**Supplementary Table S1.** Characteristics by risk group for SJYC07 participants (*n*=52)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Risk Group** | | *P* |
| **Intermediate**  **(*n*= 34)** | **High**  **(*n*=18)** |
| ***n* (%)** | ***n* (%)** |
| **Sex**  Female  Male | 14 (41)  20 (59) | 10 (56)  8 (44) | 0.39 |
| **Age at Diagnosis (years)**  Median  Range | 1.2  0–2.8 | 1.1  0–3.0 | 0.67 |
| **Metastatic status**  M+  M0  MXa | 0  23 (68)  11 (32) | 16 (89)  0  2 (11) | <0.001  (M+ vs. M0) |
| **Primary tumor site**  Infratentorial  Supratentorial (includes pineal region tumors) | 20 (59)  14 (41) | 7 (39)  11(61) | 0.24 |
| **Molecular group (n=48)**  MYC  SHH  TYR  Not available | 3 (9)  13 (38)  16 (47)  2 (6) | 3 (17)  12 (67)  1 (6)  2 (11) | 0.008  (MYC vs SHH vs TYR) |
| **Germline *SMARCB1/SMARCA4* alterations**  Positive  Negative  Not available | 7 (21)  17 (50)  10 (29) | 7(39)  5(28)  6(33) | 0.148  (+ vs. –) |

a Cerebrospinal fluid not obtained at diagnosis, but no evidence of metastases in imaging.

Abbreviations: M0, non-metastatic disease; M+, metastatic disease; MX, no imaging evidence of metastases.

**Supplementary Table S2.** Clinical features and associated outcomes for SJYC07 participants (n=52)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variable** | **n** | **5-year**  **OS ± SE (%)** | ***P*** | **5-year**  **PFS ± SE (%)** | ***P*** |
| **Metastases & age at presentation**  M0 (n=23)   * < 1 year * ≥ 1 year   M+ (n=16)   * < 1 year * ≥ 1 year   MX ( n=13)   * < 1 year * ≥ 1 year | 8  15  7  9  9  4 | 50 ± 20.4  52.5 ± 13.7  0  0  22.2 ± 11.3  25 ± 15.3 | p=0.77  p=0.73  p=0.58 | 25.0 ± 15.3  46.7 ± 13.9  0  0  22.2±13.9  0 | p=0.33  p=0.29  p=0.89 |
| **Gender**  Female  Male | 24  28 | 25.0 ± 9.7  32.1 ± 9.4 | 0.86 | 14.3 ± 7.6  25.0 ± 8.8 | 0.63 |
| **Site**  Supratentorial  Infratentorial | 25  27 | 19.2 ± 8.6  37.0 ± 9.8 | 0.063 | 12.0 ± 8.0  28.8 ± 9.2 | 0.122 |
| **Site [M0 participants only]**  Supratentorial  Infratentorial | 10  13 | 37.5 ± 17.1  61.5 ± 14.4 | 0.20 | 30.0 ± 17.7  46.2 ± 13.8 | 0.52 |
| **Extent of best resection**  **[Intermediate-risk participants only]**  GTR  <GTR | 27  7 | 44.1 ± 10.4  42.9 ± 18.7 | 0.73 | 31.9 ± 10.0  28.6 ± 17.1 | 0.30 |

Abbreviations: OS, overall survival; PFS, progression-free survival; SE, standard error; M0, non-

metastatic disease; GTR: gross total resection.

**Supplementary Table S3.** Clinical features and associated outcomes for SJMB03 participants (n=22)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Variable** | ***n*** | **5-year**  **OS ± SE (%)** | ***P*** | **5-year**  **PFS ± SE (%)** | ***P*** |
| **Gender**  Male  Female | 13  9 | 53.8 ± 12.9  44.4 ± 14.8 | 0.57 | 53.8 ± 12.9  33.3 ± 13.6 | 0.43 |
| **Risk Group**  Average  High | 11  11 | 81.8 ± 11.0  18.2 ± 9.5 | 0.002 | 72.7 ± 12.7  18.2 ± 9.5 | 0.004 |
| **Metastatic status**  M0  M+ | 14  8 | 64.3 ± 12.1  25.0 ± 12.5 | 0.085 | 57.1 ± 12.5  25.0 ± 12.5 | 0.105 |
| **Site Group**  Supratentorial  Infratentorial  Spine | 13  7  2 | 46.2 ± 12.8  71.4 ± 15.6  0.0 ± 0.0 | 0.32  (supra vs. infra) | 46.2 ± 12.8  57.1± 16.7  0.0 ± 0.0 | 0.35  (supra vs. infra) |
| **Molecular subgroup**  MYC  SHH  TYR | 7  5  4 | 42.9 ± 16.2  20.0 ± 12.6  50.0 ± 20.4 | 0.47 | 42.9 ± 16.2  20.0 ± 12.6  50.0 ± 20.4 | 0.47 |

Abbreviations: OS, overall survival; PFS, progression-free survival; SE, standard error; M0, non-metastatic disease; M+, metastatic disease.

**Supplementary Table S4.** Germline *SMARCB1* and *SMARCA4* alterations for the 16 participants with positive results

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Patient** | **Gene** | **Germline Variant** | **Protein Alteration** | **Variant Classification** |
| 1 | *SMARCB1* | c.141C>A | p. Y47\* | LP |
| 2 | *SMARCB1* | c.959delG | p. R320fs | P |
| 3 | *SMARCB1* | c.500+1G>A | p. W158\* resulting in abnormal splicing | LP |
| 4 | *SMARCB1* | c.233-5\_233-3delTACinsAGATCTGT | Intronic variant expected to result in abnormal splicing | LP |
| 5 | *SMARCB1* | c.157C>T | p. R53\* | LP |
| 6 | *SMARCB1* | c.94-2A>G | Splice acceptor site mutation resulting in deletion of exon 2 | LP |
| 7 | *SMARCB1* | c.157C>T | p.R53\* | LP |
| c.1143delG | p.T381fs | VUS |
| 8 | *SMARCB1* | c.157C>T | p. R53\* | LP |
| 9 | *SMARCB1* | c.(34\_232+25)\_(795+10\_803) | Deletion of exons 2b-6 of *SMARCB1* | LP |
| 10 | *SMARCB1* | c.986G>C | p. S329T resulting in abnormal splicing (skipping of exon 7) | LP |
| 11 | *SMARCB1* | arr 22q11.2q11.23 (21,465,661-24,781,563)x1 | Microdeletion including the whole *SMARCB1* gene | P |
| 12 | *SMARCB1* | c.601C>T | p.R201\* | P |
| 13 | *SMARCB1* | c.344\_345delAG | p.E115fs | LP |
| 14 | *SMARCA4* | c.2920delC | p.P974fs | P |
| 15 | *SMARCB1* | c.986G>C | p.S329T resulting in abnormal splicing (skipping of exon 7) | LP |
| *SMARCA4* | c.964G>A | p.A322T | VUS |
| 16 | *SMARCB1* | c.152G>A (possibly mosaic) | p.W51\* | P |

Abbreviations: LP, likely pathogenic; P, pathogenic; VUS, variant of unknown significance.

It is unknown if the 2 *SMARCB1* variants in patient 7 are in *cis* or *trans*. Patient 15 had one likely pathogenic variant in the *SMARCB1* gene and one variant of uncertain significance in the *SMARCA4* gene. Variant classification was assigned based on the 2015 American College of Medical Genetics and Genomics and the Association for Molecular Pathology consensus recommendations. The variant in

patient 4 was classified as likely pathogenic, given the expected effect on abnormal splicing. The variant in patient 6 was classified as likely pathogenic, as the deletion of exon 2 is predicted to result in a frameshift.

**Supplementary Table S5:** Disease progression following completion of maintenance phase of chemotherapy for participants in the intermediate risk arm of SJYC07

|  |  |  |
| --- | --- | --- |
| **Participant** | **Molecular group** | **Time from completion of maintenance chemotherapy to PD (in months)** |
| 1 | TYR | 13.0 |
| 2 | TYR | 67.2 |
| 3 | TYR | 9.1 |
| 4 | TYR | 0.0 |
| 5 | SHH | 12.7 |

Abbreviations: PD, progressive disease

**Supplementary Table S6.** Grade 3 and 4 CTCAE toxicities for SJYC07 and SJMB03 participants

|  |  |  |
| --- | --- | --- |
| **Toxicity** | **SJYC07 (*n*=52)** | **SJMB03 (*n*=22)** |
| ***n* (%)** | ***n* (%)** |
| Febrile neutropenia | 25 (48.1) | 9 (40.9) |
| Vomiting | 15(28.8) | 5 (22.7) |
| Infection with normal ANC or Grade 1 or 2 neutrophils | 11(21.2) | 1 (4.5) |
| Mucositis/stomatitis | 6 (11.5) | 1 (4.5) |
| Hypoxia | 6 (11.5) | 0 |
| Diarrhea | 4 (7.7) | 2 (9.1) |
| Colitis, infectious (e.g., *Clostridium difficile*) | 3 (5.8) | 2 (9.1) |
| Dehydration | 3 (5.8) | 2 (9.1) |
| ALT elevation | 3 (5.8) | 1(4.5) |
| Weight loss | 3 (5.8) | 0 |
| AST elevation | 1 (1.9) | 1 (4.5) |
| Hearing loss | 1 (1.9) | 2 (9.1) |
| Cystitis | 0 | 2 (9.1) |

Abbreviations: ANC, absolute neutrophil count; ALT, alanine aminotransferase; AST: aspartate aminotransferase.