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Evaluation of four fluoroquinolone treatment regimens for acute bovine mastitis

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Aim of the study

- Acute mastitis constitutes a major cause of economic loss in dairy industry.
- Acute mastitis accompanied by generalised disease is potentially life threatening and requires systemic antibiotic medication in combination with anti-inflammatory products where appropriate.
- This field study aimed to assess four fluoroquinolone (FQ) treatment regimens for acute bovine mastitis with generalised disease.
- The products tested in this trial have a claim for the treatment of acute coliform mastitis. However acute mastitis with generalised disease may also be associated with gram-positive bacteria.
- As medical intervention is urgent for such cases and microbiological results are not available before onset of treatment, all inclusion compliant cases, irrespective of causative bacterium, were enrolled in this trial.

Materials and methods

- Multicenter GCP trial (9 sites, 28 farms)
- 173 cows: 1st to 7th lactation, 88% ≤3rd lactation
- **Inclusion criteria**
 - Acute mastitis
 - Local clinical score (LCS) ≥2
 - Generalised disease
 - General condition score (GCS) ≥3
 - Temperature ≥39.6 °C
- Enrolled randomly at day 0 (inclusion and first treatment) until ~25 bacteriologically positive cases were obtained per group.

Study population

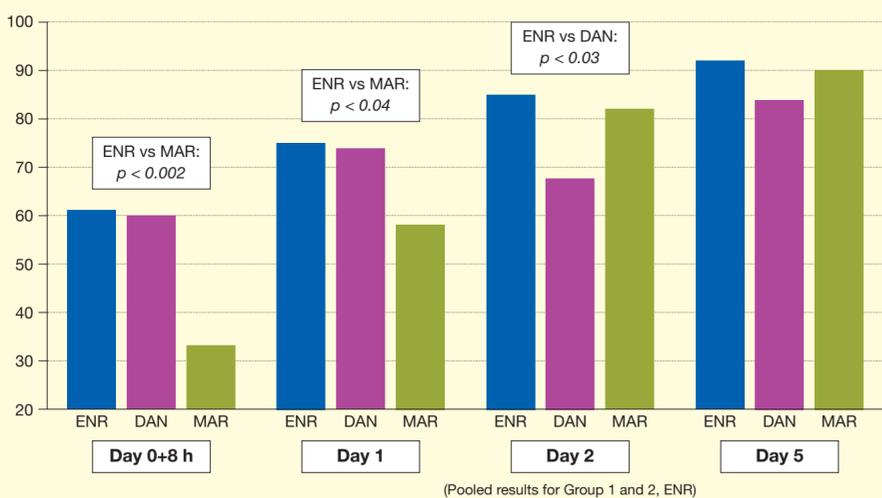
| | Group 1 | Group 2 | Group 3 | Group 4 |
|---------------------------------------------------------|-----------------------|---------------------|-----------------------|------------------------|
| | ENR, 5 mg, day 0, [1] | ENR, 5 mg, day 0, 1 | DAN, 6 mg, day 0, [2] | MAR, 2 mg, day 0, 1, 2 |
| Number enrolled and treated | 37 | 48 | 43 | 45 |
| Number enrolled, treated and microbiologically positive | 24 | 31 | 29 | 24 |

Treatments

- All antimicrobial treatments were given intravenously. In all groups, except group 1, the products were used per label.
- Products used:
 - Baytril 10% (Bayer HealthCare): enrofloxacin (ENR)
 - Marbocyl 10% (Vétoquinol): marbofloxacin (MAR)
 - Advocid 180 (Pfizer): danofloxacin (DAN)
 - In cows with temperature at ≥ 39.5°C by day 1, supportive intravenous NSAID treatment was given (0.5 mg meloxicam/kg).
- Treatment groups

| | | |
|-----------------|-------------|-------------------------------------------------------------------|
| Group 1 (n= 37) | 5 mg ENR/kg | 1 single injection if clinically required, second dose 24 h later |
| Group 2 (n= 48) | 5 mg ENR/kg | 2 daily injections |
| Group 3 (n= 43) | 6 mg DAN/kg | 1 single injection if clinically required, second dose 48 h later |
| Group 4 (n= 45) | 2 mg MAR/kg | 3 daily injections |

Clinical cure rates (%)



Clinical parameters

- Observations
 - Day 0
 - Day 0+8h
 - Day 1, 2, 3, 4 and 5
- General clinical parameters (rectal temperature, attitude, appetite, pulse rate, rumen movements, respiration rate): general condition score (GCS)
- Udder inspection (swelling, pain, heat) and milk inspection (flakes/clots, consistency, colour, smell, CMT): local clinical score (LCS)
- Milk sample for culture at days 0 to 5
- Statistical analysis. Comparisons between ENR and other FQ treatments
 - ANCOVA for mean scores
 - Chi-square for clinical cure rates (CCR)

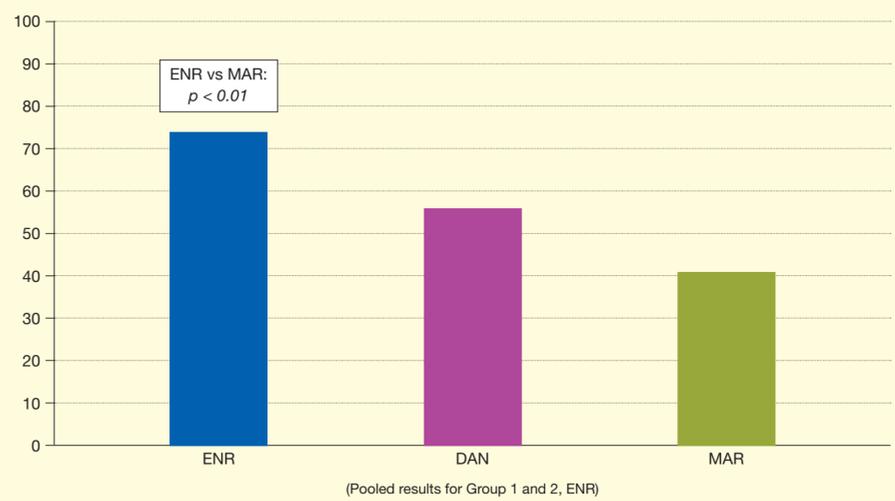
Speed of clinical recovery

| | | Study day | | | | | |
|---------|------------------------|----------------------------------------------------------------|---|---|---|---|-----|
| | | 0 | 1 | 2 | 3 | 4 | 5 |
| | | GCS ◆ down from ≥ 6.5 to < 1.0 | | | | | |
| | | LCS ■ down from ≥ 7 to < 3 | | | | | |
| Group 1 | ENR, 5 mg, day 0, [1] | | | | ◆ | ■ | |
| Group 2 | ENR, 5 mg, day 0, 1 | | | ◆ | ■ | | |
| Group 3 | DAN, 6 mg, day 0, 2 | | | | | | ◆ ■ |
| Group 4 | MAR, 2 mg, day 0, 1, 2 | | | | ◆ | ■ | |

Efficacy criteria

- Clinical cure: decrease of rectal temperature to ≤39.0 C
- Clinical improvement: decrease of rectal temperature to 39.1-39.5 C
- Bacteriological cure: negative milk sample at day 5
- Overall cure rate of clinical mastitis: cases clinically cured and LCS ≤ 1
- GCS, LCS

Milk yield increase from Day 0 (baseline) to Day 5, as % from baseline



Results and discussion

- From 173 cows treated, 108 fulfilled all inclusion criteria and were bacteriologically positive, thereof 55% for *E. coli* and 23% for *Str. uberis*.
- Across treatment groups bacteriological cure rate was 79% for coliform mastitis and 54% for *Str. uberis* cases.
- Redosing in group 1 and group 3 was required for 22% and 37% of cows, respectively.
- Fever decreased rapidly in all animals within 8 hours (≥1.5 °C).
- At study end CCRs were 93%, 91%, 84%, and 90% in groups 1, 2, 3 and 4, respectively
- Overall mastitis cure rates (clinically cured and LCS ≤ 1) were 69%, 77%, 58% and 68%, respectively.
- Mean milk yield at day 5 compared to baseline was increased by 74% in ENR, 56% in DAN and 41% in MAR treated cows.
- A dedicated study with a larger population would be needed to substantiate further whether a single intravenous enrofloxacin dose with optional redosing 24 later is as efficacious as 2 daily doses.
- All in all, among FQ treatments, Baytril showed most rapid cure from mastitis symptoms and general disease symptoms and is therefore a preferred therapy for acute mastitis with generalised disease.