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NCI-CONNECT rare CNS tumor initiative: current progress and anticipated future impact

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Background on the NCI-CONNECT Initiative

In oncology, primary tumors of the central nervous system (CNS) are a comparatively rare group of tumors comprised of a diverse range of histologies and molecular characteristics.[1,2] As such, a comprehensive understanding of the diagnosis, natural history, and prognostic factors associated with these tumors is challenging, impeding progress in evidence-based care for patients, healthcare providers, and tumor scientists.

In 2016, the US Congress approved the 21st Century Cures Act, with the intent to authorize funding toward improving our cancer diagnostic and prevention methods while also expanding access to effective therapies. Within this framework, the Beau Biden Cancer Moonshot Program designated funds for the establishment of the *Rare Tumor Patient Engagement Network (RTPEN).* The NCI Comprehensive Oncology Network Evaluating Rare CNS Tumors (NCI-CONNECT) program has received funds from the RTPEN to specifically focus on 12 types of rare adult CNS tumors. The full list of tumors can be found at https://ccr.cancer.gov/neuro-oncology-branch/connect. The incidence of these tumor types constitutes less than 2000 individuals per year or an age-adjusted incidence rate of 1.47 per 100 000 people in the United States.[3]

Objectives of NCI-CONNECT and Currently Active Initiatives

In conjunction with available highly trained experts in neuro-oncology, NCI-CONNECT seeks to leverage these funds to (1) establish an international network for better capturing and studying adults with rare CNS tumors, (2) centralize the analysis and dissemination of data for improving our understanding of the biology of these tumors, and (3) establish a comprehensive infrastructure for the acceleration of translational research. To accomplish these goals, a multi-faceted pathway has been established for individuals at any stage of their cancer diagnosis/treatment (Figure 1). Individuals in need of treatment or a second opinion can be seen for an in-person evaluation at the National Institutes of Health (NIH), while those with stable tumors have the option of participating in online health questionnaires. In the latter option, participants can also submit saliva samples for genomic studies. Following a consultation, individuals can be enrolled in the Natural History study, which collects longitudinal clinical and genomic data based on banked specimens. Where eligible, participants can be enrolled in any of 4 of the currently active clinical trials: (1) immunotherapy for rare CNS tumors, (2) sunitinib for recurrent gliosarcomas or primary CNS sarcomas, (3) marizomib for recurrent ependymomas, and (4) bevacizumab and carboplatin for recurrent ependymomas. The NCI-CONNECT program will also soon be launching a first in-human study of ONC206, an imipridone with potent dopamine receptor D2 antagonist activity. This agent will be tested in individuals with histone mutated gliomas, one of the NCI-CONNECT program rare CNS cancers. The rationale for this trial is based on preclinical studies that have demonstrated that ONC206 was most effective in cells with elevated MYC1/MYCN expression.[4] With all of these trials, subsequent continuity of care is ensured through a connection of NCI experts with local healthcare providers. In addition to having access to world experts in neuro-oncology, all transportation and medical costs to patients are covered by the NIH.

The Neuro-Oncology Branch (NOB) at the NCI is optimally positioned to conduct the above-stated goals. As part of the Brain Tumor Trials Consortium, the NOB has already established a network with 30 of the top cancer centers in the United States. In addition to the combined content expertise in the field, experts at these institutions are collectively a strong advocacy voice for neuro-oncology research at the

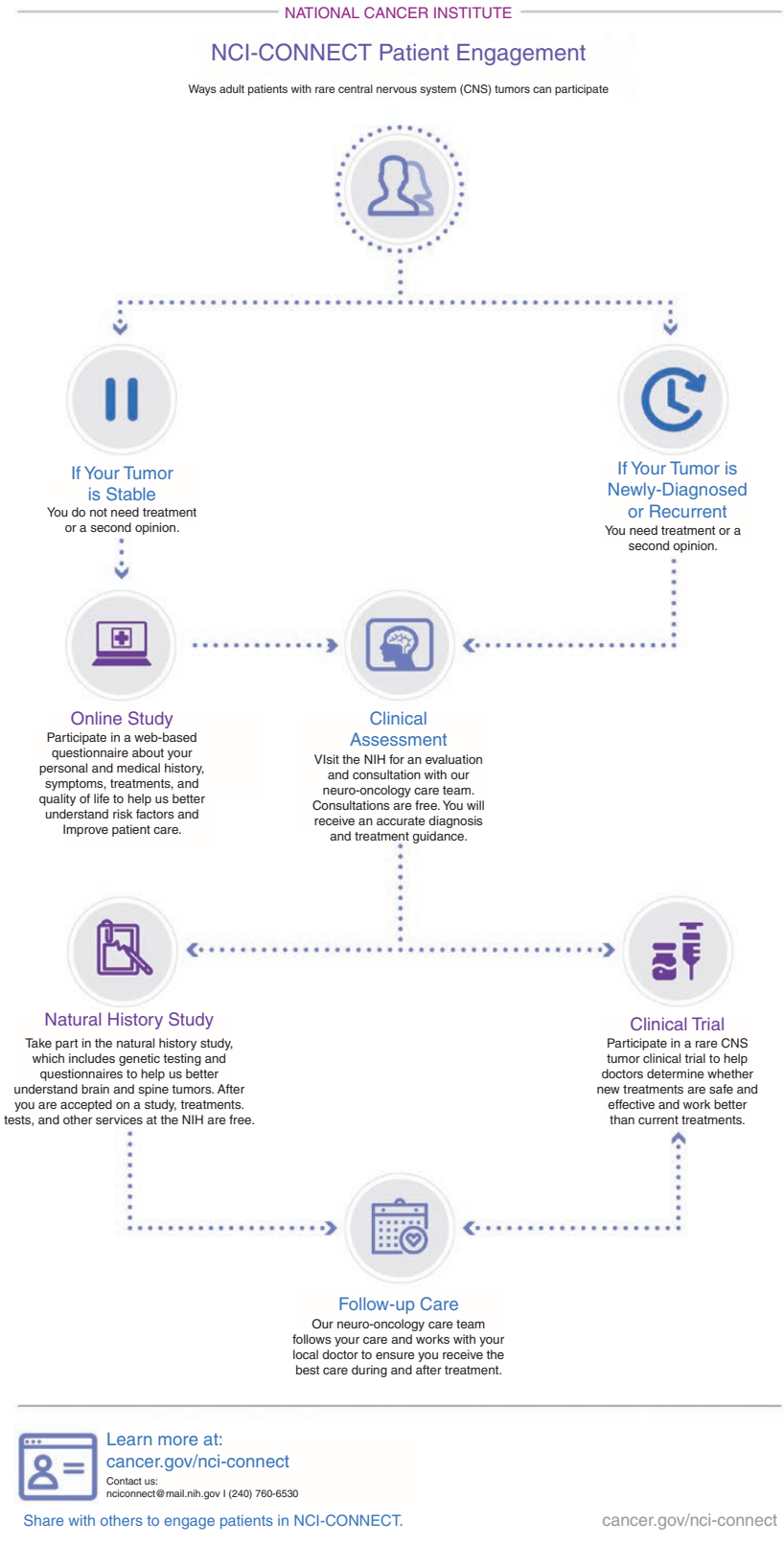

Figure 1. Clinical study pipeline of NCI-CONNECT. Credit: National Cancer Institute.

national and international stage. Already, NCI-CONNECT has been able to orchestrate 2 multi-disciplinary workshops aimed at outlining current challenges and future areas of research for histone mutated midline gliomas and oligodendrogliomas (please see Theeler et al. and Penas-Prado et al. for respective articles in the current issue of the journal). Furthermore, partnerships with other federal agencies such as the Cancer Therapy Evaluation Program help accelerate potentially novel therapies into clinical trials. Combined with dedicated federal funding, these resources create a fertile ground for establishing a large and effective research infrastructure that includes clinical trials, centralized tumor tissue repositories, along with a prospective collection of genomic and clinical data. In line with the mission of the Cancer Moonshot Program a dedicated patient engagement and outreach team—comprised of personnel for advocacy, care navigation, and communications—has also been established, enabling the dissemination of up-to-date and accurate information on CNS tumors for the neuro-oncology community.

Opportunities for Further Impact

Lessons learned from the glioblastoma population have shown that age, race, and ethnicity are correlated with incidence and prognosis.[5,6] Furthermore, studies have shown that the demographics of individuals enrolled in clinical trials—including age, sex, and race/ethnicity—are vastly different from that of the general population with glioblastomas.[7] Concerningly, only 8–11% of those with glioblastomas are enrolled in clinical trials.[8] It is conceivable that similar demographic disparities and issues with access to clinical trials may arise with the rare adult CNS tumors investigated by NCI-CONNECT.

The robust clinical research infrastructure established at the NCI, along with the facilitated access granted to potential participants from national and international arenas, provides the unique opportunity to better identify potential demographic and socioeconomic disparities in this patient population. Subsequent targeting of dedicated patient engagement and outreach efforts by the NCI-CONNECT team toward under-represented geographical areas would then potentially provide more accurate data on natural history and risk factors, empower the underserved population, and increase clinical trial enrollment.

Although the scope of the NCI-CONNECT vision is international, access by potential participants outside of the United States could potentially be limited, which could influence natural history data. Therefore, a comprehensive strategy for collaboration and data-sharing with other ongoing international efforts, such as the Canadian Cancer Registry[9] and the National POLA Network (France), is necessary. As we move toward the era of large-scale data for diagnostic, prognostic, and therapeutic purposes, the issue of protection of patient privacy will continue to loom large. As such, alongside the scientific and methodological topics, future workshops dedicated to refining the vision of large-scale international collaboration are needed.

Keywords

clinical trials | neuro-oncology | rare tumors

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