Neuroblastoma Metastatic to the Central Nervous System: Survival Analyses from the German Childhood Cancer Registry and the Literature

Abstract

Background: Therapeutic innovation has resulted in an overall decline in childhood mortality from neuroblastoma, however, metastatic disease to the central nervous system (CNS-NB), which has emerged as a sanctuary site for NB metastases, remains difficult to treat and is typically fatal. The objective of this study was to describe the natural course of CNS-NB.

Methods: Data were abstracted from a cancer registry of the German Childhood Cancer Registry (GCCR) and from relevant published studies. Survival statistics were presented from a diverse, thus, non-exhaustive, pool of CNS-NB patients. Data were presented by secondary overview and overall survival (OS) and OS after diagnosis of first CNS recurrence from birth to age 18.

Results: The GCCR query identified 86 patients with CNS NB diagnosed from 1990-2010, including 27 with prior CNS metastases. The median OS, 95% confidence (CI), and OS time were 2.6 (1.9–4.6) and 4.7 (2.1–7.2) months, respectively, for all CNS-NB patients. Secondary OS (OS) and 6.8 (2.1–11.5) months, respectively, for isolated CNS-NB patients. Secondary OS at 12, 18, and 36 months at reporting were 24%, 12%, and 3.6%, respectively, for the inclusive analysis. The proportion of patients surviving 12, 18, and 36 months at reporting were 29.4%, 18.8%, and 8.2%, respectively, for all CNS NB patients, and 35.1%, 22.8%, and 12.3%, respectively, for isolated CNS-NB patients.

Conclusions: An assessment of the natural course of CNS-NB from two sources arrived at similar conclusions with respect to age and grouped survival in general. Median secondary OS is 4 months and <1% of patients survive 12 months. The findings were consistent across geographic regions and have not changed appreciably in the 4 decades.

Results

Figure 1. German Neuroblastoma Trials: Event-Free and Overall Survival

Table 1. German Neuroblastoma Trials: Summary of Treatment Provided

Table 2. Literature Analysis: References for Included Studies

Table 3. Literature Analysis: Summary of Survival, Presented by Study

Table 4. Literature Analysis: Summary of Survival, Presented by Study

Conclusions

CNS-NB remains unacceptably low; findings were consistent across multiple study sites and treatment modalities.

LITERATURE REVIEW

A systematic search identified the references listed in Table 2. Individual patient information was extracted from the selected publications to generate the following CNS-NB analysis populations:

• Included population: Included all patients with survival data reported in the selected studies.

• Restricted population: Restricted only those remaining after reviewing patients who either (1) died before receiving therapy for CNS NB; (2) received only palliative treatment; or (3) presented with rapidly progressing systemic disease of CNS NB.

Table 2. Literature Analysis: References for Included Studies

Table 3. German Neuroblastoma Trials: Summary of Survival

Table 4. Literature Analysis: Summary of Survival, Presented by Study

Figure 2. Literature Analysis: Overall Survival Probability Curves

Background

Primary Neuroblastoma Treatment: Strategies and Trends in Overall Survival

• Innovative therapies to treat primary NB has resulted in improved clinical outcomes.

• Low-risk NB treated with surgery plus chemotherapy or with surgery alone has cure rates for stage IV-S patients of 30-35%.

• High-risk NB treated with a combination of surgery, chemotherapy, and radiation therapy has cure rates of 15-20%.

• Intensive-risk NB treated with chemotherapy plus autologous stem cell transplantation has cure rates of 10-15%.

Metastatic Neuroblastoma with Central Nervous System Involvement

• The CNS has emerged as a sanctuary site for NB metastases in ~6-8% of patients.

• Neuroblastoma with CNS involvement has a better survival than primary CNS NB; however, it typically fatal.

• The objective of the current analysis was to describe the natural course of CNS-NB with the context of the therapeutic options available at the time of treatment.