EP040

Efficacy and safety of dalbavancin as suppressive therapy

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Background

Dalbavancin is currently mainly used in off-label indications, especially in Gram-positive chronic infections, justified by: i) a prolonged half-life (149-250h) and documented tissue penetration, predicting prolonged *in situ* exposition; ii) an antibiofilm activity *in vitro* and in experimental models; and iv) a randomized clinical trial supporting its use in BJI. In the setting of device-associated infections, **suppressive antimicrobial therapy** (SAT) is an increasingly used strategy, driven by the evaluation of the risk and impact of a potential relapse, related to patients' age and comorbidities, and the quality of surgical infection source control. PK of dalbavancin makes it an attractive SAT option for Gram-positive chronic infections, but this prolonged off-label use has poorly been evaluated.

Methods

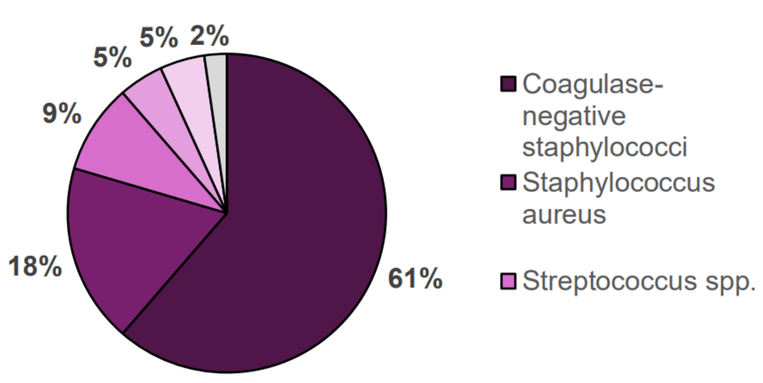
- **Retrospective observational cohort** from July 2019 to December 2024
- **Definitions**
  - **Adequate surgical strategy**: correct source control according to current guidelines (i.e., DAIR for acute infection, and ablation or 1- or 2-stage exchanges for chronic infection)
  - **Dalbavancin susceptibility** (broth microdilution [Sensititre, ThermoFisher Scientific] for staphylococci and enterococci, and E-test® gradient strips [bioMérieux] for other bacteria: MIC ≤0.25 mg/L for staphylococci and enterococci, and ≤0.125 mg/L for streptococci

Results

DEMOGRAPHICS CHARACTERISTICS OF THE 33 INCLUDED PATIENTS

Sex, male, *n [%]*	23 [69.7%]
Age, *median [IQR]*	71 [59 – 80]
Charlson comorbidity index, *median [IQR]*	4 [3 – 6]
Diabetes, *n [%]*	13 [39.4%]
Peripheral vascular disease, *n [%]*	8 [24.2%]
Chronic renal failure, *n [%]*	8 [24.2%]
Indication, *n [%]*	
Total knee arthroplasty	15 [45.4%]
Total hip arthroplasty	6 [18.2%]
Total femur arthroplasty	1 [3%]
Cardiovascular device-related infection	6 [18.2%]
Orthopedic device-associated osteomyelitis	3 [9.1%]
Spinal implant infection	2 [6.1%]

MICROBIOLOGICAL DOCUMENTATION



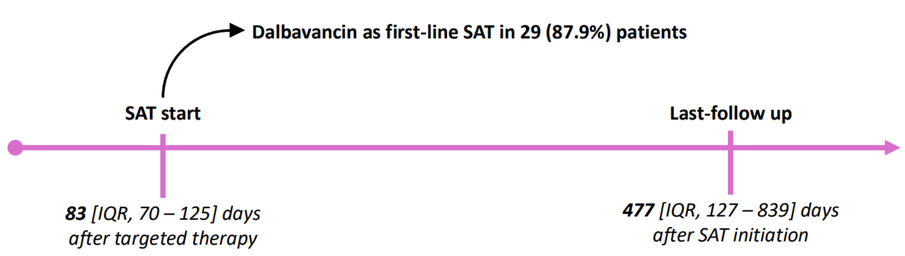
All isolates were dalbavancin-susceptible
Median MIC value: 0.03 (IQR 0.03-0.047) mg/L

SURGICAL MANAGEMENT

29 (87.9%) patients underwent surgery at the initial management phase of the index infection; 12 (41.4%) were deemed inadequate for properly addressing the infectious focus. DAIR, prosthesis replacement and abstention were proposed in 13 (59.1%), 8 (36.4%) and 1 (4.5%) patients with PJI, respectively. Device-associated osteomyelitis or spinal infections were managed by DAIR (n=4, 80%) or complete implant removal (n=1, 20%). Among patients with cardiovascular device-related infections, only 3 (50%) underwent surgery for abscess drainage (n=2) and vascular allograft after prosthesis removal (n=1).

WHY SAT ?

- **Absence of appropriate surgical infection control** (n=13, **39.4%**)
- **High impact of a potential relapse** (n=13, **39.4%**)
- **Multiple previous treatment failures** (n=7, **21.3%**)



DALBAVANCIN DOSING

- Initial doses: 1500 mg (n=28, 84.8%), with a second of 1500 mg (n=19, 57.6%) in a median interval of 14 (IQR, 7-15) days. The third administration was performed 28 (IQR, 27–31) days after (1000 mg [n=13, 39.4%] or 1500 mg [n=12, 36.4%])
- Next injections were guided by therapeutic drug monitoring in most patients.
- Total number of doses: 7 (IQR, 5-11; min-max, 3-49) over a period of 210 (IQR, 107-532) days
- Last injection: 42 (IQR, 28-56) days after the previous one, at 1500 (n=13, 39.4%), 1000 (n=13, 39.4%) or 500 (n=7, 21.2%) mg.

OUTCOMES

At the last follow-up, 21 patients were still on dalbavancin SAT with favorable outcome, 3 had stopped SAT with no sign of infection. Dalbavancin was discontinued in 9 additional patients: 7 relapses with the same pathogen, including 4 with dalbavancin-resistant isolates (median MIC, 0.5 mg/L; IQR, 0,375-0,5) (see Table).

Patient	**1**	**2**	**3**	**4**	**5**
Demographics					
Age (years), sex	64, M	90, F	87, M	81, M	69, M
Charlson Index Score	4	4	6	7	8
Index infection					
Type	PJI, knee	PJI, knee	PJI, knee	PJI, knee	PJI, hip
Surgical strategy	Partial exchange	DAIR	DAIR	No surgery	DAIR
Appropriate surgical source control	No	Yes	Yes	No	No
Microbiological data (dalbavancin MIC, mg/L)					
Index pathogens	MRSE (0.032)	MSSE (≤ 0.03) *Abiotrophia defectiva* (0.012)	MSSE (≤ 0.03)	MRSA (≤ 0.03)	*S. capitis* (≤ 0.03) MRSE (≤ 0.03)
Failure type and pathogens	Relapse MRSE (0.500)	Relapse *Abiotrophia defectiva* (0.032)	Superinfection MRSE (0.250) MRSE (0.500) MRSE (2)	Relapse MRSA (0.500)	Relapse *S. capitis* (0.500) *S. capitis* (0.125) Gram-negative
Dalbavancin therapy					
Dalbavancin initiation	Second-line targeted therapy	Second-line targeted therapy	First-line SAT	I Second-line targeted therapy	First-line SAT
Combination therapy	Rifampicin	Rifampicin	No	Rifampicin	No
Reason for SAT	Unappropriated surgical source control	High impact of a potential relapse	Multiple previous failures	Unappropriated surgical source control, multiple previous failures	Unappropriated surgical source control
Clinical status at SAT	Good	Sinus tract	Good	Persistant signs of infection	Good
Dalbavancin doses (n)	7	10	8	5	4
Delay from first to last injection (days)	134	360	324	171	59
Last dalbavancin trough concentration (mg/L)	8.0	4.8	7.9	4.1	14.8
Last follow-up					
Additional surgical procedure	Yes	No	Yes	Yes	Yes
New SAT	Doxycycline	Amoxicillin	Tedizolid and rifampicin	Pristinamycin	No
Clinical status	Relapse	Persistent signs of infection	Good	Good	Relapse

TOLERANCE : No dalbavancin-related adverse event was observed

Conclusions

Dalbavancin SAT is well tolerated and associated with an acceptable success rate in patients with chronic Gram-positive implant-associated infections. However, relapses with increased dalbavancin MICs advocate for a close monitoring of patients – especially in case of insufficient surgical source control – and dalbavancin TDM to guide dosing and avoid underexposure.