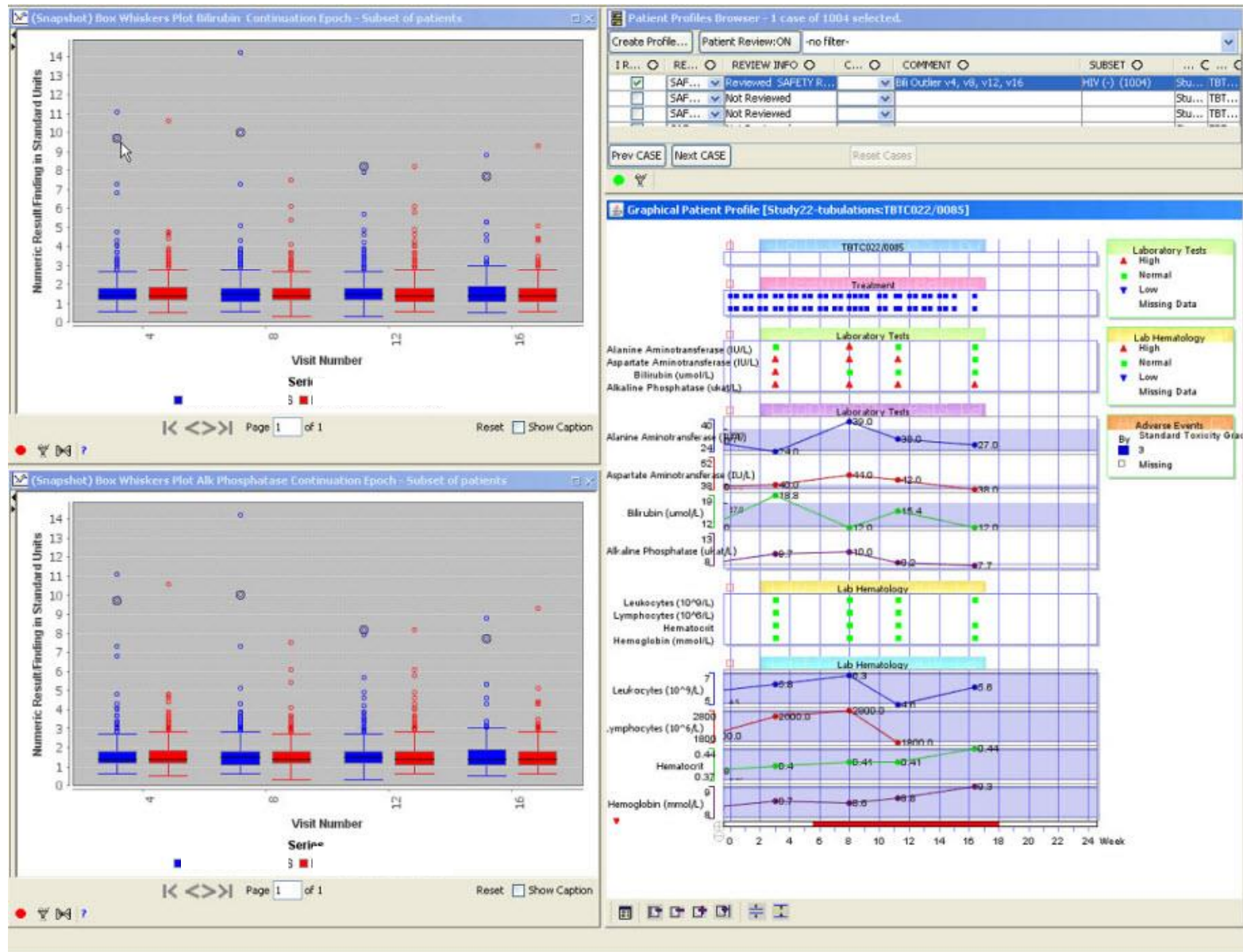
JReview: Chg from Baseline Box Whiskers

Identifying the outliers and reviewing their data



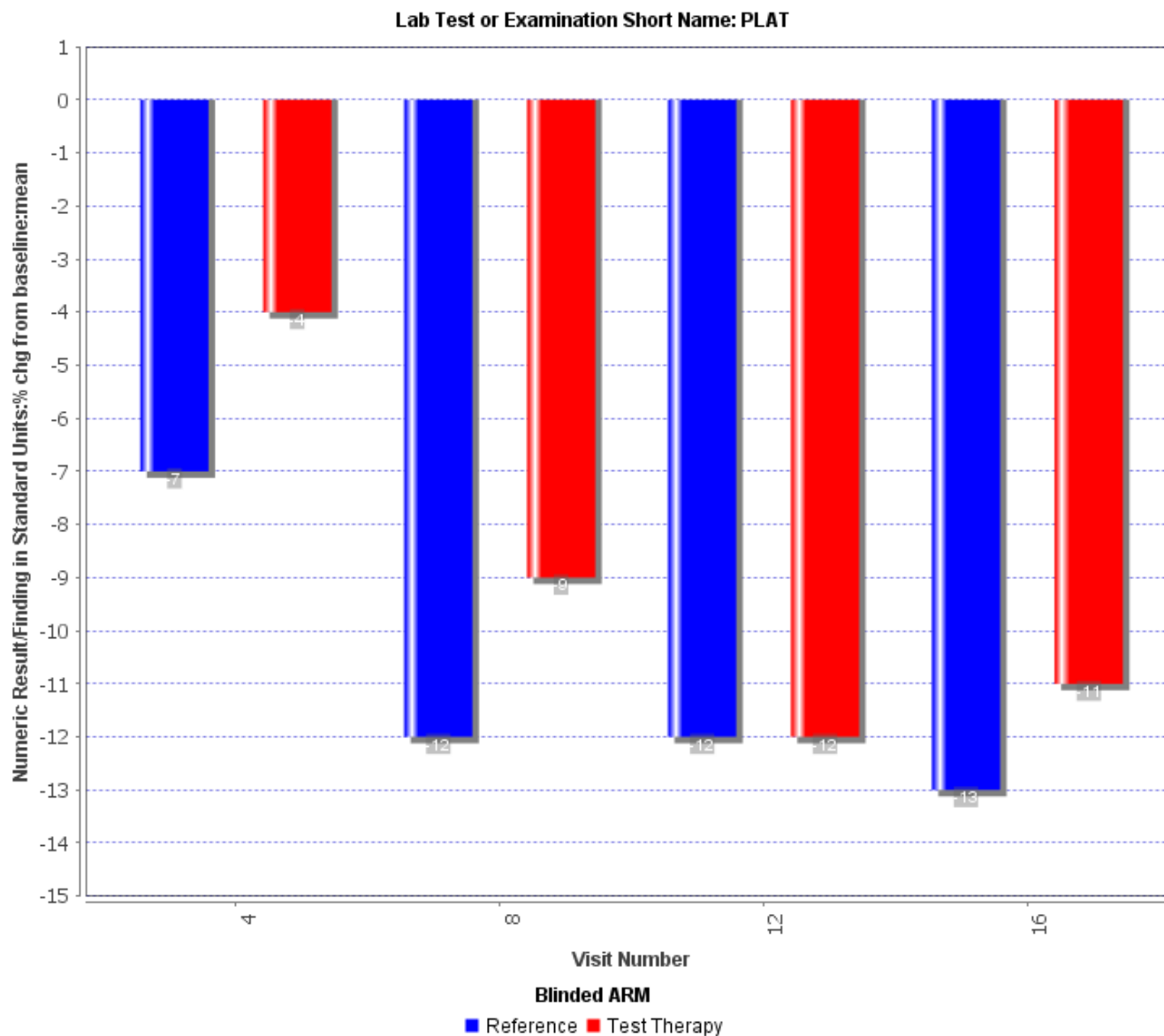
JReview: Chg from Baseline Box Whiskers

Identifying the outliers and reviewing their data



JReview: %Chg from Baseline Bar Charts

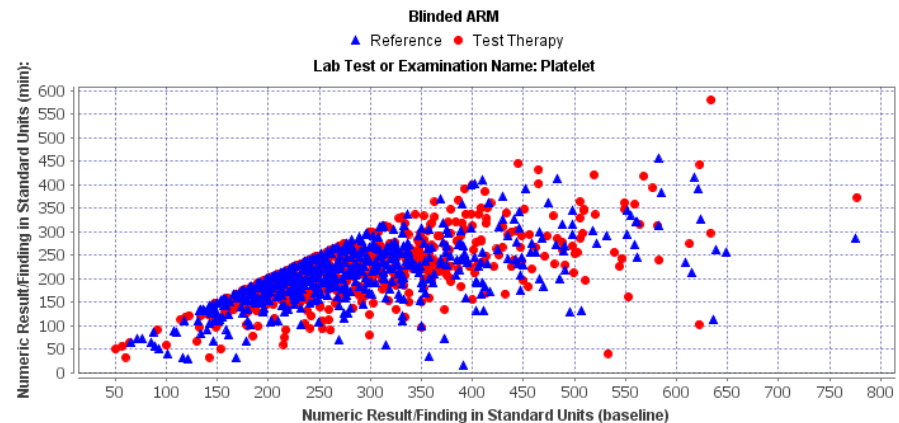
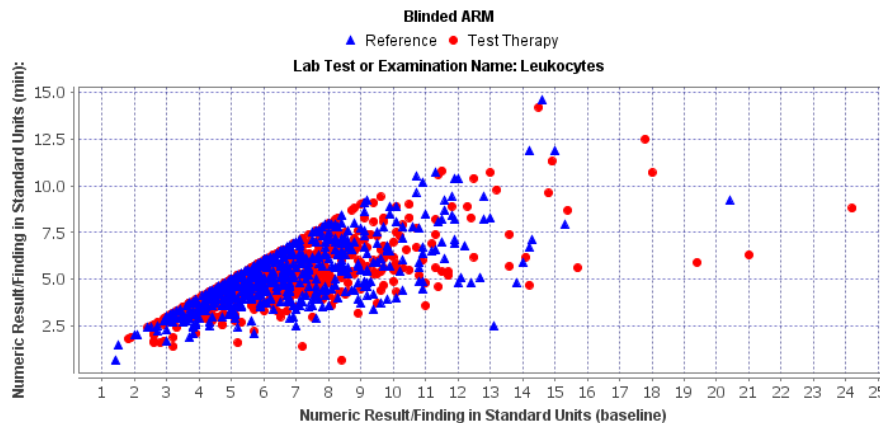
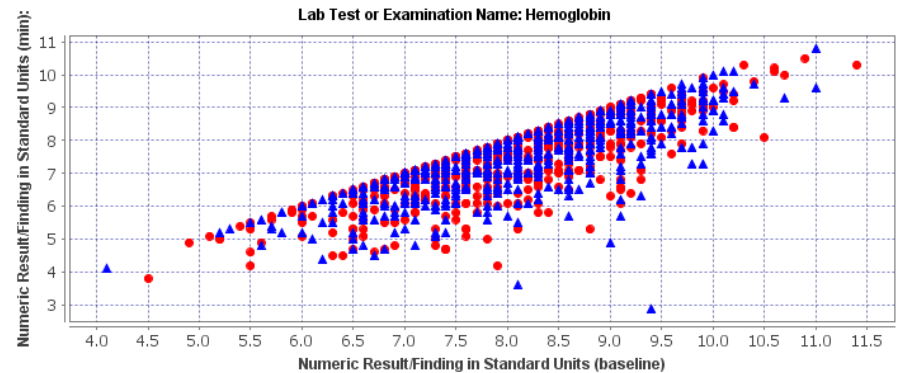
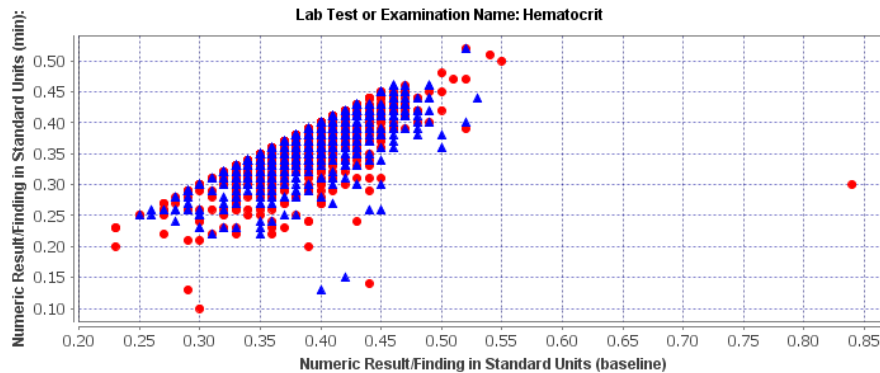
Hematology: Platelets lab test % Chg from Baseline



JReview: Shifts from Baseline Laboratory Analysis

C. Shifts from Baseline – Laboratory Analysis

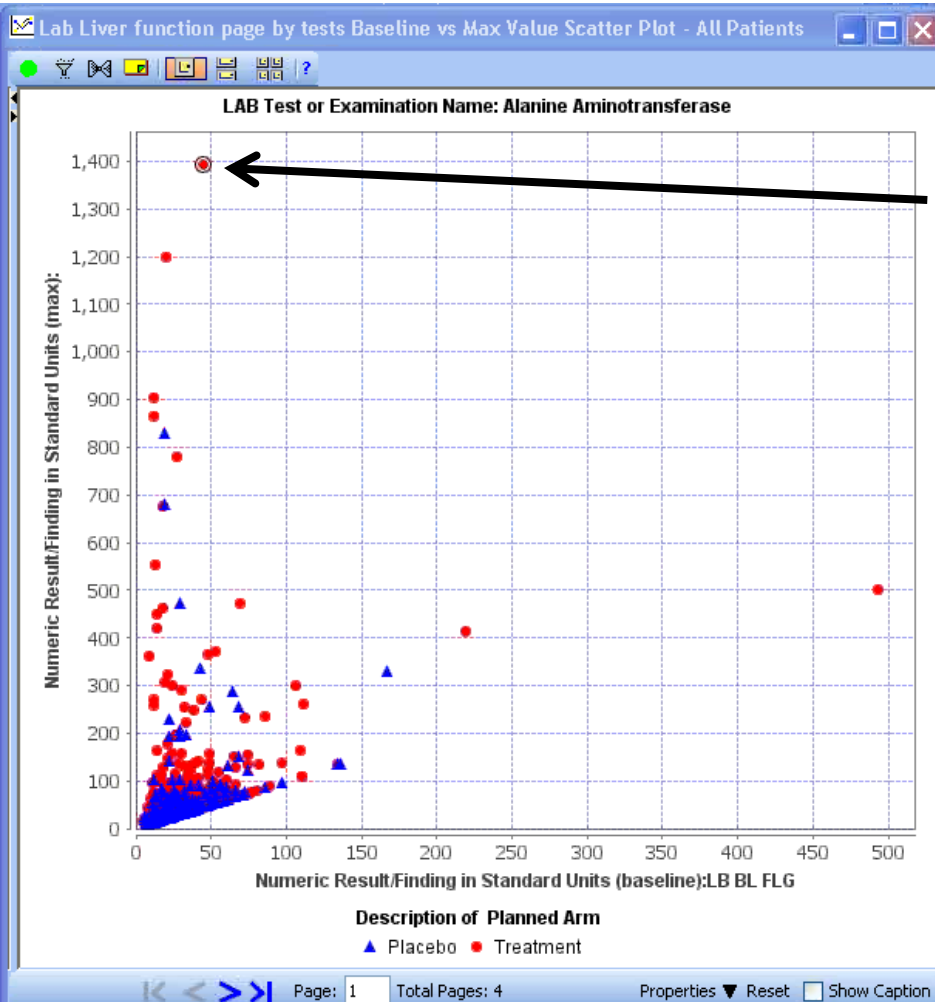
1. Identify patients with abnormal lab results and shift from Baseline
 - a) Scatter Plot Baseline vs Max, Baseline vs Min for example
 - b) Power of PageBy Variable



JReview:Shifts from Baseline Laboratory Analysis

C. Shifts from Baseline – Laboratory Analysis

1. Identify patients with abnormal lab results and shift from Baseline
 - a) Scatter Plot Baseline vs Max, Baseline vs Min for example
 - b) Report Listings: Highlighting abnormal results

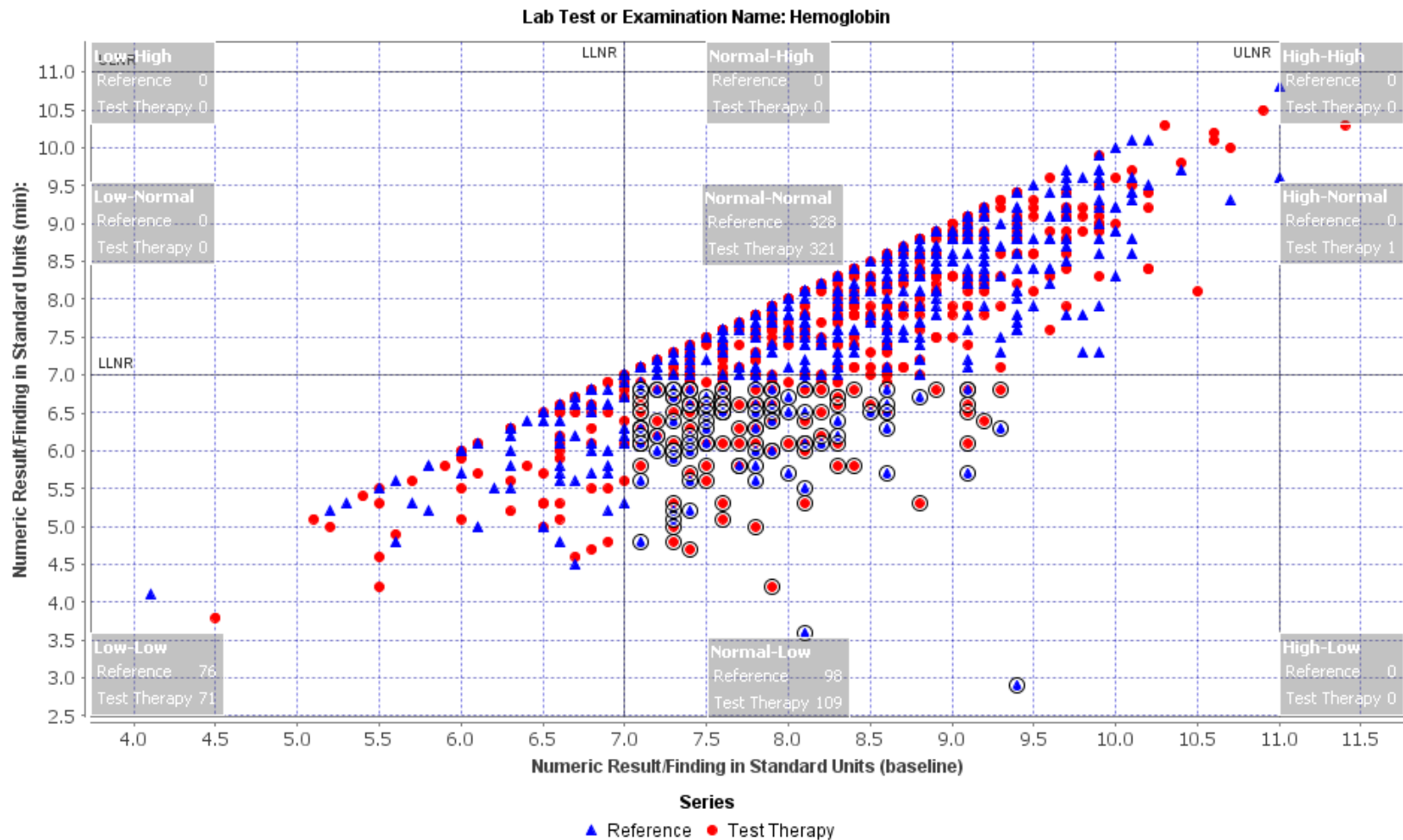


Lab Listing Liver function highlight abnormal results lows/highs 1x, 2x, 3x - All Patie...

Unique	Study	Visit	Visit	LAB	Result	Ref Range	Ref Range	Ref Range	
Subject ID	Day	Number	Name	Test	in Std Units	Indicator	LLN-Std Units	ULN-Std Units	2xU
200010002	-7	0	SCREENING/BASELINE	ALP	102		40	129	258
				ALT	45		0	45	90
				AST	36		0	41	82
				BILI	.		.	.	.
	15	1.02	CYCLE 1, DAY 15		0.8		0.1	1.2	2.4
				ALP	91		40	129	258
				ALT	36		0	45	90
				AST	37		0	41	82
	29	2.01	CYCLE 2, DAY 1		1.2		0.1	1.2	2.4
				ALP	95		40	129	258
				ALT	45	HIGH	0	45	90
				AST	41	HIGH	0	41	82
200010003	-7	0	SCREENING/BASELINE		1.1		0.1	1.2	2.4
				ALP	102	HIGH	40	129	258
				ALT	1393	HIGH	0	45	90
				AST	1261	HIGH	0	41	82
	15	1.02	CYCLE 1, DAY 15		9.2	HIGH	0.1	1.2	2.4
				ALP	118	HIGH	35	104	208
				ALT	24		0	45	90
				AST	31		0	41	82
	29	2.01	CYCLE 2, DAY 1		0.6		0.1	1.2	2.4
				ALP	136	HIGH	35	104	208
				ALT	33		0	45	90
				AST	41		0	41	82

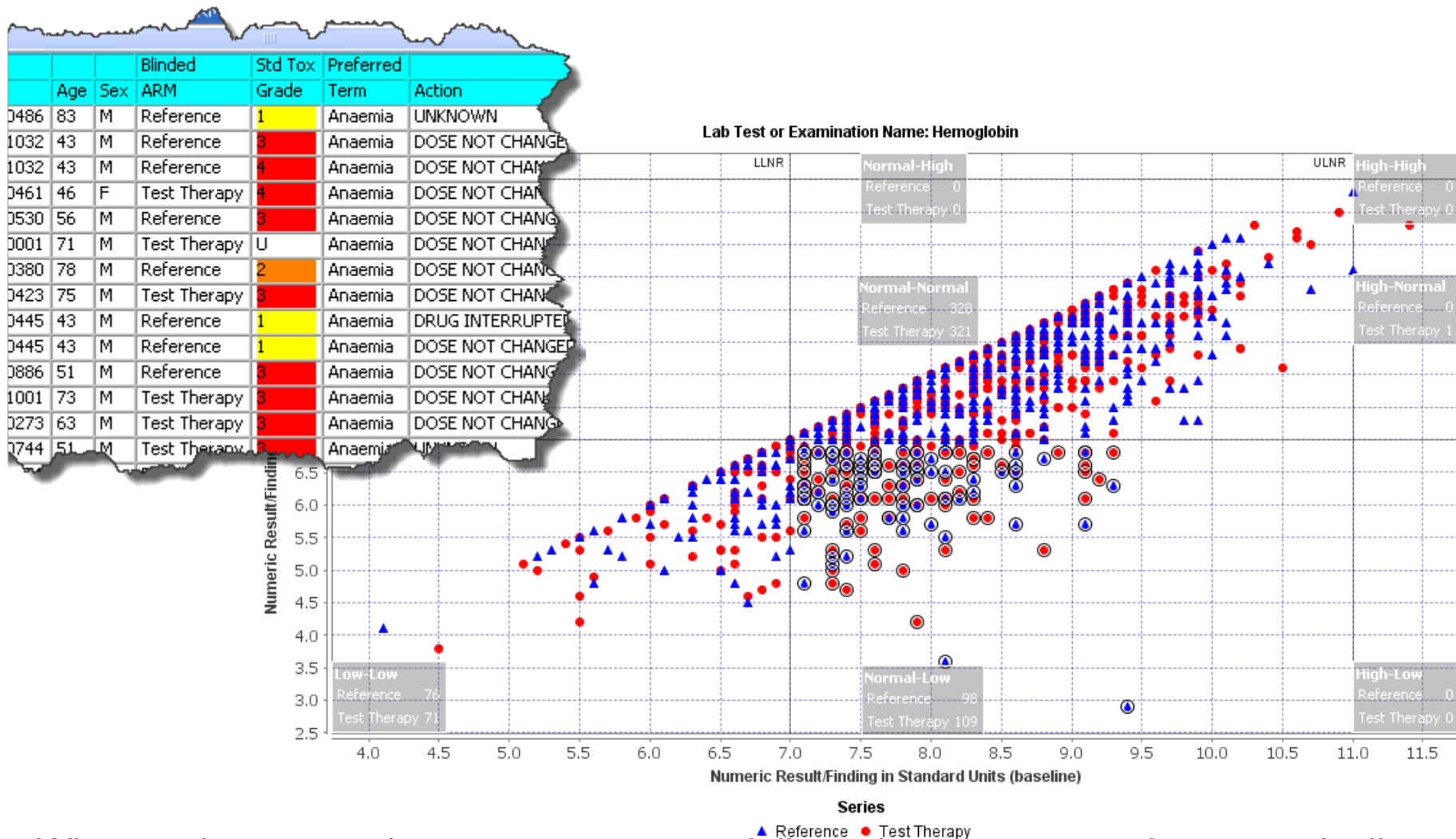
JReview: Hemoglobin Shift from Baseline

Identify patients with abnormal lab results and shift from Baseline



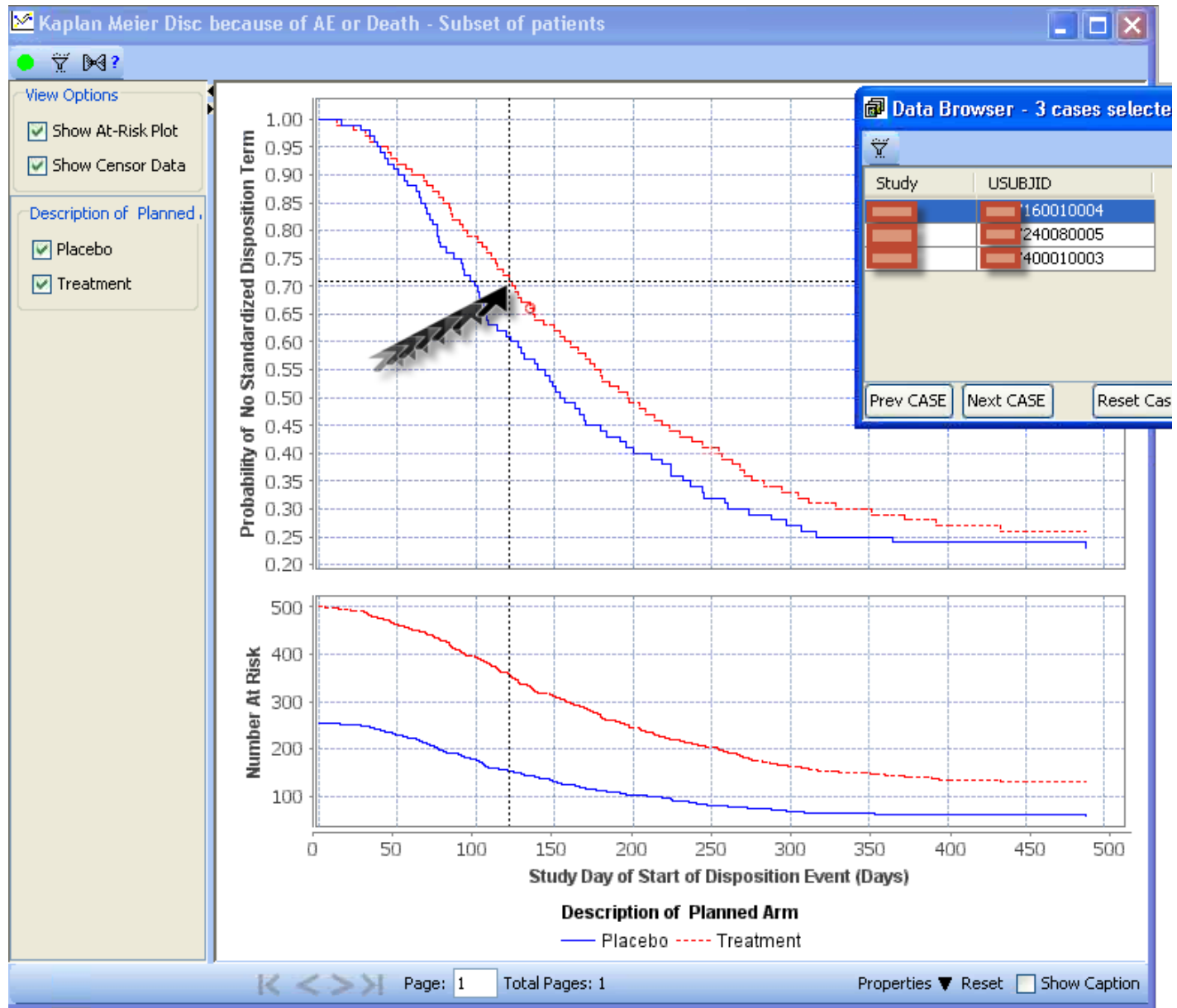
JReview: Hemoglobin Shift from Baseline

Identify patients with abnormal lab results and shift from Baseline



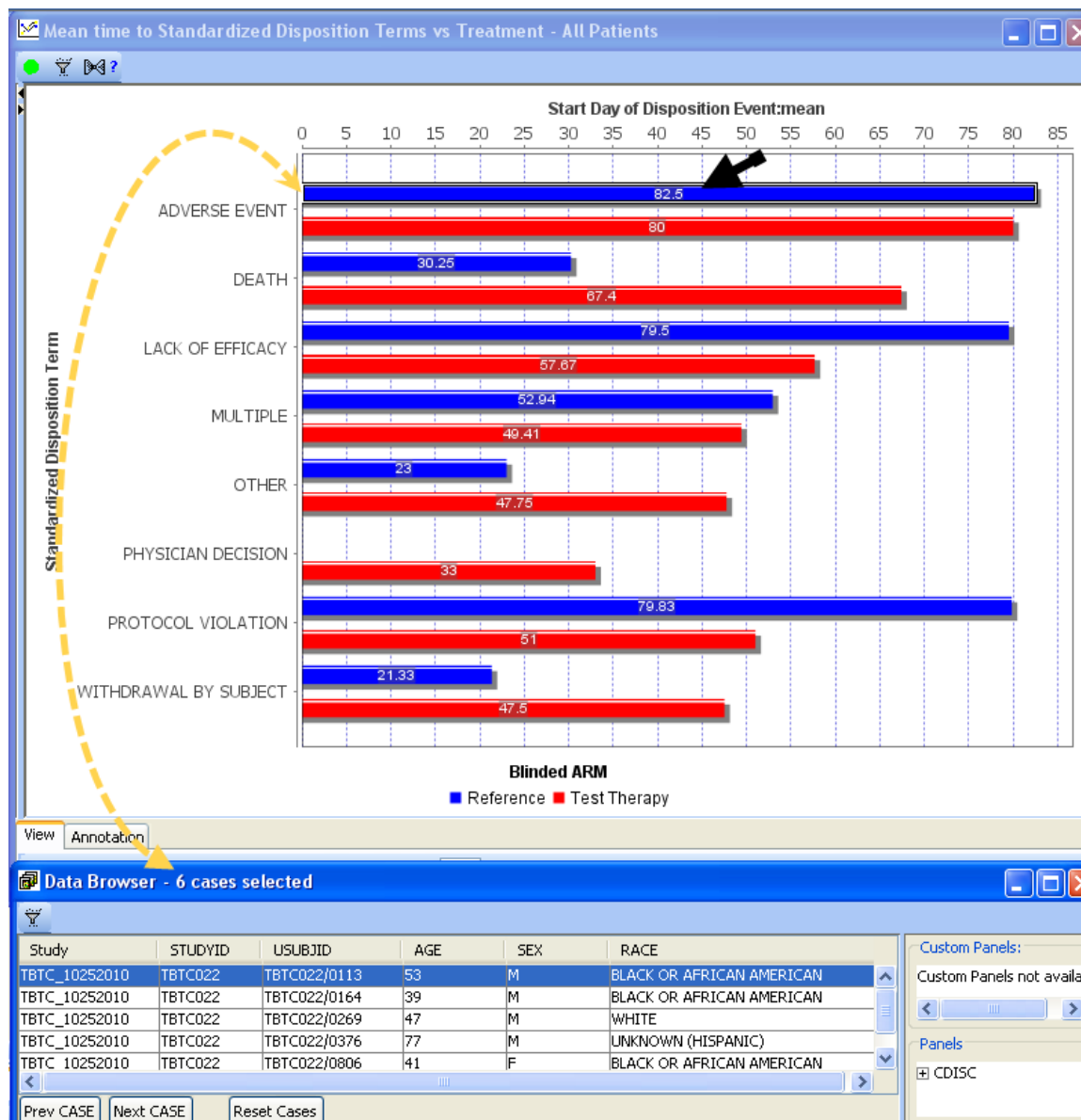
When patients experience events – especially serious event – reviewers typically want to note how patients were triaged. Dose modified? Re-challenged?

JReview: Kaplan Meier Rate/Time to death analysis



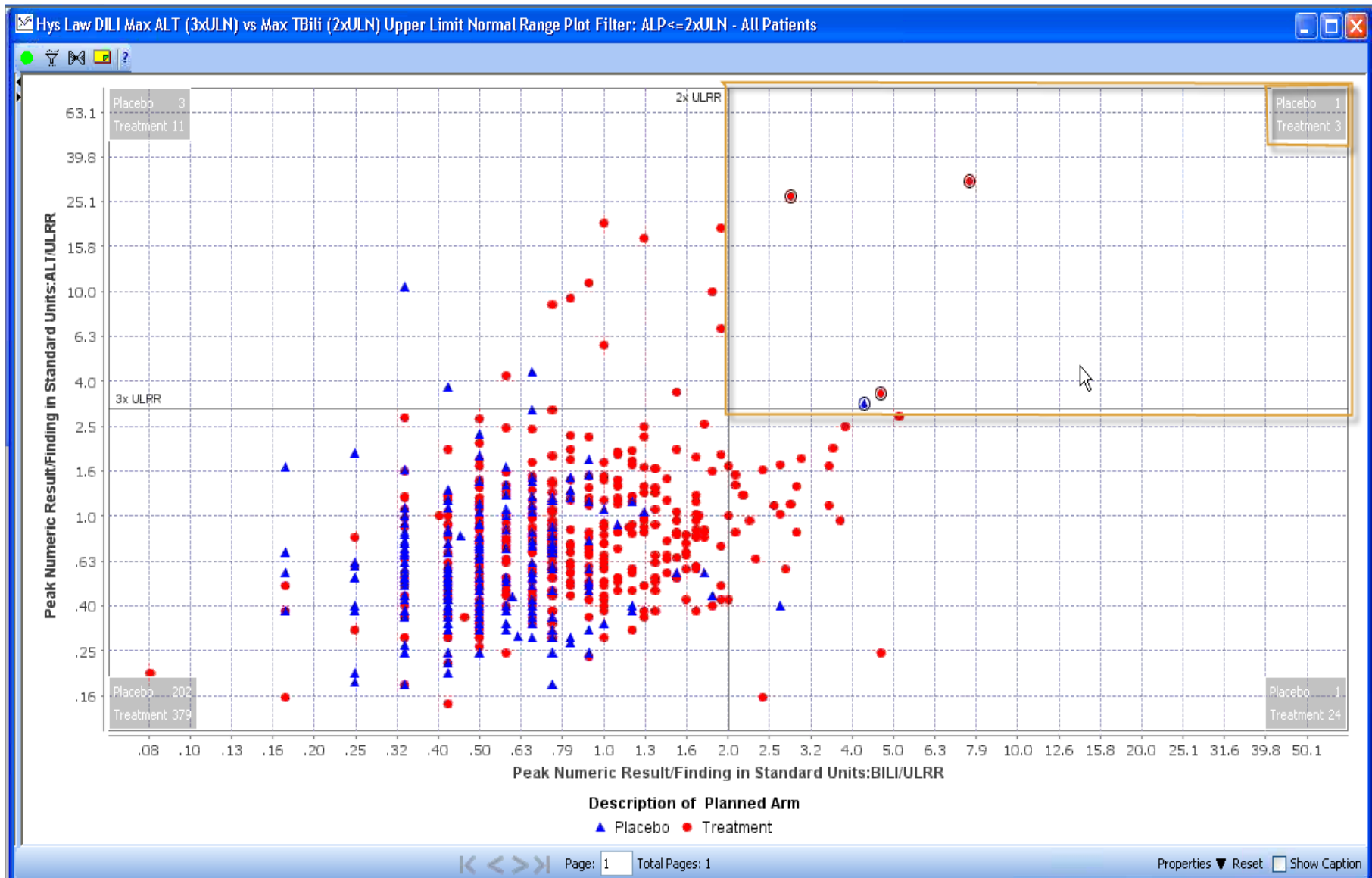
JReview: Mean Time to Disposition Events

Interactivity between objects answers many questions instantaneously



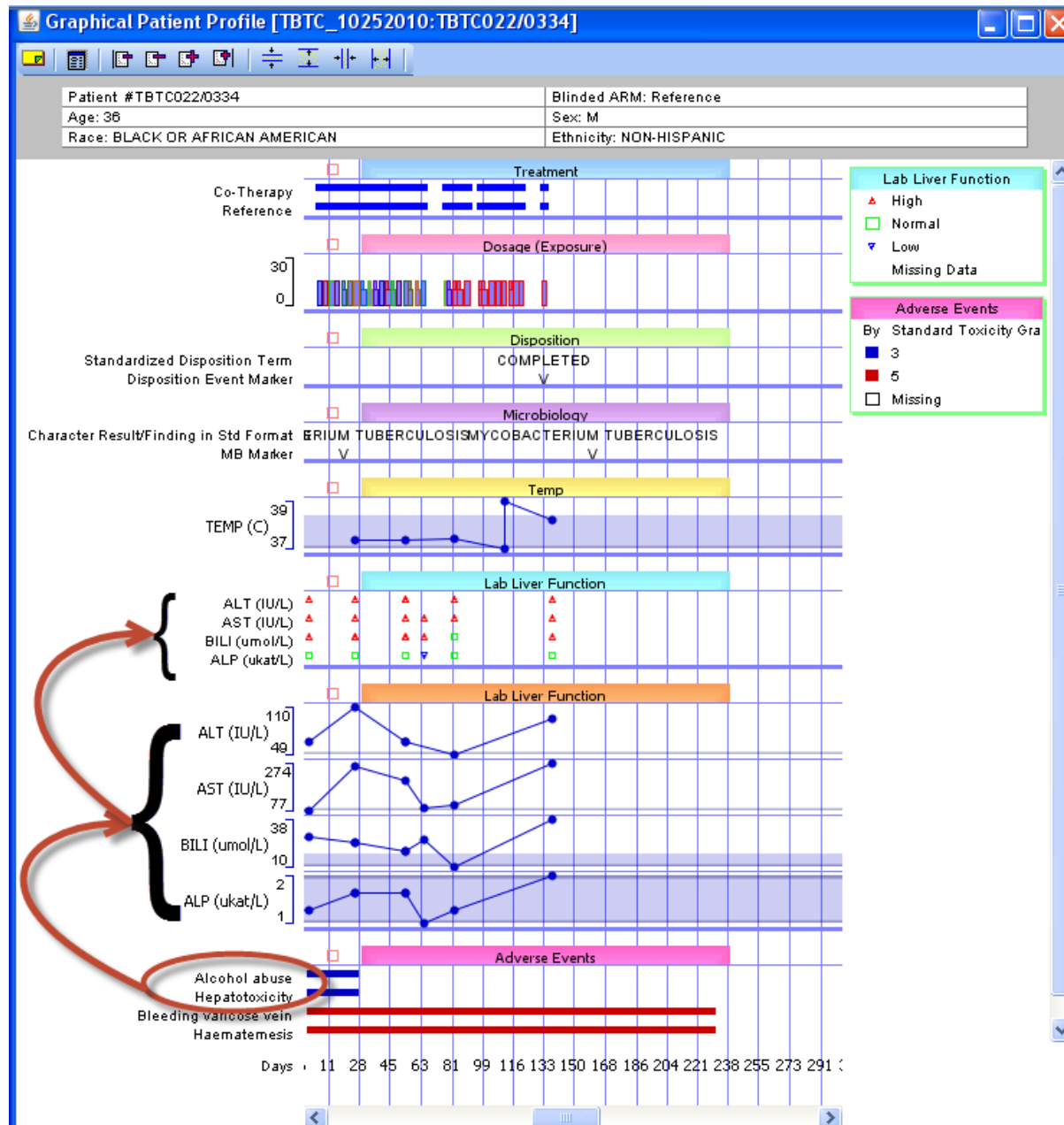
JReview:Special Assessments Hepatotoxicity

Hy's Law example – explore why patients meet the criteria

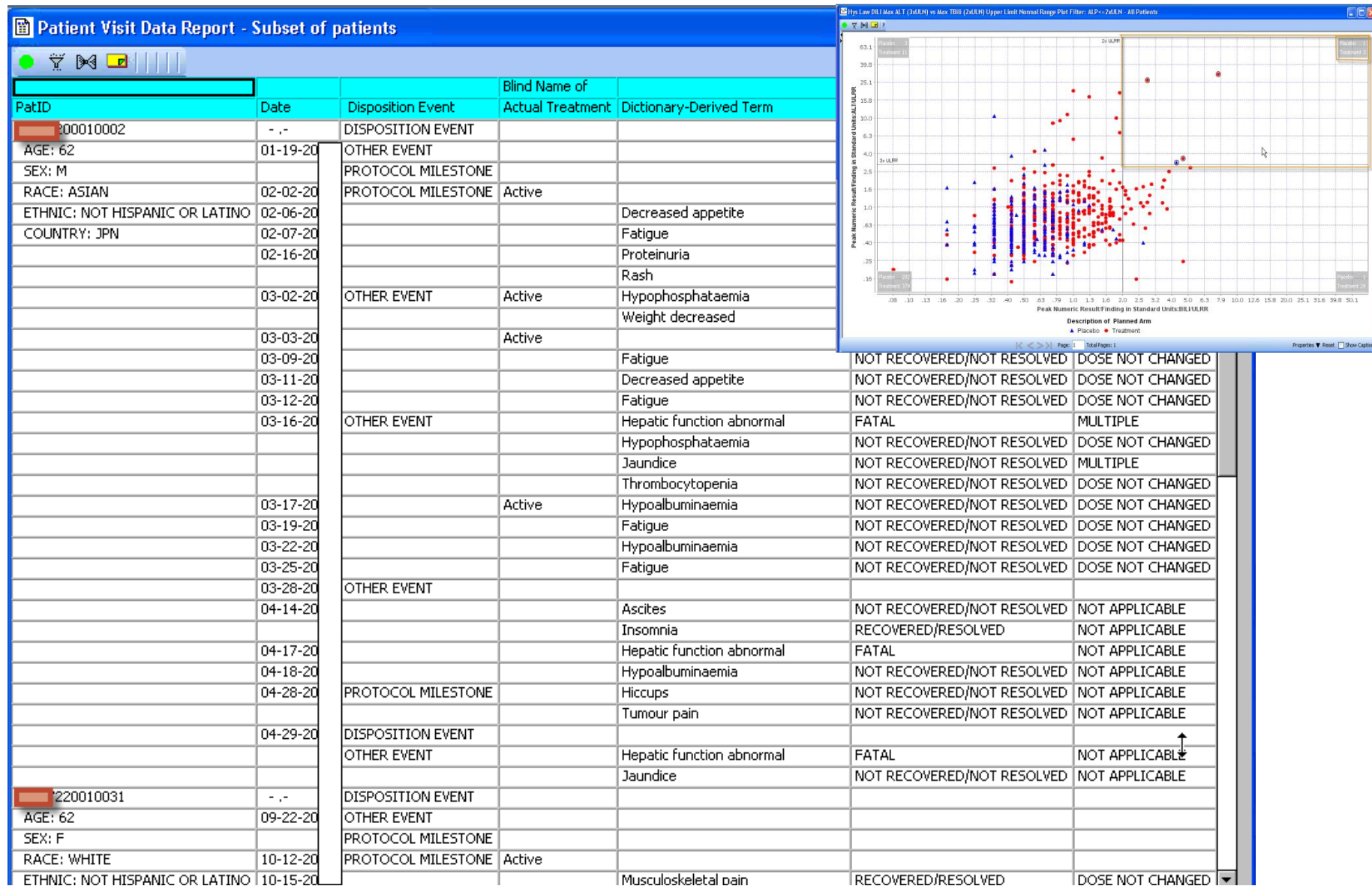


JReview: Graphical Patient Profiles

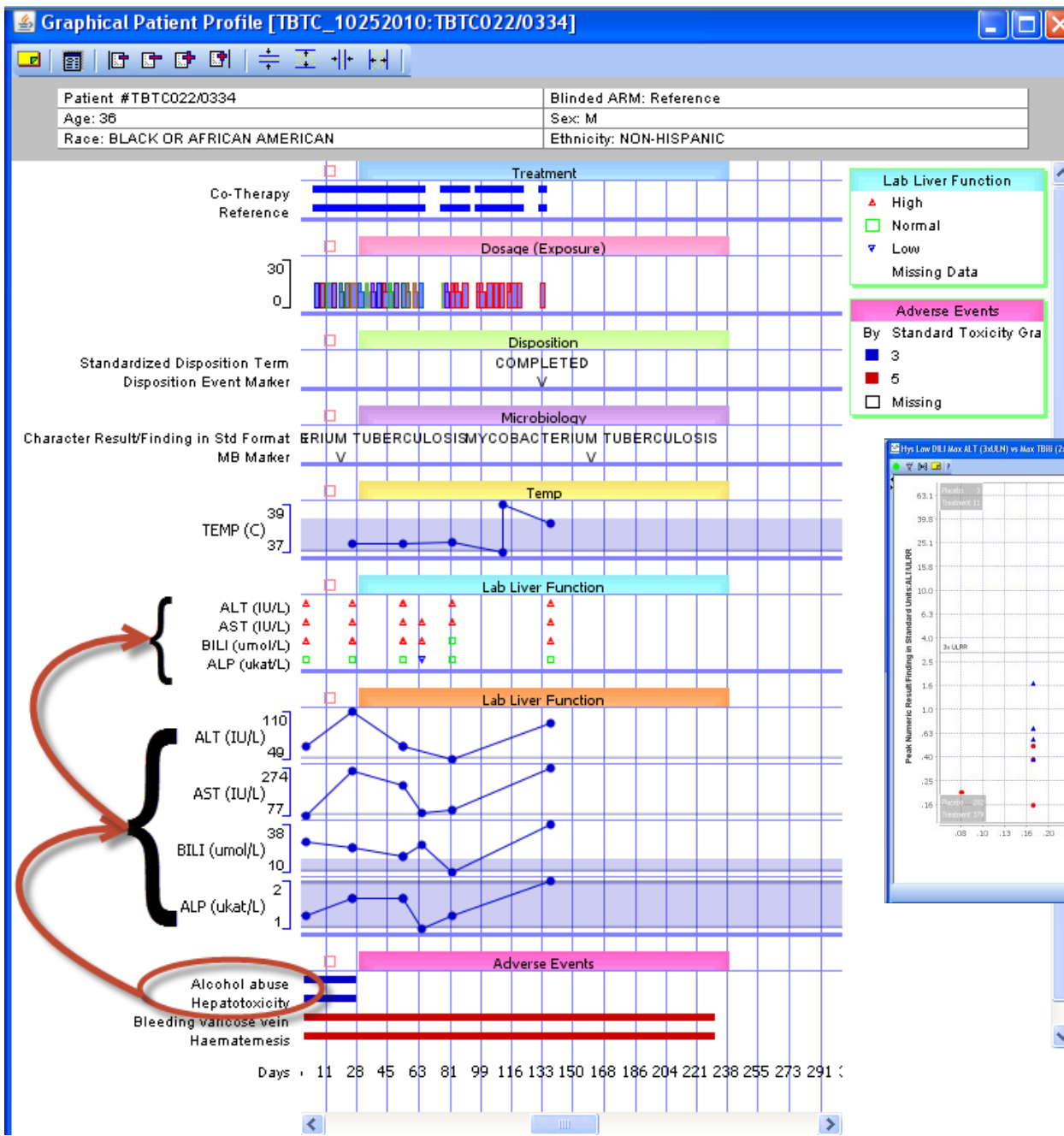
Getting to know patients: Hy's Law candidates - explained



Using Patient Visit Data Report and Simple Listings



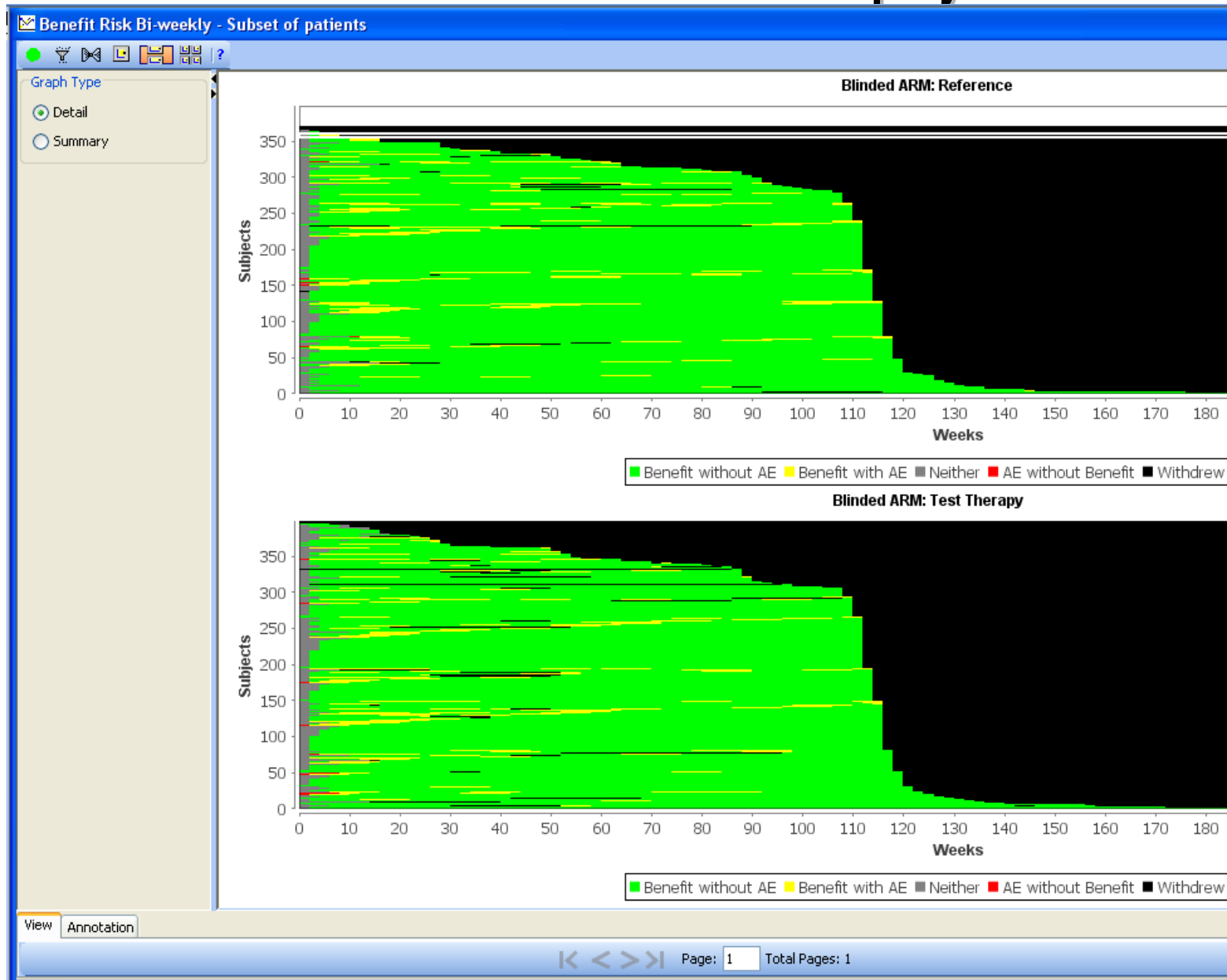
JReview:Special Assessments Hepatotoxicity



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

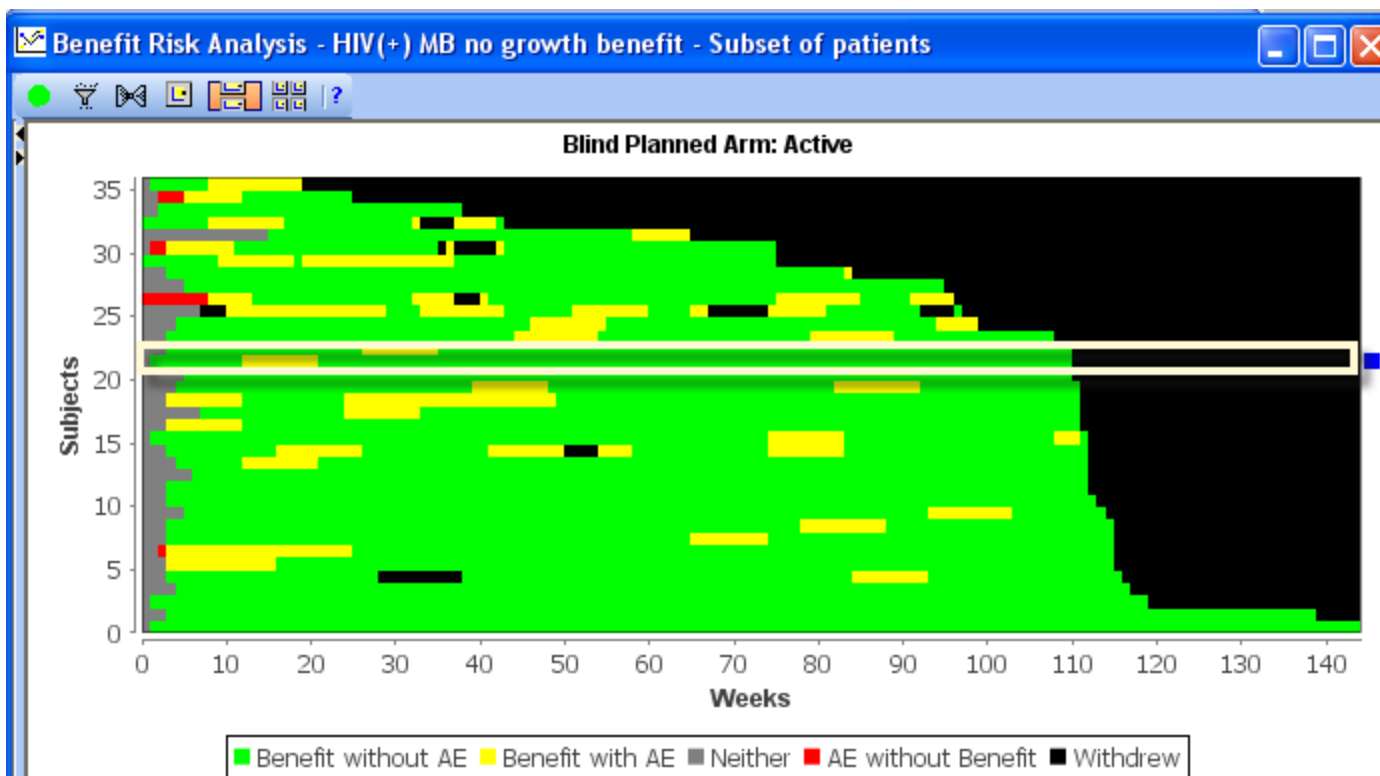


JReview : Benefit Risk Assessment Interactive Patient Level Display



[illegible]

JReview : Benefit Risk Assessment Interactive Patient Level Display



AE Patient Listing highlighting Toxicity Grade - Subset of patients / Output Filter applied

	Unique	AE Start	Dictionary	Standard	Action Taken with	Serious	Outcome	Results in
Arm	Subject ID	Study Day	-Derived Term	Tox Grade	Study Treatment	Event	of Adverse Event	Death
Active	14	84	Alcohol abuse	4	DRUG INTERRUPTED		UNKNOWN	
Active		84	Hepatotoxicity	4	DRUG INTERRUPTED		UNKNOWN	
Active	157	519	Night sweats	1	UNKNOWN		UNKNOWN	
Active		519	Pneumonia	1	UNKNOWN		UNKNOWN	

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