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

|  |  |  |
| --- | --- | --- |
|   | **Risk Group** | *P* |
| **Intermediate****(*n*= 34)** | **High****(*n*=18)** |
| ***n* (%)** | ***n* (%)** |
| **Sex**FemaleMale | 14 (41)20 (59) | 10 (56) 8 (44) | 0.39 |
| **Age at Diagnosis (years)**MedianRange | 1.20–2.8 | 1.10–3.0 | 0.67 |
| **Metastatic status**M+M0MXa  | 023 (68)11 (32) | 16 (89)0 2 (11) | <0.001(M+ vs. M0) |
| **Primary tumor site** InfratentorialSupratentorial (includes pineal region tumors) | 20 (59)14 (41) |  7 (39)11(61) | 0.24 |
| **Molecular group (n=48)**MYCSHHTYRNot 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**PositiveNegativeNot 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
 | 8157994 | 50 ± 20.452.5 ± 13.70022.2 ± 11.325 ± 15.3 | p=0.77p=0.73p=0.58 | 25.0 ± 15.346.7 ± 13.90022.2±13.90 | p=0.33p=0.29p=0.89 |
| **Gender**FemaleMale | 2428 | 25.0 ± 9.732.1 ± 9.4 | 0.86 | 14.3 ± 7.625.0 ± 8.8 | 0.63 |
| **Site** SupratentorialInfratentorial |  2527 |  19.2 ± 8.637.0 ± 9.8 |  0.063  |  12.0 ± 8.028.8 ± 9.2 |  0.122 |
| **Site [M0 participants only]**SupratentorialInfratentorial |  1013 |  37.5 ± 17.161.5 ± 14.4 |  0.20  |  30.0 ± 17.746.2 ± 13.8 |  0.52 |
| **Extent of best resection****[Intermediate-risk participants only]**GTR<GTR |   277 |   44.1 ± 10.442.9 ± 18.7 |   0.73  |   31.9 ± 10.028.6 ± 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**MaleFemale | 139 | 53.8 ± 12.944.4 ± 14.8 | 0.57 | 53.8 ± 12.933.3 ± 13.6 | 0.43 |
| **Risk Group**AverageHigh | 1111 | 81.8 ± 11.018.2 ± 9.5 | 0.002 | 72.7 ± 12.718.2 ± 9.5 | 0.004 |
| **Metastatic status**M0M+ | 148 | 64.3 ± 12.125.0 ± 12.5 | 0.085 | 57.1 ± 12.525.0 ± 12.5 | 0.105 |
| **Site Group**SupratentorialInfratentorialSpine | 1372 | 46.2 ± 12.871.4 ± 15.60.0 ± 0.0 | 0.32(supra vs. infra) | 46.2 ± 12.857.1± 16.70.0 ± 0.0 | 0.35(supra vs. infra) |
| **Molecular subgroup**MYCSHHTYR | 754 | 42.9 ± 16.220.0 ± 12.650.0 ± 20.4 | 0.47 | 42.9 ± 16.220.0 ± 12.650.0 ± 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.