ID Week 2021
Novel Antimicrobial Agents and Antimicrobial Stewardship

Marisa Winkler, MD, PhD

Second year Infectious Disease Fellow

MGH-BWH Joint ID Fellowship

Gram negatives

IDWEEK 2021

The β-Lactamase Inhibitor QPX7728 Restores the Activity of β-Lactam Agents against Contemporary ESBL-Producing and CRE Isolates, Including Isolates Producing Metallo-β-Lactamases

Jill Lindley[1], Yahse Edah[1], Olga Lomovskaya[2], Mariana Castanheira[1]
[1]JMI Laboratories, North Liberty, Iowa; [2]Qpex Biopharma, San Diego, California

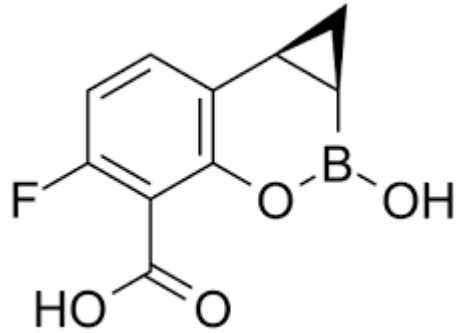
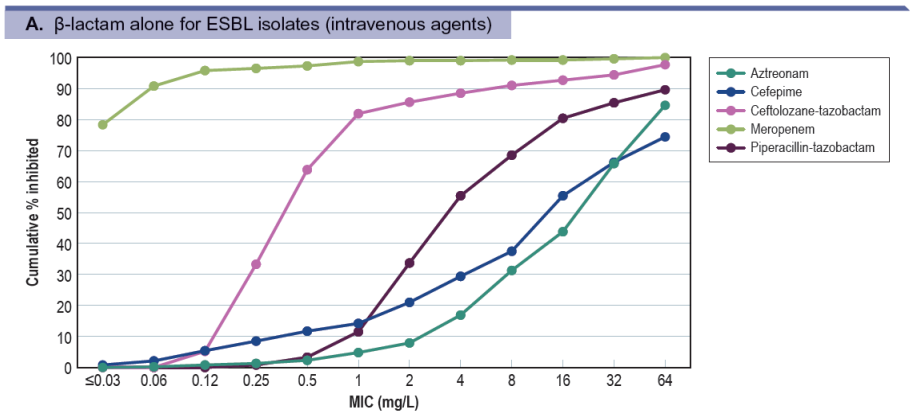
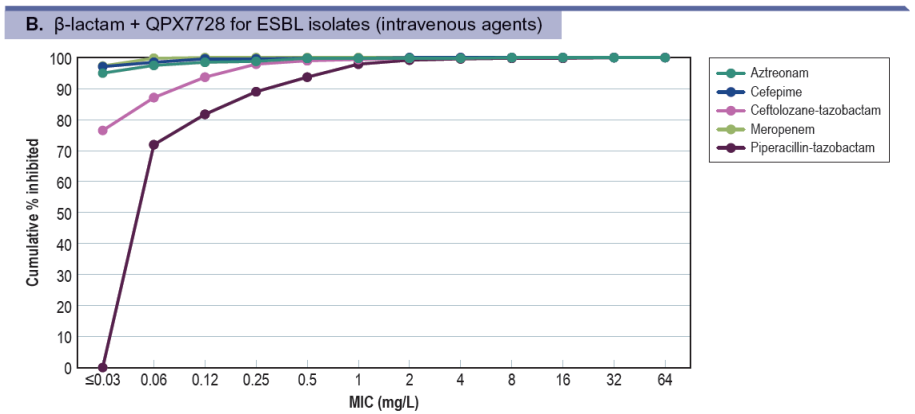
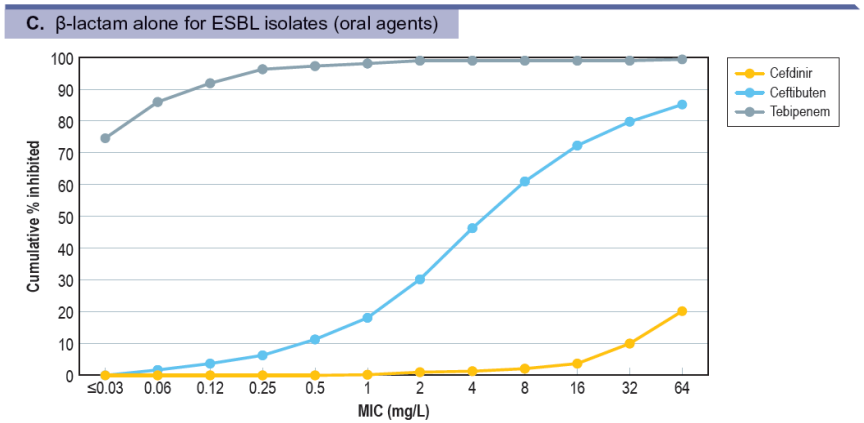


Figure 1. Antimicrobial activity of QPX7728 in combination with β-lactam agents tested against ESBL-carrying isolates







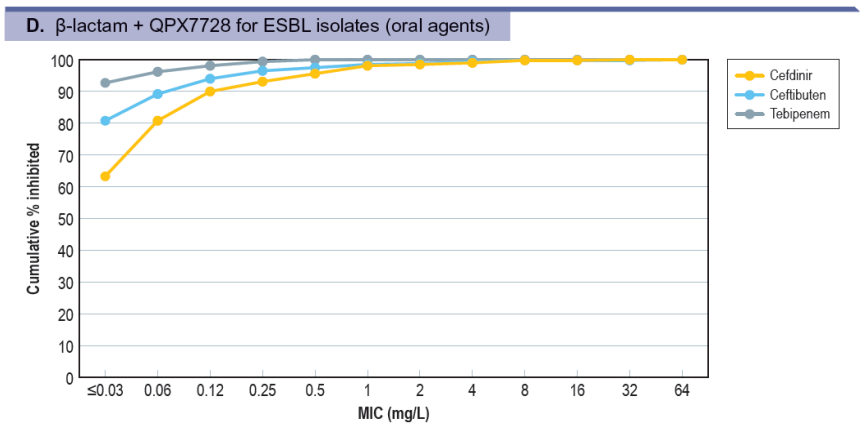
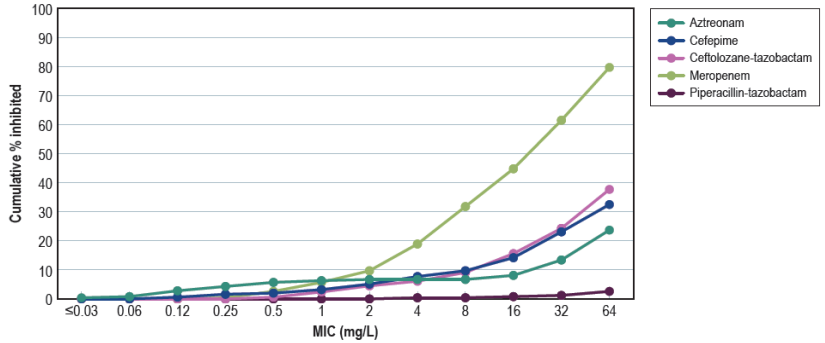
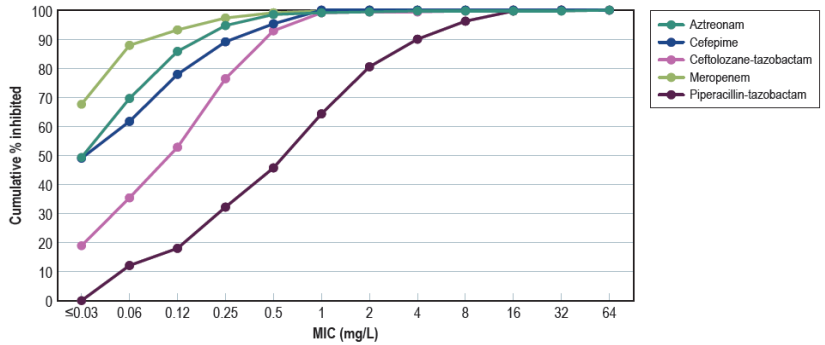


Figure 2. Antimicrobial activity of QPX7728 in combination with β-lactam agents tested against CRE isolates

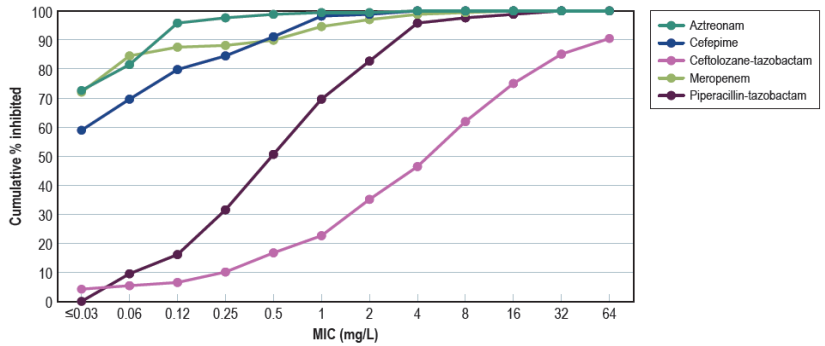
A. β-lactam alone for CRE isolates (intravenous agents)



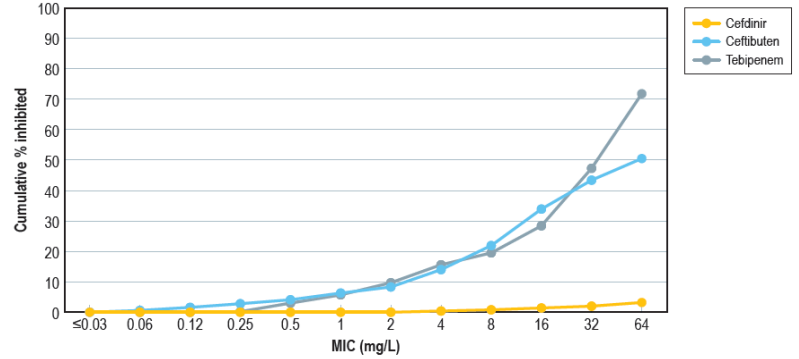
B. β-lactam + QPX7728 for CRE isolates not producing MBLs (intravenous agents)



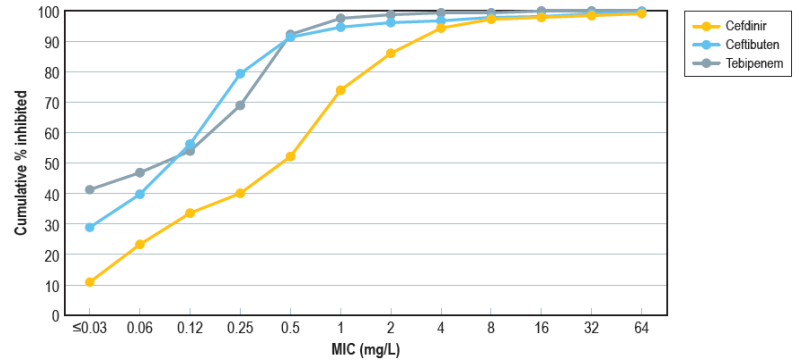
C. β-lactam + QPX7728 for CRE isolates producing MBLs (intravenous agents)



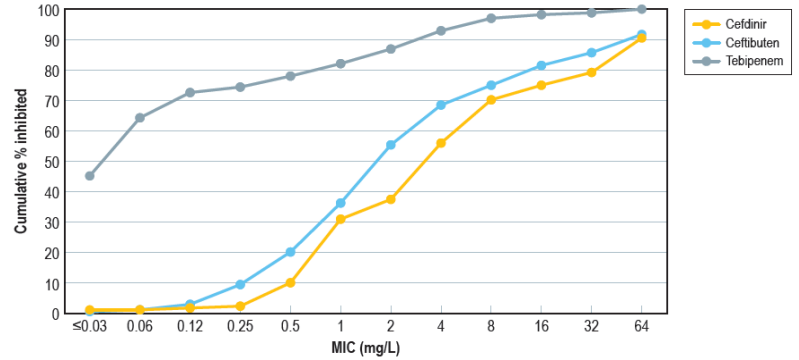
D. β-lactam alone for CRE isolates (oral agents)



E. β-lactam + QPX7728 for CRE isolates not producing MBLs (oral agents)

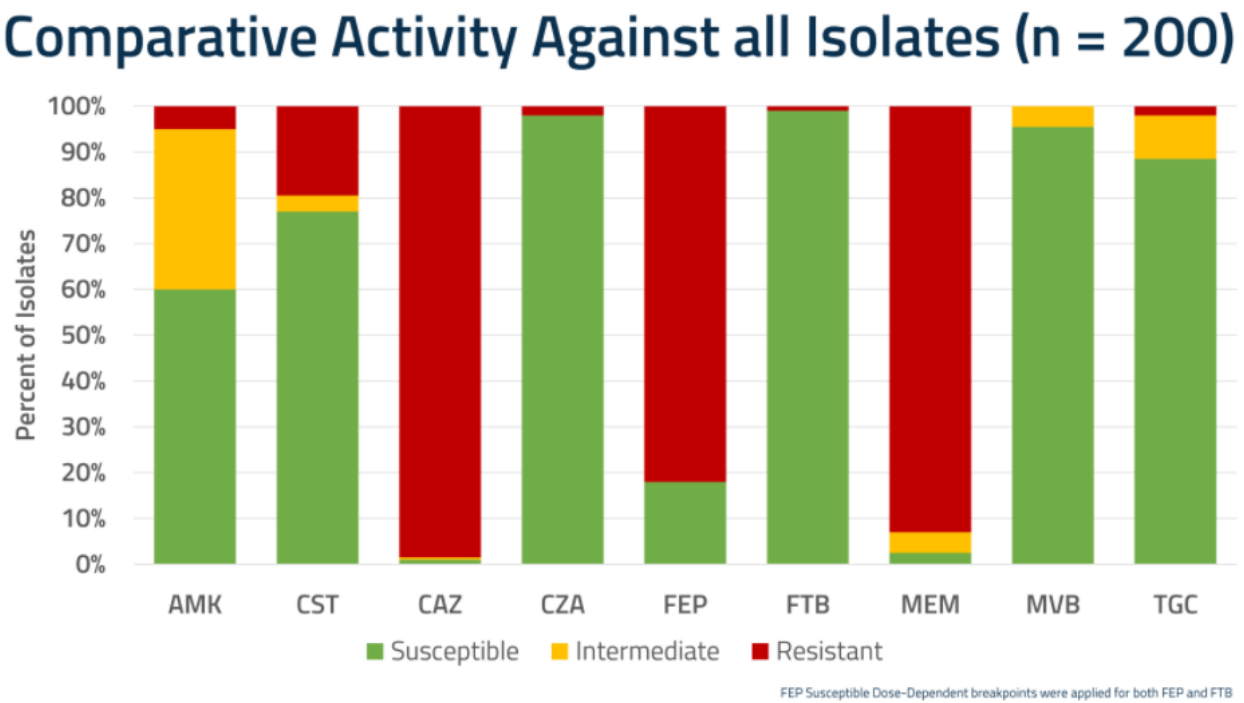


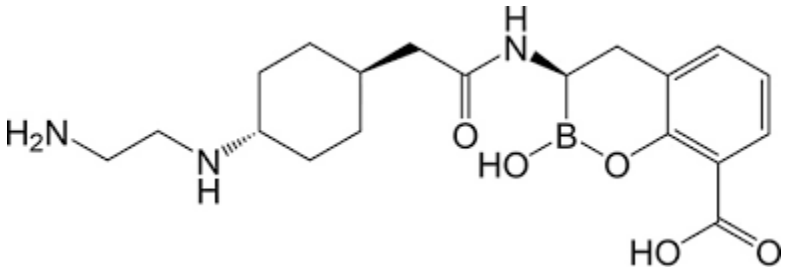
F. β-lactam + QPX7728 for CRE isolates producing MBLs (oral agents)



ARGONAUT-III: Susceptibility of Carbapenem-resistant *Klebsiellae* to Cefepime-Taniborbactam

Andrew R. Mack, Christopher R. Bethel, Steven Marshall, Robin Patel, David van Duin, Vance G. Fowler, Daniel D. Rhoads, Michael R. Jacobs, Focco van den Akker, David A. Six, Greg Moeck, Krisztina M. Papp-Wallace, Robert A. Bonomo





200 known carbapenemase-containing *K pneumoniae* isolates
In vitro assays with MICs in comparison to several other agents
Activity against all classes of β-lactamases
Phase 3 with cefepime compared to meropenem for cUTI
2 strains resistant to cefepime-taniborbactam, one with NDM, one with KPC-5 and loss of 2 porins
Few MBL-expressing isolates and few OXA-48 containing isolates

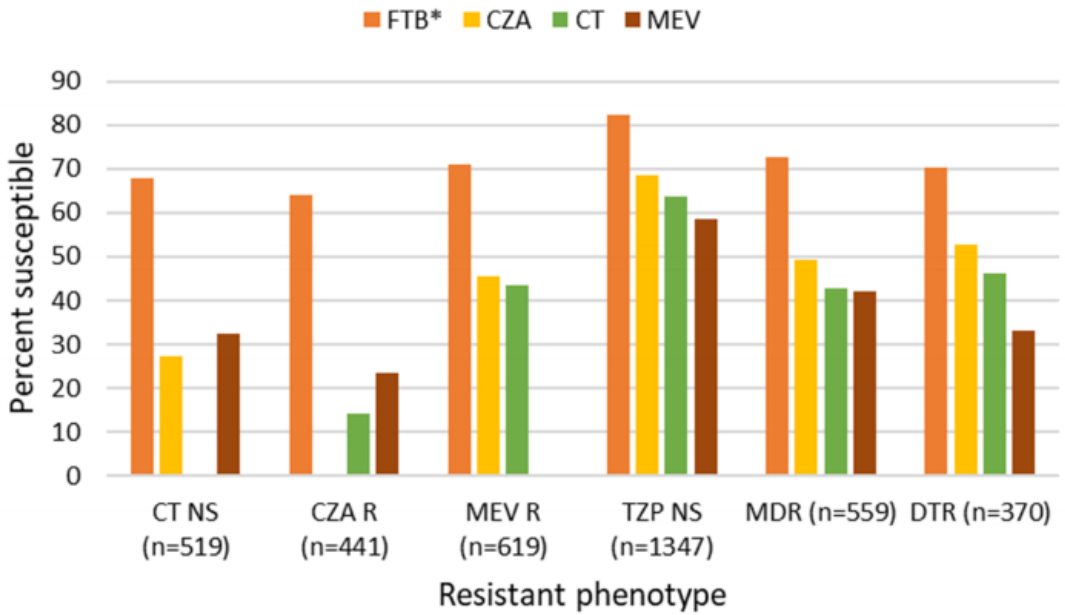
Andrew R. Mack [1,2], Christopher R. Bethel [2], Steven Marshall [2], Robin Patel [3], David van Duin [4], Vance G. Fowler [5], Daniel D. Rhoads [6], Michael R. Jacobs [6], Focco van den Akker [1], David A. Six [7], Greg Moeck [7], Krisztina M. Papp-Wallace [1,2], Robert A. Bonomo [1,2]

ARGONAUT-V: Susceptibility of multidrug-resistant (MDR) *Pseudomonas aeruginosa* to Cefepime-Taniborbactam

1 Case Western Reserve University, Cleveland, OH, USA.
2 Veterans Affairs Northeast Ohio Healthcare System, Cleveland, OH, USA.
3 Mayo Clinic, Rochester, MN, USA.
4 University of North Carolina, Chapel Hill, NC, USA.
5 Duke University Medical Center, Durham, NC, USA
6 University Hospitals Cleveland Medical Center, Cleveland, OH, USA.
7 Venatorx Pharmaceuticals, Inc., Malvern, PA, USA.

Activity of Cefepime in Combination with Taniborbactam (formerly VNRX-5133) Against *Pseudomonas aeruginosa* from a Global 2018-2020 Surveillance Collection

M. Hackel, M. Wise, D. Sahm
IHMA, Inc. Schaumburg, IL, USA



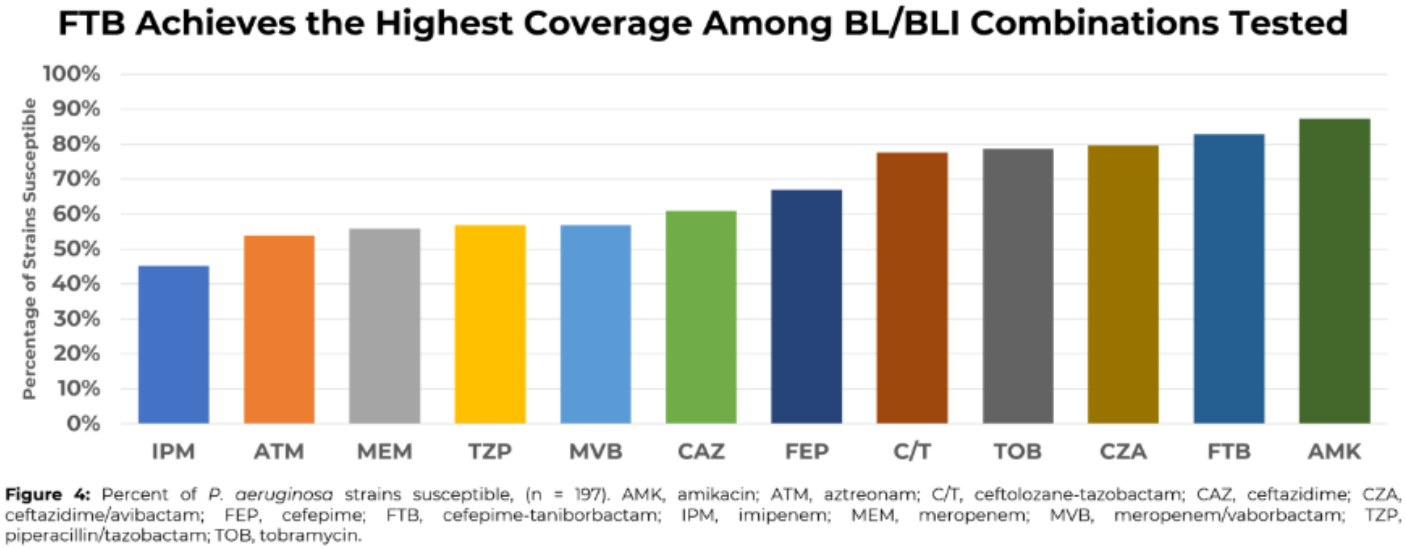
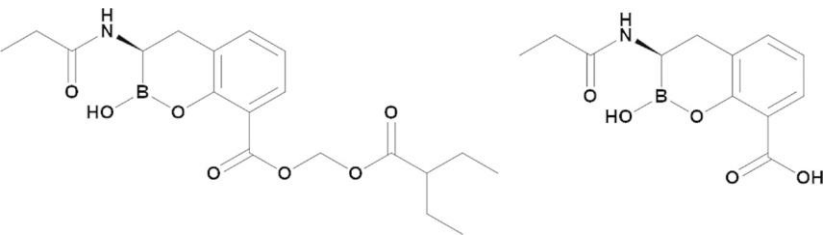


Figure 4: Percent of *P. aeruginosa* strains susceptible, (n = 197). AMK, amikacin; ATM, aztreonam; C/T, ceftolozane-tazobactam; CAZ, ceftazidime; CZA, ceftazidime/avibactam; FEP, cefepime; FTB, cefepime-taniborbactam; IPM, imipenem; MEM, meropenem; MVB, meropenem/vaborbactam; TZP, piperacillin/tazobactam; TOB, tobramycin.

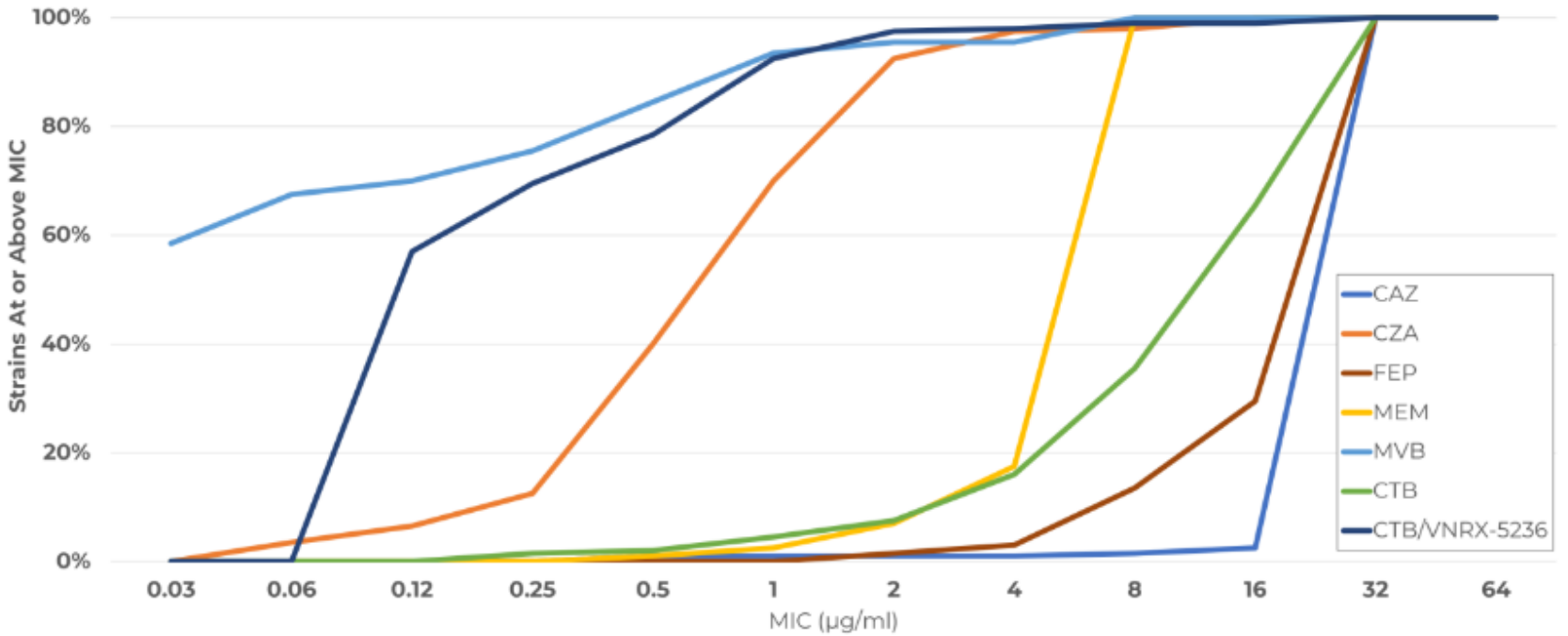
ARGONAUT-IV: Susceptibility of Carbapenem-resistant *Klebsiellae* to Ceftibuten/VNRX-5236

Andrew R. Mack [1,2], Christopher R. Bethel [2], Steven Marshall [2], Robin Patel [3], David van Duin [4], Vance G. Fowler [5], Daniel D. Rhoads [6], Michael R. Jacobs [6], Focco van den Akker [1], David A. Six [7], Greg Moeck [7], Krisztina M. Papp-Wallace [1,2], Robert A. Bonomo [1,2]

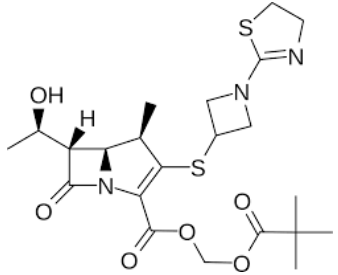
1 Case Western Reserve University, Cleveland, OH, USA.
2 Veterans Affairs Northeast Ohio Healthcare System, Cleveland, OH, USA.
3 Mayo Clinic, Rochester, MN, USA.
4 University of North Carolina, Chapel Hill, NC, USA.
5 Duke University Medical Center, Durham, NC, USA.
6 University Hospitals Cleveland Medical Center, Cleveland, OH, USA.
7 Venatorx Pharmaceuticals, Inc., Malvern, PA, USA.



VNRX-5236 Restores CTB Activity Against Carbapenem-resistant *K. pneumoniae*



Tebipenem



Tebipenem *In vitro* Activity against a Collection of Pathogens Responsible for Urinary Tract Infections in the US

R.E. Mendes[1], I.A. Critchley[2], N. Cotroneo[2], J.M. Streit[1], H.S. Sader[1], M. Castanheira[1]
[1]JMI Laboratories, North Liberty, IA, USA, [2]Spero Therapeutics, Cambridge, MA, USA

Ian A. Critchley
ID Week

October 2021
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Submission ID: 1070826
Poster

In Vitro Activity of Tebipenem and Comparators against Enterobacterales Collected from Patients with Bloodstream Infections as Part of the Global STEWARD Surveillance Program

I.A. Critchley[1], N. Cotroneo[1], M.J. Pucci[1], R.E. Mendes[2]
[1]Spero Therapeutics, Cambridge, MA, [2]JMI Laboratories, North Liberty, IA

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In Vitro Activity of Tebipenem Against Clinically Significant Gram-Negative Bacteria Isolated from Patients with Cancer

Bahgat Gerges, Ph*D; Joel Rosenblatt, PhD*; Ray Hachem, MD*; Anne-Marie Chaftari, MD* ; Issam Raad, MD*.
***University of Texas, MD Anderson Cancer Center.**

An Evaluation of Tebipenem *In Vitro* Activity Against a Panel of *Pseudomonas aeruginosa* Isolates with Efflux, AmpC, and OprD Mutations

B.D. VanScoy[1], H. Conde[1], N. Cotroneo[2], I.A. Critchley[2], T.R. Parr[2], P.G. Ambrose[1]
[1]Institute for Clinical Pharmacodynamics, Inc., Schenectady, NY; [2]Spero Therapeutics, Inc., Cambridge, MA

***In vitro* Activity of Tebipenem, an Orally Available Carbapenem Agent, against a Collection of Surveillance Gram-positive Clinical Isolates**

S.J.R. Arends[1], A.L. Klauer[1], N. Cotroneo[2], I.A. Critchley[2], R.E. Mendes[1]
[1]JMI Laboratories, North Liberty, Iowa, USA, [2]Spero Therapeutics, Cambridge, MA, USA

***In vitro* Activity of Tebipenem against a Recent Collection of Fastidious Organisms Recovered from Respiratory Tract Infections**

S.J.R. Arends[1], A.L. Klauer[1], N. Cotroneo[2], I.A. Critchley[2], R.E. Mendes[1]
[1]JMI Laboratories, North Liberty, Iowa, USA, [2]Spero Therapeutics, Cambridge, MA, USA

Summary: Oral carbapenem in late phase 3 trials
Similar to ertapenem for Gram negatives (not designed for *Pseudomonas aeruginosa*)
Low MICs against MSSA, MSSE, CoNS, *E faecalis*

Gram positive

Activity of an Anti-staphylococcal Lysin, LSVT-1701: In vitro Susceptibility of Staphylococcus aureus and Coagulase-Negative Staphylococci (CoNS) Global Clinical Isolates (2002 to 2019)

David B. Huang[1], Helio S. Sader[2], Paul R. Rhomberg[2], Katyna Borroto-Esoda[1], Eric Gaukel[1]

[1]Lysovant Sciences, Inc., New York, NY, USA; [2]JMI Laboratories, North Liberty, Iowa, USA

1070778

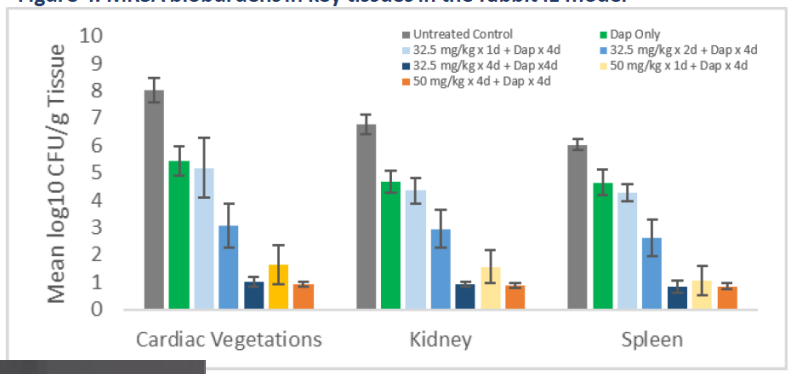
Efficacy of Anti-Staphylococcal Lysin, LSVT-1701, in Combination with Daptomycin in Experimental Left-Sided Infective Endocarditis (IE) Due to Methicillin-Resistant *Staphylococcus aureus* (MRSA)

David B. Huang,[1] Eric J. Gaukel,[1] Nancy Kerzee,[1] Katyna Borroto-Esoda,[1] Simon Lowry,[1] Yan Q. Xiong,[2,3] Wessam Abdelhady,[2] Arnold S. Bayer[2,3]

[1]Lysovant Sciences, Inc., New York, New York, USA; [2] Department of Medicine, Division of Infectious Diseases, The Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center, Torrance, California, USA; [3]The David Geffen School of Medicine at UCLA, Los Angeles, California, USA

- Bacteriophage-encoded lysin
- *In vitro* testing, low MICs including for MRSA, VRSA, and daptomycin-resistant *S. aureus*
- Rabbit model of endocarditis, significant reduction in bioburden with combination therapy vs daptomycin monotherapy

Figure 4. MRSA bioburdens in key tissues in the rabbit IE model



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In vitro Activity of Exebacase (CF-301) against *Staphylococcus aureus* Causing Bacteremia in the United States, Including Multidrug-Resistant Subsets

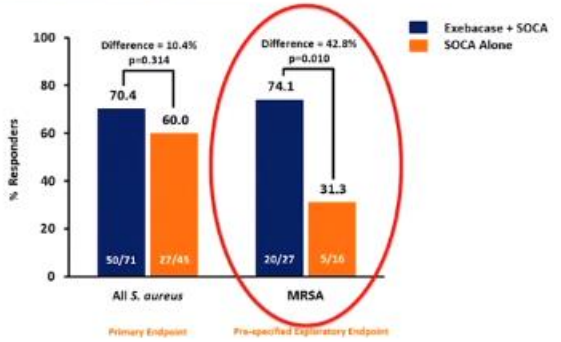
RE Mendes[1], J Lindley[1], N Gurung[1], M Castanheira[1], R Schuch[2], JE Ambler[2]

[1] JMI Laboratories, North Liberty, Iowa; [2] ContraFect Corporation, Yonkers, New York

Exebacase Shows Rapid Symptom Resolution in a Phase 2 Study in Adult Patients with *Staphylococcus aureus* bacteremia

Cara Cassino MD, Anita Das PhD, Joy Lipka, MS

42.8% Higher Clinical Responder Rate at Day 14 with Exebacase in Prespecified MRSA Subgroup



- Lysin currently in Phase 3 development of *S aureus* bacteremia including right-sided endocarditis
- *In vitro* testing, MICs similar for MSSA, MRSA, or MDR *S aureus*

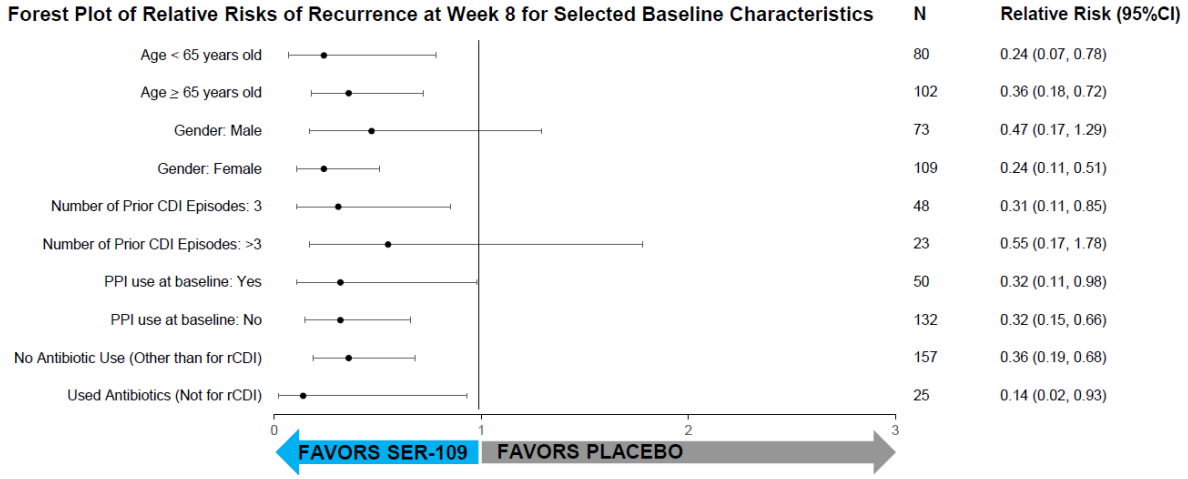
Other agents

THE IMPACT OF INVESTIGATIONAL PURIFIED MICROBIOME THERAPEUTIC SER-109 ON HEALTH-RELATED QUALITY OF LIFE (HRQoL) OF PATIENTS WITH RECURRENT CLOSTRIDIOIDES DIFFICILE INFECTION (rCDI) in ECOSPOR-III, A PLACEBO-CONTROLLED CLINICAL TRIAL

E. Hohmann[1], P. Feuerstadt[2], C. Oneto[3], C. Berenson[4], C. Lee[5], S. Pham[6], L. Zhu[6], PR Reese[6], H. Wu[7], E. Wang[8], L. von Moltke[8], **KW. Garey[9]**

[1]Massachusetts General Hospital [2]Yale University School of Medicine [3]NYU Langone [4]State University of New York at Buffalo [5]University of British Columbia [6]Aesara [7]CR Medicon Research [8]Seres Therapeutics [9]University of Houston College of Pharmacy

Relative Risk of Recurrence at Week 8 for Selected Baseline Characteristics



Investigational Microbiome Therapeutic SER-109 Reduces Recurrence of *Clostridioides difficile* Infection (rCDI) Compared to Placebo, Regardless of Risk Factors For Recurrence

S. H. Cohen[1], T. Louie[2], M. Sims[3], J. Pullman[4], E. Wang[5], B., McGovern[5], L. von Moltke[5]

UC Davis Medical Center[1], University of Calgary, Canada[2], Beaumont Health, Michigan[3], Mercury Street Medical, Butte, MT[4], Seres Therapeutics, Massachusetts[5]

TIME TO RECURRENCE OF *CLOSTRIDIOIDES DIFFICILE* INFECTION (rCDI) IS RAPID FOLLOWING COMPLETION OF STANDARD OF CARE ANTIBIOTICS: RESULTS FROM ECOSPOR-III, A PHASE 3 DOUBLE-BLIND, PLACEBO-CONTROLLED RANDOMIZED TRIAL OF SER-109, AN INVESTIGATIONAL MICROBIOME THERAPEUTIC

T. Louie[1], M. Sims[2], R. Nathan[3], S. O'Marro[4], P. Kumar[5], E. Wang[6], R. Stevens[6], K. Brady[6], B. McGovern[6] and L. von Moltke[6]

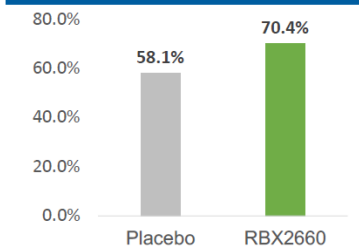
[1]University of Calgary, Canada, [2]Beaumont Health, Michigan, [3]Mountain View Hospital, Nevada, [4]Springfield Clinic, Illinois, [5]Georgetown University Hospital, Washington DC, [6]Seres Therapeutics, Massachusetts

Treatment Success in Reducing Recurrent *Clostridioides difficile* Infection with Investigational Live Biotherapeutic RBX2660 was Associated with Microbiota Restoration: Consistent Evidence from a Phase 3 Clinical Trial

Ken Blount PhD [1], Dana Walsh PhD [1], Carlos Gonzalez [2], Bill Shannon PhD MBA [2]

[1] Rebiotix Inc., A Ferring Company, Roseville, MN, USA; [2] BioRankings LLC, St. Louis, MO, USA

RBX2660 CLINICAL EFFICACY



RBX2660 MET THE PRESPECIFIED THRESHOLD OF SUCCESS, with a **0.986** posterior probability of superiority for RBX2660 vs placebo; treatment success was 70.4% for RBX2660 and 58.1% for placebo.

(reported previously by Lee et al, DDW 2021)

Viral

PRITELIVIR IN IMMUNOCOMPROMISED PATIENTS WITH MUCOCUTANEOUS ACYCLOVIR-RESISTANT HERPES SIMPLEX VIRUS-INFECTIONS – FIRST CASE SERIES

Kimberly Workowski[1], Joerg Albrecht[2], Robin Avery[3], Pranatharthi Chandrasekar[4], Roy Chemaly[5], Nicolas Issa[6], Camille Kotton[7], Princy Kumar[8], Mayur Ramesh[9], Moti Ramgopal[10], Josuha Schiffer[11], Tanya Schreibman[12], Anna Wald[13], Michael Ison[14]

1: Emory University, Department of Medicine, Atlanta/GA; 2: Cook County Hospital, Chicago/IL; 3: Johns Hopkins University, Baltimore/MD; 4: - Karmanos Cancer Center, Wayne State University, Detroit ; 5: The University of Texas MD Anderson Cancer Center, Houston/TX; 6: Brigham and Women's Hospital, Boston/MA; 7: Massachusetts General Hospital, Boston/MA; 8: Georgetown University, Washington/DC; 9: Henry Ford Health System; 10: Midway Immunology and Research Center, Ford Pierce/FL; 11: Fred Hutchinson Cancer Research Center, Seattle/WA; 12: Comprehensive Care Center Inc. d.b.a. Community AIDS Network, Sarasota/FL; 13: University of Washington, Seattle/WA; 14: Northwestern University, Feinberg School of Medicine, Chicago/IL

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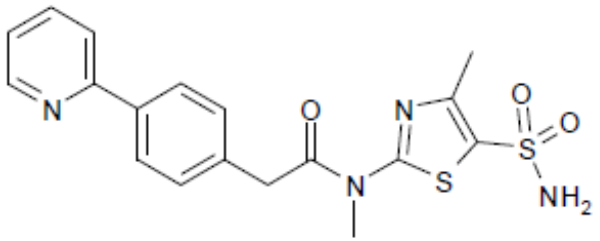


Population treated with pritelivir in Phase 2

Treatment
- 400 mg pritelivir oral loading dose on day 1
- 100 mg pritelivir oral maintenance dose daily for up to 28 days

Patients
- 23 immunocompromised patients in total
  - 11 HIV patients
  - 12 patients with malignancies, transplant or autoimmune disease
- 8 of the patients with foscarnet intolerance or resistance

Outcome
- 19 patients completely healed within 28 days
- 4 patients did not completely heal during the treatment period
- Pritelivir was well tolerated in all patients without significant adverse effects

Analysis of patients that did not heal within 28 days
- 1 patient with extensive lesions that did not heal within 28 days but in the follow-up period
- 1 case of resistance to trial medication but healed within follow-up period
- 1 patient with lesions in the oral cavity
- 1 patient with CMV reactivation therefore required stopping of pritelivir treatment

Fungal

Activity of Rezafungin and Comparator Antifungal Agents Tested Against a Worldwide Collection of Contemporaneous Invasive Fungal Isolates (2019–2020)

Cecilia G. Carvalhaes, Abby L. Klauer, Paul R. Rhomberg, Michael A. Pfaller, Mariana Castanheira

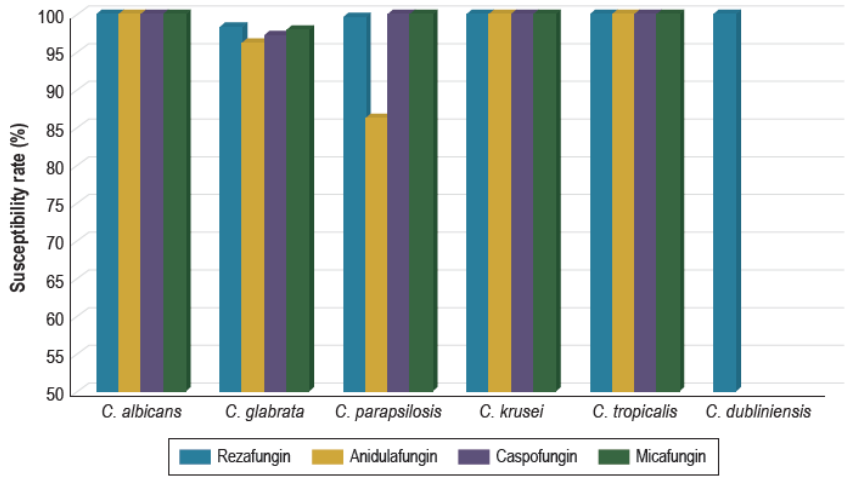
JMI Laboratories, North Liberty, Iowa, USA

Once weekly administration

In vitro testing against collected isolates of *Candida albicans, Candida glabrata, Candida parapsilosis, C. tropicalis*, *C. dublienensis*, and *C. krusei*

Similar activity as other echinocandins against *Candida spp*, *Aspergillus spp,* not effective for *Cryptococcus neoformans*

Figure 3. Echinocandin susceptibility rates against *Candida* spp. collected worldwide between 2019 and 2020



Clinical breakpoints are not available for other echinocandins against *C. dubliniensis*.

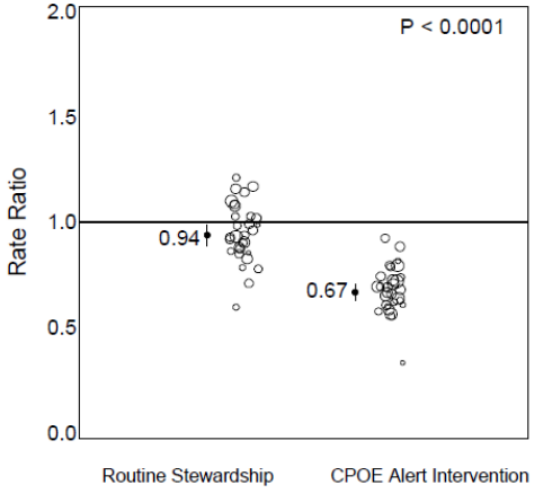
Stewardship

INSPIRE Pneumonia Trial

INtelligent Stewardship Prompts to Improve Real-time Empiric Antibiotic Selection for Patients

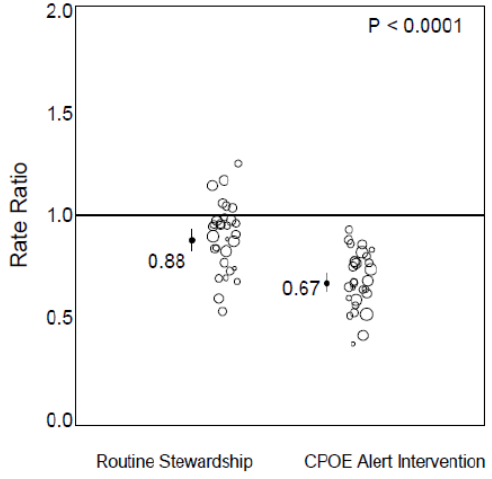
45,108 patients with pneumonia admitted to non-ICU, two arms, routine care or computerized order entry with prompt for standard spectrum antibiotics if < 10% risk of resistant organism and feedback if continued extended-spectrum use

Primary Outcome
Extended Spectrum-DOT



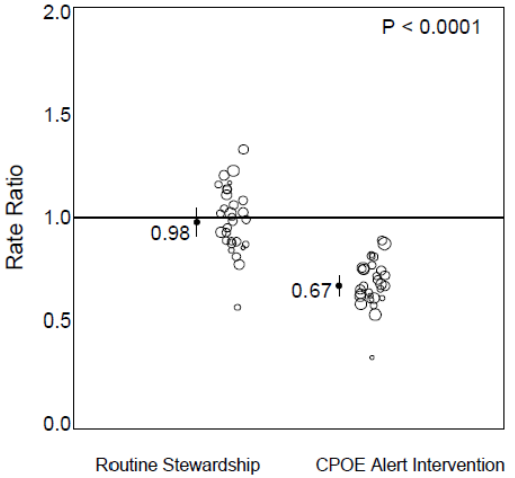
INSPIRE Prompt Group
28% reduction in
Extended-spectrum DOT

Secondary Outcome
Vancomycin-DOT



INSPIRE Prompt Group
24% reduction in
Vancomycin-DOT

Secondary Outcome
Antipseudomonal-DOT



INSPIRE Prompt Group
31% reduction in
Antipseudomonal-DOT

DETOURS

De-escalating Empiric Treatment: Opting OUt of Rx for Selected Patients with Suspected Sepsis

Moehring RW, Yarrington MY, Warren BG, Lokhnygina YL, Atkinson E, Bankston A, Coluccio J, David MZ, Davis A, Davis J, Dionne B, Dyer A, Jones T, Klompas M, Kubiak DW, Marsalis J, Omorogbe J, Orajaka P, Parish A, Parker T, Pearson JC, Pearson T, Sarubbi CS, Shaw C, Spivey J, Wolf R, Wrenn RH, Dodds Ashley ES, Anderson DJ, and the CDC Prevention Epicenters Program

- Opt-out protocol to decrease unnecessary antibiotics in some patients with suspected sepsis
- Screened patients with negative blood cultures at 48-96h (or CoNS without central line), on broad-spectrum antibiotics, and not in ICU
- Safety check performed to ensure vital signs, past medical history, and laboratory values not concerning
- Patients who passed prior checks randomized to intervention where verbal intervention recommending stopping antibiotics
- If team opted to continue antibiotics still encouraged de-escalation or identifying an end date

Design and Preclinical Characterization of SER-155, an Investigational Cultivated Microbiome Therapeutic to Restore Colonization Resistance and Prevent Infection in Patients Undergoing Hematopoietic Stem Cell Transplantation (HSCT)

September 29 – October 3, 2021

IDWeek 2021
Session: Novel Antimicrobial Agents, #130

Elizabeth Halvorsen, Marin Vulić, Edward O'Brien, Jessica Byrant, Mary-Jane Lombardo, Christopher Ford, Matthew Henn

- SER-155: designed collection of human commensal bacteria
- Goal to restore microbiome post-SCT to improve outcomes, mouse model with oral administration, now enrolling in phase 1b

ID Week 2021: HIV and Miscellaneous ID Updates

(Join CHANT today for COVID Treatment Updates)

Raj Gandhi, MD
Massachusetts General Hospital
Harvard Medical School

Disclosures: Scientific Advisory Board, Merck (> 2 years ago)

What to Start in Pregnancy: US DHHS Guidelines Feb 10, 2021

Two NRTIs

Abacavir/3TC

or

TDF/FTC or TDF/3TC

TAF/FTC – alternative NRTI

Plus

Integrase inhibitor:

Raltegravir (twice daily) or

Dolutegravir (*Preferred ARV throughout pregnancy and for those who are trying to conceive*)

or

Protease inhibitor:

Darunavir/ritonavir (twice daily) or

Atazanavir/ritonavir

Bictegravir (insufficient data)
Elvitegravir/cobi (PK concerns)
DRV/cobi (PK concerns)
ATV/cobi (PK concerns)
DOR (insufficient data)
2-drug regimens not recommended

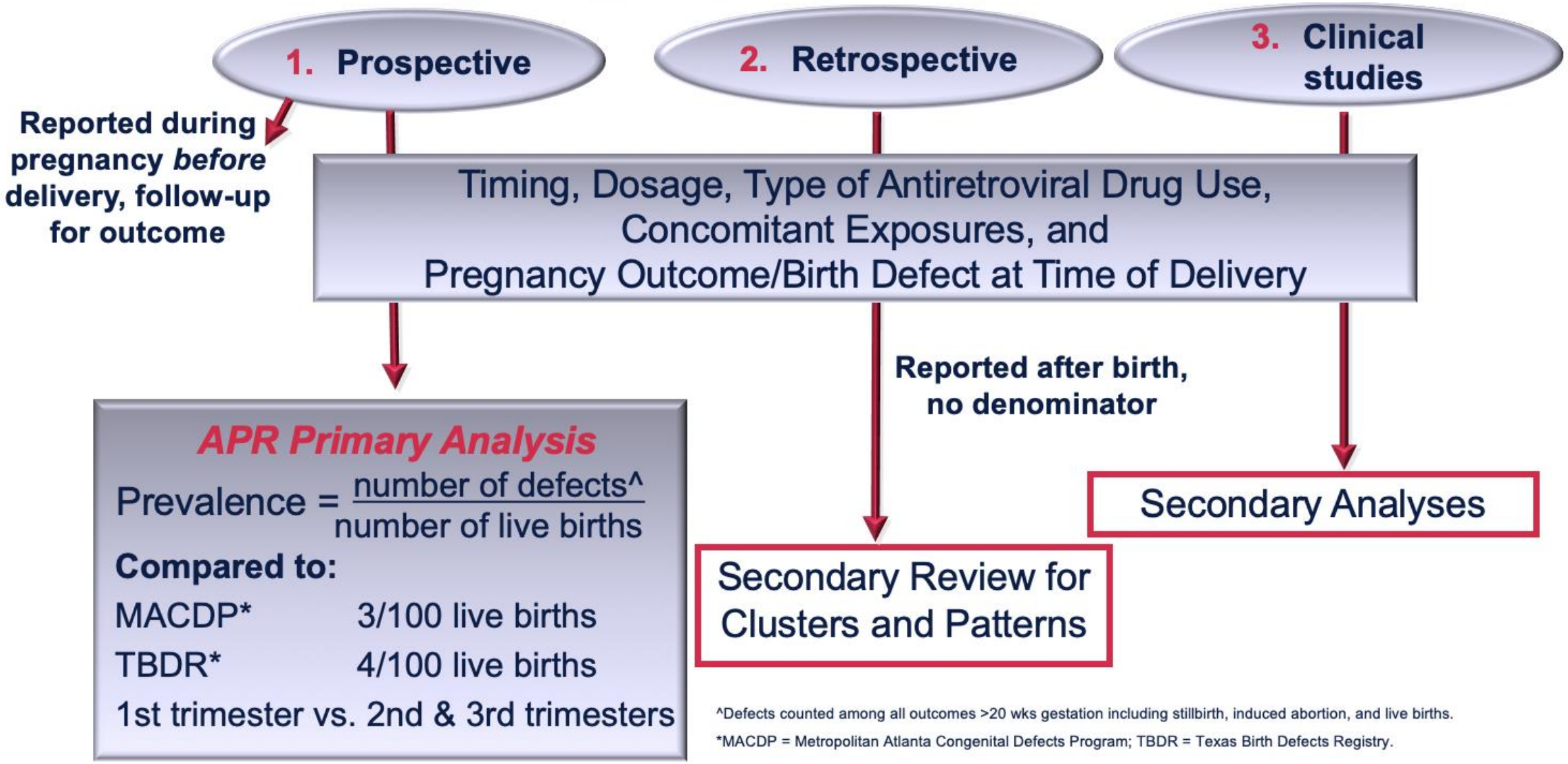
Decreasing Rate of Neural Tube Defects (NTDs) in Women with HIV who Conceive While on DTG

- 2018: Tsepamo study found increase in NTD prevalence among infants born to Botswanan women who conceived on DTG (DTG vs non-DTG: 0.94% vs. 0.12%)
- As more data have accrued, NTD prevalence with DTG has decreased; not significantly different from non-DTG ART at conception

	Conception			HIV-Negative
	DTG	Non-DTG	EFV	
Total NTDs per exposures, n/N	9/5860	22/22,475	8/13,217	97/144,967
NTD prevalence, % (95% CI)	0.15 (0.08-0.29)	0.10 (0.06-0.15)	0.06 (0.03-0.12)	0.07 (0.05-0.08)
Prevalence diff. for DTG at conception, % (95% CI)	Ref	0.06 (-0.03 to 0.20)	0.09 (-0 to 0.23)	0.09 (0.01-0.23)

1. Zash. NEJM. 2018; 379:979. 2. Zash. IAS 2021. Abstr. PE02B52.

Antiretroviral Pregnancy Registry Analyses



^Defects counted among all outcomes >20 wks gestation including stillbirth, induced abortion, and live births.

*MACDP = Metropolitan Atlanta Congenital Defects Program; TBDR = Texas Birth Defects Registry.

Vannappagari V et al, IDWeek 2021

Prevalence of Birth Defects – DTG Exposed Pregnancies

Prevalence and 95% Confidence Intervals for Birth Defects

Number of live births	956
Number of live births with at least one defect	39 (39/956 = 4.1%, 95% CI: 2.92-5.53)

Timing of Exposure	Birth Defects/Live Births	Prevalence % (95% CI)**
First trimester	19/576	3.3 (95% CI: 2.00-5.10)
Periconception	16*/475	3.4 (95% CI: 1.94-5.41)
Later first trimester	3/101	3.0 (95% CI: 0.62-8.44)
Second/Third trimester	20/380	5.3 (95% CI: 3.24-8.01)

*Includes one neural tube defect.

**Based on Clopper-Pearson exact method.

Vannappagari V et al, IDWeek 2021

Drug-Specific Overall Birth Defect Rates

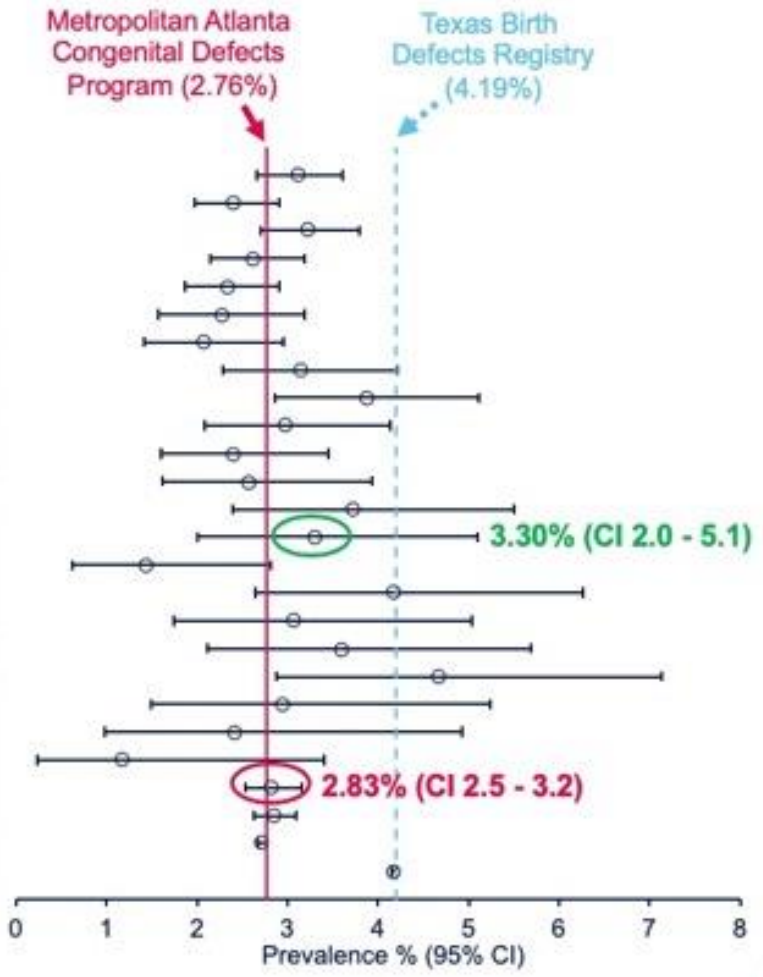
- **Prevalence of birth defects (95% CI) with 1st trimester exposure: 1 January 1989 to 31 January 2021**
  - For drug to be included for comparison with population rates, must meet threshold of having ≥200 1st trimester exposed pregnancies
  - 22 ARVs have ≥200 first trimester exposures

	Defects/Live births	Prevalence (95% CI), %
Lamivudine	169/5433	3.11 (2.66-3.61)
Tenofovir DF	108/4483	2.41 (1.98-2.90)
Zidovudine	136/4225	3.22 (2.71-3.80)
Emtricitabine	104/3952	2.63 (2.15-3.18)
Ritonavir	81/3453	2.35 (1.87-2.91)
Atazanavir	33/1447	2.28 (1.57-3.19)
Lopinavir	30/1439	2.08 (1.41-2.96)
Abacavir	43/1368	3.14 (2.28-4.21)
Nelfinavir	47/1212	3.88 (2.86-5.12)
Nevirapine	35/1171	2.99 (2.09-4.13)
Efavirenz	28/1166	2.40 (1.60-3.45)
Stavudine	21/811	2.59 (1.61-3.93)
Darunavir	24/643	3.73 (2.40-5.50)
Dolutegravir	**19/576**	3.30 (2.00-5.10)
Rilpivirine	8/557	1.44 (0.62-2.81)
Tenofovir alafenamide	22/526	4.18 (2.64-6.27)
Raltegravir	15/486	3.09 (1.74-5.04)
Cobicistat	17/473	3.59 (2.11-5.69)
Didanosine	20/427	4.68 (2.88-7.14)
Elvitegravir	11/371	2.96 (1.49-5.24)
Indinavir	7/289	2.42 (0.98-4.93)
Telbivudine	3/254	1.18 (0.24-3.41)
First Trimester APR	**310/10950**	2.83 (2.53-3.16)
Any Trimester APR	590/20686	2.85 (2.63-3.09)
MACDP		2.72 (2.68-2.76)
TBDR		4.17 (4.15-4.19)

MACDP = Metropolitan Atlanta Congenital Defects Program.

TBDR = Texas Birth Defects Registry.

95% CIs are calculated using the Clopper-Pearson exact binomial method.



Overall birth defect rate with DTG use (4.1%) no different than population expected rate (2.8% and 4.2%).

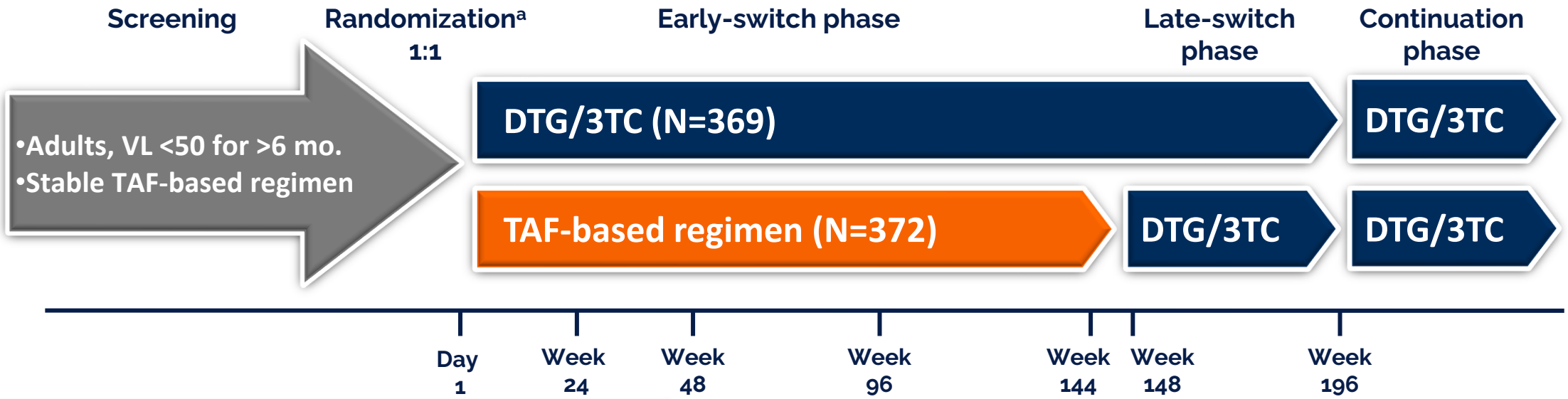
One NTD with 475 periconception DTG exposures (0.21%)

Vannappagari V et al, IDWeek 2021

New Insights into Weight Gain and Metabolic Complications

TANGO: Switching from TAF-based ART to DTG/3TC

Phase 3, non-inferiority open label study in people on stable TAF-based ART with VL<50



- No HBV infection
- No prior VF and no documented NRTI/INSTI resistance
- TAF/FTC + INSTI 79% (about 66% EVG/c), 12% RPV, 7% bDRV
- Median duration of ART before switch: (~3 yr)

At week 144, rate of virologic suppression similar with DTG/3TC and TAF-based ART

Wang. IAS 2021. Abstr OAB0301

SALSA: DTG/3TC for Maintenance Therapy

- SALSA: efficacy of switching to DTG/3TC compared with continuing any current 3- or 4-drug ART regimen (n=493)

Who was in SALSA?
- Duration of ART: ≅5-6 yr
- NRTI: TDF (44%)
- Baseline 3rd agent:
  - INSTI (40%)
  - NNRTI (50%)
  - PI (10%)

CAR: current antiretroviral therapy

At week 48, rate of virologic suppression similar with DTG/3TC and 3-or 4-drug ART

Llibre J et al, IAS 2021, Abstract OALB0303

Weight Gain after Switching to DTG/3TC: Lessons from TANGO and SALSA

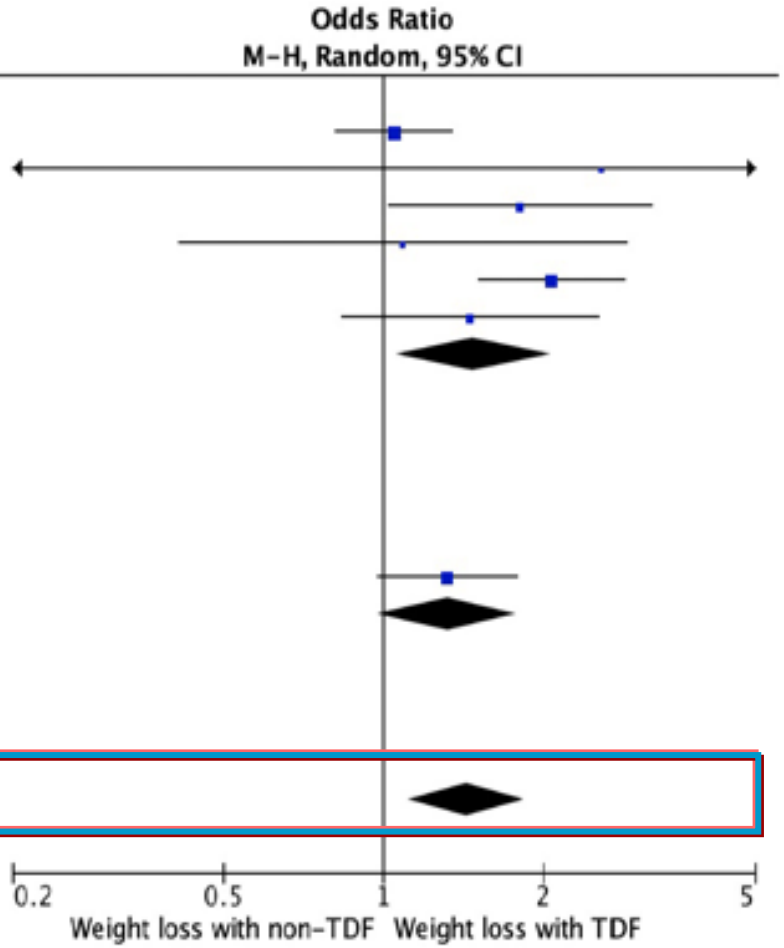
Study	Weight change (kg): DTG/3TC vs. CAR	Demographics	Baseline TDF use	Baseline EFV use
TANGO	0.81 vs. 0.76 kg	8% female 23% ≧50 yr 21% non-white	0%	<1.5%
SALSA	2.1 vs. 0.6 kg	39% female 39% ≧50 yr 41% non-white	44%	32%

- **Potential reasons more weight gain seen with DTG/3TC in SALSA than in TANGO**
  - Higher risk population: greater proportion female, non-white, > age 50
  - Higher proportion were on medication that may attenuate weight gain (TDF, EFV); withdrawal of those medicines may have led to greater weight gain

Llibre J et al, IAS 2021, Abstract OALB0303; van Wyk J et al, CID, 2020

TDF Associated with Weight Loss: Meta-analysis of 7 Clinical Trials in >19,000 People Without HIV

Study or Subgroup	TDF Events	TDF Total	non-TDF Events	non-TDF Total	Weight	Odds Ratio M-H, Random, 95% CI
1.2.1 TDF or TDF/FTC vs Placebo						
BKK (TDF vs Placebo)	140	1204	135	1209	24.7%	1.05 [0.81, 1.35]
FEM-PrEP (TDF/FTC vs Placebo)	1	1205	0	1033	0.6%	2.57 [0.10, 63.26]
iPrEX (TDF/FTC vs Placebo)	34	1251	19	1248	12.4%	1.81 [1.03, 3.19]
Partners (TDF/FTC vs Placebo)	13	3163	6	1584	5.6%	1.09 [0.41, 2.86]
TDF-2 (TDF/FTC vs Placebo)	133	611	72	608	21.8%	2.07 [1.52, 2.83]
VOICE (TDF or TDF/FTC vs Placebo)	49	2010	17	1009	12.6%	1.46 [0.84, 2.54]
Subtotal (95% CI)		**9444**		**6691**	**77.8%**	**1.48 [1.06, 2.07]**
Total events	370		249			
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 12.40$, df = 5 (P = 0.03); $I^2 = 60\%$						
Test for overall effect: Z = 2.28 (P = 0.02)						
1.2.2 TDF/FTC vs Cabotegravir						
HPTN 084 (TDF/FTC vs CAB)	101	1610	78	1614	22.2%	1.32 [0.97, 1.79]
Subtotal (95% CI)		**1610**		**1614**	**22.2%**	**1.32 [0.97, 1.79]**
Total events	101		78			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.78 (P = 0.07)						
Total (95% CI)		**11054**		**8305**	**100.0%**	**1.44 [1.12, 1.85]**
Total events	471		327			
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 12.53$, df = 6 (P = 0.05); $I^2 = 52\%$						
Test for overall effect: Z = 2.81 (P = 0.005)						
Test for subgroup differences: $Chi^2 = 0.25$, df = 1 (P = 0.62), $I^2 = 0\%$						

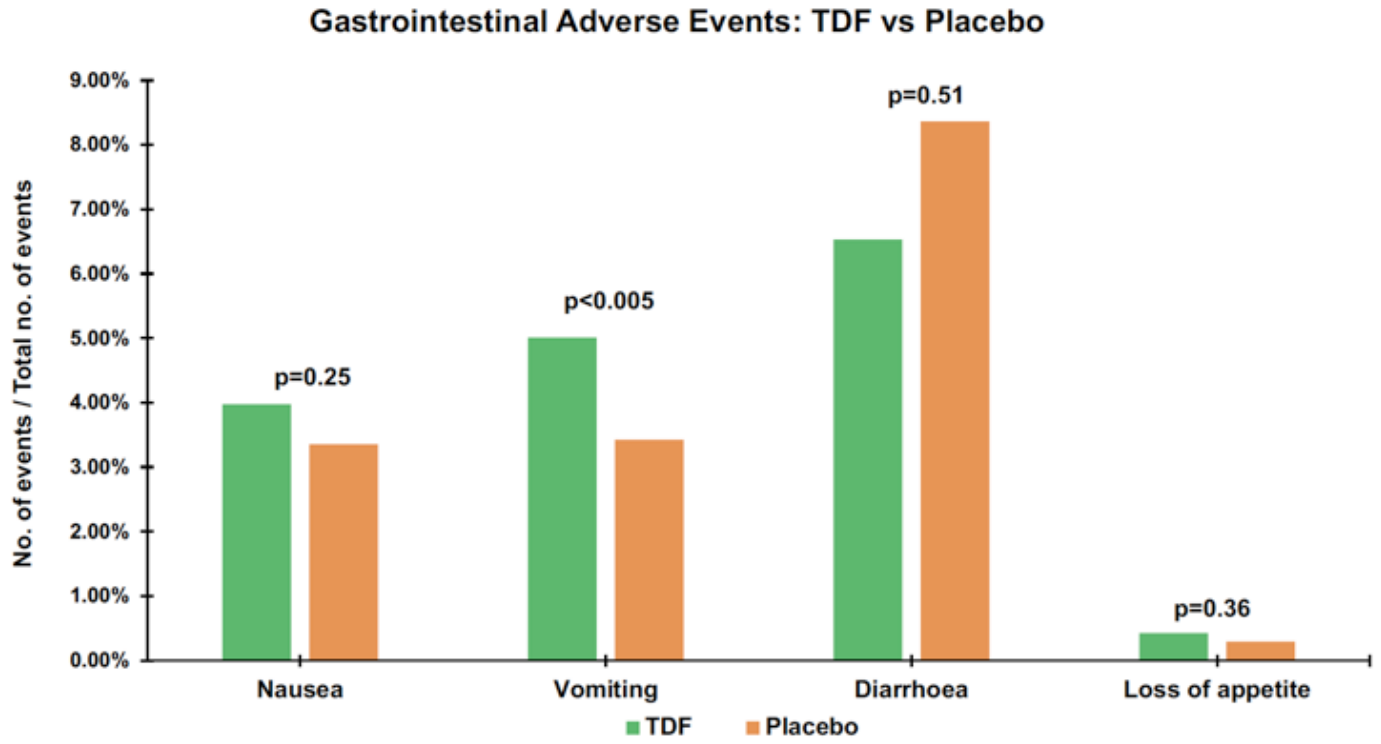


Shah S et al, IDWeek 2021

TDF Associated with Weight Loss: Meta-analysis of 7 Clinical Trials in >19,000 People Without HIV

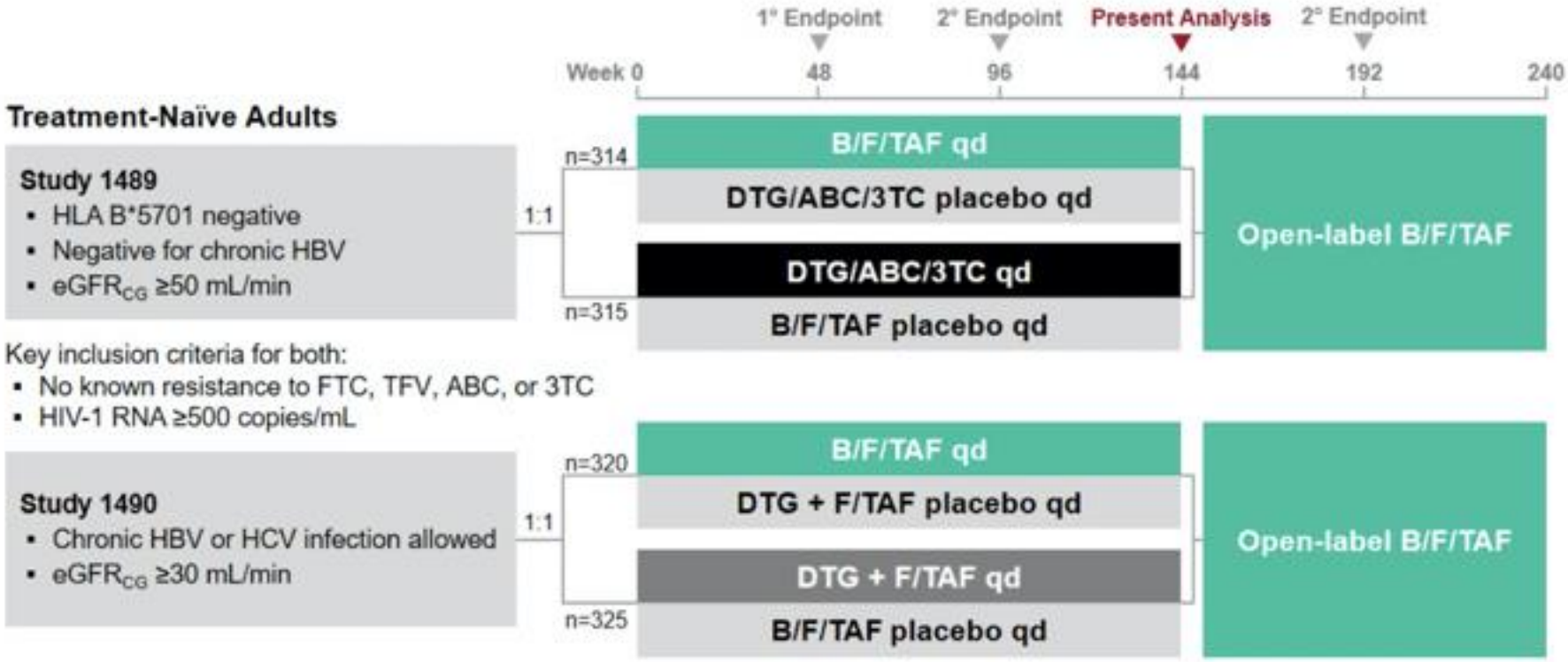
Gastrointestinal adverse events

In a separate analysis of GI AEs, exposure to TDF was also linked to greater odds of vomiting (OR 1.81 95% CI (1.20, 2.73) p <0.005). There were no increased odds of nausea, diarrhoea, or loss of appetite.



Shah S et al, IDWeek 2021

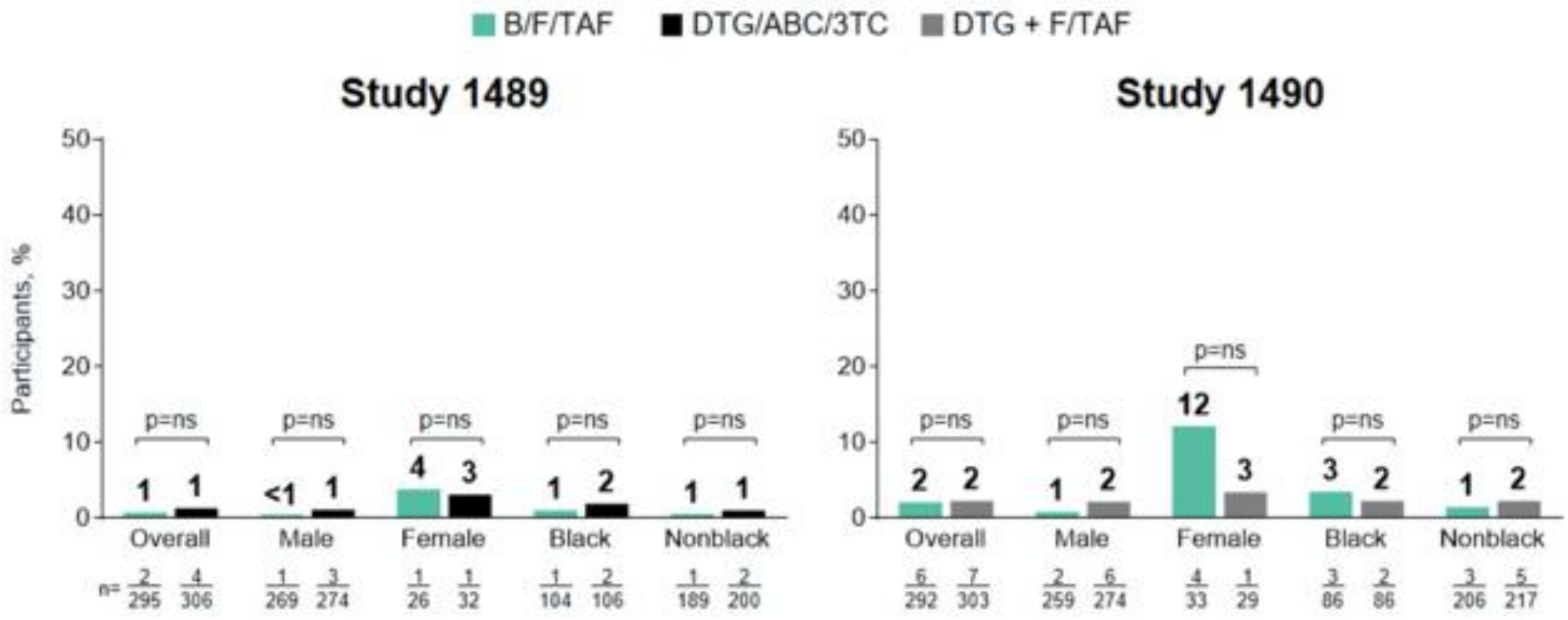
Incidence of Metabolic Complications in PWH Randomized to BIC/TAF/FTC, DTG/ABC/3TC or DTG + TAF/FTC



- Median age: early 30s. Male sex: about 90%. About 30-36% African American
- Median CD4 cell count: mid-400s

Daar E et al, IDWeek 2021

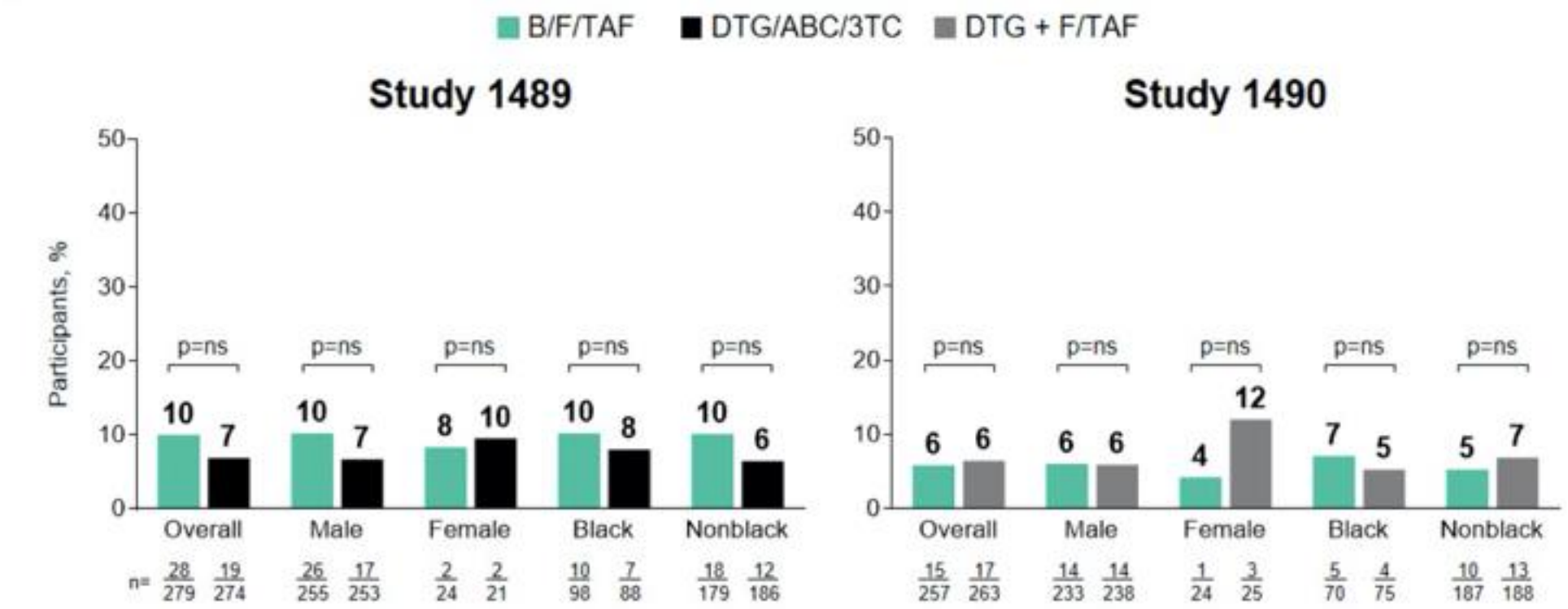
Treatment-emergent DM over 144 weeks: 1-2%



- Treatment-emergent diabetes events occurred at low rates in both studies (1–2% of overall population)
  - Subgroup analyses showed similar findings when evaluating participants by sex at birth or race

Daar E et al, IDWeek 2021

Treatment-emergent Hypertension over 144 weeks: <10%



- Treatment-emergent hypertension events occurred ≤10% in both studies in the overall population
- Subgroup analyses showed similar findings when evaluating participants by sex at birth or race

*Excluding those with medical history of hypertension; p-values from Fisher exact test to compare treatment groups; hypertension events defined using search list "hypertension (SMQ)" in MedDRA version 23.1; ns, nonsignificant (p≥0.05).

Daar E et al, IDWeek 2021

Does changing ART ameliorate weight gain?

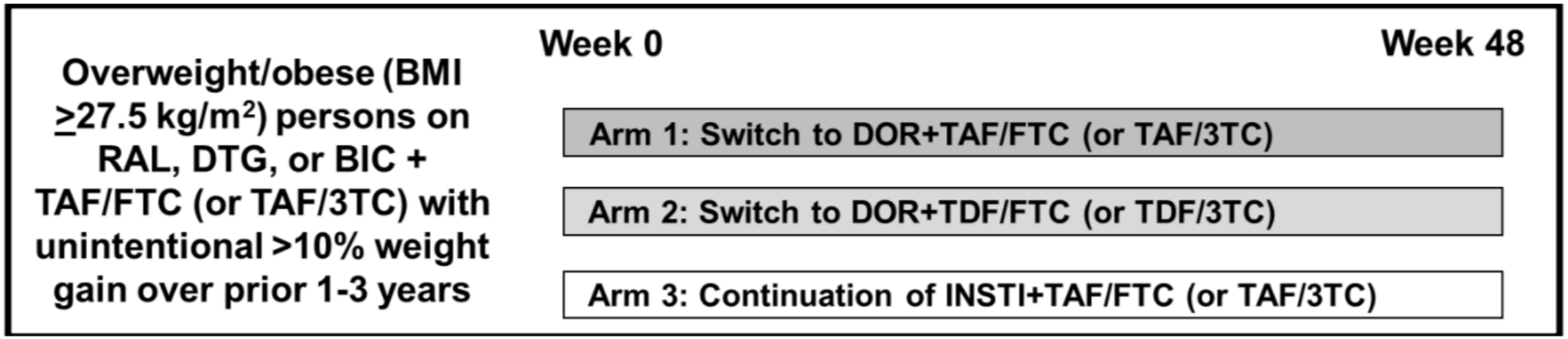
Open Forum Infectious Diseases

NOVEL ID CASES (INVITED)

Case Report: Reversal of Integrase Inhibitor– and Tenofovir Alafenamide–Related Weight Gain After Switching Back to Efavirenz/Emtricitabine/Tenofovir DF

F. Will Pohlman,[1] Kara S. McGee,[2,3] and Mehri S. McKellar[2]

ACTG A5391 (Do-IT study): Doravirine for Persons with Excessive Weight Gain on Integrase Inhibitors and TAF



Invasive Pneumococcal Disease (IPD) in PWH

- Risk of IPD is increased in PWH, even in era of widespread ART
- **PCV13** recommended for adults with immunocompromising conditions, including HIV, in 2012
- Following this recommendation, IPD rates in PWH fell by as much as 40%
  - Rate of PCV13 serotypes fell by up to 73%
- Nevertheless, 2017-18 IPD incidence rate **17-fold higher in people with HIV than in people without HIV**
  - PCV13 serotype IPD was 13-fold higher

Marcus. AIDS Patient Care STDS. 2016;30:463. CDC. MMWR Morb Mortal Wkly Rep. 2010; 59: 1-18.
CDC. MMWR Morb Mortal Wkly Rep. 2012;61:816. Kobayashi. IDWeek 2021. Abstr 70.

Vaccine-type IPD in PWH

- Two new pneumococcal conjugate vaccines recently approved, but not yet included in CDC recommendations on prevention of IPD
  - **PCV15** targets PCV13 serotypes plus 2 other serotypes
  - **PCV20** targets PCV15 serotypes plus 5 other serotypes
- Newly approved pneumococcal conjugate vaccines with higher valency may be effective to reduce disease burden against broad range of IPD serotypes observed in people with HIV

% Vaccine-Type IPD, 2017-2018	PWH
PCV13 type*	35
PCV15 unique	15
PCV20 unique	17
PPSV23, non-PCV20†	11
Nonvaccine type	22

*PCV13 serotypes 1, 5, and 14 were not detected.
†PCV23, non-PCV20 serotype 2 was not detected.

Kobayashi. IDWeek 2021. Abstr 70.

Slide credit: clinicaloptions.com

COVID-19 Treatment Highlights
(join CHANT today for more)

- In high-risk outpatients with mild-moderate COVID-19 and within 7 days of symptom onset, 3 days of iv remdesivir reduced hospitalization/death by 87%
- In high-risk outpatients with mild-moderate COVID-19, single iv infusion of BRII-196/BRII-198 anti-SARS CoV-2 monoclonal antibodies reduced hospitalization/death by 78%
- In high-risk outpatients with mild to moderate COVID-19 within 5 days of symptom onset, molnupiravir reduced hospitalization/death by 48%
- In seronegative hospitalized patients requiring low flow or no oxygen and who are within 10 days of symptom onset, casirivimab/imdevimab associated with decreased mortality
- In a phase 3 pre-exposure prophylaxis trial (PROVENT; n=5197)), single dose of tixagevimab/cilgavimab (AZD7442) reduced risk of symptomatic COVID-19 by 77%

Hill J et al, IDWeek, 2021; Evering T et al, IDWeek 2021; Mylonakis E et al, IDWeek 2021; Levin M et al, IDWeek 2021

Other IDWeek 2021 Highlights

- Currently, monthly doses of palivizumab during RSV season used to prevent RSV in infants at high risk (eg, prematurity).
  - In phase 3 trial (MELODY, n=1490), single IM dose of nirsevimab (longer half-life) reduced medically attended RSV lower respiratory tract infections by 75% in otherwise healthy infants (NNT: 11)
- In phase 2b trial in older adults (CYPRESS), Ad26.RSV.preF-based vaccine reduced RSV lower respiratory tract infection by 70-80%. Several RSV vaccines, including this one, in phase 3 trials
- In a retrospective study involving 132 adults with osteomyelitis, two doses of dalbavancin compared favorably to standard of care antibiotics (oral or iv)
  - About 75% had lower extremity osteomyelitis; about 45% had diabetic foot infection
  - Treatment failure about 20% in both groups
  - Shorter hospital length of stay, fewer catheter related complications in the dalbavancin group
  - Larger, prospective and randomized trials needed

Hammitt L et al, IDWeek 2021, LB13; Falsley A et al, IDWeek 2021, LB14; Cain A et al, IDWeek 2021, #108