27th ECCMID Vienna, Austria 22 – 25 April 2017
The congress of ESCMID

Session: P066 Various agents against Gram-positive bacteria

Category: 5c. New antibacterial agents: clinical trials

24 April 2017, 12:30 - 13:30
P1352

Delafloxacin (DLX) is effective and well-tolerated in treatment of European patients with acute bacterial skin and skin structure infections (ABSSSI) versus vancomycin/aztreonam (VAN/AZ)

Lajos Kemeny[1], Carmen Giuglea[2], Megan Quintas[3], Laura Lawrence[3], Shujui Liang[4], Sue Cammarata*[5]

[1]*University of Szeged*

[2]*St. Ioan Emergency Clinical Hospital*

[3]*Melinta Therapeutics*

[4]*H2o Clinical*

[5]*Melinta; Clinical*

Background: DLX, an investigational anionic fluoroquinolone antibiotic with Gram-positive and Gram-negative activity, including MRSA, is in development for treatment of ABSSSI. Two global phase 3 ABSSSI trials included patients from Europe (studies 302 and 303).

Material/methods: Two multicenter, double-blind, double-dummy trials of adults with ABSSSI randomized patients 1:1 to receive either DLX monotherapy or VAN 15 mg/kg (actual body weight) with AZ for 5 – 14 days. Study 302 used DLX 300mg BID IV only; study 303 used IV DLX for 3 days with a mandatory blinded switch to DLX 450 mg oral BID. Key endpoints were objective response at 48-72 hours with ≥20% reduction in lesion size and Investigator assessment of signs and symptoms at Follow-up (FU day 14) and Late follow-up (LFU day 21-28).

Results: In the 2 studies, 456 patients were randomized in Europe (Latvia, Hungary, Estonia, Moldova, Ukraine, Romania, Bulgaria, Georgia, Spain, Croatia, Israel). 52% were male with mean age 57 yrs. Average erythema area at baseline was 466 cm^2. 65% had cellulitis, 18% abscesses, 15% wound and 2% burn infections; 283 (62%) patients had pathogens identified at baseline. *S. aureus* was the most frequent isolate. *E.coli* was the most frequent Gram-negative pathogen. Patients received mean ~8 days of therapy. Key endpoints are shown below:

Key Endpoints	DLX n/Total (%)	VAN/AZ n/Total (%)	DLX - VAN/AZ (95% CI) Stratified by study
Objective response 48-72h (ITT)	178/228 (78.1%)	174/228 (76.3%)	2.0 (-5.7, 9.8)
Investigator-Assessed Success (FU ITT)	210/228 (92.1%)	206/228 (90.4%)	1.7 (-3.7, 7.2)
Investigator-Assessed Success (LFU ITT)	205/228 (89.9%)	202/228 (88.6%)	1.4 (-4.6, 7.3)
Micro Success (FU ME) for *S aureus*	54/54 (100.0)	48/51 (94.1)	8 (-2.0, 17.9)
Micro Success (FU ME) for *E.coli*	8/8 (100.0)	8/9 (88.9)	10.9 (-25.6, 47.5)

The overall % of patients with at least one treatment-emergent AE (TEAE) was comparable for DLX (27.6%) compared to VAN/AZ (26.8%). The most frequent treatment-related adverse events were gastrointestinal in nature including diarrhea seen in 2.2% and 1.8% of DLX and VAN/AZ patients respectively. There were no cases of *C.difficile* diarrhea. There were 5 DLX and 10 VAN/AZ patients who had serious adverse events; there were 3 DLX and 4 VAN/AZ patients who discontinued due to treatment-related AEs.

Conclusions: Fixed dose monotherapy DLX was comparable to VAN/AZ combination therapy in treatment of ABSSSI based on the early objective response as well as investigator assessment of response. DLX was also comparable to VAN/AZ in treating patients with *S. Aureus* including MRSA. DLX appears effective and well tolerated in European patients with ABSSSI.