

**Table 6.** Minimal inhibitory concentrations (MICs), Cyp51A amino acid alterations and genotype by patients with azole resistant *A. fumigatus* isolates

| Id no.    | Patient # | Sample, date | Acc#      | ITC agar | EUCAST MIC |      |       | E test MIC |       |                     | cyp51A alteration | Genotype |    |    |    |    |    |        |    |
|-----------|-----------|--------------|-----------|----------|------------|------|-------|------------|-------|---------------------|-------------------|----------|----|----|----|----|----|--------|----|
|           |           |              |           |          | ITC        | VRC  | POS   | AMB        | CAS   | 2A                  |                   | 2B       | 2C | 3A | 3B | 3C | 4A | 4B     | 4C |
| R1-07-1*  | R1        | 04.01.2007   | T43729    | +        | >4         | 4    | >4    | 1          | 0.064 | M220K               | 23                | 23       | 15 | 35 | 10 | 20 | 13 | 9      | 5  |
| R1-07-2   | R1        | 22.11.2007   | F45297    | +        | >4         | 2    | >4    | 0.5        | ND    | M220K               | 23                | 23       | 15 | 35 | 10 | 20 | 13 | 9      | 5  |
| R2-07-1   | R2        | 22.10.2007   | M10731    | +        | >4         | 0.5  | 0.5   | 0.25       | ND    | TR+L98H+S297T+F495I | 14                | 20       | 8  | 40 | 9  | 11 | 8  | 10     | 20 |
| R3-07-1   | R3        | 07.08.2007   | T16102    | -        | 0.5        | 0.5  | 0.125 | 0.5        | ND    | Y431C               | 19                | 26       | 9  | 31 | 11 | 36 | 20 | 9      | 8  |
| R3-07-2   | R3        | 21.08.2007   | H21791    | -        | 0.25       | 0.25 | 0.5   | 0.5        | ND    | Y431C               | 19                | 26       | 9  | 31 | 11 | 36 | 20 | 9      | 8  |
| R3-07-3   | R3        | 27.08.2007   | T18267 II | -        | NA         | NA   | NA    | NA         | NA    | Y431C               | 19                | 26       | 9  | 31 | 11 | 36 | 20 | 9      | 8  |
| R3-07-4   | R3        | 14.09.2007   | H28093    | +        | >4         | 4    | 2     | 0.5        | 0.032 | Y431C               | 19                | 26       | 9  | 31 | 11 | 36 | 20 | 9      | 8  |
| R4-07-1   | R4        | 17.07.2007   | F15877    | -        | 1          | 1    | 0.25  | 0.5        | 0.032 | Not found           | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 9      | 10 |
| R4-07-2   | R4        | 05.12.2007   | T40280    | -        | 0.5        | 1    | 0.5   | 0.5        | 0.016 | Not found           | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 9      | 10 |
| R4-09-1   | R4        | 09.07.2009   | M46330    | +        | >4         | 1    | 4     | 0.5        | 0.016 | M220I + V101F       | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 9      | 10 |
| R4-09-2   | R4        | 16.07.2009   | M46200    | +        | >4         | 1    | 4     | 0.25       | 0.032 | M220I + V101F       | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 12     | 10 |
| R4-09-3   | R4        | 21.07.2009   | T21639    | +        | >4         | 2    | 4     | 0.5        | 0.016 | M220I + V101F       | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 12 & 9 | 10 |
| R4-09-4   | R4        | 10.08.2009   | T26530    | +        | >4         | 1    | 4     | 0.25       | 0.032 | M220I + V101F       | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 9      | 10 |
| R4-09-5   | R4        | 07.09.2009   | T33127    | +        | >4         | 1    | 4     | 1          | 0.032 | M220I + V101F       | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 12     | 10 |
| R4-09-6   | R4        | 25.09.2009   | H42463    | +        | >4         | 4    | 0.5   | 0.5        | 0.125 | Not found           | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 9      | 10 |
| R4-09-7   | R4        | 23.10.2009   | T47842    | +        | >4         | 4    | 4     | 0.5        | 0.032 | M220I + V101F       | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 12     | 10 |
| R4-09-8   | R4        | 24.11.2009   | W64844    | +        | >4         | 2    | 1     | 1          | 0.094 | M220I + V101F       | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 9      | 10 |
| R4-09-9   | R4        | 26.11.2009   | W64734    | -        | 0.5        | 0.5  | 0.25  | 1          | 0.016 | Not found           | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 9      | 10 |
| R4-09-10  | R4        | 14.12.2009   | M13176    | +        | >4         | 2    | 4     | 0.5        | 0.016 | M220I + V101F       | 18                | 23       | 16 | 35 | 13 | 18 | 15 | 9      | 10 |
| R5-07-1   | R5        | 01.08.2007   | W19437a   | +        | >4         | 1    | 0.5   | 0.5        | 0.016 | TR+L98H+S297T+F495I | 14                | 20       | 8  | 40 | 9  | 11 | 8  | 10     | 20 |
| R5-07-2   | R5        | 16.11.2007   | F36888    | +        | >4         | 1    | 1     | 0.5        | 0.032 | TR+L98H+S297T+F495I | 14                | 20       | 8  | 40 | 9  | 11 | 8  | 10     | 20 |
| R5-07-3   | R5        | 20.11.2007   | T35448a   | +        | >4         | 1    | 0.5   | 0.5        | 0.016 | TR+L98H+S297T+F495I | 14                | 20       | 8  | 40 | 9  | 11 | 8  | 10     | 20 |
| R5-07-4   | R5        | 06.12.2007   | M19486    | +        | >4         | 1    | 1     | 0.5        | 0.016 | TR+L98H+S297T+F495I | 14                | 20       | 8  | 40 | 9  | 11 | 8  | 10     | 20 |
| R5-09-1** | R5        | 12.05.2009   | F12895    | +        | >4         | 4    | 2     | 0.5/4      | 0.032 | TR+L98H+S297T+F495I | 14                | 20       | 8  | 40 | 9  | 11 | 8  | 10     | 20 |
| R5-09-2   | R5        | 28.07.2009   | W33602a   | -        | 0.25       | 0.25 | 0.06  | 0.5        | 0.064 | Not found           | 23                | 24       | 15 | 34 | 12 | 19 | 13 | 9      | 5  |

|           |    |            |          |   |       |       |       |     |       |                     |    |       |    |    |       |       |    |    |    |
|-----------|----|------------|----------|---|-------|-------|-------|-----|-------|---------------------|----|-------|----|----|-------|-------|----|----|----|
| R5-09-3   | R5 | 31.08.2009 | F34426a  | + | >4    | 2     | 1     | 1   | 0.032 | TR+L98H+S297T+F495I | 14 | 20    | 8  | 40 | 9     | 11    | 8  | 10 | 20 |
| R5-09-4   | R5 | 13.11.2009 | T50586a  | - | 0.25  | 0.25  | 0.06  | 0.5 | 0.064 | Not found           | 13 | 20    | 9  | 34 | 9     | 10    | 10 | 10 | 19 |
| R5-09-5   | R5 | 24.11.2009 | W64719.2 | + | >4    | 2     | 1     | 0.5 | 0.032 | TR+L98H+S297T+F495I | 14 | 20    | 8  | 40 | 9     | 11    | 8  | 10 | 20 |
| R5-09-6   | R5 | 24.11.2009 | W64719.1 | + | >4    | 4     | 1     | 0.5 | 0.016 | TR+L98H             | 23 | 10    | 9  | 10 | 10    | 6     | 8  | 10 | 20 |
| R6-07-1   | R6 | 01.08.2007 | W19455   | - | NA    | NA    | NA    | NA  | NA    | NA                  | 25 | 20    | 12 | 34 | 9     | 10    | 2  | 10 | 17 |
| R6-07-2   | R6 | 27.08.2007 | T18260   | - | NA    | NA    | NA    | NA  | NA    | Not found           | 23 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| R6-07-3   | R6 | 11.10.2007 | M9255    | - | NA    | NA    | NA    | NA  | NA    | NA                  | 23 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| R6-09-1** | R6 | 09.03.2009 | H70083   | - | 0.5   | 1     | 0.25  | 0.5 | 0.125 | Not found           | 23 | 23    | 15 | 37 | 11    | 20    | 13 | 9  | 5  |
| R6-09-2   | R6 | 14.07.2009 | M46277a  | - | NA    | NA    | NA    | NA  | NA    | NA                  | 23 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| R6-09-3   | R6 | 10.08.2009 | T26532c  | + | >4    | 2     | 0.5   | 2   | 0.064 | Not found           | 18 | 19    | 8  | 37 | 15    | 20    | 9  | 9  | 5  |
| R6-09-4   | R6 | 23.08.2009 | T28585a  | - | NA    | NA    | NA    | NA  | NA    | NA                  | 18 | 19    | 8  | 37 | 15    | 20    | 9  | 9  | 5  |
| R6-09-5   | R6 | 27.08.2009 | F34423a  | - | NA    | NA    | NA    | NA  | NA    | NA                  | 23 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| R6-09-6   | R6 | 21.09.2009 | T33879   | - | NA    | NA    | NA    | NA  | NA    | NA                  | 23 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| R6-09-7   | R6 | 06.10.2009 | W51261a  | - | NA    | NA    | NA    | NA  | NA    | NA                  | 14 | 19    | 8  | 36 | 18    | 7     | 8  | 27 | 5  |
| R6-09-8   | R6 | 13.10.2009 | M67310   | + | >4    | 2     | 0.25  | 2   | 0.064 | Not found           | 24 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| R6-09-9   | R6 | 18.11.2009 | H57334   | - | NA    | NA    | NA    | NA  | NA    | NA                  | 23 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| R6-09-10  | R6 | 07.12.2009 | M11218   | - | NA    | NA    | NA    | NA  | NA    | NA                  | 23 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| R6-09-11  | R6 | 28.12.2009 | F64207   | - | NA    | NA    | NA    | NA  | NA    | NA                  | 23 | 23    | 15 | 36 | 11    | 20    | 13 | 9  | 5  |
| S1-07-1   | SI | 07.08.2007 | M68381   | - | 0.125 | 0.25  | 0.06  | 0.5 | 0.125 | NA                  | 18 | 17    | 15 | 35 | 21    | 24    | 16 | 9  | 8  |
| S1-07-2   | SI | 25.10.2007 | T35395   | - | 1     | 0.25  | 0.125 | 0.5 | ND    | NA                  | 18 | 23    | 19 | 32 | 13    | 27    | 17 | 9  | 5  |
| S1-07-3   | SI | 26.10.2007 | W38943   | - | 0.5   | 1     | 0.25  | 0.5 | 0.094 | Not found           | 18 | 17    | 15 | 36 | 21    | 24    | 16 | 9  | 8  |
| S1-07-4   | SI | 10.12.2007 | M19504   | - | 0.25  | 0.125 | 0.06  | 0.5 | ND    | NA                  | 18 | 17    | 15 | 35 | 21    | 24    | 16 | 9  | 8  |
| S1-09-1   | SI | 03.08.2009 | M48698   | - | 0.125 | 0.5   | 0.125 | 0.5 | 0.032 | NA                  | 18 | 17    | 15 | 35 | 21    | 24    | 16 | 9  | 8  |
| S1-09-2   | SI | 07.09.2009 | F36605   | - | NA    | NA    | NA    | NA  | NA    | NA                  | 18 | 23    | 19 | 33 | 13    | 27    | 17 | 9  | 5  |
| S1-09-3   | SI | 26.10.2009 | T47850a  | - | NA    | NA    | NA    | NA  | NA    | NA                  | 18 | 23    | 19 | 32 | 13    | 27    | 17 | 9  | 5  |
| S1-09-4   | SI | 04.12.2009 | W68546   | - | NA    | NA    | NA    | NA  | NA    | NA                  | 18 | 17    | 15 | 35 | 21    | 24    | 16 | 9  | 8  |
| S1-09-5   | SI | 07.12.2009 | M11123   | - | NA    | NA    | NA    | NA  | NA    | NA                  | 18 | 17&23 | 15 | 35 | 13&21 | 24&27 | 16 | 9  | 8  |
| S2-09-1   | S2 | 23.11.2009 | W64620   | - | 0.25  | 1     | 0.06  | 1   | 0.064 | Not found           | 25 | 20    | 8  | 10 | 10    | 21    | 9  | 10 | 5  |
| T11       | E1 |            | T11      | + | >4    | 4     | 2     |     |       | TR+L98H             | 14 | 21    | 12 | 31 | 9     | 38    | 8  | 10 | 5  |
| T18       | E2 |            | T18      | + | >4    | 4     | 0.5   |     |       | TR+L98H             | 10 | 20    | 8  | 32 | 9     | 7     | 8  | 9  | 19 |

|     |    |     |   |    |   |      |           |    |    |    |        |    |    |   |    |    |
|-----|----|-----|---|----|---|------|-----------|----|----|----|--------|----|----|---|----|----|
| T22 | E3 | T22 | + | >4 | 4 | 0.25 | TR+L98H   | 14 | 24 | 14 | 39     | 10 | 7  | 8 | 11 | 5  |
| R13 | E4 | R13 | + | >4 | 4 | 1    | TR + L98H | 20 | 10 | 12 | 0 & 84 | 10 | 13 | 8 | 9  | 11 |

ITC = itraconazole, VRC = voriconazole, POS = posaconazole, CAS = caspofungin, ND = not determined, NA = not analysed.

\*Isolates obtained prior to sample periods. \*\*Isolates obtained between sample periods.