Primary intracranial germ cell tumors (GCTs) represent 3-5% of all central nervous system (CNS) tumors and occur most commonly in the pineal and suprasellar region with a male preponderance. Germinomas account for approximately two-thirds of intracranial GCTs and the remaining third are non-germinomatous germ cell tumors (NGGCTs). 1-4 NGGCTs include endodermal sinus tumor or yolk sac tumor (YST), choriocarcinoma (CC), embryonal carcinoma (EC) and more commonly mixed malignant germ cell tumors. GCTs may secrete measurable proteins into the blood and/or cerebrospinal fluid (CSF). Human chorionic gonadotropin-beta (hCG\textbeta) and alpha-fetoprotein (AFP) are internationally used for diagnostic purposes.

Moderate elevation of hCG\textbeta only in serum and/or CSF with characteristic neuroimaging features is considered diagnostic for bifocal germinoma and a biopsy is generally not mandated. Abnormal AFP levels and/or hCG\textbeta levels in the serum or CSF >50 mIU/mL are generally considered to be consistent with NGGCTs and a biopsy is not required for diagnosis. However, biopsied germinomas have been reported to secrete hCG\textbeta levels of up to 200 mIU/mL with no adverse impact upon survival. Surgery/tissue biopsy is required for diagnosis in the absence of tumor marker elevation. The late effects of CSI have long been recognized, particularly in children. Long term sequelae include auditory and visual impairment, endocrine and neurocognitive dysfunction and secondary malignancies.

This protocol aims to reduce treatment burden in select groups of CNS GCTs, that is, localized NGGCT and germinoma. Localized disease as defined by this study includes tumors involving the suprasellar region, pineal region, both (bifocal), or elsewhere within the ventricles. The objective of this study is to investigate whether pre-radiation therapy followed by response based radiation therapy (RT) will yield a high progression free survival (PFS) while reducing the risk of long term neurocognitive sequelae and maintaining quality of life (QoL). Cognitive, social, emotional and behavioral functioning will be evaluated and longitudinally modeled for all patients (on both strata) using the ALTE07C1 protocol.

This study consists of 2 treatment strata: Stratum 1 for patients with localized NGGCTs and Stratum 2 for patients with localized germinomas. Treatment for NGGCTs (Stratum 1) will determine, as measured by the 3-year progression-free survival (PFS) rate, whether dose and volume of irradiation can be safely reduced to 30.6 Gy whole ventricular field irradiation (WVI) and 23.4 Gy primary site boost in the subgroup of children and young adults (ages 3-21 yrs) with localized NGGCT who have a magnetic resonance imaging (MRI) confirmed complete response (CR) or partial response (PR) in response to induction chemotherapy and negative serum and cerebrospinal fluid (CSF) tumor markers or in patients who have less than a PR after induction therapy with
negative tumor markers who undergo second-look surgery and are found to have only mature teratoma, residual scar or fibrosis and meet the criteria for CR or PR.

Treatment for germinoma (Stratum 2) will determine, as measured by the 3-year PFS rate, whether simplified chemotherapy prior to dose-reduced radiation therapy is effective for treating children and young adults (ages 3-21 yrs) with localized germinoma who present with serum and CSF hCGb ≤ 50 mIU/ml. PFS and survival distributions of localized germinoma patients who present with serum and/or CSF hCGb > 50 mIU/ml and ≤ 100 mIU/ml will be estimated.