

Resistance-guided antimicrobial therapy:

Efficacy and tolerability of doxycycline-moxifloxacin and doxycycline-2.5g azithromycin for the treatment of *Mycoplasma genitalium* infections



Duygu Durukan
MD/PhD candidate
Monash University
duygu.durukan@monash.edu

Background

Macrolide resistant MG strains have become more common than wild type

- 50-70% in Japan (Deguchi, J Infect Chemother 2018) and Australia (Murray, Emerg Infect Dis 2017);
- 58% in Canada (Gesink, Can Fam Phys 2016), 51% in USA (Getman, J Clin Micro 2016)

Quinolone resistant strains have also been reported

- Australia – 15% (Murray, Emerg Infect Dis 2017) and 47% in Japan (Kikuchi J Antimicrob Chemother 2014)

In 2016 we introduced resistance guided therapy for all MG infections

Urethritis

Proctitis

Cervicitis

PID

MG
contact

ResistancePlus[®] MG



n=77

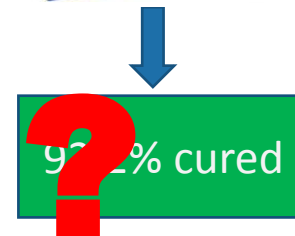
Macrolide susceptible

2.5g: 1 g STAT, then
500mg for 3 days



Macrolide resistant

100 mg BD for 7 days



Clinical Infectious Diseases
MAJOR ARTICLE

IDSA
Infectious Diseases Society of America

hivma
hiv medicine association

OXFORD

Outcomes of Resistance-guided Sequential Treatment
of *Mycoplasma genitalium* Infections: A Prospective
Evaluation

Tim R. H. Read,^{1,2} Christopher K. Fairley,^{1,2} Gerald L. Murray,^{1,2,3,4,5,6} Jorgen S. Jensen,⁷ Jennifer Danielewski,^{3,4} Karen Worthington,²
Michelle Doyle,⁸ Elisa Mokany,⁸ Litty Tan,⁸ Eric P. F. Chow,^{1,2} Suzanne M. Garland,^{2,4,6,9} and Catriona S. Bradshaw,^{1,2}

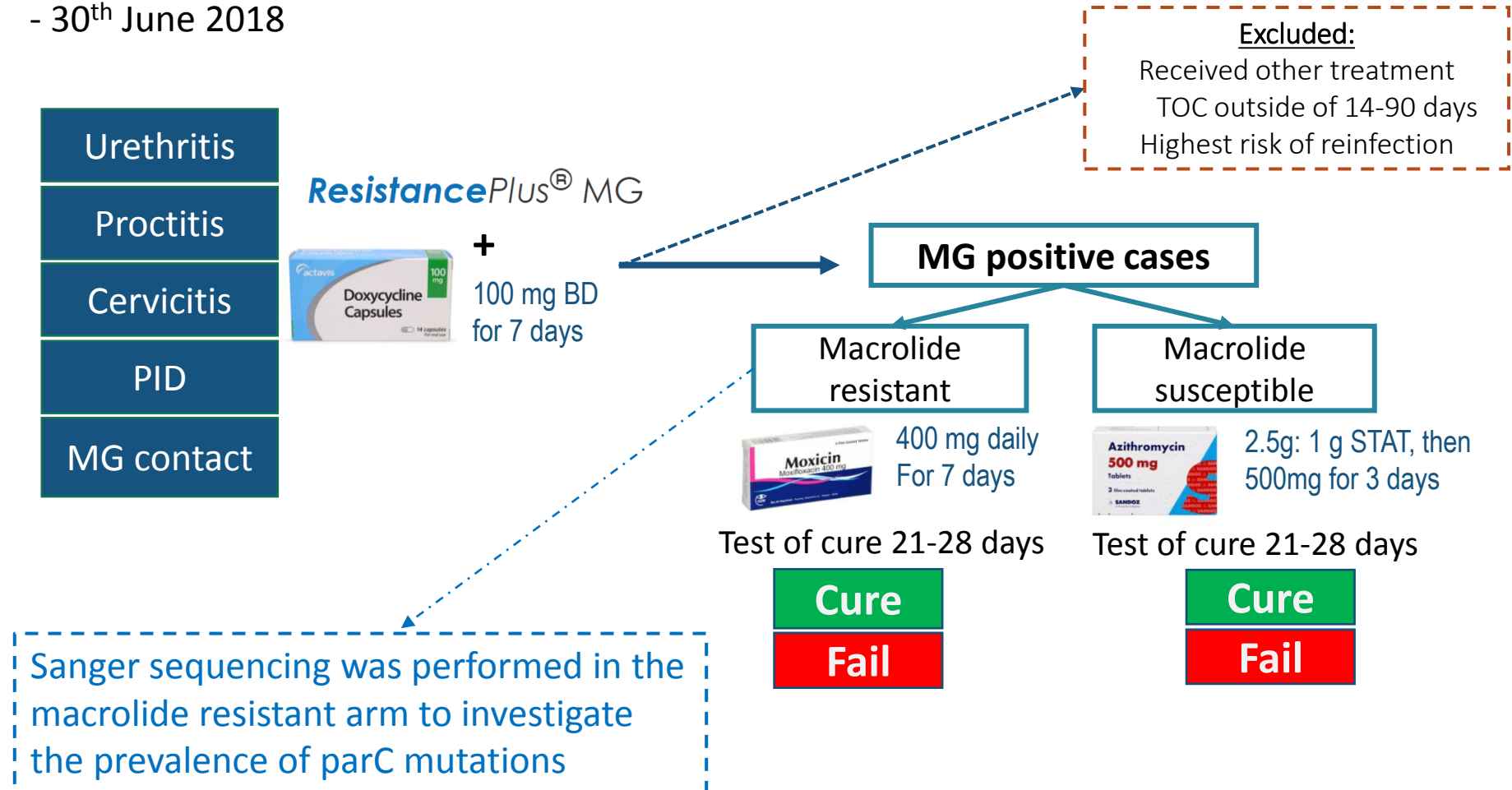


Read, Clin Infect Dis 2018

Methods

Can resistance guided therapy with moxifloxacin or 2.5g azithromycin cure >95% of MG and result in less *de novo* resistance (<5%)?

Prospective clinical evaluation at Melbourne Sexual Health Centre between 11th April 2017 - 30th June 2018



Methods

At test of cure, clinicians recorded symptoms, side effects of each drug, adherence and sexual behaviour at test of cure.

Participants were asked “Have you had sex since starting treatment?”



Primary analysis: Efficacy of the resistance guided therapy 

Secondary analysis: Univariable logistic regression to assess the impact of sexual behaviour on microbial cure 

High risk: Condomless sex with an ongoing untreated partner

Ethics approval was obtained from Alfred Health Ethics Committee
(Approval no: 232/16)

Results: Primary Analysis

Median age:
28

Median time to TOC:
27 days

Symptomatic:
82.5%

81 Women 21% 106 MSW 28% 196 MSM 51%

383 patients on RGT

274 Macrolide
Resistant
(71.5%)

109 Macrolide
Susceptible
(28.5%)



92.0% cured
(n=252)
(95% CI 88.1-94.6)

8.0% failed
(n=22)
(95% CI 5.4-11.9)

95.4% cured
(n=104)
(95% CI 89.7-98.0)

4.6% failed
(n=5)
(95% CI 2.0-10.3)

ParC mutations were present up to 22% of the macrolide resistant cases
71.5% (196/274) were sequenced

- Position S83: 15.3% (30/196) – key mutations
- Position D87 : 6.6% (13/196) – implicated in failure

[Murray et al. 2019](#)

16% of this study population have dual resistance

5/5 had de novo resistance on TOC = **4.6%**

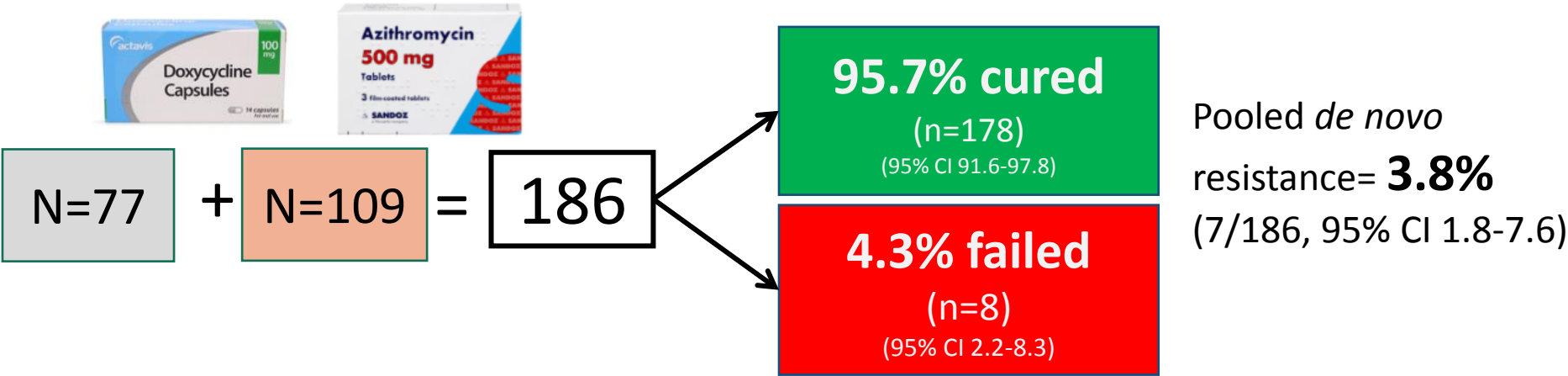
Results: Secondary analysis and pooled cure estimate

Table 3 Microbial failure by the reported reinfection risk

	Reinfection risk category (N= 366)	Positive TOC, n(%[95% CI])	Odds Ratio (95% CI)	p Value
1-No risk	No sex (n=154)	15 (9.7 [6.0-15.1])	1 (ref)	
2-Low risk	Condoms always or fully treated ongoing partner (n=138)	6 (4.4 [2.0-9.7])	0.44 (0.18-1.20)	0.11
3-Mod.risk	Inconsistent condom use with a new partner/unknown treatment status (n=42)	5 (11.9 [5.2-25.0])	1.23 (0.42-3.62)	0.70
4-High risk	Inconsistent condom use with an untreated regular partner (n=32)	9 (28.1 [15.6-45.4])	3.73 (1.46-9.58)	0.006

The only group with an increased risk of treatment failure was the “High risk” patients, justifying their exclusion from the efficacy analysis (Read Clin Infect Dis, 2018)

We combined the doxycycline-2.5g Azithromycin arms from two RGT studies to calculate a pooled estimate of cure and de novo resistance



Results: Adherence and side effects

	Doxycycline n(%)	Azithromycin, n(%)	Moxifloxacin, n(%)
Adherence	298 (77.8)	81 (74.3)	215 (78.5)
Took all doses	280 (94.0)	81 (100)	209 (97.2)
Missed 1-4	16 (5.4)	0	6 (3.0)
Missed >4	2 (0.6)	0	0
Adverse effects (%)	348 (90.9)	97 (90.0)	251 (91.6)
Yes	53 (15.2)	22 (22.7)	62(24.5)
Nausea	9	9	13
Vomiting	1	0	3
Diarrhoea	13	8	10
Gastrointestinal	1	3	0
Photosensitivity (Rash)	8	0	0
Tendon/Joint Pain	0	0	6
Neuropathy	0	0	3
Headache	2	0	5
Anxiety	1	0	3
Fatigue	5	0	6
Dizziness	1	2	9

One case of Achilles tendonitis that self resolved over three days

Limitations:

This was not a controlled clinical trial

- We cannot disentangle the relative effects of antimicrobials
- Side effects, adherence and reinfection risk were self reported
- Antimicrobial resistance may be higher in our STI clinic than general population
- Cure rate is likely to be conservative as we had a 23% loss to follow up and those who don't return were probably more likely to be cured

Conclusion

In the context of high levels of macrolide resistance and at least 20% quinolone resistance, we achieved high levels of microbial cure and low levels of de novo resistance



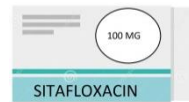
Doxycycline-2.5 g Azithromycin cure:
95.7% (95% CI 91.6-97.8)

De novo macrolide resistance: **3.8%** (95% CI 1.8-7.6)

De novo macrolide resistance following 1g Azithromycin is **12.0%** (95% CI 7.1-16.9) (Horner, Sex Transm Infect 2016)



Doxycycline-Moxifloxacin cure:
92.0% (95% CI 88.1-94.6)



Doxycycline-Sitafloxacin cure was **92.2%**
(Read et al. 2018 Clin Infect Dis)

In 2017 dual class resistance was **8.6%** (Murray, Emerg Infect Dis 2017).

It is **16%** in this study

Resistance guided strategies are essential for optimising treatment and antimicrobial stewardship

Conclusion

This study provides the evidence that underpins the recommendations in the UK, Europe and Australian guidelines for treatment of Mycoplasma Genitalium



- Resistance guided therapy using 2.5g azithromycin or moxifloxacin cures >90% of MG infections
- It is currently the most effective therapy that uses common antimicrobials
- This regimen is easily implemented in high case load STI services and is associated with high adherence

Thank you

Acknowledgements:

Supervisors: A/Prof Catriona Bradshaw, Prof Christopher Fairley, A/Prof Eric Chow, Dr Tim Read

MSHC Staff: All nurses and doctors who were involved in patient care
IT: Afrizal Afrizal, Jun Kit Sze

MSHC Genital Microbiota and Mycoplasma group: Michelle Doyle, Dr Lenka Vodstrcil

Royal Women's Hospital: Gerald Murray, Kaveesha Bodiyaadu
Disclosures: SpeedX Pty Ltd, Australia, provides research funding to Melbourne Sexual Health Centre