CLSI Methodology June 2013 FQWG

Members of the FQ Working Group

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Whenever you are
going somewhere it
is helpful to know
where you have been

History of FQ Working Group

Established following the June 2009 CLSI AST Subcommittee meeting, based on a vote by the Subcommittee that an M23, section 6 condition potentially exists for re-evaluation of quinolone and fluoroquinolone breakpoints for *Salmonella* spp. and perhaps other *Enterobacteriaceae*

FQ WG: Original *Raison d'Etre*

- Assess validity and utility of NA disk test for Salmonella
- Assess validity and need for change of FQ breakpoints for Salmonella

History of FQ WG: Data Reviewed

- MIC data summarized by H. Sadar
- PK/PD data: summarized by S. Bhavnani
- Clinical: collected and summarized by J. Adler included several recent publications

Conclusion of WG: Break points were too high and NA test performed poorly

FQ WG: What has been accomplished

Assess validity and need for change of FQ breakpoints for Salmonellae

- Based on available data (MIC distribution, PK/PD, clinical) the breakpoints for Salmonellae were changed (lowered) for testing the FQs in clinical usage

FQ WG: What has been accomplished

Assess validity and need for change of FQ breakpoints for Salmonellae

- CIP: MIC and DD
  - Ciprofloxacin: S/I/R <0.06 / 0.12-.05 / ≥1
  - Ciprofloxacin S/I/R ≥31 / 21-30 / ≤20
- LVX and OFX: MIC only (correlation of DD data with MIC not acceptable)
  - Levofloxacin: S/I/R <0.12 / 0.25-1 / ≥2
  - Ofloxacin: S/I/R <0.12 / 0.25-1 / ≥2

FQ WG: What has been learned

Assess validity and utility of NA disk test for Salmonellae

- Current 30 ug NA disk does NOT work as a screening test for Salmonellae. It neither identifies nor excludes resistant strains.
- Screening test is useful (needed) in geographic areas in which MIC testing is not readily available
- There can be difficulties in reading CIP/OFX/LVX DD tests. The NA DD is easier to read

FQ WG: What has been done

Assess validity and utility of NA disk test for Salmonellae

- Took out NA comment (Jan 2011) and put it back (June 2011) with the understanding that alternative/improvement in screening test would be pursued
- Clarified intentions in comments 32-34 and 36-37
  - MIC testing is preferable
  - NA test may be used to test for reduced FQ susceptibility in *Salmonella*. Strains with that test R to NA may be associated with clinical failure in FQ treated patients.
  - NA may not detect all mechanisms of FQ resistance

FQ WG: What has been done

Assess validity and utility of NA disk test for Salmonellae

- Investigation by Robert Skov (Pilot study data presented Jan 2013): Detection of reduced susceptibility to fluoroquinolones for salmonellae spp using alternative fluoroquinolone disks

Detection of reduced susceptibility to fluoroquinolones for *salmonellae spp* using alternative fluoroquinolone disks

Robert Skov, Mia Torpdahl,
Statens Serum Institut, Copenhagen, Denmark

Erika Matuschek, Gunnar Kahlmeter,
EUCAST Laboratory for AST, Växjö, Sweden

Maria Karlsson, Rebecca Howie
CDC, National Antimicrobial Resistance Surveillance Team, Atlanta, US

Materials and methods

- 126 isolates
  - Examined by PCR for qnr, QRDR and aac6
    - 43 isolates with no identified resistance mechanisms
    - 37 isolates with qnr genes
    - 45 isolates with QRDR mutations
    - 1 isolate with an aac6-Ib-cr gene
      - Possible also an additional resistance mechanism – not identified

Materials and Methods

- Disks (µg)
  - Ciprofloxacin 5
  - Ofloxacin 5
  - Levofloxacin 5
  - Nalidixic acid 30

  - Ciprofloxacin 1
  - Enoxacin 10
  - Norfloxacin 2
  - Pefloxacin 5

Materials and methods

- MIC
  - BMD, Frozen panels, Trek ML1FNFQ, lot 12494

    - Ciprofloxacin 0.016 – 16 mg/L
    - Levofloxacin 0.016 – 32 mg/L
    - Ofloxacin 0.016 – 32 mg/L
    - Nalidixic acid 0.016 – 32 mg/L

- QC
  - *E.coli* ATCC 25922 and *P. aeruginosa* ATCC 27853

Summary/Conclusion I

- By MIC using current CLSI break points, all three FQ (CIP, LVX, OFX) distinguished between isolates with and without resistance mechanisms.

- By DD neither CIP 5µg, LVX 5, OFX 5 or NA 30 were able to reliably distinguish isolates with resistance mechanisms from WT.

Summary/Conclusion II

- DD
  - Alternative disks were identified
  - **Pefloxacin 5** was able to reliably distinguish between isolates with and without resistance mechanisms on all tested batches of MH agar
  - Pooling all results (readers, media etc) a breakpoint of

    S≥ 25 mm

    R< 25 mm

  yielded a sensitivity of 100%

  specificity of 99,6%

FQ WG: Next Steps

Goal is to have a reliable, robust, low cost screen test available for publication in CLSI documents 2014

Based on presentation of study data, in Jan 2013 SC recommended moving forward to develop pefloxacin 5 disc as screening test

- Specific activities for Robert
  - Generate sufficient data to establish QC guidelines. Conduct a full QC study consistent with M-23
  - Additional testing with characterized strains from Marcelo or other labs.
  - Present data on MIC correlation consistent with M-23 guidelines
- Anticipate presentation of data package to SC in Jan 2014


Thank you!