Trends of Genotypic Sensitivity Scores of HIV-1 in Taiwan: Potential Application in the Selection of Single-Tablet Antiretroviral Regimens

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Background: Trends of cART in Taiwan

Trend of STRs

Trends of third agents

2019 IMS data

*STR, single-tablet regimen
MTR, multi-tablet regimen
Objectives

• To update the prevalence of transmitted drug resistance (TDR) in Taiwan after increasing use of single-tablet regimens (STRs)

• To determine the trends of genotypic sensitivity scores (GSS) of HIV strains among treatment-naïve and treatment-experienced patients
Materials and Methods

• Genotypic resistance assays were performed in HIV strains from antiretroviral-naïve and -experienced patients in Taiwan from 2016 to 2018.

• Resistance mutations were identified using the HIVdb program of the Stanford University HIV Drug Resistance Database.

• Genotypic Sensitivity Score (GSS) was determined based on the RAMs detected in each specimen.
## Genotypic sensitivity score (GSS)

<table>
<thead>
<tr>
<th>Stanford HIVdb</th>
<th>High</th>
<th>Intermediate</th>
<th>Low</th>
<th>Potential low</th>
<th>Susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>0</td>
<td>0.25</td>
<td>0.5</td>
<td>0.75</td>
<td>1</td>
</tr>
</tbody>
</table>

### Antiretroviral Agents

<table>
<thead>
<tr>
<th></th>
<th>NRTI</th>
<th>NNRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-level resistant</td>
<td>3TC and FTC</td>
<td>NVP</td>
</tr>
<tr>
<td>Intermediate-level resistant</td>
<td>EFV and ETR</td>
<td></td>
</tr>
<tr>
<td>Low-level resistant</td>
<td>ABC</td>
<td></td>
</tr>
<tr>
<td>Potential low-level resistant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Susceptible</td>
<td>AZT and TDF</td>
<td></td>
</tr>
</tbody>
</table>

**Example Calculation:**

ABC + 3TC + EFV

= 0.5 + 0 + 0.25

= 0.75
# CART regimens

<table>
<thead>
<tr>
<th>CART Regimens</th>
<th>DHHS</th>
<th>EACS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended Regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2NRTIs + INSTI</td>
<td>ABC/3TC/DTG (Triumeq)</td>
<td>ABC/3TC/DTG (Triumeq)</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC or TDF/FTC+DTG</td>
<td>TAF/FTC or TDF/FTC+DTG</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC or TDF/FTC+RAL</td>
<td>TAF/FTC or TDF/FTC+RAL</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC/BIC (Biktarvy)</td>
<td>TAF/FTC/RPV or TDF/FTC/RPV (Complera)</td>
</tr>
<tr>
<td>2NRTIs + nNRTI</td>
<td></td>
<td>TAF/FTC/RPV or TDF/FTC/RPV (Complera)</td>
</tr>
<tr>
<td>2NRTIs + PI</td>
<td></td>
<td>TAF/FTC or TDF/FTC+DRV/r</td>
</tr>
<tr>
<td><strong>Alternative Regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2NRTIs + INSTI</td>
<td>ABC/3TC+RAL</td>
<td>ABC/3TC+RAL</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC/EVG/c (Genvoya)</td>
<td>TAF/FTC/EVG/c (Genvoya)</td>
</tr>
<tr>
<td>2NRTIs + nNRTI</td>
<td>TAF/FTC/EFV or TDF/FTC/EFV (Atripla)</td>
<td>TAF/FTC/EFV or TDF/FTC/EFV (Atripla)</td>
</tr>
<tr>
<td></td>
<td>TDF/3TC/DOR (Delstrigo)</td>
<td>ABC/3TC+EFV</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC/RPV or TDF/FTC/RPV (Complera)</td>
<td></td>
</tr>
<tr>
<td>2NRTIs + PI</td>
<td>TAF/FTC or TDF/FTC+ATV/r</td>
<td>TAF/FTC or TDF/FTC+ATV/r</td>
</tr>
<tr>
<td></td>
<td>TAF/FTC or TDF/FTC+DRV/r</td>
<td>ABC/3TC+DRV/r</td>
</tr>
<tr>
<td></td>
<td>ABC/3TC+DRV/r</td>
<td>ABC/3TC+ATV/r</td>
</tr>
<tr>
<td><strong>Other combinations</strong></td>
<td>DTG+3TC</td>
<td>DTG+3TC</td>
</tr>
<tr>
<td></td>
<td>RAL+DRV/r</td>
<td>RAL+DRV/r</td>
</tr>
<tr>
<td></td>
<td>DRV/r+3TC</td>
<td></td>
</tr>
</tbody>
</table>

*STRs labeled in red are the first-line recommended regimens in Taiwan*
Prevalence of transmitted drug resistance in northern Taiwan

Transmitted genetic resistance (%)

<table>
<thead>
<tr>
<th>Year</th>
<th>PI</th>
<th>NRTI</th>
<th>NNRTI</th>
<th>INSTI</th>
<th>MDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>1166</td>
<td>581</td>
<td>102</td>
<td>39</td>
<td>89</td>
</tr>
<tr>
<td>2013</td>
<td>740</td>
<td>645</td>
<td>39</td>
<td>89</td>
<td>536</td>
</tr>
<tr>
<td>2014</td>
<td>536</td>
<td>591</td>
<td>295</td>
<td>374</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>428</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Updated 2019/06/24**
Trends of drug-resistance in treatment-naïve patients in northern Taiwan

Updated 2019/06/24
Distribution of **NRTI**-related genotypic mutations in treatment-naïve patients in northern Taiwan
Distribution of \textbf{nNRTI}-related genotypic mutations in treatment-naïve patients in northern Taiwan

Updated 2019/06/24
Distribution of **INSTI**-related genotypic mutations in treatment-naïve patients in northern Taiwan

% of mutations detected

- H51Y
- T66I/A/K
- E92G/Q/N
- T97A
- F121Y
- E138A/K
- G140A/C/S
- Y143C/H/K/R
- P145S
- Q146P
- S147G
- Q148H/K/R
- V151A/L
- S153Y
- N155H/S/T
- E157Q
- G163K/R
- S230R
- R263K

Updated 2019/06/24
Prevalence of genotypic resistance to various ARV classes in treatment-naïve patients

Updated 2019/06/24
Trends of drug-resistance in treatment-experienced patients in northern Taiwan
Prevalence of genotypic resistance to various ARV classes in treatment-experienced patients

Updated 2019/06/24
Comparison of GSS of STR in treatment-naïve patients, 2016-2018

% of study subjects

2016 | 2017 | 2018
---|---|---
Atripla | 0.06 | 0.008 | 0.06
Complera | 0.06 | 0.008 | 0.06
Genvoya | 0.11 | 0.15 | 0.21
Triumeq | 0.11 | 0.15 | 0.21

Updated 2019/06/24
Comparison of GSS of NRTI-backbone in treatment-naïve patients, 2016-2018
Comparison of GSS of STR in treatment-experienced patients, 2016-2018

Updated 2019/06/24
Comparison of GSS of NRTI-backbone in treatment-experienced patients, 2016-2018

Updated 2019/06/24
Summary-1

• Of 1,555 blood specimens from treatment-naïve patients, the overall prevalence of TDR was 14.9% (n=232)
  – NRTIs: 4.5% (n=70)
  – nNRTIs: 10.9% (n=169)
  – PIs: 1.4% (n=22)
  – INSTIs: 1.3% (n=10; N=758)
  – MDR: 1.6% (n=25)

• A significant increase of TDR to nNRTIs and to any class of ARV was observed, from 6.9% to 13.3% (P<0.001) and 11.9% to 18.0% (P=0.008), respectively.
Summary-2

• Of 873 blood specimens from treatment-experienced patients, the overall prevalence of RAM was 51.2% (n=447)
  – NRTIs: 33.7% (n=294)
  – nNRTIs: 39.7% (n=347)
  – PIs: 3.2% (n=28)
  – INSTIs: 10.1% (n=62; N=613)
  – MDR: 27.4% (n=239)

• A significant decrease of RAM to NRTIs, nNRTIs, MDR and any class of drugs was observed, from 37.4% to 28.5% (P=0.03), 45.0% to 29.4% (P<0.001), 32.6% to 20.1% (P=0.002), and 54.6% to 45.3% (P=0.04), respectively.
In treatment-naïve patients, a significant increased percentage of GSS <2.5 was observed for two nNRTI-based STR since 2016, from 6.7% to 11.4% for TDF/FTC/EFV ($P = 0.01$) and 2.2% to 5.5% for TDF/FTC/RPV ($P = 0.008$), while the percentage of GSS <2.5 for two INSTI-based STRs remained relatively low (1.7% to 2.3%).
• In treatment–experienced patients, an increase percentage of GSS >2.5 was observed between 2016 and 2018 for all STRs, probably reflecting the effectiveness of STR in preventing emergence of RAMs as compared to non-STRs.
Conclusions

• For treatment-naïve patients who are to initiate nNRTI-based STR as the first-line regimen in Taiwan, an ARV resistance testing should be performed at baseline, while drug resistance testing is not required for those in whom INSTI-based STR is to be initiated as the first-line regimen.

• For treatment-experienced patients, an increase percentage of GSS >2.5 was observed between 2016 and 2018 for all STRs, although a TFV/FTC-based backbone is preferred as compared to 3TC/ABC-based backbone based on the recent evolution of GSS.
Acknowledgments

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