INNOVIVA Specialty Therapeutics™

Zoliflodacin Phase 3 clinical trial topline data

November 6, 2023

Top line summary: positive zoliflodacin Phase 3 results

- An estimated 82 million patients contract gonorrhea each year[1], with rising rates of resistance to standard of care regimens in many countries[2].
- We, in collaboration with GARDP, ran a global pivotal phase 3 trial to evaluate the efficacy of a single 3g oral dose of zoliflodacin in treatment of uncomplicated gonorrhea compared to treatment with a combination of intramuscular injection of ceftriaxone and oral azithromycin.
- Zoliflodacin met the primary efficacy endpoint and was non-inferior to the comparator arm in participants with urogenital disease (point estimate 5.3% (95% confidence interval: 1.4%, 8.7%)).
- For the key secondary analyses of infections at rectal and pharyngeal sites, rates of cure in the zoliflodacin arm were comparable to those observed in the comparator arm, though these analyses were not powered for statistical significance.
- In this study, zoliflodacin was safe and generally well-tolerated; majority of adverse events were mild to moderate with no discontinuations due to adverse events, serious adverse events, or deaths.
- The study outcome could provide an important therapeutic option for patients and is a positive milestone in the development of zoliflodacin and the fight against antimicrobial resistance.

1 – WHO global antimicrobial resistance suveillance. Lancet Microbe 2021; 2: e627–36
2 – Lancet 2023; 9: e332-33

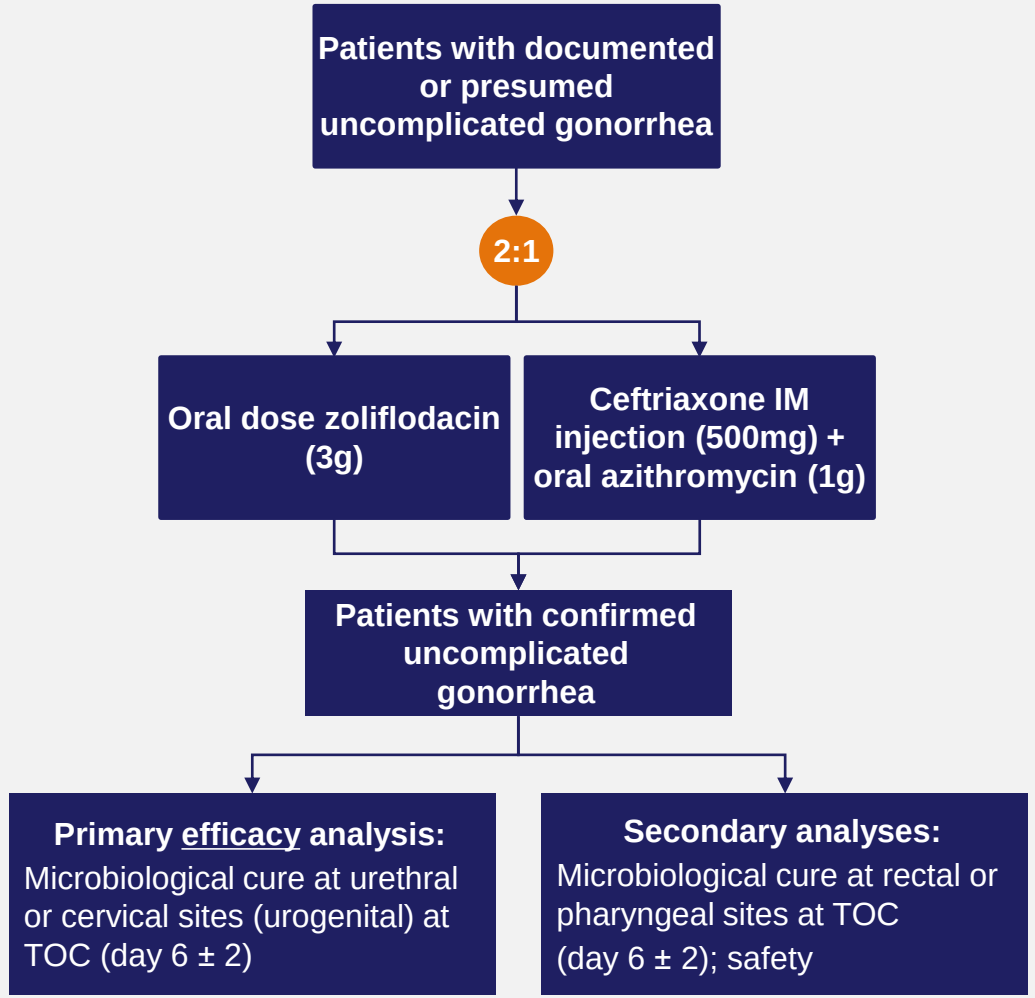
Zoliflodacin Phase 3 registration study design

The zoliflodacin pivotal Phase 3 registration trial was conducted to evaluate the efficacy of a single 3g oral dose of zoliflodacin in treatment of uncomplicated gonorrhea compared to treatment with intramuscular injection of ceftriaxone and oral azithromycin, a current global standard of care regimen.

The primary efficacy endpoint was microbiological test of cure at urethral or cervical sites (urogenital) in participants who had a positive culture for gonorrhea at baseline.

Secondary analyses were microbiological cure at rectal or pharyngeal sites and safety. The trial was designed with a 90% power and a 10% noninferiority margin.

This was a global study, conducted at 16 sites in the United States, South Africa, Belgium, Netherlands, and Thailand.



Abbreviations: CRO-AZI – ceftriaxone and azithromycin; IM – intramuscular injection

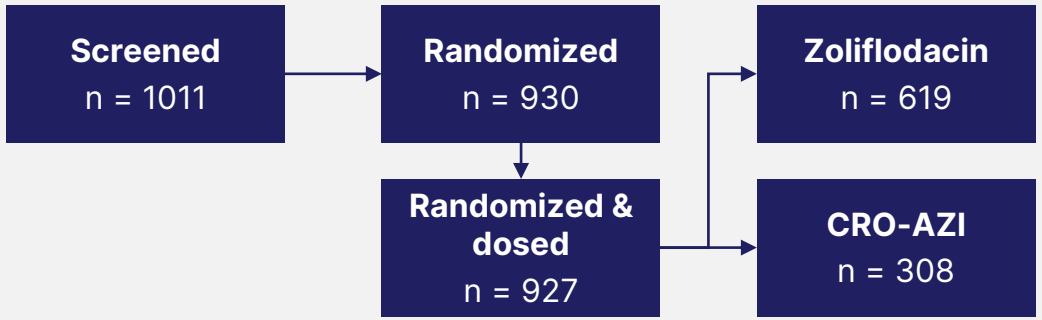
Study enrollment

1011 patients were initially screened, with 927 randomized and dosed.

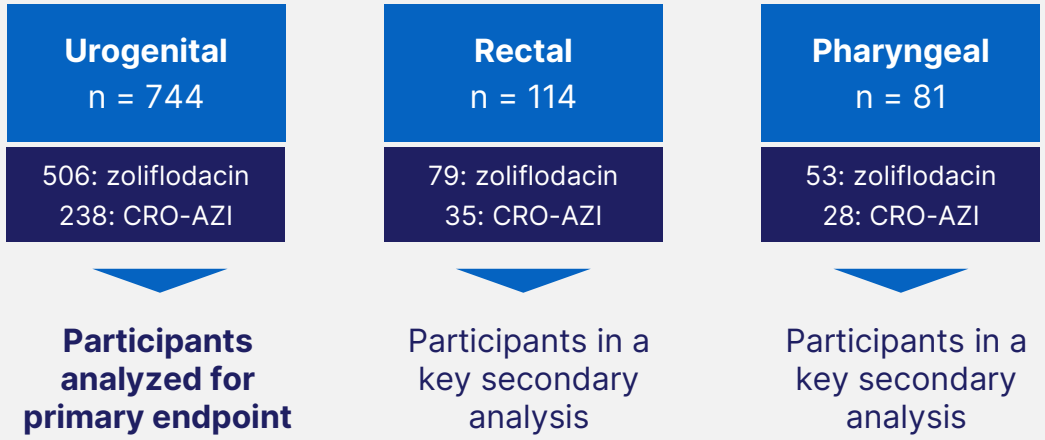
The majority of participants (744) presented with urogenital infections, followed by rectal infections (114) and pharyngeal infections (81). Participants could be in more than one group.

Overall, the trial participants were 87% male, 13% female, 55% Black or Black African, and 20% were positive for human immunodeficiency virus (HIV).

Enrollment and dosing



Sites of infection (participants could be in more than one group)

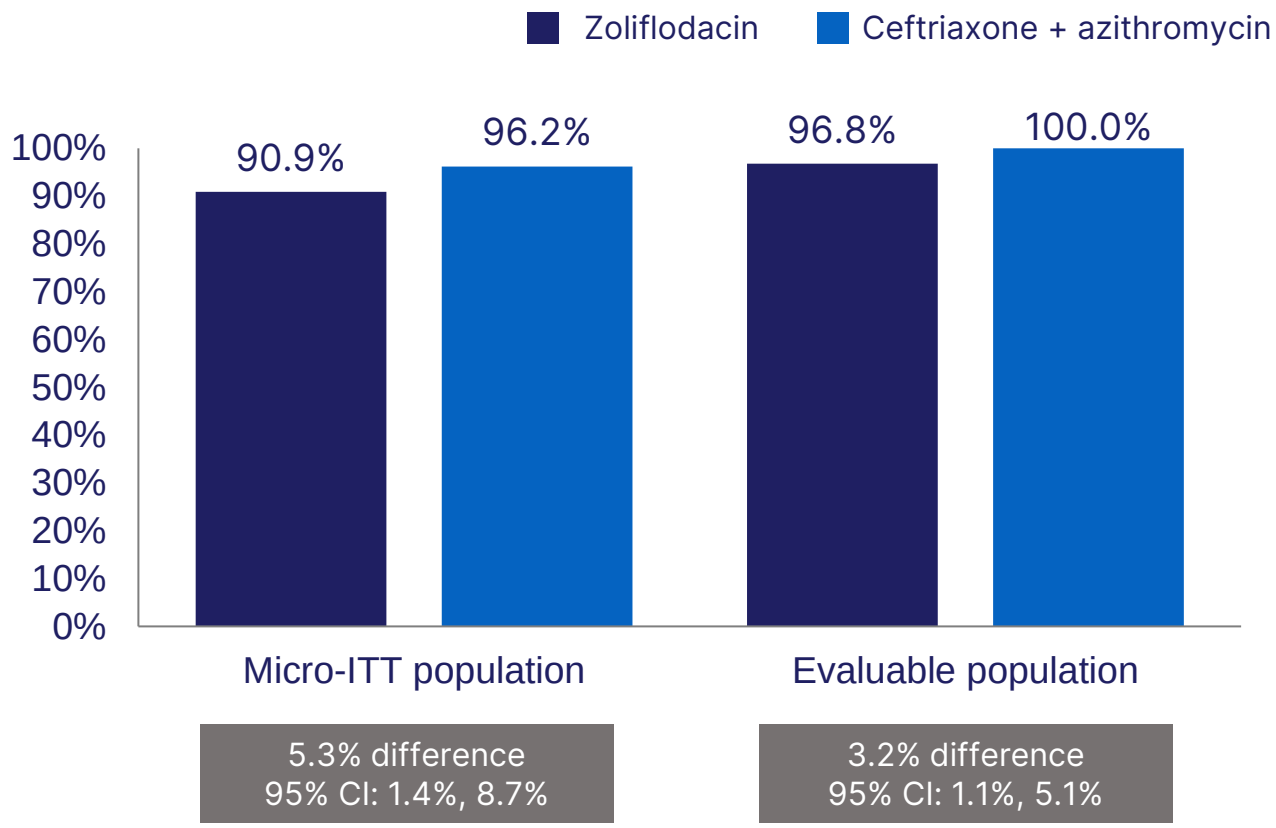


Abbreviations: CRO-AZI – ceftriaxone and azithromycin

The primary endpoint was achieved

A high microbiological cure rate (>90% in both arms) was observed

Microbiological cure rate at test of cure visit



Zoliflodacin met the primary efficacy endpoint and was non-inferior to the comparator (point estimate 5.3% (95% confidence interval (CI): 1.4%, 8.7%)).

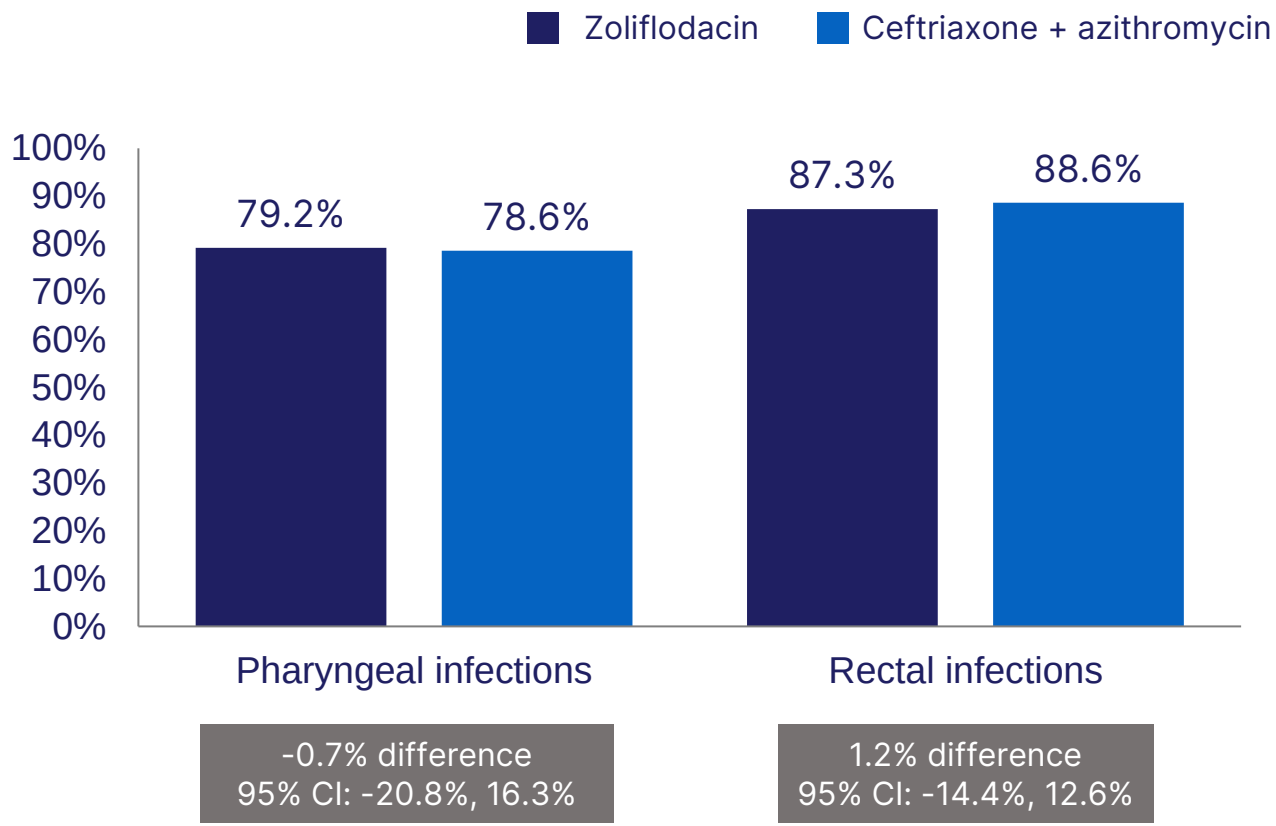
The intent to treat analysis included all participants with a positive baseline culture for gonorrhea; those who missed the test of cure culture, were out of window, or had demonstrated microbiologic failure, were recorded as failures.

When participants who had both baseline and follow up cultures were evaluated, the point estimate was reduced to 3.2% (95% CI, 1.1%, 5.1%).

Clinical cure rates, as assessed by improvement in symptoms in the subset of male participants with urogenital disease, were also comparable between zoliflodacin and the comparator arms

Key secondary analyses showed comparable results in comparison to ceftriaxone and azithromycin

Microbiological cure rate at test of cure visit



Key secondary analysis included participants with pharyngeal and rectal gonorrhea. Historical rates of cure for these populations have been lower than those observed in urogenital disease.

Rates of cure in the zoliflodacin arm were comparable to those observed in the comparator arm.

These secondary analyses were not powered for statistical significance.

Favorable safety and tolerability profile in this study

In this study, zoliflodacin was safe and generally well-tolerated

The overall rate of adverse events was comparable between the two arms

The majority of adverse events were mild to moderate

There were no discontinuations reported due to adverse events, serious adverse events, or deaths

	Zoliflodacin N=619 n (%)	CRO-AZI N=308 n (%)
All TEAEs	286 (46.2)	143 (46.4)
Drug-related TEAEs	117 (18.9)	76 (24.7)
SAEs	0	0
Drug-related SAEs	0	0
Withdrawals due to adverse events	0	0
TEAEs leading to death	0	0

TEAE	Zoliflodacin	CRO-AZI
Headache	61 (9.9)	14 (4.5)
Neutropenia	42 (6.8)	24 (7.8)
Leukopenia	24 (3.9)	7 (2.3)
Neutrophil count decreased	21 (3.4)	15 (4.9)
Dizziness	21 (3.4)	5 (1.6)
Nausea	16 (2.6)	12 (3.9)
Diarrhea	15 (2.4)	22 (7.1)

Abbreviations: TEAE – Treatment emergent adverse event; SAE – Serious adverse event; CRO-AZI – ceftriaxone and azithromycin