SUPPLEMENTARY DATA

**Supplementary data 1:** Features of the neuroendocrine tumour in each individual patient

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Patient** | **Age at NET diagnosis, y** | **Gender** | **Primary site** | **Ki67** | **Metastases at NET diagnosis** |
| #1 | 71 | M | rectum | 5-10% | yes |
| #2 | 74 | F | pancreas | 10% | yes |
| #3 | 51 | M | small bowel | 20-30% | yes |
| #4 | 61 | M | small bowel | 1-5% | no |
| #5 | 64 | F | pancreas | 5-10% | yes |
| #6 | 80 | M | pancreas | 3-5% | yes |
| #7 | 66 | M | unknown | <10% | yes |
| #8 | 49 | M | small bowel | <1% | yes |
| #9 | 35 | M | duodenum | 2% | yes |
| #10 | 51 | F | pancreas | NA | yes |
| #11 | 59 | F | colon | 2% | yes |
| #12 | 50 | F | pancreas | 2% | yes |
| #13 | 69 | F | pancreas | 5% | yes |

M, male; F, female; NA, not available

**Supplementary data 2:** Neurological features in each individual patient

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patients** | **Treatment before neurological symptom onset** | **Time between NET diagnosis and neurological symptom onset, monthsa** | **Metastases at**  **diagnosis of neurological**  **symptoms** | **Site**  **of metastases** | **Tumor Tumor**  **volumeb status** |  |  |  |
| #1 | So, Su | 31 | yes | Liver, peritoneum | High stable |  |  |  |
| #2 | So, Su | 18 | yes | Liver | High progressing |  |  |  |
| #3 | TACE, So, Te, Ca | 9 | yes | Liver, bone | High stable |  |  |  |
| #4 | S | 24 | no | - | Low stable |  |  |  |
| #5 | So, Su, Te, Ca, Ev, FOLFIRI | 19 | yes | Liver, bone, lymph nodes | Low progressing |  |  |  |
| #6 | TACE, So, Su, Ca | 36 | yes | Liver, bone | High progressing |  |  |  |
| #7 | RFA | -36 | no | - | Low stable |  |  |  |
| #8 | none | -36 | no | - | Low stable |  |  |  |
| #9 | S, Su | 72 | yes | Liver, lymph nodes | Low stable |  |  |  |
| #10 | STZ-ADA, So | 264 | yes | Liver, lymph nodes | Low stable |  |  |  |
| #11 | S, TACE | 60 | yes | Liver, lymph nodes | High stable |  |  |  |
| #12 | S | 120 | yes | Liver | High stable |  |  |  |
| #13 | none | 0 | yes | Liver | High stable |  |  |  |

So: somatostatin analogue; Su: sunitinib; TACE: transcatheter oily chemoembolization; Te: temozolomide; Ca: capecitabine; S: surgery; RFA: radiofrequency ablation;

Ev: everolimus; FOLFIRI: Folinic acid, 5-fluorouracil, and irinotecan; STZ-ADA: streptozotocin-adriamycin

aIn 2 patients, the neurological symptoms antedated the diagnosis of NET.

b High tumor volume is defined as liver tumor volume >50 % of total liver volume calculated on CT

**Supplementary data 3:** Results of the investigations in each individual patient

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Patients | Clinical  symptoms | Anti-neuronal antibodies | Imaging studies | EEG | EMG | CSF |
| #1 | upper extremity motor deficit | anti-Hu | spinal metastasesa | NA | AN | normal |
| #2 | lower extremity motor deficit | negative | spinal metastasesa | NA | AN | NA |
| #3 | upper extremity motor deficit | anti- amphi-physin | spinal metastasesa | NA | AN | normal |
| #4 | hearing loss | anti-Hu | Normal | NA | NA | normal |
| #5 | lower extremity motor deficit | anti-GAD | Normal | NA | AN | normal |
| #6 | encephalopathy | NA | Normal | generalised slowing | NA | normal |
| #7 | sensory and motor neuropathy | NA | Normal | NA | AN | normal |
| #8 | diplopia | NA | Normal | NA | NA | normal |
| #9 | peripheral neuropathy | anti-recoverin | Normal | NA | AN | normal |
| #10 | convulsion | NA | Normal | temporal lobe epilepsy | NA | NA |
| #11 | confusions, hallucinations | NA | Normal | generalised slowing | NA | normal |
| #12 | encephalopathy | NA | Normal | generalised slowing | NA | NA |
| #13 | encephalopathy | NA | Normal | generalised slowing | NA | normal |

NA: not available; AN: axonal neuropathy

awithout evidence of spinal cord compression

**Supplementary data 4:** Treatment received and clinical response in each individual patient

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Patients | Clinical  symptoms | Anti-neuronal antibodies | Treatment | Clinical response |
| #1 | upper extremity motor deficit | anti-Hu | steroids | complete response |
| #2 | lower extremity motor deficit | negative | radiotherapy | no response |
| #3 | upper extremity sensory deficit | anti-amphiphysin | NA | NA |
| #4 | hearing loss | anti-Hu | steroids | no response |
| #5 | lower extremity motor deficit | anti-GAD | steroids | complete response |
| #6 | encephalopathy | NA | lactulose, rifaximin | partial response |
| #7 | sensory and motor neuropathy | NA | IVIG | complete response |
| #8 | diplopia | NA | NA | NA |
| #9 | peripheral neuropathy | anti-recoverin | steroids | complete response |
| #10 | convulsion | NA | levetiracetam | partial response |
| #11 | confusions, hallucinations | NA | lactulose, rifaximin | partial response |
| #12 | encephalopathy | NA | hepatectomy | complete response |
| #13 | encephalopathy | NA | TACE | complete response |

TACE: transcatheter oily chemoembolization