Evaluation Of Resources Used During Care Of Children With High-risk Neuroblastoma Via Merging Of Cooperative Group Trial Data & Administrative Data

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BACKGROUND

- Standard multimodality therapy for high-risk neuroblastoma (HR NBL) includes intensive multi-agent chemotherapy, surgery, myeloablative chemotherapy with autologous stem cell rescue, external beam radiation, and immunotherapy (anti-GD2 antibody ch14.18 +cytokines) with a differentiating agent (Figures 1 and 2).

Figure 1: COG A3973

VDC – Vincristine, Doxorubicin, Cyclophosphamide
CE – Cisplatin, Etoposide
SURG – Resection of Primary Tumor
ASCT – Autologous Stem Cell Transplant
XRT – Radiation Therapy

Figure 2: COG ANBL0032

ch14.18- Chimeric anti-G_{D2} monoclonal antibody
GM-CSF- Sargramostim
IL-2- Interleukin-2
cis-RA- 13-cis-retinoic acid

- Cooperative group trials have improved outcomes for children with HR NBL.
- Trial data provide reliable information regarding patient characteristics, treatment, and response but do not include information regarding resource utilization.
- Merging of trial and administrative data would facilitate comparative effectiveness studies.

PRIMARY OBJECTIVES

- To determine if clinical trial data from the Children's Oncology Group (COG) Protocols A3973 and ANBL0032 can be merged with administrative data from the Children's Hospital Association (CHA) Pediatric Health Information (PHIS) database.
- To describe the resources associated with providing therapy to patients with high-risk neuroblastoma (HR NBL).

METHODS

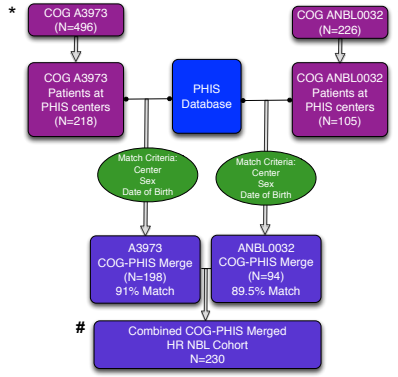
- COG is the largest international pediatric cooperative oncology group, and enrolls approximately 4,400 patients annually on therapeutic trials.
- The PHIS database consists of inpatient data from 43, not-for-profit tertiary pediatric hospitals affiliated with CHA **(Figure 3)**.
- PHIS data include the following information:
  - Level 1: Demographics, ICD-9 codes, procedure codes, dates of service, discharge disposition, and payor information
  - Level 2: Daily billing data for medications, laboratory tests, imaging procedures, clinical services, and supplies
- Patients are assigned a unique identifier in the PHIS database and can be followed from one admission to another.

Figure 3: 43 PHIS Centers

- Data from COG and PHIS were merged for patients enrolled on Phase III COG trials for HR NB (A3973 and and ANBL0032).
- Patients were matched based on the center, sex, and date of birth.
- Inpatient resource utilization summary statistics were tabulated based on PHIS data using Poisson regression (Rate=days of resource exposure per 1000 hospital days). Pearson scale was used to adjust for potential overdispersion.

RESULTS:

Figure 4: Match results for COG trials A3973 and ANBL0032 with PHIS data



* COG A9732 (Figure 1): Phase III randomized study of purged versus non-purged peripheral blood stem-cell transplantation for HR NBL.
** COG ANBL0032 (Figure 2): Phase III randomized study of immunotherapy versus 13-cis-retinoic acid alone for HR NBL.
A portion of patients treated on A3973 were also treated on ANBL0032.

Table 1: Patient Characteristics at Diagnosis

Age	**Years**
Median	3.19
Range	0.3-16.09
Stage	**Number (%)**
2a	1 (0.52)
2b	1 (0.52)
3	18 (9.38)
4	163 (84.89)
4S	2 (1.04)
Unknown	7 (3.65)
***MYCN* Status**	**Number (%)**
Amplified	66 (34.38)
Non-amplified	93 (48.44)
Unknown	33 (17.18)
Shimada classification	**Number (%)**
Favorable histology	3 (1.56)
Unfavorable Histology	145 (75.52)
Unknown	44 (22.92)

Table 2: COG Study Duration and Days in Hospital for A3973 and ANBL0032

COG Protocol	A3973 Combined Arms N=184 Mean ± SD (Range)	ANBL0032 Immunotherapy Arm N=45 Mean ± SD (Range)	ANBL0032 13-cis-retinoic acid Arm N=21 Mean ± SD (Range)
COG Study Period (Days)	279.70 ± 137.66 (1 - 997)	149.16 ± 54.88 (25 - 207)	128.95 ± 71.43 (9 - 238)
Days in Hospital	100.53 ± 51.73 (1 - 356)	36.64 ± 16.34 (2 - 85)	12.29 ± 12.92 (1 - 59)
Intensive Care Days*	3.98 ±13.03 (0 - 123)	1.24 ± 2.53 (0 - 14)	0.14 ± 0.65 (0 - 3)

RESULTS (continued) :

Table 3: A3973 (Combined Arms) Merged Cohort Resource Utilization Data (N=184)

Resources Measured	Resource Utilization Rate (Days of resource exposure per 1000 hospital days)
Aminoglycosides	113.66
Other ototoxic antibiotics	60.69
Antifungals	343.49
Analgesics	
Non-opioid	230.91
Opioid	326.38
PCA	69.49
Parenteral Nutrition	290.21
Antihypertensives	150.50
Diuretics	143.49
Dialysis	14.68

A3973 Resource Utilization

- Median number of days in hospital was 100 (range 1-356d)
- ICU level care delivered to 39% of pts (median 4d per pt, range 0-123)
- Ototoxic antibiotics administered to 44% of pts (median 6d per pt, range 1-93)

Table 4: ANBL0032 Merged Cohort Resource Utilization Data (N=66)

Resources Measured	Immunotherapy Arm N=45 Resource Utilization Rate (Days of resource exposure per 1000 hospital days)	13-cis-retinoic acid Arm N=21 Resource Utilization Rate (Days of resource exposure per 1000 hospital days)	p-value
Aminoglycosides	52.76	85.27	0.51
Other ototoxic antibiotics	25.47	38.76	0.63
Antifungals	280.17	116.28	0.16
Analgesics			
Non-opioid	502.12	170.54	*<0.0001*
Opioid	431.78	166.67	*<0.0001*
PCA	132.81	23.26	0.10
Parenteral Nutrition	72.77	38.76	0.53
Antihypertensives	41.84	15.5	0.56
Diuretics	163.13	77.52	0.09
Vasopressors			
Dopamine	21.23	0	0.07
Other	87.33	23.26	*0.03*
Dialysis	1.21	0	0.56

ANBL0032 Resource Utilization

- Fifteen (33%) pts in the immunotherapy arm received ICU level of care. One (4.8%) pt in the cis-RA arm received ICU level of care.
- Patients in the immunotherapy arm had a higher exposure to both opioid and non-opioid analgesics.

CONCLUSIONS:

- Patients enrolled on cooperative group HR NBL studies can be successfully identified and resource utilization data can be collected across trials using an administrative dataset.
- Characteristics of patients in this cohort are consistent with those of patients on recent HR NBL studies.
- Information regarding length of stay and supportive care required for treatment of children with HR NBL will be used in comparative effectiveness studies and will aid in patient/family education.
- A larger cohort, created by adding patients from future trials, will permit additional analyses.
- Future directions include linking this merged cohort with biology data.

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