Dalbavancina

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Conflict of interest

Nothing to declare.

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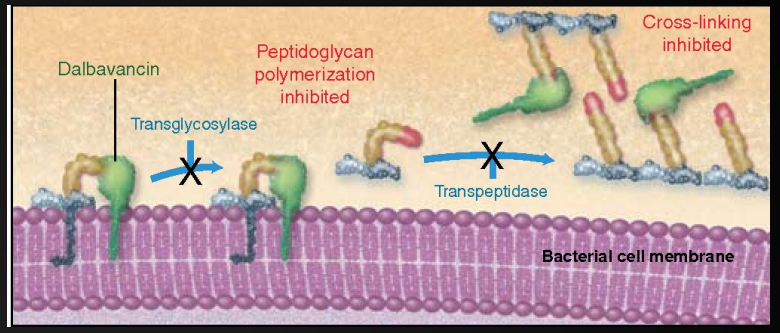
Pharmacology
Dalbavancin



- Semysynthetic lipoglycopeptides
- Binds to the **D-alanyl-D-alanine** terminus of cell wall peptidoglycan inhibiting crosslinking
- **AUC/MIC** predictor of pharmacodynamic activity

FDA access.gov (access package inserts dalbavancin)

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Proprierties of Dalbavancin

CHARACTERISTICS	
Dosing FDA approved	Single dose 1500 mg or 1 gram X 1 followed by 500 mg q 1 week
Infusion time	30 minutes
Half life	150-250 hours
Renal dose adjustment	Requires dose adjustment at CrCl<30ml/min
Drug-drug interactions	No clinically relevant DDI
Spectrum of activity	Gram-positive organisms including van-B VRE

FDA access.gov (access package inserts dalbavancin)
Zhanel GG et al. Drugs 2010; 70: 859-86

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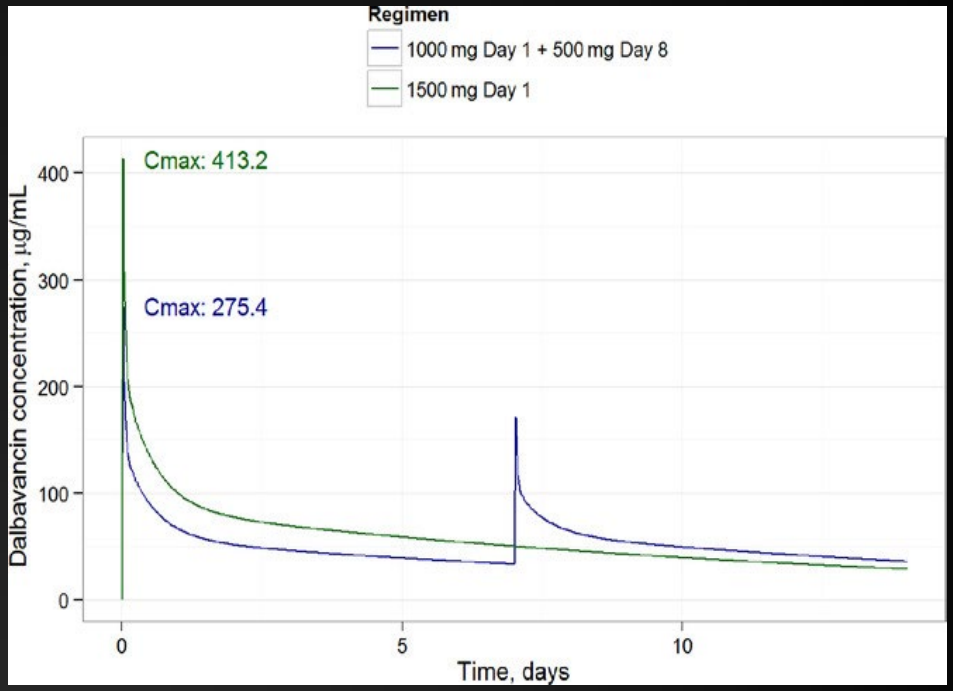
Dalbavancin PK/PD in details

- 3-compartment distribution model w/first- order elimination
- Vs ~ 15 L; 93% protein bound
- Only factors maiorly PK is severe renal impairment.
- >99% target attainment up to MIC of 2 mcg/mL
  - ➢ Breakpoints: MIC ≤ 0.25 mcg/mL



MIC_{90} *S. aureus*= 0.12 mcg/mL

Carrothers TJ, et al. Clin Pharmacol Drug Dev 2020
Andes D, et al AAC 2007

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Clinical application based on pharmacological properties

- Facilitate early discharge, thus decreasing HLOS
- Suppression therapy
- Alternative to protracted courses of oral therapy (especially in patients with low adherence to treatment)
- Facilitate discharge in patient **NOT a candidate** for home health or PICC placement

Personal view

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Currently FDA and EMA approval for dalbavancin

Once-Weekly Dalbavancin versus Standard-of-Care Antimicrobial Regimens for Treatment of Skin and Soft-Tissue Infections

Elyse Seltzer, Mary Beth Dorr, Beth P. Goldstein, Marc Perry, James A. Dowell, Tim Henkel, and the Dalbavancin Skin and Soft-Tissue Infection Study Group[a]
Vicuron Pharmaceuticals, King of Prussia, Pennsylvania

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 5, 2014 VOL. 370 NO. 23

Once-Weekly Dalbavancin versus Daily Conventional Therapy for Skin Infection

Helen W. Boucher, M.D., Mark Wilcox, M.D., George H. Talbot, M.D., Sailaja Puttagunta, M.D., Anita F. Das, Ph.D., and Michael W. Dunne, M.D.

Boucher TJ, et al. NEJM 2014
Seltzer et al. Clin Infect Dis 2014

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Real life mismatch

Area of need Vs Registration trial

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Highly pressing scenarios in which dalbavancin could play an important role

- **Complicated and uncomplicated BSIs**
  - Including IE and cardiac device-related infections
- **Acute and chronic bone and joint infections**
  - With and without foreign material
  - Vertebral osteomyelitis and spondylodiscitis
  - Acute and chronic PJI
- **Other specific situations…**

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Dalbavancin is an effective treatment option for CR-BSIs

Efficacy and Safety of Weekly Dalbavancin Therapy for Catheter-Related Bloodstream Infection Caused by Gram-Positive Pathogens

- 75 adults with CR-BSI caused by CoNS or *S. aureus* randomized to either dalbavancin or vancomycin (1 g bid 14 d)
- **CVC removal:** mandatory for *S. aureus;* discretionary for CoNS.

Overall success rate:

87% Dalbavancin Vs 50% Vancomycin (p= 0.05) **regardless** of catheter removal.

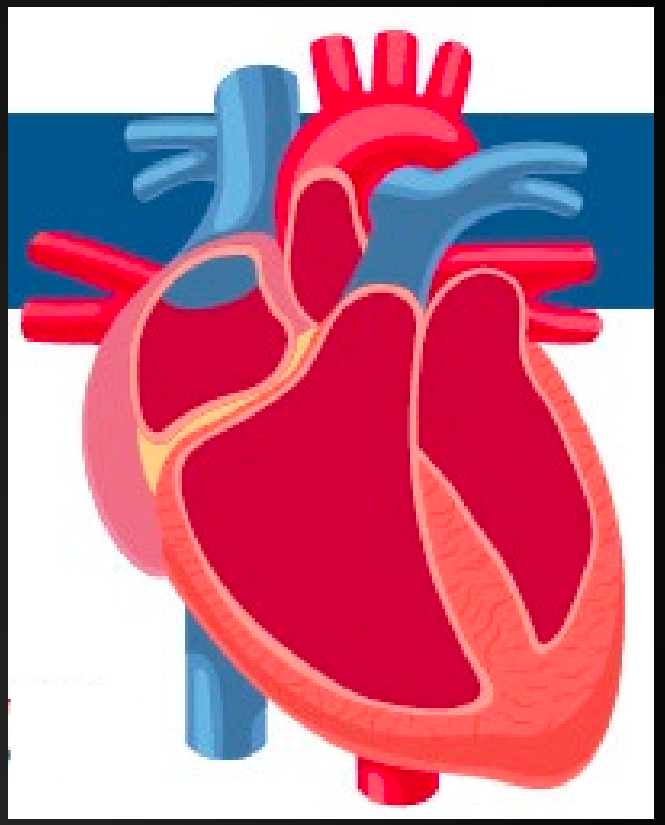
Dalbavancin and infective endocarditis (at least 5 cases)

Ref.	n	NV/PV/CD	Bacteria	Dosing	Success
Tobudic, 2018	27	15/7/5	*S. aureus* (9), CoNS (7), *E. faecalis* (4), other (9)	1,5 g LD then 1 g every 2 wk or 1g LD then 500 mg wk	93%
Bouza, 2018	7	Not specified	*S. aureus* (1), CoNS (2), *Enterococcus* (2), other (2)	1 g LD then 500 mg weekly	86%
Hidalgo-Tenorio ,2019	34	11/15/8	*S. aureus* (10), CoNS (15), *E. faecalis* (3), other (7)	1 g once or 1,5 g LD then 500 mg at day 8	97%
Bryson-Cahn,2019	9	9/-/-	S. aureus (9	1 g once or 1,000– 1,5 g LD then 500 mg day 7	100%
Wunsch,2019	25	15/6/4	Not specified	1 g LD then 500 mg weekly or 1,5 g once or 1,5 g weekly × 2g	92%
Dinh,2019	19	9/10/-	Not specified	1,5 g once or 1,5 g LD then 1–1,5 g at day 7	68%
Bork,2019	7	Not specified	Not specified	Not specified	57%
Veve,2020	12	Not specified	Not specified	1 g once or 1,000– 1,5 g LD then 500 mg day 7	91%

Dalbavancin and infective endocarditis

…in conclusion..

- 8 studies, n =140 patients
- Native valve (n=59), prosthetic valve (n=38) and cardiac device related (n=18)
- *S. aureus* (n=29), CoNS (n=24), *Enterococcus* (n=9)
- Dalbavancin as a second-line agent for consolidation therapy >>>>rescue therapy.
- **Success: 88%** **(ranges from 57% to 100%)**



Tran T. et al. AAC 2022

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Dalbavancin as a suppressive therapy

Dalbavancin as chronic antibiotic suppression therapy for left ventricular assist device driveline infection due to methicillin-resistant *Staphylococcus aureus*: a case report

34 weeks of dalbavancin!

Dalbavancin as long-term suppressive therapy for patients with Gram-positive bacteremia due to an intravascular source—a series of four cases

1 prosthetic valve IE
2 LVAD infection
1 TAVI

Lenght of therapy:
5-52 weeks

1 patient developed *E. faecalis* Vanco-S BSI

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Pallotto G. et al. J. Chemother. 2022
Hitzenbichler F et al. Infection 2021

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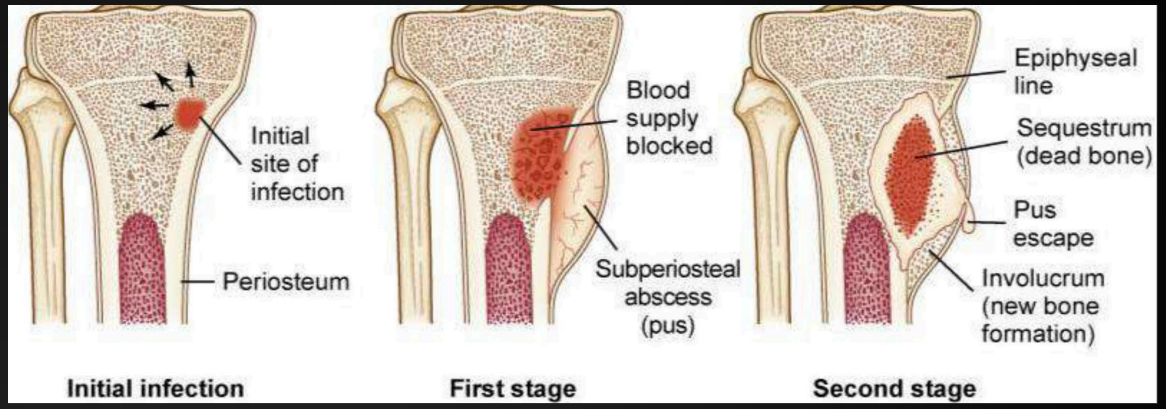
Dalbavancin for non-implant-related acute or chronic osteomyelitis

- Patients were randomized 7:1 to dalbavancin (1500 mg IV on d 1 and 8) or SOC (vancomycin followed by oral linezolid or FQ) for osteomyelitis per investigator judgment for 4-6 weeks

- All eligible patients underwent surgical debridement at baseline and had **a Gram-positive pathogen** recovered from a bone culture.



- **Primary outcome:** clinical response at day 42, defined as recovery without need for additional antibiotics in the clinically evaluable (CE) population.
- **Secondary outcome**: Clinical response at day 21, 6 months, and 1 year.

Rappo U et al Open Forum Infect Dis. 2018

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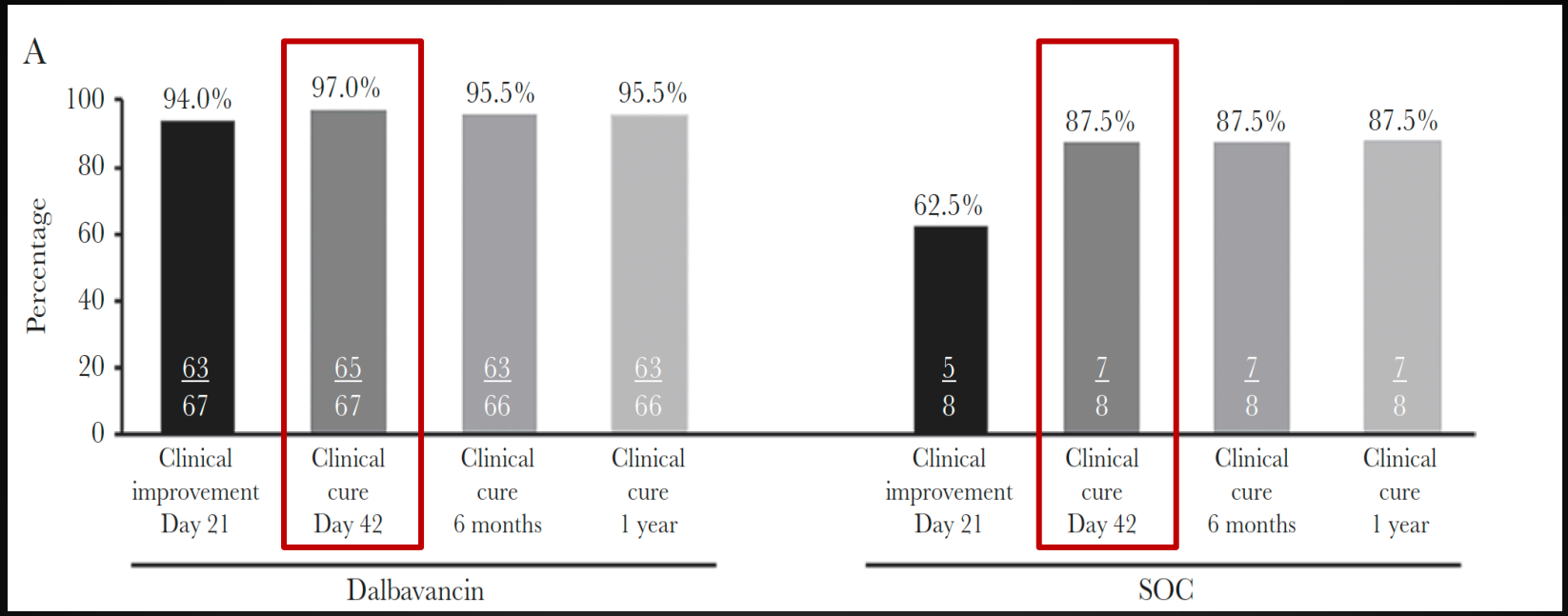
Clinical outcomes in the clinically evaluable populations.



- A 2-dose regimen of weekly dalbavancin **is effective** and well tolerated for the treatment of osteomyelitis in adults.

Rappo U et al Open Forum Infect Dis. 2018

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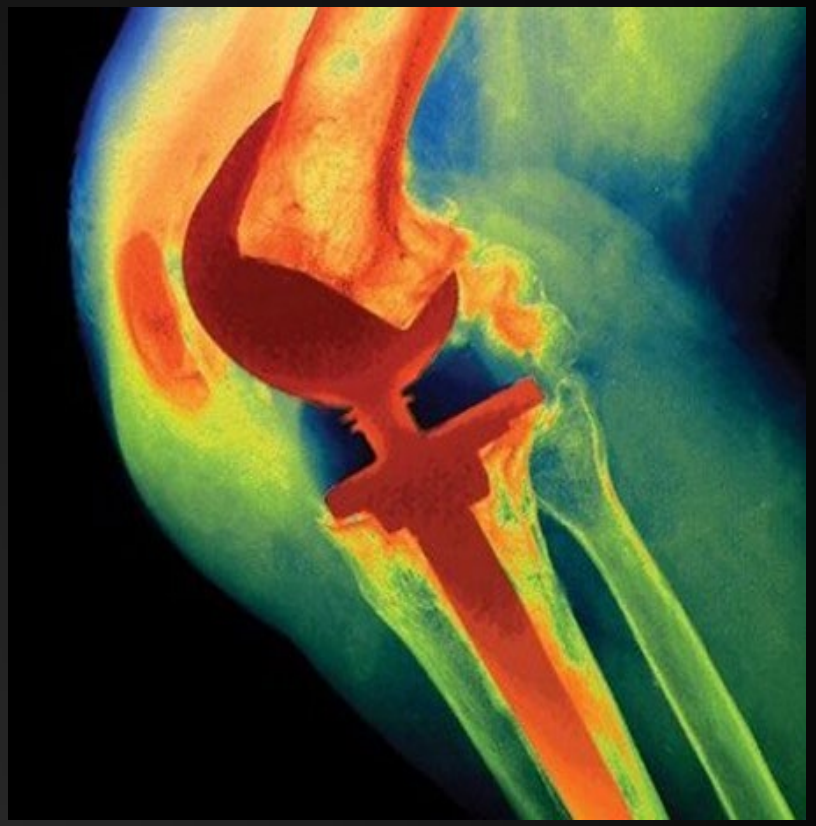
Bone and Joint infections

- 12 studies, n =463 patients
- Prosthesis associated infections in 149 patients (32.1%)
- *S. aureus* (n=113), CoNS (n=90), *Enterococcus* (n=28)
- Dalbavancin as a second-line agent for consolidation therapy >>>>salvage therapy.
- **Success: 79%** **(range from 47% to 97%)**



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Effectiveness of Dalbavancin Compared With Standard of Care for the Treatment of Osteomyelitis: A Real-world Analysis

Alexander R. Cain,[o] Derek N. Bremmer,[o] Dustin R. Carr,[o] Carley Buchanan, Max Jacobs, Thomas L. Walsh, Matthew A. Moffa,[o] Nathan R. Shively,[o] and Tamara L. Trienski

- Matched cohort (1:2 according to the Charlson Comorbidity Index, site of infection, and causative pathogen) Dalbavancin (2 doses 1 week apart; n=42) to SOC (n=90)
- **Key results**
  - Treatment success at 1 year similar (79% vs 77%)
  - Shorter LOS with dalba (5.2 days vs 7.2 days; p = .01)
  - **17.8%** of patients in SOC had **PICC-line complications!**

Cain AR et al Open Forum Infect Dis. 2022

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Other opportunities…

1

ORIGINAL RESEARCH

A Dalbavancin Lock Solution Can Reduce Enterococcal Biofilms After Freezing

2

Postexposure Prophylaxis and Treatment of *Bacillus anthracis* Infections: A Systematic Review and Meta-analyses of Animal Models, 1947–2019

Jordan L. Kennedy,[1] Jürgen B. Bulitta,[2] Kevin Chatham-Stephens,[3] Marissa K. Person,[1] Rachel Cook,[4] Thitipong Mongkolrattanothai,[4] Eunjeong Shin,[2] Patricia Yu,[5] Maria E. Negron,[1] William A. Bower,[1,*] and Katherine Hendricks[1]

3

Letter to the Editor

Long-term use of repeated doses of dalbavancin as prophylaxis for recurrent Gram-positive bacteraemic cellulitis

F. Escrihuela-Vidal [1], E. Benavent [1], O. Servitje [2], E. Gonzalez-Barca [3], R. Rigo-Bonnin [4], O. Murillo [1,*]

4

Short Communication

Clinical experience with dalbavancin for the treatment of deep sternal wound infection

Michele Bartoletti[a,*], Elisa Mikus[b], Renato Pascale[a], Maddalena Giannella[a], Sara Tedeschi[a], Simone Calvi[b], Elena Tenti[c], Fabio Tumietto[a], Pierluigi Viale[a]

SAFETY

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Adverse events

- AEs documented are typically mild (e.g. GI, headache, non severe rash) and infrequent in occurrence **(3-11%)**

- **Lack of cross reactivity** demonstrated in patients with history of **vancomycin-associated DRESS** (HLA-A32:01-positive individuals)

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Nakkam N, et al. J Aller Clin Immunol 2020
Freeman K, et al. OFID Nov 2021 (Abstract)

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COST-EFFECTIVINESS

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Is it cost-effectiveness?

The overall cost reduction of dalbavancin treatment has been estimated at €3064 per patient.

Bouza E., Vena A Int J Infect Dis 2017

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Conclusions

- The tale of the dalbavancin illustrates the increasing complexity of AB use and the ever-growing need for high-quality data to inform clinical decisions aimed to optimize critical antimicrobials.

- Its remarkable PK/PD characteristics make dalbavancin attractive as alternatives that may facilitate quicker hospital discharge, limit long-term iv accesses, and decrease the need for strict outpatient FU.

- Nevertheless, further high-quality clinical data should be obtained in order to consolidate the broader than labeled use generally done by clinicians and institutions.

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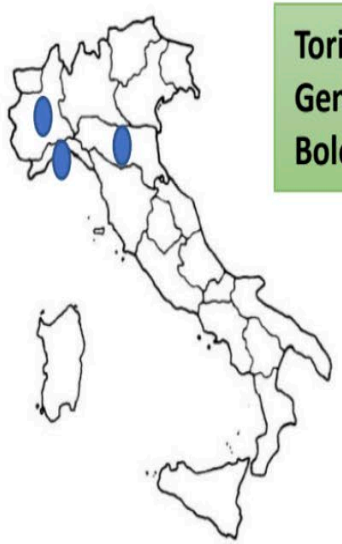
1° Edizione Observership SITA GIOVANI

L'observership SITA giovani si rivolge ai giovani infettivologi; 2 giorni di corso

- Clinico (round)
- Educativo (lezioni frontali e casi clinic)
- Ricerca clinica (progetto ricerca SITA Giovani)



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