Comparative efficacy of tildipirosin (Zuprevo®) in the treatment of bovine respiratory disease

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Background:

The novel 16-membered semi-synthetic macrolide tildipirosin (Zuprevo® 180 mg/mL solution for injection for cattle, MSD Animal Health) has recently been approved for treatment and prevention of bovine respiratory disease (BRD) associated with *M. haemolytica, P. multocida* and *H. somni* in the EU.

Objective:

To demonstrate therapeutic efficacy of Zuprevo® under field conditions at the recommended label dose.

Materials and Methods:

Experimental design:

- Investigator-blinded, positive-controlled multi-site field study.
- 10 farms in Germany, France and Italy.
- Beef cattle and dairy replacement heifers.
- Clinical signs of BRD (fever + abnormal respiration + abnormal attitude).
- Animals fulfilling all per protocol inclusion criteria (n = 345) were randomly assigned to study groups.

Treatment (see Table 1):

Group A (n=171): Single subcutaneous injection of Zuprevo® at 4 mg tildipirosin/kg body weight (BW).
Group B (n=174): Single subcutaneous injection of Draxxin® at 2.5 mg tulathromycin/kg BW.

Parameters:

- Transtracheal lavage (TTL) samples of bronchial fluid were collected from pre-treatment and from withdrawn animals (failures, late failures) for confirmation of target pathogens *(see Figure 1)*.
- Paired serum samples were taken from these animals for detection of concomitant respiratory viral and *Mycoplasma (M.) bovis* infection.
- Animals were observed daily over a period of 21 days, and assessed clinically by a fixed set of withdrawal criteria.
- Overall treatment success was determined on day 14 and relapse rate was determined on day 21.
- Testimate (IDV Gauting) was used for statistical analysis.

Results:

- Treatment success on day 14 was 84.8% (n = 145 of 171) for Zuprevo®, and 79.3% for Draxxin® (n = 138 of 174) *(see Figure 1)*.
- Relapse rate was 7.6% (n = 11 of 145) for Zuprevo®, and 5.8% for Draxxin® (n = 8 of 138) *(see Figure 2)*.
- Mortality was 0.0% (n = 0 of 171) for Zuprevo® and 0.6% (n = 1 of 174) for Draxxin®.
- Mean rectal temperatures decreased markedly in both treatment groups from D1 on (see Figure 3).
- Target bacterial pathogens were found in 46.2% (n = 156 of 338) of pre-treatment TTLs and 16.2% (n = 11 of 68) of TTLs from withdrawn animals *(see Table 2)*.
- Seroconversion indicating at least one respiratory viral or a *M. bovis* infection was detected in 60.5% of study animals *(see Table 3)*.
- Zuprevo® was significantly non-inferior to the positive control for treatment success and relapse rates.

Conclusions:

Zuprevo® (tildipirosin) is highly efficacious in the treatment of bovine respiratory disease (BRD) associated with *M. haemolytica, P. multocida* and *H. somni*.

Table 1: Study schedule

Study day	Action	Sample	Evaluation injection site reaction
Day 0	Clinical examination Weighing Allocation to the study groups	TTL and serum	Yes
	Group A: Treatment with Zuprevo®: 4 mg tildipirosin/kg BW		
	Group B: Treatment with Draxxin®: 2.5 mg tulathromycin/kg BW		
Day 1 - day14	Clinical examination		Yes
Day 15 - day 20	Observation by owner, investigator visit on demand (unscheduled examination)		Yes
Day 2 - day 21 ±1	Withdrawal	TTL	
Day 21 ±1	Clinical examination, weighing, end of animal phase	Serum	Yes

Table 2: Number of TTL samples taken and target bacteria detected pre-treatment and in animals withdrawn from the two study groups.

	Zuprevo®	Draxxin®
Number of TTL samples	167 at inclusion	171 at inclusion
	34 at withdrawal	34 at withdrawal
Number of pathogens	Inclusion: 38 *M. haemolytica*	Inclusion: 32 *M. haemolytica*
	38 *P. multocida*	36 *P. multocida*
	15 *H. somni*	9 *H. somni*
	Withdrawal: 2 *M. haemolytica*	Withdrawal: 3 *M. haemolytica*
	2 *P. multocida*	1 *P. multocida*
	2 *H. somni*	1 *H. somni*

Table 3: Study animals with increase in antibody titers.

	Zuprevo® (n=170)		Draxxin® (n=172)	
	N	%	N	%
BHV1	15	8.9	18	10.6
PI 3	41	24.1	39	22.7
BRSV	42	24.7	56	32.6
BVD/MD	21	12.4	13	7.6
M. bovis	59	34.7	62	36.1
No seroconversions	68	40.0	67	39.0

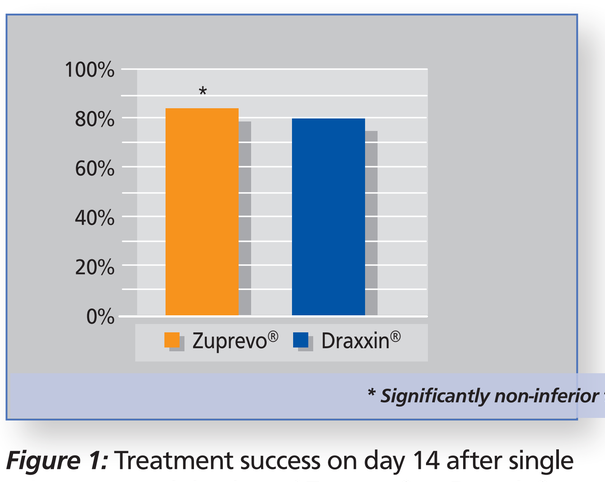
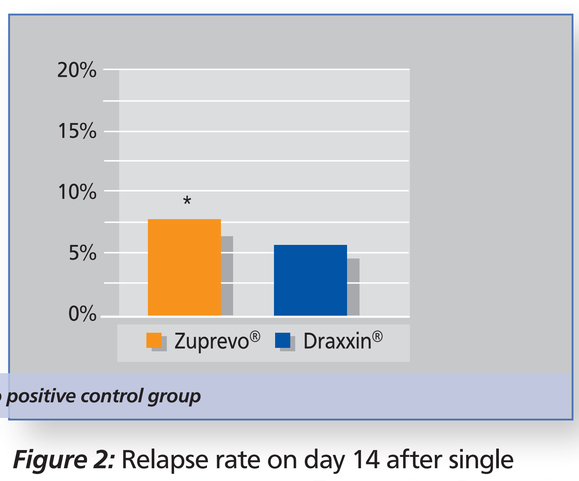


Figure 1: Treatment success on day 14 after single subcutaneous injection of Zuprevo® or Draxxin® at the recommended doses.



**** Significantly non-inferior to positive control group***

Figure 2: Relapse rate on day 14 after single subcutaneous injection of Zuprevo® or Draxxin® at the recommended doses.

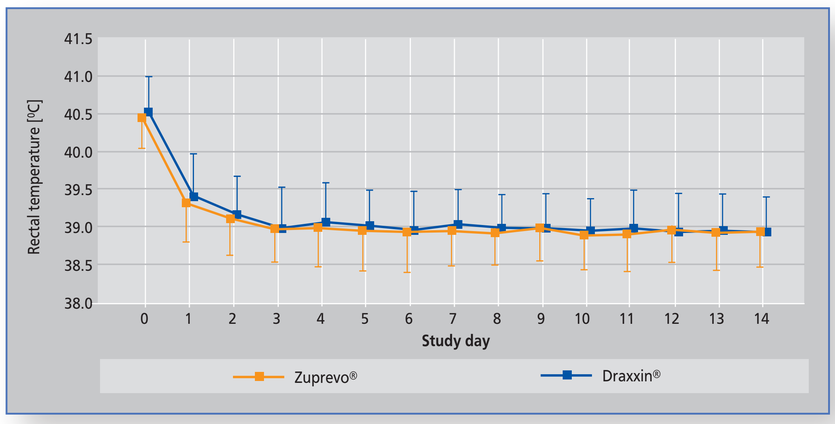


Figure 3: Rectal temperatures after single subcutaneous injection of Zuprevo® or Draxxin® at the recommended doses.

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