2015 Strategic Priorities

Brain Malignancies Steering Committee (BMSC)

The following summary is based upon input from a series of strategic planning activities: 1) a preliminary teleconference on October 9, 2014 dedicated to the Strategic Priorities planning process, which formulated broad features of clinical trials that BMSC views as key priorities for concept development, 2) a face-to-face meeting in conjunction with the Society of Neuro-Oncology meeting on November 14, 2014, and 3) a subsequent conference call on January 9, 2015, which provided additional discussion and feedback. Each of the pediatric and adult cooperative groups and consortia presented their recent and ongoing development plans in the context of these meetings.

Common themes that emerged from these discussions were: 1) That there was a wealth of molecular data driving genomically-targeted therapeutic strategies for newly identified subsets of common tumor types in both pediatric and adult neuro-oncology; 2) The diversity of tumor types and relevant targets in pediatric neuro-oncology, and the recognition of molecularly distinct subsets of adult gliomas necessitates a broad and inclusive approach to prioritization; 3) Implementation of novel modalities (e.g. immunotherapy) should also be prioritized; 4) BMSC should be open to consider the most promising new ideas, based on rapidly evolving genomic and tumor biologic insights, rather than prioritizing particular agents or modalities to the exclusion of others.

The general Strategic Priorities that arose from these discussions are as follows:

1) **Biologically or genomically based trial designs**, which take into consideration **molecular subsets of tumors** (e.g., MGMT methylated or unmethylated GBMs, 1p/19q codeleted gliomas, GBMs with molecular alterations that predict potential sensitivity to a novel agent (INSIGHT trial), SHH or beta catenin subsets of medulloblastomas in children and adults, BRAF-targeted therapies for pediatric LGG and HGG), in which case the **biomarkers are integral** to the study design.

2) Studies that **pair administration of a novel agent (e.g., small molecule) or modality (e.g., immunotherapy), with pharmacodynamic or immunological measures or tissue analyses of the drug target and studies of drug penetration into the tumor**, such that **mechanistic hypotheses** directly relevant to the agent/modality in question can be tested that may form a foundation for subsequent trials.

3) Studies that pair novel agents or modalities with **imaging biomarkers or molecular biomarkers** as hypothesis-testing or hypothesis-generating tools.

4) Studies that focus on "**process improvement**" approaches that may enhance QOL and/or influence outcome (e.g., whether temozolomide adds benefit post-RT vs. only during RT; use of proton vs. photon irradiation).