1. Purpose of the Study

- To develop an enhanced genotypic algorithm for detecting resistance to ETR, by applying a combination of 2 weighted score systems, and other resistance associated mutations identified thru correlation analysis with phenotypic response.

- The 2 independent studies that reported extended lists of ETR resistance associated mutations and their weight factors are:
  - MGRM: developed by Monogram Biosciences thru minimizing discordance to phenotypic susceptibility [1].
  - TBTC: developed by Tibotec thru correlation with virologic outcome [2].

2. Optimizing Genotypic Weighted Score by Minimizing Discordance to Phenotype

- Samples reported after 2009 that included at least one NNRTI resistance associated mutation, or one of the mutations in the expanded list, were included in the test set.
- Weights in range of 1 – 4 were assigned to mutations based on the rank order of both score systems.
- Weights for individual mutations and threshold factors applied to more extensive list of mutations.

3. Results: Mutations and Weight Factors

4. Distribution of ETR FC by Enhanced Genotypic Score

5. Performance of the Enhanced Genotypic Score

- Sensitivity to detect ETR FC ≥ 2.9 was 90.1% and discordance rate for all samples was 13.6% compared to 83.7% and 12% for the original MGRM weighted score, respectively. The improved sensitivity was accompanied by modest increase in number of samples with FC < 2.9 but a weighted score ≥ 4, from 11 by the original score to 14.5 by the enhanced algorithm.

6. Performance of the Original MGRM Score in the New Test Set

- Overall Discordance = 12%
- False Positive Rate = 11% (Specificity = 89%)

ACKNOWLEDGEMENTS

We are grateful to the Monogram Biosciences Clinical Reference Laboratory for performance of all phenotypes and genotype assays. This work was supported in part by SBIR grant # 5R44AI057068-05.

REFERENCES