**Supplementary Table 1** Patient case study survey

|  |  |
| --- | --- |
| Respondent profile | * Respondent characteristics (eg specialty)
* Type of hospital
* AADCd patient population (pediatric/adult)
 |
| General questions | * Number of patients with AADC that clinician has diagnosed/cared for (ever and currently)
* Overall patient characteristics (eg any biological relations severity of AADCd)
* Current use of standard management/treatment protocols (if any)
 |
| Patient case study survey(completed separately for each patient) | * Patient characteristics (eg age, age at diagnosis, best achieved motor milestone)
* Patient symptoms (presence of central nervous system symptoms, autoimmune system symptoms, and other specified symptoms)

Healthcare resource use associated with the care of each patient:* Medical management (annual frequency of HCP interactions/visits)
* Paramedical support (annual frequency)
* Drug treatments (annual frequency)
* Medical devices (annual frequency)
* Technical procedures (annual frequency)
* Laboratory tests (annual frequency)
* Surgery (at any time)
* Hospitalizations and emergency room (annual frequency; reasons for hospitalizations)
* Other resources (annual frequency)
 |

**Abbreviations:** AADCd, aromatic L-amino acid decarboxylase deficiency.

**Supplementary Table 2** AADCd genotype according to best achieved motor milestone

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Walking assisted or unassisted**(n = 10) | **Sitting unassisted or standing with support**(n = 2) | **No motor function or full head control only**(n = 8) | **Overall**(n = 20) |
| Mutation known |  |  |  |  |
| Yes | 8 (80) | 2 (100) | 4 (50) | 14 (70) |
| Type of mutation |  |  |  |  |
| c.1543C>T (p.Ser250Phe) | 1 (13) | 0 | 2 (50) | 3 (21) |
| c.105delC (p.Tyr37Thrfs\*5)/c.710 T>C (p.F237S) | 2 (25) | 0 | 0 | 2 (14) |
| p.Arg375 Cys | 2 (25) | 0 | 0 | 2 (14) |
| AADC gene variants: p.Ala91Val (c.272C> T) and p.Cys410Gly (c.1228T> G) | 1 (13) | 0 | 0 | 1 (7) |
| c.843C>G (p.Cys281Trp)/c.1085T>C (p.Met362Thr) | 1 (13) | 0 | 0 | 1 (7) |
| Homozygotic variant c.734C>T/p.Thr245Ile | 0 | 0 | 1 (25) | 1 (7) |
| Two new mutations (7p11) p.G123R (c.367G>A) + p.T245I (c.734C>T) | 1 (13) | 0 | 0 | 1 (7) |
| Missense mutation (not specified) | 0 | 2 (100) | 0 | 2 (14) |
| Not recorded | 0 | 0 | 1 (25) | 1 (7) |

**Notes:** Data are n (%).

**Abbreviations:** AADCd, aromatic L-amino acid decarboxylase deficiency.

**Supplementary Table 3** Key patient characteristics by country

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Key characteristics** | **France**(n = 7) | **Italy**(n = 11) | **Spain**(n = 2) | **Pooled**(n = 20) |
| Age at onset of symptoms, months, mean (SD) | 2.4 (2.4) | 8.6 (9.0) | 5.0 (1.4) | 6.1 (7.3) |
| Age at diagnosis, months, mean (SD) | 20.3 (29.6) | 131.0 (146.7) | 8.5 (3.5) | 80.0 (122.3) |
| Follow-up duration, years, mean (SD) | 4.2 (3.6) | 5.4 (2.5) | 7.5 (6.4) | 5.2 (3.2) |
| Alive at time of survey | 5 (71.4) | 11 (100.0) | 1 (50.0) | 17 (85.0) |
| If alive, age at time of survey, years, mean (SD) | 10.0 (5.8) | 21.5 (11.7) | 3.0 (–) | 17.1 (11.6) |
| If deceased, age at last follow-up, years, mean (SD) | 7.0 (1.4) | N/A | 12.0 (–) | 8.7 (3.1) |
| Male sex | 4 (57.1) | 8 (72.7) | 0  | 12 (60.0) |
| Ethnicity  |  |  |  |  |
| Caucasian | 1 (14.3) | 9 (81.8) | 2 (100.0) | 12 (60.0) |
| African | 1 (14.3) | 2 (18.2) | 0 | 3 (15.0) |
| Other | 4 (57.1) | 0 | 0 | 4 (20.0) |
| Not mentioned | 1 (14.3) | 0 | 0 | 1 (5.0) |
| Best achieved motor milestone  |  |  |  |  |
| No motor function | 5 (71.4) | 0  | 1 (50.0) | 6 (30.0) |
| Full head control only | 0 | 2 (18.2) | 0 | 2 (10.0) |
| Sitting unassisted | 0 | 2 (18.2) | 0 | 2 (10.0) |
| Standing with support | 0 | 0 | 0 | 0 |
| Walking assisted | 0 | 0 | 0 | 0 |
| Walking unassisted | 2 (28.6) | 7 (63.6) | 1 (50.0) | 10 (50.0) |

**Notes:** Data are n (%) unless otherwise indicated.

**Abbreviations:** SD, standard deviation.

**Supplementary Table 4.** Drug treatments reported at the time of the survey.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Current drug treatments1** | **Walking assisted or unassisted**(n = 10) | **Sitting unassisted or standing with support**(n = 2) | **No motor function or full head control only**(n = 8) | **Overall**(n = 20) |
| **Vitamin B6** | 8 (80) | 2 (100) | 7 (88) | 17 (85) |
|  Pyridoxine | 7 (70) | 2 (100) | 5 (63) | 14 (70) |
|  Pyridoxalphosphate | 2 (20) | 0 | 2 (25) | 4 (20) |
| **Dopamine agonists** | 9 (90) | 0 | 8 (100) | 17 (85) |
|  Pramipexole | 2 (20) | 0 | 2 (25) | 4 (20) |
|  Ropinirole | 0 | 0 | 2 (25) | 2 (10) |
|  Rotigotine | 6 (60) | 0 | 4 (50) | 10 (50) |
|  Bromocriptine | 2 (20) | 0 | 2 (25) | 4 (20) |
| **Monoamine oxidase inhibitors** | 8 (80) | 0 | 6 (75) | 14 (70) |
|  Selegiline | 6 (60) | 0 | 4 (50) | 10 (50) |
|  Tranylcypromine | 2 (20) | 0 | 2 (25) | 4 (20) |
| **Anticholinergic agents** | 0 | 0 | 1 (13) | 1 (5) |
|  Benztropine | 0 | 0 | 1 (13) | 1 (5) |
| **Sleep and mood disorder treatments** | 2 (20) | 1 (50) | 3 (38) | 6 (30) |
|  Melatonin | 2 (20) | 1 (50) | 3 (38) | 6 (30) |
|  Benzodiazepines | 0 | 1 (50) | 2 (25) | 3 (15) |
| **Other drug treatments** | 4 (40) | 1 (50) | 8 (100) | 13 (65) |
|  Levodopa | 3 (30) | 1 (50) | 2 (25) | 6 (30) |
|  Vitamin B9 | 2 (20) | 0 | 6 (75) | 8 (40) |
|  Dietary supplement | 1 (10) | 0 | 1 (13) | 2 (10) |
|  Enteral nutrition | 0 | 0 | 2 (25) | 2 (10) |
|  Other2 | 1 (10) | 0 | 4 (50) | 5 (25) |

Values are n (%). 1Results are not mutually exclusive as patients may have been om more than one type of treatment at the time of the survey. 2Other drug treatments included one patient able to walk receiving for fluoxetine and of the patients with no motor function or head control only, one patient each received amitriptyline drops, vitamin D, methylphenidate and parenteral nutrition.