**Supplementary Table 1: Serum tumour markers of histological subtype12**

|  |  |  |
| --- | --- | --- |
| Histology | β-HCG | αFP |
| Pure germinoma | -- | -- |
| Germinoma with STGC |  | -- |
| Immature/Malignant teratoma |  |  |
| Mature teratoma | -- | -- |
| Choriocarcinoma |  | -- |
| Yolk sac tumour | -- |  |
| Embryonal carcinoma |  |  |

β-HCG – beta-human chorionic gonadotropin; αFP – alpha-fetoprotein; STGC - syncytiotrophoblastic giant cells

**Supplement Table 2: Univariate analysis**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable |  | Number | 5-year PFS (%) | p value | 5-year OS (%) | p value |
| Age | <15 | 24 | 88 | 0.478 | 91 | 0.774 |
| >15 | 35 | 80 | 88 |
| Sex | Male | 41 | 82 | 0.256 | 81 | 0.981 |
| Female | 18 | 84 | 83 |
| Biopsy | Yes | 25 | 91 | 0.140 | 95 | 0.109 |
| No | 34 | 74 | 77 |
| Location | Pineal | 31 | 75 | 0.043 | 88 | 0.947 |
| Non-pineal | 28 | 90 | 90 |
| Group | PG | 26 | 91 | 0.232 | 100 | 0.113 |
| SG | 15 | 81 | 82 |
| NGGCT | 18 | 59 | 68 |
| Group 2 | **PG+SG** | **41** | **87** | **0.089** | **89** | **0.149** |
| **NGGCT** | **18** | **59** | **68** |
| Chemotherapy | Yes | 53 | 80 | 0.370 | 82 | 0.491 |
| No | 6 | 90 | 100 |
| Sequencing of chemo | Before RT | 39 | 80 | 0.159 | 85 | 0.051 |
| After RT | 14 | 64 | 65 |
| RT type | WVRT | 42 | 82 | 0.938 | 82 | 0.968 |
| CSI | 16 | 86 | 88 |
| RT dose | ≤50.4Gy | 39 | 80 | 0.468 | 84 | 0.701 |
| >50.4Gy | 19 | 72 | 78 |
| RT technique | Conventional | 36 | 81 | 0.887 | 82 | 0.857 |
| Conformal (3DCRT/IMRT) | 22 | 86 | 86 |

PG – Pure germinoma, SG – Secreting germinoma, NGGCT – Non germinomatous germ cell tumour,RT – radiotherapy, WVRT – Whole ventricular radiotherapy, CSI – Craniospinal irradiation, 3DCRT – 3 dimensional conformal radiotherapy, IMRT – intensity modulated radiotherapy, OS – Overall survival, PFS – Progression-free survival

**Supplementary Table 3: Characteristics of patients who progressed/recurred**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient | Age (years)/Sex | Diagnosis (site) | Tumour markers at diagnosis | | Biopsy | Chemo | | RT field | RT dose | | Tumour markers at progression | | | Progression type | Time to progression (months) | Intervention at progression | Status | Overall survival (months) |
| β-HCG (mIU/ml) | αFP (IU/ml) | β-HCG (mIU/ml) | | αFP (IU/ml) |
| 1 | 7/F | SG  (Suprasellar) | 30 | 1 | No | CarboPIE x 4 | WVRT | | | 50.4 | | <0.1 | 0.776 | IC | 41 | 2nd line chemo and RT | D | 95 |
| 2 | 15/F | NGGCT  **(Multifocal)** | 13 (CSF – 127) | 0.637 | No | CarboPIE x 4 | WVRT | | | 50.4 | **199.3** | | 0.7 | EC | 35 | 2nd line chemo + excision of liver metastases | D | 59 |
| 3 | 25/M | NGGCT  (Pineal) | <1 | 574 | No | EP x 6 | WVRT | | | 30.6 (defaulted) | <0.1 | | 232 | Local | 9 | 2nd line chemo | D | 11 |
| 4 | 26/M | PG  (Pineal) | <1 | 1.84 | No | EP x 6 | WVRT | | | 45 | 0.9 | | 2.1 | Local & Sp | 102 | 2nd line chemo f/b RT (CSI) | A | 118 |
| 5 | 20/M | PG  (Pineal) | <0.1 | 1.9 | No | EP x2,  BEP x 2 | WVRT | | | 50.4 | <0.1 | | 1.78 | EC | 23 | 2nd line Chemo | LFU | 40 |
| 6 | 7/M | NGGCT  (Pineal) | 5377 | 1.03 | No | CarboPIE x 4 | CSI | | | 54 | 4631 (CSF 28340) | | 2 (CSF 0.4) | Local | 63 | 2nd line chemo | A | 66 |
| 7 | 19/M | NGGCT  (Pineal) | 21.9 | 124 | No | EP x 4 | CSI | | | 54 | 27.6 | | 264 | Local | 15 | 2nd line chemo | D | 22 |
| 8 | 15/M | SG  (Pineal & sellar - bifocal) | 5.4 (CSF – 17.4) | 1.8 | No | EP x 4 | WVRT | | 50.4 | | 0.732 | | 2.74 | IC & Sp | 19 | 2nd line chemo | D | 20 |
| 9 | 13/M | NGGCT  (Pineal) | <0.1 | 19300 | Yes (yolk sac tumour) | CarboPIE x 4 | CSI | | 54 | | <0.1 | | 6420 | IC & Sp | 9 | Supportive care | D | 10 |
| 10 | 22/M | PG  (Pineal) | 0.1 | 0.873 | Yes | EP x 4 | WVRT | | 45 | | <0.1 | | 1.19 | IC (LM) | 8 | Supportive care | LFU | 10 |

*Diagnosis*: PG – pure germinoma, SG – Secreting germinoma, NGGCT – non-germinomatous germ cell tumours; *Chemo*: CarboPIE – Carboplatin+Etoposide alternating with Ifosfamide+Etoposide, EP – Cisplatin+Etoposide, BEP – Bleomycin+Cisplatin+Etoposide; *RT field*: WVRT – Whole ventricular radiotherapy, CSI – Craniospinal radiotherapy; Progressiontype: IC – intracranial, EC – Extracranial metastases, Local – Local recurrence, Sp - Spinal dissemination, LM – Leptomeningeal metastases; *Status*: A – Alive, D- Dead, LFU – Lost to follow up

**Supplementary Table 4: Characteristics of all patients included in the study**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Patient | Age/  Sex | Diagnosis (site) | Tumour markers at diagnosis (Serum) | | Tumour markers at diagnosis (CSF) | | Biopsy | Chemo | RT field | Disease status | Progression free survival (months) | Intervention at progression | Status | Overall survival (months) |
| β-HCG (mIU/ml) | αFP (IU/ml) | β-HCG (mIU/ml) | αFP (IU/ml) |
| 1 | 18/M | NGGCT  (Pineal) | 527 | 1.15 | 355 | 1 | No | EP x 6 | WVRT | NP | 89 | NA | A | 89 |
| 2 | 18/M | SG  (Pineal) | 63.6 | 0.915 | 50.3 | <0.2 | Yes (germinoma) | BEP x 3, EP x 1 | WVRT | NP | 18 | NA | LFU | 18 |
| 3 | 15/F | PG  (Pineal) | <1 | 1.8 | <1 | 0.364 | Yes (germinoma) | BEP x 3, EP x 1 | WVRT | NP | 48 | NA | A | 48 |
| 4 | 11/F | NGGCT  (Pineal) | 1161 | 840 | NA | NA | No | CarboPIE x 4 | CSI | NP | 160 | NA | A | 160 |
| 5 | 20/M | PG  (Pineal) | 2.73 | 1.87 | 13 | 0.495 | Yes (germinoma) | EP x 4 | WVRT | NP | 16 | NA | LFU | 16 |
| 6 | 16/M | PG  (Pineal) | <1 | 1.12 | 1.18 | <0.2 | Yes (germinoma) | No | WVRT | NP | 5 | NA | LFU | 5 |
| 7 | 13/M | PG  (Pineal) | 4.65 | 1.72 | 4.55 | 0.263 | Yes (germinoma) | CarboPIE x 4 | WVRT | NP | 134 | NA | A | 134 |
| 8 | 22/F | PG  (Pineal) | <1 | 1.22 | 4.88 | 0.247 | Yes (germinoma) | EP x 4 | WVRT | NP | 144 | NA | A | 144 |
| 9 | 7/F | SG  (Suprasellar) | 30 | 1 | NA | NA | No | CarboPIE x 4 | WVRT | P | 41 | 2nd line chemo and RT | D | 95 |
| 10 | 15/F | NGGCT  (Multifocal) | 13 (CSF – 127) | 0.637 | 127 | <0.2 | No | CarboPIE x 4 | CSI | P | 35 | 2nd line chemo + excision of liver metastases | D | 59 |
| 11 | 19/M | PG (thalamus) | 11.3 | 1.42 | NA | NA | Yes (germinoma) | EP x 4 | WVRT | NP | 71 | NA | A | 71 |
| 12 | 7/M | NGGCT (Pineal) | <1 | 96.5 | 2.79 | 0.55 | Yes (Yolk sac tumour and immature teratoma) | CarboPIE x 4 | WVRT | NP | 76 | NA | A | 76 |
| 13 | 15/F | PG  (Suprasellar) | <1 | 1.39 | NA | NA | Yes (germinoma) | EP x 4 | CSI | NP | 125 | NA | A | 125 |
| 14 | 24/M | SG  (Bifocal) | 6.88 | 1.85 | 26 | 0.426 | No | EP x 4 | CSI | NP | 125 | NA | A | 125 |
| 15 | 25/M | NGGCT  (Pineal) | <1 | 574 | 2.71 | 239 | No | EP x 6 | WVRT | P | 9 | 2nd line chemo | D | 10 |
| 16 | 12/M | NGGCT  (Pineal) | 239 | 465 | 436 | 157 | No | CarboPIE x 4 | WVRT | NP | 4 | NA | LFU | 4 |
| 17 | 26/M | PG  (Pineal) | <1 | 1.84 | 5.86 | 0.247 | No | EP x 6 | WVRT | P | 102 | 2nd line chemo f/b RT (CSI) | A | 118 |
| 18 | 11/F | SG  (Suprasellar) | 28.22 | 1.28 | 38.22 | 1.18 | No | CarboPIE x 4 | WVRT | NP | 115 | NA | A | 115 |
| 19 | 11/F | NGGCT  (Suprasellar) | 237.4 | 97.4 | NA | NA | No | CarboPIE x 4 | WVRT | NP | 78 | NA | A | 78 |
| 20 | 18/M | PG  (Pineal) | 1.59 | 1.07 | NA | NA | Yes (germinoma) | EP x 2 | WVRT | NP | 33 | NA | A | 33 |
| 21 | 16/M | SG  (Multifocal) | 8.02 | 2.5 | 35.9 | 0.909 | No | EP x 4 | WVRT | NP | 59 | NA | D | 59 |
| 22 | 11/M | SG  (Multifocal) | 95.81 | 1.02 | <0.1 | 0.801 | Yes (germinoma) | CarboPIE x 4 | WVRT | NP | 99 | NA | A | 99 |
| 23 | 20/M | PG  (Pineal) | <0.1 | 1.9 | 3.27 | 0.7 | No | EP x2,  BEP x 2 | WVRT | P | 23 | 2nd line Chemo | LFU | 40 |
| 24 | 25/M | SG  (Pineal) | 2.92 | 1.49 | 13.59 | <0.2 | No | EP x 3 | WVRT | NP | 88 | NA | A | 88 |
| 25 | 15/M | PG  (Bifocal) | 5.17 | 0.624 | 4.28 | 0.428 | No | CarboPIE x 4 | WVRT | NP | 82 | NA | A | 82 |
| 26 | 20/M | NGGCT  (Bifocal) | 142.59 | 0.66 | 189.58 | <0.2 | No | EP x 4 | CSI | NP | 80 | NA | A | 80 |
| 27 | 23/F | PG  (Suprasellar) | 4.5 | 1 | NA | NA | Yes (germinoma) | EP x 4 | WVRT | NP | 80 | NA | A | 80 |
| 28 | 38/M | PG  (Pineal) | 0.864 | 1.61 | 6.1 | <0.2 | No | EP x 4 | WVRT | NP | 5 | NA | LFU | 5 |
| 29 | 22/M | PG  (Pineal) | 0.1 | 0.873 | 1.33 | <0.2 | Yes (germinoma) | EP x 4 | WVRT | P  IC (LM) | 8 | Supportive care | LFU | 9 |
| 30 | 27/M | NGGCT  (Bifocal) | 34.16 | 0.69 | 343.1 | <0.2 | No | EP x 4 | WVRT | NP | 55 | NA | A | 55 |
| 31 | 12/M | SG  (Basal ganglia) | 77.4 | 1.38 | NA | NA | Yes (germinoma) | CarboPIE x 4 | WVRT | NP | 47 | NA | A | 47 |
| 32 | 26/F | SG  (Pineal) | <0.1 | 1.15 | 0.119 | 6.41 | No | EP x 4 | CSI | NP | 21 | NA | LFU | 21 |
| 33 | 17/F | PG  (Basal ganglia) | 0.17 | 0.615 | 4.41 | 0.794 | Yes (germinoma) | EP x 4 | WVRT | NP | 41 | NA | A | 41 |
| 34 | 7/M | NGGCT  (Pineal) | 5377 | 1.03 | NA | NA | No | CarboPIE x 4 | CSI | P | 63 | 2nd line chemo | A | 66 |
| 35 | 37/M | PG  (Pineal) | 0.597 | 0.688 | 2.67 | <0.2 | No | EP x 4 | WVRT | NP | 48 | NA | A | 48 |
| 36 | 20/M | PG  (Thalamus) | <0.1 | 1.6 | 9.41 | <0.2 | Yes (germinoma) | EP x 4 | CSI | NP | 52 | NA | A | 52 |
| 37 | 6/F | SG  (Suprasellar) | 22.2 | 16.8 | 27.02 | 2.1 | No | CarboPIE x 4 | No RT | NP | 3 | NA | D | 3 |
| 38 | 11/M | PG  (Pineal) | <0.1 | 1.16 | 0.759 | <0.2 | Yes (germinoma) | No | CSI | NP | 57 | NA | A | 57 |
| 39 | 26/F | PG  (Thalamus) | 0.6 | 1.02 | 2.59 | <2 | Yes (germinoma) | No | WVRT | NP | 48 | NA | A | 48 |
| 40 | 12/F | PG  (Suprasellar) | 6.7 | 1.26 | 0.785 | <0.2 | No | No | WVRT | NP | 46 | NA | A | 46 |
| 41 | 9/F | NGGCT  (Suprasellar) | 9.1 | 10400 | 1.6 | 2960 | No | CarboPIE x 4 | CSI | NP | 54 | NA | A | 54 |
| 42 | 6/M | NGGCT  (Suprasellar) | 219 | 11.7 | NA | NA | Yes  (germinoma) | CarboPIE x 4 | WVRT | NP | 4 | NA | LFU | 4 |
| 43 | 14/M | NGGCT  (Suprasellar) | 172.4 | 7580 | 6.7 | 275 | Yes  (Yolk sac tumour) | CarboPIE x 2 | CSI | NP | 43 | NA | A | 43 |
| 44 | 9/F | NGGCT  (Suprasellar) | 184.2 | 816 | 574.4 | 278 | No | CarboPIE x 4 | WVRT | NP | 34 | NA | A | 34 |
| 45 | 17/M | PG  (Thalamus) | 3.3 | 1 | 22.7 | <0.2 | Yes (germinoma) | EP x 4 | WVRT | NP | 48 | NA | A | 48 |
| 46 | 18/M | SG  (Pineal) | 26 | 0.78 | 0.1 | <2 | No | EP x 4 | WVRT | NP | 47 | NA | A | 47 |
| 47 | 11/F | PG  (Suprasellar) | 15.9 | 0.8 | 1 | 0.1 | No | CarboPIE x 4 | CSI | NP | 33 | NA | A | 33 |
| 48 | 11/M | PG  (Pineal) | 2 | 0.95 | 4.3 | <0.2 | Yes (germinoma) | No | WVRT | NP | 46 | NA | A | 46 |
| 49 | 19/M | NGGCT  (Pineal) | 21.9 | 124 | 9 | 10.8 | No | EP x 4 | CSI | P | 15 | 2nd line chemo | D | 22 |
| 50 | 16/M | NGGCT  (Suprasellar) | 673 | 189 | NA | NA | No | No | CSI | NP | 3 | NA | LFU | 3 |
| 51 | 16/M | PG  (Pineal) | 2.9 | 1.4 | 6.6 | <0.2 | Yes (germinoma) | EP x 4 | WVRT | NP | 37 | NA | A | 37 |
| 52 | 13/M | SG  (Pineal) | 37.9 | 1.7 | 12.37 | 1.14 | No | CarboPIE x 4 | CSI | NP | 32 | NA | A | 32 |
| 53 | 7/M | SG  (Pineal) | 25.2 | 2.1 | 16.6 | 8.5 | No | CarboPIE x 4 | WVRT | NP | 32 | NA | A | 32 |
| 54 | 3/M | NGGCT  (Pineal) | <0.1 | 2.4 | 5.1 | <0.2 | Yes (Malignant teratoma) | CarboPIE x 4 | CSI | NP | 11 | NA | LFU | 11 |
| 55 | 15/M | SG  (Bifocal) | 5.4 | 1.8 | 17.2 | <0.2 | No | EP x 4 | WVRT | P | 19 | 2nd line chemo | D | 20 |
| 56 | 13/F | PG  (Pineal) | 1.4 | 0.5 | 2.79 | <0.2 | No | CarboPIE x 4 | WVRT | NP | 29 | NA | A | 29 |
| 57 | 17/M | PG  (Pineal) | 0.1 | 1.1 | 7.2 | <0.2 | No | EP x 4 | WVRT | NP | 28 | NA | A | 28 |
| 58 | 17/M | SG  (internal capsule) | 23 | 0.6 | 33.7 | <0.2 | No | EP x 4 | WVRT | NP | 26 | NA | A | 26 |
| 59 | 13/M | NGGCT  (Pineal) | <0.1 | 19300 | <0.1 | 2650 | Yes (Yolk sac tumour) | CarboPIE x 4 | CSI | IC & Sp | 9 | Supportive care | D | 10 |

PG – pure germinoma, SG – Secreting germinoma, NGGCT – non-germinomatous germ cell tumours; *Chemo*: CarboPIE – Carboplatin+Etoposide alternating with Ifosfamide+Etoposide, EP – Cisplatin+Etoposide, BEP – Bleomycin+Cisplatin+Etoposide; RT – Radiotherapy, WVRT – Whole ventricular radiotherapy, CSI – Craniospinal radiotherapy; P – Progressed, NP – Not progressed/remission; *Status*: A – Alive, D- Dead, LFU – Lost to follow up