ABSTRACT

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Hypofractionated radiotherapy for Diffuse Intrinsic Pontine Glioma (DIPG): A non-inferiority prospective randomized study including 253 children.

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BACKGROUND: Pediatric Diffuse intrinsic pontine glioma (DIPG) is an orfen disease. The study aims at confirming the non-inferiority of hypofractionated (HF) radiotherapy. Identification of the prognostic factors that determine the overall survival (OS) and progression-free survival (PFS) is the secondary objective.

METHODS: 253 patients were randomized into 3 arms; HF1 receiving 39 Gy /13 fractions, HF2 receiving 45 Gy /15 fractions, and Conventional fractionation (CF) 54 Gy/30 fractions. The OS and PFS were calculated using Kaplan-Meier methods and the non-inferiority was estimated against the CF arm.

RESULTS: The median OS for the HF1, HF2, and CF were: 9.6, 8.2, and 8.7 months, respectively. The 1-, 1.5-, and 2- year OS were: 34.6 %, 17.9 %, and 10.7 % for HF1, 26.2 %, 13.1, and 4.8 % for HF2 compared to 25.3 %, 12.1 %, and 8.4 % for CF, respectively (p=0.3). The hazard ratio was 0.776 and 1.124 for HF1 and HF2, respectively. Considering the non-inferiority margin (Δ) of 15% and a power of 90%, the lower inferiority confident interval for HF1= -14.34% & HF2= 11.37% (both below Δ) confirming its non-inferiority at 18-months OS. Younger patients (2 - 5 years) have better median OS in the whole cohort (11.6 months), HF1(13.5), and CF (12.1) but not HF2 (6.2) (p=0.003). Furthermore, the overall survival rates at 1-,1.5- and 2- year for Children 2 - 5 years belonging to HF2 arm was lower than that for HF1 and CF arms. However, similar acute and late side effects were reported in the 3 arms.

CONCLUSIONS: Two Hypofractionated radiotherapy proved to be non-inferior to conventional fractionation. Young age (2 - 5 years) is the only prognostic factor determining both OS and PFS. The young age superiority was lost with a higher hypofractionated RT dose necessitating more caution in applying 45 Gy/15 fractions in younger (2 - 5 years) children.

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