**Supplemental file 1**

In SIOP-WT-2001, Stage V was defined as both sides WT (BWT), andboth sides hyperplastic nephrogenic rest (nephroblastomatosis - NB) or one-sided WT+ contralateral NB

The study included specific recommendations for these bilateral diseases, particularly for Bilateral Wilms Tumors as follows:

1. A complete clinical examination to detect specific anomalies indicating a possible underlying predisposition syndrome.
2. A complete radiological examination by computed tomography (CT) and/or magnetic resonance imaging (MRI) was strongly recommended to establish the number, size, aspects and extension of the tumors at diagnosis and during follow-up. Indeed, for small nodular lesions, it is highly important to try to distinguish Wilms tumor and Nephrogenic rests.

3) The treatment was first line-prolonged chemotherapy by vincristine (VCR) + actinomycin-D (VA) (Vincristine 1.5mg/m²; (max 2mg, weekly), plus Actinomycine D 45µg/kg (max 2mg, every 2 weeks). This chemotherapy had to be performed as long as the tumors showed signs of regression and up to the time of kidney sparing surgery if possible. The response assessment was carried out every four weeks. In the event of continuous response, chemotherapy was continued with VA. The duration of chemotherapy had to be geared to its effectiveness as checked by imaging procedures. If the response was insufficient, a modification of chemotherapy could be discussed: adding Doxorubicin (50mg/m² every 6 weeks, so VAD), or replacement by another association as etoposide (VP16) 150 mg/m² + Carboplatin 200mg/m,² for 3 consecutive days.

4) Surgery was planned after optimal tumor reduction by pre-operative chemotherapy. Both the best kind of surgery and the best time to operate was decided by a multidisciplinary committee (oncologist, radiologist and surgeon). The aim of surgery was to obtain a sufficient nephron sparing surgery with a carcinologic efficacy. If possible, it was recommended to perform bilateral partial nephrectomy or wedge resections to preserve functional renal tissue. A CT scan prior to surgery was mandatory to assess the feasibility of partial resection. Complete nephrectomy on one side with NSS on the opposite side could be a good solution, providing enough functional renal tissue can be preserved (9).

An experienced surgeon in renal parenchymal-sparing procedures were advised to participate to the discussion and it was advised pursue surgery in a center specialized in the treatment of bilateral cases and with a lot of experience in NSS.

5) The post-operative chemotherapy was according to the highest stage and the highest- histology risk group of the lesions. The dose of Doxorubicin was adapted according to the preoperative chemotherapy given, and was recommended not to exceed a total dose of 300 mg/m2. During treatment, a secure follow up imaging with short intervals was recommended.

6) Radiotherapy in the treatment of bilateral WT was recommended in local stage III cases, as, in the previous SIOP-9 Study, incomplete surgery followed by low-dose (10 Gy) radiotherapy and chemotherapy may result in a long-term remission [10].

7) For BWT, the follow-up was recommended as follow: every 2 months for the first year and second year with chest X-ray and US every time; every 3 months for the third and fourth year with sonography every time. A long follow-up with annual US was recommended up to 8 years.

Renal function should be checked at 3 months, 1 year and 3 years after surgery. According to the results, the follow-up was planned by the pediatric nephrologist.

Concerning nephroblastomatosis, guidelines were as follow:

1) Chemotherapy first:

Nephroblastomatosis to be treated with a combination of vincristine-actinomycin D as in stage I WT. The duration of chemotherapy had to be geared to the response documented by

imaging. As long as the NB shrinked, the treatmentwas advised to be continued.

2) Rarely, surgery was advised to be performed in these particular situations:

- if there was stabilization or progression of lesions in spite of chemotherapy

- if a nodular spherical lesion appeared within the initial lesion

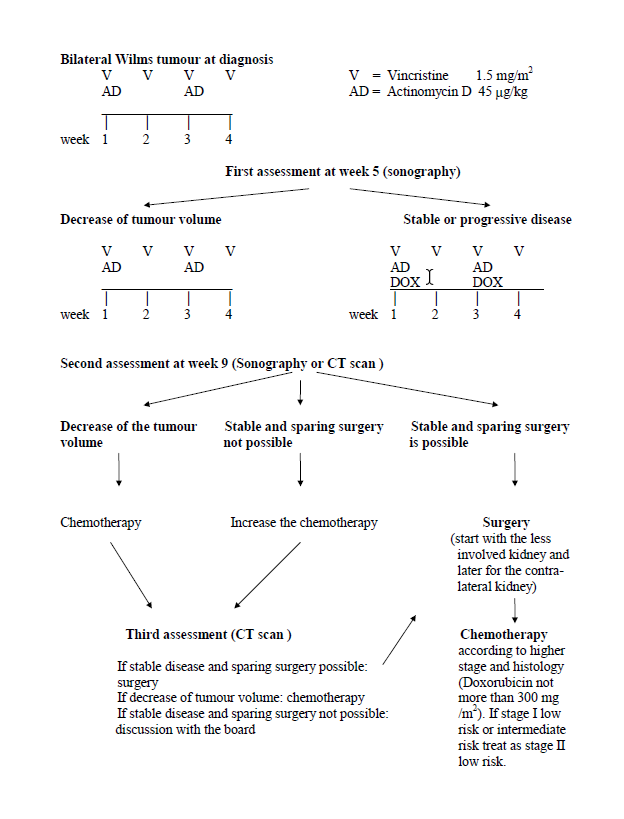
- if the lesion became heterogeneous

Partial nephrectomy or wedge excision of the lesion to be performed as in the case of bilateral

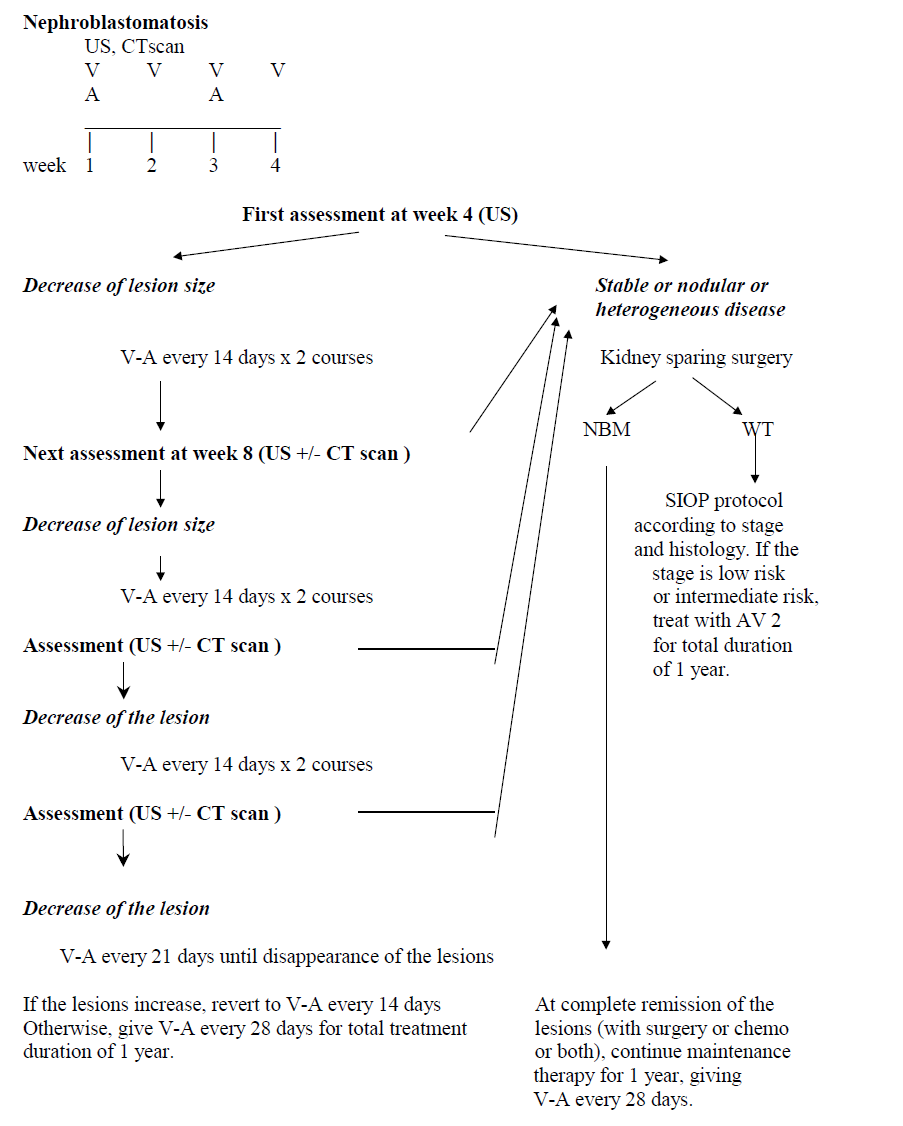
Wilms tumour.

3) Even, when the lesions had disappeared with chemotherapy or chemotherapy plus surgery, a maintenance therapy to be continued to a total duration of 1 year from diagnosis

**Below, the scheme for BWT p151 of Nephroblastoma clinical trial and study SIOP 2001 PROTOCOL**



**Below, the scheme for nephroblastomatosis , p 155 of Nephroblastoma clinical trial and study SIOP 2001 PROTOCOL**

****