SUPPLEMENTAL DIGITAL CONTENT 2

Monogram Genotypic and Phenotypic Susceptibility Scoring

The genotypic susceptibility score (GSS) was created by calculating a genetic susceptibility rating (GSR) for each antiretroviral (ARV) drug in the initial optimized background therapy (OBT) and then summing up those ratings. The GSS was missing if at least 1 ARV drug in the initial OBT had a missing GSR.

For drugs in the protease inhibitor (PI), nucleoside reverse transcriptase inhibitor (NRTI), non-nucleoside reverse transcriptase inhibitor (NNRTI), and integrase inhibitor (INI) classes, the GSR for each drug was based on the baseline genotypic susceptibility (genotype) from the Monogram PhenoSense GT Plus Integrase assay. Non-protocol assays were excluded. The GSR for drugs in these ARV classes was calculated as follows:

- 1, if the genotype had evidence of drug sensitivity

- 0.5, if the genotype had evidence of partial drug sensitivity

- 0, if the genotype had evidence of drug resistance

- Missing, if the genotype was non-reportable or missing

For the fusion inhibitor (FI) enfuvirtide in the absence of a genetic test, the GSR was based on the Monogram PhenoSense Entry assay and was calculated as follows:

- 1, if the susceptibility assessment was sensitive

- 0, if the susceptibility assessment was reduced susceptibility

- Missing, otherwise

For the CCR5 receptor antagonist (RA) maraviroc in the absence of a genetic test, the GSR was based on the Monogram Trofile assay and was calculated as follows:

- 1, if the CCR5 antagonist activity was yes

- 0, if the CCR5 antagonist activity was no

- Missing, if the CCR5 antagonist activity was non-reportable or missing

Experimental ARV drugs other than fostemsavir in the initial OBT were assigned GSR = 1. Boosting agents such as ritonavir and cobicistat were assigned GSR = 0. The GSR of tenofovir alafenamide fumarate (TAF) and tenofovir disoproxil fumarate (TDF) was based on the GSR of tenofovir.

The phenotypic susceptibility score (PSS) was created by calculating a phenotypic susceptibility rating (PSR) for each ARV drug in the initial OBT and then summing up those ratings. The PSS was missing if at least 1 ARV drug in the initial OBT had a missing PSR.

For drugs in the PI, NRTI, NNRTI, and INI ARV classes, the PSR for each drug was based on the baseline phenotypic susceptibility (phenotype) from the Monogram PhenoSense GT Plus Integrase assay. Non-protocol assays were excluded. The PSR for drugs in these ARV classes was calculated as follows:

- 1, if the phenotype had evidence of drug sensitivity
- 0.5, if the phenotype had evidence of partial drug sensitivity
- 0, if the phenotype had evidence of drug resistance
- Missing, if the phenotype was non-reportable or missing

For the FI enfuvirtide, the PSR was based on the Monogram PhenoSense Entry assay and was calculated as follows:

- 1, if the susceptibility assessment was sensitive
- 0, if the susceptibility assessment was reduced susceptibility
- Missing, if the susceptibility assessment was non-reportable or missing

For the CCR5 RA maraviroc, the PSR was based on the Monogram Trofile assay and was calculated as follows:

- 1, if the CCR5 antagonist activity was yes
- 0, if the CCR5 antagonist activity was no
- Missing, if the CCR5 antagonist activity was non-reportable or missing

Experimental ARV drugs other than fostemsavir in the initial OBT were assigned PSR = 1. Boosting agents such as ritonavir and cobicistat were assigned PSR = 0. The PSR of TAF and TDF was based on the PSR of tenofovir.

The overall susceptibility score (OSS) captures both genotypic and phenotypic assessments of susceptibility. The OSS was created by calculating an overall susceptibility rating (OSR) for each ARV in the initial OBT and then summing up those ratings. The OSS was missing if at least 1 OSR was missing.

For drugs in the PI, NRTI, NNRTI, and INI ARV classes, the OSR for each drug was based on the baseline combination genotype/phenotype net assessment from the Monogram PhenoSense GT Plus Integrase assay. Non-protocol assays were excluded. The OSR for drugs in these ARV classes was calculated as follows:

- 1, if the net assessment was sensitive
- 0.5, if the net assessment was partially sensitive
- 0, if the net assessment was resistant
- Missing, if the net assessment was non-reportable or missing

For the FI enfuvirtide, the OSR was based on the Monogram PhenoSense Entry assay and was calculated as follows:

- 1, if the susceptibility assessment was sensitive
- 0, if the susceptibility assessment was reduced susceptibility
- Missing, if the susceptibility assessment was non-reportable or missing

For the CCR5 RA maraviroc, the OSR was based on the Monogram Trofile assay and was calculated as follows:

- 1, if the CCR5 antagonist activity was yes
- 0, if the CCR5 antagonist activity was no
- Missing, if the CCR5 antagonist activity was non-reportable or missing

Experimental ARV drugs other than fostemsavir in the initial OBT were assigned OSR = 1. Boosting agents such as ritonavir and cobicistat were assigned OSR = 0. The OSR of TAF and TDF was based on the OSR of tenofovir.