Monitoring Adverse Events using an Interactive Web-Based Tool

Ryan Bailey

Rho, Inc.

Immune Tolerance Network (ITN)

- International Research Consortium sponsored by the NIH
  - 27 active studies
  - >2500 participants enrolled
- Rho serves as the Statistics and Data Coordinating Center

ITN027AI AbATE Trial

- Autoimmunity-blocking Antibody for Tolerance in type 1 diabetes (AbATE)
- Randomized, open-labeled, controlled trial
- Randomly assigned at a 2:1 ratio to receive:
  - Teplizumab plus standard diabetes management

    vs
  - Standard diabetes management alone
- 77 participants
- >1400 adverse events

Traditional Reporting Method

Table 14.3.1.1
Adverse Events

	hOKT3		Control		Total	
	Subjects (N=52) [1] N (%)	Events [2] n (%)	Subjects (N=25) [1] N (%)	Events [2] n (%)	Subjects (N=77) [1] N (%)	Events [2] n (%)
Total Adverse Events	52	1227	23 (92.0)	228	75 (97.4)	1455
Infections and infestations	48 (92.3)	205 (16.7)	21 (84.0)	71 (31.1)	69 (89.6)	276 (19.0)
Upper respiratory tract infection	32 (61.5)	80 (6.5)	14 (56.0)	23 (10.1)	46 (59.7)	103 (7.1)
Influenza	10 (19.2)	11 (0.9)	5 (20.0)	8 (3.5)	15 (19.5)	19 (1.3)
Pharyngitis	11 (21.2)	14 (1.1)	3 (12.0)	6 (2.6)	14 (18.2)	20 (1.4)
Skin papilloma	9 (17.3)	10 (0.8)	2 (8.0)	2 (0.9)	11 (14.3)	12 (0.8)
Acne pustular	5 (9.6)	6 (0.5)	3 (12.0)	3 (1.3)	8 (10.4)	9 (0.6)
Diarrhoea infectious	6 (11.5)	6 (0.5)	2 (8.0)	2 (0.9)	8 (10.4)	8 (0.5)
Gastroenteritis viral	7 (13.5)	7 (0.6)	1 (4.0)	1 (0.4)	8 (10.4)	8 (0.5)
Sinusitis	5 (9.6)	5 (0.4)	3 (12.0)	6 (2.6)	8 (10.4)	11 (0.8)
Bronchitis	3 (5.8)	3 (0.2)	4 (16.0)	4 (1.8)	7 (9.1)	7 (0.5)
Rhinitis	5 (9.6)	6 (0.5)	1 (4.0)	2 (0.9)	6 (7.8)	8 (0.5)
Ear infection	4 (7.7)	4 (0.3)	1 (4.0)	1 (0.4)	5 (6.5)	5 (0.3)
Conjunctivitis infective	3 (5.8)	4 (0.3)	1 (4.0)	1 (0.4)	4 (5.2)	5 (0.3)
Gastroenteritis	3 (5.8)	3 (0.2)	1 (4.0)	1 (0.4)	4 (5.2)	4 (0.3)
Nasopharyngitis	3 (5.8)	3 (0.2)	1 (4.0)	1 (0.4)	4 (5.2)	4 (0.3)
Pharyngitis streptococcal	1 (1.9)	1 (<0.1)	2 (8.0)	2 (0.9)	3 (3.9)	3 (0.2)
Viral infection	3 (5.8)	4 (0.3)	0	0	3 (3.9)	4 (0.3)
Body tinea	1 (1.9)	1 (<0.1)	1 (4.0)	1 (0.4)	2 (2.6)	2 (0.1)
Cellulitis	2 (3.8)	2 (0.2)	0	0	2 (2.6)	2 (0.1)
Implant site infection	1 (1.9)	1 (<0.1)	1 (4.0)	1 (0.4)	2 (2.6)	2 (0.1)
Laryngitis	2 (3.8)	2 (0.2)	0	0	2 (2.6)	2 (0.1)
Otitis media	2 (3.8)	2 (0.2)	0	0	2 (2.6)	2 (0.1)
Tinea infection	0	0	2 (8.0)	2 (0.9)	2 (2.6)	2 (0.1)
Tooth abscess	2 (3.8)	2 (0.2)	0	0	2 (2.6)	2 (0.1)
Urinary tract infection	2 (3.8)	2 (0.2)	0	0	2 (2.6)	2 (0.1)
Varicella	2 (3.8)	2 (0.2)	0	0	2 (2.6)	2 (0.1)
Viral skin infection	2 (3.8)	2 (0.2)	0	0	2 (2.6)	2 (0.1)
Viral upper respiratory tract infection	2 (3.8)	2 (0.2)	0	0	2 (2.6)	2 (0.1)

Note: Events are displayed in descending order of frequency of the System Organ Class and by preferred term within System Organ Class, based on the overall frequency of subjects experiencing the event. Adverse events are coded according to MedDRA V11.1.

[1] Percentages for the number of subjects with AEs are based on the number of subjects in the ITT population (N). If a subject experienced more than one episode of an adverse event, the subject is counted once for that Preferred Term. If a subject had more than one adverse event in a System Organ Class, the subject is counted only once in that System Organ Class.

[2] Percentages for the number of AEs are based on the total number of AEs.

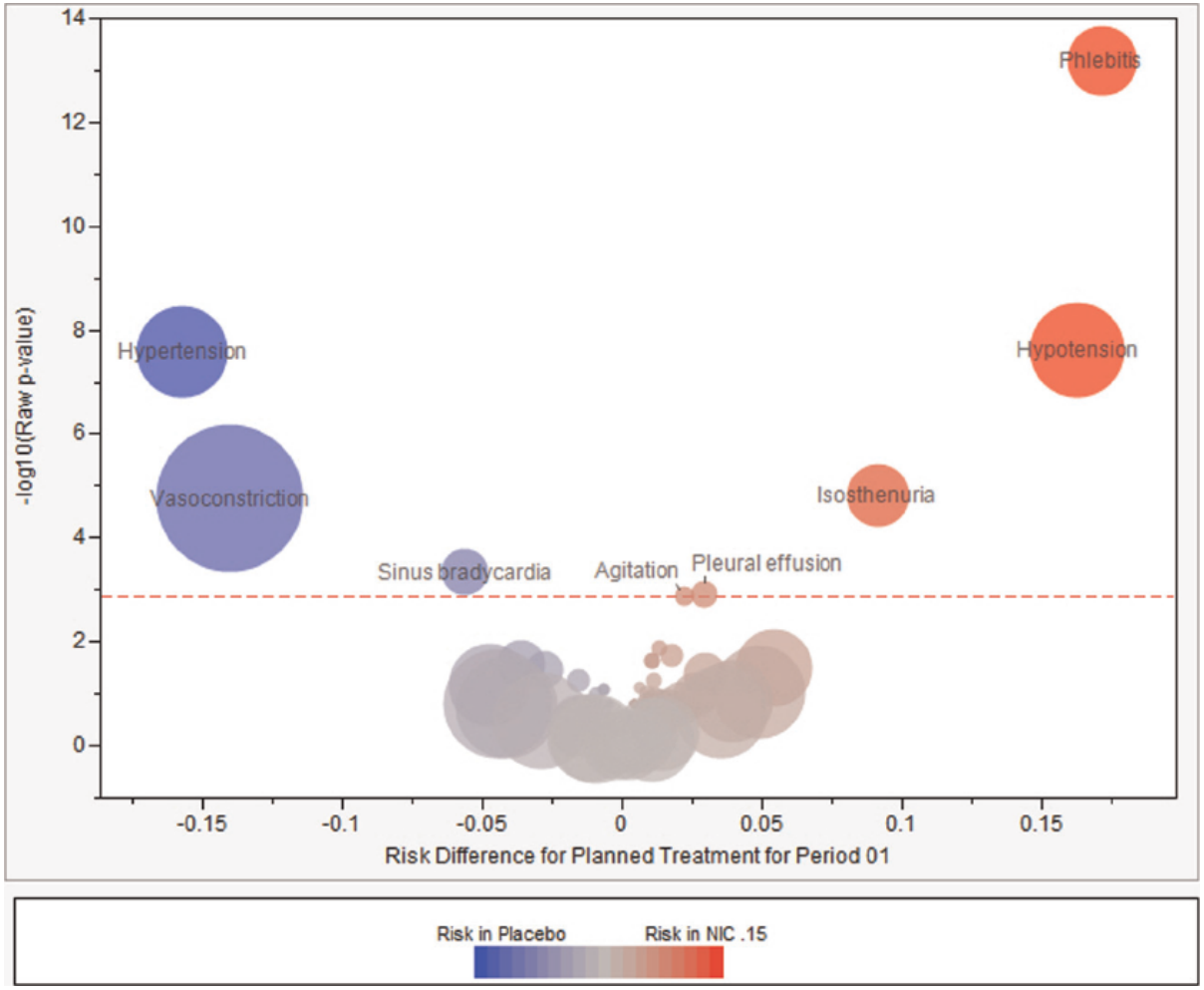
The Problem with Traditional Reporting

Long and tedious

Static and unresponsive

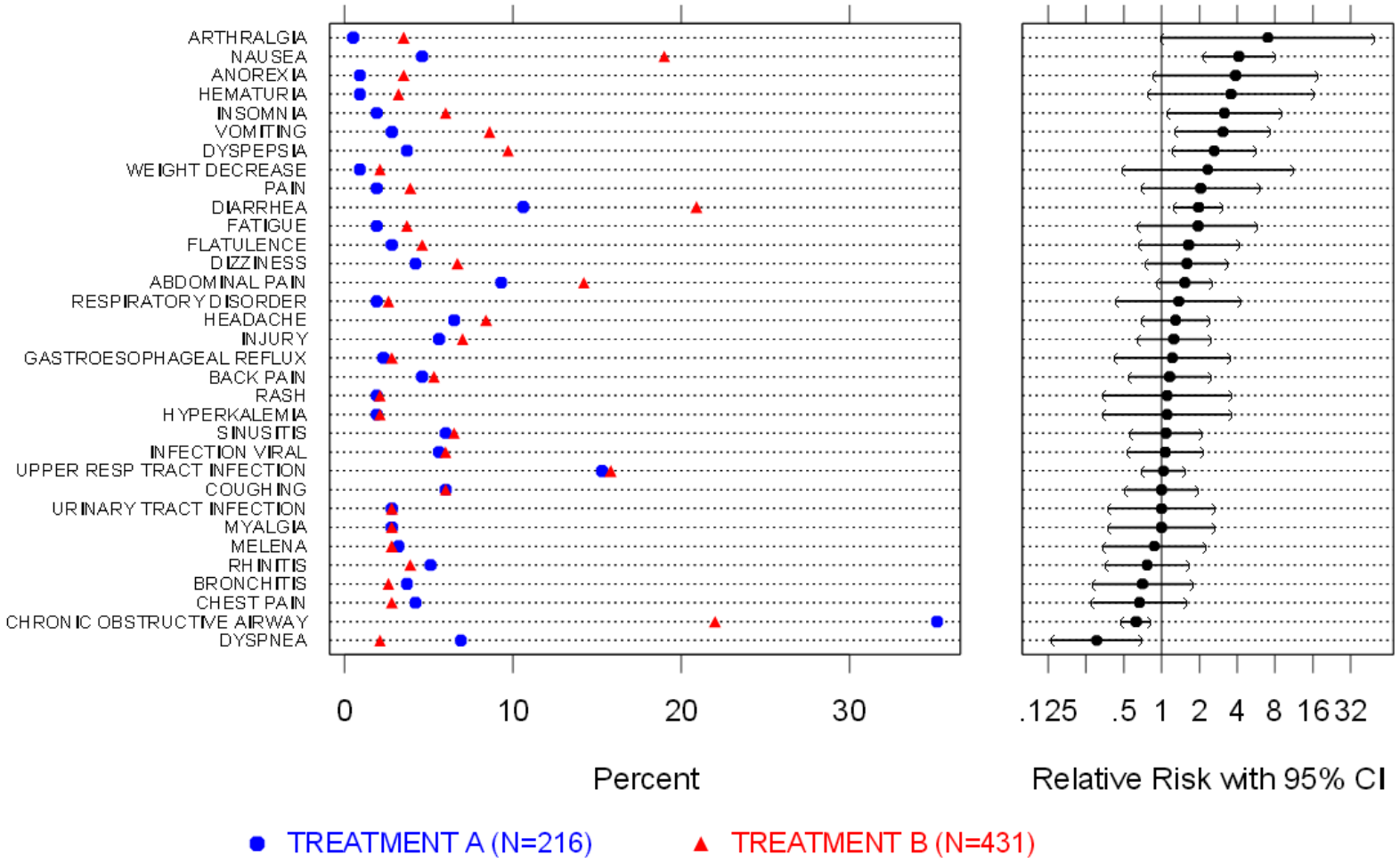
Signal:NOISE

Possible Solutions



Zink RC, Wolfinger RD, Mann G. Summarizing the incidence of adverse events using volcano plots and time intervals. *Clin Trials* 2013; 10: 398-406.

Possible Solutions



Amit O, Heiberger RM, Lane PW. Graphical approaches to the analysis of safety data from clinical trials. *Pharmaceut Statist* 2008; 7: 20-35.

The Challenge

Give medical monitors and safety monitoring committees a better way of digesting these data…

…without sacrificing our ethical obligation to provide a comprehensive listing of all adverse events.

The Solution

Create an interactive

Adverse Events Explorer

Note:

Live Demonstration Presented at SCT

A demonstration of the Interactive AE Explorer is available on YouTube at the following link:

https://www.youtube.com/watch?v=f-jlA0q6Nfw

The Value

- Speeds comprehension
- Eases the burden on the reviewers
- Limits the “Noise” in the data
- Gives the experts control

Future Uses

- Analyzing outcomes data
- Conducting meta-analyses
- Mining mechanistic datasets
- Exploring data

Technical Details

- Programmed in HTML and JavaScript

- Interactivity comes from a JavaScript library called “D3” or Data Driven Documents

Disclosures

This project funded with federal funds from the NIAID, NIH under contract HHSN272200800029C

Data presented are from ITN027AI AbATE study

Acknowledgments

- Jeremy Wildfire
- Emily Wilson
- Nathan Bryant
- Brandy Lind
- James Rochon, PhD

Questions

Comments

Discussion

Contact us with questions:

graphics@rhoworld.com