How is the management of HIV changing?  
(assuming there is no cure)

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Hon. Professor LSHTM

IAS President
Disclosures

- **Type of affiliation / financial interest**
  - Receipt of grants/research supports:
  - Receipt of honoraria or consultation fees:
  - Participation in a company sponsored speaker’s bureau:
  - Stock shareholder:
  - Spouse/partner:

- **Name of commercial company**
  - To my unit from Janssen, Merck, Viiv and Gilead
  - To me from Janssen, Merck, Viiv, Gilead, Cipla
  - None
  - None
  - None
  - None
The Future of ART - introduction

• Immediate start ART
• What ART to Start-
  – Integrase for all
  – Which Nucleosides
  – 2Drug or 3 Drug
  – Role of new drugs
• Adverse effects
  – Pregnancy and NTDs
  – Weight gain/Diabetes
• Injectables-implantables
Immediate Start
AKA Rapid start, Same Day Start.....

Everyone starts on same day as HIV diagnosis

(May be essential for AHIV infection and very Late presenters)

But what about asymptomatic patients?
Current Recommendations for Same-Day ART Initiation

- Rapid start or initiating ART on same day as HIV is diagnosed is an emerging strategy to reduce loss to follow-up and decrease time to viral suppression
- Evidence base limited but growing, and outcomes favorable thus far

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Investigational</strong></td>
<td></td>
<td></td>
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<tr>
<td>- Resource intensive</td>
<td></td>
<td></td>
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<tr>
<td>- Long-term benefits not yet proven in the US</td>
<td></td>
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</tr>
<tr>
<td><strong>WHO[2]</strong></td>
<td><strong>Recommended</strong> where feasible</td>
<td></td>
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<tr>
<td><strong>Start ART as soon as possible, including immediately after diagnosis, if patient is ready</strong></td>
<td></td>
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</table>

Will Rapid Start be better than what we do now?
Same-Day ART compared to standard of care, Thai Red Cross Anonymous Clinic

Cumulative proportion of ART initiation

Cumulative proportion of VL suppression

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>Same-Day ART</th>
<th>Standard Care</th>
</tr>
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<tbody>
<tr>
<td>Time to ART initiation (days)</td>
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<td></td>
</tr>
<tr>
<td>0</td>
<td>1429</td>
<td>5373</td>
</tr>
<tr>
<td>60</td>
<td>152</td>
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<tr>
<td>360</td>
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<td>1502</td>
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P-value < 0.001

Number at risk

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<th>Standard Care</th>
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<tbody>
<tr>
<td>Time to VL suppression (days)</td>
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<tr>
<td>0</td>
<td>181</td>
<td>2513</td>
</tr>
<tr>
<td>60</td>
<td>178</td>
<td>2507</td>
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<td>120</td>
<td>147</td>
<td>2300</td>
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<td>180</td>
<td>71</td>
<td>1566</td>
</tr>
<tr>
<td>240</td>
<td>11</td>
<td>901</td>
</tr>
<tr>
<td>300</td>
<td>11</td>
<td>674</td>
</tr>
</tbody>
</table>

P-value < 0.001

Those in Same-Day ART program were 3.9 times more likely to start ART

Those in Same-Day ART program were 2.2 times more likely to be viral suppressed
The data in high-income Settings is Limited- Engagement in Treatment and Time to Suppression

- **56 DS, London: n=178 in 2015 vs n=101 in 2016**
  - Appointment offered within 2 days of diagnosis
  - Median time to appointment vs 2015: 7 vs 15 days, p < 0.00001
  - Median time to ART vs 2015: 8 vs 21 days, p < 0.00001

- **RAPID cohort, San Francisco: n=38**
  - 39/86 eligible for rapid ART (same/next day)
  - Faster suppression: 56 vs 79 days from referral (p=0.009)
  - Numerically less loss to follow-up: 10.3% vs 14.9% (p=0.52)

- **Other US Cohorts –in abstracts**
  - New Orleans and other Cities rolling out programs

56DS: Whitlock G et al. HIV Medicine; August 2019
Other Concerns re: Immediate Start

- Readiness to start
- Time to counsel
- Clinic capacity
- Long-term adherence & satisfaction
- Long term virologic outcomes
- Resistance
- Screen for Hep B (if 2DR)
- Cost
If we adopt rapid Start
What initial Therapy is best?

Everyone starts on an Integrase plus
Plus One other?
Plus Two other?
Plus More than two other Drugs?
Rapid ART What RX? Guidelines

EACS, IAS-USA
If ART initiated before resistance available, a high genetic barrier drug is recommended (boosted PI, dolutegravir or bictegravir)

DHHS
If start ARV before resistance available, recommended regimens: boosted darunavir or dolutegravir + a tenofovir/emtricitabine

Integrase for all?
- will we only use these in first line?
What will be the long term outcomes of doing this?

Will we use NNRTIs or Pi/b as a first line choice anymore?
Which 3\textsuperscript{rd} agent? NNRTI, PI or INSTI

The age of integrase

- Guidelines & integrase-based initial ART 1\textsuperscript{st} line:
  - \textbf{Exclusively:} IAS-USA
  - \textbf{Primarily:} DHHS, EACS, WHO

- Issues for integrase inhibitors
  - Barrier to resistance (raltegravir, elvitegravir)
  - Drug interactions (TB drugs, cations)
  - Toxicity....
Which InSTI-What is the difference?
Resistance and STR

Spring -2 Raltegravir versus Dolutegravir

GS-1490: BIC/FTC/TAF vs DTG + FTC/TAF

% Treatment Difference (95% CI)

<table>
<thead>
<tr>
<th>Treatment Difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG + FTC/TAF</td>
<td>-7.9</td>
</tr>
<tr>
<td>BIC/FTC/TAF</td>
<td>3.2</td>
</tr>
</tbody>
</table>

Favors DTG + FTC/TAF
Favors BIC/FTC/TAF

BIC vs DOL No treatment-emergent resistance detected in any patient through Wk 96

Role of NNRTIs in First Line- If Toxicities of INSTIs?

**Drive-Ahead - Doravirine vs EFV**  
**Virologic Outcomes at Wk 96**

**FDA Snapshot Analysis**

- Treatment difference: 3.8% (95% CI: -2.4% to 10.0%)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HIV-1 RNA &lt; 50 copies/mL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOR/3TC/TDF</td>
<td>77.5</td>
</tr>
<tr>
<td>EFV/FTC/TDF</td>
<td>73.6</td>
</tr>
</tbody>
</table>

- **DOR has potent activity against WT, K103N, Y181C, and K103N/Y181C**
  - Resistance:
    - DOR-R in 6 patients (1.6%) in DOR arm vs EFV-R in 13 patients (3.8%) in EFV arm
    - NRTI-R in 1.4% vs 1.6%, respectively
  - Small decreases in fasting LDL-C, non-HDL-C with DOR vs increases with EFV
  - Less frequent A/E, D/Cs especially neuropsychiatric AEs with DOR/3TC/TDF vs EFV/FTC/TDF

PIs and Boosted agents?

Limited use in first line-transmitted resistance

Avoid for actual and potential drug interactions

Switches away to/from InSTIs

Long term future? ? in Implants as no issue with PgP (if low CYP P450 metabolism)
Single Pill Regimens

Oral Fixed-Dose Combinations
Will every combination be available?
We Have many Oral Fixed-Dose Combinations

- EFV/FTC/TDF
- RPV/FTC/TDF
- EVG/COBI/FTC/TDF
- BIC/FTC/TAF
- DRV/COBI/FTC/TAF
- DTG/3TC
- DTG/RPV
- DOR/3TC/TDF
- DTG/ABC/3TC
- EVG/COBI/FTC/TAF
- RPV/FTC/TAF
- EVG/COBI/FTC/TAF

Two-drug single-tablet regimens

DTG/3TC

DTG/RPV
Will we see the end of Some Nucleos(t)ides?

NRTI: tenofovir-DF and abacavir

Concerns re Toxicity
Less Drugs then Less Toxicity
So will everyone be on a 2DR?

• Increasing concern about NRTI toxicities
• Unboosted high barrier agents
• Lower costs?
• Fewer drugs may be a good thing
  – Ageing, multi-morbidity, polypharmacy....
Dolutegravir-based 2DR

• **SWORD: dolutegravir + rilpivirine**
  – Non-inferior to continued 3DR (suppressed switch only)
  – **Resistance common in small number of failures**

• **GEMINI: dolutegravir + lamivudine 1\textsuperscript{st} line**
  – Non-inferior to tenofovir-DF/emtricitabine + dolutegravir 1\textsuperscript{st} line at 96 weeks (including high VL & sensitive assays)
  – **No resistance emergence**

• **TANGO: dolutegravir + lamivudine suppressed switch**
  – Non-inferior to continued TAF-based 3DR at 48 weeks
  – **No resistance emergence**
## GEMINI-1 and -2: Wk 48 Subgroup Analysis

<table>
<thead>
<tr>
<th>HIV-1 RNA &lt; 50 copies/mL, n/N (%)</th>
<th>DTG + 3TC (n = 716)</th>
<th>DTG + FTC/TDF (n = 717)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 35</td>
<td>386/420 (92)</td>
<td>381/408 (93)</td>
</tr>
<tr>
<td>35 to &lt; 50</td>
<td>211/231 (91)</td>
<td>216/229 (94)</td>
</tr>
<tr>
<td>≥ 50</td>
<td>58/65 (89)</td>
<td>72/80 (90)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>100/113 (88)</td>
<td>89/98 (91)</td>
</tr>
<tr>
<td>Male</td>
<td>555/603 (92)</td>
<td>580/619 (94)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>447/480 (93)</td>
<td>471/497 (95)</td>
</tr>
<tr>
<td>Black</td>
<td>83/99 (84)</td>
<td>64/76 (84)</td>
</tr>
<tr>
<td>Asian</td>
<td>67/71 (94)</td>
<td>68/72 (94)</td>
</tr>
<tr>
<td>HIV-1 RNA, copies/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 100,000</td>
<td>526/576 (91)</td>
<td>531/564 (94)</td>
</tr>
<tr>
<td>&gt; 100,000</td>
<td>129/140 (92)</td>
<td>138/153 (90)</td>
</tr>
<tr>
<td>&gt; 250,000</td>
<td>45/51 (88)</td>
<td>41/46 (89)</td>
</tr>
<tr>
<td>&gt; 400,000</td>
<td>16/18 (89)</td>
<td>20/24 (83)</td>
</tr>
<tr>
<td>CD4+ count, cells/mm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 200</td>
<td>50/63 (79)</td>
<td>51/55 (93)</td>
</tr>
<tr>
<td>&gt; 200</td>
<td>605/653 (93)</td>
<td>618/662 (93)</td>
</tr>
</tbody>
</table>

Emergent Resistance With Two-Drug Regimens?

GEMINI (initial DTG + 3TC)[1]
- No treatment-emergent resistance mutations in patients with VF

SWORD (switch to DTG + RPV)[2]
- Treatment-emergent NNRTI mutations (n = 4) and INSTI mutations (n = 3) in 8 patients with VF

ATLAS, FLAIR (switch to LA CAB + RPV)[3,4]
- Treatment-emergent NNRTI mutations (n = 6) and INSTI mutations (n = 4) in the 6 patients with VF

## Advantages - Cost

<table>
<thead>
<tr>
<th>Combination treatment</th>
<th>Estimated price per patient-year</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF/3TC/ATV/r</td>
<td>$279</td>
<td>13</td>
</tr>
<tr>
<td>TDF/FTC/ELV/COBI</td>
<td>$184</td>
<td>14</td>
</tr>
<tr>
<td>ABC/3TC/DTG</td>
<td>$179</td>
<td>14</td>
</tr>
<tr>
<td>TDF/FTC/EFV600</td>
<td>$144</td>
<td>13</td>
</tr>
<tr>
<td>TDF/3TC/EFV600</td>
<td>$130</td>
<td>13</td>
</tr>
<tr>
<td>TDF/3TC/EFV400</td>
<td>$100 to $110</td>
<td>13</td>
</tr>
<tr>
<td>IAF/3TC/DTG</td>
<td>$60</td>
<td>14</td>
</tr>
<tr>
<td>DTG/3TC</td>
<td>$46</td>
<td>14</td>
</tr>
</tbody>
</table>

Table 1. Target prices for key first-line combination treatments in low or low-middle income countries
2DR-Limitations

- Hepatitis B co-infection
- Access to resistance testing
  - No evidence for DTG + 3TC if 3TC resistance
- TB treatment
  - Need for twice daily DTG?
- Pregnancy
  - Efficacy
- High VL and Low CD4
  - Not studied in patients with HIV-1 RNA > 500,000 copies/mL
- Rapid Start-can you use it without resistance test
- Women, adolescent data
- Will we see bictegravir-based 2DR at some stage....?
Less Drugs Less Toxicity
Will patients only take their drugs 4 days a week?
ANRS 170 QUATUOR: Study Design

- Multicenter, randomized, open-label phase III noninferiority study

- Primary endpoint: HIV-1 RNA < 50 copies/mL and no strategy interruption (except for pregnancy and within-class switches)
  - Noninferiority margin: -5%

HIV-infected adults with HIV-1 RNA < 50 c/mL for ≥ 12 mos on ART,* no genotypic resistance, CD4+ cell count > 250 cells/mm³ (N = 640)

- ART regimen based on either PI, NNRTI, or INSTI with 2 NRTIs.

- Primary endpoint: HIV-1 RNA < 50 copies/mL and no strategy interruption (except for pregnancy and within-class switches)

Landman. IAS 2019. Abstr WEAB0406LB.
ANRS 170 QUATUOR: Treatment Failure by Third Agent
Maybe only useful in high resistance barrier regimens

<table>
<thead>
<tr>
<th>Virological non-response</th>
<th>4 D/7 (n = 318)</th>
<th>7 D/7 (n = 318)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed VL &gt; 50 c/mL</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>INI group (n = 304)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R emergence</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>1 (on RAL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTI group (n = 296)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R emergence</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>2 (on RPV)</td>
<td></td>
<td>1 (on RPV)</td>
</tr>
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</table>

Difference (95% CI) of Proportion

WILL TOXICITY & CO-MORBIDITIES DETERMINE THE NEXT 10 YEARS

Will we have to rethink what we use in therapy if new toxicities/adverse events arise post marketing?

Will Integrase still be first line in 10 years?
‘Novel’ ART toxicities-
Will they move us away from INSTIs?

Pregnancy safety
Weight gain
Dolutegravir and Pregnancy
Since May 2018
1 NTD/1275 additional exposures to DTG at conception

Tsepamo (Botswana): NTD Prevalence by Exposure at Conception

<table>
<thead>
<tr>
<th>NTDs/Exposures</th>
<th>DTG-CONCEPTION</th>
<th>ANY NON-DTG ART-CONCEPTION</th>
<th>EFV-CONCEPTION</th>
<th>DTG-PREGNANCY</th>
<th>HIV-NEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>% with NTD (95% CI)</td>
<td>5/1683</td>
<td>15/14792</td>
<td>3/7959</td>
<td>1/3840</td>
<td>70/89372</td>
</tr>
<tr>
<td>Prevalence Difference (95% CI)</td>
<td>ref</td>
<td>0.20% (0.01, 0.59)</td>
<td>0.26% (0.07, 0.66)</td>
<td>0.27% (0.06, 0.67)</td>
<td>0.22% (0.05, 0.62)</td>
</tr>
</tbody>
</table>

Zash R, IAS 2019, Abs. MOAX0105LB
The antagonism of folate receptor by dolutegravir: developmental toxicity reduction by supplemental folic acid

Robert M. Cabrera\textsuperscript{a}, Jaclyn P. Souder\textsuperscript{a,b}, John W. Steele\textsuperscript{a}, Lythou Yeo\textsuperscript{a}, Gabriel Tukeman\textsuperscript{a}, Daniel A. Gorelick\textsuperscript{a} and Richard H. Finnell\textsuperscript{a,c}

**DTG treatment, 3 hours post-fertilization**

- (a) 60ng/mL folate
- (b) 100\textmu M DTG
- (c) 60ng/mL folate + 100\textmu M DTG
Do Integrases cause weight Gain?
What about TAF?
Weight Gain and INSTIs:

Positive Association

• NA-ACCORD, initial therapy (N = 24,001)\(^1\)
• ACTG A5001, A5322 switch cohort (N = 691)\(^2\)
• Women’s Interagency HIV Study, switch cohort (N = 1118)\(^3\)

No Association

• TRIO retrospective switch cohort (N = 3468)\(^4\)
• HPTN 077 cohort of HIV-uninfected people receiving cabotegravir (N = 199)\(^5\)

The initial signal from Controlled Trial data

**NEAT 022 Study: switch to DTG**

Post-Hoc Analysis of Change in Weight and BMI in Patients With High CVD Risk

**Weight Change**

- Dolutegravir: +0.8 kg
- PI: +0.3 kg

**BMI Change**

- Dolutegravir: +0.3 kg/m²
- PI: +0.06 kg/m²

All patients received 2 NRTIs.


ADVANCE study: 1st line open-label randomized ART

- TAF/FTC + DTG (N = 351) vs TDF/3TC + DTG (N = 351) vs TDF/3TC/EFV600 (N = 351)

Percentage weight change (%) to w96 (incomplete data W48-W96)

MEN

<table>
<thead>
<tr>
<th>Weeks</th>
<th>TAF/FTC+DTG</th>
<th>TDF/FTC+DTG</th>
<th>TDF/FTC/EFV</th>
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<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>+2%</td>
<td>+6%</td>
<td>+7%</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>24</td>
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<td>72</td>
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<tr>
<td>96</td>
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</table>

WOMEN

<table>
<thead>
<tr>
<th>Weeks</th>
<th>TAF/FTC+DTG</th>
<th>TDF/FTC+DTG</th>
<th>TDF/FTC/EFV</th>
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</thead>
<tbody>
<tr>
<td>0</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>+4%</td>
<td>+8%</td>
<td>+16%</td>
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<tr>
<td>96</td>
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* P <0.05 ; ** p < 0.01 ; *** p < 0.001

Hill A, IAS 2019, Abs. MOABX0102LB
# Randomised trials – effects of DTG and BIC on weight

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gilead 1490</td>
<td>TAF/FTC/DTG</td>
<td>+3.9kg rise in body weight to Week 96</td>
</tr>
<tr>
<td>N=645, naïve</td>
<td>TAF/FTC/BIC</td>
<td>+3.5kg rise in body weight to Week 96</td>
</tr>
</tbody>
</table>
The risk of incident DM in 21,516 eligible ART initiators

INSTIs vs. NNRTIs (HR=1.22; CI: 0.95-1.57) NS

RAL- vs. NNRTIs (HR=1.50, CI: 1.11-2.03)
PI- vs. NNRTI-initiators (HR=1.25; CI: 1.05-1.49)

Confounders age, CD4, time of follow up
LONG ACTING ARVS

Forget Pills!
In the next ten years
Is this where HIV treatment is really going?
Long Acting – What’s the attraction?

- Prevents poor adherence
- Infrequent dosing
- Use in patients with pill fatigue /aversion?
- Better protects health privacy
- Lower overall drug dose
Less Drug Less Toxicity
Yearly intake of ARV by regimen

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Daily Dose (mg)</th>
<th>Yearly dose (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3-Drug Regimens:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV/r + FTC/TDF</td>
<td>800/100 + 200/300</td>
<td>511.0</td>
</tr>
<tr>
<td>RAL + F/TAF</td>
<td>800 + 200/10</td>
<td>368.7</td>
</tr>
<tr>
<td>DTG/ABC/3TC</td>
<td>50/600/300</td>
<td>346.8</td>
</tr>
<tr>
<td>EVG/c/FTC/TAF</td>
<td>150/150/200/10</td>
<td>186.2</td>
</tr>
<tr>
<td><strong>2-Drug Regimens:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTG + 3TC</td>
<td>50 + 300</td>
<td>127.8</td>
</tr>
<tr>
<td>DTG + RPV</td>
<td>50 + 25</td>
<td>27.4</td>
</tr>
<tr>
<td>CAB&lt;sub&gt;oral&lt;/sub&gt; + RPV&lt;sub&gt;oral&lt;/sub&gt;</td>
<td>30 + 25</td>
<td>20.1</td>
</tr>
<tr>
<td>CAB&lt;sub&gt;im&lt;/sub&gt; + RPV&lt;sub&gt;im&lt;/sub&gt;</td>
<td>400 + 600 (every 2 mo)</td>
<td>6g</td>
</tr>
</tbody>
</table>

50 years of tx
DRUG DELIVERY SYSTEMS:
Injectables
Injectable drugs: Cabotegravir and Rilpivirine
Evidence for Injectable Long-Acting Therapy in Virologically Suppressed Patients
Phase 3 results: in a Nutshell

• Two large RCTs of injectable cabotegravir + rilpivirine vs oral therapy
  – **ATLAS**: suppressed switch
  – **FLAIR**: naïve with a lead-in phase

• Very high rates of viral suppression
  – Injectables non-inferior to oral treatment
  – Injectables preferred by patients
  – Small failure/resistance signal in subtype A
Challenges

- Pregnancy safety
- Hep B not covered
- Cold chain – managing injections
- IM injections
  - Long-term acceptability of injection site reactions
  - Impact of: BMI, other IM injections
- Drug-drug interactions e.g. rifampicin
- Resistance
- Delayed/missed doses
  - Adherence VERY high in trials to date....real life?
- Drug tails: long half-lives in PrEP trials
  - **Cabotegravir:** 17% detectable 52 weeks post-injection
  - **Rilpivirine:** detected for a mean of 541 days post-dose

David Back, CROI 2019; Ford et al. HIVR4P 2016; Chicago, IL. Abstract OA12.06LB.
**FIRST-IN-HUMAN TRIAL OF MK-8591-ELUTING IMPLANTS DEMONSTRATES CONCENTRATIONS SUITABLE FOR HIV PROPHYLAXIS FOR AT LEAST ONE YEAR**

July 23, 2019
Randolph Matthews, MD, PhD
Sr. Principal Scientist
Translational Pharmacology, Merck & Co., Inc., Kenilworth, NJ, USA

**Ilatravir (MK-8591):**
A First-in-Class Nucleoside Reverse Transcriptase Translocation Inhibitor (NRTTI) With Multiple Mechanisms of Action

- **Translocation Inhibition Due to the 4'-ethynyl Group**
- **Delayed Chain Termination Due to the 4'-ethynyl and 3'-hydroxyl Groups**
A Tunable, Biodegradable, Thin-Film Polymer Device as a Long-Acting Implant Delivering Tenofovir Alafenamide Fumarate for HIV Pre-exposure Prophylaxis

Erica Schlesinger¹, Daniel Johengen², Ellen Luecke⁵, Ginger Rothrock³, Ian McGowan⁴, Ariane van der Straten⁵,⁶, and Tejal Desai²,§

(A) 2.5mm diameter, 40mm long prototypes loaded with 230mg 1:1 TAF:PEG300 (w/w)

(B) 0.6mm diameter, 20mm long prototype loaded with 26mg 1:1 TAF:PEG300 (w/w)
Conclusions

• Immediate start ART-not certain
• What ART to Start-
  – Integrase for all- ? Still in 2030?
  – 2Drug or 3 Drug- still areas of 2DR to be resolved
  – Role of new drugs moving away from conventional drugs
• Recently reported adverse effects
  – Pregnancy and NTDs-for LMICs resolved ? For HICs
  – Weight gain/Diabetes-still need data
• Injectables-Implantables
  – The way to go !!!