microsurgery SRS might also be an alternative that balances tumor control, hearing preservation and adverse effects. The purpose of this analysis was to evaluate the efficacy and toxicity of SRS for different Koos grades including AN I, Koos II and III.

METHODS: In this single center retrospective analysis (1991 - 2015) we included all patients with previously untreated AN who underwent single session LINAC or Cyberknife® based SRS with a minimum follow-up of 3 months. Outcomes were analyzed and correlated (Pearson’s coefficient) with the different Koos grades in terms of radiological tumor control, preservation of serviceable hearing, course of median pure tone averages (PTA) and adverse events rated by Common Terminology Criteria for Adverse Events (CTCAE; ver. 5.0).

RESULTS: 301 patients (f:m = 151:150, median age 59 years ±13.6, range 17-84) were identified with a mean follow-up of 50.9 months (range 3-265). Mean tumor volume was 1.85 ml ±2.4 (range 0.1-23.7, the mean marginal dose was 12.4 Gy ± 0.8 (range 11-20) and the prescription isodose was 95.3 ± 1.2% (range 92.9-96.2). Within regard to the Koos classification 52 patients were considered as grade I, 162 as grade II, 42 and 45 as grade III and IV, respectively.

At last follow-up after SRS 94% of the patients showed radiological tumor control. There was no significant correlation (p = 0.113) between Koos grades I II vs III IV and radiological tumor control.

Median PTA of Koos I/II tumors increased about 49% (37.2 dB prior to SRS up to 53.6 dB at last follow-up). In case of Koos III IV tumors the increase of median PTA was similar (47.2 dB up to 68.2 dB).

The rate of transient focal nerve dysfunction CTCAE grade 1 or 2 in Koos I/II tumors was 2.3% and 4.6% in Koos III/IV. Permanent focal nerve dysfunction CTCAE grade 1 was observed in one patient with Koos I grade I (2.3%) and transient trigeminal nerve impairment CTCAE grade 1/2 occurred with 3.7% in Koos III/II and with 6.9% in Koos III/IV. Four patients (4.6%) with Koos III/IV tumors had permanent trigeminal nerve impairment CTCAE grade 1/2.

CONCLUSION: SRS for AN shows reliable long term tumor control and a high rate of hearing preservation and without considerable permanent side effects. Therefore, SRS can be proposed as safe and effective treatment option for AN, even with higher Koos grades.

P19.03 RANDOMIZED DOUBLE ARM PHASE III STUDY TO EVALUATE FEASIBILITY AND SAFETY OF GAMMA KNIFE RADIOTHERAPY VERSUS LINAC BASED (EDGE) RADIOTHERAPY IN BRAIN METASTATIC PATIENTS

P. Navarra1, A. Ascolese1, L. Cozzi1, S. Tomatis1, P. Picciozi1, G. Pecchioldi1, L. Attu1, E. Clerici1, G. Maggi1, M. Scorsetti1,2,3,4,5

1Humanitas Cancer Center, Rozzano, Italy, 2Humanitas University, Rozzano, Milan, Italy.

INTRODUCTION: For limited brain disease the treatment choice is radiosurgery(RS) that obtain a local control in 90% of patients. Different technological modalities have been used: Gammaknife, Cyberknife, Linac with comparable results and different incidence of symptomatic radionecrosis. To date no comparative randomized studies have been published in this matter. We draw this randomized study with the objective to evaluate incidence of symptomatic radionecrosis, local control (LC) and patient overall survival using two different modalities of RS, gammaknife vs linac.

METHODS AND MATERIALS: The present prospective phase III study includes patients with limited BMs (up to 4) treated with RS. Inclusion criteria were a KPS ≥70, RPA class I-II, maximum diameter <3cm and/or a total tumor volume <30 cc. The total dose delivered was 24 Gy at 50% isodose for BMs ≤20 mm or ≤42 cc, 20 Gy for BMs 21-30 mm or volume <14.1 cc and ≥43.2 cc for Gamma Knife RS and 24 Gy at mean dose to PTV for LINAC RS. Outcome evaluation consisted of physical examination and brain MRI performed every 3 months. Local progression was defined as radiographic increase of the enhancing abnormality in the irradiated volume on serial MR imaging, and distant failure by the presence of new brain metastases or leptomeningeal enhancement outside the irradiated volume. Suggestive of radionecrosis was considered the presence of central hypodensity and peripheral enhancement on T1-weighted post-contrast imaging, with edema on T2-weighted images. The median follow-up was 3 months. No symptomatic radionecrosis was recorded in Edge arm. The 6 months and 1 year PFS were 100% and 95.2% and the 6 months and 1 year OS 86.6% and 80.2% respectively.

CONCLUSION: Gamma-knife and LINAC RS are comparable in terms of LC. The risk of radionecrosis is greater in GK arm.

P20 NEW DEVELOPMENTS IN DRUG DELIVERY

P20.01 MEVITEM: A EUROPEAN, RANDOMIZED, OPEN-LABEL PHASE II/III STUDY OF VISMODEGIB IN COMBINATION WITH TEOZOMOLIDE VERSUS TEOZOMOLIDE ALONE IN ADULT PATIENTS WITH RECURRENT OR REFRACTORY MEDULLOBLASTOMA PRESENTING AN ACTIVATION OF THE SONIC HEDGEHOG PATHWAY

D. Frappaz1, D. Meyronnet2, G. Garn1, F. Laigle-Donadery4, E. Le Rhun1, A. Bonniveille-Levard1, J. Frene1, A. Idhbaa1, C. Gourmelon1, O. Chinton1

1Centre leon Bérard, Lyon, France, 2Centre de Pathologie et Neurpathologie Est, Lyon, France, 3DRCC- Centre leon Bérard, Lyon, France, 4Centre Rene Gauducheau, Saint-Herblain, France, 5Universite Pierre et Marie Curie Paris VI, Paris, France, 6Centre Rene Gauducheau, Saint-Herblain, France, 7CHU La Timone, Marseille, France.

BACKGROUND: Therapeutic options are limited for refractory/relapsed adult medulloblastoma with activation of sonic hedgehog pathway (SHH-MB). Inhibition of this pathway may offer an attractive therapy. Vismodegib suppresses SHH signaling by binding to and interfering with the SMO transmembrane receptor. We postulate that vismodegib together with chemotherapy may kill more tumor cells than chemotherapy alone by blocking cell proliferation at different molecular levels (“vertical association strategy”).

METHODS: MEVITEM is a multicenter, randomized (2:1 ratio), open-label, Phase II/III aiming to evaluate the safety and clinical activity of the association vismodegib (V; daily 150mg/d, po) + temozolomide (T; D-5: 150 mg/m2 for Cycle 1 and 200mg/m2or subsequent cycles) versus T alone in adult patients with recurrent or refractory SHH-MB. Main eligibility criteria are histologically confirmed recurrent or refractory SHH-MB with which known curative therapy exists, not previously treated with T, with evidence of measurable disease and documented activation of SHH pathway. Pathological review and analysis of SHH pathway are performed centrally by IHC. This Phase II/III includes i) a safety Run aiming to evaluate the safety of V+T and ii) a Phase II part aiming to evaluate the clinical activity of V+T measured by the 6-month non-progression rate. Patients enrolled in the safety Run are included in the evaluation of the Phase II part. Considering that V would be uninteresting if 6-month non-progression rate ≤ 30% and promising if ≥ 55% and using Simon’s optimal two-stage design (type I error rate of 5%, power of 80%), a sample size of 25 evaluable patients is required for Arm V+T (including 9 in stage I). The sample size in Arm T alone is 13 patients.

Considering the rarity of the disease, the few therapeutic options and the promising results reported with V in adult SHH-MB the Sponsor considered the enrolment of patients previously treated by T in a 3rdindependent and parallel arm with V as single agent (Arm C). To date, 18 patients were enrolled (Arm V+T: 7, Arm T: 4, Arm C: 7), the Phase II part is ongoing.

P20.02 GRAPHENE IN NEUROSURGERY: A POTENTIAL AND INNOVATIVE STRATEGY IN THE TREATMENT OF CEREBRAL GLIOMAS

M. Calti1, R. V. Abbruzzeti1, G. Caruso1, V. Barresi2, L. Minutoli3, A. Germani1, F. Tomaselli1

1Department of Neurosurgery, University of Messina, A.O.U. Polichinico G. Martino, Messina, Messina, Italy, 2Department of Human Pathology, University of Messina, A.O.U. Polichinico G. Martino, Messina, Messina, Italy, 3Department of Clinical and Experimental Medicine, University of Messina, A.O.U. Polichinico G. Martino, Messina, Messina, Italy.

Glomas account for around 45% of primary brain tumors. The treatment of malignant gliomas depend on the person’s age, the type of tumor, and the location of the tumor. These tumors tend to grow into the normal brain tissue, with the result that complete surgical removal can be very difficult to obtain. Current therapy is usually unsatisfactory due to low therapeutic efficacy and strong systemic side effects of chemo- and/or radiotherapy protocols.

The standard protocol includes maximal surgical resection with postoperative combination of radiation therapy with concomitant and adjuvant chemotherapy. Surgical treatment represents the first initial treatment. However, in spite of the recent innovations in surgical techniques, including intraoperative mapping, we only got a slight improvement of the prognosis. Additionally, radiation therapy is also used to treat gliomas in locations where surgery is not safe and for recurrent gliomas. Chemotherapy is recom-