## **Supplementary Material**

## **Figure e1.** SRS treatment plans with isodose lines (cGy) of: (A) a local recurrence of a left frontal ependymoma 20 months after GTR and EBRT that was subtotally resected and treated with SRS (24 Gy in 3 fractions prescribed to the 71% isodose line to resection cavity, with a boost to 27 Gy in 3 fractions to gross disease); patient was stable without local or distant recurrence at last follow-up 13 months after SRS; (B) a T3-4 spinal ependymoma distant recurrence 12 years after STR of initial lesion and resection and irradiation to multiple distant spinal and intracranial recurrences, treated with SRS (24 Gy in 3 fractions prescribed to the 69% isodose line to two adjacent nodules); patient was stable without local or distant recurrence at last follow-up 5 years after SRS. Abbreviations: stereotactic radiosurgery (SRS), gross total resection (GTR), external beam radiation therapy (EBRT).

**Figure e2.** Cumulative incidence of local failure for intracranial and spinal ependymoma lesions treated with SRS. Abbreviation: confidence interval (CI).

**Figure e3.** Cumulative incidence of distant failure after SRS treatment courses for intracranial and spinal ependymoma (A); for local and distant recurrences after initial treatment (B). Abbreviation: confidence interval (CI).

## **Table e1**. Patient characteristics. Abbreviations: stereotactic radiosurgery (SRS).

|  |  |
| --- | --- |
| **Characteristics** | **Number/Median (range)** |
| Age group |  |
| Pediatric (< 19 years) | 11 |
| Adult (≥ 19 years) | 10 |
| Sex |  |
| Female | 12 |
| Male | 9 |
| Race/ethnicity |  |
| White | 12 |
| Hispanic/Latino | 6 |
| Asian/Pacific Islander | 3 |
| African American | 0 |
| Initial tumor location |  |
| Intracranial | 15 (supratentorial, n=3; infratentorial, n=12) |
| Spinal | 6 (cervical, n=1; thoracic, n=3; lumbosacral, n=2) |
| *RELA* fusion (among 3 patients with supratentorial ependymoma) |  |
| Positive | 2 |
| Not tested | 1 |
| Total number of lesions treated with SRS  |  |
| Intracranial | 1 (1-4) |
| Spinal | 1 (1-8) |
| Extent of disease at first SRS (Number of patients) |  |
| With intracranial lesion(s) only | 14 |
| With spinal lesion(s) only | 5 |
| With both intracranial and spinal lesions | 2 |
| Chemotherapy prior to SRS |  |
| Yes | 5 |
| No | 16 |

## **Table e2.** Lesion and treatment characteristics. Abbreviations: external beam radiotherapy (EBRT), craniospinal irradiation (CSI), World Health Organization (WHO), gross total resection (GTR), subtotal resection (STR), stereotactic radiosurgery (SRS), not applicable (n/a).

|  |  |  |
| --- | --- | --- |
|  | Intracranial lesions (n=30) | Spinal lesions (n=10) |
|  | Number/Median (range) | Number/Median (range) |
| Location |  |  |
| Supratentorial | 11 | n/a |
| Infratentorial | 19 | n/a |
| Cervical | n/a | 1 |
| Thoracic | n/a | 5 |
| Lumbosacral | n/a | 4 |
| Recurrence location |  |  |
| At initial lesion location | 14 | 3 |
| At new location | 16 | 7 |
| WHO grade  |  |  |
| I | 0 | 2 |
| II | 19 | 8 |
| III | \*11 | 0 |
| Repeat resection prior to SRS  |  |  |
| No resection | 21 | 10 |
| GTR | 4 | 0 |
| STR | 5 | 0 |
| Radiation to area prior to first SRS |  |  |
| No prior radiation | 16 | 8 |
| Prior EBRT | 11 | 2 |
| Prior CSI | 3 | 0 |
| Interval between most recent radiation to area and first SRS treatment (months) | 21 (1-88) | 0 (boost)  |
| Radiation Dose to area prior to SRS (Gy) | 54 (45 - 59.4) | 45 |
| First SRS treatment |  |  |
| Planning target volume (cm3) | 0.95 (0.03-17.50) | 0.74 (0.17-1.45) |
| Dose (Gy)/Fractions | 20 (12-27.5) in 1 (1-5) fractions | 19 (6-24) in 2 (1-3) fractions |
| †Single fraction equivalent dose (SFED) | 18 (12-24) | 18.1 (4.2-20.4) |
| Additional SRS treatments after first SRS treatment | 1 (n=4), 3 (n=1) | 0 |
| ‡Total cumulative equivalent doses in 2-Gy fractions (EQD2) | 68 (22-252.4) | 36 (12.5-95.1) |

\*2 patients with 5 lesions total had Grade II primary lesion and Grade III recurrent lesion

†SFED = D − (n − 1) ⋅1.8 Gy, where n is number of fractions, D is prescribed dose

‡EQD2 = D × [(d + α/β) / (2 Gy + α/β)], where D is the total dose, d is dose per fraction, and the α/β ratio is assumed to be 10. All intracranial and spinal EBRT had 1.8 Gy per fraction. Total cumulative dose includes EBRT and all SRS treatments to each lesion.

**Table e3.**

Dosing regimens of 47 SRS treatments for 40 ependymoma lesions by location.

|  |  |  |  |
| --- | --- | --- | --- |
| Location of lesion | Dose (Gy) | Fraction | Number of treatments with this regimen |
| *Spine* |  |  |  |
|  | 24 | 3 | 3 |
|  | 22 | 2 | 2 |
|  | 20 | 1 | 1 |
|  | 18 | 1 | 1 |
|  | 16 | 1 | 3 |
|  | 10 | 2 | 1 |
|  | 6 | 2 | 1 |
| *Infratentorial* |  |  |  |
|  | 27.5 | 5 | 1 |
|  | 25.5 | 3 | 1 |
|  | 25 | 5 | 1 |
|  | 24 | 3 | 2 |
|  | 20 | 1 | 5 |
|  | 18 | 1 | 5 |
|  | 16 | 1 | 1 |
|  | 14 | 1 | 2 |
|  | 12 | 1 | 2 |
| *Supratentorial* |  |  |  |
|  | 30 | 5 | 1 |
|  | 27 | 3 | 1 |
|  | 25 | 5 | 1 |
|  | 25 | 3 | 1 |
|  | 24 | 3 | 1 |
|  | 24 | 1 | 2 |
|  | 22 | 1 | 2 |
|  | 20 | 1 | 1 |
|  | 18 | 1 | 3 |
|  | 16 | 1 | 2 |

## **Table e4**. Published series of SRS treatment for intracranial and spinal ependymoma. Abbreviations: adverse radiation effect (ARE), stereotactic radiosurgery (SRS).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Number of Patients/Lesions** | **SRS dose (Gy; median, range)** | **SRS fraction (median, range)** | **Lesion volume (cm3; median, range)** | **Median follow-up (months)** | **Overall survival** | **ARE (number, percentage)** | **Progression-free survival (median or percentage)** | **Local failure** | **Distant failure** |
| Loeffler et al., 1990[39] | 2 (intracranial) | Unknown | Unknown | Unknown | 9 | Both patient alive at follow-up | unknown | 100% | 0% | 0% |
| Hirato et al., 1995 | 3 (intracranial)/4 |  | 1 | Unknown | Unknown | Unknown | Unknown | 75% | 25% | 0% |
| Grabb et al., 1996[40] | 7 (intracranial)/7 | Unknown | Unknown | Unknown | 6 | 14.3% | unknown | 14.3% (5-year) | 42.9% | 57.1% |
| Weprin et al., 1996[41] | 3 (intracranial)/3 | 20 (12.5-22) | Unknown | 7.54 (2.03-22.20) | 17 | 33.% | 1 (33.3%) | 33.3% | 33.3% | 0% |
| Aggarwal et al., 1997[42] | 5 (intracranial)/5 | 10 (9-15) | Unknown | Unknown | 24 | 80% (last follow-up) | 1 (20%) | 80% at last follow-up | 20% | 0% |
| Jawahar et al., 1999[43] | 22 (intracranial)/22 | 16.1 (10-20) | 1 | 13.7 (0.84-36.8) | 21 | Median 26.4 months | 1 (4.5%) | 32.4% (3-year) | 37.7% (3-year) | 36.3% (3-year) |
| Stafford et al., 2000[44] | 12 (intracranial)/17 | 18 (12-24) | unknown | 3.2 (0.3-15.5) | 22.5 | Median 40 months | 2 (17%) | Median 18 months | 32% (3-year) | 16.7% |
| Hodgson et al., 2001[45] | 28 (intracranial)/unknown | 12.5 (6-25) | Unknown | 4.5 (0.08-29.3) | 24 | Unknown | unknown | Median 8.5 months; 22% (3-year) | 71% (3-year) | unknown |
| Endo et al., 2004[46] | 2 (intracranial - nodular disseminationof anaplastic ependymoma)/11 | 22 (16-25) | Unknown | Unknown | 85.5 | Both patients alive at follow-up | 0 (0%) | Tumor control over 21 months | N/A | N/A |
| Lo et al., 2006[47] | 8 (intracranial)/13 | 14 (12-20) | 1 | 1 (0.151-10.7) | 30.2 | 75% | 2 (25%) | 62.5%, 50%, 50% (1-year, 2-year, 3-year) | 26.8%, 39% (1-year, 3-year) | 13.5%, 27.1% (1-year, 3-year) |
| Mansur et al., 2004[48] | 9 (intracranial)/9 | 16 (14-20) | unknown | 5.4 (0.9-11.1) | 28 | 71.1% (3-year) | 2 (22%) | 55.6% at 3-year | Unknown | unknown |
| Combs et al., 2006[49] | 19 (intracranial)/19 | 36 (20-60) | 5 | 17.8 (4.5-28.1)  | 32 | 77% and 64% (5-year, 10-year) | 0 | 60% (5-year) | 26.3% | 31.6% |
| Merchant et al., 2008[26] | 6 (intracranial)/6 | 18 (15-20) | Unknown | unknown | 18.5 | 20% (5-year) | 1 (16.7%) | Median 18.5 months | 66.7% (last follow-up) | 33.3%  |
| Liu et al., 2009[50] | 6 (intracranial)/6 | 24 (24-30) | Unknown | Unknown | 28 | 100% | 3 (50%) | 100% | 0% | 0%x |
| Kano et al., 2010[51] | 21 (intracranial)/32 | 15 (9-22) | unknown | 2.2 (0.1-21.4) | 27.6 | 85.2%, 53.2%, 23.0% (1-year, 2-year, 3-year) | 2 (10%) | 78.4%, 55.5%, 41.6% (1-year, 2-year, 3-year) | 28% (follow-up) | 33.6%, 41.0%, 80.3% (1-year, 2-year, 3-year) |
| Stauder et al., 2012[52] | 26 (intracranial)/49 | 18 (12 - 24) | unknown | 2.2 (0.3-66.6) | 36.1 | 96%, 69 % (1-year, 3-year) | 2 (8%) | 80%, 66% (1-year, 3-year) | 15%, 28% (1-year 3-year) | 27% |
| Hoffman et al., 2014[53] | 12 (intracranial)/12 | 24 (24-30) | 3 | 1.4 (0.4-19.3) | 25 | 71% (2-year) | 6 (50%) | Median 40 months | 11% (3-year) | 86.7% |
| Murai et al., 2016[54] | 8 (intracranial)/38 (20 unfractionated; 18 fractionated) | 15.3 (23-10.4); 23 (18-35) (unfractionated; fractionated)  | 1; 4 (2-5) (unfractionated; fractionated) | 0.9 (0.1-44.7) | 23 | 100%, 38% (1-year, 3-year) | 3 (37.5%) | Median 8 months; 26%, 21% (1-year, 3-year) | 24% (3-year) | unknown |
| Lobón et al., 2016[33] | 8 (intracranial)/8 | 35 (14-44) | 8 (1-10) | Unknown | 32.5 | 75%, 50% (1-year, 3-year) | 2 (25%) | Median 30.6 months | 25% | 37.5% |
| Kano et al., 2018[35] | 89 (intracranial)/113 | 15 (9-24) | 1 | 2.2 cc (0.03-36.8) | 18 | 86%, 50%, 44% (1-year, 3-year, 5-year) | 9 (10%) | 71%, 56%, 48% (1-year, 3-year, 5-year) | 37%% (last follow-up) | 61%, 74%, 85% (1-year, 3-year, 5-year) |
| Ryu et al., 2003[18] | 2 (spinal) | 18 (18-18) | unknown | Unknown | 6.5 | 100% | 0 | 100% | 0% | 0% |
| Benzil et al., 2004[55] | 1 (spinal) | Unknown | Unknown |  Unknown | 12 | Patient died at 12 months | 1 (100%) | 6 months | 6 months | 6 months |
| Elibe et al., 2018[56] | 2 (spinal) | 16 (10-24) | 1 | Results reported together with other non-ependymoma spinal lesions |
| Current series | 15 (intracranial)/30;6 (spinal)/10 | Intracranial: 20 (12-27.5);Spinal: 19 (6-24) | Intracranial: 1 (1-5);Spinal: 2 (1-3) | Intracranial: 0.95 (0.03-17.5);Spinal: 0.74 (0.17-1.45) | 45.5 | Median 117 months; 89.4% (1-year) | 3 (14.3%) | Median 54 months; 90.0%, 67.3% (1-year, 5-year) | 18.5% (2-year) | 33.8% (2-year) |