**Supplemental Table 1**: Characteristics of individuals diagnosed with cryptococcosis from 2002-2007 vs 2008-2017

|  |  |  |  |
| --- | --- | --- | --- |
|  | Pre-modern ART era (n=56) (%) | Modern ART era (n=49) (%) | p-value |
| **Mean age at diagnosis (SD), years** | 39 (8) | 41 (11) | 0.644 |
| **Male sex** | 46 (82) | 38 (78) | 0.557 |
| **Race** |  |  | 0.759 |
| *African American* | 42 (75) | 38 (78) | - |
| *Non-African American* | 14 (25) | 11 (22) | - |
| **Site of Infection** | | | |
| *CNS* | 38 (68) | 33 (67) | 0.956 |
| *Pulmonary* | 7 (13) | 3 (6) | 0.267 |
| *Bloodstream* | 26 (46) | 12 (25) | **0.020** |
| *Other* | 2 (4) | 0 (0) | 0.182 |
| **Presenting Symptoms** | | | |
| *Fever* | 41 (73) | 32 (65) | 0.380 |
| *Fatigue* | 43 (77) | 38 (78) | 0.926 |
| *Stiff neck* | 12 (21) | 17 (35) | 0.129 |
| *Headache* | 27 (48) | 33 (67) | **0.048** |
| *AMS* | 21 (38) | 18 (37) | 0.935 |
| *Visual changes* | 4 (7) | 6 (12) | 0.374 |
| **Serum CrAg Completed** | 40 (71) | 41 (84) | 0.136 |
| **Serum CrAg titers \*** |  |  | 0.796 |
| *0* | 1 (3) | 2 (5) | - |
| *1:2 – 1:8* | 4 (10) | 5 (15) | - |
| *1:16 – 1:512* | 17 (43) | 18 (44) | - |
| *≥1:1024* | 18 (45) | 15 (37) | - |
| **CSF CrAg Completed** | 37 (66) | 44 (90) | **0.004** |
| **CSF CrAg titers \*\*** |  |  | **0.039** |
| *0* | 5 (14) | 15 (34) | - |
| *1:2 – 1:8* | 4 (11) | 6 (14) | - |
| *1:16 – 1:512* | 14 (38) | 6 (14) | **-** |
| *≥1:1,024* | 14 (38) | 17 (39) | - |
| **Treatment** ꝉ | | | |
| *Amphotericin* | 36 (95) | 29 (88) | 0.300 |
| *Amphotericin ≥14 days* | 24 (63) | 19 (58) | 0.631 |
| *+ Flucytosine* | 24 (63) | 27 (82) | 0.081 |
| **Mortality** | | | |
| *Survivor* | 19 (34) | 36 (74) | **<0.001** |
| *Early-Mortality* | 7 (14) | 10 (18) | 0.620 |
| *Late-Mortality* | 27 (48) | 6 (12) | **<0.001** |

Data are presented as No. (%) unless otherwise indicated. CNS = central nervous system. CrAg = cryptococcal antigen. CSF = cerebrospinal fluid. Modern ART era defined as 2008 or later.

\*Denotes number of individuals that had serum CrAg testing (n=81) with pre-modern ART era (n=40) and modern ART era (n=41).

\*\*Denotes number of individuals that had lumbar puncture and CSF CrAg (n=81) with pre-modern ART era (n=37) and modern ART era (n=44)

ꝉ Denotes number of individuals with CNS involvement (n=71) with pre-modern ART era (n=38) and modern ART era (n=33).

**Supplemental Table 2**: HIV characteristics of individuals diagnosed with cryptococcosis from 2002-2007 vs 2008-2017

|  |  |  |  |
| --- | --- | --- | --- |
|  | Pre-modern ART era (n=56) (%) | Modern ART era (n=49) (%) | p-value |
| **Median CD4+ T CELL at time of cryptococcal diagnosis (cells/mm3) (IQR)** | 17 (7, 49) | 26 (8, 42) | 0.533 |
| **Median HIV viral load at cryptococcal diagnosis (log copies/mL) (IQR)** | 5.26 (4.88, 5.80) | 4.83 (4.05, 5.28) | **0.011** |
| **Median HIV viral load at last observation (log copies/mL) (IQR)** | 5.16 (4.47, 5.65) | 4.46 (2.92, 5.27) | 0.099 |
| **New HIV diagnosis at time of cryptococcal diagnosis** | 12 (21) | 10 (20) | 0.898 |
| **Median time from HIV diagnosis to Cryptococcal diagnosis (Years) (IQR)** | 6.5 (1.0, 12.0) | 6.0 (1.0, 12.5) | 0.971 |
| **ART-Experienced at time of cryptococcal diagnosis** | 32 (57) | 33 (67) | 0.283 |
| **Prescribed ART at time of cryptococcal diagnosis** | 17 (30) | 21 (43) | 0.184 |
| **HIV Viral Load Suppressed at time of cryptococcal diagnosis** | 5 (9) | 8 (16) | 0.251 |
| **HIV Viral Load Suppressed at last observation** | 16 (29) | 28 (57) | **0.003** |
| **History of previous OIs (at time of cryptococcal diagnosis)** |  |  | 0.273 |
| *Pneumocystis Pneumonia* | 18 (32) | 12 (25) | - |
| *Disseminated MAC* | 4 (7) | 4 (8) | - |
| *Histoplasmosis* | 1 (2) | 0 (0) | - |
| *Tuberculosis* | 3 (5) | 0 (0) | - |
| *Oral Candidiasis* | 4 (7) | 5 (10) | - |
| *Cryptosporidium* | 0 (0) | 1 (2) | - |
| **Insurance** |  |  | **0.026** |
| *Private* | 7 (13) | 17 (35) | **-** |
| *Government (Medicaid, Medicare,*  *Ryan White)* | 43 (77) | 28 (57) | **-** |
| *None* | 6 (11) | 4 (8) | - |
| **History of substance abuse** | 29 (52) | 22 (45) | 0.481 |
| **History of psychiatric illness** | 19 (34) | 14 (29) | 0.555 |

Data are presented as No. (%) unless otherwise indicated. HIV= Human Immunodeficiency Virus, CD4+ T cell= Cluster of Differentiation 4, ART = antiretrovirals, OI= opportunistic infections, MAC= mycobacterium avium complex. Modern ART era defined as 2008 or later.