- Treatment of *Mycoplasma genitalium* with azithromycin 1 g is less efficacious and associated with induction of macrolide resistance compared to a 5 day regimen.

Dr Paddy Horner

University of Bristol

University of BRISTOL

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Disclosures

Research studies/consultancy

Hologic

Cepheid

Aquarius Population Health

Mycoplasma genitalium

- 1-3% young people
- 5-7% young people attending GUM
- Associated NGU, cervicitis and PID (mild)
  - Non-gonococcal non-chlamydial disease
  - 5-10% co-infection with chlamydia
- Increases HIV transmission
- 3-7% rectum MSM - ?proctitis
- Limited availability NAAT diagnosis

Horner et al Curr Opin inf Dis 2014; 27: 68-74.

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M. genitalium life cycle

- Very slow growing
- Replication
  - Extracellular
  - Intracellular
  - Epithelial cells –
    - Columnar: urethral and endocervical
    - non-keratinized squamous: Vaginal and ?sub-preputial
- High mutation rate

Macrolide antimicrobial resistance (AMR)

- Distinct mutations associated with
  - Macrolide AMR
- Prevalence
  - Increasing
  - 10-40% worldwide
  - Hypothesised driven by use of azithromycin 1g

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Azithromycin

- Treatment should be >95% effective (WHO)
- Azithromycin (macrolide sensitive)
  - 1grm
    - 80-90% effective
    - Evidence efficacy decreasing
  - 500mgs then 250mgs od 4/7 (5 day regimen)
    - >95% effective
- Prolonged half-life
  - Intracellular > extracellular
  - Chlamydia

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Horner P et al Curr Opin Inf Dis 2014

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Methods

- Systematic review and meta-analysis
  - *Mycoplasma genitalium*, macrolide, azithromycin
  - Up to March 2015
  - AMR genotyping available pre and post treatment failure
    - No AMR prior to treatment

Results

- Six studies identified
- All observational
  - Men and women
- 6: azithromycin 1g
- 1: azithromycin 1.5g (5 days)

Study	Setting	Sample size for analysis	Treated with 5 day regimen			Number treated with 1g regimen			Diff in failure rate (95% CI) (1g compared to 5 day)	Diff in resistance rate (95% CI) (1g compared to 5 day)
			Total	Failure	Resistance	Total	Failure	Resistance		
Anagrius	Swedish STD clinic. Men and women.	191	77	0 (0%)	0	114	7 (6.1%)	7 (6.1%)		
Twin	Melbourne Sexual Health Centre. Men and women.	66	0			66	14 (21.2%)	14 (21.2%)		
Couldwell	Western Sydney Sexual Health Centre. Men and women.	12	0			12	4 (33.3%)	3 (25%)		
Walker	Australian primary care clinics. Women only.	28	0			28	3 (10.7%)	3 (10.7%)		
Bissessor	Melbourne Sexual Health Centre. Men and women.	99	0			99	11 (11.1%)	11 (11.1%)		
Ito	Urologic clinic in Sendai, Japan, during 2006 through 2008	24	0			24	7 (29.2%)	4 (16.7%)		
Total		**420**	**77**	**0 (0%)**	**0**	**343**	**46 (13.4%)**	**42 (12.2%)**	**13.4% (9.8%, 17.0%)**	**12.2% (8.8%, 15.7%)**

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Azithromycin 1g: 13.4% fail treatment

Azithromycin 5 days: no treatment failures

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Azithromycin 1g: 12.2% develop AMR

Resistance Heterogeneity p=0.068 I-squared = 51.3% (moderate)

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Azithromycin 1g vs 5 day : 12.2% (8.8%-15.7%) develop AMR (91% of failures)
: 10% (7%-13%) Forest plot analysis

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52 patients given azithromycin 5 days and pre-treated with doxycycline: excluded

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No difference in failure or AMR rate if not pre-treated with doxycycline

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Strengths and weaknesses

- Strengths
  - Includes all studies in which antimicrobial resistance genotype known prior to treatment
- Weaknesses
  - Observational studies only
    - Loss to follow-up
  - Clinical presentation and gender not considered
  - Only one study reporting efficacy of azithromycin 5 day regimen

Conclusions

- Azithromycin 1g results in:
  - Treatment failure in ~13%
  - AMR 10%-12%
- Azithromycin 5 days (500mg then 250mgs od 4/7)
  - No treatment failures (numbers are small)
  - Duration vs total dose vs combination

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