Nuovi long acting e altre opzioni nella terapia delle infezioni difficili da Gram-positivi

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Conflicts of interest

- Investigator-initiated grants (Pfizer, Gilead Italia, Shionogi)
- Personal fees for speaker/consultant (Pfizer, Tillotts Pharma, Menarini)

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Place in therapy - Scenarios

- On label (choice by parameters other than efficacy)
- Off label (best option or failure of on label options)

Place in therapy - Scenarios

- Nuovi long acting vs. altre opzioni

Characteristics of dalbavancin

- Semisynthetic lipoglycopeptide
- Structurally similar to teicoplanin
- Some modifications and a lipophilic tail, that confer extended half-life and improve its anti-staphylococcal activity

Bailej J et al. Am J Health Syst Pharm 2008; 65:599–610
Bassetti M et al. Curr Opin Infect Dis 2021; 34:96-108

Mechanism(s) of action

- Inhibition of transglycosylation
- Inhibition of transpeptidation

Ciabatti R et al. Farmaco 1997; 52:313–321
Bassetti M et al. Curr Opin Infect Dis 2021; 34:96-108

PK characteristics

- Prolonged terminal half-life of 346 hours
- High protein binding (93%)
- Most of the drug is excreted in the urine (adjustment for CLCr <30 mL/min)

Marbury T et al. J Clin Pharmacol 2009; 49:465–476
Bassetti M et al. Curr Opin Infect Dis 2021; 34:96-108

Dalbavancin - Efficacy in RCTs

Study [ref] (type of study)	Investigational drugs (dosage)	Comparator/s (dosage)	Primary endpoint	Disease and study population of the primary analysis	Cured/total (rates, %)	Percent difference (95% CI)
DISCOVER 1 [30] (noninferiority)	Dalbavancin (1 g i.v. on day 1 and 500 mg i.v. on day 8)	Vancomycin (15 mg/kg q12h i.v. for at least 3 days, with possible switch after day 4 to oral linezolid 600 mg q12h for a total of 10–14 days of treatment)	*Early clinical response* (no increase in the surface area of the lesion as compared with baseline and a temperature of 37.6 °C or lower at three consecutive readings performed 6 h apart; assessed at 48–72 h)	ABSSSI *ITT population* Dalbavancin Vancomycin-linezolid	 240/288 (83.3) 233/285 (81.8)	 1.5 (−4.6 to 7.9) Reference
DISCOVER 2 [30] (noninferiority)	Dalbavancin (1 g i.v. on day 1 and 500 mg i.v. on day 8)	Vancomycin (15 mg/kg q12h i.v. for at least 3 days, with possible switch after day 4 to oral linezolid 600 mg q12h for a total of 10–14 days of treatment)	*Early clinical response* (no increase in the surface area of the lesion as compared with baseline and a temperature of 37.6 °C or lower at three consecutive readings performed 6 h apart; assessed at 48–72-h)	ABSSSI *ITT population* Dalbavancin Vancomycin-linezolid	 285/371 (76.8) 288/368 (78.3)	 −1.5 (−7.4 to 4.6) Reference
Dunne *et al.* [34] (noninferiority)	Dalbavancin (1 g i.v. on day 1 and 500 mg i.v. on day 8)	Dalbavancin (1,5 g i.v. on day 1)	*Treatment response* (≥20% reduction in the size of the erythema; assessed at 48–72-h)	ABSSSI *ITT population* Dalbavancin single-dose Dalbavancin 2-dose	 284/349 (81.4) 294/349 (84.2)	 −2.9 (−8.5 to 2.8) Reference

Boucher HW et al. N Engl J Med 2014; 370:2169–2179
Dunne MW et al. Clin Infect Dis 2016; 62:545–551
Bassetti M et al. Curr Opin Infect Dis 2020; 33:110-120

Safety of dalbavancin

- Pooled data from RCTs
- Lower rates of nephrotoxicity than 10 days of iv vancomycin (3.7% vs. 9.3%

Gonzalez PL et al. Infect Dis Ther 2021; 10:471-481

Table 2. Characteristics of published studies on the use of dalbavancin for indications other than acute bacterial skin and skin structure infections[a]

Reference	Type of study	Type of infections other than ABSSSI treated with dalbavancin (no. patients)	Outcome/s data	Safety data AE (no. patients)
Bouza *et al.* [15]	Retrospective Multicenter	Prosthetic joint infection (20) Osteomyelitis (12) CRBSI (8) Endocarditis (7) Intra-abdominal infection (3) Other endovascular infections (2) Septic arthritis (1) Sinusitis (1)	*Successful clinical outcome* Prosthetic joint infection (80%, 16/20) Osteomyelitis (91.7%, 11/12) CRBSI (75%, 6/8) Endocarditis (85.7%, 6/7) Intra-abdominal infection (100%, 3/3) Septic arthritis (100%, 1/1)	*Assessed in the entire cohort, n = 69, including also patients with ABSSSI* Any AE (9) Mild AE (7) Severe AE (2) *Type of AE* Rash (2) Tachycardia (2) Impaired renal function (2) Nausea (1) Rectal bleeding (1) Candidiasis (1)
Nair *et al.* [80]	Retrospective Single center	Endocarditis (2) Osteomyelitis (5) BSI (5) Septic shock with puerperal sepsis (1)	*Outcome assessed in the entire cohort, n = 52, including also patients with ABSSSI* Complete resolution or improvement observed in 44/52 patients (84.6%)	*Assessed in the entire cohort, n = 52, including also patients with ABSSSI* Red man type reaction (2)
Tobudic *et al.* [81]	Retrospective Single center	Endocarditis (27)	Microbiological and clinical success observed in 25/27 patients (92.6%), with the note that dalbavancin was used after clearance of blood cultures in 24/27 cases (88.9%)	Nausea and vomiting (1) Increase in serum creatinine levels (1)

Bassetti M., et al. Curr Opin Infect Dis. 2021 Apr 1;34(2):96-108

Reference	Type of study	Type of infections other than ABSSSI treated with dalbavancin (no. patients)	Outcome/s data	Safety data AE (no. patients)
Dinh *et al.* [75]	Retrospective Multicenter	BJI (48) Endocarditis (19) Vascular infection (5) Catheter line infection (4) BSI (3) Mediastinitis (2) Disseminated disease (19)	*Cure at last visit (exclusion of patients lost to follow-up)* BJI (76.1%, 35/46) Endocarditis (72.2%, 13/18) Vascular infection (100%, 5/5) Catheter line infection (100%, 2/2) BSI (100%, 1/1) Mediastinitis (50%, 1/2)	Erythematous rash, chills and fever (2) Headache (1) Self-resolving hypereosinophilia (1) Local inflammatory signs (1)
Almangour *et al.* [82]	Retrospective Multicenter	Osteomyelitis (36)	Clinical success at 3-month after the end of antibiotic course equal to 90% (28/31, missing 5)	No AE
Bartoletti *et al.* [83]	Retrospective Multicenter	DSWI (15)	At 6-month follow-up, 14/15 patients (93%) showed no relapse, did not received further coursed of antibiotics, and were not readmitted	NA
Bork *et al.* [84]	Retrospective Multicenter	Osteomyelitis (13) Endovascular infection (6) BSI (4) Septic arthritis (1) Prosthetic joint infection (1) Cardiac device infection (1) MRSA pneumonia (1) Pyelonephritis (1)	Clinical cure at 30-day was 71% (15/21 patients with available follow-up)	Acute kidney injury (2) Pruritus and rash (1)
Bryson-Cahn *et al.* [85]	Retrospective Single center	MSSA endocarditis (2) MRSA endocarditis (7) Osteomyelitis (7) Uncomplicated or complicated BSI (14) Septic arthritis (2)	Clinical response observed in 18/32 patients (56%)	NA
Buzón Martín *et al.* [86]	Retrospective Single center	Prosthetic joint infection (16)	Infection resolved in 12/16 patients (75%)	Mild skin rash (1) Mild transient leukopenia (1)

Bassetti M., et al. Curr Opin Infect Dis. 2021 Apr 1;34(2):96-108

Hidalgo-Tenorio *et al.* [87]	Retrospective Multicenter	Endocarditis (34) Uncomplicated or complicated BSI (49)	*Clinical cure of dalbavancin as consolidation therapy* Endocarditis (100%, 34/34) Uncomplicated or complicated BSI (100%, 49/49)	Asthenia (1) Self-limited rash (1) Fever with self-limited shivering (1) Impaired renal function (1)
Morata *et al.* [88]	Retrospective Multicenter	BJI with orthopedic implant (45) BJI without orthopedic implant (19)	*Success or improvement (missing = 1)* BJI with implant retention (100%, 23/23) BJI with implant removal (95.2%, 20/21) BJI without implant (89.5%, 17/19)	Gastrointestinal (3) Self-limited rash (1) Phlebitis (1) Self-reported asthenia (1) Increase of serum creatinine (1)
Morrisette *et al.* [52,53]	Retrospective Multicenter	*Numbers include both dalbavancin-treated and oritavancin-treated patients:* Osteomyelitis (15) Endocarditis (5) CRBSI (2) Pneumonia (2) Various other infections (14)	*Numbers include both dalbavancin-treated and oritavancin-treated patients for whom outcome data was available:* 92% clinical success (11/12) for osteomyelitis, 100% (3/3) for endocarditis, and 100% (2/2) for CRBSI	*The following mild AE include both dalbavancin-treated and oritavancin-treated patients:* Infusion reaction (1) Nausea (1) Chest tightness (1) Line infiltration with edema (1) Acute kidney injury (1) Headache (1)
Streifel *et al.* [89]	Retrospective Single center	Osteomyelitis (11) Joint infection (4) Uncomplicated or complicated BSI (12) Endocarditis (2)	*Outcome assessed in the entire cohort, n = 37, including also patients with ABSSSI* 30-day readmission for any reason (24%, 9/37) 30-day readmission due to recurrence of infection or potential AE of dalbavancin (5%, 2/37) Recurrence of infection (3%, 1/37)	*Assessed in the entire cohort, n = 37, including also patients with ABSSSI* Thrombophlebitis at the peripheral intravenous insertion site (1) Pruritus (1) Chest pain and acute on chronic increase in serum creatinine (1)

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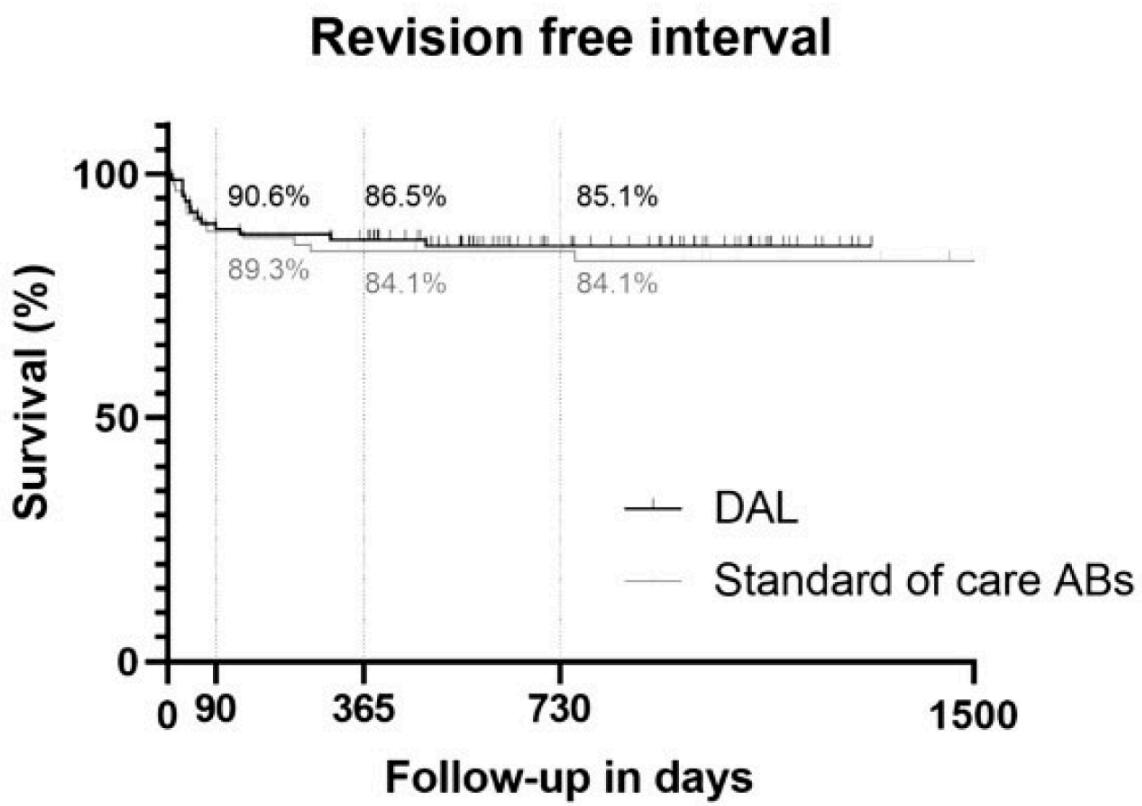

Figure 1. Kaplan–Mayer curve showing the relative (%) revision-free interval of knee and hip PJIs in the dalbavancin and Standard of Care antibiotics groups after 90, 365 and 730 days. DAL, dalbavancin; ABs, antibiotics.

Simon S., et al. J Antimicrob Chemother 2022; 77: 2274–2277

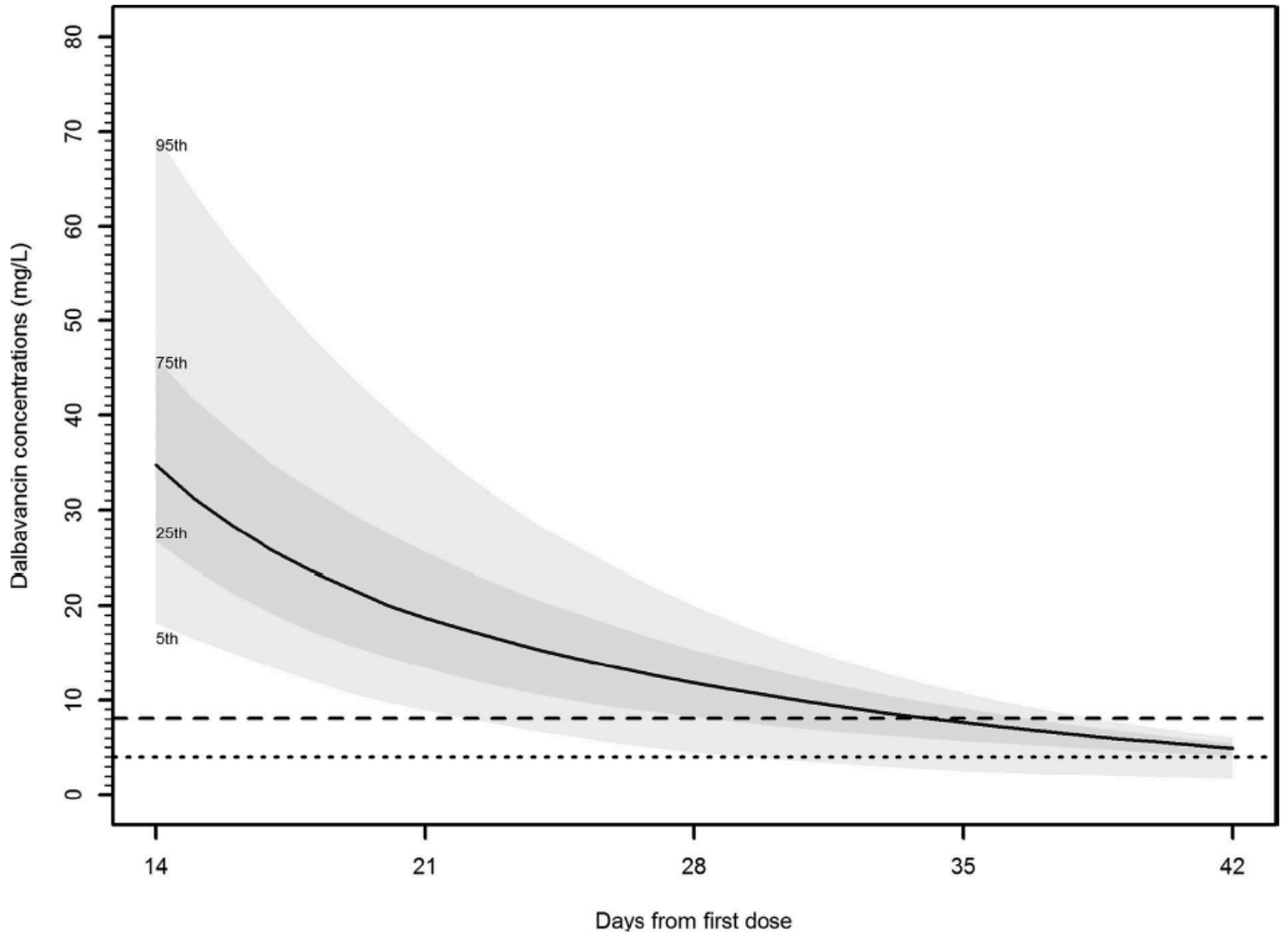

Fig. 1. Median and percentiles of the simulated total dalbavancin plasma concentrations estimated from Day 14 onwards in a previous population pharmacokinetic study with the two 1500 mg dalbavancin dosing regimen 1 week apart [9]. The dashed line refers to the threshold of total dalbavancin concentration of 8.04 mg/L, which may ensure a very high probability (≥90%) of optimal pharmacodynamic target attainment against *Staphylococcus aureus* with an MIC up to the EUCAST clinical breakpoint of susceptibility for dalbavancin (0.125 mg/L). The dotted line refers to the threshold of total dalbavancin concentration of 4.02 mg/L, which may ensure very high probability (≥90%) of optimal pharmacodynamic target attainment against *S. aureus* with an MIC up to the MIC_{90} (0.0625 mg/L). MIC, minimum inhibitory concentration; MIC_{90}, MIC required to inhibit 90% of the isolates; EUCAST, European Committee on Antimicrobial Susceptibility Testing.

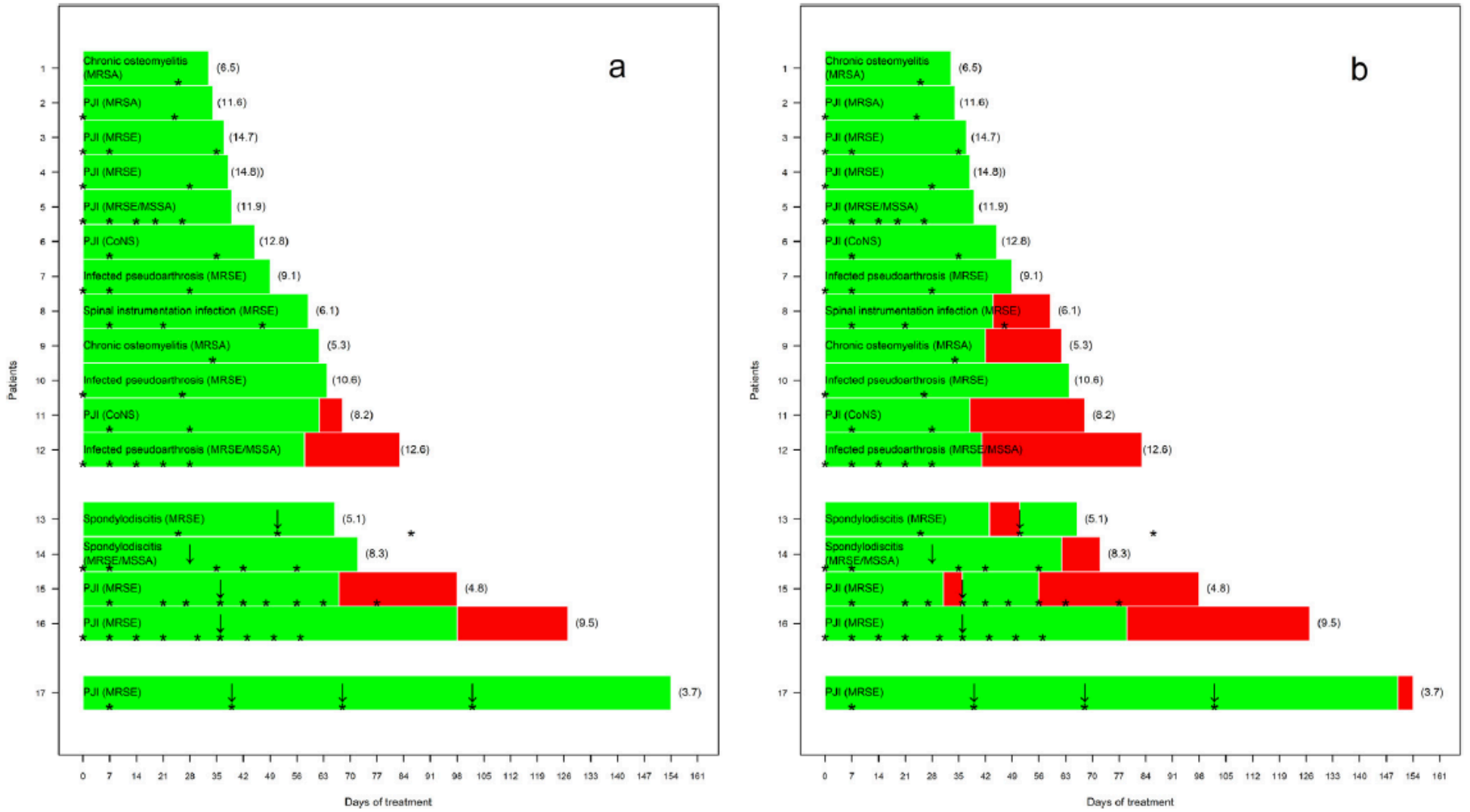

Fig. 1. Estimated distribution of time with dalbavancin concentrations above or below the pharmacokinetic/pharmacodynamic (PK/PD) efficacy thresholds of 4.02 mg/L (a) and 8.04 mg/L (b) during the overall treatment period in each patient. Green box, attainment of the PK/PD efficacy thresholds [≥4.02 or ≥8.04 mg/L, corresponding to an $fAUC_{24h}$/MIC ratio >111.1 against staphylococci with a minimum inhibitory concentration (MIC) of 0.06 and 0.125 mg/L, respectively]; red box, non-attainment of PK/PD efficacy thresholds (<4.02 or <8.04 mg/L, corresponding to an $fAUC_{24h}$/MIC ratio <111.1 against staphylococci with an MIC of 0.06 and 0.125 mg/L, respectively); arrows indicate timing of additional dalbavancin doses other than basic dosing regimen (namely 1500 mg on day 1 plus 1500 mg on day 8). Numbers in parentheses () are the months of follow-up elapsed since positive test of cure (TOC). *Time of TDM assessments. PJI, prosthetic joint infection; MRSA, methicillin-resistant *Staphylococcus aureus*; MRSE, methicillin-resistant *Staphylococcus epidermidis*; CoNS, coagulase-negative staphylococci; MSSA, methicillin-susceptible *S. aureus*.

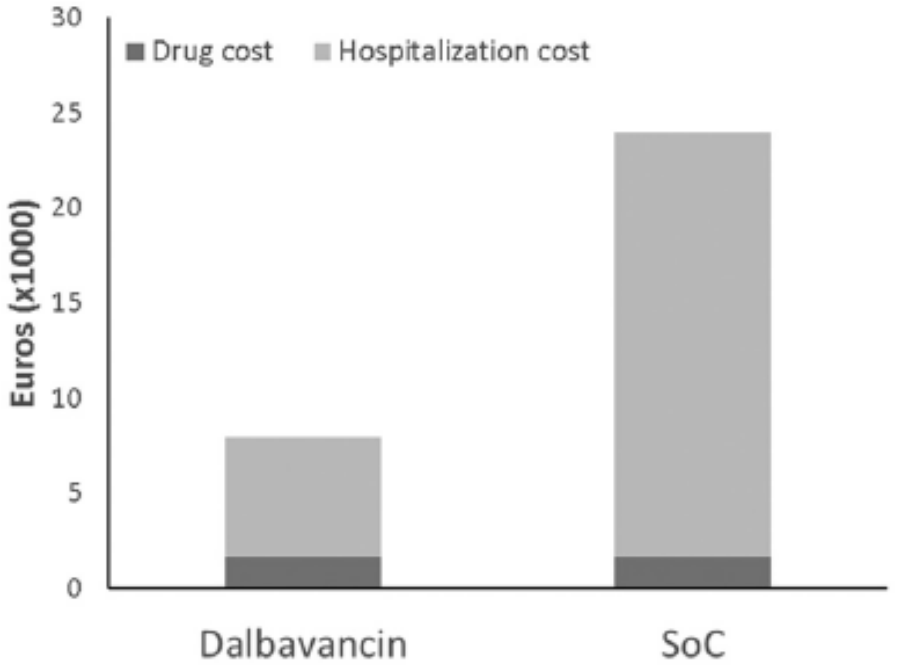

Fig. 2. Cost minimization analysis of patients treated with dalbavancin compared to SoC. SoC, standard of care.

Comparison of Sequential Dalbavancin With Standard-of-Care Treatment for *Staphylococcus aureus* Bloodstream Infections

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Background. Dalbavancin (DAL) is a long-acting lipoglycopeptide with activity against *Staphylococcus aureus,* including methicillin-resistant *S. aureus* (MRSA). This study investigates DAL as sequential therapy in *S. aureus* bloodstream infections (BSIs).

Methods. We conducted a retrospective cohort study from 2014 to 2021 comparing sequential DAL with standard-of-care therapy (SoC) for *S. aureus* BSI. The primary outcome was 90-day clinical failure (90-day all-cause mortality or 90-day recurrence). Secondary outcomes were incidence of acute kidney injury, creatinine phosphokinase elevations, catheter-related thrombosis, and hospital-acquired infections. Analyses were adjusted using inverse probability of treatment weighting (IPTW).

Results. Overall, 225 patients (45 DAL, 180 SoC) were included. DAL patients had a higher incidence of community-acquired infection and persons who use drugs; SoC patients had more comorbidities and a longer duration of bacteremia. MRSA incidence was similar between the DAL and SoC groups. The median length of stay was 16 days among DAL recipients compared with 24 days among SoC recipients. Central catheter placement was 17.8% compared with 57.2% in the SoC group. Ninety-day clinical failure occurred in 13.3% and 18.3% of participants in the DAL and SOC groups, respectively. In IPTW-adjusted analysis, sequential DAL was not associated with 90-day clinical failure (adjusted odds ratio, 0.94; 95% CI, 0.333–2.32).

Conclusions. This study provides preliminary evidence that select patients with *S. aureus* BSI treated with sequential DAL have similar clinical failure rates, with significant reductions in catheter placement and hospital length of stay compared with SoC. Further prospective evaluation is needed.

Keywords. long-acting lipoglycopeptides; MRSA; SAB; BSI.

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Characteristics of oritavancin

- Semisynthetic lipoglycopeptide
- Structurally similar to vancomycin
- May retain some activity in presence of VanA and VanB-mediated vancomycin-resistance

Brade KD, et al. Infect Dis Ther 2016; 5:1–15
Biavasco F, et al. Antimicrob Agents Chemother 1997; 41:2165–2172
Cooper RD, et al. J Antibiot (Tokyo) 1996; 49:575–581
Domenech O, et al. Biochim Biophys Acta 2009; 1788:1832–1840

Mechanism(s) of action

- Inhibition of transglycosylation (similar to vancomycin)
- Inhibition of transpeptidation (contributing to its activity against vancomycin-resistant strains)
- Membrane depolarization and permeabilization

Zhanel GG, et al. Drugs 2010; 70:859–886
Munch D, et al. Antimicrob Agents Chemother 2015; 59:772–781
Zhanel GG, et al. Clin Infect Dis 2012; 54(Suppl 3):S214–S219.

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Mechanism(s) of action

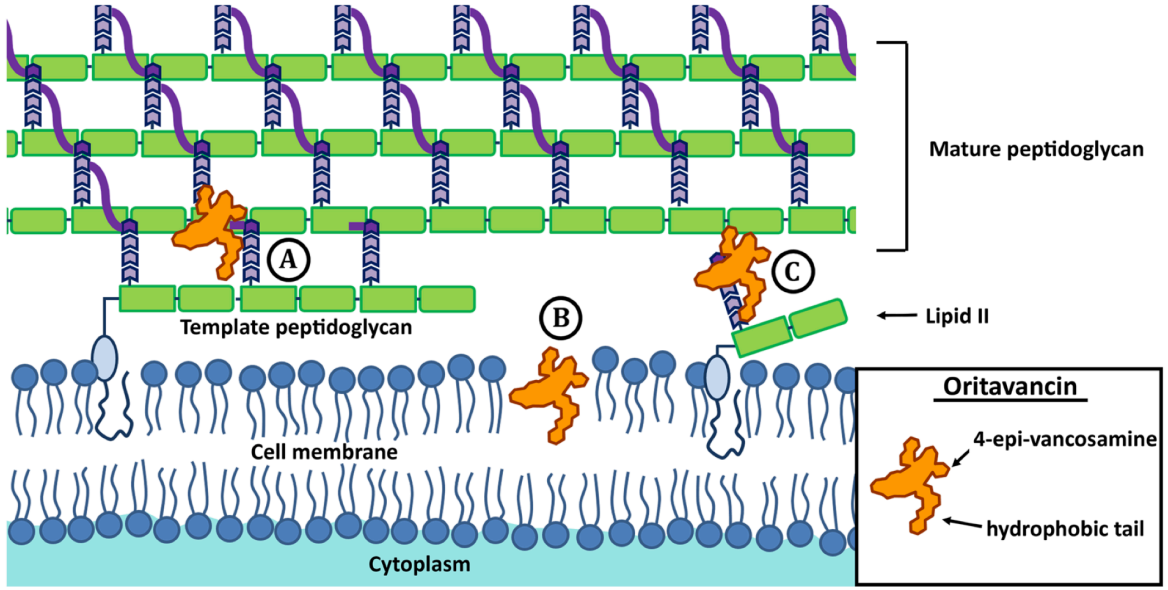

Fig. 3 Oritavancin bacterial binding sites. **a** Oritavancin binding to template peptidoglycan at cleft between hydrophobic tail group and 4-epi-vancosamine. **b** Oritavancin hydrophobic tail group insertion into bacterial cell membrane. **c** Oritavancin binding to D-alanyl-D-alanine stabilized by hydrophobic tail group

Brade KD, et al. Infect Dis Ther 2016; 5:1–15

PK characteristics

- Prolonged terminal half-life of 200–300 hours
- Large Vd and high protein binding (85–90%)
- Elimination mainly through the reticuloendothelial system (no adjustments for kidney or hepatic failure)

Rubino CM, et al. Antimicrob Agents Chemother 2015; 59:3365–3372.
Mitra S, et al. Infect Drug Resist 2015; 8:189–197
Brade KD, et al. Infect Dis Ther 2016; 5:1–15
Bassetti M, et al. Expert Opin Drug Saf 2019; 18:635–650

Drug interactions

- Oritavancin is a weak inhibitor of CYP2C9 and CYP2C19, and an inducer of CYP3A4 and CYP2D6
- Patients treated with warfarin and receiving oritavancin should be monitored for possible bleeding

Bassetti M, et al. Curr Opin Infect Dis 2021; 34:96-108

Alteration of lab tests

- Possible alterations of some coagulation tests in the first hours/days after oritavancin administration (e.g., prolonged PT and prolonged aPTT) because of interaction of oritavancin with the phospholipid reagent
- i.v. unfractionated heparin sodium is contraindicated for up to 5 days after oritavancin administration, owing to inability to reliably monitor coagulation tests
- The results of the chromogenic factor Xa and the thrombin time assays are not affected by oritavancin administration
- False increase in vancomycin concentrations

Bassetti M, et al. Curr Opin Infect Dis 2021; 34:96-108
Smelter FM, et al. J Clin Pharmacol 2022; 62:472-478
Belley A, et al. Antimicrob Agents Chemother 2017; 61:e01968–16

Indication and dosage (EMA)

- ABSSSI in adults
- 1,200 mg administered as a single dose by intravenous infusion over 3 hours (in glucose 5%)

https://www.ema.europa.eu/

Oritavancin - Efficacy in RCTs

Study [ref] (type of study)	Investigational drugs (dosage)	Comparator/s (dosage)	Primary endpoint	Disease and study population of the primary analysis	Cured/total (rates, %)	Percent difference (95% CI)
SOLO I [45] (noninferiority)	Oritavancin (1200 mg i.v. on day 1)	Vancomycin (15 mg/kg q12h i.v. for 7–10 days)	*Early clinical response* (cessation of spreading or a reduction in the size of the baseline lesion, the absence of fever, and the absence of a need for rescue antibiotic medication; assessed at 48–72-h)	ABSSSI *MITT population* Oritavancin Vancomycin	 391/475 (82.3) 378/479 (78.9)	 3.4 (−1.6 to 8.4) Reference
SOLO II [44] (noninferiority)	Oritavancin (1200 mg i.v. on day 1)	Vancomycin (15 mg/kg q12h i.v. for 7–10 days)	*Early clinical response* (cessation of spreading or reduction in the size of the baseline lesion, absence of fever, and no rescue antibiotic medication; assessed at 48–72-h)	ABSSSI *MITT population* Oritavancin Vancomycin	 403/503 (80.1) 416/502 (82.9)	 −2.7 (−7.5 to 2.0) Reference

Corey GR et al. N Engl J Med 2014; 370:2180–2190
Corey GR et al. Clin Infect Dis 2015; 60:254–262
Bassetti M et al. Curr Opin Infect Dis 2020; 33:110-120

Safety in RCTs

- Safety of oritavancin in the SOLO studies was similar to vancomycin (most common AEs were nausea and headache in both arms)
- SAE were 7.4% for oritavancin vs. 7.3% for vancomycin in SOLO I
- SAE were 4.4% for oritavancin vs. 4.6% for vancomycin in SOLO II

Corey GR, et al., N Engl J Med 2014; 370:2180–2190
Corey GR, et al., Clin Infect Dis 2015; 60:254–262

Table 1. Characteristics of published studies on the use of oritavancin for indications other than acute bacterial skin and skin structure infections[a]

Reference	Type of study	Type of infections other than ABSSSI treated with oritavancin (no. patients)	Outcome/s data	Safety data AE (no. patients)
Stewart *et al.* [50]	Retrospective Single center	MSSA BSI (5) MRSA bursitis (1) Group B streptococcal BSI with infective endocarditis (1) CoNS bacteremia (1) MSSA deep tissue infection (1) *Enterococcus* spp. BSI (1)	7/10 Patients (70%) were successfully treated	Nausea (2) Hearing loss (1)
Co *et al.* [43]	Retrospective Single center	Cardiac device infection (7) Diabetic foot infection (3) Osteomyelitis (8) Bacteremia (3)	No readmission within 14 days	NA
Schulz *et al.* [51]	Retrospective Single center	MRSA pneumonia (2) Osteomyelitis (4) VRE hepatic abscess (1) *Staphylococcus lugdunensis* endovascular graft infection (1) VRE bacteremia (1)	Success or improvement in 9/9 cases (100%)	*Assessed in the entire cohort, n = 17, including also patients with ABSSSI* Infusion-related infections (2) Anemia and leukopenia (1)
Chastain and Davis [16]	Retrospective Single center	Osteomyelitis (9)	Clinical cure in 9/9 cases (100%) at 6-month follow-up	No treatment-emergent AE reported
Morrisette *et al.* [52,53]	Retrospective Multicenter	*Numbers include both dalbavancin-treated and oritavancin-treated patients:* Osteomyelitis (15) Endocarditis (5) CRBSI (2) Pneumonia (2) Various other infections (14)	*Numbers include both dalbavancin-treated and oritavancin-treated patients for whom outcome data was available:* 92% clinical success (11/12) for osteomyelitis, 100% (3/3) for endocarditis, and 100% (2/2) for catheter-related bacteraemia	*The following mild AE include both dalbavancin-treated and oritavancin-treated patients:* Infusion reaction (1) Nausea (1) Chest tightness (1) Line infiltration with edema (1) Acute kidney injury (1) Headache (1)

Bassetti M., et al. Curr Opin Infect Dis. 2021 Apr 1;34(2):96-108

Table 1 (*Continued*)

Reference	Type of study	Type of infections other than ABSSSI treated with oritavancin (no. patients)	Outcome/s data	Safety data AE (no. patients)
Brownell *et al.* [42]	Retrospective Single center	Osteomyelitis/septic arthritis (10) Diabetic foot infection (3) Endocarditis (4) Line infection (2) Pneumonia (5) Prosthetic device infection (4) Sepsis (5) Surgical wound infection (12) Other (5)	*Clinical cure or improvement* Osteomyelitis/septic arthritis (100%, 10/10) Diabetic foot infection (100%, 3/3) Endocarditis (100%, 4/4) Line infection (100%, 2/2) Pneumonia (100%, 5/5) Prosthetic device infection (3/3, 100%, 1 missing) Sepsis (3/5, 60%) Surgical wound infection (11/12, 91.7%) Other (4/5, 80%)	Any AE (5) The most frequent AE was back pain (3/75, including also patients with ABSSSI at the denominator)
Van Hise *et al.* [55]	Retrospective Multicenter	Osteomyelitis (134)	Clinical success at the end of treatment (118/134, 88.1%) Relapse or persistent infection (13/134, 9.7%)	Hypoglycemia (3) Tachycardia (1) Tachycardia with chest pain (1)
Redell *et al.* [48]	Retrospective Multicenter	Primary bacteremia (5) Osteomyelitis (18) Septic Arthritis/synovitis (4) Prosthetic joint infection (3) Infected bursa (3) Catheter exit site (1) Maxillary sinus infection (1) Hardware, posterior lumbar tissue (1) Lymphadenitis (1)	In patients with osteomyelitis receiving single-dose oritavancin for completion of treatment, clinical success or improvement was observed in 9/10 cases (90%) Clinical success in patients receiving oritavancin for joint infections was 71.4% (5/7)	*Assessed in the entire cohort, n = 440, including also patients with ABSSSI* Any AE (29) Pruritus (14) *Six AE leading to discontinuation* Infusion site reaction (2) Pruritus, urticaria, and headache (1) Urticaria and pruritus (1) Headache and throat tightness (1) Back pain and flushing (1)
Ahiskali and Rhodes [54]	Retrospective Single center	Bone or joint infections (14) Endocarditis (2) Isolated BSI (3)	*Outcome includes also patients with ABSSSI* Clinical cure was observed in 19/24 patients (79%)	*Assessed in the entire cohort, n = 24, including also patients with ABSSSI* Infusion-related reaction (1) Abdominal pain (1)

Bassetti M., et al. Curr Opin Infect Dis. 2021 Apr 1;34(2):96-108

Discussion

- Clinical need
- Lack of large RCT
- Good response rates in available experiences
- Need for economic studies
- Comparison with other new options

ABSSSI

	Switch to oral therapy and early discharge	Poor adherence to outpatient therapy	Avoidance of hospitalization	Low risk of CDI	Patients with kidney impairment	Allergy to β-lactams
APPROVED						
Tedizolid	✓		✓	✓	✓	✓
Ceftaroline					✓	
Delafloxacin	✓					✓
Omadacycline	✓		✓		✓	✓
Dalbavancin		✓	✓	✓		✓
Oritavancin		✓	✓	✓		✓
Telavancin				✓		✓
IN DEVELOPMENT						
Ceftobiprole					✓	
Iclaprim	✓		✓	✓	✓	✓
Brilacidin				?	?	✓
Gepotidacin				?	?	✓
Afabicin	✓		✓	?	?	✓
CG-549	✓		✓	?	?	✓
Cefilavancin				?	?	
TNP-2092				?	?	✓
Radezolid	✓		✓	?	?	✓
Contezolid	✓		✓	?	?	✓
Lefamulin					✓	✓
Levonadifloxacin	✓		✓	?	?	✓
Avarofloxacin	✓		✓	?	?	✓

Giacobbe et al. Curr Opin Infect Dis 2020

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Investigational agent	Phase II studies for ABSSSI	Other indications (development phase)
Brilacidin	X	Oral mucositis (II)/Ulcerative colitis (I-II)
Lefamulin	X	CABP (FDA approved)
Afabicin	X	Staphylococcal BJI (II)
CG-400549	X	
Delpazolid		Pulmonary tuberculosis (II)
Radezolid	X	Acne vulgaris (I)
Contezolid	X	ABSSSI (III in China)
Levonadifloxacin		ABSSSI (III in India)
Avarofloxacin	X	
TNP-2092	X	
Gepotidacin	X	uUTI (III), urogenital gonorrhoea (III)
Cefilavancin	X	
Exebacase		*S. aureus* BSI/right-sided endocarditis (II)
SAL200		Persistent *S. aureus* BSI (II)
Monoclonal antibodies		Various (see text)

Bassetti et al. Expert Opinion on Investigational Drugs 2020, DOI: 10.1080/13543784.2020.1750595

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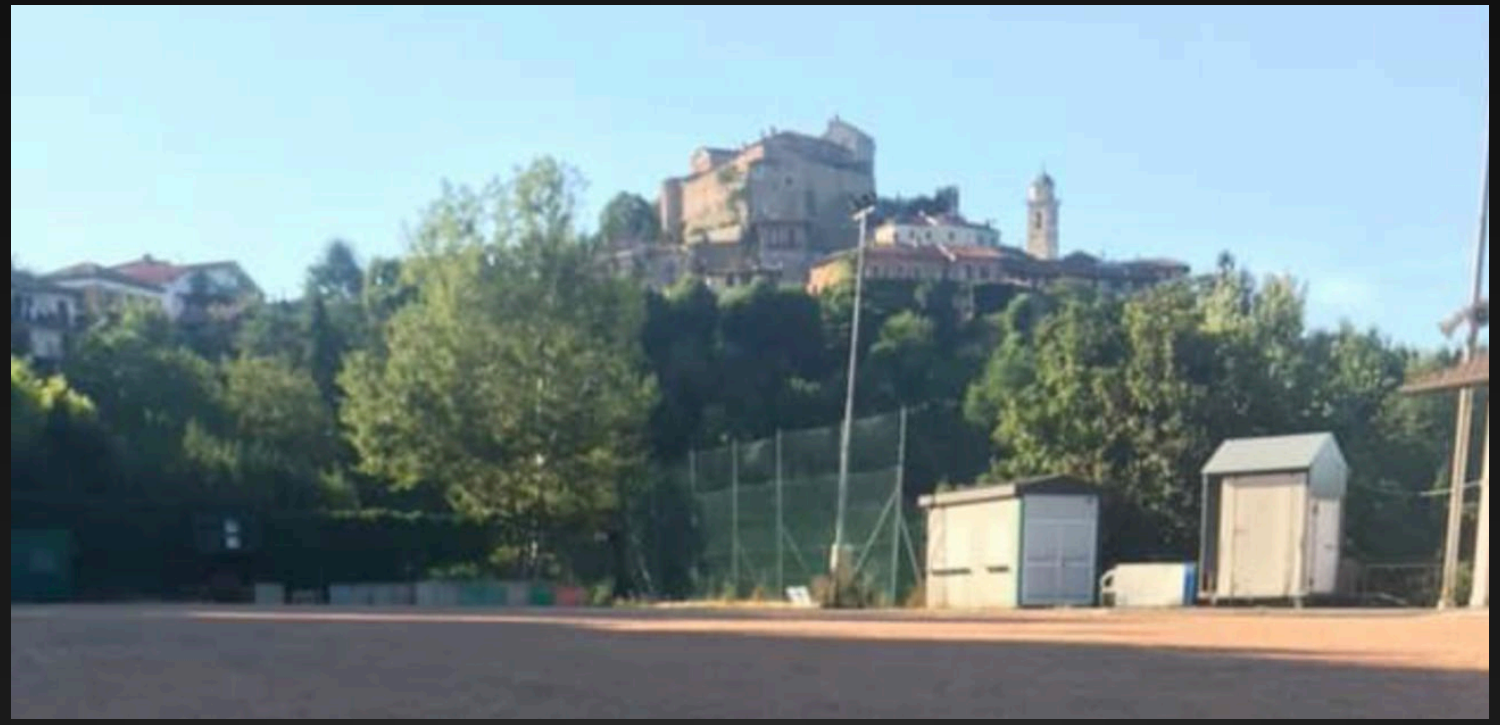
Thank you



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