小児腎がんの予後改善 (Abstract 10009)

標準治療の強化により高リスクのWilms腫瘍の治癒率が上昇する

Augmenting standard therapies increase cure rates for high-risk Wilms tumor

2つの第III相試験の結果、薬剤を追加することによる治療強化は高リスクWilms腫瘍の小児の予後を改善する、と第51回American Society of Clinical Oncology年次集会で発表された。このスタディは、いわゆる予後良好な組織型のWilms腫瘍（小児腎腫瘍の75%を占める）の小児に焦点を当てた。これらの腫瘍のうち、約5～6%が染色体1pと16qにヘテロ接合性の消失（LOH）として知られる染色体異常を腫瘍内に有していた。研究者らは過去に、LOH 1pおよび16qを有する患者は再発リスクが高いことを明らかにした。LOH 1pおよび16qはステージI/IIの患者35人、およびステージIII/IVの患者52人において検出された。ステージI/IIの患者に対しては標準治療（ビンクリスチン／アクチノマイシンDによる化学療法）にドキソルビシンを追加し強化された。ステージIII/IVの患者はRegimen M（ビンクリスチン／アクチノマイシンDによる化学療法および放射線療法）に4サイクルのシクロフォスファミド／エトポシドの外来での投与を追加することにより強化された。先行研究では、これらの患者の4年無再発生存率はステージI/IIで74.9%であり、ステージIII/IVでは65.9%であった。今回の新たなスタディにおいて、強化療法はこの率をステージI/IIで83.9%、ステージIII/IVで91.5%に上昇させた。

Full Text

Two phase III Children's Oncology Group studies found that augmenting therapy with additional drugs improves outcomes for children with a high-risk form of Wilms tumor according to researchers at the American Society of Clinical Oncology's 51st Annual Meeting. These patients have a specific chromosomal abnormality associated with poorer prognosis. In prior research, such patients had four-year relapse-free survival rates of 74.9% for stage I/II disease and 65.9% for stage III/IV disease. In the new studies, augmented therapy increased the rates to 83.9% for stage I/II and 91.5% for stage III/IV disease.

"Tailoring therapy to match each patient's risk for relapse has been a major focus of pediatric oncology. For cancers with a low risk of recurrence, we strive to decrease therapy and minimize exposure to potentially toxic agents. On the other hand, we want to augment the therapy for those patients who are at higher risk of relapse so that we can hopefully increase the chance for cure," said lead study author David B. Dix, M.D., a physician at the British Columbia Children's Hospital in Vancouver, Canada. "Our study is an example of successful augmentation of therapy for a higher risk group. We were very encouraged to see that augmentation of therapy can overcome the negative influence of a biologic marker in children with Wilms tumor."

Wilms tumor is a rare form of kidney cancer that mainly affects children under the age of five years. This study focused on children with so-called favorable histology Wilms tumor, which accounts for 75% of childhood renal cancers. Of those, about 5-6% of have a chromosome abnormality in the tumor that is known as loss of heterozygosity (LOH) on chromosomes 1p and 16q. Researchers previously found that patients with LOH 1p and 16q have a higher risk of relapse.

In the studies, LOH 1p and 16q was detected in 35 patients with stage I/II disease and 52 with stage III/IV disease. For patients with stage I/II disease, the standard therapy (vincristine/dactinomycin chemotherapy) was augmented with the addition of doxorubicin. Patients with stage III/IV disease received Regimen M: the standard therapy (vincristine/dactinomycin/doxorubicin and radiation therapy) was augmented with 4 cycles of outpatient cyclophosphamide/etoposide.

At a median follow-up of 3.6 years, the four-year relapse-free survival rates were 83.9% for stage I/II disease and 91.5% for stage III/IV disease. When comparing these rates to outcomes with standard treatment regimens (75% for early- stage disease and 66% for late-stage disease), these studies suggest that augmentation of therapy markedly improves outcomes for patients with advanced disease. Given the small numbers in the study sample, the benefit is less clear for patients with lower stage disease but suggestive of an improved outcome.

Overall, the treatment was well tolerated. For stage I/II patients, augmented therapy was not associated with any significant short term increase in side effects. For stage III/IV patients, the most common severe side effect of Regimen M was suppression of bone marrow function, occurring in 60% of patients; however, the side effect was manageable. According to the authors, Regimen M substantially reduces the number of patients who would otherwise have to undergo very intensive relapse therapy. However, the regimen is predicted to be associated with some risk of reduced fertility. The authors recommend a clear discussion with families regarding the risks and benefits of augmented therapy for these higher risk patients with LOH.

ASCO President-Elect Julie M. Vose, M.D., MBA, FASCO commented on the study: "It's very encouraging that we're making progress even for kids with a rare, high-risk form of this disease. The ability to easily identify a small subset of patients with a poorer prognosis means these children can receive treatment that's right for them, while decreasing side effects for lower risk patients. And that means a better shot at surviving their cancer."

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