Improved Data Quality and Site Collaboration Through Blinded Data Analytics

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Disclosures

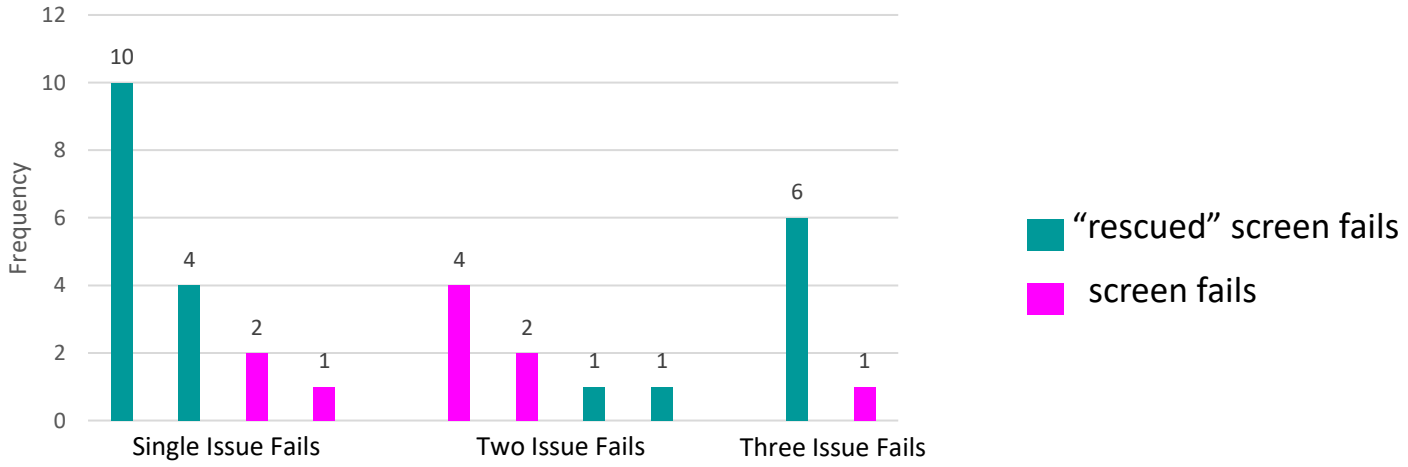
- Employee of and Stockholder in Neurocrine Biosciences Inc.
- Stockholder in JNJ, Pfizer, BMS, Gilead, GSK

Intent of Blinded Data Analytics Is to Ensure Protocol Is Executed as Intended

- Prioritize relationship with sites through open communication
- Blinded data analytics (BDA) is an additional mechanism for site feedback by identifying potential problems with protocol interpretation or assessment administration
- Important to combine BDA with source document review, tailored to individual study
- Early intervention allows for correction to reduce long-term impact of misunderstanding, misrepresentation and misinformation

Site collaboration begins at eligibility review

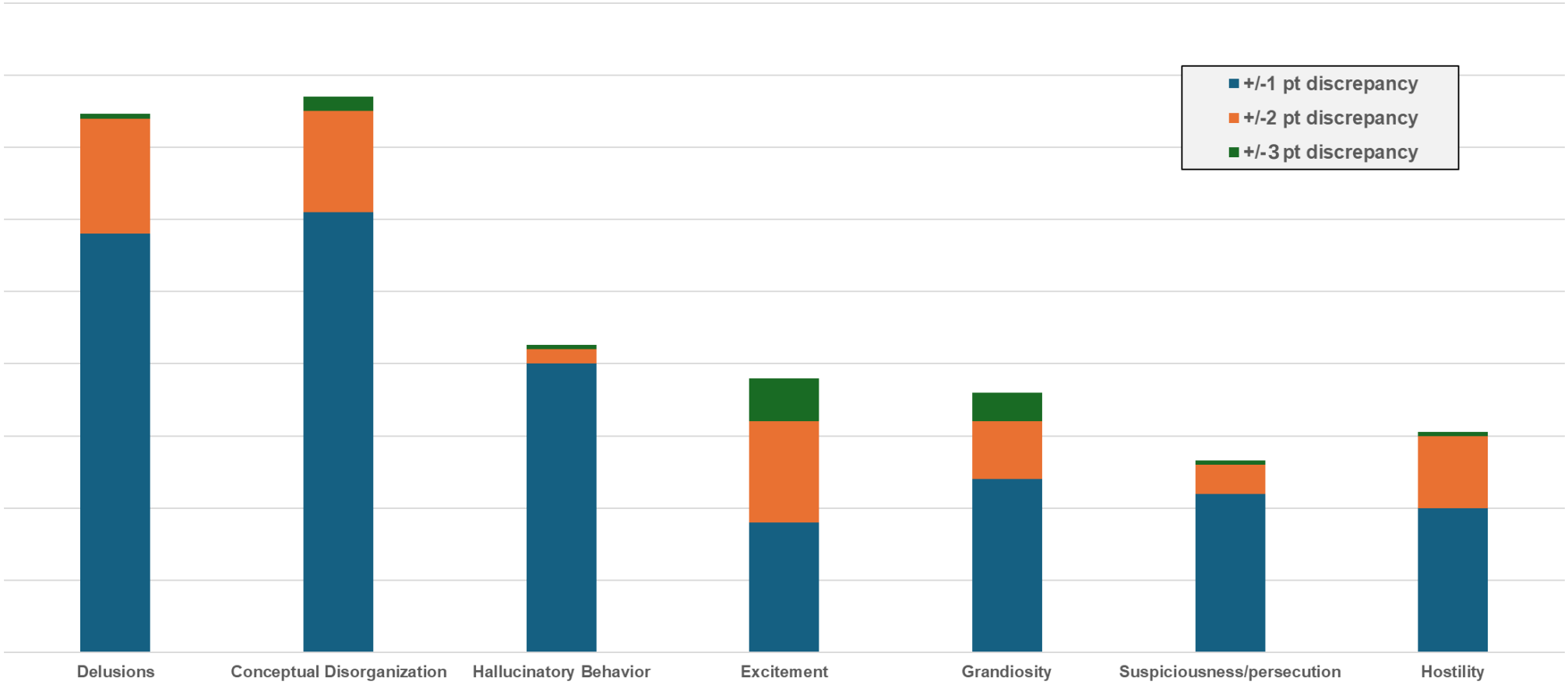
- Centralized review of MINI recordings at screening and subsequent collaboration with the sites clarified potential screen failures.
- 22 subjects ultimately deemed eligible for participation who would have screen failed without further discussion



Monthly Blinded Data Analytics During Study Conduct Inform Areas for Potential Intervention

- Identify potential problem areas for additional training through review of interrater reliability between site-based raters (primary raters for the program) and centralized raters (quality monitoring only)
  - Individual PANSS items scoring discrepancies
  - Significant total score differences
  - Total PANSS score discrepancies by “responder” categories
  - Rater responsiveness to interactions

Individual Item Scoring Discrepancies Can Inform Training Needs



Representative Data

Site Level Analytics Further Hone Potential Interventions

- Rater performance and operational metrics comparisons between individual site and rest of study
- Underscore desire for consistency of execution and evaluation across sites

Category Distribution for Site vs. (Central)

	Responders	Minimal Responders	Deterioration	Rho Correlation
Overall Study	**33.3% (33.3%)**	**33.3% (33.3%)**	**33.3% (33.3%)**	**0.850, p<0.001**
Site 1	65.4% (27.7%)	17.1% (54.4%)	17.5% (17.9%)	0.923, p<0.001
Site 2	20.9% (31.9%)	76.3% (65.3%)	2.8% (2.8%)	0.776, p=0.002
Site 3	13.1% (13.1%)	50% (34.7%)	36.9% (52.2%)	0.882, p=0.007

Representative Data

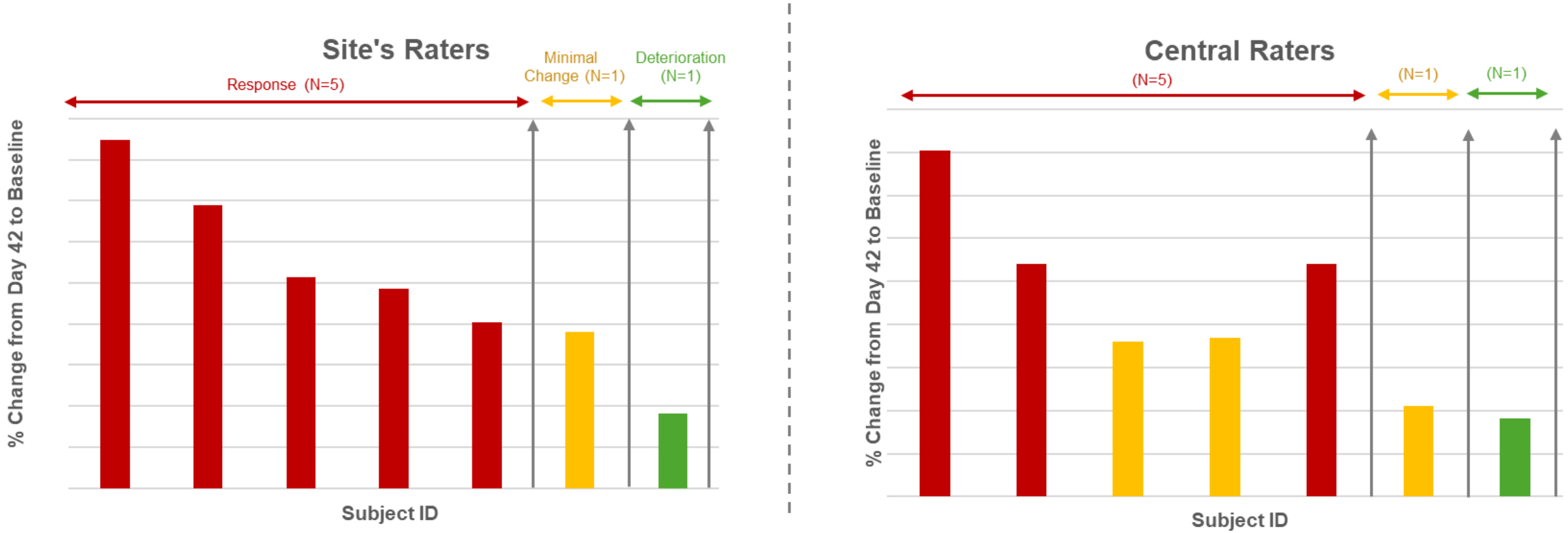
Analysis of Individual Categorical Discrepancies Can Identify Rater Issues

Case ID	Point Difference	Site Rater PANSS Improvement	Central Rater PANSS Improvement
1	28	-42.98%	-8.05%
2	15	-30.67%	-9.89%
3	13	-19.00%	0.00%
4	11	-8.90%	-23.60%
5	9	12.17%	-8.05%
6	7	-20.43%	-14.89%

≥ 20% improvement
≥ 0% improvement and < 20%
< 0% improvement/worsening

Representative Data

Interrater Reliability Shared on a subject, site and study-wide level



Rho = .881, p = .004

- ≥ 20% improvement
- ≥ 0% improvement and < 20%
- < 0% improvement/worsening

Representative Data

Additional Site-Specific Metrics complement Efficacy Measure Correlations

Category Discrepancy (Completers)	Responder (Central)	Minimal Responder (Central)	Non-Responder (Central)	N Discrepancies / N Total Cases (%)
Site (N=16)	37.5% (31.2%)	43.7% (56.3%)	18.8% (12.5%)	6/37 (16.2%)
Study Wide	34.9% (32%)	45.3% (47.1%)	19.8% (20.9%)	37/172 (21.5%)

Blinded Analytics	Underperforming	Performing As Expected	Study Median
# Category Discrepancies	X (16.2% vs 6.7% study avg)		2 (5.4%)
Escalated Raters	X (3 vs 1.33/site study avg)		1
Eligibility Issues		X (7.4% vs 25.2% study avg)	23.3
Threshold PANSS	X (14% vs 12% studywide)		8%
Early Terminations		X (10% vs 12.3% study avg)	11.9%

Representative Data

Rater Name	Rater Status	# Cases	# Interventions (%)*	# RAPS Fails
Doe, Jane	Lead Rater	72	2 (3%)	1 (1.4%)
Bizness, Nunya	Active	27	2 (7%)	2 (7.4%)
Per site	99 vs 82 site avg		4 (4% vs 9% site avg)	3 (3% vs 2% avg)

Actions Related to Ongoing Analytics Feedback to Sites

- Proactive discussion of potential study participants to identify potential eligibility hurdles and how to overcome them
- Raters removed from any trial-based activities (globally as well as study-specific)
- Reprioritization of raters for study
- Changes in recruitment methods
- Voluntary reduction in recruitment/enrollment to focus on quality

We’re All In This Together

- Through open communication of study-level and site-focused data, we sought to establish a team-based culture across the study
- Providing data and rationale for requests and decisions minimizes chances for mistrust, confusion or frustration between sites and sponsor
- Post-hoc analysis of data suggests early interventions based on BDA were effective at minimizing negative outcomes