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| **Table e-1: FLUOXETINE SAFETY** |
|  | Fluoxetine Exposed (n=30) |
| **TREATMENT REGIMEN** |
| Dosinga | Below 0.75mg/kg/day | 8 (27%) |
|  | 0.75mg/kg/day, max 40mg/dayb | 21 (70%) |
| Timinga | Days after Neurologic Onset (median, IQR) | 5 (3, 7)  |
|  | Before Nadir | 11 (37%) |
|  | Between Nadir and Latest Follow-up | 18 (60%) |
| Duration  | Days Receiving Fluoxetine (median, IQR) | 7 (7, 12) |
| **SERIOUS ADVERSE EVENTS** | 0 (0%) |
|  | Prolonged Hospitalization | 0 (0%) |
|  | Disability or Permanent Damage | 0 (0%) |
|  | Life-threatening | 0 (0%) |
|  | Required Intervention | 0 (0%) |
|  | Death | 0 (0%) |
| **ELECTROCARDIOGRAPHIC EFFECTS** |
|  | Prolonged QTc for Age (% of those with ECG)c | 2 (12%) |
| **TREATMENT STOPPED PREMATURELY** | 2 (7%) |
|  | Perceived adverse effectsd | 1 (3%) |
|  | No foreseen benefite | 1 (3%) |
| *aFluoxetine dose and timing was unavailable for one patient each.**bDose received was nearest 5mg dose increment to 0.75mg/kg/day and did not exceed 40mg/day.**cn=17 with ECG obtained after fluoxetine initiation. Prolonged QTc noted in two patients of 450 ms and 495 ms (no ECG prior to initiation).* |
| *dDue to multifactorial anxiety.* |
| *eDue to mild weakness.* |

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| **Table e-2: FLUOXETINE TOLERABILITY** |
| REPORTED ADVERSE EFFECTS | Fluoxetine Exposed (n=30) | Fluoxetine Unexposed (n=26) | Overall (n=56) | P value |
| **GASTROINTESTINAL (%)** | 7 (23%) | 12 (46%) | 19 (34%) | 0.07 |
| Nausea  | 1 (3%) | 3 (12%) | 4 (7%) | 0.33 |
| Vomiting | 3 (10%) | 3 (12%) | 6 (10%) | >0.99 |
| Diarrhea | 3 (10%) | 1 (4%) | 4 (7%) | 0.62 |
| Abdominal Pain | 3 (10%) | 0 (0%) | 3 (5%) | 0.24 |
| Othera | 0 (0%) | 3 (12%) | 3 (5%) | 0.09 |
| **PSYCHIATRIC (%)** | 11 (37%) | 4 (15%) | 15 (27%) | 0.07 |
| Anxiety | 9 (30%) | 3 (12%) | 12 (21%) | 0.09 |
| Agitation | 5 (17%) | 2 (8%) | 7 (13%) | 0.43 |
| Panic Attack | 0 (0%) | 0 (0%) | 0 (0%) | NA |
| Insomnia | 2 (7%) | 0 (0%) | 2 (4%) | 0.49 |
| Otherb | 3 (10%) | 0 (0%) | 3 (5%) | 0.24 |
| **ALLERGIC (%)** | 0 (0%) | 2 (8%) | 2 (4%) | 0.21 |
| Rash | 0 (0%) | 2 (8%) | 2 (4%) | 0.21 |
| Anaphylaxis | 0 (0%) | 0 (0%) | 0 (0%) | NA |
| Serotonin Syndrome | 0 (0%) | 0 (0%) | 0 (0%) | NA |
| **LABORATORY (%)** | 1 (3%) | 2 (8%) | 3 (5%) | 0.59 |
| Hyponatremia | 0 (0%) | 2 (8%) | 2 (4%) | 0.21 |
| Elevation in AST/ALT  | 0 (0%) | 0 (0%) | 0 (0%) | NA |
| Double in BUN/Cr | 0 (0%) | 0 (0%) | 0 (0%) | NA |
| INR > 2 | 0 (0%) | 0 (0%) | 0 (0%) | NA |
| Otherc | 1 (3%) | 0 (0%) | 1 (2%) | 1 |
| **TOTAL PATIENTS WITH REPORTED ADVERSE EFFECTS (%)** | 14 (47%) | 17 (65%) | 31 (55%) | 0.16 |

***a****constipation (n=3).*

*baggression (n=1), depression (n=2).*

*canemia and thrombocytopenia (n=1).*

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| **Table e-3: SECONDARY OUTCOMES** |
|  | Fluoxetine-Treated (n=28) | Fluoxetine-Untreated (n=28) | Overall (n=56) | P value |
| **HOSPITAL COURSE** |  |  |  |  |
| Length of Stay (days; median, IQR) | 14 (8.5, 42.5) | 7 (5, 11) | 9.5 (6.5, 19) | 0.007 |
| ICU Care Needed (%) | 17 (61%) | 8 (29%) | 25 (45%) | 0.02 |
|  *ICU Length of Stay (days; median, IQR)* | 9 (3, 40.5) | 5.5 (3.5, 9) | 7 (3.5, 28) | 0.36 |
| Rehabilitation Stay Needed (%) | 22 (79%) | 13 (46%) | 35 (62.5%) | 0.01 |
|  *Rehabilitation Length of Stay (days; median, IQR)* | 54 (21, 71) | 31.5 (14, 44.5) | 37 (20, 62) | 0.09 |
| **VENTILATORY/FEEDING SUPPORT** |  |  |  |  |
| Persistent Cranial Nerve Deficita (% affected) | 7 (50%) | 4 (44%) | 11 (48%) | 1 |
| Ventilatory Support (%)b | 12 (43%) | 3 (11%) | 15 (27%) | 0.007 |
|  *Persistent Need for Ventilatory Support (%)ab* | 6 (21%) | 0 (0%) | 6 (11%) | 0.02 |
|  *Days of Respiratory Support (median, IQR)* | 245 (29, 327) | 5 (1, 7) | 18 (5, 245) | 0.10 |
| Tracheostomy Support (%) | 8 (29%) | 0 (0%) | 8 (14%) | 0.004 |
|  *Persistent Need for Tracheostomy Support (%)a* | 5 (18%) | 0 (0%) | 5 (9%) | 0.05 |
|  *Days with Tracheostomy (median, IQR)* | 294 (11, 300) | NA | 294 (11, 300) | NA |
| Supplemental Feeding Support (%)c | 10 (36%) | 3 (11%) | 13 (23%) | 0.03 |
|  *Persistent Need for Supplemental Feeding Support (%)ac* | 7 (25%) | 0 (0%) | 7 (13%) | 0.01 |
|  *Days of Supplemental Feeding Support (median; IQR)* | 56 (14, 234) | 8 (7, 47) | 35 (9.5, 159.5) | 0.16 |
| **MORTALITY** |  |  |  |  |
| Death | 1 (4%) | 0 (0%) | 1 (2%) | >0.99 |
| *aPersistent defined as still present/requiring support at latest follow-up.* |
| *bIncludes need for invasive (intubation, tracheostomy) or non-invasive (CPAP, BiPAP) ventilation.* |
| *cIncludes supplemental feeding by gastrostomy or nasogastric feeding tube.* |

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| **Table e-4: ASSOCIATION OF CORTICOSTEROIDS AND INTRAVENOUS IMMUNE GLOBULIN WITH LIMB STRENGTH OUTCOMES** |
|  | **Change in Summative Limb Strength Score: Initial to Follow-up** | **Change in Weakest Limb Strength Score: Initial to Follow-up** |
| **Corticosteroids** | Steroid Treated (n=33) | Steroid Untreated (n=23) | P value | Steroid Treated (n=33) | Steroid Untreated (n=23) | P value |
| Unadjusted Mean Change (95%CI) | +1.1 (-1.1, +3.6) | +0.5 (-1.6, +2.6) | 0.68 | +0.5 (-0.1, +1.0) | +0.4 (-0.3, +1.2) | 0.90 |
| Adjusted Mean Change (95%CI)\*  | +0.8 (-1.1, +2.7) | +1.0 (-0.8, +2.9) | 0.83 | +0.5 (-0.0, +1.0) | +0.4 (-0.3, +1.0) | 0.74 |
| **Intravenous Immune Globulin (IVIG)** | IVIG Treated (n=46) | IVIG Untreated (n=10) | p value | IVIG Treated (n=46) | IVIG Untreated (n=10) | p value |
| Unadjusted Mean Change (95%CI) | +0.7 (-1.1, +2.6) | +1.6 (+0.6, +2.6) | 0.40 | +0.4 (-0.1, +0.9) | +0.6 (-0.3, +1.5) | 0.69 |
| Adjusted Mean Change (95%CI)\*  | +0.7 (-0.9, +2.3) | +2.2 (+1.5, +2.9) | 0.09 | +0.4 (-0.1, +0.8) | +0.5 (-0.6, +1.5) | 0.90 |
| *\*Adjusted for age, sex, and strength score at initial exam using doubly robust, propensity score weighted ATE model* |

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| **Table e-5: ANALYSIS OF FLUOXETINE-TREATED PATIENTS WITH AND WITHOUT ENTEROVIRUS D68 IDENTIFIED** |
|  | Fluoxetine-treated: EV-D68 Identified (n=16) | Fluoxetine-treated: No EV-D68 Identified (n=12) | P value |
| **DEMOGRAPHICS** |  |  |  |
| Age in Years (median; IQR) | 3.0 (1.8, 4.3) | 6.0 (3.0, 7.8) | 0.11 |
| Sex (% male) | 11 (69%) | 3 (25%) | 0.02 |
| Race (% non-white) | 5 (31%) | 6 (50%) | 0.44 |
| Ethnicity (% hispanic or latino) | 5 (33%) | 4 (33%) | >0.99 |
| **HOST CHARACTERISTICS** |  |  |  |
| Underlying Medical Condition (%) | 8 (50%) | 2 (17%) | 0.11 |
|  Asthma (%) | 6 (38%) | 0 (0%) | 0.02 |
|  Immunocompromised (%) | 3 (19%) | 0 (0%) | 0.24 |
|  Abnormal Neurologic Baseline (%) | 2 (13%) | 0 (0%) | 0.49 |
|  Psychiatric (%) | 0 (0%) | 0 (0%) | NA |
| **PRODROME** |  |  |  |
| Preceding Illness (%) | 15 (94%) | 12 (100%) | >0.99 |
| Fever (%) | 13 (81%) | 9 (75%) | >0.99 |
|  Respiratory (%) | 13 (81%) | 10 (83%) | >0.99 |
|  Gastrointestinal (%) | 2 (13%) | 4 (33%) | 0.35 |
| **NEUROLOGIC ONSET** |  |  |  |
| Days from Prodromal Illness (median, IQR) | 6 (3, 10) | 11.5 (4, 18.5) | 0.14 |
| Fever (%) | 12 (75%) | 6 (50%) | 0.24 |
| Meningeal Signs (%) | 4 (25%) | 4 (33%) | 0.69 |
| Limb Pain (%) | 1 (6%) | 4 (33%) | 0.13 |
| Altered Mental Status or Seizures (%) | 0 (0%) | 2 (17%) | 0.18 |
| CSF Pleocytosis (% of those with lumbar puncture) | 14 (88%) | 12 (71%) | 0.40 |
| **AFM INITIAL PRESENTATION** |  |  |  |
| Days from Neurologic Onset (median, IQR) | 1 (0, 3) | 3.5 (1.5, 5) | 0.02 |
| Number of Limbs with Weakness (median; IQR) | 2 (1, 3) | 2.5 (1.5, 4) | 0.30 |
| Leg Involvement (%) | 8 (50%) | 9 (75%) | 0.25 |
| Arm Involvement (%) | 12 (75%) | 12 (100%) | 0.11 |
| Cranial Nerve Involvement (%) | 4 (25%) | 9 (75%) | 0.009 |
| **AFM TIME COURSE** |  |  |  |
| Days from Onset to Nadir (median, IQR) | 4.5 (3, 7.5) | 5.5 (3.5, 14.5) | 0.25 |
| Days from Onset to Latest Follow-up (median, IQR) | 273 (130, 326) | 172 (92, 242) | 0.06 |
| **SUMMATIVE LIMB STRENGTH SCORES (SLSS)** |
| Initial (mean, 95%CI) | 12.6 (9.9, 15.4) | 13.2 (10.4, 16.0) | 0.75 |
| Nadir (mean, 95%CI) | 7.9 (5.0, 10.7) | 11.1 (7.5, 14.7) | 0.14 |
| Follow-up (mean, 95%CI) | 12.0 (9.3, 14.7) | 13.1 (9.0, 17.2) | 0.63 |
| Unadjusted Mean Change: Initial to Follow-up (95%CI) | -0.6 (-4.0, +2.8) | -0.1 (-2.9, +2.7) | 0.80 |
| Adjusted Mean Change: Initial to Follow-up (95%CI)\* | 0.0 (-2.2, +2.2) | -0.1 (-3.1, +3.0) | 0.98 |
| *\*Adjusted for age, sex, and strength score at initial exam, using doubly robust, propensity score weighted ATE model* |