

| Drug                                   | Gene(s)                            | Mutation  | Pathway   |
|--|------------------------------------|---|---|
| INH (Isoniazid) 1 <sup>st</sup>        | Rv1484 (inhA)                      | <b>-8 T/A</b> and Ser94Ala                                      | mycolic acid biosynthesis   |
|  | Rv1908c (katG)                     | <b>Ser315Thr</b>  | tryptophan metabolism and methane metabolism  |
|  | Rv3795 (embB)                      | Met306Ileu  | arabinosyl transferase  |
|  | Rv2428 (ahpC)                      | Ser315Thr   | glutathione metabolism  |
|  | Rv2245 (kasA)                      | Asp66Asn  | N.A   |
|  | Rv1854c (ndh)                      | Thr110Ala and Arg268His   | oxidative phosphorylation   |
| PZA (Pyrazinamide) 1 <sup>st</sup>     | Rv2043c (pncA)                     | <b>Ala132Gly</b> , Thr114Met                                    | nicotinate and nicotinamide metabolism  |
| RIF (Rifampicin) 1 <sup>st</sup>       | Rv0667 (rpoB)                      | <b>Asp435Gly, Leu452Pro, Ile1106Thr, Ser531Leu</b> or His526Tyr | purine metabolism, pyrimidine metabolism, RNA polymerase                                    |
|  | Rv3795 (embB)                      | <b>Met306Val</b>  | arabinosyl transferase  |
| EMB (Ethambutol) 1 <sup>st</sup>       | Rv3795 (embB)                      | Met306Ileu  | arabinosyl transferase  |
|  | Rv3793 (embC)                      | Met306Val   | arabinosyl transferase  |
|  | Rv3794 (embA)                      | Met306Ileu  | arabinosyl transferase  |
|  | Rv3266c (rmlD)                     | N.A   | nucleotide sugars metabolism, streptomycin biosynthesis, polyketide sugar unit biosynthesis |
|  | STR (Streptomycin) 1 <sup>st</sup> | Rv3919c (gidB)  | <b>Indel</b>  |
| ETH (Ethionamide) 2 <sup>nd</sup>      | Rv1483 (mapA, fabG1)               | Ser94Ala  | mycolic acid biosynthesis   |
|  | Rv3854c (ethA, ethR)               | N.A   | aminobenzoate degradation   |
| FLQ (flouroquinolones) 2 <sup>nd</sup> | Rv0005 (gyrB)                      | N.A   | N.A   |
|  | Rv0006 (gyrA)                      | <b>Ala90Val</b> , Asp94Gly                                      | N.A   |
| AMI (Aminoglycosides) 2 <sup>nd</sup>  | MTB000019 (rrs)                    | <b>Ala1401Gly</b>   | N.A   |
|  | Rv1694 (tlyA)                      | N.A   | N.A   |

The 10 mutations (eight genes) indicated in bold were verified by the BROAD institute, while the remainder were identified from literature. Abbreviations used: A-Adenine, Ala-Alanine, Arg-Arginine, Asn-Glutamine, Asp-Aspartate, Gly-Glycine, His-Histidine, indel-insertion deletion, Ileu-Isoleucine, Leu-Leucine, Met-Methionine, N.A-Not available, Pro-Proline, Ser-Serine, T-Thymidine, Thr-Threonine, Tyr-Tyrosine, Val-Valine.