The nephroblastoma, a malignant neoplasm of the kidney, is seen mostly in children. It was first categorized as a mixed tumor by the German surgeon, Max Wilms in 1899 and it has since been universally known as the Wilms tumor in acknowledgement of his work. It is the most common primary renal tumor in childhood. An annual incidence of Wilms tumor is 2.2 cases per million individuals-24 cases per year in Thailand. The peak incidence of Wilms tumor occurs between 2 and 5 years of age, with 95% of children being diagnosed before the age of 10 years. Affected children most commonly present with a palpable abdominal mass and less frequently abdominal pain or hematuria.

Wilms tumor is a great therapeutic success story within pediatric oncology. The continued achievement of clinical trials over the past 30 years has led to an overall survival of 85%, and treatment-related morbidity has now been reduced. The current management of Wilms tumor continues to evolve with the two notably different approaches being taken by two large multi-institutional cooperatives, the National Wilms Tumor Study Group (NWTSG) in North America (now incorporated into the Children’s Oncology Group, COG) and the International Society of Pediatric Oncology (SIOP) in Europe. The NWTS has recommended early nephrectomy to define the uncorrected stage and histology, on which further treatment stratification is decided. By contrast, SIOP has advised initial treatment with pre-operative chemotherapy, mainly on the basis of radiographic diagnosis and showed that pretreatment made surgery safer, reduced tumor rupture rates, and increased the proportion of children with a lower tumor stage requiring less overall treatment. Both treatment approaches yield excellent clinical outcomes. Although overall survival is similar with both the NWTS/COG and SIOP approaches, each has distinct advantages and disadvantages. In this review, we discuss the advances of Wilms tumor therapy and the debated issues about the different strategies in North America and Europe.

### Prognostic Factors

Treatment regimens for Wilms tumor are selected based on an individual’s risk of recurrence, which is defined by tumor stage, patient age, histological, and biological prognostic factors.

#### Staging

The staging criteria for Wilms tumor are based exclusively on the anatomic extent of the tumor, without consideration of genetic, biologic, or molecular markers.

The COG (formerly NWTSG) has developed a pre-chemotherapy/up-front, surgery-based system that incorporates surgical and pathological information that is gathered at the time of initial surgery, generally before chemotherapy. This system allows for stage-based adjuvant therapy and the avoidance of unnecessary chemotherapy for some children. In SIOP studies, local (abdominal) staging of the primary tumor is done following surgery after pre-operative chemotherapy (post-chemotherapy-based system). The presence/absence of metastases is evaluated at presentation, on the basis of imaging studies. Both staging systems have proven valuable in predicting outcomes. However, the difference in surgical timing makes a direct stage-to-stage comparison of these two systems difficult. The criteria for NWTS/COG staging and SIOP staging are given in Table 1.

#### Histology

Histology is the most powerful prognostic indicator for patients with Wilms tumor.

### The NWTS/COG classification

Anaplasia is characterized by irregular mitotic figures, large nuclear size and hyperchromasia and is firmly established as a means of differentiating those with adverse outcomes, after a retrospective analysis of histopathology samples from the first NWTSG study (NWTS-1). NWTSG classifies Wilms tumors as having a favorable histology (FH) or anaplastic histology (AH) based on the presence or absence of anaplasia. Anaplasia may be diffuse or focal. Focal anaplasia is defined as the presence of one or a few sharply localized regions of anaplasia within a primary tumor and there is a...
different prognosis between that of tumors with favorable histology (without anaplasia) and that of tumors with diffuse anaplasia. Anaplastic histology occurs in approximately 10% of patients, and the prevalence varies with the patient’s age. Anaplastic Wilms tumor is rarely present in children younger than 2 years old, but is reported in about 13% of children older than 5 years.

The SIOP classification

The use of pre-operative chemotherapy by SIOP allows a histological risk stratification of tumors dependent on the tumor response before removal. This adds another dimension which makes direct comparison to NWTSG data difficult. The revised SIOP histological classification divides Wilms’ tumors into three risk groups:

- low risk (completely necrotic nephroblastoma or cystic partially differentiated nephroblastoma),
- intermediate risk (regressive, epithelial, stroma, mixed, or focal anaplastic nephroblastoma), and
- high risk (blastemal or diffuse anaplastic nephroblastoma).

Patient Age

The youngest patients have the best survival as well as the highest chance that a renal mass is not a Wilms tumor. Studies undertaken by SIOP and NWTSG have shown that increasing patient age is associated with increased risk of recurrence in non-metastatic Wilms tumor. A subset with an outstanding prognosis are patients younger than 2 years old, with tumors less than 550 g, with stage I favorable histology. Furthermore, retrospective data from a collaborative study undertaken by SIOP, NWTSG and the UK Children’s Cancer Study Group (UKCCSG), which

<table>
<thead>
<tr>
<th>Stage</th>
<th>NWTSG/COG§</th>
<th>SIOP§</th>
</tr>
</thead>
</table>
| I     | a) Tumor limited to the kidney and completely resected  
    (43% of patients)  
    b) Renal capsule intact  
    c) Tumor not ruptured or biopsied before removal  
    d) No involvement of renal sinus vessels  
    e) No evidence of tumor at/or beyond margins of resection | a) Tumor limited to the kidney or, if outside the normal kidney contour, surrounded with a fibrous pseudocapsule that may be infiltrated with tumor that does not reach the outer surface, and is completely resected  
    b) Tumor may protrude into the renal pelvis and  
        ureter, but not infiltrate their walls  
    c) Vessels of the renal sinus are uninvolved  
    d) Intrarenal vessels may be involved |
| II    | Tumor extends beyond kidney, but completely resected with negative margins  
    (20% of patients)  
    a) Regional extension of tumor (penetration of renal sinus capsule, or extensive invasion of soft tissue of the renal sinus) or tumor thrombus or invasion in renal or extrarenal vessels (thrombus removed complete) | a) Tumor extends beyond kidney or penetrates through renal capsule and/or fibrous pseudocapsule into perirenal fat, but completely resected  
    b) Tumor infiltrates renal sinus and/or invades blood and lymphatic vessels outside the renal parenchyma, but is completely resected  
    c) Tumor infiltrates adjacent organs or vena cava but is completely resected |
| III   | Residual tumor after surgery confined to tumor bed  
    (21% of patients)  
    a) Lymph nodes within the abdomen or pelvis are  
        involved by tumor  
    b) Tumor penetrates through the peritoneal surface  
    c) Tumor implants on peritoneal surface  
    d) Gross or microscopic residual tumor  
    e) Tumor incompletely resectable owing to local infiltration into vital structures  
    f) Tumor spillage before or during surgery  
    g) Tumor biopsied (using Tru-cut® needles, open biopsy, or fine-needle aspiration) before removal  
    h) Tumor removed in more than one piece (e.g. tumor cells found in a separated excised adrenal gland or a renal vein tumor thrombus removed separately)  
    i) Extension of the primary tumor within vena cava into thoracic vena cava and heart considered stage III, rather than stage IV, even through outside the abdomen. | a) Incomplete tumor excision that extends beyond resection margins (gross or microscopic tumor remains)  
    b) Any involved abdominal lymph nodes  
    c) Tumor rupture before or during surgery (irrespective of other staging criteria)  
    d) Tumor penetrates the peritoneal surface  
    e) Tumor implants on peritoneal surface  
    f) Tumor thrombi present at resection margins of vessels or ureter, transected or removed piecemeal  
    g) The tumor has been surgically biopsied before pre-operative chemotherapy or surgery |
| IV    | Hematogenous metastases (lung, liver, bone, brain, etc.)  
    (11% of patients)  
    or lymph node metastases outside the abdominal and pelvic region | Hematogenous metastases (lung, liver, bone, brain, etc.) or lymph node metastases outside the abdominal and pelvic region |
| V     | Bilateral renal tumors present at diagnosis  
    (5% of patients) | Bilateral renal tumors present at diagnosis |

TABLE 1. NWTSG/COG§ and SIOP schemes for staging Wilms tumors.  

§Originally developed by the National Wilms Tumor Study Group and still used by the Children’s Oncology Group  

NWTSG/COG staging is done before chemotherapy, whereas SIOP staging is done after it. Abbreviations: NWTSG, National Wilms Tumor Study Group; SIOP, International Society of Pediatric Oncology.
reviewed the clinical characteristics and survival of infants diagnosed with a primary renal tumor in the first 7 months of life, showed that only 58% of patients had Wilms tumors, and 18% had benign congenital mesoblastic nephromas. Among the patients with Wilms tumors, 82% had stage I or II disease, and the 5-year overall survival in this subgroup was 93.4%.17

Molecular prognostic factors

The NWTSG discovered that loss of heterozygosity (LOH) for both chromosomes at 16q and 1p is associated with a poorer prognosis for patients with favorable histology (FH). In NWTS-5, the incidence of LOH was 17.4% at 16q and 11.3% at 1p in FH tumors. Patients with stage I/II FH disease with combined LOH had only a 74.9% 4-year relapse-free survival (RFS), clearly worse than their counterparts without LOH who had a 91.2% RFS.18 Ongoing COG trials will study the benefit from the addition of doxorubicin to their therapy in this group of patients. Likewise, patients with advanced stage II FH disease, whose tumors harbor LOH for 1p and 16q, also have an inferior outcome, even when treated with a three-drug therapy. These patients may benefit from intensification of their therapy with the addition of other chemotherapeutic agents, such as cyclophosphamide and etoposide or carboplatin and etoposide.

Other promising prognostic markers are an increase in gene copy number or expression at chromosome 1q25 and telomerase expression level.21 Gene expression profiling also shows promise to identify new prognostic factors.22

Treatment of Wilms tumor

Current treatment stratification is based on histology and tumor staging and comprises multimodality chemotherapy and surgery, with or without radiation therapy. The activity of dactinomycin and vincristine against WT was demonstrated in the 1950s and 1960s, and these drugs have served as the backbone chemotherapy for Wilms tumor ever since. Doxorubicin was added to WT therapy in the 1970s, followed by carboplatin and etoposide later on. The main objectives of today’s trials are to treat patients according to well-defined risk groups in order to achieve the maximize cure rates, and to decrease the frequency and intensity of acute and late toxicity.

National Wilms tumor study group

The NWTSG was established in 1969 and is now incorporated into the Children’s Oncology Group (COG), which includes almost all pediatric oncology centers in North America. The hallmark of NWTSG and upcoming COG trials is initial nephrectomy with pathologic tumor staging before chemotherapy. At present, five major trials (NWTS 1–5) have been conducted. Table 2 summarizes the main conclusions of these trials.16,18,23-25 Nearly all patients with Wilms tumors receive chemotherapy, usually adjuvant. Most patients undergo primary nephrectomy and those with stage III or IV tumors have additional radiation therapy. Although COG recommends initial nephrectomy for most patients with Wilms tumors, pre-operative chemotherapy is recommended under certain circumstances, including the occurrence of Wilms tumor in a solitary kidney, bilateral Wilms tumor, tumor in a horseshoe kidney, tumor thrombus in the inferior vena cava above the level of the hepatic veins, and respiratory distress resulting from the presence of extensive metastatic tumors.

COG protocols recommend that stage I and most FH stage II tumors should initially be treated by nephrectomy, followed in most patients by 18 weeks of vincristine and dactinomycin. However, there may be a subset of patients in this group that may benefit from surgery alone. The NWTS-5 pilot trial allocated patients younger than 24 months of age with stage I FH tumors and tumor weight less than 550 g to a no post-operative treatment group. This trial was stopped prematurely because of a stringent stopping rule after interim analysis which put the relapse free rate at 86.5 %.26 However, the overall survival was shown to be 98%. Therefore, the new COG trial (COG protocol AREN0532) continues a similar method to definitively resolve this issue. Owning to their adverse outcome in NWTS-5, COG AREN0532 also adds doxorubicin therapy to stage I, II FH tumors that demonstrate LOH at chromosome 1p and 16q. Patients with stage III Wilms tumors

<table>
<thead>
<tr>
<th>Study</th>
<th>Conclusions</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>NWTS-1</td>
<td>Post-operative radiotherapy was unnecessary for stage I disease.</td>
<td>D’Angio GJ, et al. (1976)24</td>
</tr>
<tr>
<td>NWTS-2</td>
<td>For stage I tumor; 6 months and 15 months of dactinomycin and vincristine had comparable efficacy. Addition of doxorubicin increased 2-year relapse-free survival in advanced stage disease</td>
<td>D’Angio GJ, et al. (1981)25</td>
</tr>
<tr>
<td>NWTS-3</td>
<td>For stage I tumors: 11 weeks of vincristine and dactinomycin was sufficient. Doxorubicin was unnecessary to treat stage II disease Radiation dose for stage III tumors could be reduced from 20 Gy to 10 Gy. Addition of cyclophosphamide did not improve prognosis for patients with stage IV FH tumors.</td>
<td>D’Angio GJ, et al. (1989)26</td>
</tr>
<tr>
<td>NWTS-4</td>
<td>Dactinomycin and doxorubicin could be given safely in pulse intensive regimens, which were associated with a reduced incidence of severe hematological toxicity. For stage II, III and IV tumors: a total duration of 6 months of chemotherapy was sufficient. Tumor spillage conferred an increased risk of local recurrence</td>
<td>Green DM, et al. (1998)27 Shamberger RC, et al. (1999)27</td>
</tr>
<tr>
<td>NWTS-5</td>
<td>Loss of heterozygosity for combined chromosomes 1p and 16q predicted recurrence of FH tumors. Children &lt;24 months old with small (&lt;550 g), stage I, FH tumors treated with nephrectomy only had a 2-year overall survival of 100%, but decreased relapse-free survival of 86.5%, which led to closure of this arm</td>
<td>Grundy PE, et al. (2005)28</td>
</tr>
</tbody>
</table>
receive aggressive therapy that comprises 24 weeks of vincristine, dactinomycin and doxorubicin (triple therapy) followed by 10.8 Gy of radiotherapy administered to the affected flank. For stage III tumors with LOH, current COG ARENO532 recommends this standard triple-therapy regimen plus cyclophosphamide and etoposide. Patients with stage IV tumors are given 24 weeks of triple therapy with 10.8 Gy of abdominal radiotherapy for local residual disease, and/or 12 Gy of whole-lung radiotherapy if lung metastases are visualized on chest radiography. In an ongoing COG ARENO532 trial, stage IV FH tumors with lung lesions are reassessed by chest CT after 6 weeks of chemotherapy. Those patients with a complete response finish the 24-week course without radiation therapy, whereas those who have persistent pulmonary metastases receive supplemental cyclophosphamide and etoposide as well as extra whole-lung radiation therapy.²

### International society of pediatric oncology

SIOP was established in the late 1960s and includes most European pediatric oncology centers and other centers worldwide. The SIOP trials and studies largely focus on the issue of preoperative therapy. Preoperative chemotherapy in SIOP trials has lead to refinements in a treatment strategy customized to the response of the tumor to preoperative chemotherapy. Table 3 summarizes the main conclusions of clinical trials conducted by SIOP.²⁵⁻³³

Nearly all patients with stage I–IV tumors receive chemotherapy before nephrectomy. Children without evidence of metastases are given 4 weeks of vincristine and dactinomycin, while those with metastases receive 6 weeks of pre-operative chemotherapy with vincristine, dactinomycin and doxorubicin. Post-operative therapy is tailored according to tumor staging.

After nephrectomy, children with stage I tumors usually receive a short post-operative treatment with 4 weeks of vincristine and dactinomycin without radiotherapy. Children with stage II and III tumors are treated with 27 weeks of adjuvant vincristine, dactinomycin and doxorubicin. Patients with stage II tumors and regional lymph node involvement, and all patients with stage III tumors, receive an additional 15 Gy of radiotherapy. Children with stage IV disease are initially started on vincristine, dactinomycin and doxorubicin, and then reassessed after 9 weeks. In the SIOP studies, only chest x-ray is used to evaluate lung metastasis. If lung metastases completely disappear within 9 weeks of initial treatment, patients do not receive lung irradiation. Those patients with complete remission finish the 27-week regimen, whereas those with incomplete remission are switched to ifosfamide, carboplatin, etoposide and doxorubicin for an additional 34 weeks.³

### Outcomes

Despite their different approaches, event-free survival (EFS) and overall survival (OS) outcomes of patients treated according to SIOP and COG protocols are similar. Regardless of the management strategy used, EFS vary substantially with tumor histology, stage, size, and the age of the patient at diagnosis. Table 4 summarizes the EFS and OS outcomes from recently reported large studies of Wilms tumor with FH characteristics.¹⁶,²³,²⁹,³⁰,³⁵,³⁶ Although the OS outcomes are

---

### TABLE 3. Summarizes the main conclusions of studies by the International Society of Pediatric Oncology.

<table>
<thead>
<tr>
<th>Study</th>
<th>Conclusions</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIOP-1</td>
<td>There was no difference in survival rate between the pre-operative radiation therapy and immediate surgery groups. Significantly fewer tumor ruptures occurred in the pretreated group, and the RFS was lower for patients who experienced intraoperative rupture.</td>
<td>Lemerle J, et al. (1976)³¹</td>
</tr>
<tr>
<td>SIOP-2</td>
<td>Patients treated with radiotherapy and 5 days of dactinomycin before surgery had a reduced rate of tumor rupture (5%) compared with those managed by primary resection (20%)</td>
<td>Graf N, et al. (2000)³²</td>
</tr>
<tr>
<td>SIOP-5</td>
<td>Pre-operative chemotherapy with vincristine and dactinomycin was as effective as radiation therapy with dactinomycin in preventing tumor rupture.</td>
<td>Lemerle J, et al. (1983)³³</td>
</tr>
<tr>
<td>SIOP-6</td>
<td>For stage I tumors, treatment with vincristine and dactinomycin was as effective for 17 weeks as for 38 weeks in terms of RFS and OS. Patients with stage II tumors and negative lymph nodes who did not receive radiotherapy had a higher recurrence rate than those who did receive it.</td>
<td>Tournade MF, et al. (1993)³⁴</td>
</tr>
<tr>
<td>SIOP-9</td>
<td>Pre-operative vincristine and dactinomycin was as effective for 4 weeks as for 8 weeks in terms of stage distribution and tumor shrinkage.</td>
<td>Tournade MF, et al. (2001)³⁵</td>
</tr>
<tr>
<td>SIOP-93-01</td>
<td>For stage I, intermediate-risk, anaplastic tumors, 4 weeks or 18 weeks of adjuvant chemotherapy resulted in similar event free survival at 2 years</td>
<td>de Kraker J, et al. (2004)³⁶</td>
</tr>
</tbody>
</table>

---

### TABLE 4. RFS and OS of Favorable Histology Wilms Tumor.

<table>
<thead>
<tr>
<th>Study</th>
<th>Stage</th>
<th>RFS/EFS (%)</th>
<th>OS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NWTS-3³⁵</td>
<td>I</td>
<td>92.5</td>
<td>97.6</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>89.6</td>
<td>92.9</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>80.4</td>
<td>86.2</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>76.5</td>
<td>79.5</td>
</tr>
<tr>
<td>NWTS-4³⁵</td>
<td>I</td>
<td>94.9 (2-year)</td>
<td>98.7 (2-year)</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>83.6 (8-year)</td>
<td>93.8 (8-year)</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>88.9 (8-year)</td>
<td>93.0 (8-year)</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>80.6 (2-year)</td>
<td>89.5 (2-year)</td>
</tr>
<tr>
<td>NWTS-5³⁶</td>
<td>I (age &lt; 24 months, tumor weight &lt; 550 g)</td>
<td>86.5</td>
<td>100</td>
</tr>
<tr>
<td>SIOP-9³⁵</td>
<td>I</td>
<td>88</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>II N0</td>
<td>85</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>II N1 and III</td>
<td>71</td>
<td>85</td>
</tr>
<tr>
<td>SIOP 93-01</td>
<td>I</td>
<td>88.3</td>
<td>97.0</td>
</tr>
</tbody>
</table>

**Abbreviations:** EFS: event-free survival; N0, no lymph node involvement; N1, lymph node involvement; NWTS, National Wilms Tumor Study; OS: overall survival; RFS: relapse-free survival; SIOP, International Society of Pediatric Oncology
low in patients with bilateral Wilms tumors, the 4-year survival rate in patients with bilateral, favorable histology Wilms tumor treated with renal salvage procedures is still 81.7%. By contrast, children with diffuse anaplastic histology have poor outcomes despite intensive therapy. In NWTS-5, patients with stage I tumors with diffuse or focal anaplasia had a 4-year EFS of only 69.5% and OS of 82.6% compared to 92.4% and 98.3% in patients with favorable histology. Moreover, for tumors with anaplastic histology, the OS worsens as the stage increases: 81.5% for stage II tumors, 66.7% for stage III, and just 33.3% for stage IV.

Advantages and disadvantages of the NWTSG and SIOP approaches

Although overall survival is similar with both the NWTSG and SIOP approaches to Wilms tumor treatment, each have distinct advantages and disadvantages. The primary strength of the NWTSG approach is that immediate nephrectomy allows accurate assessment on diagnosis including histology, molecular markers and tumor staging, on which further treatment stratification is decided. By contrast, the pre-treatment strategy in the SIOP approach makes surgery safer and more widely applicable by reducing tumor rupture rates, and increasing the proportion of children with a lower tumor stage (downstaging) requiring less overall treatment.

Most patients treated on the SIOP Wilms tumor studies do not undergo tumor biopsy before starting therapy. The diagnostic error rate in the ninth SIOP study was approximately 5% (28 of 511 patients). Twenty patients had malignant renal neoplasms of other types. However, the risk of administering chemotherapy to a patient with benign tumor was low, affecting only 1.5% and 1.6% of patients in the SIOP-6 and SIOP-9 trials, respectively. The resolution to this particular argument could be provided by the adoption of the United Kingdom Children’s Cancer Study Group (UK CSG) approach of percutaneous needle biopsy before therapy starts which reduced the risk of diagnostic error to virtually zero and did not appear to be associated with an increased risk of local recurrence or upstaging.

The primary strength of the SIOP approach is that pre-operative chemotherapy usually reduces the tumor volume, thereby decreasing the frequency of tumor rupture and spillage of malignancy into the abdominal cavity. As a result, fewer patients received local irradiation on SIOP-9 than on NWTS-5. The frequency of spill in SIOP-5 was 6% compared to a much higher rate of 20% in comparable stage patients in NWTS-4. Although, on current data, the survival rate for patients suffering tumor spillage has not been statistically significantly worse than the rate of non-spill patients (92% vs. 94%, respectively), the relapse rate is higher. Clearly, it is better to avoid the medical and psychological burdens for the patients and family that occur after recurrence.

Another advantage claimed by the proponents of pre-operative therapy is the downstaging of patients which leads to reduction in surgical complications and overall treatment toxicity. Certainly, SIOP has a higher proportion of stage I patients in their studies, but this does not truly reflect the stage at diagnosis. The pre-operative therapy can mask pre-existing or residual tumor deposits, for example, in lymph nodes. This is particularly important when stage III, favorable histology tumors are downstaged to stage II, favorable histology tumors. The SIOP-6 trial had a proportion of stage II, node negative patients relapsing locally in the non-irradiated arm, indicating possible occult stage III at the time of surgery. This has led SIOP investigators to cover unirradiated SIOP stage II children by adding an anthracycline to the basic two agents, daunomycin and vincristine. This is done even though many of the children are true stage II patients and, therefore, receive the cardioactive agent unnecessarily.

The advantage of the NWTSG approach is that immediate nephrectomy allows an accurate assessment on histology and molecular study especially the presence of allele loss at specified loci which identifies a higher risk group which needs more intensive therapy. Preoperative chemotherapy can be so effective as to lead to total necrosis of all the tumor cells in the operative specimen. In contrast, SIOP see an advantage on the modification of tumor histology from pre-operative chemotherapy. This allows individualized assessment of tumor response to chemotherapy and allows a new histological classification for treatment. The use of radiotherapy and anthracyclines may be restricted to patients whose tumors do not respond adequately to first-line pre-operative chemotherapy.

Another difference between the NWTSG and SIOP studies is the management of lung metastases. The NWTSG approach recommends whole-lung irradiation for all cases with lung metastases, regardless of the speed of response. The 2-year relapse free survival for patients with stage IV disease treated on NWTS-4 was 81%. In the SIOP studies, if lung metastases completely disappeared with chemotherapy or surgical resection, patients did not receive lung irradiation. As a result, fewer patients received local irradiation on SIOP. This policy has reduced the proportion of patients receiving pulmonary irradiation to approximately 15%. With this approach, SIOP reported a 4-year EFS rate of 83%.

CONCLUSION

Continued cooperation as part of national and international study groups have been substantially improving the outcome of Wilms tumor. Although, the NWTSG and SIOP approaches are different, both focus on risk-based management that aims to reduce treatment morbidity while preserving survival in patients with low-risk tumors, and to improve the survival in individual patients with high-risk disease. Understanding the advantages and disadvantages of each approach, individual physicians and institutions can select the method that seems best suited to their patients and the capability of each institution.

REFERENCES


