A REVIEW OF DALBAVANCIN USE IN NHS GRAMPIAN

OPAT REGIONAL WORKSHOP GLASGOW 2023

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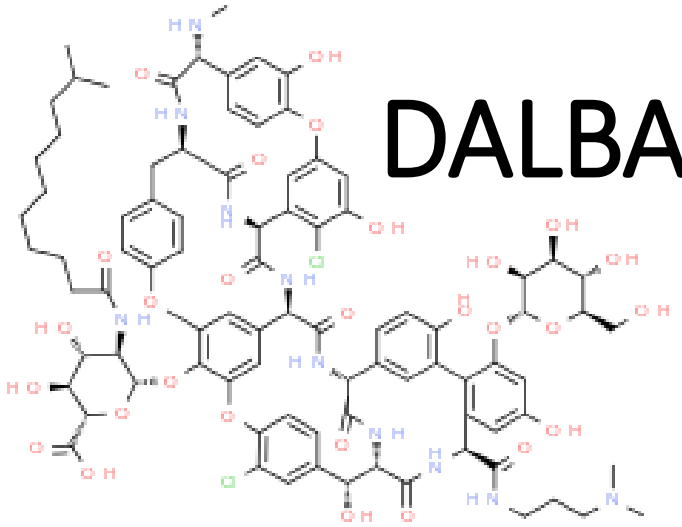
OPAT Outpatient Parenteral Antimicrobial Therapy



DALBAVANCIN

- Long acting lipoglycopeptide, bactericidal activity against Gram-positive bacteria with minimal reported side effects.
- Licensed for acute bacterial skin and skin structure infection.
- Administered parenterally, single 30 minute infusion using dextrose 5% via cannula - removes longer term IV Access requirement.
- Extended interval antibiotic suitable for single dose or two dose regimens – useful in OPAT.
- Limited published scientific data on its use for other indications however considerably large practical experience in its use, based on expert consensus

NHS GRAMPIAN SERVICE: DALBAVANCIN

Consultant-led that assists by

Facilitating quicker discharge

- Referral from any inpatient wards
  - Based on oncall ID Consultant/Reg recommendation
  - Via duty microbiologist suggestion/advice
  - Various discipline that refer to OPAT: enables OPAT ID Team to review, suggest and manage antibiotics (promotes AMS)
  - Direct referral from ID Unit

Avoiding admission altogether

- Adapting SAPG Cellulitis Pathway in ED/Acute Medical Initial Assessment/Observation Unit
  - Referral to OPAT Clinic - First dose IV antibiotics given as per guidelines, patient referred to OPAT Clinic.
  - Followed up and managed under OPAT clinic

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NHS GRAMPIAN SERVICE: DALBAVANCIN DOSING AS PER SAPG

OPAT Outpatient Parenteral Antimicrobial Therapy

Licensed indication(s) in the OPAT setting	Dose
Acute bacterial skin and skin structure infections	Day 1; 1000mg one-off dose and review on Day 8 for consideration of oral therapy or further 500mg one-off dose **OR** Day 1; 1500mg one-off dose (equivalent to a 2 week course of treatment)

Off-label indications in the OPAT setting	Dose
Uncomplicated *Staphylococcus aureus* bacteraemia (no deep source of infection identified or suspected and clinically well)	• If suitable for OPAT and it is 7 days or less since last positive blood culture; 1500mg one-off dose • If suitable for OPAT and it is more than 7 days since last positive blood culture; 1000mg one-off dose
Bone and joint infection (eg first stage revision of joint)	1500mg dosed on Day 1 and repeated on Day 8 Equivalent duration 4-6 weeks
Bone and joint infection (eg debridement and implant retention)	1000mg one-off dose on Day 1 then 500mg on Day 8 and weekly thereafter Duration dependent upon source of infection and availability of oral antibiotic options
Infective Endocarditis (Native and Prosthetic valves)	1000mg one-off dose on Day 1 then 500mg on Day 8 and weekly thereafter Duration usually to complete 6 weeks total effective therapy

Table adapted from SAPG Good Practice Prescribing Guide Feb 2023

NHS GRAMPIAN SERVICE: CHOOSING DALBAVANCIN

Various factors influence decision making:

- Primarily decided by ID Consultant/OPAT ID Consultant on rota
- Based on microbiology and sensitivities (where available)
- Patient specific parameters (elderly, comorbidities, dexterity for self administration, living alone)
- Patient geographical location (linking with community hospitals)
- IVDU patients (no other means available in Grampian)
- Influence of hospital capacity
- Cost
  - Grampian Finance Department quote £554 per night of hospital stay, per vial dalbavancin approximately £560
  - Once daily antibiotics - risk of line infection, does incur cost even in OP setting, utilizes specialist nurse resources

Experience with Dalbavancin in various Gram-positive infections at ARI OPAT Service

Background:

- Retrospective observational study at Aberdeen Royal Infirmary
- 9 months (December 2021 – October 2022)
- All patients receiving ≥1 dose dalbavancin and ≤48 hours of other active agents were eligible :- 102 patients
- Key demographics were age, sex, Charlson comorbidity index (CCI), drug allergies, causal pathogens, dosing regimen, surgery
- Primary outcome :- cure ?
- Secondary outcomes :- adverse events ? primary or consolidation therapy ?

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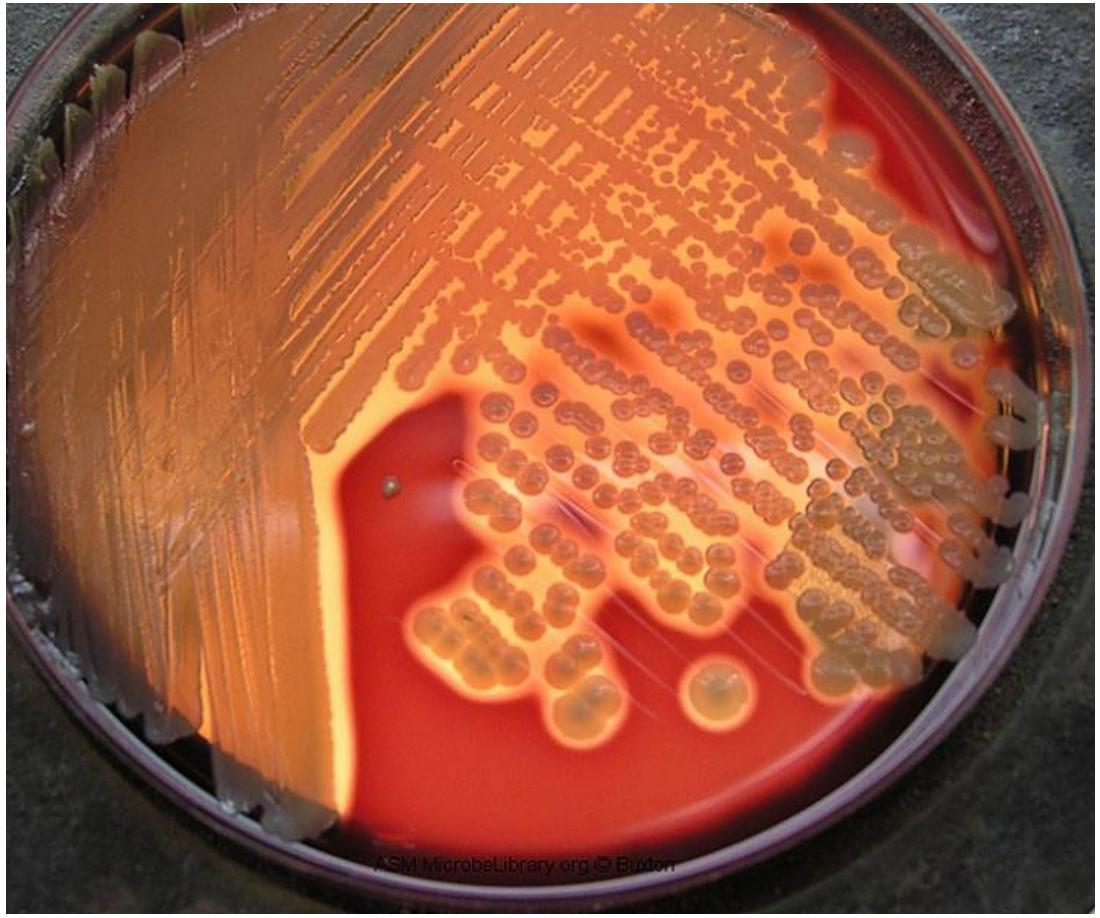
PATIENTS TREATED	TOTAL	CLINICAL FAILURES	CURES	IMPROVED	PRIMARY DALBAVANCIN
Age (range)	31-97				
Sex (M/F)	(71/31)	(12/7)	(50/19)	(9/7)	
1. ABSSSI	45	3	42	0	34
2. OSTEOMYELITIS	35	14	9	13	24
3. SEPTIC ARTHRITIS	10	2	5	3	4
Native joint	4	0	3	1	1
Prosthetic joint	6	2	2	2	3
4. BACTERAEMIA	12	0	12	0	0
Endovascular graft	1	0	1	0	0
IV drug abuse	4	0	4	0	0
Dental extraction	1	0	1	0	0
Pneumonia	1	0	1	0	0
Discitis	2	0	1	0	0
ABSSSI	2	0	2	0	0
Other	1	0	1	0	0

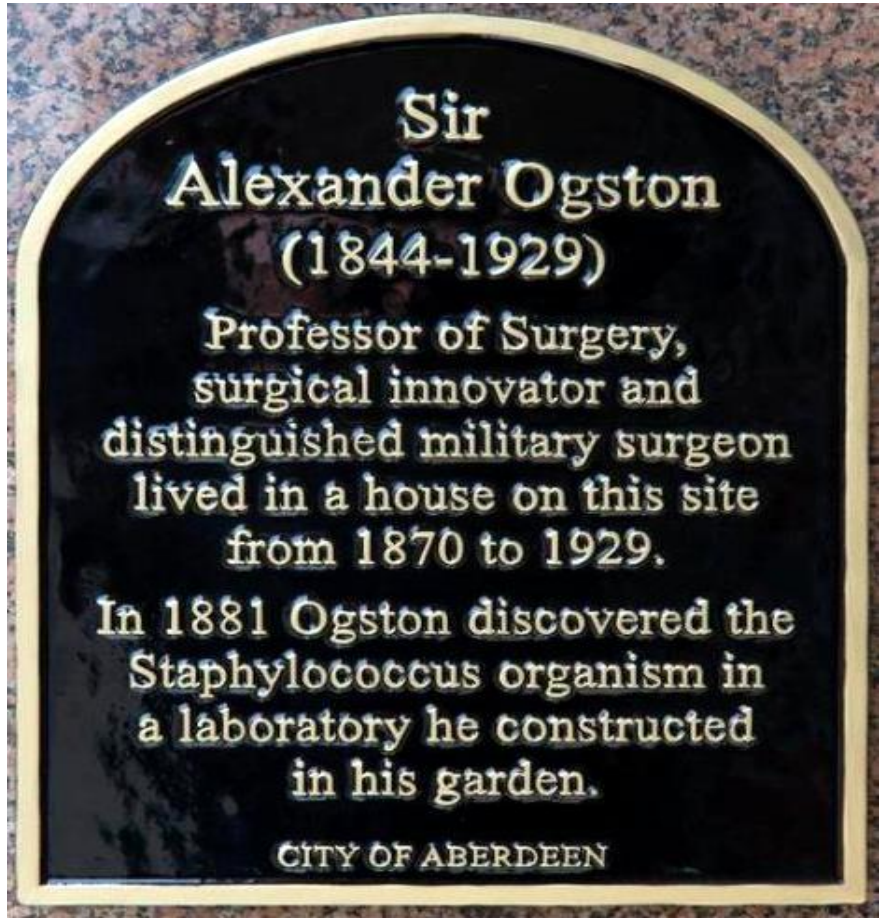
Experience with Dalbavancin in various Gram-positive infections at ARI OPAT Service

PATHOGEN	TOTAL (CLINICAL FAILURES)
Staphylococcus aureus (MS)	27(7)
Staphylococcus aureus (MR)	4(1)
CoN Staphylococcus spp.	9(4)
β-haemolytic Streptococcus	13(4)
viridans group Streptococcus	2(0)
Streptococcus pneumoniae	1(0)
Enterococcus faecalis (VS)	4(2)
Enterococcus faecium (VS)	1(1)
Corynebacterium tuberculostearicum	1(0)
*Corynebacterium afermentans**	1(0)
Lactobacillus spp.	1(0)
Kocuria spp.	1(0)
Bacillus licheniformis	1(0)
*Niallia circulans**	1(0)
*Clostridium sporogenes**	1(0)
Parvimonas micra	1(1)
Total	69(20)

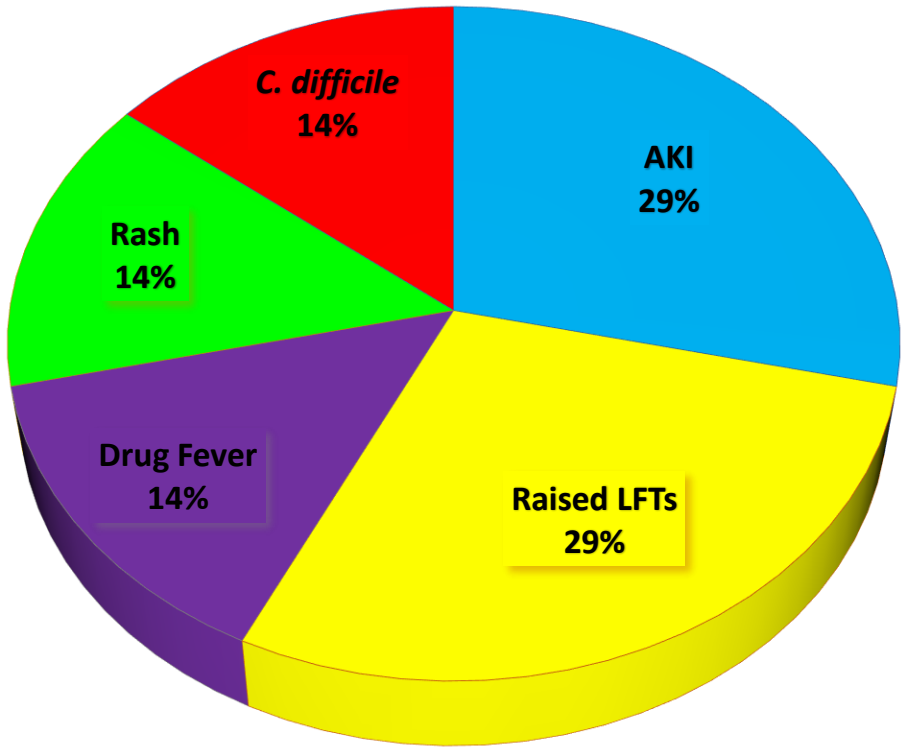


Experience with Dalbavancin in various Gram-positive infections at ARI OPAT Service

Microbiology



Experience with Dalbavancin in various Gram-positive infections at ARI OPAT Service



Experience with Dalbavancin in various Gram-positive infections at ARI OPAT Service

Our findings:

- 93% curative as primary therapy for ABSSSI including one by Panton Valentine Leucocidin +ve MRSA (n=45).
- 100 % curative as consolidation therapy for bacteraemia including 2 IVDUs with septic emboli who received less than 5 days IV flucloxacillin (n=12).
- 100 % cure rates for native joint septic arthritis and acute osteomyelitis ; cure rates low for chronic osteoarticular infections without source control were low but still not obviously inferior to standard agents.
- Low incidence of adverse events (14 %) – this is probably an overestimate

Experience with Dalbavancin in various Gram-positive infections at ARI OPAT Service

Unresolved questions:

- Role as primary therapy in bacteraemia ?
- Did not stratify organisms by vancomycin MIC – possible that dalbavancin may be less effective against resistant organisms (VRE, VISA, hVISA) ?
- Formal trials to assess non-inferiority vs other agents as a suppressive agent in chronic infections
- Synergistic with other drugs e.g. ‘seesaw’ effects with β-lactams ? [1]
- Success in one PVL-MRSA infection – effective in toxin mediated disease similar to clindamycin/linezolid ? [2]
- Long terminal half life – liable to select for resistance ? [3]

Experience with Dalbavancin in various Gram-positive infections at ARI OPAT Service

References:

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