Adolescent and Young Adults (AYA) *vs*. Adult Subjects with Advanced Malignancies Involving the Central Nervous System (CNS) Respond Differently to Drugs

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Malignancies of the central nervous systems (brain and spinal cord) occur at every age level of human life; no age group is spared the possibility of developing a primary or secondary central nervous system (CNS) malignancy (1).

Almost 700,000 people in the US are living with tumors in the CNS. An additional 400,000 individuals are estimated to be living in other parts of the world with malignancies in the CNS. Although the age range that is most affected by CNS malignancies are the 50-70s, no age range is spared (1). It is estimated that nearly 15% of CNS tumors worldwide involve the adolescent/young adult (AYA) age group, 15-39 years of age. It is predicted that in the US alone 10,617 AYA aged individuals will be diagnosed with CNS tumors resulting in 434 deaths this year (2, 3).

The AYA age group of individuals with malignancies deserves special attention since they generally lack histories of comorbidities - hypertension, pulmonary and liver diseases, etc. and may tolerate drugs differently from older subjects. They may also be more at risk for toxicities with the newer immuno/chemotherapy regimens in current use. In general AYA individuals with cancer demonstrate different host biology, tumor pathophysiology and metabolize chemotherapy drugs differently than do either younger or older individuals.

Generally, there is a significant difference between AYA (15-39 years of age) and adult individuals (>39 years of age), as compared to their metabolism and distribution of all types of drugs (4).

The above generalization was re-enforced by Weiner, *et. al*., whom presented early Phase I results and experiences with a new drug, 4-demethyl-4-cholesteryl-oxypenclomedine (DM-CHOC-PEN), administered as intravenous treatment for cancers involving the central nervous system (CNS) in both adults and in AYA individuals (5). The same intravenous doses resulted in different blood levels in adult and AYA individuals; the former group had a drug peak in the blood that occurred earlier (at ~72 hrs), but the maximum drug concentration – peak in the blood, was greater for the AYA subjects. However, for the older aged group the drug had a longer blood half–life (remained in the circulation for almost a week longer than for the AYA subjects) (6, 7).

This was not surprising in view of the differences in the natural host biology and the chronic aging process that everyone undergoes, especially in the ability to metabolize and utilize drugs that pass through the liver (8).

The AYA individuals, especially the 15-20 year old group are of major interest since they are typically managed by pediatric or adult oncologists, rather than by AYA hematology/oncology specialists that also appreciate their physical, psychosocial, emotional, sexual, spiritual, financial, dietary, etc. issues and have the ability to relate to them and solve their problems, as well as treat them for their malignancies. Also, the AYA age group is not commonly enrolled in clinical trials, thus not afforded assess to the newer drugs and specialty counselling.

DEKK-TEC will be adding notes from consulting specialists/advisors and other support services on a regular schedule to this web site regarding these topics.

A Phase II clinical trial with 4-demethyl-4-cholesteryl-oxypenclomedine (DM-CHOC-PEN) as treatment for AYA subjects (15-39 years old) with malignancies involving the CNS is now enrolling subjects nationwide. Please contact DEKK-TEC for more information.

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Suggested reading and references:

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