**Supplement table no. 1: Course of disease case no 1**

|  |  |  |  |
| --- | --- | --- | --- |
| Year | Date | Therapy | Staging |
| **2010** | 04/2010 |  | initial diagnosis of a NET G2 of the larynx with metastases of the lungs, brain, orbita and cutis  synaptophysin +, CEA+, EMA+, Pancytokeratin+, SMA-, S100-, CT31- |
|  | 04/2010 | local resection of left ary cartilage |  |
| **2012** | 09/2012 | right neck dissection with lymph node resection | relapse of the primary tumor with synchronous lymph node and pulmonary metastases  Ki-67 12%. |
| **2012** | 11/12-02/14 | temzolomide (15 cycles) | Stable disease |
| **2014** | 11/14 |  | PD with testicular metastases |
|  | 12/14-09/15 | FOLFOX (12 cycles) discontinued due to peripheral motor neuropathy Grade 2 according to CTCAE [23] |  |
| **2015** | 02/15 | right orchiectomy |  |
| **2016** | 06-09/16 | everolimus | PD with cutaneous metastasis |
|  | 09/16 | resection of cutaneous metastasis | several SNV’s in POLE, BRCA1, BRACA2, CHEK2, HRAS  Ki-67 15% |
|  | 10/16-03/17 | CAP/TEM |  |
|  | 11/16 | stereotactic radiation of orbita metastasis (54 Gy) |  |
| **2017** | 04/17-01/20 | pembrolizumab | PR with regression of pulmonary, osseous and cerebral metastases |
|  | 06/2017 | stereotactic radiation of cerebral metastases (49,4 Gy) |  |
|  | 07/17 |  | mixed response with stable disease despite of a newly diagnosed cerebellar metastasis |
|  | 11/2017 | stereotactic radiation of cerebellar metastasis (25,6 Gy) |  |
|  | 12/2017-09/2018 |  | SD |
| **2018** | 10/2018 |  | progression in a retrotracheal lymph node |
|  | 10/2018 | stereotactic radiation of retrotracheal lymph node |  |
|  |  |  | SD |
| **2019** | 11/2019 |  | bronchoscopy: bronchial metastasis  stenosis of the right main bronchus |
| **2020** | 01/2020 | CAP/TEM |  |

neuroendocrine tumor (NET), progressive disease (PD), stable disease (SD), capecitabin/temozolomide (CAP/TEM), single nucleotide variant (SNV)