What’s Hot in Infectious Diseases - Clinical Science?

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No Disclosures
Pakistan: Salmonella enterica serovar typhi
MDR → XDR

• November 2016, Hyderabad Pakistan
• Appearance of a H58 haplotype strain resistant to antibiotics of 5 classes
• Resulted from acquisition of chromosomal and plasmid mediated mechanisms by dominant H58 haplotype
• Plasmid carrying qnrS, bla_{CTX-M-15} acquired from *E. coli*
• Susceptible only to imipenem, azithromycin

Integrated transposon encoding amp, chloro, T/S resistance + gyrA single mutation

*IncY plasmid*

\[ \text{bla}_{CTXM-15} \]
\[ qnrS \]

MDR – chloramphenicol\(^R\), T/S\(^R\), ampicillin\(^R\)
XDR – MDR plus ceftriaxone\(^R\), fluoroquinolone\(^R\)

mBio. January/February 2018 Volume 9 Issue 1 e00105-18
Rapid increase in case numbers with spread to Karachi
WHO prequalified use of conjugate vaccine (Typbar-TCV®) – single dose, immunogenic in children >6 months of age

At least 3 travelers returned with infection - one to UK, 2 to US
“Novartis joins the Big Pharma exodus out of antibiotics, dumping research, cutting 140 and out-licensing programs”
### Selected Antibacterials Expected to Be Submitted to the FDA for Approval by Mid-2019

<table>
<thead>
<tr>
<th>Investigational drug name</th>
<th>Manufacturer</th>
<th>Class</th>
<th>Proposed indication(s)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefiderocol</td>
<td>Shinogi</td>
<td>Siderophore-cephalosporin</td>
<td>cUTI, HABP/VABP, CRE</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Eravacycline</td>
<td>Tetraphase</td>
<td>Tetracycline</td>
<td>clAI (failed cUTI study)</td>
<td>PDUFA date Aug 28, 2018</td>
</tr>
<tr>
<td>Fosfomycin (intravenous)</td>
<td>Zavante</td>
<td>Phosphonic acid derivative</td>
<td>cUTI, clAI, HABP/VABP, ABSSSI</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Iclaprim</td>
<td>Motif Bio PLC</td>
<td>Dihydrofolate reductase inhibitor</td>
<td>ABSSSI, HABP</td>
<td>NDA filed Q2 2018</td>
</tr>
<tr>
<td>Lefamulin</td>
<td>Nabriva</td>
<td>Pleuromutilins</td>
<td>CABP, ABSSSI</td>
<td>Estimated NDA filing Q4 2018</td>
</tr>
<tr>
<td>Omadacycline</td>
<td>Paratek</td>
<td>Tetracycline</td>
<td>CABP, ABSSSI</td>
<td>NDA filed Q2 2018 (PDUFA estimated Oct 2018)</td>
</tr>
<tr>
<td>Plazomicin</td>
<td>Achaogen Inc.</td>
<td>Aminoglycoside</td>
<td>cUTI</td>
<td>Approved Jun 25, 2018</td>
</tr>
<tr>
<td>Imipenem-cilastatin/relebactam</td>
<td>Merck</td>
<td>Carbapenem</td>
<td>cUTI, AP, HABP/VABP</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>

*a Adapted from Pew Charitable Trusts.3

[https://cdn2.hubspot.net/hubfs/498900/Jul2018_DrugPriceForecast_Media_FINAL.pdf](https://cdn2.hubspot.net/hubfs/498900/Jul2018_DrugPriceForecast_Media_FINAL.pdf)
Cefiderocol

- Siderophore cephalosporin
- Panel (N=315) of carbapenemase-producing MDR GNR – MIC ≤4 mcg/ml:
  - Enterobacteriaceae – 87.5%
  - *P. aeruginosa* - 100%
  - *A. baumanii* - 89%
- Activity by carbapenemase type:
  - A – 91.8%     B - 74.8%     D – 98.0%

IDWeek 2017. Abstract 1230

Also active against *Stenotrophomonas maltophilia*
Minocycline
Oxytetracycline derivative

Tigecycline
Glycylglycine

Eravacycline
Fluorocycline

Omadacycline
Aminomethylcycline
Tigecycline, Eravacycline, Omadacycline
Tissue-Directed Pharmacokinetics

<table>
<thead>
<tr>
<th></th>
<th>Tigecycline</th>
<th>Eravacycline*</th>
<th>Omadacycline**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (µg/mL)</td>
<td>0.82</td>
<td>1.8 – 2.1</td>
<td>1.8</td>
</tr>
<tr>
<td>T1/2 (hours)</td>
<td>36</td>
<td>20</td>
<td>16.8</td>
</tr>
<tr>
<td>Vd (L)</td>
<td>350-500</td>
<td>320</td>
<td>200</td>
</tr>
<tr>
<td>Renal Excretion (%)</td>
<td>33</td>
<td>16</td>
<td>14</td>
</tr>
</tbody>
</table>

*1.0 mg/kg IV
**100 mg IV

### Eravacycline Vs. FDA Breakpoints & Tigecycline

<table>
<thead>
<tr>
<th>Organism</th>
<th>Eravacycline (mcg/ml)</th>
<th>Tigecycline (mcg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC90 (µg/ml)</td>
<td>FDA Breakpoint (µg/ml)</td>
</tr>
<tr>
<td>MRSA</td>
<td>0.12</td>
<td>&lt;0.06</td>
</tr>
<tr>
<td>VRE</td>
<td>0.06</td>
<td>&lt;0.06</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>1.0</td>
<td>≤0.5</td>
</tr>
<tr>
<td>E. coli (ESBL)</td>
<td>0.5</td>
<td>≤0.5</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>16</td>
<td>None</td>
</tr>
<tr>
<td>S. maltophilia</td>
<td>0.5</td>
<td>None</td>
</tr>
<tr>
<td>B. fragilis</td>
<td>2.0</td>
<td>≤0.5</td>
</tr>
<tr>
<td>C. difficile</td>
<td>0.12</td>
<td>≤0.5</td>
</tr>
</tbody>
</table>

Drugs 2016; 76:567-88.
Eravacycline (Xerava)

• Failed in two Phase 3 cUTI studies (q24h dosing)  Note: 16% in urine.
  • IGNITE 2: Vs. levofloxacin (both IV -→ oral) – LL of difference (95%CI): -14.2%
  • IGNITE 3: Vs. ertapenem (both IV only) – LL of difference (95%CI): -14.2%

• Non-inferior to carbapenemems in 2 Phase 3 cIAI studies (q12h dosing); micro ITT
  • IGNITE 1: 1 mg/kg q12h vs. ertapenem – success in 86.8% Vs. 87.6% [1]
  • IGNITE 4: 1 mg/kg q12h vs. meropenem – success in 90.8% vs. 91.2% [2]

• FDA approval for cIAI August 27, 2018

Efficacy of Eravacycline in Secondary Bacteremia: A Post Hoc Analysis of Two Phase 3 studies of Complicated Intra-Abdominal Infection

Table 1. Microbiological Eradication at the Test of Cure Visit by Baseline Pathogen from Blood Specimen

<table>
<thead>
<tr>
<th>Baseline Pathogen</th>
<th>Eravacycline (N=415)</th>
<th>*Comparators (N=431)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Gram-negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14/15 (93.3)</td>
<td>14/15 (93.3)</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>5/6 (83.3)</td>
<td>6/7 (85.7)</td>
</tr>
<tr>
<td>Gram-positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus spp.</em></td>
<td>15/15 (100)</td>
<td>11/11 (100)</td>
</tr>
<tr>
<td><em>Enterococcus spp.</em></td>
<td>8/8 (100)</td>
<td>4/4 (100)</td>
</tr>
<tr>
<td><em>Anaerobes</em></td>
<td>2/2 (100)</td>
<td>5/5 (100)</td>
</tr>
<tr>
<td><em>Bacteroides spp.</em></td>
<td>9/9 (100)</td>
<td>13/14 (92.9)</td>
</tr>
<tr>
<td>*Meropenem and Ertapenem</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2018 IDWeek Abstract 1978
Omadacycline

- IV/PO q24h dosing (2 doses 1st d)
- CABP (OPTIC) – non-inferior to moxifloxacin, each IV (≥3 days) → PO
- ABSSI (OASIS I, II) – non-inferior to linezolid (both PO)

- August 29, 2018: FDA Advisory Committee voted approval for ABSSI and CABP
- FDA Approval October 3, 2018

AAC 2018; PMID 28223386  
AAC 2016; 60:7431-5.
Plazomicin (ZEMDRI)

- Sisomicin derivative
- Unaffected by 15/17 aminoglycoside modifying enzymes; Exceptions:
  - AAC(2')-Ia (only in *P. stuartii*)
  - APH(2'')-IVa (only in Enterococc)
- Methyltransferases cause resistance - highly associated with NDM-carrying organisms

<table>
<thead>
<tr>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 mcg/ml</td>
<td>4 mcg/ml</td>
<td>&gt;8 mcg/ml</td>
</tr>
</tbody>
</table>

- 97 CRE – MIC90 1.0 mcg/ml (amikacin – 32 mcg/ml)
- *P. aeruginosa, Acinetobacter* – MIC90: 16 mcg/ml (72%, 65% inhibited at <4 mcg/ml)
- 64% amikacin-resistant Enterobacteriales inhibited at <4 mcg/ml)

Plazomicin cUTI – FDA approval – June 26, 2018
For “Patients with limited or no options”

EPIC Trial

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Response</th>
<th>Plazomicin N=191 N (%)</th>
<th>Meropenem N=197 N(%)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 5</strong></td>
<td>Cure</td>
<td>168 (88.0)</td>
<td>180 (91.4)</td>
<td>-3.4 (-10.0, 3.1)</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>20 (10.5)</td>
<td>15 (7.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Indeterminate</td>
<td>3 (1.6)</td>
<td>2 (1.0)</td>
<td></td>
</tr>
<tr>
<td><strong>TOC</strong></td>
<td>Cure</td>
<td>156 (81.7)</td>
<td>138 (70.1)</td>
<td>11.6 (2.7, 20.3)</td>
</tr>
<tr>
<td></td>
<td>Failure</td>
<td>29 (15.2)</td>
<td>51 (25.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Indeterminate</td>
<td>6 (3.1)</td>
<td>8 (4.1)</td>
<td></td>
</tr>
</tbody>
</table>

https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM607642.pdf
Plazomicin Vs. Colistin (Each + Meropenem or Tigecycline) in MDR BSI, HABP/VABP

FDA: Complete Response Letter

Figure 2. Mortality-Based Outcomes
Difference (plazomicin minus colistin) (90% CI)
-39.0 (-65.5 to -9.4)
-32.9 (-60.1 to -4.0)

All-cause mortality at day 28 or significant complications

All-cause mortality at day 28

Plazomicin Colistin
14.3 2/14
53.3 8/15
7.1 1/14
40.0 6/15

Two-sided 90% CI calculated based on the unconditional exact method.

Figure 3. Survival Through Day 60

HR for death through day 60 (plazomicin vs colistin) (90% CI)
0.37 (0.15-0.91)

Time to death through day 60 was estimated with the Kaplan-Meier approach and the hazard ratio (HR) was calculated using a Cox proportional hazards regression model.

Approximately 2100 pts screened over 2 years; <2% met inclusion criteria CRE. Planned 286 with.

McKinnell JA, et al. IDWeek 2017. Poster 1853
IV Fosfomycin (Contepo) Vs. Pip/Tazo ZEUS Trial: cUTI and Acute Pyelonephritis

- 465 inpatients randomized to 7d days IV Rx (14 days if bacteremic)
  - Fosfomycin: 6 g q8h over 1 hour
  - Pip/Tazo: 4.5 g q8h over 1 hour
- 1° outcome: Clinical + Micro in MITT @ TOC
- NDA filing expected Q4 2018
- Upcoming problem:
  - Agar dilution Only reliable method of susceptibility testing

Success: Clinical + Micro

<table>
<thead>
<tr>
<th></th>
<th>Percent</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosfomycin</td>
<td>64.7</td>
<td>119/184</td>
</tr>
<tr>
<td>Pip/Tazo</td>
<td>54.5</td>
<td>97/178</td>
</tr>
</tbody>
</table>

Difference 10.8% (95% CI, -0.4 to 20.8)

MRSA Bacteremia: Open-Label Multicenter Randomized Trial -- Daptomycin +/- Fosfomycin

- Daptomycin 10 mg/kg/d; Fosfomycin 2 g q6h
- Rx duration: Uncomplicated 10-14 days; Complicated 28-42 days

<table>
<thead>
<tr>
<th></th>
<th>Dapto</th>
<th>Dapto + Fosfomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>81</td>
<td>74</td>
</tr>
<tr>
<td><strong>7 days of Rx</strong></td>
<td>62 (76.5%)*</td>
<td>69 (93.2%)*</td>
</tr>
<tr>
<td><strong>Difference</strong></td>
<td></td>
<td>16.7% (5.4% to 27.7%)</td>
</tr>
<tr>
<td><strong>TOC</strong></td>
<td>34 (42%)*</td>
<td>40 (54.1%)*</td>
</tr>
<tr>
<td><strong>Difference</strong></td>
<td></td>
<td>12.1% (0% to 27.0%)</td>
</tr>
<tr>
<td><strong>Micro Failure @ TOC Visit</strong></td>
<td>9</td>
<td>0 (P = 0.009)</td>
</tr>
</tbody>
</table>

- *7 day success: Alive, bacteremia cleared without relapse
- **Test-of-cure success: 6 wks after end of Rx

IDWeek 2018 Abstract LB3
Lefamulin (Nabriva): First Systemic Antibiotic Representative of a New Class

• A pleuromutilin – binds to peptidyl transferase component of 50S ribosome subunit, inhibiting protein synthesis
  • Retapumulin approved for topical use

• Active against respiratory pathogens (including “atypicals”), STD pathogens (including *M. genitalium* and resistant gonococci) plus MRSA and VRE

• IV and oral formulations

• Non-inferior to moxifloxacin +/- linezolid in CABP

• NDA (CABP) planned 4th quarter 2018

Pharmacotherapy 2018; doi: 10.1002/phar.2166
Iclaprim (Motif Bio PLC)

• Tricyclic diaminopyrimidine
• 20X more potent against *S. aureus* DHFR than trimethoprim (TMP)
• Active against many TMP-resistant *S. aureus* & *S. pneumoniae* DHFR
• Also active against *H. influenzae* & *M. catarrhalis*

• Targeted Infections: ABSSI, HAP/VAP, CF with *S. aureus*
• ABSSI – non-inferior to vanco
• PDUFA (ABSSI): February 13, 2019

https://www.motifbio.com/iclaprim/
Make Antibiotics Great Again
MERINO: Pip/Tazo Vs. Meropenem

• Ceftriaxone-nonsusceptible, pip/tazo susceptible *E. coli* or *K. pneumoniae* bacteremia
• 26 sites in 9 countries; open-label

• Randomized within 72 h of blood culture draw to:
  • Pip/tazo 4.5 g Q 6h (30 minute infusion) OR
  • Meropenem 1 g Q 8h
• Study stopped at 3rd interim analysis for “futility and harm” based on 30-day mortality in mITT population (the primary outcome measurement).

JAMA 2018; 320:984-94.
MERINO: Kaplan-Meier Failure Estimates for Primary Outcome

86.2% *E. coli*

Primary outcome – 30-day mortality

23/187 (12.3%)

7/191 (3.7%)

$\Delta 8.6\%$ (1-sided 97.5% CI, $-\infty$ to 14.5%; $P = 0.90$ for noninferiority

# Needed to Harm = 12

Median observation time for both meropenem (MER) and piperacillin-tazobactam (PTZ) groups = 30 days; includes primary analysis population

JAMA 2018; 320:984-94.
MERINO: Day of Clinical & Micro Resolution (mITT)

- Clinical & micro resolution @ Day 4
  - Pip/Tazo – 68.4%
  - Meropenem – 74.6% (P = 0.19)

- Median day of resolution of signs of infection
  - Pip/Tazo – 3
  - Meropenem – 2 (P = 0.18)

- No significant differences in: micro resolution by Day 4, micro relapse, 2° MDR infection, CDI

JAMA 2018; 320:984-94.
MERINO: Secondary Outcomes

All subgroup and secondary analyses favored meropenem.

Measure of Success

Clinical and microbiological success at day 4
Microbiological success at day 4

Measure of Failure

Microbiological relapse
Secondary infection with multiresistant organism or Clostridium difficile

a. Survival, neg BC, T <38°C, WBC <12K

JAMA 2018; 320:984-94.
No association between MIC and 30-day mortality
Some MERINO Issues

- Is a 30 minute infusion adequate?
  - MIC of 8 → 81% PTA\(^1\) (PTA: >50% T>MIC)
  - 3 h infusion → 100% PTA

- What accounts for the low mortality (7.9% overall)?
  - No significant difference in microbiological, clinical resolution
  - Only 2.6% high-risk – nonurinary and PITT>4
  - Had to survive to randomization at up to 72 hours

- Effect of empiric Rx, including X-overs

- Step-down allowed after 5 days – 20% of each group received ertapenem

- If no significant difference in clinical & microbiological response, what accounts for the 30-day mortality difference?

\(^1\)AAC 2012; 56:4087-94.

### Potential Bias Favors:

<table>
<thead>
<tr>
<th>Factor</th>
<th>Pip/Tazo</th>
<th>Meropenem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pip/Tazo 30 minute infusion</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Mero 30 minute infusion??</td>
<td>✔</td>
<td>??</td>
</tr>
<tr>
<td>Low mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Empiric Rx; carba in 13.8% PT</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Step-down; carba in 20.2% PT</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>AmpC (10%), ESBL+AmpC (2%)</td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>
POET: Endocarditis Rx -- IV -→ PO Conversion

Entry Criteria

- Age >18 years
- Left-sided infective endocarditis
  - Fulfills modified Duke criteria
  - Native or prosthetic valve
- *Streptococcus, E. faecalis,*
  - *S. aureus,* or coagulase-negative staph
- IV antibiotic for >10 days and T <38°C for >2 days, WBC <15K, CRP <2 or decreased to <25% of peak
  - >7 days after valve surgery (if performed)
- No abscess or valve dysfunction requiring surgery (by trans-esophageal echo) within 48 hours of randomization

POET: Endocarditis Rx -- IV → PO Conversion
Enrollment, Population, Management

- Multiple cardiac centers in Denmark
- 400 of 1954 referred were randomized to all IV or IV → PO
  - 90% power to confirm non-inferiority with 1-sided CI of 97.5%
- Major reasons for exclusion: not meeting criteria, no consent
- Mean age 67 y; 38% with significant comorbidity

- Aortic valve – 54.7%, AV + MV – 10.8%, MV – 34.3%; Prosthetic valve – 27%
- Strep – 40.1%, E. faecalis – 24.3%, MSSA – 21.3%, CNS - 5.7%
- 38% had valve surgery prior to randomization at median of 17 days after which IV Rx continued for median 19 days and PO median 17 days
- PO Rx based on PK/PD principles & always included 2 antibiotics from different classes, targets, PK; rifampin frequently used
  - 7 PO patients below target levels for 1 of 2 drugs; no effect on outcome despite no change in Rx

### Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

<table>
<thead>
<tr>
<th>Component</th>
<th>Intravenous Treatment (N=199)</th>
<th>Oral Treatment (N=201)</th>
<th>Difference</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number (percent)</td>
<td>percentage points</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>13 (6.5)</td>
<td>7 (3.5)</td>
<td>3.0 (-1.4 to 7.7)</td>
<td>0.53 (0.21 to 1.32)</td>
</tr>
<tr>
<td>Unplanned cardiac surgery</td>
<td>6 (3.0)</td>
<td>6 (3.0)</td>
<td>0 (-3.3 to 3.4)</td>
<td>0.99 (0.32 to 3.07)</td>
</tr>
<tr>
<td>Embolic event</td>
<td>3 (1.5)</td>
<td>3 (1.5)</td>
<td>0 (-2.4 to 2.4)</td>
<td>0.97 (0.20 to 4.82)</td>
</tr>
<tr>
<td>Relapse of the positive blood culture†</td>
<td>5 (2.5)</td>
<td>5 (2.5)</td>
<td>0 (-3.1 to 3.1)</td>
<td>0.97 (0.28 to 3.33)</td>
</tr>
</tbody>
</table>

* Six patients, three in each group, had two outcomes.

<table>
<thead>
<tr>
<th>1° Outcome N (%)</th>
<th>Risk Diff (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV Only</td>
<td>24 (12.1%)</td>
</tr>
<tr>
<td></td>
<td>3.1% (-3.4% to -9.6%)</td>
</tr>
<tr>
<td>IV -→ PO</td>
<td>18 (9.0%)</td>
</tr>
</tbody>
</table>

Strep
*E. faecalis*
*S. aureus*
CNS

POET: Endocarditis Rx -- IV → PO Conversion
Primary Composite Outcome


IV: 12.1%
IV to PO: 9.0%

Risk Difference (95% CI):
3.1% (-3.4% to 9.6%)
P = 0.40

Conclusion: IV→PO switch in the selected population was non-inferior to all IV Rx.
Tuberculosis

• Preventive Vaccination
  • Repeat BCG prevent Mtb efficacy in prevention of infection (by sustained QFT conversion). Efficacy 45.4% (P=0.03)\(^1\)

• Latent TB Infection (LTBI) – Prevention of Activation
  • 12 wks weekly rifapentine + INH without DOT is effective\(^2\)
  • 4 months daily rifampin non-inferior to 9 months daily INH in adults & children; rifampin better tolerated, more completions\(^3,4\)
  • 1 month daily rifapentine/INH non-inferior to daily INH for 9 months in HIV-infected\(^5\)
  • M72/AS01\(_E\) recombinant adjuvanted vaccine in LTBI (most BCG vaccinated in infancy) provided 54% protection\(^6\)

• Treatment
  • WHO revised recommendations for Rx of MDR TB (additions, re-prioritization, dropped kanamycin & capreomycin)\(^7\)

Inhaled Liposomal Amikacin (Arikayce) for Pulmonary MAC

- FDA approval Sept 28, 2018 as part of combination Rx of pulmonary MAC in adults with limited or no treatment options.

Convertors (3 monthly consecutive negative cultures) had significantly improved 6 minute walk test results.

Malaria

- **Tafenoquine**\(^1\).  
  - July 20, 2018 single 300 mg dose FDA approved for radical cure (relapse prevention) in *P. vivax* malaria in \(>16\) years receiving appropriate antimalarial therapy.  
  - Aug 8, 2018 prophylaxis age \(>18\) years

- Higher chloroquine dose\(^2\). Increasing dose in \(<5\)y to 30 mg/kg in absence of radical cure significantly reduces recurrences (LID)

- **Ivermectin**\(^3\). Ivermectin mass drug administration to humans disrupts malaria parasite transmission in Senegalese villages. For at least 2 weeks.

Viral Infections

• Smallpox - tecovirimat\(^1\)
  • Monkeypox?

• Influenza – Baloxavir\(^2\) – inhibits CAP-dependent endonuclease
  • Single dose – symptom resolution noninferior to oseltamivir; greater decrease viral load at 24 h; 9.7% emergence of resistance in Phase 3 trial
  • FDA Priority Review granted 28 June 2018

• CAR T-Cell antiviral therapy\(^3\)

• HAV – continued outbreaks homeless, drug users\(^4\)

• HPV – rate of oropharyngeal cancers in men > cervical cancers\(^5\)

5. https://www.cdc.gov/mmwr/volumes/67/wr/mm6733a2.htm
And Even More Hot Topics...

- Opioid abuse – Infectious Disease Syndemic: e.g., HIV, HCV, Endocarditis (incl Candida), pneumococcal infection
- CHEMSEX: STIs
- Microbiome & checkpoint inhibitor response
- Rapid diagnostics
- Unbiased metagenomic next generation sequencing for diagnosis
- Whole genome sequencing for epidemiologic purposes
- Phage therapy
- CDI prophylaxis
- FMT for non-CDI
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