Forecasting pipeline ARVs

Joseph Perriëns
Sandeep Juneja
Aastha Gupta
Presently: lack of visibility causes a gap between demand and generic production for new drugs.
Creating early visibility of demand (forecasts) can speed benefits of generic competition.

But to plan ahead, manufacturers need to understand: in future:
- Which products are likely to be in demand?
- When?
- In which country?
- In what quantity?

Longer term benefit of generic competition

Forecasted demand
Ensure availability of recommended ARVs by signalling the needs to manufacturers in advance, thus facilitating planning and financing of procurement, achieving treatment targets, and maximizing public health impact.
• Consolidated forecast: for both pipeline AND current ARVs for 10 years
• Draws from and builds upon existing forecasts
• Accounts for current and likely use of ARVs, technical/medical aspects and country/regional information
• Allows better definition of markets
Forecasting Model
Extent and timing of public health usage of ARVs, especially new drugs, was a key area for the MPP to understand when we commenced our licensing work with originator and generic companies.

MPP started its forecasting exercise in 2011, including all ARVs but focusing on new drugs:
- Prioritisation of voluntary licences with originators to achieve key public health objectives
- Early visibility by generic manufacturers on new ARVs: portfolio planning and prioritisation
- Resulting in timely development of required FDCs

To further supplement this, MPP requires knowledge of futuristic FDCs which would be needed in resource limited settings.

Consultations with WHO HIV department and the TAC team to understand FDCs needed in future, scenario building and refine assumptions on uptake.

Consultations with other stakeholders in the TWG.
MPP’s Concluded Agreements

- Abbvie
  - Lopinavir (paed)
  - Ritonavir (paed)

- Bristol-Myers Squibb
  - Atazanavir

- Gilead
  - Cobicistat
  - Elvitegravir
  - Emtricitabine
  - Tenofovir Alafenamide
  - Tenofovir Disoproxil

- Merck
  - Raltegravir (paed)

- NIH
  - Darunavir related

- Roche
  - Valganciclovir (pricing agreement)

- ViiV Healthcare
  - Abacavir (paed)
  - Dolutegravir

MPP has concluded licence agreements with 6 patent holders and a pricing agreement.
Out-Licensing Partners and Agreements

MPP is currently running 52 development projects with 10 partners
Principles of the Model

- Currently does not include estimates of number of people who may need PrEP (e.g. number of IDUs at high risk of HIV acquisition) or TasP
- Borrows average usage forecast from currently available forecasts till 2018
- Borrows epidemiological estimates from available estimates till 2018
- Assumptions:
  - Linear regression on market share increase
  - Healthy and timely generic competition
  - Introduction of new drugs based on projected development timelines of generic manufacturers and estimated inclusion in WHO Guidelines
  - Price considerations: lower priced medicines would potentially have higher usage
  - Country inclusion: accounts for all low and middle income countries including those with well established ARV treatment programs such as Brazil
  - Accounts mainly for the public market
Considered three possibilities:

**Scenario 1: Status Quo**
- WHO Guidelines remain consistent with current guidelines
- New products when introduced show only a marginal uptake
- Use of Integrase Inhibitors (INIs) limited to 3rd line

**Scenario 2: Likely Use**
- WHO Guidelines accept and recommend new products using the treatment optimisation framework
- New products have a good uptake; assumed that new FDCs such as those containing DTG, TAF and heat stable DRV/r are made available as generics
- Use of INIs is recommended as preferred options in 2nd and 3rd line in initial years, and later progressing to 1st line use (when more safety data is available)

**Scenario 3: Aggressive Adoption**
- WHO Guidelines recommend aggressive use of new products
- Use of INIs as preferred option recommended in 1st line
Adults
Scenario 1: Status Quo

Guidelines remain consistent with current recommendations

In this scenario:
- **1st line:**
  - INI-based regimens used minimally in 1st line
  - As per current recommendations, use of NVP declines and EFV increases
- **2nd line**
  - LPV continues to be the main option initially
  - ATV is used due to the potential low cost and once daily dose
  - DRV/r in combination with DTG is used marginally
  - DTG used marginally with NRTIs
- **3rd line**
  - DTG slowly replaces RAL in 3rd line

This scenario is less likely, as generics are already developing low cost FDCs which may be compelling for potential use in developing countries.
Consistent with current Guidelines

- Uptake of TDF increases further, consolidating its positions as the main backbone in 1\textsuperscript{st} line
- Due to higher use of TDF in 1\textsuperscript{st} line, AZT becomes preferred option in 2\textsuperscript{nd} line
- Minimal uptake of TAF from 2020, taking share from TDF
- DTG introduced marginally in 2\textsuperscript{nd} line with PIs
Scenario 2: Likely Use

bPIs: recommended in in 2\textsuperscript{nd} line and 3\textsuperscript{rd} line either with NRTIs or with INIs.

New INIs: initially in 2\textsuperscript{nd} & 3\textsuperscript{rd} line; recommended in 1\textsuperscript{st} line after 3-4 years of introduction

In this scenario:
- 1\textsuperscript{st} line
  - Continues to be NNRTI based initially
  - INI-based regimens used minimally in initial years, then increase
- 2\textsuperscript{nd} line
  - Development of co-formulations of bPI with INI (trials in plan)
  - bPIs used with either NRTIs (as per current Guidelines) or with INIs (such as DTG)
- 3\textsuperscript{rd} line
  - Mainly RAL-based, DTG uptake increases initially, then then stabilizes

This may be a likely scenario in the initial years. Clinical trials of bPI+INI regimens in experienced patients underway.
Likely Use: Backbones

Introduction of INI in 2\textsuperscript{nd} line

- Uptake of TDF increases further, consolidating its positions as the main backbone in 1\textsuperscript{st} line
- Due to higher use of TDF in 1\textsuperscript{st} line, use of AZT increases in 2\textsuperscript{nd} line, however, the market is shared with TAF as well as DTG
- Medium uptake of TAF from 2020, mainly taking share from TDF in 1\textsuperscript{st} and 2\textsuperscript{nd} line
- DTG used in 2\textsuperscript{nd} line with PIs (mainly with DRV)
Scenario 3: Aggressive Adoption

INIs recommended in 1st line based on low cost and FDC availability

In this scenario:
• 1st line
  • DTG is rapidly used in 1st line from year 2018, becoming the main option
• 2nd line
  • LPV/r is replaced steadily by ATV/r due to lower cost and once daily regimen
  • bPIs used with either NRTIs (as per current Guidelines) or with INIs (such as DTG)
• 3rd line
  • Mainly RAL-based; DTG is used by patients who have not used it in 1st line

This scenario may be a reality in future once WHO gets more data with respect to INIs on TB co-infection and use in pregnant women.
Aggressive Adoption: Backbones

Introduction of INI in 2\textsuperscript{nd} line

- Uptake of TDF increases, becoming the main backbone in 1\textsuperscript{st} line, and being replaced later by TAF
- Due to higher use of TDF in 1\textsuperscript{st} line, AZT becomes preferred option in 2\textsuperscript{nd} line
- High uptake of TAF from 2020, taking share from TDF and AZT
- DTG used in 2\textsuperscript{nd} line with PIs (mainly with DRV)
Above graphs show likely uptake of TAF and DTG.

The two products show quite significant number of people on treatment, going up to >5mn in 5 years for TAF and >6mn for DTG.
## Formulations Usage for Adults

<table>
<thead>
<tr>
<th>PLHIVs using each formulation</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
<th>2023</th>
<th>2024</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVP/AZT/3TC</td>
<td>3,025,000</td>
<td>2,716,000</td>
<td>2,425,000</td>
<td>1,963,000</td>
<td>1,736,000</td>
<td>1,502,000</td>
<td>1,264,000</td>
</tr>
<tr>
<td>NVP/TDF/XTC</td>
<td>1,964,000</td>
<td>1,763,000</td>
<td>1,574,000</td>
<td>1,274,000</td>
<td>1,127,000</td>
<td>975,000</td>
<td>820,000</td>
</tr>
<tr>
<td>EFV/AZT/3TC</td>
<td>1,690,000</td>
<td>1,430,000</td>
<td>1,157,000</td>
<td>917,000</td>
<td>583,000</td>
<td>285,000</td>
<td>-</td>
</tr>
<tr>
<td>EFV/TDF/XTC</td>
<td>11,550,000</td>
<td>12,009,000</td>
<td>11,717,000</td>
<td>11,920,000</td>
<td>11,075,000</td>
<td>10,276,000</td>
<td>9,638,000</td>
</tr>
<tr>
<td>EFV/TAF/XTC</td>
<td>-</td>
<td>-</td>
<td>723,000</td>
<td>1,528,000</td>
<td>2,040,000</td>
<td>2,855,000</td>
<td>3,492,000</td>
</tr>
<tr>
<td>LPV/r/AZT/3TC</td>
<td>240,000</td>
<td>218,000</td>
<td>217,000</td>
<td>218,000</td>
<td>214,000</td>
<td>200,000</td>
<td>182,000</td>
</tr>
<tr>
<td>LPV/r/TDF/XTC</td>
<td>328,000</td>
<td>251,000</td>
<td>186,000</td>
<td>116,000</td>
<td>58,000</td>
<td>28,000</td>
<td>3,500</td>
</tr>
<tr>
<td>LPV/r/TAF/XTC</td>
<td>-</td>
<td>-</td>
<td>21,000</td>
<td>39,000</td>
<td>53,000</td>
<td>48,000</td>
<td>42,000</td>
</tr>
<tr>
<td>ATV/r/AZT/3TC</td>
<td>149,000</td>
<td>199,000</td>
<td>236,000</td>
<td>284,000</td>
<td>338,000</td>
<td>393,000</td>
<td>453,000</td>
</tr>
<tr>
<td>ATV/r/TDF/XTC</td>
<td>203,000</td>
<td>229,000</td>
<td>202,000</td>
<td>152,000</td>
<td>92,000</td>
<td>55,000</td>
<td>9,000</td>
</tr>
<tr>
<td>ATV/r/TAF/XTC</td>
<td>-</td>
<td>-</td>
<td>22,000</td>
<td>50,000</td>
<td>85,000</td>
<td>94,000</td>
<td>104,000</td>
</tr>
<tr>
<td>DRV/r/AZT/3TC</td>
<td>-</td>
<td>3,000</td>
<td>5,000</td>
<td>9,000</td>
<td>13,000</td>
<td>17,000</td>
<td>21,000</td>
</tr>
<tr>
<td>DTG/TDF/XTC</td>
<td>-</td>
<td>1,182,000</td>
<td>1,913,000</td>
<td>2,017,000</td>
<td>2,991,000</td>
<td>3,449,000</td>
<td>3,865,000</td>
</tr>
<tr>
<td>DTG/TAF/XTC</td>
<td>-</td>
<td>-</td>
<td>109,000</td>
<td>243,000</td>
<td>528,000</td>
<td>939,000</td>
<td>1,410,000</td>
</tr>
<tr>
<td>DTG/LPV/r</td>
<td>25,000</td>
<td>44,000</td>
<td>62,000</td>
<td>82,000</td>
<td>94,000</td>
<td>100,000</td>
<td>101,000</td>
</tr>
<tr>
<td>DTG/ATV/r</td>
<td>16,000</td>
<td>40,000</td>
<td>67,000</td>
<td>107,000</td>
<td>148,000</td>
<td>196,000</td>
<td>252,000</td>
</tr>
<tr>
<td>DTG/DRV/r</td>
<td>15,000</td>
<td>38,000</td>
<td>60,000</td>
<td>91,000</td>
<td>106,000</td>
<td>132,000</td>
<td>157,000</td>
</tr>
<tr>
<td>RAL/DRV/r</td>
<td>228,000</td>
<td>229,000</td>
<td>230,000</td>
<td>220,000</td>
<td>224,000</td>
<td>216,000</td>
<td>203,000</td>
</tr>
</tbody>
</table>
Thank You