SUPPLEMENTARY MATERIAL

Supplementary table 1: Fungal isolates and secondary outcomes in lung transplant recipients and other SOTR.

| Identified fungal species          | Lung transplant recipients (n = 44) | Kidney, liver and combined transplant recipients (n = 9) | All SOTR (n = 53) |
|-----------------------------------|------------------------------------|--------------------------------------------------------|------------------|
| Aspergillus spp                   | 36 (80)                            | 7 (100)                                               | 43 (82.7)        |
| A. flavus                         | 14 (38.9)                          | 2 (28.6)                                              | 16 (30.2)        |
| A. terreus                        | 11 (30.6)                          | 0 (0)                                                 | 11 (20.8)        |
| A. fumigatus                      | 8 (17.8)                           | 4 (57.1)                                              | 12 (22.6)        |
| Other Aspergillus spp             | 3 (6.7)                            | 1 (14.3)                                              | 4 (7.6)          |
| Mucormicosis                      | 1 (2.2)                            | 0 (0)                                                 | 1 (1.9)          |
| Other filamentous fungi           | 5 (11.1)                           | 0 (0)                                                 | 5 (9.4)          |
| Yeasts                            | 4 (8.9)                            | 0 (0)                                                 | 4 (7.5)          |
| Trichosporon asahii               | 2 (4.5)                            | 0 (0)                                                 | 2 (3.8)          |
| Candida albicans                  | 1 (2.2)                            | 0 (0)                                                 | 1 (1.9)          |
| Saccharomyces cerevisiae          | 1 (2.2)                            | 0 (0)                                                 | 1 (1.9)          |
| No fungal isolate                 | 6                                  | 3                                                     | 9 SOTR           |

| Type of Fl³                       | 45 infections in 44 lung transplant recipients | 9 infections in 9 kidney, liver and combined transplant recipients | 54 infections in 53 SOTR³ |
|-----------------------------------|-----------------------------------------------|--------------------------------------------------------------------|--------------------------|
| Tracheobronchitis                 | 22 (48.9)                                     | 3 (33.3)                                                           | 25 (46.3)                |
| Fungal pneumonia                  | 7 (15.6)                                      | 0 (0)                                                              | 7 (13)                   |
| Bronchial anastomotic infection   | 2 (4.4)                                       | 0 (0)                                                              | 2 (3.7)                  |
| Other:                            |                                               |                                                                    |                          |
| Micetoma                          | 5 (11.1)                                      | 1 (11.1)                                                           | 6 (11.1)                 |
| Cutaneous infection               | 3 (6.7)                                       | 0 (0)                                                              | 3 (5.6)                  |
| Disseminated FI                   | 1 (2.2)                                       | 1 (11.1)                                                           | 2 (3.7)                  |
| Osteomyelitis                     | 1 (2.2)                                       | 0 (0)                                                              | 1 (1.9)                  |
| Chronic otitis media              | 0 (0)                                         | 1 (11.1)                                                           | 1 (1.9)                  |
|                             | 35 lung transplant recipients | 9 kidney, liver and combined transplant recipients | 44 SOTR |
|-----------------------------|-------------------------------|-----------------------------------------------|--------|
| Isolation in donor          | 1 (2.2)                       | 0 (0)                                         | 1 (1.9) |
| No proven or probable FI    | 3 (6.7)                       | 3 (33.3)                                      | 6 (11.1) |
| Clinical cure at EOT         | 22 (50)                       | 5 (55.6)                                      | 27 (50.9) |
| Culture conversion at EOT    | 14 (40)                       | 3 (33.3)                                      | 17 (38.6) |
| Fungal persistence at EOT    | 14 (40)                       | 1 (11.1)                                      | 15 (34.1) |
| Cultures were not performed at EOT | 7 (20)                      | 5 (55.6)                                      | 12 (27.3) |

aAll cases were definite or probable fungal infection according to ISHLT and EORTC/MSGERC criteria except when indicated.
bOne patient was treated for fungal tracheobronchitis and subcutaneous infection at the same time.

Data are expressed as numbers (%) unless otherwise indicated. EORTC/MSGERC, European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium; FI, fungal infection; ISHLT, International Society for Heart and Lung Transplantation; SOTR, solid organ transplant recipient.
Supplementary table 2: *Aspergillus* spp MIC and susceptibility rates to the antifungal agents tested (n = 43).

|                | A. *flavus* (n =16, 37.2%. Fifteen MIC could be assessed) | A. *fumigatus* (n =12 , 27.9%. Ten MIC could be assessed) | A. *terreus* (n =11, 25.6%. Ten MIC could be assessed) | A. *nidulans* (2), A. *niger* (1), A. *lentulus* (1) |
|----------------|-----------------------------------------------------------|----------------------------------------------------------|---------------------------------------------------|-------------------------------------------------|
| **Isavuconazole** |                                            |                                                          |                                                   |                                                 |
| MIC50          | 0.25                                                     | 0.19                                                     | 0.38                                             | 0.125                                          |
| MIC90          | 0.38                                                     | 0.38                                                     | 0.5                                              | NC                                             |
| IQR MIC50      | 0.125-0.38                                               | 0.125-0.25                                               | 0.19-0.5                                         | 0.047-0.051                                    |
| **Voriconazole** |                                            |                                                          |                                                   |                                                 |
| MIC50          | 0.25                                                     | 0.125                                                   | 0.38                                             | 0.125                                          |
| MIC90          | 0.5                                                      | 0.25                                                    | 1.5                                             | NC                                             |
| IQR MIC50      | 0.19-0.38                                                | 0.125-0.25                                              | 0.25-0.5                                        | 0.094-0.19                                     |
| **Posaconazole** |                                            |                                                          |                                                   |                                                 |
| MIC50          | 0.25                                                     | 0.125                                                   | 0.094                                           | 0.38                                           |
| MIC90          | 0.5                                                      | 0.38                                                    | 0.38                                            | NC                                             |
| IQR MIC50      | 0.19-0.38                                                | 0.064-0.25                                              | 0.064-0.25                                     | 0.19-0.5                                       |
| **Amphotericin B** |                                 |                                                          |                                                   |                                                 |
| MIC50          | 4                                                        | 0.38                                                    | 2                                               | 1                                              |
| MIC90          | 12                                                       | 2                                                       | 30                                              | NC                                             |
| IQR MIC50      | 1.5-6                                                    | 0.025-1                                                 | 1.5-8                                           | 0.38-4                                         |
| **Anidulafungin** |                                 |                                                          |                                                   |                                                 |
| MIC50          | 0.002                                                    | 0.008                                                   | 0.008                                           | 0.016                                          |
| MIC90          | 0.006                                                    | 0.047                                                   | 0.03                                            | NC                                             |
| IQR MIC50      | 0.002-0.004                                              | 0.003-0.03                                              | 0.006-0.16                                     | 0.004-0.064                                    |
| **Micafungin** |                                            |                                                          |                                                   |                                                 |
| MIC50          | 0.003                                                    | 0.012                                                   | 0.007                                           | 0.008                                          |
| MIC90          | 0.006                                                    | 0.06                                                    | 0.012                                           | NC                                             |
| IQR MIC50      | 0.003-0.004                                              | 0.006-0.016                                             | 0.004-0.008                                     | 0.006-0.047                                    |
| Caspofungin | MIC50 | 0.032 | 0.125 | 0.094 | 0.094 |
|------------|------|------|------|------|------|
|            | MIC90| 0.125| 0.19 | 0.25 | NC   |
|            | IQR  | 0.016-0.064 | 0.064-0.125 | 0.032-0.125 | 0.064-0.125 |

Data are expressed as numbers (%) unless otherwise indicated. IQR, interquartile range; MIC (μg/dL), Minimum Inhibitory Concentration (MIC50 and MIC90 values were defined as the lowest concentration of the antifungal at which 50 and 90% of the isolates were inhibited); NC, Not Calculated; S%, susceptibility percentage of isolates according to antifungal breakpoints established by CLSI.
Supplementary table 3: non *Aspergillus* species MIC to antifungal agents tested (n = 10)

|                     | ISA  | VOR  | POS  | AMPB | ANID | MICA | CASP |
|---------------------|------|------|------|------|------|------|------|
| *Candida albicans*  |      | 0.008| 1    | 0.015| 0.125| 0.125|      |
| *Trichosporon asahii* | 0.094| 0.06 | 0.25 | 0.5  | 32   | 32   | 32   |
| *Lomentospora prolificans* | 32   | 32   | 32   | 32   | 32   | 32   | 32   |
| *Alternaria alternata* | 8    | 8    | 8    | 2    | 0.03 | 0.06 | 0.5  |
| *Purpureocillium lilacinus* | 0.25 | 0.125| 0.38 | 32   | 32   | 32   | 32   |

*Trichosporon asahii, Saccharomyces cerevisiae, Mucor spp, Diaporthe spp, and unidentified new mold species*  Antifungal susceptibility could not be performed

MIC (μg/dL) = minimum inhibitory concentration.
Supplementary table 4: Dosage and plasmatic levels of tacrolimus and m-TOR inhibitors after starting isavuconazole

|                     | Before start | 1-2 days     | 4 days       | 7 days       | 10 days      | 14 days      |
|---------------------|--------------|--------------|--------------|--------------|--------------|--------------|
| **Tacrolimus dose (mg)** | n = 47       | n = 38       | n = 46       | n = 40       | n = 37       | n = 37       |
| Tacrolimus          | 4 (2-6)      | 3 (2-5.3)    | 2.3 (1.4-4)  | 2 (1.1-4)    | 2 (1.3-4)    | 2 (1-4)      |
| measured levels     | 8.6 (5.7-11.4) | 7.4 (4.8-15.2) | 9.8 (5.7-15.2) | 9.2 (4.8-10.9) | 7.9 (6.1-9.4) | 7.5 (5.6-10) |
| n = 47              | n = 28       | n = 34       | n = 24       | n = 27       | n = 28       |
| **mTOR dose**       | n = 7        | n = 7        | n = 7        | n = 7        | n = 7        | n = 7        |
| mTOR measured levels| 1.75 (1-2)   | 1 (1-2)      | 1 (0-1)      | 0.5 (0-1)    | 0.5 (0-1)    | 0.5 (0-1)    |
| n = 7               | n = 4        | n = 3        | n = 4        | n = 2        | n = 4        |

Data are expressed as median (IQR) unless otherwise indicated.
Supplementary table 5: Dosage and plasmatic levels of tacrolimus and m-TOR inhibitors after discontinuation of isavuconazole.

|                         | Initial | 1-2 days | 4 days | 7 days | 10 days | 14 days |
|-------------------------|---------|----------|--------|--------|---------|---------|
| **Tacrolimus dose (mg)**| 3 (2-4) | 4 (2-4.9)| 4 (2-4)| 4 (2-6)| 4 (2-5.3)| 4 (2-6) |
| n = 39                  | n = 30  | n = 31   | n = 31 | n = 30 | n = 30  | n = 30  |
| **Tacrolimus measured levels** | 6.8 (5.1-10) | 7.9 (5.3-12.1) | 9.3 (5.2-13.6) | 6.7 (4.7-12.6) | 7.3 (5.2-8.5) | 7.2 (5.2-10.6) |
| n = 39                  | n = 14  | n = 17   | n = 19 | n = 15 | n = 22  |         |
| **mTOR dose (mg)**      | 1 (0.5-2.8) | 1.5 (0.8-3.5) | 1.5 (0.8-3.5) | 1.5 (0.8-3.5) | 1.5 (0.8-3.5) | 1.5 (0.8-3.5) |
| n = 5                   | n = 5   | n = 5    | n = 5  | n = 5  | n = 5   | n = 5   |
| **mTOR measured levels**| 5.7 (2.7-7.6) | 7 (0.8-10.7) | 5.1 (0.8-10.7) | 3      | 1.9     | 3.9     |
| n = 4                   | n = 1   | n = 3    | n = 2  | n = 2  | n = 2   | n = 2   |

Data are expressed as median (IQR) unless otherwise indicated.
Supplementary table 6: Evolution of SOTR treated with ISA

Black, deceased; Blue, duration of treatment with isavuconazole; Green, transplant date; Orange, discontinuation of treatment due to a clinically relevant adverse event. ISA, isavuconazole; SOTR, solid organ transplant recipient.