|  |  |  |  |
| --- | --- | --- | --- |
| **Patient characteristics** | **Typical N=73 (72%)** | **Atypical N=29 (28%)** | **P-value** |
| **Gender** |  |  | .603 |
| Male | 24 (75%) | 8  |  |
| Female | 49 (70%) | 21 (30%) |  |
| **Age at diagnosis** |  |  | .391 |
| <40 | 14 (70%) | 6  |  |
| 40-50 | 16 (76.2%) | 5  |  |
| 50-60 | 21 (75%) | 7 |  |
| 60-70 | 15 (78.9%) | 4  |  |
| >70 | 7  | 7  |  |
| **Smoking history** |  |  | **.019** |
| Unknown | 33 (60%) | 22 (40%) |  |
| Yes | 14 (82%) | 3  |  |
| No | 26 (86.7%) | 4  |  |
| **Symptoms** |  |  | .155 |
| Cough | 17 (73.9%) | 6  |  |
| SOB/Chest pain | 9  | 1  |  |
| Pneumonia | 15 (78.9%) | 4  |  |
| Haemoptysis | 8  | 5  |  |
| Atypical carcinoid syndrome | 5  | 1  |  |
| Ectopic Cushing’s syndrome | 4  | 1  |  |
| **Site** |  |  | .325 |
| RUL | 4  | 3  |  |
| RML | 11 (91.7%) | 1  |  |
| RLL | 12 (75%) | 4  |  |
| LUL | 12 (85.7%) | 2  |  |
| LLL | 14 (70%) | 6  |  |
| Right hilum | 7  | 6  |  |
| Left hilum | 5  | 1  |  |
| **Surgical Procedure** |  |  | .183 |
| Wedge resection | 5  | 1  |  |
| Lobectomy | 42 (73.7%) | 15 (26.3%) |  |
| Bilobectomy | 9  | 0 |  |
| Sleeve resection | 2  | 1  |  |
| Pneumonectomy | 5  | 4  |  |
| **Laser Treatment** |  |  | **.002** |
| No | 70 (76.1%) | 22 (23.9%) |  |
| Yes | 3  | 7  |  |
| **pT** |  |  | .848 |
| pTx | 13 (72.2%) | 5  |  |
| pT1a | 11 (73.3%) | 4  |  |
| pT1b | 22 (75.9%) | 7  |  |
| pT1c | 15 (75%) | 5 |  |
| pT2a | 4  | 2  |  |
| pT2b | 2  | 3  |  |
| pT3 | 5  | 2  |  |
| pT4 | 1  | 1  |  |
| **pN** |  |  | .204 |
| pNx | 8  | 4  |  |
| pN0 | 52 (76.5%) | 16 (23.5%) |  |
| pN1 | 9  | 4  |  |
| pN2 | 4  | 5  |  |
| **cM** |  |  | .769 |
| cMx | 7  | 4  |  |
| cM0 | 62 (72.1%) | 24 (27.9%) |  |
| cM1 | 4  | 1  |  |
| **pStage** |  |  | .245 |
| Unknown | 12 (70.6%) | 5  |  |
| IA1 | 9  | 2  |  |
| IA2 | 19 (73.1%) | 7  |  |
| IA3 | 11 (78.6%) | 3 |  |
| IB | 3  | 1  |  |
| IIA | 3  | 2 |  |
| IIB | 10 (83.3%) | 2 |  |
| IIIA | 2  | 5 |  |
| IIIB | 0 | 1 |  |
| IIIC | 0 | 0 |  |
| IVA | 3  | 0 |  |
| IVB | 1  | 1  |  |
| **WHO Grade** |  |  | **.001** |
| Grade 1 | 44 (84.6%) | 8  |  |
| Grade 2 | 18 (52.9%) | 16 (47.1%) |  |
| **Calendar year** |  |  | .336 |
| 1985-1995 | 12 (85.7%) | 2  |  |
| 1996-2005 | 36 (72%) | 14 (28%) |  |
| 2006-2012 | 24 (64.9%) | 13 (35.1%) |  |
| **Familial** |  |  | .495 |
| Yes (MEN1) | 1 | 0  |  |
| No (Sporadic) | 72(71.3%) | 29(28.7%) |  |

Supplementary Table 1. Patient characteristics divided by histopathological type.

Abbreviations: SOB: shortness of breath; RUL: right upper lobe; RML: right middle lobe; RLL: right lower lobe; LUL: left upper lobe; LLL: left lower lobe.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Systemic and targeted treatments | OS |  | RS |  |
|  | 5-year | 10-year | 5-year | 10-year |
| **Chemotherapy (n=25)** | 92 (82 – 100) | 58 (41 – 82) | 97 (87 – 108) | 71 (51 – 99) |
| **Targeted agents (mTOR, TKI, n=6)** | 100 (100 – 100) | 42 (15 – 100) | 100 (100 – 100) | 48 (20 – 120) |
| **External radiation (n=7)** | 86 (63 – 100) | 71 (45 – 100) | 88 (67 – 116) | 78 (50 – 121) |
| **SSA (n=21)** | 91 (79 – 100) | 69 (51 – 93) | 95 (83 – 109) | 81 (60 – 110) |
| **Interferon (n=7)** | 100 (100 – 100) | 86 (63 – 100) | 100 (100 – 100) | 88 (60 – 129) |

Supplementary Table 2. Overall and relative survival rates for different methods of treatment for patients undergoing systemic therapy and/or external radiation.

Abbreviations: mTOR: mammalian target of Rapamycin; TKI: tyrosine kinase inhibitors; SSA: somatostatin analogues.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **IHC marker** | **Positive** | **Negative** | **OS EFS** |  |
|  | **N** | **N** | **Adjusted log-rank p-values** | **Adjusted log-rank p-values** |
|

|  |
| --- |
| SSTR1 quantitative |

 | 51 | 27 | 1 | 1 |
|

|  |
| --- |
| SSTR1-S1 |

 | 39 | 38 | 1 | 1 |
|

|  |
| --- |
| SSTR1-S2 |

 | 16 | 61 | 1 | 1 |
|

|  |
| --- |
| SSTR1-S3 |

 | 3 | 74 | 1 | 1 |
|  SSTR2 Gramsch quantitative | 56 | 21 | 1 | 1 |
|  SSTR2 Gramsch S1 | 37 | 40 | 1 | 1 |
|

|  |
| --- |
| SSTR2 Gramsch S2 |

 | 33 | 44 | 1 | 1 |
|

|  |
| --- |
| SSTR2 Gramsch S3 |

 | 25 | 52 | 1 | 1 |
|  SSTR2 UMB1 quantitative | 48 | 21 | 1 | 1 |
|

|  |
| --- |
| SSTR2 UMB S1 |

 | 10 | 59 | 1 | 1 |
|

|  |
| --- |
| SSTR2 UMB1 S2 |

 | 25 | 44 | 1 | 1 |
|

|  |
| --- |
| SSTR2 UMB1 S3 |

 | 23 | 46 | 1 | 1 |
|

|  |
| --- |
| SSTR3 quantitative |

 | 27 | 48 | 1 | 1 |
|

|  |
| --- |
| SSTR3 S1 |

 | 21 | 45 | 1 | 1 |
|

|  |
| --- |
| SSTR4 |

 | 0 | 72 | - | - |
|

|  |
| --- |
| SSTR5 quantitative |

 | 37 | 40 | 1 | 1 |
|

|  |
| --- |
| SSTR5 S1 |

 | 42 | 35 | 1 | 1 |
|

|  |
| --- |
| SSTR5 S2 |

 | 6 | 71 | 1 | 1 |
|

|  |
| --- |
| DR2 quantitative |

 | 11 | 51 | 1 | 1 |
|

|  |
| --- |
| OR51E1 quantitative |

 | 46 | 25 | 1 | 1 |
|

|  |
| --- |
| OR51E1 S1 |

 | 2 | 69 | 1 | 1 |
|

|  |
| --- |
| OR51E1 S2 |

 | 35 | 35 | 1 | 1 |
|

|  |
| --- |
| OR51E1 S3 |

 | 28 | 43 | 1 | 1 |
|

|  |
| --- |
| CTGF |

 | 48 | 14 | 1 | 1 |
|

|  |
| --- |
| HIF |

 | 49 | 14 | 1 | 1 |
|  IGF-1 | 46 | 20 | 1 | 1 |
|  IGF-1R | 47 | 20 | 1 | 1 |

Suplementary Table 3. Log-rank P values from Mantel–Cox test on overall survival and event-free survival analysis in connection to IHC marker positivity with Holm–Bonferroni correction for multiple testing.

Abbreviations: IHC:immunohistochemical; OS: overall survival; EFS: event-free survival; SSTR: somatostatin receptor; DR2: dopamine receptor 2; OR51E1: olfactory receptor; IGF-1: insulin-like growth factor-1; IGF-1R: IGF-1 receptor; CTGF: connective tissue growth factor; and HIF-1: hypoxia factor-1.