Introductory Remarks - Anti-Infective Drugs Advisory Committee Meeting for Dalbavancin

March 31, 2014

John Alexander, MD, MPH
Medical Team Leader, DAIP

Meeting Objectives

Discuss NDA 21-883: Dalbavancin for Injection (Dalvance™)

- Applicant: Durata Therapeutics International B.V.
- Formulation: Lyophilized Powder for Injection (500 mg/Vial)
- Dose: Two-Dose Regimen (Day 1/Day 8)
- Proposed Indication: Treatment of Acute Bacterial Skin and Skin Structure Infections

Dalbavancin Hydrochloride

- Lipoglycopeptide Antibacterial
  - Derived from Fermentation Product of *Nonomuraea* Species
  - Mechanism of Action: Interruption of Cell Wall Synthesis by Binding to D-Alanyl-D-Alanine
  - Active Against Selected Gram-Positive Organisms Including Staphylococci and Streptococci
- Product Previously Owned by Other Applicants
  - Trials of Complicated and Uncomplicated Skin Infections
  - Safety Data Used in Support of Current Application
- New Studies of ABSSSI Conducted by Durata Therapeutics

Dalbavancin NDA Package: Two Phase 3 Trials

- Studies DUR001-301 and DUR001-302
  - Randomized, Active-Controlled, Double-Blind, Double-Dummy, Multicenter, Noninferiority Trials of Dalbavancin vs. 14 days of IV Vancomycin +/- Switch to Oral Linezolid for Treatment of ABSSSI
  - Dalbavancin Given in Two Doses
    - 1 g on Day 1 Followed by 500 mg on Day 8
    - Dose Adjustment for Severe Renal Impairment (750 mg/375 mg)
  - Randomized 1:1
  - Primary Endpoint: Early Clinical Response at 48-72 h Visit in ITT
    - Cessation of Spread of Lesion Compared to Baseline
    - Afebrile at 48-72 Hours

Afternoon Agenda

- Applicant Presentations by Durata Therapeutics
  - Michael Dunne, MD, Chief Medical Officer
  - Sailaja Puttagunta, MD, Executive Director
- FDA Presentations
  - Safety Evaluation by Dmitri Iarikov, MD, PhD
  - Efficacy Results by Christopher Kadoorie, PhD
- Open Public Hearing
- Charge/Questions to the Committee

Question for the Committee

1. Has the applicant provided substantial evidence of the safety and effectiveness of dalbavancin for the treatment of ABSSSI caused by susceptible isolates of the designated microorganisms? **VOTE**
   - If yes, please provide any recommendations concerning labeling.
   - If no, what additional studies/analyses are needed?

Dalbavancin for the Treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI)

NDA 21883

Durata Therapeutics International B.V.

Anti-Infective Drugs Advisory Committee Meeting

March 31, 2014

Dmitri Iarikov, MD, PhD
Medical Officer
Division of Anti-Infective Products
FDA/CDER

Presentation Outline

- Dalbavancin characteristics
- Nonclinical toxicology
- Sources of clinical data
- Primary efficacy analyses
- Safety analyses
  - Hepatotoxicity
  - Adverse reactions related to hemorrhages
- Other adverse events of interest

Dalbavancin Characteristics

- Lipoglycopeptide antibacterial drug
- Active against *S. aureus* including MRSA strains and against S*treptococci*
- Dosing regimen:

Creatinine clearance	**Day 1**	**Day 8**
≥ 30 mL/min or on renal dialysis	1000 mg	500 mg
<30 mL/min and not on renal dialysis	750 mg	375 mg

Major Nonclinical Toxicology Findings

- Liver toxicity: transaminase elevations and hepatocellular centrilobular necrosis
- Renal toxicity: increased BUN and creatinine, tubular necrosis, and interstitial inflammation
  - Liver and renal toxicity was observed in rats and dogs at 5-7 times the plasma exposure expected in humans
- Infusion reactions (systemic and local)
- Abortions in rabbits

Dalbavancin Clinical Development Program

	Phase 1	Phase 2	Phase 3	All Trials	DUR001-301 & 302
No of Trials	14	2	5	21	
Dalbavancin	307	81	1704	**2092**	659
Comparator	124	55	1171	1350	653

Intent to treat (ITT) population

Dalbavancin Phase 2 and 3 Trials

Trials	Phase	Indication	Dalbavancin (N)	Comparator (N)
DUR001-301	3	Acute Bacterial Skin and Skin Structure Infections (ABSSSI)	284	284
DUR001-302	3		368	367
VER001-4	2	Catheter-Related Bloodstream Infections	40	34
VER001-5	2	Complicated SSSI	41	21
VER001-9	3	Complicated SSSI	571	283
VER001-8	3	Uncomplicated SSSI	367	186
VER001-16	3	SSSI with MRSA	107	49
Total*			**1778**	**1224**

SSSI – skin and skin structure infections; * Safety population

DUR001-301 and -302 Trials

- Randomized (1:1) double-blind non-inferiority phase 3 trials (NI margin 10%)
- **Study arms**:

❑ Dalbavancin on Day 1 and Day 8

❑ Vancomycin IV with optional switch to oral linezolid x 10-14 days after at least 72 hours of IV therapy

- **Primary Efficacy Endpoint**: Early Clinical Response - cessation of spread of ABSSSI and no fever at 48 to 72 hours in the intent-to-treat (ITT) population (all randomized subjects regardless of receiving study drug).

Baseline Characteristics (ITT Population)[a]

	DUR001-301		DUR001-302	
	Dalbavancin N=288 n (%)	Comparator N=285 n (%)	Dalbavancin N=371 n (%)	Comparator N=368 n (%)
Age ≥ 65 years	37 (12.8)	43 (15.1)	70 (18.7)	81 (22)
T ≥ 38°C at baseline	236 (81.9)	235 (82.5)	303 (81.7)	303 (82.3)
US enrollment	120 (41.7)	118 (41.4)	115 (31)	114 (31)
CrCl < 30 mL/min	11 (3.8)	7 (2.5)	8 (2.2)	7 (1.9)
Cellulitis	156 (54.2)	147 (51.6)	198 (53.4)	202 (54.9)
Major Abscess	72 (25)	86 (30.2)	90 (24.3)	87 (23.6)
Wound Infection	60 (20.8)	52 (18.2)	82 (22.1)	79 (21.5)
Cellulitis area (cm^2) [b]	348.5	496	452	466

[a] 9 subjects in the ITT are not included in the Safety population; [b] Median

Baseline Characteristics (cont.)

Safety Population

	DUR001-301		DUR001-302	
	Dalbavancin N=284 n (%)	Comparator N=284 n (%)	Dalbavancin N=368 n (%)	Comparator N=367 n (%)
ALT > ULN	49 (17.2)	44 (15.5)	49 (13.1)	56 (15.3)
ALT ≥ 3x ULN	6 (2.1)	8 (2.8)	4 (1.1)	6 (1.6)
Elevated Hepatobiliary Status [a]	17 (6)	19 (6.7)	16 (4.3)	20 (5.4)
h/o Hepatitis C	27 (9.5)	32 (11.3)	23 (6.3)	27 (7.4)

[a] Baseline hepatobiliary status: elevated if either baseline ALT or AST was >3 times the ULN, or if the subject's baseline alkaline phosphatase level was >1.5 times the ULN

Primary Efficacy Endpoint
Early Clinical Response at 48–72 hours

	Dalbavancin n/N (%)	Comparator n/N (%)	Difference (95% CI)
DUR001-301	240/288 (83.3)	233/285 (81.8)	1.5 (-4.6, 7.9)
DUR001-302	285/371 (76.8)	288/368 (78.3)	-1.5 (-7.4, 4.6)

Exposure to Dalbavancin
Safety Population

	DUR001-301 & 302 N=652 n (%)	All Phase 2 and 3 N=1778 n (%)
2 doses (Day 1 and 8)	620 (95.1)	1408 (79.2)
1 dose (Day 1)	32 (4.9)	370 (20.8)

1 dose provides a 7-day exposure
2 doses provide a 14-day exposure

Comparator Regimen
Trials DUR001-301 and DUR001-302

	Trial 301	Trial 302	Total	
Vancomycin	66	34	100 (15.4%)	**651**
Vancomycin/Linezolid	218	333	551 (84.6%)	

Time to Oral Switch and Total Duration of Treatment in DUR001-301 and -302 Trials

Days (mean)*	DUR001-301		DUR001-302	
	Dalbavancin N=288	Comparator N=285	Dalbavancin N=371	Comparator N=368
IV therapy	4.8	4.8	3.8	3.8
Total therapy (IV and oral)	10.6	11.0	11.1	11.1

* Due to dalbavancin PK characteristics the majority of dalbavancin-treated subjects were exposed to the drug for 14 days regardless of the decision to stop study treatment; ITT population

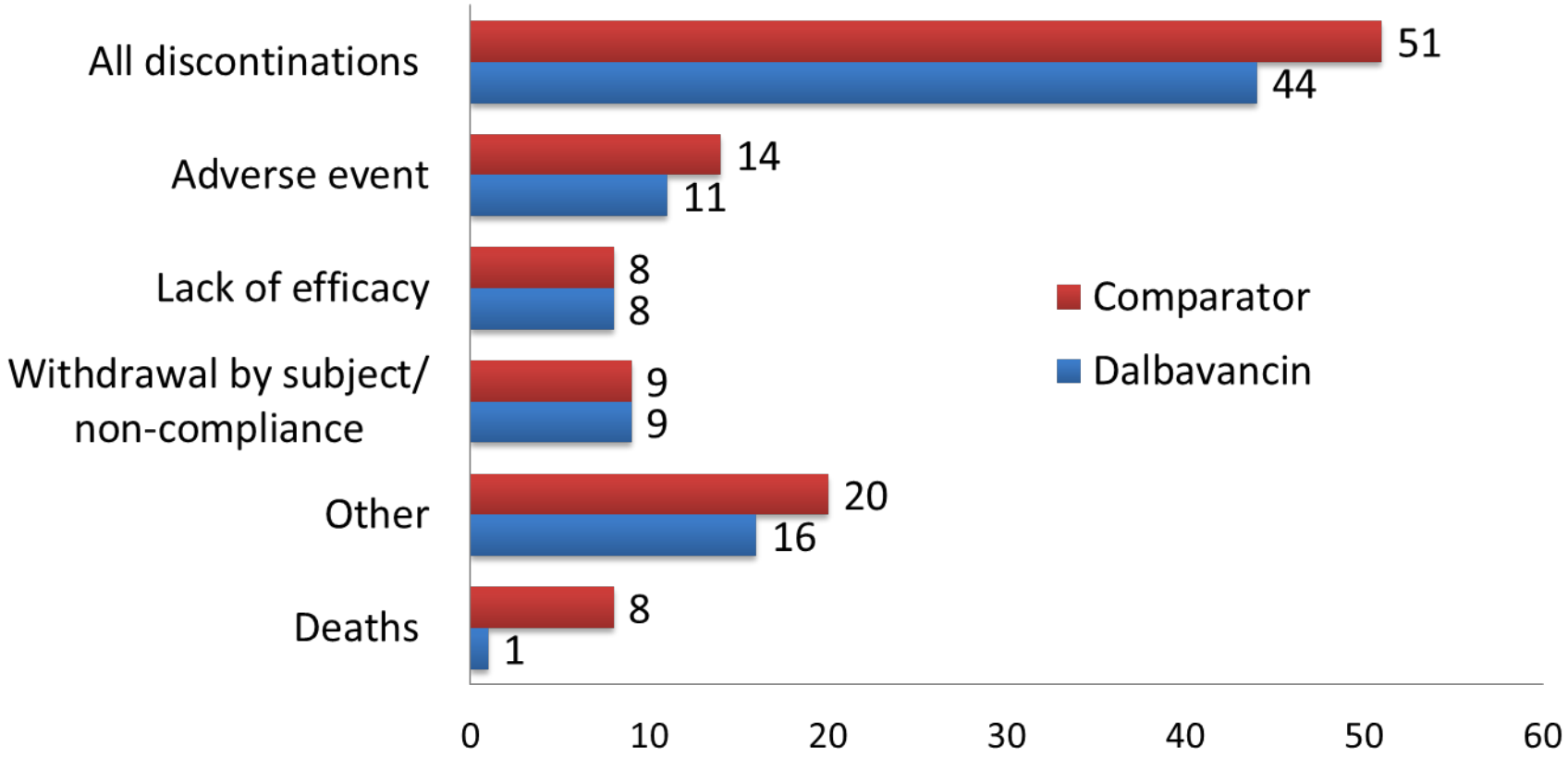
Adverse Experiences in DUR001-301 and 302 Trials

	Dalbavancin N=652 n (%)	Comparator N=651 n (%)
Deaths	1 (0.2)	8 (1.2)
Study Drug Discontinuations	44 (6.7)	51 (7.8)
Nonfatal Serious TEAEs	17 (2.6)	26 (4)
Subjects with any TEAE	214 (32.8)	247 (37.9)

AE – adverse event; TEAE – treatment emergent AE

Study Drug Discontinuations and Deaths

DUR001-301 and -302 Trials



Deaths in Dalbavancin Trials

Prior Phase 2/3 Trials		DUR001-301 and 302		All Phase 2/3 trials	
Dalbavancin (N=1126)	Comparator (N=573)	Dalbavancin (N=652)	Comparator (N=651)	Dalbavancin (N=1778)	Comparator (N=1224)
9 (0.8%)	7 (1.2%)	1 (0.2%)	8 (1.2%)	10 (0.6%)	15 (1.2%)

Deaths in DUR001-301 and -302 Trials

#	Age Sex	Days on Study Drug	Study Day of Death	Cause to Death
Dalbavancin				
1	78 F	11	32	Retroperitoneal abscess
Vancomycin				
1	73 F	10	32	Congestive heart failure
2	62 F	15	49	Systemic lupus erythematosus
3	79 F	3	4	Acute cardiac failure
4	69 F	5	5	Pulmonary embolism
5	68 M	14	52	Cardiopulmonary failure
6	57 M	13	38	Sudden death
7	78 F	7	41	Cardiopulmonary failure
8	50 M	7	24	Gram-negative bacterial sepsis

Submission Safety Concerns
ALT Elevations
DUR001-301 and -302 Trials

	Dalbavancin N = 652		Vancomycin N = 651	
Post-dose ALT	n	%	n	%
> 3x ULN – 5x ULN	26	4.0	15	2.3
> 5x ULN – 10x ULN	6	0.9	0	0
> 10x ULN	3	0.5	0	0

ULN – the upper limit; subjects may have abnormal baseline levels and may be counted more than once.

ALT Elevations in Subjects with Normal Baseline Transaminase Levels

	DUR001-301&302		All Phase 2/3 Trials	
	Dalbavancin N=505	Comparator N=521	Dalbavancin N=1406	Comparator N=957
> 3x ULN – 5x ULN	3	1	7	1
> 5x ULN – 10x ULN	1	0	2	1
> 10x ULN	2	0	3	0
Total n (%)*	6 (1.2)	1 (0.2)	12 (0.8)	2 (0.2)

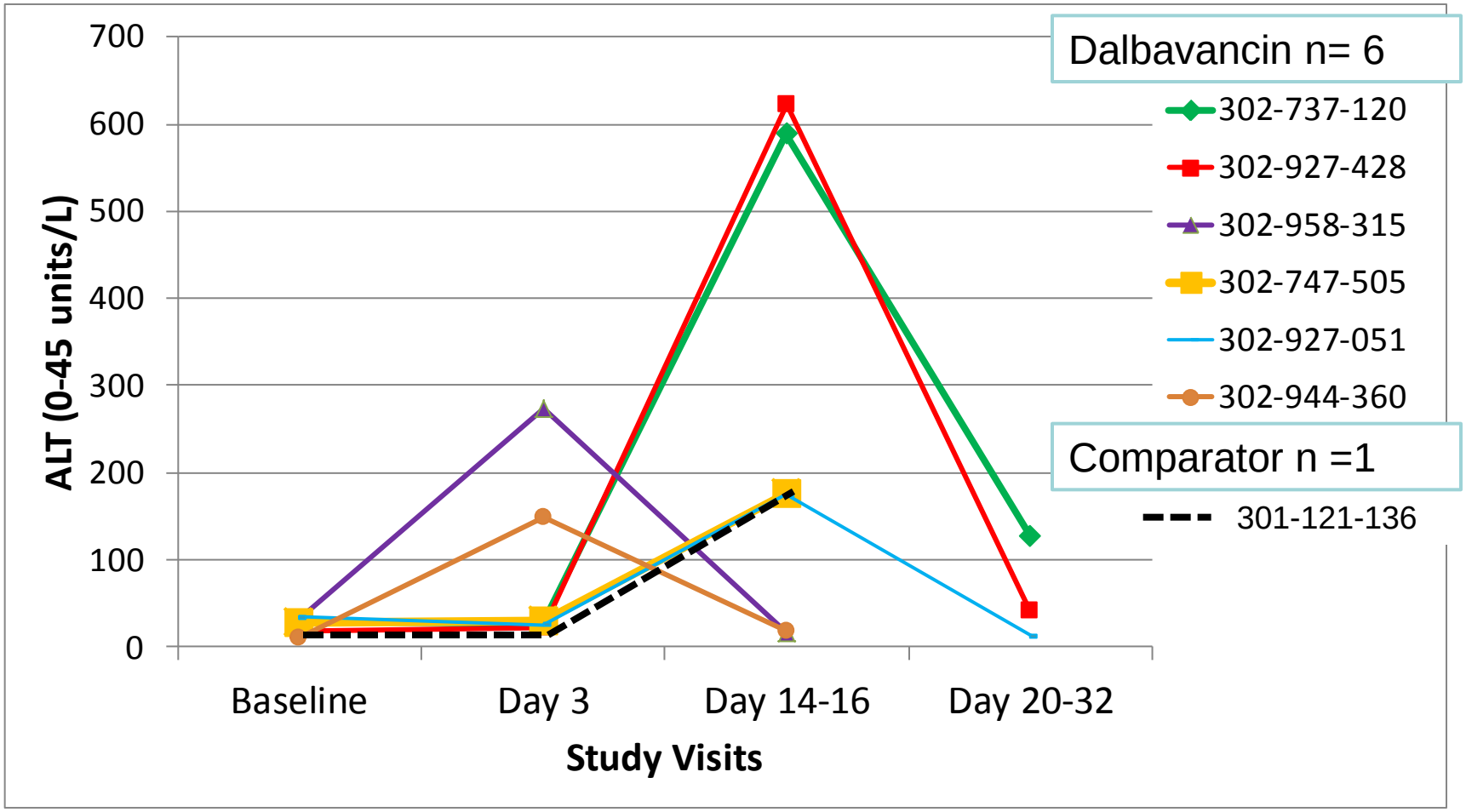
N = subjects with baseline ALT < the upper limit of normal;
* Subjects counted once

ALT Shifts in Dalbavancin Subjects with ALT > ULN (Trials 301 & 302)

ALT	Baseline	Post-dose				
	N =98	< ULN	>ULN - 3xULN	>3xULN - 5xULN	>5xULN - 10xULN	> 10x ULN
> ULN - < 3xULN	88*	9	65	11	1	1
> 3xULN - 5xULN	8	1	2	5	0	0
> 5xULN - 10xULN	1	0	0	1	0	0
> 10xULN - 20xULN	1	0	0	0	1	0

*** Post-dose levels are available for 87 out of 88 subjects**
Only the highest level is counted; subjects are counted once

Timing of ALT Elevations in Subjects with Normal Baseline Transaminases
Trials DUR001-301 and 302

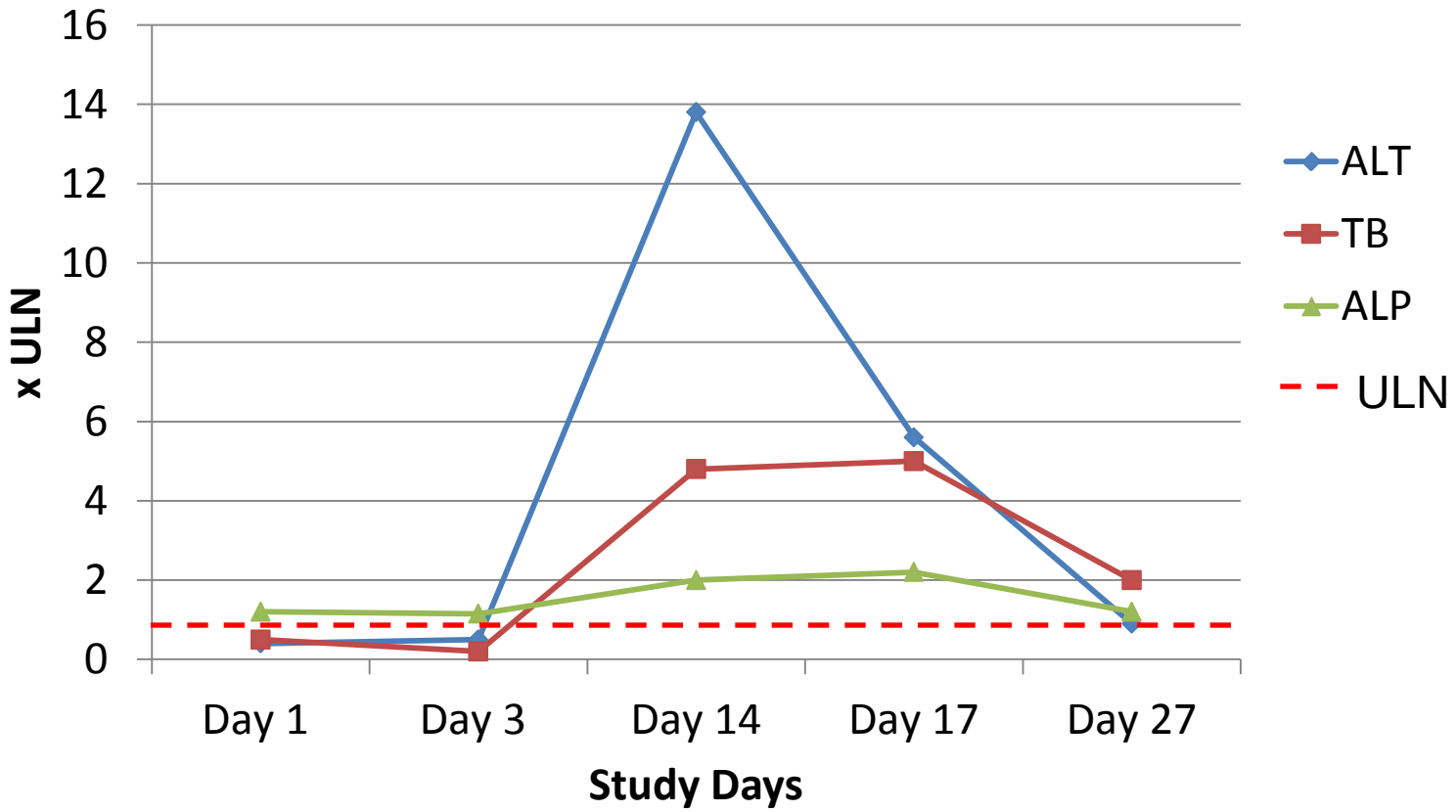


Concomitant Elevations in Liver Tests in Dalbavancin Subjects with Risen ALT

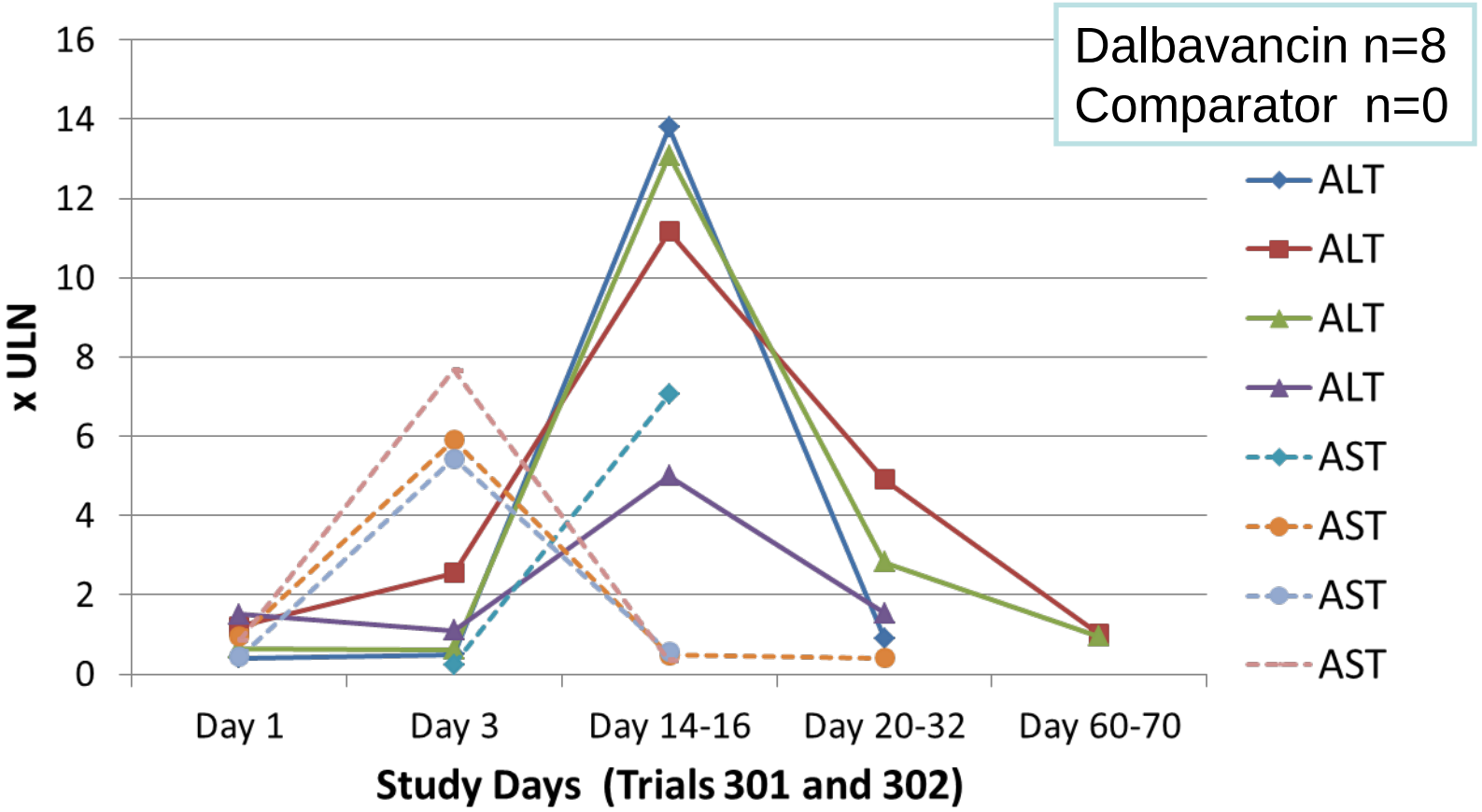
Subject ID* ***Med. Hist.***	**Highest ALT 0- 45 units/L**	**AST 0- 41 units/L**	**TB 0.1-1.2 mg/dL**	**ALP**	**Baseline ALP**
927-428 *Hepatitis C*	622	85	**5.8**	210	121 (35-104 U/L)
737-120 *Hepatitis C*	589	248	0.6	274	135 (40-129 U/L)
958-315 *Alcoh. abuse*	274	315	0.4	244	91 (40-129 U/L)
747-505 *IV drug use*	177	77	0.4	247	117 (40-129 U/L)
927-051 *None*	175	119	1.4	65	60 (35-104 U/L)
944-360 *Chronic HBV*	148	223	0.9	257	222 (35-104 U/L)

* All subjects are from trial 302 *and had normal baseline ALT, AST and total bilirubin* (TB) levels; ALP – alkaline phosphatase

Subject 302-927-428 with Concomitant ALT and TB Elevation

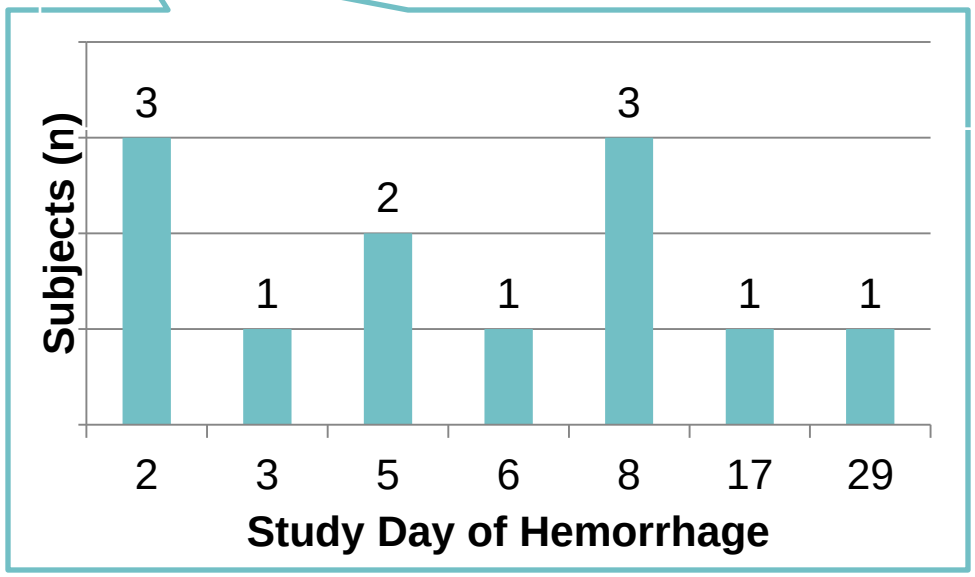


Subjects with ALT or AST Elevations of ≥ 5x ULN (Baseline ALT/AST levels of < 2x ULN)



Subjects with TEAE Identified by a MedDRA SMQ "Haemorrhages" *

DUR001-301 and -302		All Phase 2 and 3	
Dalbavancin N=652	Comparator N=651	Dalbavancin N=1778	Comparator N=1224
12 (1.8%)	3 (0.5%)	36 (2%)	19 (1.6%)



Severity (Trials 301&302)

- Severe – 2
- Moderate -2
- Mild – 8

All event resolved

Study drug was continued in all but 1 case

TEAE of Hemorrhages
Trials DUR001301 and -302 (MedDRA PT)

Dalbavancin arm :

Severe events (n=2):

Gastrointestinal hemorrhage –in 70 year-old male, occurred on day 8, required RBC transfusion, drug was stopped, the event resolved and was attributed to gastric ulcer.

Epistaxis – in 58 year-old female, occurred on day 5, required external nasal tamponade, resolved, study drug continued.

Other TEAE (n=10): upper gastrointestinal hemorrhage, melena, hematochezia, petechiae, vessel puncture site hematoma, spontaneous hematoma, hemorrhagic anemia (2), and hematuria (2).

Comparator arm: rectal haemorrhage, *gastrointestinal haemorrhage (severe)*, and epistaxis.

Other AEs of Interest

	DUR001-301 and -302		All Phase 2 and 3 trials	
	Dalbavancin N=652	Comp. N=651	Dalbavancin N=1778	Comp. N=1224
Infusion site reactions	12 (1.8%)	17 (2.1%)	51 (2.9%)	53 (4.3%)
Hypersensitivity	43 (6.6%)	52 (8%)	140 (7.9%)	115 (9.4%)
Renal Toxicity	1 (0.15%)	4 (0.6%)	7 (0.4%)	12 (1%)
WBC decreased	9 (1.4%)	6 (1%)	18 (1%)	12 (1%)
Platelet decreased	5 (0.8%)	2 (0.3%)	9 (0.5%)	9 (0.7%)
Hypoglycemia	1 (0.15%)	4 (0.6%)	7 (0.4%)	5 (0.4%)

Acknowledgments

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NDA 21883, Dalbavancin for ABSSSI: Efficacy Evaluation

Christopher Kadoorie, Ph.D.

Statistical Reviewer

Division of Biometrics IV

Office of Biostatistics

Outline

- Studies 301 & 302 (Brief Review)
- Evaluation of Early Endpoints (48-72 hrs)
- Evaluation of Later Endpoints
  - End of Treatment (EOT)
  - Short Term Follow-up (SFU)
- Concordance Analyses (48-72 hrs & SFU)
- Reasons for Incomplete Resolution in Responders
- Summary & Conclusions

Studies 301 & 302 Design

- Randomized, double-blind, double-dummy, multicenter, Phase 3 studies in patients w/ ABSSSI (Gram$^+$ bacteria)
- IV dalbavancin vs. IV vancomycin/oral linezolid
- 573 & 739 randomized patients w/ cellulitis, major abscess or wound infection
- Entry Criteria included:
  - Lesion area ≥ 75cm^2 w/ sufficient erythema
  - ≥ 2 local signs: purulent drainage/discharge, fluctuance, heat/warmth, tenderness, swelling
  - ≥ 1 systemic sign (Temp. ≥ 38°C, elevated WBC)
  - Infection severity requiring ≥ 72 hrs of IV therapy

Studies 301 & 302 Endpoints (ITT Population)

- Primary endpoint: Early clinical response
  - Cessation of spread of lesion & afebrile at 48-72 hrs
  - Tested for non-inferiority (10% NI margin)
- Key secondary endpoint (Reviewer)
  - 20% reduction in lesion area at 48-72 hrs (10% NI margin)
  - Recommended primary endpoint in 2013 ABSSSI guidance
- Secondary endpoint
  - Clinical status at EOT- Success Rates (No inferential testing)
  - No pre-specified 'win/lose' criteria

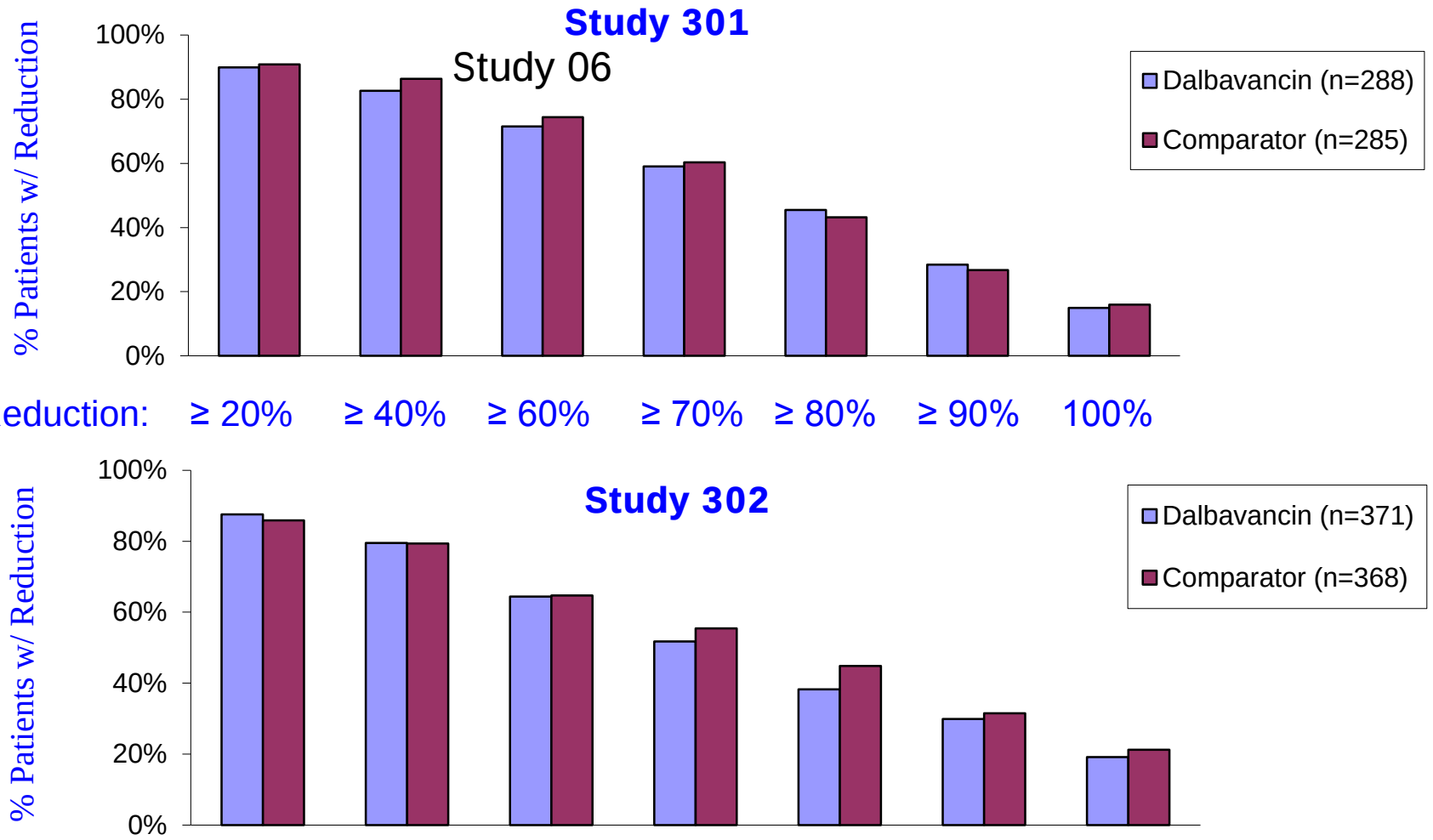
*Study visits occurred on Days 2, 3, 4, 8, EOT, SFU, LFU (Long term follow-up)

Primary & Key Secondary Endpoints at 48-72 hrs

	Dalbavancin	Comparator	Difference (95% CI)
Primary: Early Clinical Response at 48-72 hrs (Responders)			
Study 301	240/288 (83%)	233/285 (82%)	1.5 (-4.6, 7.9)
Study 302	285/371 (77%)	288/368 (78%)	-1.5 (-7.4, 4.6)
Secondary: ≥ 20% Reduction in Lesion Area at 48-72 hrs (Responders)			
Study 301	259/288 (90%)	259/285 (91%)	-1.0 (-5.7, 4.0)
Study 302	325/371 (88%)	316/368 (86%)	1.7 (-3.2, 6.7)

Responders must be alive, not use non-study systemic abx up to 48-72 hrs.

Patients with ≥ x% Reduction in Lesion Area at 48-72 hrs



Patients meeting % reductions must also be alive, not use nonstudy systemic abx up to 48-72 hrs

Evaluation of Later Endpoints

Will those patients achieving efficacy at 48-72 hours achieve similar efficacy at later endpoints (EOT and SFU)?

Clinical Status at EOT/SFU: Success Rates

- Success for clinical status at EOT/SFU required:
  - Temp. ≤ 37.6°C
  - Lesion size (length & width): decreased from baseline
  - Purulent d/d: absent or mild, improved (wound infections)
  - Fluctuance & heat/warmth: absent
  - Tenderness & swelling: absent or mild
- Successes also could not have any of the following in the study period up to EOT/SFU visit:
  - A death
  - Use of non-study systemic antibacterials
  - Surgical intervention (after 72 hrs of treatment)
- Indeterminates counted as failures in the ITT analysis

Clinical Status at EOT/SFU: Success Rates

ITT	Dalbavancin	Comparator	Difference (95% CI)
Study 301	**N=288**	**N=285**	
Success, EOT	234 (81%)	247 (87%)	-5.4% (-11.5, 0.6)
Failure	40 (14)	29 (10)	3.7
Indeterminate	14 (5)	9 (3)	1.7
Success, SFU	241 (84%)	251 (88%)	-4.4% (-10.2, 1.3)
Failure	18 (6)	13 (5)	1.7
Indeterminate	29 (10)	21 (7)	2.7
Study 302	**N=371**	**N=368**	
Success, EOT	329 (89%)	314 (85%)	3.4% (-1.5, 8.3)
Failure	32 (9)	34 (9)	-0.6
Indeterminate	10 (3)	20 (5)	-2.7
Success, SFU	327 (88%)	311 (85%)	3.6% (-1.3, 8.7)
Failure	18 (5)	23 (6)	-1.4
Indeterminate	26 (7)	34 (9)	-2.2

Clinical Status at EOT/SFU: Reasons for Failure

	Study 301		Study 302	
	Dalbavancin	Comparator	Dalbavancin	Comparator
# Failures due to reason (# Failures due to reason ONLY)				
Clinical Failures, EOT	N=40	N=29	N=32	N=34
Heat/warmth present	**31 (19)**	**21 (11)**	**16 (5)**	**20 (6)**
Non-study systemic abx	13 (1)	4 (0)	9 (1)	14 (0)
Lesion size not decreased	10 (2)	3 (1)	7 (1)	5 (2)
Swelling worse than mild	6 (1)	6 (1)	8 (2)	13 (2)
Clinical Failures, SFU	N=18	N=13	N=18	N=23
Nonstudy systemic abx	**16 (9)**	**7 (3)**	**11 (7)**	**15 (8)**
Heat/warmth present	5 (2)	2 (0)	1 (1)	3 (1)

Sensitivity Analyses at EOT/SFU: S1-S4

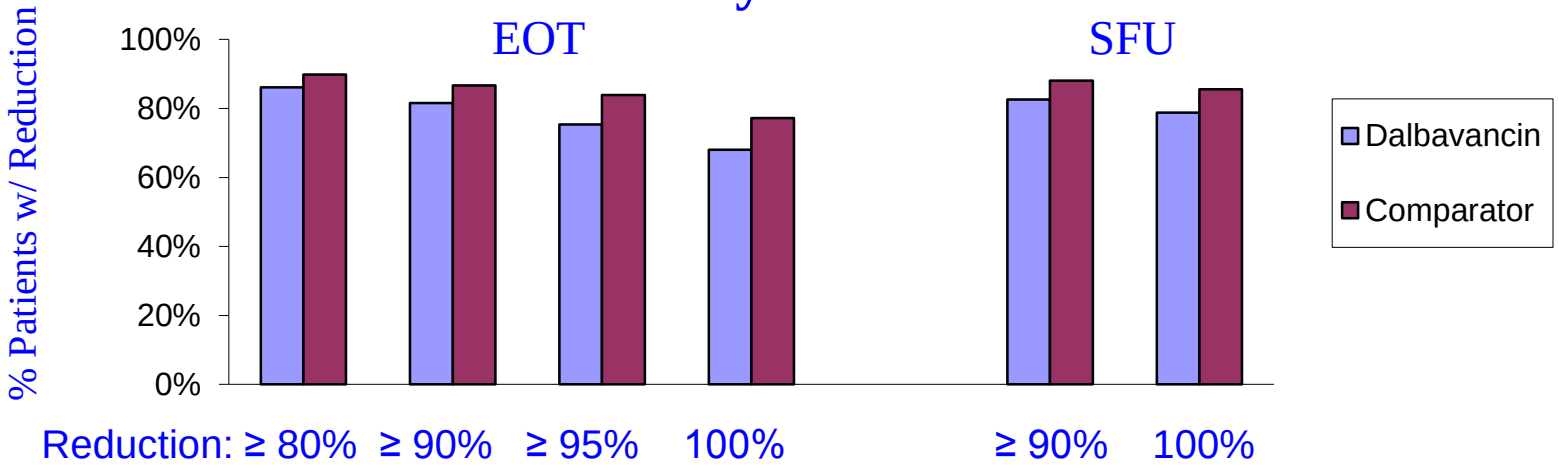
- S1-S4 were performed to address limitations in the success criteria for clinical status at EOT/SFU:
  - Investigator rating of erythema
  - Magnitude of decrease in lesion size
  - Unresolved local signs at SFU
- S1 & S2 require successes at EOT to also have:
  - 80% & 90% reduction in lesion area at EOT, resp.
  - Erythema no worse than mild
- S3 & S4 require successes at SFU to also have:
  - Complete resolution of all local signs except for mild erythema, if residual lesion area ≤ 10% (S3)
  - Complete resolution of all local signs, incl. erythema (S4)

Sensitivity Analyses at EOT/SFU: Success Rates

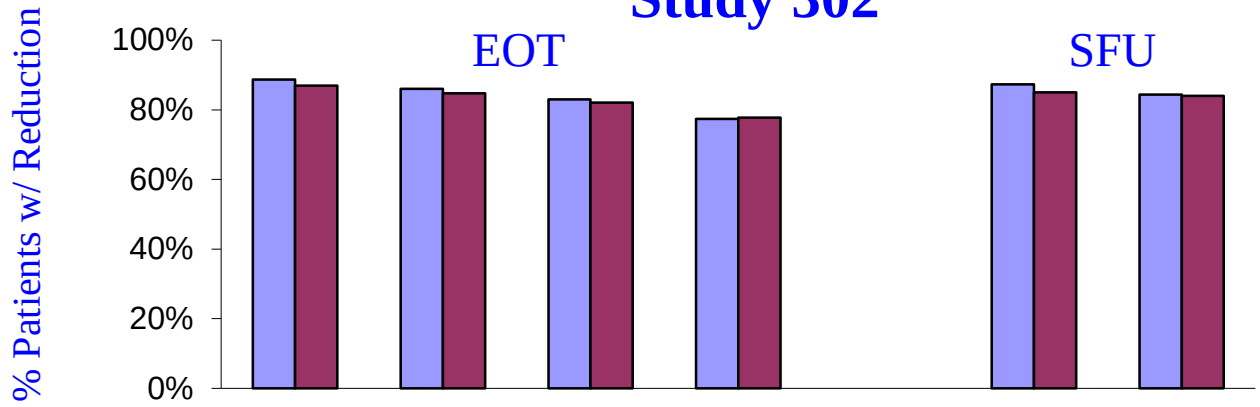
	Dalbavancin	Comparator	Difference (95% CI)
Study 301	**N=288**	**N=285**	
Clinical Status, EOT	234 (81%)	247 (87%)	-5.4% (-11.5, 0.6)
S1	226 (78)	242 (85)	-6.4 (-12.8, -0.1)
S2	218 (76)	237 (83)	-7.5 (-14.1, -0.8)
Clinical Status, SFU	241 (84%)	251 (88%)	-4.4% (-10.2, 1.3)
S3	229 (80)	241 (85)	-5.1 (-11.4, 1.3)
S4	220 (76)	239 (84)	-7.5 (-14.0, -0.9)
Study 302	**N=371**	**N=368**	
Clinical Status, EOT	329 (89%)	314 (85%)	3.4% (-1.5, 8.3)
S1	318 (86)	306 (83)	2.6 (-2.7, 7.8)
S2	309 (83)	299 (81)	2.0 (-3.5, 7.6)
Clinical Status, SFU	327 (88%)	311 (85%)	3.6 (-1.3, 8.7)
S3	298 (80)	288 (78)	2.1 (-3.8, 7.9)
S4	292 (79)	286 (78)	1.0 (-5.0, 7.0)

Patients with ≥ x% Reduction in Lesion Area at EOT/SFU

Study 301



Study 302



Patients meeting % reductions must also be alive, not use nonstudy systemic abx, not have a surgical intervention (after 72 hrs. of treatment) up to EOT/SFU visit.

Concordance Analyses

- Concordance analyses assessed relationship between early and later endpoints:
  - Clinical response at 48-72 hrs (responder/non-responder)
  - Resolution of local signs, incl. erythema, at SFU (complete/ incomplete)
- Concordance analyses were performed separately in responders and non-responders at 48-72 hrs.

*Patients with complete resolution of local signs must also be alive, not use nonstudy systemic abx, not have a surgical intervention (after 72 hrs. of treatment) up to SFU visit.

Concordance- Responder/Non-responders at 48-72 hrs w/ Complete/Incomplete Resolution of Local Signs at SFU

Short Term Follow-up ↓	Dalbavancin	Comparator	Dalbavancin	Comparator
	Responders (48-72 hrs)		Non-responders (48-72 hrs)	
Study 301	N=240	N=233	N=48	N=52
Complete resolution	194 (80.8%)	207 (88.8%)	26 (54.2%)	32 (61.5%)
Incomplete resolution	**46 (19.2%)**	**26 (11.2%)**	22 (45.8%)	20 (38.5%)
Study 302	N=285	N=288	N=86	N=80
Complete resolution	235 (82.5%)	242 (84.0%)	57 (66.3%)	44 (55.0%)
Incomplete resolution	**50 (17.5%)**	**46 (16.0%)**	29 (33.7%)	36 (45.0%)

Reasons for Incomplete Resolution at SFU Among Responders at 48-72 hrs

Incomplete Resolution of Local Signs at SFU (Clinical Failures & Indeterminates):	Study 301		Study 302	
	Dalbavancin N = 46	Comparator N = 26	Dalbavancin N = 50	Comparator N = 46
Local signs unresolved:	**25**	**12**	**26**	**24**
– **Erythema:**	**21**	**6**	**12**	**7**
– Heat/warmth:	5	1	0	1
– Tenderness:	5	6	4	11
– Swelling:	11	5	12	13
Missing local signs:	**18**	**13**	**18**	**17**
Non-Study Systemic Abx:	8	3	4	3
Surgical Intervention:	2	0	7	6

Patients with missing local signs who also had a death, surgical intervention or non-study systemic abx use were considered as indeterminates.

Summary & Conclusions

- Efficacy of dalbavancin was demonstrated at 48-72 hrs, but still some uncertainty at later endpoints.
- Clinical status at EOT/SFU was limited:
  - Success criteria for local signs, esp. erythema
  - Variability in findings for Studies 301 & 302
- Sensitivity analyses at EOT/SFU (S1-S4) and concordance analyses showed Dalbavancin was:
  - Less favorable to comparator in Study 301
  - More similar to comparator in Study 302

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