Oral zoliflodacin for treatment of uncomplicated gonorrhea

Subgroup analyses by sex at birth, race and region of a global Phase 3 randomized controlled clinical trial

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on behalf of the zoliflodacin Phase 3 study group

STI Prevention Conference, Atlanta, GA, USA - 19 September 2024

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Conflicts of interest disclosure

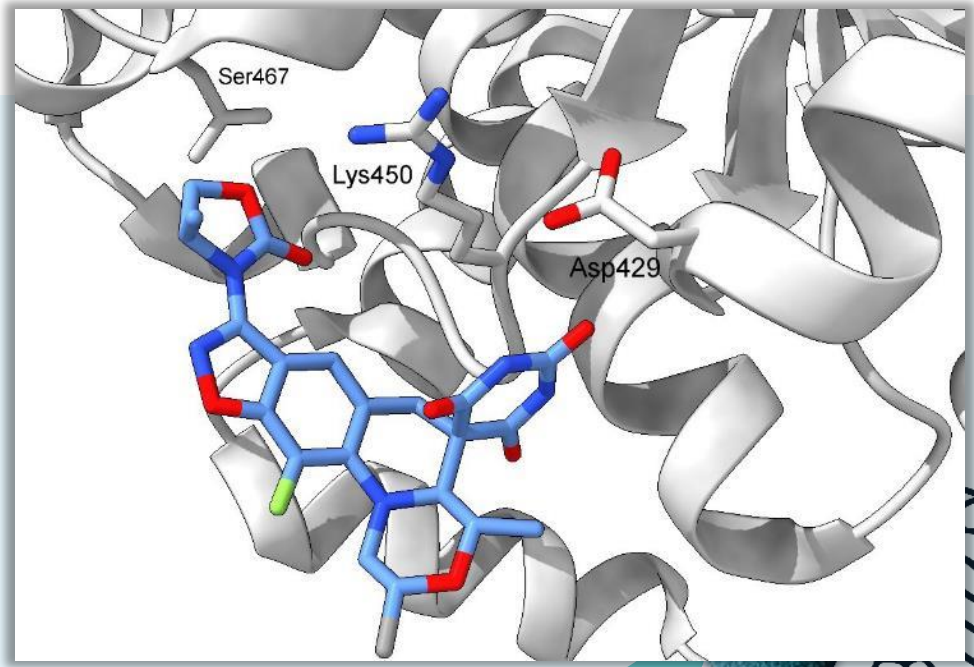
- Edward W Hook III – has received honoraria or consulting fees from GARDP, Visby Diagnostics, and Debio Pharmaceuticals.
- Zoliflodacin is co-developed by GARDP in collaboration with Entasis Therapeutics, Inc., an affiliate of Innoviva Specialty Therapeutics, Inc., and a subsidiary of Innoviva, Inc. (Nasdaq: INVA).

Funding acknowledgments

- This trial was fully publicly funded with support from the governments of Germany (BMBF and BMG), UK (GAMRIF, part of DHSC, and DFID), Japan (MHLW), the Netherlands (Ministries of VWS and BZ), Switzerland (FOPH), The Grand Duchy of Luxembourg, as well as the Canton of Geneva, the South African Medical Research Council (SAMRC), and the Leo Model Foundation.
- The views expressed in this presentation are those of the authors and not necessarily those of the funding bodies.

Zoliflodacin: investigational oral treatment for uncomplicated gonorrhea

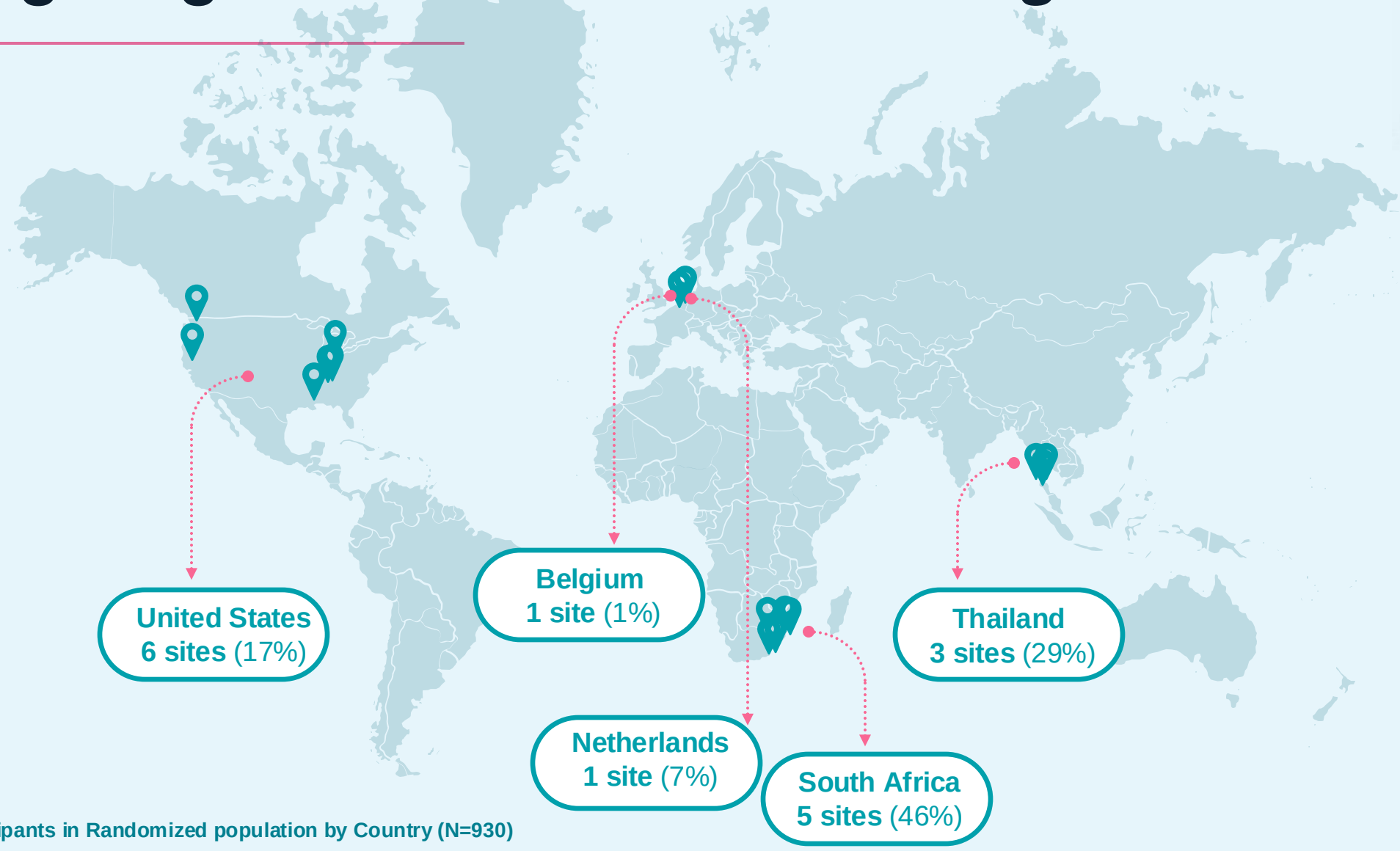
- **Developed within a novel public-private partnership model**
  by AZ/Entasis/IST, NIAID and GARDP
- **First-in-class antibiotic**
  with distinct mode of action through interaction with topoisomerase II complex (GyrB)
- **Microbiological potency**
  against *Neisseria gonorrhoeae* (MIC_{90} of 0.12 mg/L) including multi-drug resistant strains
- **Low propensity**
  to development of *in vitro* resistance
- **Single oral dose**
  for the proposed indication of uncomplicated gonorrhea



Abbreviations: AZ: AstraZeneca; GARDP: Global Antibiotic R&D Partnership; IST: Innoviva Specialty Therapeutics, Inc.; NIAID: National Institute of Allergy and Infectious Diseases

References: Bradford PA, *et al.*, ACS Infectious Diseases 2020; 6(6);1332-1345
Diagram derived from Morgan H, *et al.*, Int. J. Mol. Sci. 2023; 24(2); 1634

Largest global Phase 3 trial for *N. gonorrhoeae*

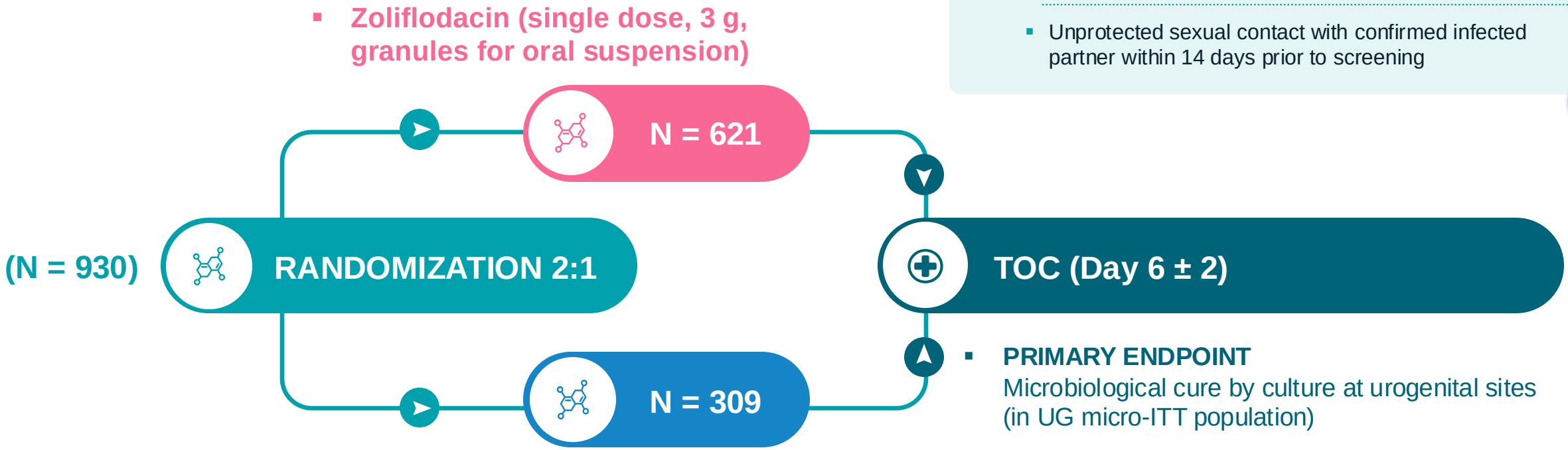


% of participants in Randomized population by Country (N=930)

GARDP-sponsored zoliflodacin Phase 3 registration trial design

KEY INCLUSION CRITERIA

- Age ≥ 12 years
- Signs and symptoms of uncomplicated urethral or endocervical gonorrhea **and/or**
- Culture, Gram stain or NAAT positive for NG within 14 days prior to screening **and/or**
- Unprotected sexual contact with confirmed infected partner within 14 days prior to screening



- Zoliflodacin (single dose, 3 g, granules for oral suspension)
- Ceftriaxone (single dose, 500 mg, IM), plus
- Azithromycin (single dose, 1 g, oral)

- **PRIMARY ENDPOINT**
  Microbiological cure by culture at urogenital sites (in UG micro-ITT population)
- **NON-INFERIORITY MARGIN 12%**

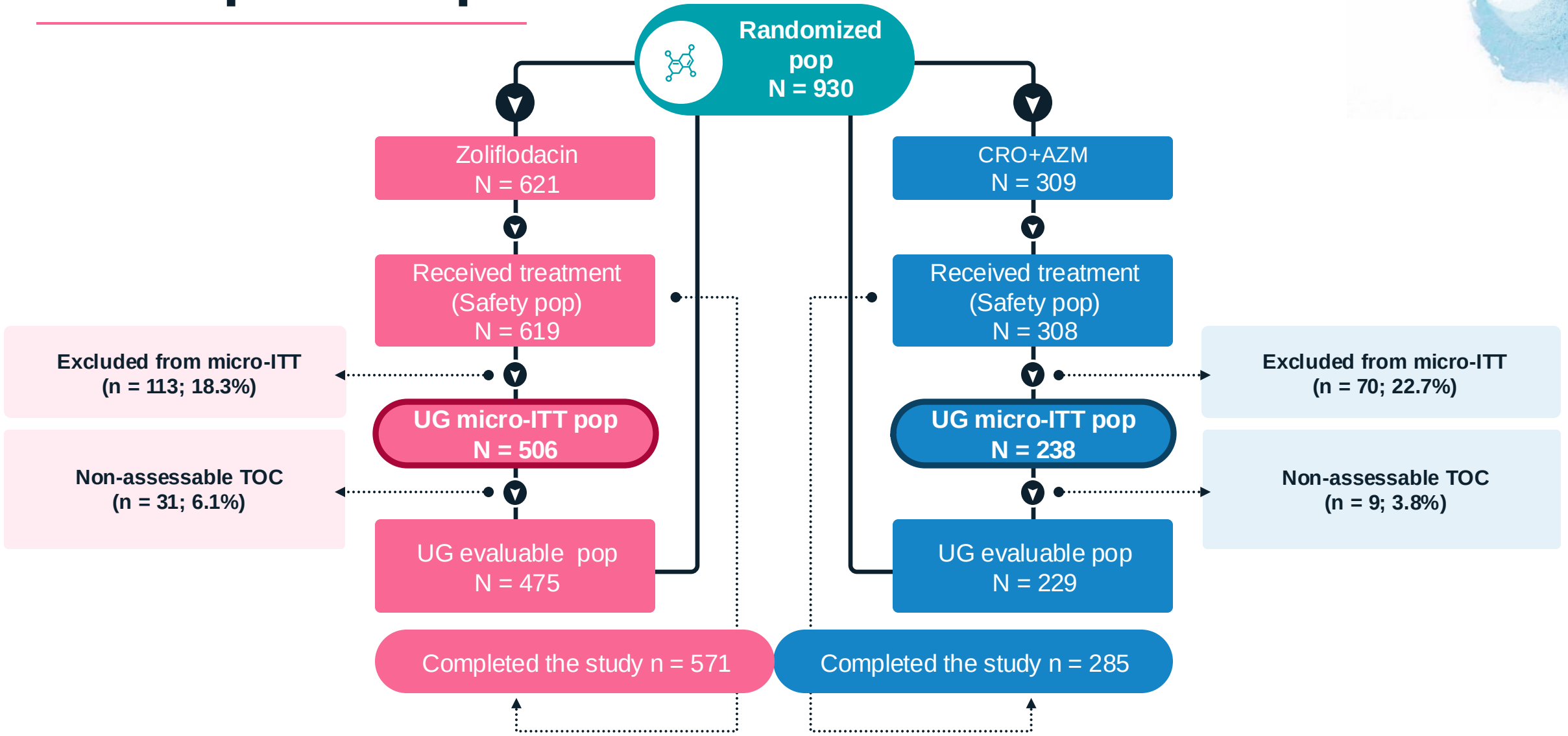
Abbreviations: IM = intramuscular; micro-ITT = microbiological ITT; NAAT: nucleic acid amplification test; N = number of participants; NG = *Neisseria gonorrhoeae*; TOC = test of cure; UG = urogenital (urethral or cervical).

Baseline participant characteristics (Randomized Population)

PARAMETER	Zoliflodacin (N = 621)	CRO+AZM (N = 309)	Overall (N = 930)
AGE [years]			
Mean (SD)	30.0 (9.56)	29.2 (9.13)	**29.7** (9.42)
Min – Max	16 – 73	15 – 67	15 – 73
≥ 18 years [n (%)]	609 (98.1)	307 (99.4)	916 (**98.5**)
ASSIGNED SEX AT BIRTH [n (%)]			
Male	544 (87.6)	271 (87.7)	815 (**87.6**)
RACE* [n (%)]			
White	66 (10.6)	47 (15.2)	113 (12.2)
Black/African American	349 (56.2)	165 (53.4)	514 (**55.3**)
American Indian or Alaska Native	8 (1.3)	1 (0.3)	9 (1.0)
Native Hawaiian or Other Pacific Islander	2 (0.3)	1 (0.3)	3 (0.3)
Asian	193 (31.1)	92 (29.8)	285 (30.6)
White, Asian	1 (0.2)	2 (0.6)	3 (0.3)
Other	2 (0.3)	1 (0.3)	3 (0.3)
HIV STATUS [n (%)]			
Positive	134 (21.6)	65 (21.0)	199 (**21.4**)

Abbreviations: CRO+AZM = ceftriaxone+azithromycin; n = number of participants by treatment arm or overall; SD = standard deviation.
Percentages calculated as n/N x 100.
*as per FDA categorization

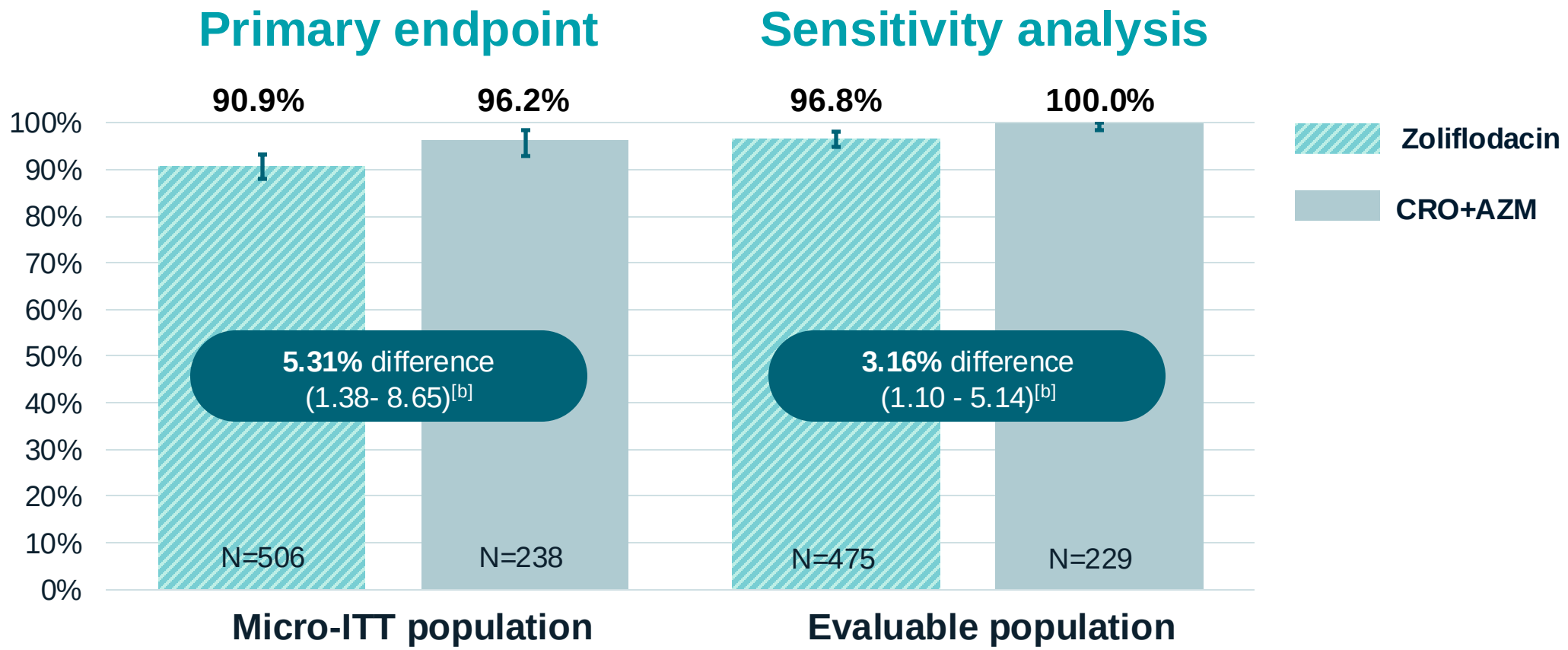
Participant disposition



Abbreviations: CRO+AZM = ceftriaxone+azithromycin; micro-ITT = microbiological ITT; N = number of participants in specified population; n = number of participants; pop: population; TOC = test of cure; UG = urogenital (urethral or cervical).

Zoliflodacin was non-inferior to the comparator*

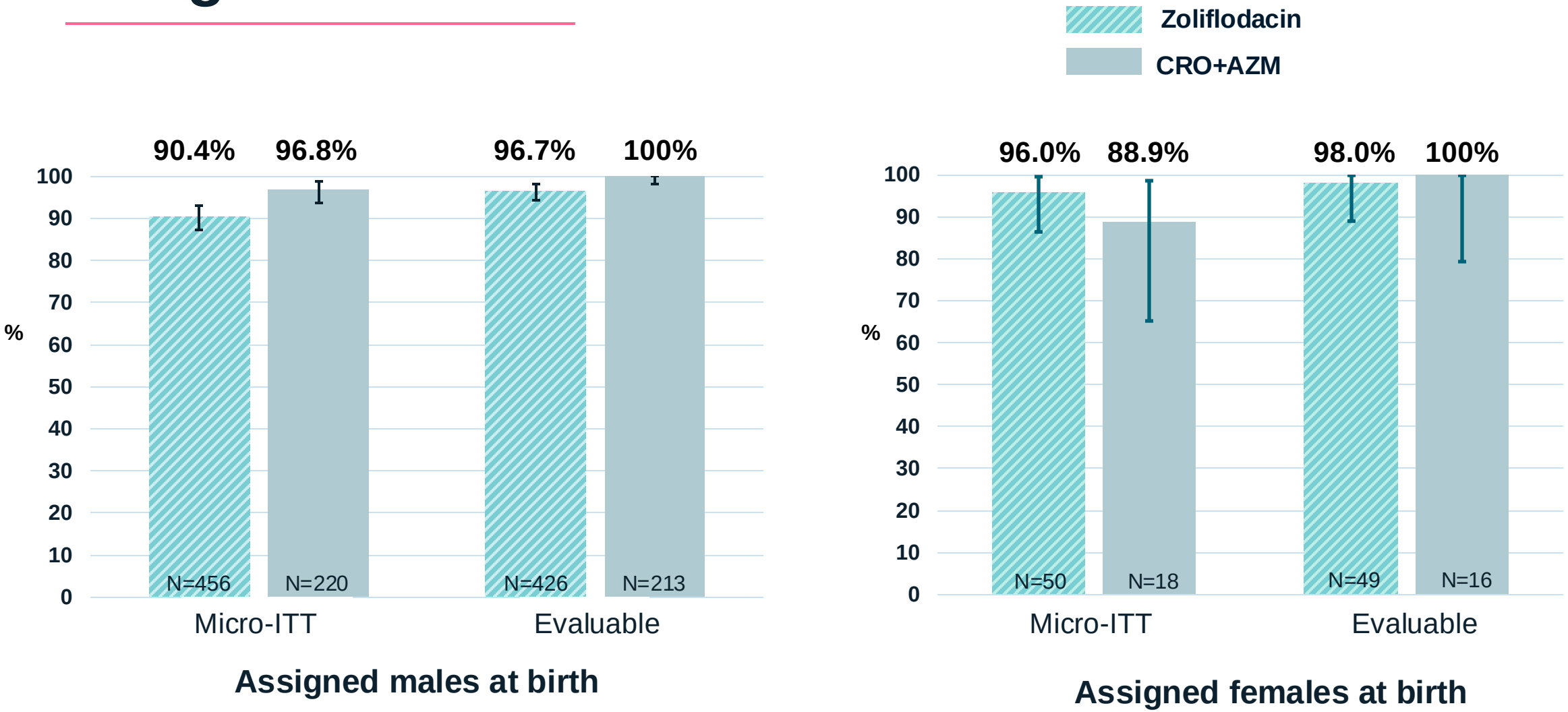
UROGENITAL MICROBIOLOGICAL CURE RATE (95%CI)[a] AT TOC VISIT



Abbreviations: CI = confidence interval; CRO+AZM = ceftriaxone+azithromycin; micro-ITT = microbiological ITT; N = number of participants in the micro-ITT/Evaluable Population for the specified body site; TOC = test of cure.
The percentages are calculated as 100 x (n/N).
[a] Calculated with the Clopper-Pearson method.
[b] Calculated with the Newcombe score method.

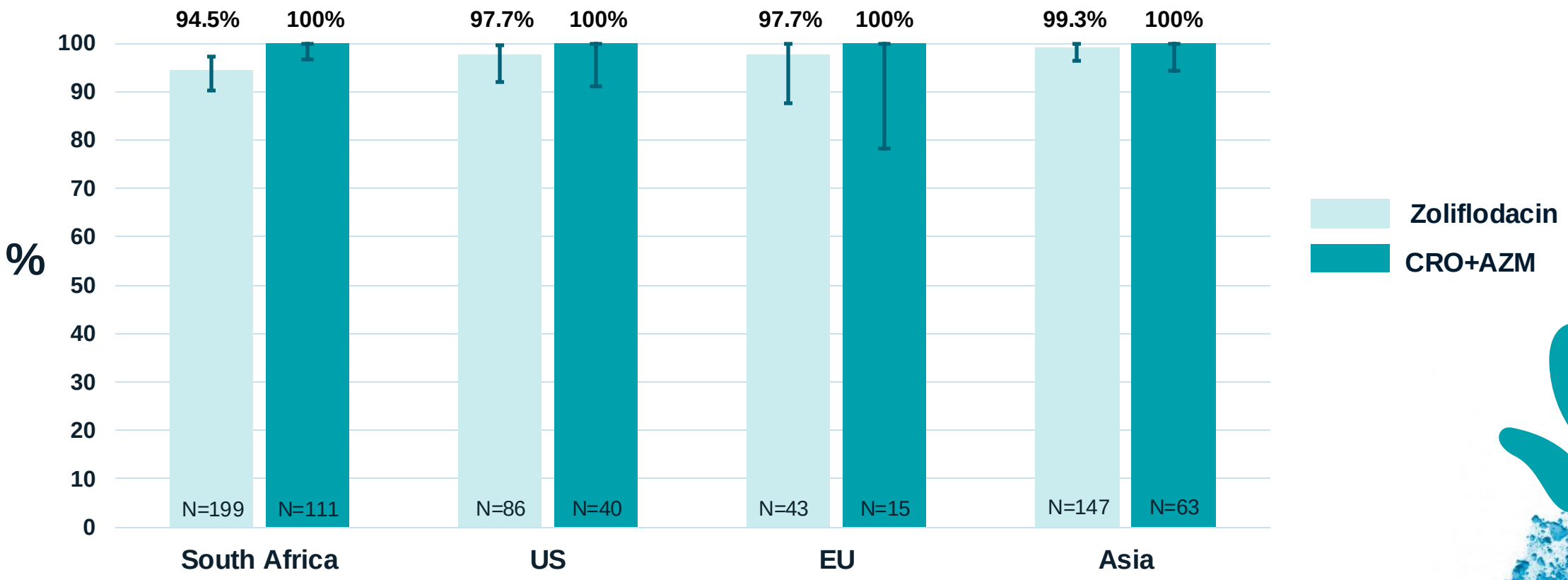
***Reference:** A Luckey, H Broadhurst, P Daram, S Delany-Moretlwe, HJC de Vries, R Kittiyaowamarn, D Lewis, JP Mueller, S O'Brien, MA Richardson, S Srinivasan, SN Taylor, M Unemo, E Hook III, for the zoliflodacin Phase 3 study group. Abstract number 01099; ESCMID Global, April 27-30 2024, Barcelona, Spain.

Urogenital microbiological cure rate (95%CI) by assigned sex at birth



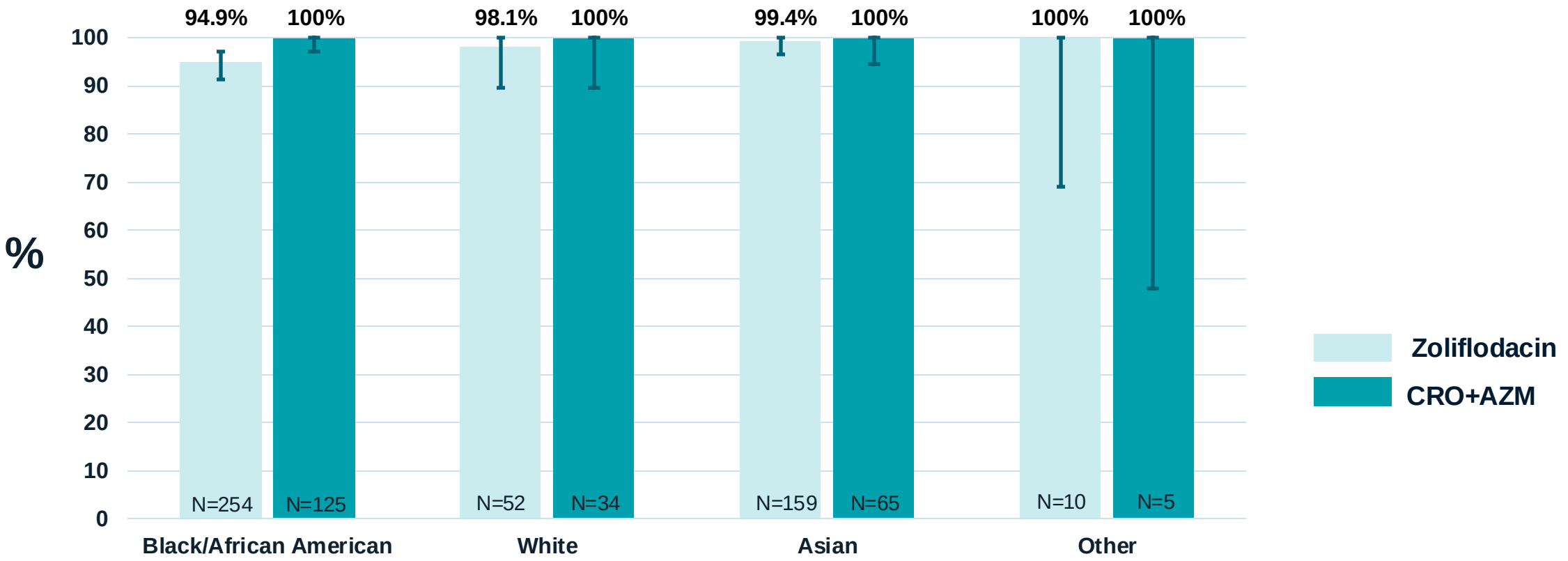
Abbreviations: CI = confidence interval; CRO+AZM = ceftriaxone+azithromycin; micro-ITT = microbiological ITT; N = number of participants in the micro-ITT/EP for the specified sex at birth; TOC = test of cure.
The percentages are calculated as 100 x (n/N). 95% CI are calculated with the Clopper-Pearson method.

Urogenital microbiological cure rate (95%CI) by region (Evaluable population)



Abbreviations: CI = confidence interval; CRO+AZM = ceftriaxone+azithromycin; N = number of participants for the specified subgroup.
The percentages are calculated as 100 x (n/N).

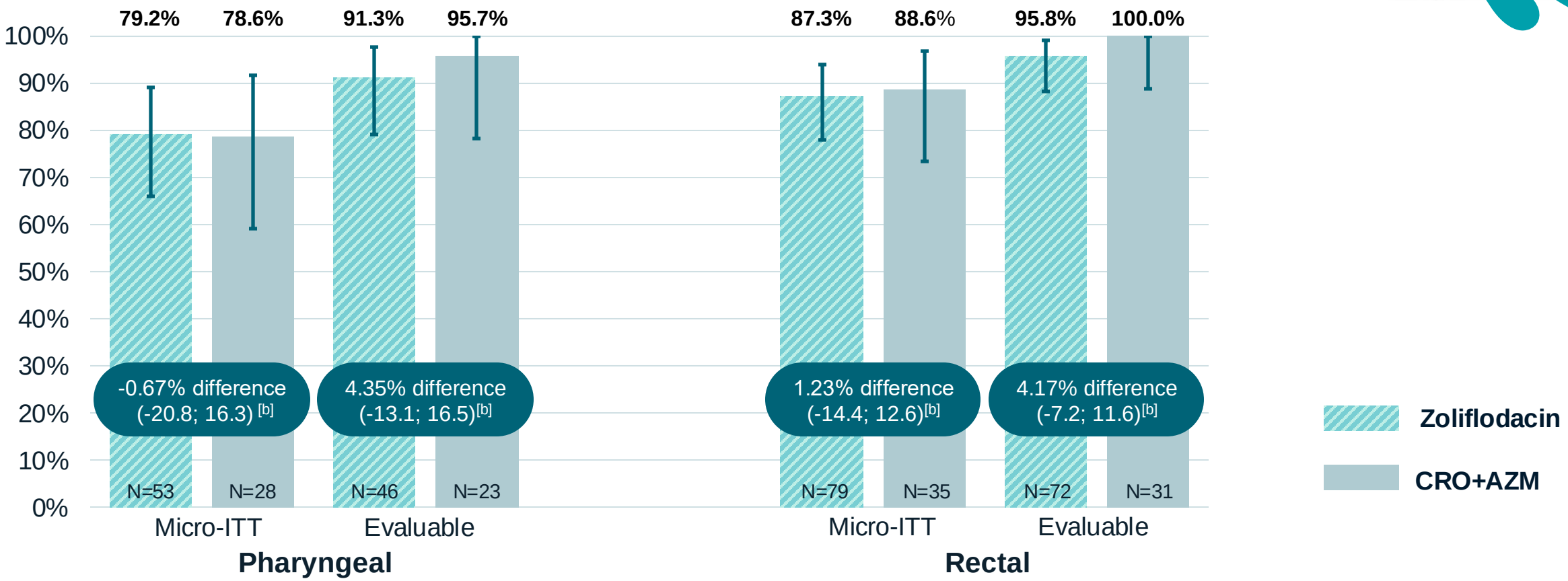
Urogenital microbiological cure rate (95% CI) based on race (Evaluable population)



Abbreviations: CI: confidence interval; CRO+AZM = ceftriaxone+azithromycin; EP = evaluable population; N = number of participants for the specified subgroup.
The percentages are calculated as 100 x (n/N).

Microbiological efficacy at extragenital sites*

MICROBIOLOGICAL CURE RATE (95%CI)[a] AT TOC VISIT



Abbreviations: CI = confidence interval; CRO+AZM = ceftriaxone+azithromycin; micro-ITT = microbiological ITT; N: number of participants in micro-ITT/Evaluable population for the specified body site; TOC = test of cure. The percentages are calculated as 100 x (n/N).
[a] Calculated with the Clopper-Pearson method.
[b] Calculated with the Newcombe score method.

***Reference:** Luckey, A. et al. Oral zoliflodacin is non-inferior to a combination of ceftriaxone and azithromycin for treatment of uncomplicated urogenital gonorrhoea: results of a large global Phase 3 randomised controlled trial. Abstract number 01099; ESCMID Global 2024; oral presentation, April 27-30 2024, Barcelona, Spain.

Zoliflodacin has a similar adverse event profile to comparator

	Zoliflodacin (N = 619) n (%)	CRO+AZM (N = 308) n (%)	Overall (N = 927) n (%)
All AEs	287 (46.4)	144 (46.8)	431 (46.5)
Related AEs	117 (18.9)	76 (24.7)	193 (20.8)
Serious AEs	0	0	0
Related serious AEs	0	0	0
AEs leading to treatment discontinuation	0	0	0
AEs leading to death	0	0	0
AEs by maximum severity[a]			
▪ Grade 1 – Mild	157 (25.4)	82 (26.6)	239 (25.8)
▪ Grade 2 – Moderate	109 (17.6)	44 (14.3)	153 (16.5)
▪ Grade 3 – Severe	20 (3.2)	18 (5.8)	38 (4.1)
▪ Grade 4 – Life-Threatening	1 (0.2)	0	1 (0.1)
▪ Grade 5 – Death	0	0	0

Abbreviations: AE = Adverse event; CRO+AZM = ceftriaxone-azithromycin; n = number of participants with AEs; N = number of participants in the Safety population. The percentages are calculated on the number of participants per treatment arm = 100 x (n/N).
[a] Based on Common Terminology Criteria for Adverse Events (CTCAE).

***Reference:** Luckey, A. et al. Abstract number 01099; ESCMID Global 2024; oral presentation, April 27-30 2024, Barcelona, Spain.

Favourable safety and tolerability profile

TREATMENT EMERGENT ADVERSE EVENT BY PREFERRED TERM (≥3% Overall)	Zoliflodacin (N = 619) n (%)	CRO+AZM (N = 308) n (%)	Overall (N = 927) n (%)
Subjects with at least one TEAE	286 (46.2)	143 (46.4)	429 (46.3)
Headache	61 (9.9)	14 (4.5)	75 (8.1)
Neutropenia	42 (6.8)	24 (7.8)	66 (7.1)
Injection site pain	5 (0.8)	38 (12.3)	43 (4.6)
Diarrhoea	15 (2.4)	22 (7.1)	37 (4.0)
Neutrophil count decreased	21 (3.4)	15 (4.9)	36 (3.9)
Leukopenia	24 (3.9)	7 (2.3)	31 (3.3)
Nausea	16 (2.6)	12 (3.9)	28 (3.0)

Abbreviations: CRO+AZM = ceftriaxone+azithromycin; n = number of participants with TEAEs, N = number of participants in the Safety population; TEAE = treatment emergent adverse event. The percentages are calculated on the number of participants per treatment arm = 100 x (n/N).

Summary

1. This is a large, well conducted, global pivotal Phase 3 trial
2. Non-inferiority of zoliflodacin microbiological cure rate at TOC at urogenital site has been demonstrated
3. High microbiological cure rates are observed at urogenital and extragenital sites of infection
4. Descriptive efficacy sensitivity and subgroup analyses are consistent with the primary endpoint analysis
5. A single oral 3 g dose of zoliflodacin is generally well tolerated with a comparable safety profile to the standard of care
5. Favorable benefit/risk supports progression to new drug application (NDA) submission to FDA

Acknowledgments – Zoliflodacin Phase 3 Study Group

All Trial Participants

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  - Teodora Wi, WHO
- Current and former GARDP and IST collaborators and consultants

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