A Phase II Trial of Single-Dose Oral ETX0914 (AZD0914) for Treatment of Uncomplicated Urogenital Gonorrhea

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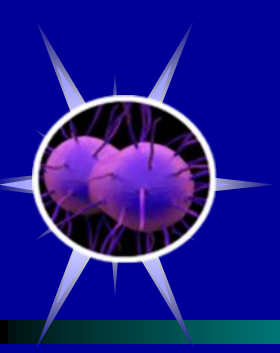
Urgent Public Health Threat

The Emerging Threat of Untreatable Gonococcal Infection
Gail A. Bolan, M.D. et al. N Engl J Med 2012; 366:485-487

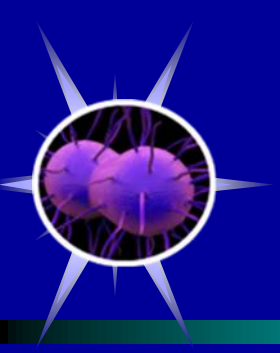
Antibiotic Resistance Threats in the United States, 2013

- 2013 – CDC issued a call to action for development of new antibiotics for treatment of gonorrhea
- 2014 – FDA issued guidance for industry on new drug development
- 2016 – WHO re-emphasized the need for new drug development to combat resistant GC



ETX0914

- ETX0914 is a novel spiropyrimidinetrione antibiotic unlike any marketed antibiotics
- Inhibits DNA synthesis by accumulation of double stranded cleavages that interfere with DNA gyrase
- Similar to fluoroquinolones but active against quinolone and vancomycin resistant Staph
- Active against NG isolates resistant to both ciprofloxacin and ceftriaxone



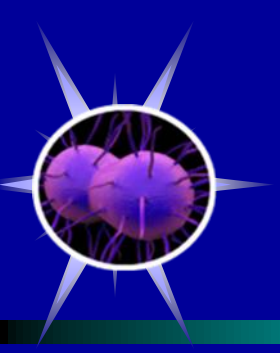
Primary Objectives

- To assess the efficacy by microbiological cure rate of oral 2g or 3g ETX0914 alone compared to 500 mg intramuscular ceftriaxone alone for the treatment of uncomplicated urogenital gonorrhea

- To assess the safety and tolerability of a single dose of oral 2g or 3g ETX0914 alone compared to 500 mg intramuscular ceftriaxone alone

Study Design

- Multi-center, Phase II randomized controlled trial
- Evaluated ETX0914 for treatment of uncomplicated urogenital (urethral and cervical) gonorrhea in men and women.
- Five sites (LSUHSC, UAB, IU, UW, UNC)
- Entasis and NIAID



Methods

- Enrolled 180; Ages 18-53 years old in good health
- Eligibility Criteria
  - Signs and symptoms of urogenital gonorrhea
  - Confirmed urogenital gonorrhea in the past 14 days
  - Sexual contact with an individual diagnosed with gonorrhea in the past 14 days
- Randomized approximately 70:70:40 to receive 2g or 3g ETX0914 orally alone or single intramuscular injection of 500 mg ceftriaxone alone

Methods

- Enrollment: November 2014 – December 2015
- Test-of-cure visit: 6±2 days – Assess clinical cure and safety
- Safety follow-up visit: 31±2 days
- **The primary efficacy outcome measure:**

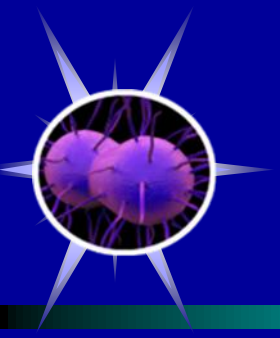
  Microbiological cure rate of uncomplicated urogenital gonorrhea at test-of-cure visit

Demographics

	n	%
Men	167	93
Women	13	7
Heterosexual	90	54
Homosexual/Gay	66	40
Bisexual	11	6
Non-Hispanic	167	93
Hispanic	13	7
Black/African American	107	59
White	58	32
Multi-racial/Other/Hawaiian/Native American/Alaskan Nat./Asian	15	9

Urogenital Microbiological Cure Rates Per Protocol

Therapy	Confirmed Infections	Cures	Micro. Cure Rate %	Micro. Cure % 95% CI
ETX0914 2g	49	48	**97.96**	89.15, 99.95
ETX0914 3g	47	47	**100.00**	92.45, 100.00
Ceftriaxone 500 mg	21	21	**100.00**	83.89, 100.00



Rectal Microbiological Cure Rates Per Protocol

Therapy	Confirmed Infections	Cures	Micro. Cure Rate %	Micro. Cure % 95% CI
ETX0914 2g	4	4	**100.00**	39.76, 100.00
ETX0914 3g	6	6	**100.00**	54.07, 100.00
Ceftriaxone 500 mg	3	3	**100.00**	29.24, 100.00

Pharyngeal Microbiological Cure Rates Per Protocol

Therapy	Confirmed Infections	Cures	Micro. Cure Rate %	Micro. Cure % 95% CI
ETX0914 2g	6	4	**66.67**	22.28, 95.67
ETX0914 3g	9	7	**77.78**	39.99, 97.19
Ceftriaxone 500 mg	4	4	**100.00**	39.76, 100.00

ETX0914 Safety Results
*Participants with Non-solicited AEs**

	Non-solicited AEs **(n=59)** n (%)	Related to Drug (**ETX0914 – 21)** n (%)	Mild n (%)	Mod. n (%)
ETX0914 2g	18 (25)	**9 (13)**	8 (89)	1(11)
**ETX0914 3g	23 (34)	**12 (18)**	12 (100)	---
Ceftriaxone 500 mg	18 (45)	6 (15)	5 (83)	1 (17)

*~2:2:1 enrollment – More participants in ETX0914 arms than ceftriaxone arm

** 1 Participant with Severe AE - Non-fatal gunshot wound

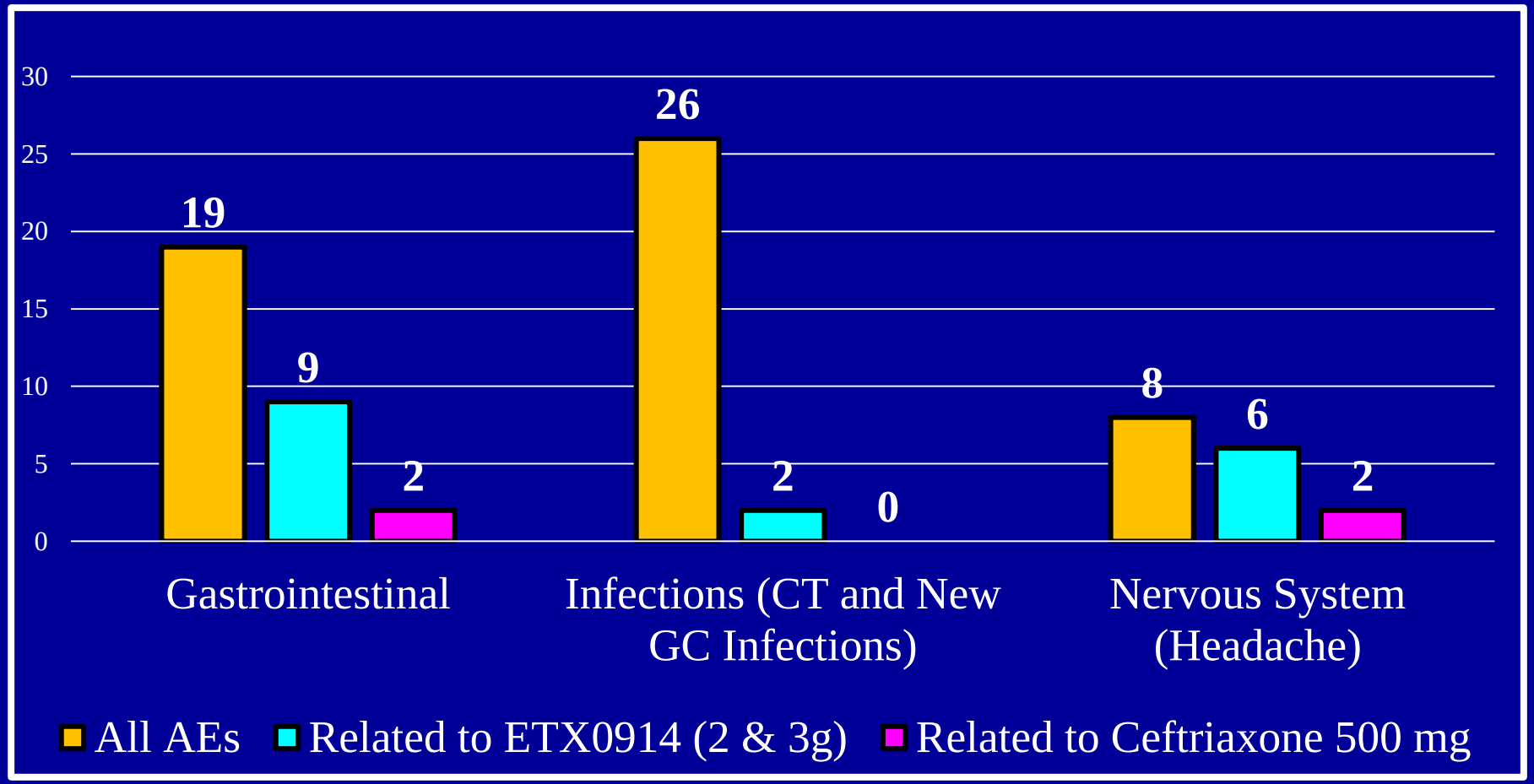
ETX0914 Safety Results
*Number of Non-solicited AEs**

	Non-solicited AEs **n = 84**	Related to Drug **n = 27**	Mild n=72	Mod. n=11
ETX0914 2g	24	**10**	20	4
**ETX0914 3g	37	**17**	33	3
Ceftriaxone 500 mg	23	6	19	4

*~2:2:1 enrollment – More participants in ETX0914 arms than ceftriaxone arm

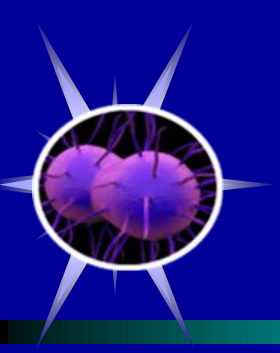
** 1 Participant with Severe AE - Non-fatal gunshot wound

Most Common AEs and Relationship to ETX0914



Conclusions

- ETX0914 was well tolerated and has a favorable side effect profile
- Efficacy of ETX0914 was lower at the pharyngeal site with no difference in the MIC between baseline and test of cure *N. gonorrhoeae* isolates (Data not shown)
- Pharyngeal findings consistent with historical difficulty in treating pharyngeal gonorrhea



Conclusions

- Single-dose ETX0914 was safe and effective in eradicating *N. gonorrhoeae* from urogenital and rectal sites
- ETX0914 shows promise for the treatment of uncomplicated gonorrhea

Acknowledgements

- Our patients
- Jeanne Marrazzo, MD, MPH
- Byron E. Batteiger, MD
- Edward W. Hook, III, MD
- Arlene C. Seña, MD, MPH
- Site sub-PIs, clinical, laboratory and research teams
- Supported by NIAID Contract HHSN272201300012I
- Entasis Therapeutics, Inc.
- STICTG; FHI 360; EMMES Corporation
- UAB Infectious Diseases Laboratory (Central Microbiology Laboratory)