of Merck & Co., Inc.: Employee and Shareholder, May hold stock/stock options in the company and Salary. **S. Kumar**, Merck & Co., Inc.: Employee and Shareholder, Salary. **P. Sklar**, Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.: Employee and Shareholder, Salary. **G. J. Hanna**, Merck Sharp & Dohme, a subsidiary of Merck & Co., inc.: Employee and Shareholder, May hold stock/stock options in the company. and Salary. **C. Hwang**, Merck Sharp & Dohme, a subsidiary of Merck & Co., Inc.: Employee and Shareholder, Salary. **W. Greaves**, Merck Sharp & Dohme, a subsidiary of Merck & Co., Inc.: Employee, May hold stock/stock options within the company.

DRIVE-SHIFT Phase 3 Trial: Efficacy & Safety Outcomes

| Efficacy (FDA Snapshot Approach) | DOR/3TC/TDF QD (ISG) N=447 | | Baseline Regimen (DSG) N=223 | | ISG minus DSG |
|---|---|---|---|---|---|
| ISG vs DSG, Week 24 | n | (%) | n | (%) | Difference (95% CI) |
| HIV-1 RNA <50 copies/mL | 419 | (93.7) | 211 | (94.6) | -0.9 (-4.7, 3.0) |
| HIV-1 RNA ≥50 copies/mL | 8 | (1.8) | 4 | (1.8) | -0.0 (-2.3, 2.3) |
| ISG Week 48 vs DSG Week 24 | n | (%) | n | (%) | Difference (95% CI) |
| HIV-1 RNA <50 copies/mL | 406 | (90.8) | 211 | (94.6) | -3.8 (-7.9, 0.3) |
| HIV-1 RNA ≥50 copies/mL | 7 | (1.6) | 4 | (1.8) | -0.2 (-2.5, 2.1) |
| **Safety Outcomes, Week 24** | **DOR/3TC/TDF QD (ISG) N=447** | | **Baseline Regimen (DSG) N=223** | | **ISG minus DSG** |
| Lipids, Change from Baseline (PI+rtv Stratum) | Mean Change (95% CI) | | Mean Change (95% CI) | | Difference (95% CI) |
| Fasting LDL-C (mg/dL) | -16.5 (-19.4, -13.7) | | -1.9 (-6.5, 2.6) | | -14.6 (-18.9, -10.4) |
| Fasting non-HDL-C (mg/dL) | -24.7 (-28.3, -21.2) | | -1.3 (-6.2, 3.6) | | -23.0 (-28.0, -18.1) |
| Adverse Event (AE) Summary | n | (%) | n | (%) | Difference (95% CI) |
| One or more AE | 308 | (68.9) | 117 | (52.5) | 16.4 (8.6, 24.2) |
| Drug-related† (DR) AE | 87 | (19.5) | 5 | (2.2) | 17.2 (13.0, 21.5) |
| Discontinued due to AE | 11 | (2.5) | 1 | (0.4) | 2.0 (-0.2, 4.0) |
| Discontinued due to DR AE | 7 | (1.6) | 0 | (0.0) | 1.6 (-0.1, 3.2) |

† Determined by the investigator to be related to study treatment.
ISG = Immediate Switch Group; DSG = Delayed Switch Group. Baseline Regimen = ritonavir or cobicistat-boosted PI, or cobicistat-boosted elvitegravir, or NNRTI, each administered with two NRTIs.

### LB3. Daptomycin Plus Fosfomycin vs. Daptomycin Monotherapy for Methicillin-Resistant *Staphylococcus aureus* Bacteremia: A Multicenter, Randomized, Clinical Trial

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**Session:** 48. Late Breaker Oral Abstracts: HIV and Antibiotic Trials
*Thursday, October 4, 2018: 10:30 AM*

***Background***. Daptomycin plus fosfomycin combination has demonstrated synergistic and bactericidal effect in animal models of methicillin-resistant *Staphylococcus aureus* bacteremia (MRSAB), but there is lack of data in humans.

***Method***. A randomized (1:1), open-label, clinical trial involving adults with MRSAB was conducted at 18 medical centers in Spain. Patients were assigned to receive daptomycin, 10 mg/kg IV daily plus fosfomycin, 2 g IV/6 hour (combination therapy) or to receive daptomycin 10 mg/kg/24 h IV (monotherapy) during 10 up to 14 days for uncomplicated bacteremia and 28 up to 42 days for complicated bacteremia. The primary efficacy endpoints were: (a) treatment success at Test-of-Cure visit (ToC: 6 weeks after end of therapy) and (b) treatment success at 7 days (defined as alive at day 7 and clearance of bacteremia without relapse from 8 to 90 days after randomization), according with the proposed primary endpoints for use in clinical trials in bloodstream infections in adults.

***Result***. Between December 2013 and November 2017, 674 patients with MRSAB were evaluated and 155 patients were randomized: 74 received combination therapy and 81 monotherapy. In intention-to-treat analysis, (a) at ToC visit successful outcome was achieved in 40 of 74 patients (54,1%) who received combination therapy as compared with 34 of 81 patients (42%) who were given monotherapy (54.1% vs. 42.0%; absolute difference, 12.1%; 95% confidence interval, 0%-27.0%); (b) at 7 days after starting the therapy: a successful outcome was achieved in 69 of 74 patients who received combination therapy as compared with 62 out of 81 patients who received monotherapy (93.2% vs. 76.5%; absolute difference, 16.7%; 95% confidence interval, 5.4%–27.7%). Combination therapy was associated with lower rates of microbiologic failure than monotherapy at ToC visit (0 vs. 9 patients, $P = 0.009$). Combination therapy, as compared with daptomycin monotherapy, was associated with a nonsignificantly higher rate of adverse events due to study medication leading to treatment failure and discontinuation of therapy: 6/74 (8.1%) vs. 3/81 (3.7%) ($P = 0.31$).

***Conclusion***. The combination of daptomycin plus fosfomycin was more effective than daptomycin alone for treating MRSAB (NCT01898338).

***Disclosures***. **All authors:** No reported disclosures.

### LB4. A Phase 3, Randomized, Controlled Clinical Trial of Bictegravir in a Fixed-Dose Combination, B/F/TAF, vs. ABC/DTG/3TC in Treatment-Naïve Adults at Week 96

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**Session:** 48. Late Breaker Oral Abstracts: HIV and Antibiotic Trials
*Thursday, October 4, 2018: 10:30 AM*

***Background***. Bictegravir (B), a potent INSTI with a high barrier to resistance, is coformulated with emtricitabine (F) and tenofovir alafenamide (TAF) as the FDA-approved single-tablet regimen B/F/TAF. We report Week 96 results from an ongoing phase 3 study comparing B/F/TAF to coformulated dolutegravir, abacavir, and lamivudine (DTG/ABC/3TC) in treatment-naïve adults living with HIV-1. Primary outcome at W48 demonstrated noninferior virologic responses, similar bone and renal profiles, and no viral resistance.

***Methods***. We randomized 1:1 HLA-B*5701-negative adults, without HBV and with estimated glomerular filtration rate (eGFR) ≥50 mL/minute to receive blinded B/F/TAF (50/200/25 mg) or DTG/ABC/3TC (50/600/300 mg) with matching placebos QD. Primary endpoint was proportion with HIV-1 RNA <50 copies/mL at W48 (FDA snapshot), with secondary analyses at W96. Noninferiority was assessed with 95% confidence intervals (CI) (12% margin). Other secondary endpoints were safety (adverse events [AEs], laboratory abnormalities) and predefined analyses of bone mineral density (BMD) and measures of renal function (eGFR, proteinuria).

***Results***. A total of 629 adults were randomized/treated (314 B/F/TAF, 315 DTG/ABC/3TC). At W96, B/F/TAF was noninferior to DTG/ABC/3TC: 87.9% vs. 89.8%, respectively, achieved HIV-1 RNA <50 copies/mL (difference −1.9%; 95%CI −6.9% to 3.1%, $P = 0.45$). In per-protocol analysis, 99.6% on B/F/TAF vs. 98.9% on DTG/ABC/3TC achieved HIV-1 RNA <50 copies/mL ($P = 0.33$). Most common AEs overall were nausea (11% B/F/TAF, 24% DTG/ABC/3TC, $P < 0.001$), diarrhea (15%, 16%), and headache (13%, 16%). Through W96, no participant had emergent resistance to study drugs. No participant discontinued B/F/TAF due to AEs; five (2%) discontinued DTG/ABC/3TC due to AEs (one after W48). Treatment-related AEs occurred in 28% B/F/TAF vs. 40% DTG/ABC/3TC ($P = 0.002$); most common was nausea (6%, 17%. $P < 0.001$). At W96, mean percentage changes in spine and hip BMD were small and similar between groups (table); median change in eGFR was significantly less with B/F/TAF, while median % changes in proteinuria were similar.

***Conclusion***. At W96, B/F/TAF was virologically noninferior to DTG/ABC/3TC, with no viral resistance or safety-related discontinuations. B/F/TAF was well tolerated with less nausea than DTG/ABC/3TC and similar bone and renal safety.

**Table. Changes from baseline in safety parameters at W96**

| | B/F/TAF (n=314) | DTG/ABC/3TC (n=315) | P value |
|---|---|---|---|
| **eGFR, median (mL/min)** | -7.8 | -9.6 | 0.01 |
| **Renal Biomarkers, median (%)** | | | |
| Urine Albumin: Creatinine Ratio | -0.3 | +5.2 | 0.25 |
| Urine Retinol Binding Protein: Creatinine Ratio | +21.2 | +22.1 | 0.91 |
| Urine Beta-2-Microglobulin: Creatinine Ratio | -30.8 | -29.4 | 0.96 |
| **BMD, mean (%)** | | | |
| Spine[a] | -0.71 | -0.22 | 0.14 |
| Hip[b] | -1.13 | -1.26 | 0.59 |

[a] n=256 (B/F/TAF), n=258 (DTG/ABC/3TC)
[b] n=250 (B/F/TAF), n=258 (DTG/ABC/3TC)

***Disclosures***. **D. A. Wohl**, Gilead: Grant Investigator and Scientific Advisor, Consulting fee and Research grant. **Y. Yazdanpanah**, AbbVie: Consultant, Consulting fee. Bristol-Myers Squibb: Consultant, Consulting fee. Gilead: Consultant, Consulting fee. MSD: Consultant, Consulting fee. Pfizer: Consultant, Consulting fee. Johnson & Johnson: Consultant, Consulting fee. ViiV Healthcare: Consultant, Consulting fee. **A. Baumgarten**, AbbVie: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium. BMS: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium. Gilead: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium. Janssen-Cilag: Consultant and Speaker's Bureau, Consulting fee and Speaker