Purpose or Objective: The aim of this study was to investigate the patterns of failure after radiotherapy for pediatric intracranial ependymoma and their correlation to dose parameters.

Material and Methods: Between 2000 and 2013, 206 patients with intracranial ependymoma were treated in the 13 french reference pediatric radiotherapy centers . The magnetic resonance imaging obtained at recurrence were registered with the original planning CT for topographic analysis of the patterns failure. Clinical target volume (CTV) and planning target volume (PTV) margins were extracted ; several dosimetric quality indices were derived from Dose Volume Histogram (DVH) to compare relapse with no-relapse patient.

Results: With a median follow-up of 44.81 months (95% CI [36.80; 56.51]), 85 (41.3%) patients presented with recurrence. The topographic analysis of patterns of failure showed 50 (58.8%) patients with local recurrence in the radiation field (LF), 6 (4.1%) in the edge of field (EFG), 6 (7.1%) were loco-regional outside the field (LRF), 8 (9.4%) in spine (SF), 5 supratentorial (SUF) and 10 (11.8%) local and distant (LDF). The median prescription dose was respectively: 55.8 Gy [50.4; 60] in LF, 54 Gy [48.6; 59.4] in EF, 56.7 Gy [50.4; 60] in LRF, 54 Gy [50.4; 59.4] in LDF, 59.4 Gy [48.6-59.4] in SUF and 56.7Gy [54; 60] in SF. The median PTV margins was 0.5 mm [0.3; 1]. The median Coverage index and The Target Coverage index of the PTV were both lower in the relapse group as they were respectively 0.97 and 94.8% in the relapse group compared with 0.98 and 95.99% in the no-relapse group. The median Homogeneity index was 0.097 in the relapse group versus 0.091 in the no-relapse group. The median volume of relapse was 1.29 cc [0.11; 27] in the LF group, with a median dose of 58.81 Gy [50.86; 61.38].

Conclusion: In patients with intracranial ependymoma, local failure in the tumor bed was the major pattern of failure. The preliminary results showed that all dosimetric indices on the PTV were worse in the relapse group. Improving the coverage of target volume may be an effective way to reduce the local failures. Thus a complementary correlation of relapse patterns with dose parameters to PTV and organs at risks and the irradiation techniques is under statistical analysis and final results will be presented at the meeting.

OC-0346

Pediatric diffuse intrinsic pontine glioma re-irradiation: better survival and better time

L. Gandola[1], E. Pecori[1], V. Biassoni[2], B. Diletto[1], E. Schiavello[2], S. Meroni[3], F. Spreafico[2], E. Pignoli[3], M. Massimino[2]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Radiation Oncology- Pediatric Radiotherapy Unit, Milan, Italy

[2]Fondazione IRCCS Istituto Nazionale dei Tumori, Pediatric Oncology, Milan, Italy

[3]Fondazione IRCCS Istituto Nazionale dei Tumori, Medical Physics, Milan, Italy

Purpose or Objective: Since 2009 we launched a strategy for children with centrally reviewed MRI diagnosis of diffuse intrinsic pontine glioma (DIPG) implying the intravenous administration of vinorelbine with nimotuzumab –an anti-EGFR monoclonal antibody- weekly, for a total of 12 weeks, during radiotherapy delivery of 54 Gy, 1.8 Gy/fraction daily. After radiotherapy completion, vinorelbine and nimotuzumab were administered any other week until tumor progression or for a total of two years. In the attempt to improve survival and quality of life of our children, a protocol amendment in July 2011 introduced re-irradiation at relapse/progression.

Material and Methods: Local re-irradiation consisted of 19.8 Gy, fractionated over 11 days. A 3DCRT with 5-6 coplanar beams was adopted with a beam geometry possibly not overlapping that of the first line irradiation; the most demanding planning issue of re-irradiation was to meet optic chiasm dose constraints. Three additional children were re-irradiated to distant sites of relapse, spine (2) or ventricular system at doses of 36 Gy or 54 Gy respectively.

Results: Of the 39 patients treated from 8/2009, 28 had local (23) or disseminated (5) progression and 18 were given local (15) or distant (3) relapse re-irradiation at a median of 8 months after first radiotherapy (2.5-19 months). Reasons for not re-irradiating the other 10 children were: progression before July 2011 (4), parents refusal (4), too poor Lansky status (2); median PFS and progression site were not different in the two subgroups. Survival after re-irradiation lasted between two weeks and 14 months, median 6 months, and determined a statistically difference in median OS between the two groups of re-irradiated or not children, being 16 and 12 months, respectively (P=0.004). In 16 radiologically evaluated patients, re-irradiation induced: reduction of tumor volume in 8, stable volume in 3 while 5 had progression; 13 had symptom amelioration and 12 steroid suspension. Volume reductions were obtained in 7/8 children that have shown the same response after first line irradiation while one was obtained after stable disease in first line treatment. No adverse event was reported and all children were re-irradiated as outpatients .

Conclusion: Re-irradiation after relapse/progression represented a significant benefit for both OS and quality of life of children with DIPG with symptom amelioration in 13/18. This option is worth to be offered also in case of disseminated progression.

Partially supported by Associazione Italiana per la Ricerca sul Cancro (AIRC)

OC-0347

Outcome and prognosticators in adult patients with medulloblastoma: a Rare Cancer Network study

B. Atalar[1], M. Ozsahin[2], J. Call[3], A. Napieralska[4], S. Kamer[5], V. Salvador[6], P. Erpolat[7], L. Negretti[2], Y.L. Ramstad[8], C. Onal[9], S. Akyurek[10], G. Ugurluer[1], B. Baumert[11,12], S. Servagi-Vernat[13], R.C. Miller[14], E. Ozyar[1], T. Sio[15]

[11]Acıbadem University, Department of Radiation Oncology, Istanbul, Turkey

[2]Centre Hospitalier Universitaire Vaudois, Department of Radiation Oncology, Lausanne, Switzerland

[3]Mayo Clinic, Department of Radiation Oncology, Rochester, USA

[4]Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Department of Radiotherapy, Gliwice, Poland

[5]Ege University, Department of Radiation Oncology, Izmir, Turkey

[6]Catalan Institute of Oncology, Department of Radiation Oncology, Badalona, Spain

[7]Gazi University, Department of Radiation Oncology, Ankara, Turkey

[8]Aarhus University Hospital, Department of Oncology, Aarhus, Denmark

[9]Baskent University, Department of Radiation Oncology, Ankara, Turkey

[10]Ankara University, Department of Radiation Oncology, Ankara, Turkey

[11]Maastricht University (MAASTRO) GROW Research Institute, Department of Radiation Oncology, Maastricht, The Netherlands

[12]MediClin Robert Janker Clinic & Clinical Cooperation Unit Neurooncology, University of Bonn MC, Bonn, Germany

[13]University Hospital of Besancon, Department of Radiation Oncology, Besancon, France

[14]Mayo Clinic, Department of Radiation Oncology, Jacksonville, USA

[15]Mayo Clinic, Department of Radiation Oncology, Phoenix, USA

Purpose or Objective: For the treatment of adult patients newly diagnosed with medulloblastoma, there is no standard to guide multimodality therapy. With a multi-institutional cohort, we investigated and reported the multidisciplinary approach, clinical outcome, and prognostic factors of medulloblastoma in adult patients treated with postoperative radiotherapy (RT).

Material and Methods: Thirteen (13) institutions from the RCN study group among Europe and United States enrolled 206 adult medulloblastoma patients who underwent postoperative RT between 1976 and 2014. All hospitals received their respective Institutional Review Board approval, and extracted data were sent to one investigator (B.A.) for data analyses. Log-rank univariate and Cox-modeled multivariate analyses were performed.

Results: There were 118 men and 88 women, and median age was 29 (range, 16-67). The median follow-up was 31 months. Tumor resection was performed in all patients, and surgery was complete in 140 (68%) of the patients. For those patients with reported residual volume, 83 (66%) achieved <1.5 cm2 after resection. Histological subtype was classic (61%) predominantly. Postoperative RT was given in 202 (98%) patients, and 93% of them received craniospinal irradiation (CSI) to a median dose of 36 Gy, with a median RT boost of 18 Gy to the posterior fossa. Ninety-eight (48%) patients had chemotherapy before, after, or concomitant with RT; the most common chemotherapy regimens were cisplatin and vincristine-based. At 5 and 10 years' marks, the overall survival (OS) rates were 63 and 51%; local control (LC) rates were 60 and 46%; and disease-free survival (DFS) rates were 52 and 38% for all patients, respectively. On univariate analyses, Karnofsky performance status (KPS) ≥ 80%, time between surgery and RT (≤ 47 days), negative CSF, total RT dose ≥ 54 Gy, CSI completion, use of boost field, and chemotherapy were associated with better LC, DFS, and OS. Additionally, complete surgery, <1.5 cm2 residual volume, desmoplastic pathology, and age (≥ 29) were significant favorable prognostic factors for DFS and OS. In multivariate analyses, KPS ≥ 80% (P<0.001) and CSI (P=0.0002) were the remaining significantly favorable prognostic factors for DFS and OS; presence of chemotherapy (P=0.0002) and KPS ≥ 80% (p=0.03) correlated with better LC rates.

Conclusion: We retrospectively reported the largest clinical series for the treatment of adult medulloblastoma and elucidated prognostic factors for tumor control and also survival outcomes. For patients with high KPS who also received CSI, their DFS and OS were better. The use of chemotherapy may associate with better local control, possibly due to improved radio-sensitization. This information should serve as the benchmark and provide the basis for future prospective clinical trials in further improving the outcome for this group of adult patients with rare medulloblastoma.

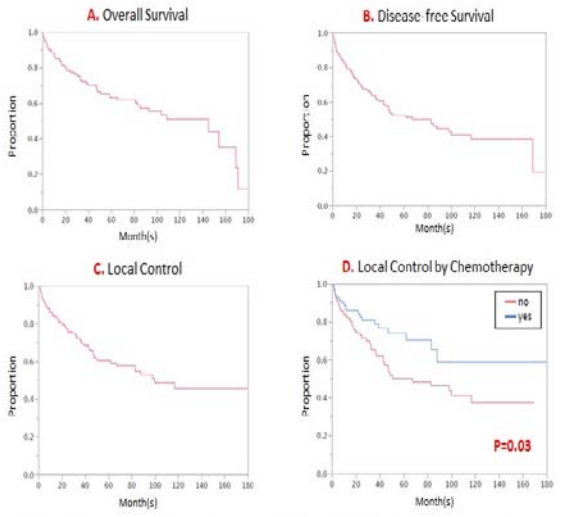

Figure: A. Overall survival of the entire cohort (N=206 patients); B. Disease-free survival, 206 pts; C. Local control rate, also 206 pts; D. Local control as stratified by the use of any adjuvant chemotherapy, P=0.0273, Log-Rank testing

OC-0348

Tumor bed radiosurgery vs. whole brain radiotherapy after surgery of single brain metastasis

L. Kepka[1], D. Tyc-Szczepaniak[2], K. Bujko[2], M. Olszyna-Serementa[2], W. Michalski[3], A. Sprawka[2], B. Trabska-Kluch[4], K. Komosinska[1], E. Wasilewska-Tesluk[1], B. Czeremszynska[1]

[1]*Independent Public Health Care Facility of the Ministry of the Interior and Warmian & Mazurian Oncology Centre, Department of Radiotherapy, Olsztyn, Poland*

[2]*Maria Sklodowska-Curie Memorial Oncology Center and Institute of Oncology, Department of Radiotherapy, Warsaw, Poland*

[3]*Maria Sklodowska-Curie Memorial Oncology Center and Institute of Oncology, Department of Biostatistics, Warsaw, Poland*

[4]*Medical University of Lodz, Department of Radiotherapy, Lodz, Poland*

Purpose or Objective: A multicenter randomized trial evaluated neurological status (including neurological deaths) and cognitive function of patients with resected single brain metastasis (BM) after stereotactic radiotherapy of the tumor bed (SRT-TB) in comparison with adjuvant whole-brain radiotherapy (WBRT). This study reports a preliminary comparison of pattern of failure and neurological deaths in this trial.

Material and Methods: A planned number of 60 patients was randomly assigned into SRT-TB (30) and WBRT (30) arms. Inclusion criteria were: total or subtotal resection of BM, single BM in the MRI before craniotomy, KPS ≥ 70, life expectancy >6 months. Patients in the SRT-TB arm received linac-radiosurgery of 15 Gy/1 fraction, or 5 x 5Gy if large cavity or proximity of critical structures. WBRT consisted of 30 Gy in 10 fractions. Evaluation at baseline (before RT), eight weeks after RT, and next every three months consisted of EORTC QLQ-C30 - BN-20, MiniMental test, KPS, neurologic status, and MRI of the brain. Neurological death was defined as every death from progression in the brain, toxicity of treatment of BM, and from undetermined cause. Crude rates of neurological deaths and relapses in the brain were compared according to the treatment actually received analysis with chi2 test. Overall survival (OS) and interval free from neurological death (IFFND) rates were compared with log-rank test.

Results: In the SRT-TB arm, six patients were ineligible (new BM detected during RT planning [5], withdrawal of consent [1]), one received WBRT by error, two had rapid extracranial progression (one had no BM treatment, one received WBRT), thus finally 21 (72%) patients received the assigned treatment in this group. In the WBRT arm, 29 (97%) received the assigned treatment. With median follow-up of 12 months (range: 1-36) for 26 living patients, one-year OS rates (intention-to-treat) were 48% (95% CI: 36-60%) and 61% (95% CI: 43-79%) for SRT-TB and WBRT arm, respectively, p=.14. In the intention-to-treat analysis, one-year IFFND rates were 59% (95% CI: 35-84%) and 74% (95% CI: 56-93%) for SRT-TB and WBRT arm, respectively, p=.10. In the treatment actually received analysis, one-year IFFND rates were 62% (95% CI: 37-88%) and 72% (95% CI: 53-90%) for SRT-TB and WBRT arm, respectively, p=.26. There were 9 (41%) and 9 (30%) neurological deaths, in the patients receiving SRT-TB and WBRT, respectively, p= .10.

Ten (45%) of 22 patients treated with SRT-TB had relapse in the brain including 5 (23%) relapses in the tumor bed; 9 (31%) of 30 patients treated with WBRT had relapse in the brain including 7 (24%) relapses in the tumor bed, p=.29.

Conclusion: Our results showed high rate of neurological deaths with omission of WBRT, thus such treatment might not be safe. Planned analysis of the results from our study that will compare neurological and cognitive functions following two treatments will be also helpful in decision making process.