**Randomized Phase III Trial Comparing Gamma Knife and Linac Based (EDGE) Approaches for Brain Metastases Radiosurgery: Results from the Gadget Trial**

P. Navarria,1 E. Clerici,1 G. Carta,2 L. Attuati,3 P. Picozzi,3 C. Franzese,1G.R. D’Agostino,4 S. Tomatis,1 P. Mancosu,3 L. Cozzi,2 G. Reggiori,2and M. Scorsetti5,6;

*1Humanitas Clinical and Research Hospital, Rozzano - Milan, Italy, 2Humanitas Clinical and Research Hospital, Rozzano-MI, Italy, 3Humanitas Research Hospital, Rozzano, Italy, 4Humanitas Cancer Center and Research Hospital, Rozzano, Italy, 5Istituto Clinico Humanitas, Rozzano (Milan), Italy, 6Humanitas University, Rozzano (Milan), Italy*

**Purpose/Objective(s):** Brain metastases (BMs) from solid tumors represent a topic of increasing interest for the higher incidence in the last years. Stereotactic radiosurgery (SRS) is the main effective local therapeutic approach used. Different technological modalities have been employed with comparable local control rate but to date no randomized trials are available on this issue. We draw a phase III trial comparing Gammaknife (GK) and Linac based (Edge) SRS. The primary aim was to evaluate the incidence of radionecrosis between the two different modality; secondary endpoints were local control (LC) and overall survival (OS).

**Materials/Methods:** Patients 18 - 85 years old, with Karnofsky performance status (KPS) ≥70, histopathologically confirmation of primary solid tumor, RPA 1-2, estimated survival ≥ 3 months as for DS-GPA score, and harboring up to 4 BMs with max tumor diameter ≤30 mm were included. Randomization was stratified according to age, presence of extracranial metastases, and the number of BMs. For Arm A (GK) a single dose of 20-24 Gy at 50% isodose was prescribed. For Arm B a single dose of 24 Gy was prescribed to PTV for all metastases. Outcome evaluation was performed every 3 months with MRI and clinical examination. Radionecrosis was assessed mismatching T1/T2 MRI images, perfusion MRI, and in doubt cases using Methionine-CT/PET. Local response was appraised according to the Response Assessment in Neuro-Oncology (RANO) Working Group criteria.

**Results:** From October 2014 to January 2018, 168 patients for 292 BMs treated were included, 80 in Arm A (GK) and 88 in Arm B (Edge), for 152 BMs in arm A and 140 in Arm B, respectively. RN occurred in 23 (7.8%) cases, 11 in Arm A and 12 in Arm B; grade II in 8 cases of GK arm at a median time of 6.5 months and in 12 cases of Edge arm at a median time of 9.4 months; grade III RN was recorded in 3 cases, only in GK arm, at a median time of 3 months. The 12, and 18 months LC rates were 97.5% and 94.5% for the whole cohort; 98.8% and 90.9% for arm A; 96.2% and 96.2% for Arm B, comparable for the two groups (p value=0.96). The median, 12, and 18 months OS rates were 17.8 months, 74.1%, and 48.9%, comparable in both arms (p value=0.36). On univariate and multivariate analysis the volume of BMs was the only factor impacting on radionecrosis occurrence (p value=0.005; p value=0.03).

**Conclusion:** Gamma-knife and LINAC based SRS for BMs were comparable in terms of LC rates. The occurrence of GIII radionecrosis was greater and earlier in the GK arm respect to Edge arm.