Viral Molecular Testing of Cerebrospinal Fluid in Adults with Suspected Central Nervous System Infection in an Italian University Hospital Laboratory: a Retrospective Study on 1462 Consecutive Patients

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Supplementary Table 1. Description of which viral PCRs were prescribed and of their positive (number in bold character) and negative result for each testing set approach (intended as number of tests requested on the sample). Data are reported as overall values for all patients who had the same number of PCRs tested. Empty cell: not included in diagnostic workflow.

| PCRs (n) | EV | HSV | VZV | CMV | EBV | HPeVs\textsuperscript{a} | WNV | HHV-6 | TBE | HAdV\textsuperscript{b} | HHV-8 | JCV | MEA | MUM | HTLV-1 | PEB19 |
|----------|----|-----|-----|-----|-----|-----------------|-----|-------|-----|-----------------|-------|-----|-----|-----|-------|-------|
| 1 (29 pts) | 1/0 | 4/24 |
| 2 (50 pts) | 1/8 | 0/46 | 5/14 | 0/4 | 0/3 | 0/3 | 0/2 | 0/1 | 1/0 | 0/2 | 0/8 | 1/0 |
| 3 (99 pts) | 0/41 | 1/93 | 3/46 | 1/44 | 0/35 | 0/12 | 0/8 | 0/3 | 0/3 | 1/0 | 0/1 | 0/2 | 0/3 |
| 4 (259 pts) | 1/122 | 7/249 | 6/217 | 1/140 | 8/124 | 0/97 | 0/19 | 0/9 | 0/8 | 1/11 | 2/1 | 0/3 | 1/8 | 0/1 |
| 5 (172 pts) | 6/96 | 5/161 | 2/139 | 0/97 | 3/97 | 0/71 | 0/77 | 0/14 | 0/32 | 0/22 | 0/2 | 1/20 | 0/1 | 0/9 | 1/1 |
| 6 (210 pts) | 11/15 | 5/200 | 5/181 | 0/176 | 7/161 | 0/142 | 0/64 | 1/19 | 0/54 | 0/24 | 0/8 | 0/8 | 2/25 | 0/3 | 0/2 | 0/4 | 0/5 |
| 7 (169 pts) | 5/130 | 4/162 | 5/146 | 1/149 | 3/151 | 0/112 | 0/65 | 1/50 | 0/61 | 0/39 | 0/30 | 0/26 | 1/24 | 0/6 | 0/4 | 0/4 | 0/4 |
| 8 (90 pts) | 4/74 | 1/87 | 3/82 | 1/85 | 1/79 | 0/64 | 1/51 | 0/34 | 0/47 | 0/32 | 0/17 | 0/18 | 0/24 | 0/3 | 0/1 | 0/6 | 0/5 |
| 9 (112 pts) | 4/88 | 4/108 | 2/102 | 0/108 | 5/91 | 0/78 | 0/59 | 1/84 | 0/61 | 0/42 | 1/50 | 0/55 | 0/34 | 1/12 | 0/5 | 0/13 |
| 10 (63 pts) | 6/51 | 1/61 | 2/59 | 0/62 | 2/59 | 0/51 | 0/38 | 1/57 | 0/33 | 0/24 | 3/36 | 0/38 | 0/23 | 0/6 | 0/9 | 0/6 | 0/2 |

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(Table S1) contd....

Supplementary Table 2. Description of number of PCRs made and of positive PCRs of the virus which had a positive result in the 353 patients who had HHV-7 tested on CSF and in the 1109 who had not. The PCRs were described both as absolute value and as percentage respect to the number of tests performed for the specific virus. The viruses are listed according to the percentage of positive PCRs found in the overall population. Only viruses which had a positive result in the overall study population were included in the table.

| Viral PCRs | Tested in patients with HHV-7* DNA tested (353 patients), n (%) | Tested in patients with HHV-7* DNA not tested (1109 patients), n (%) | p     |
|------------|---------------------------------------------------------------|---------------------------------------------------------------|-------|
| EV         | 283 (80.2)                                                   | 722 (65.1)                                                   | < 0.0001 |
| EBV        | 324 (91.8)                                                   | 714 (64.4)                                                   | < 0.0001 |
| HSV        | 344 (97.5)                                                   | 1087 (98)                                                   | 0.5206 |
| VZV        | 319 (90.4)                                                   | 902 (81.3)                                                   | < 0.0001 |
| HHV-6      | 334 (94.6)                                                   | 143 (12.9)                                                   | < 0.0001 |
| CMV        | 337 (95.5)                                                   | 741 (66.8)                                                   | < 0.0001 |
| JC         | 121 (34.3)                                                   | 162 (14.6)                                                   | < 0.0001 |
| HAdV*      | 115 (30)                                                    | 154 (13.9)                                                   | < 0.0001 |
| HPeV*      | 260 (73.7)                                                   | 559 (50.4)                                                   | < 0.0001 |
| WNV        | 191 (54.1)                                                   | 351 (31.7)                                                   | < 0.0001 |
| MEAV       | 137 (38.8)                                                   | 22 (2)                                                       | < 0.0001 |
| PvB19      | 12 (3.4)                                                     | 16 (1.4)                                                     | 0.0195 |

Positive Viral PCRs

| Patients with HHV-7* DNA tested, n (%) | Patients with HHV-7* DNA not tested, n (%) | p     |
|--------------------------------------|--------------------------------------------|-------|
| EV                                   | 19 (6.7)                                   | 33 (4.6) | 0.1679 |
| EBV                                  | 11 (3.4)                                   | 25 (3.5) | 0.9309 |
| HSV                                  | 6 (1.7)                                    | 29 (2.7) | 0.3339 |
| VZV                                  | 4 (1.2)                                    | 31 (3.4) | 0.049919 |
| HHV-6                                | 5 (1.5)                                    | 3 (2.1)  | 0.701372 |
| CMV                                  | 1 (0.3)                                    | 4 (0.5)  | 1     |
| JC                                   | 0 (0.3)                                    | 5 (3.1)  | 0.073460 |
| HAdV*                                | 2 (0.9)                                    | 0 (0.0)  | 0.515  |
| HPeV*                                | 0 (0.0)                                    | 1 (0.2)  | 1     |
| WNV                                  | 0 (0.0)                                    | 1 (0.3)  | 1     |

PCRs: real-time polymerase chain reaction pt: patient; pts: patients
EV: enterovirus; PvB19: parvovirus B19; EBV: Epstein-Barr virus; VZV: varicella zoster virus; HHV-7: human herpes virus-7; HSV: herpes simplex virus; JC: JC virus; HHV-6: human herpes virus-6; MEAV: measles virus; HAdV: human adenovirus; CMV: cytomegalovirus; WNV: West Nile Virus; HPeVs: human parechoviruses; TBEV: tick-borne encephalitis virus; HHV-8: human herpes virus-8; MUMV: mumps virus; HTLV-1: human T-cell leukemia virus type 1. HHV-8: human herpes virus-8.

HPeVs tested from May 2012; HAdV tested from February 2012; HHV-7 tested from January 2013.
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EV: enterovirus; PvB19: parvovirus B19; EBV: Epstein-Barr virus; VZV: varicella zoster virus; HHV-7: human herpes virus-7; HSV: herpes simplex virus; JCV: JC virus; HHV-6: human herpes virus-6; MEAV: measles virus; HAdV: human adenovirus; CMV: cytomegalovirus; WNV: West Nile Virus; HPeVs: human parechoviruses.

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