Cooperation and Progress in Pediatric Cancer Care: The National Wilms Tumor Study Group

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Ten year relative survival (%), adults (15-99 years), selected cancers

- Testis
- Melanoma
- Hodgkin’s lymphoma
- Breast (females)
- Prostate
- Cervix
- Larynx (males)
- Colon (males)
- Bladder
- All cancers
- Kidney
- Ovary
- Leukaemia
- Myeloma
- Stomach
- Oesophagus
- Brain
- Lung
- Pancreas

Percentage survival

Wilms Tumor: A dramatic success story in modern medicine
Wilms’ Tumor

# 1 renal
# 2 abdominal
tumor of childhood

- 8 per million in children < 15 yr
- 450 cases / yr (US)
- peak age = 2 – 3 yr
4 year old girl

bulging left renal mass
1899: German surgeon Max Wilms first describes “a mixed tumor” kidney cancer in 7 children.

Operative mortality was at least 25% at this point.
1900-1950: improvements in surgical technique and postoperative care credited with survival rate of 25-30%.

1950: Routine post-operative radiation credited with 50% survival.
1950s – discovery of dactinomycin (from mold studies) and vincristine chemotherapy

1955 – Dr. Sidney Farber - Administration of dactinomycin to WT patients observed to cause remission.
Cooperation

Radiotherapist

Surgeon

450 cases/yr

Right kidney with Wilms' tumor

Chemotherapist

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Study | Years of Registration | Total Registrants
--- | --- | ---
NWTS-1 | 1969-1975 | 741
NWTS-2 | 1975-1979 | 950
NWTS-3 | 1979-1986 | 2496
NWTS-4 | 1986-1995 | 3335
NWTS-5 | 1995-2002 | 3031

**Motto:** *Cure is not enough*

**Overall Aims:**
1. To establish best treatments for WT stratified according to extent of disease
2. To study the nature and biology of childhood renal tumors
3. To gather information regarding possible genetic correlates
4. To determine whether the intergroup mechanism was feasible
5. Accumulate data on long-term survivors
1. Dactinomycin and viscristine are better together than individually and should form the building block of WT therapy (NWTS1)

2. Doxorubicin + dactinomycin + vincristine for advanced disease results in fewer relapse (NWTS2).

3. Radiation is unnecessary for localized disease that is completely resected (NWTS1)

4. Lower doses of radiation are just as effective as higher (NWTS 1,3)

5. Chemotherapy can be given in single doses rather than in multiple divided daily doses (NWTS4)

6. Total treatment time can be reduced from 15 months to 24 weeks (NWTS4)

7. Identification of histologic (favorable vs. unfavorable histology) and molecular genetic configurations (LOH 16p, 1q) are associated with a poorer prognosis (NWTS 1-5)
NWTS was not in isolation
2000: The Children’s Oncology Group (COG) =

Children’s Cancer Group (CCG) +

Pediatric Oncology Group (POG) +

National Wilms Tumor Study Group (NWTS) +

Intergroup Rhabdomyosarcoma Study Group (IRSG)
Stage I    Stage II    Stage III    Stage IV    Stage V

Within kidney
Within resection
Tumor biopsy
Tumor rupture
Into Gerota’s fascia
Venous thrombus
Lymph nodes

Distant Mets
Bilateral

From Staging to Risk Stratification
## Favorable WT

<table>
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<tr>
<th>Age</th>
<th>Tumor Wt (gm)</th>
<th>Stage</th>
<th>LOH</th>
<th>Rapid Response</th>
<th>Final Risk Group</th>
<th>Treatment Study</th>
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Anaplastic WT, Clear Cell Sarcoma, Malignant Rhabdoid, Renal Cell Carcinoma
All Renal Tumors and extrarenal Wilms or extrarenal/extra-CNS rhabdoid

**AREN03B2 CLASSIFICATION STUDY**
(Central Review)

- **FH WT (Very Low/Standard Risk)**
- **FH WT (Standard Risk/Higer Risk)**
- **Bilateral**
- **Anaplastic WT Clear Cell Sarcoma Malignant Rhabdoid Renal Cell Carcinoma**
- **Others FH WT (Low Risk)**

- **AREN0532**
- **AREN0533**
- **AREN0534**
- **AREN0321**
- **AREN03B2**
Radiology
Pathology
Operative Notes

If all materials received by post-op day 10, institution will receive Initial Risk Assignment by day 14.

Final Risk Assignment after LOH, which will be completed by day 21.

All protocols for Stage I-IV FH identical for first 21 days.
Very Low Risk

Must be < 2 years of age, < 550 gram tumor weight, Stage I, and No 1p/16q LOH.

Must sample lymph nodes to qualify.

Constitutes a very low risk for relapse.
Those that do relapse respond to salvage chemotherapy.
National Wilms Tumor Study Group

Paradigm for intergroup, interdisciplinary collaborative research in advancement of cancer care.

On what part of the curve are we functioning for other cancers?