

Wilms Tumor

Bilateral and Predisposition Syndromes

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AGENDA

1

Historical Context

2

Treatment Algorithms

3

Modern Outcomes

4

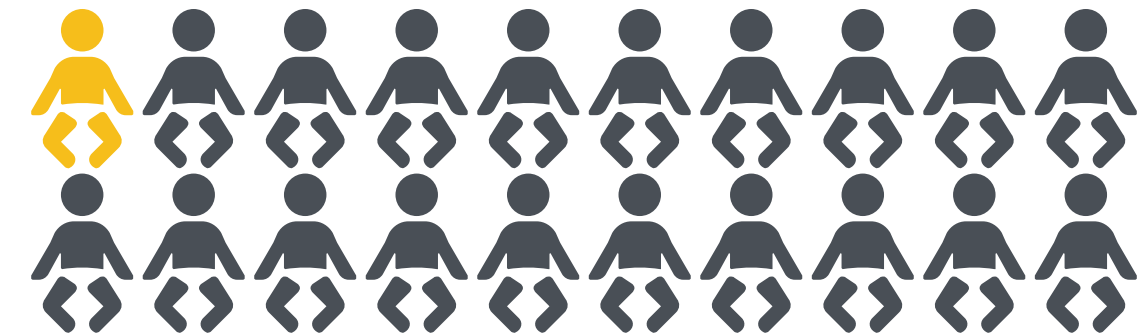
Surveillance

Recommendations

Prevelance



10% Predisposition
Syndrome



5% Bilateral



WT Predisposition Syndromes

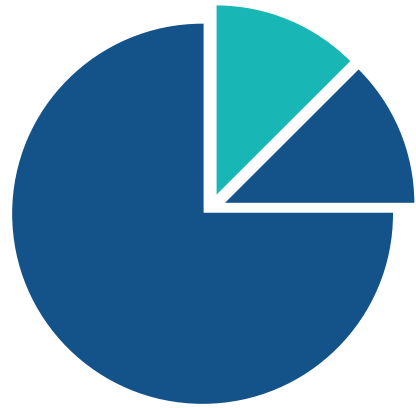
Syndrome	WT Risk (%)	Features
WAGR	50	WT, Aniridia, GU anomalies, MR
Denys-Drash	50-90	XY DSD, Hypospadias, UDT, Renal Failure
Perlman	30-60	Macrocephaly, UDT, GDD
Beckwith-Weidemann	5-10	Hemihypertrophy, Macroglassia



COG Renal Tumor Staging

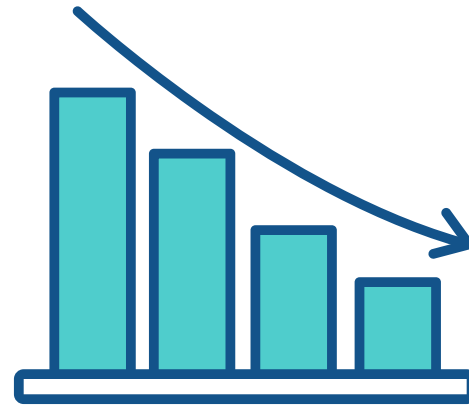
STAGE I	STAGE II	STAGE III	STAGE IV	STAGE V
Confined to kidney Negative margin N0	Spread beyond kidney Negative margins N0	+ Surgical margin Preop biopsy Tumor rupture or spillage +LN Peritoneal involvement Neoadjuvant chemotherapy	M+	Bilateral Tumors

Historical Outcomes



ERSD

~10% BWT
Highest in
predisposition
syndromes



Survival

EFS 60% vs
>85%
OS 80% vs >90%



Relapse

Earlier
relapse:
Months vs
Years



Why Poorer Outcomes?

1

No Protocol
Lack of dedicated
treatment protocols

2

Inappropriate
Therapy
Not modified based
on histology

3

Increased
Anaplasia
Higher rates of
unfavorable
histology

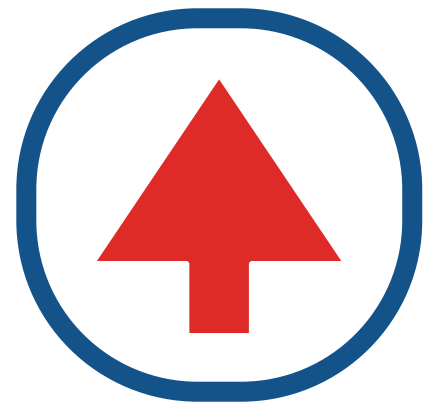
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Surgical Delay
Delay in local
disease control

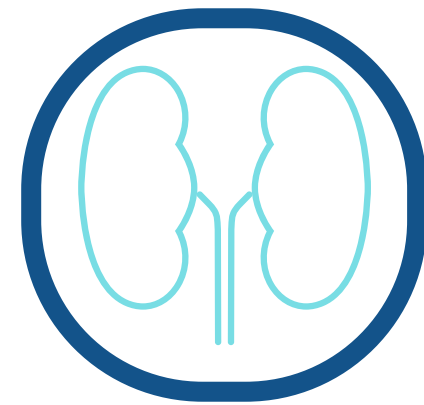
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Prolonged
Treatments
Protracted
Chemotherapy

AREN0534: Treatment for Patients with Bilateral, Multicentric, or Bilaterally-Predisposed Unilateral Wilms Tumor



Improve EFS and OS



Preserve Renal Tissue



Decrease Treatment Burden

Facilitate partial nephrectomy using pre-operative chemotherapy, complete definitive surgery by 12 weeks from diagnosis, and modify post-operative chemotherapy based on histologic response.

Pretreatment Tumor Biopsy

Pros

Confirm Histology

Detect Anaplasia

Cons

Poor Anaplasia
Detection

Staging Impact

Indications

Unusual Clinical
Scenario

Age >10

Atypical Features



Pretreatment Tumor Biopsy



XRT Exclusion

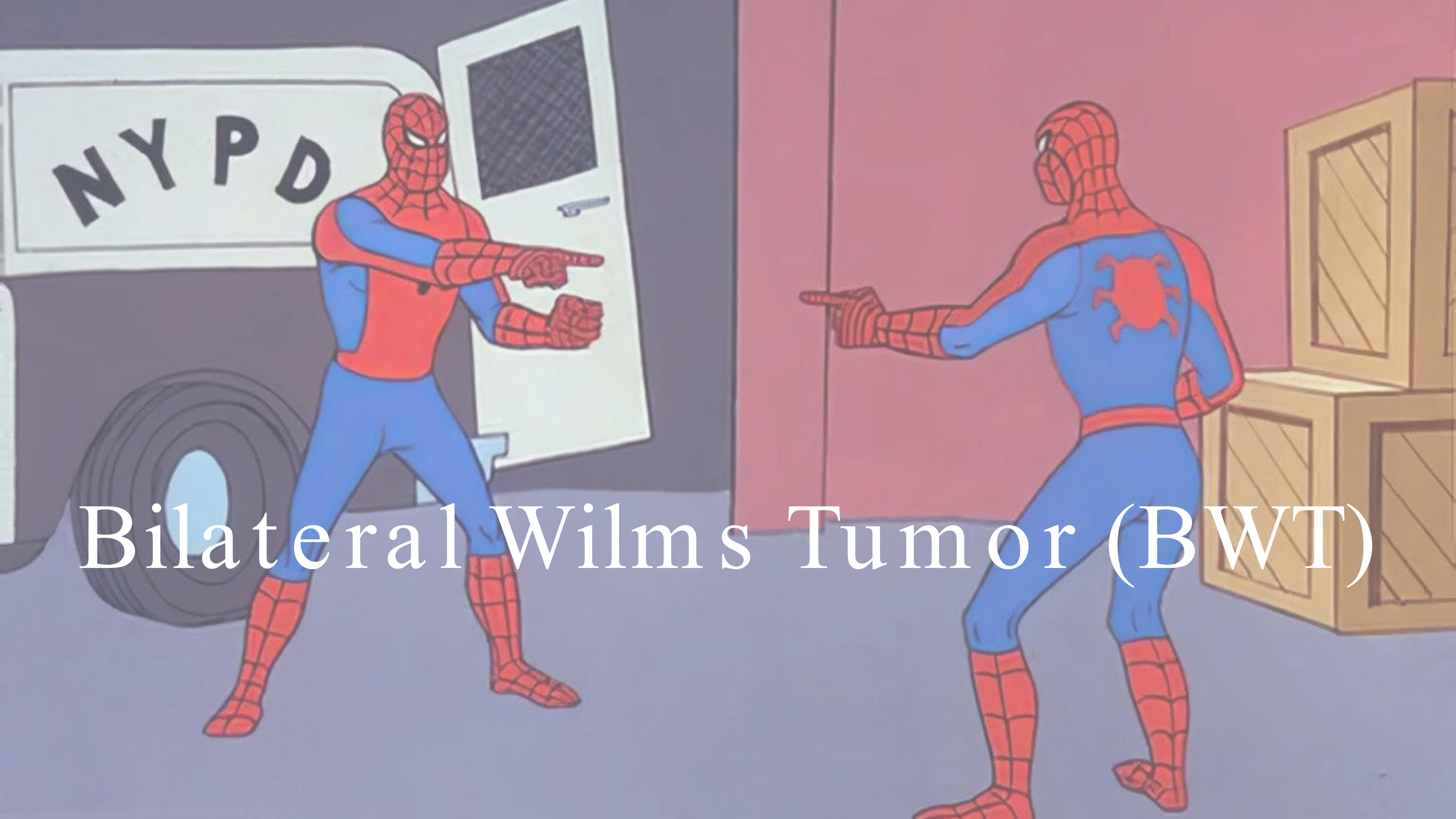
*Must be FH
No other
qualifying
criteria



Percutaneous

Posterior
approach
preferred





Bilateral Wilms Tumor (BWT)

BWT Initial Management: AREN0534

VAD Chemotherapy x6 weeks: Repeat CT/MRI

NO

Complete response in both kidneys?

YES

Bilateral partial nephrectomy feasible?

Start EE-4A

YES

NO

Greater than partial response in both kidneys?

Definitive Surgery

YES

NO

Bilateral Open Biopsy

6 More Weeks Chemotherapy

YES

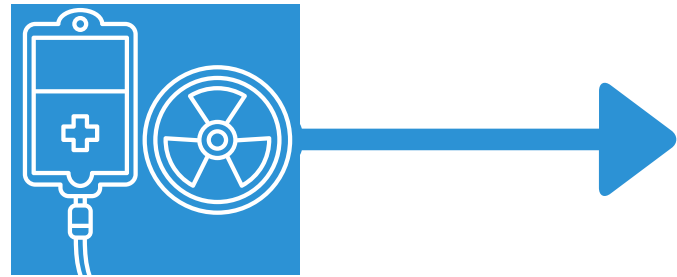
Complete response in both kidneys?

NO

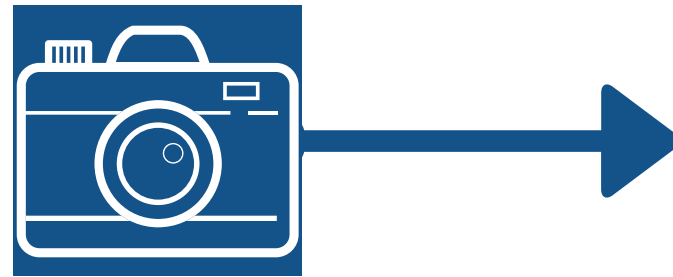
Start DD-4A

Definitive Surgery

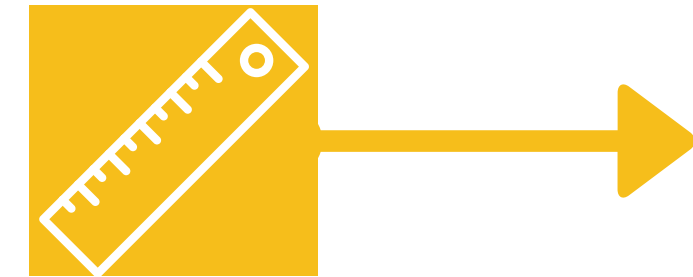
First Steps



Neoadjuvant
Chemotherapy
VAD for 6 weeks



Re-image
Assess response
after 2 cycles (6-
weeks)



Measure
Response
RECIST Criteria



RECIST Criteria

Resolution of all target lesions

Complete
Response

$\geq 30\%$ reduction in sum of
diameters of target lesions

Partial
Response

Progressive
Disease

20% increase in sum of
target lesion diameter or
new lesion

Stable Disease

No change to
qualify for PR
or PD

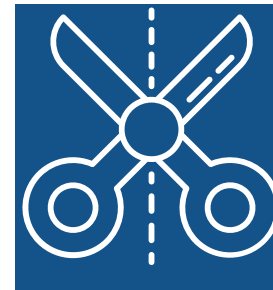


6-Week Assessment



Complete
Response

VA Chemotherapy
19 weeks



NSS
Appropriate

Bilateral Partial
Nephrectomy



Not NSS
Appropriate

>PR: Continue
chemotherapy 6
more weeks
<PR: Open biopsy

NSS Not Possible After 6-Weeks

<PR: Open Biopsy

Blastemal:
Regimen 1

Anaplasia: UH-1

All other
histologies: VAD

DEFINITIVE
SURGERY 12
WEEKS

≥PR

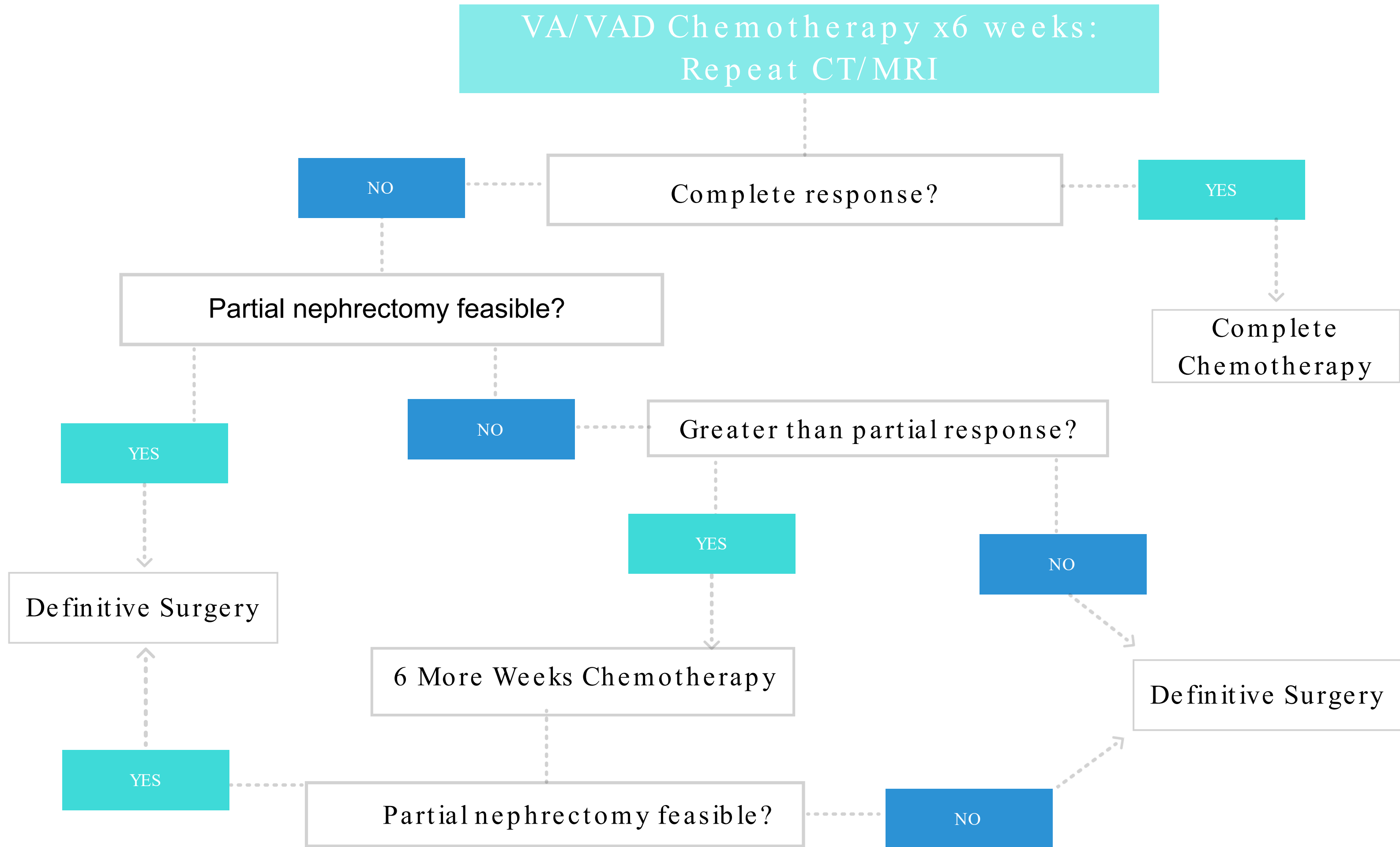
VAD 6 more
weeks



A blurred road with a 'RISK AHEAD' sign. The background shows a road curving through green fields under a blue sky with light clouds. A yellow diamond-shaped sign with a black border and two pairs of black dots at the top and bottom corners is mounted on a blue post. The sign contains the text 'RISK AHEAD' in bold, black, sans-serif capital letters.

Unilateral, Predisposition Syndromes

Unilateral Tumors (Predisposition Syndrome)/ Multicentric Tumors/ Solitary Kidney



First Steps



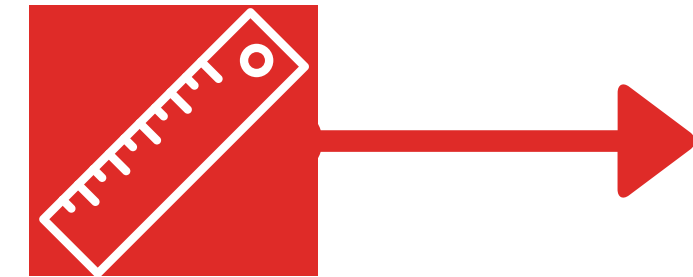
Neoadjuvant
Chemotherapy

VA (non -
metastatic) or VAD
for 6 weeks



Re-image

Assess response
after 2 cycles (6-
weeks)



Measure
Response

RECIST Criteria

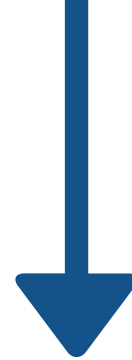
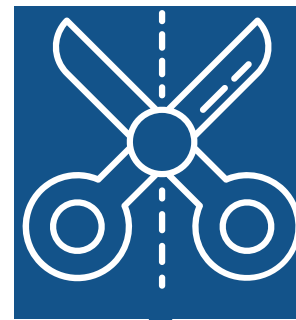


6-Week Assessment



Complete
Response

VA Chemotherapy
19 weeks



NSS
Appropriate

Partial
Nephrectomy



Not NSS
Appropriate

>PR: Continue
chemotherapy 6
more weeks
<PR: Radical or
Partial Nx



Surgeon

Checklist

Partial Nephrectomy

Ureteral Stent

Warm Ischemia/Parenchymal Compression

Avoid Vascular Clamping

Margins vs Enucleation

LNS Bilaterally

Drain

Surgeon Checklist

Radical Nephrectomy

BWT: Not Amenable to NSS at 12 weeks

Unilateral Predisposition: PD at 6 weeks

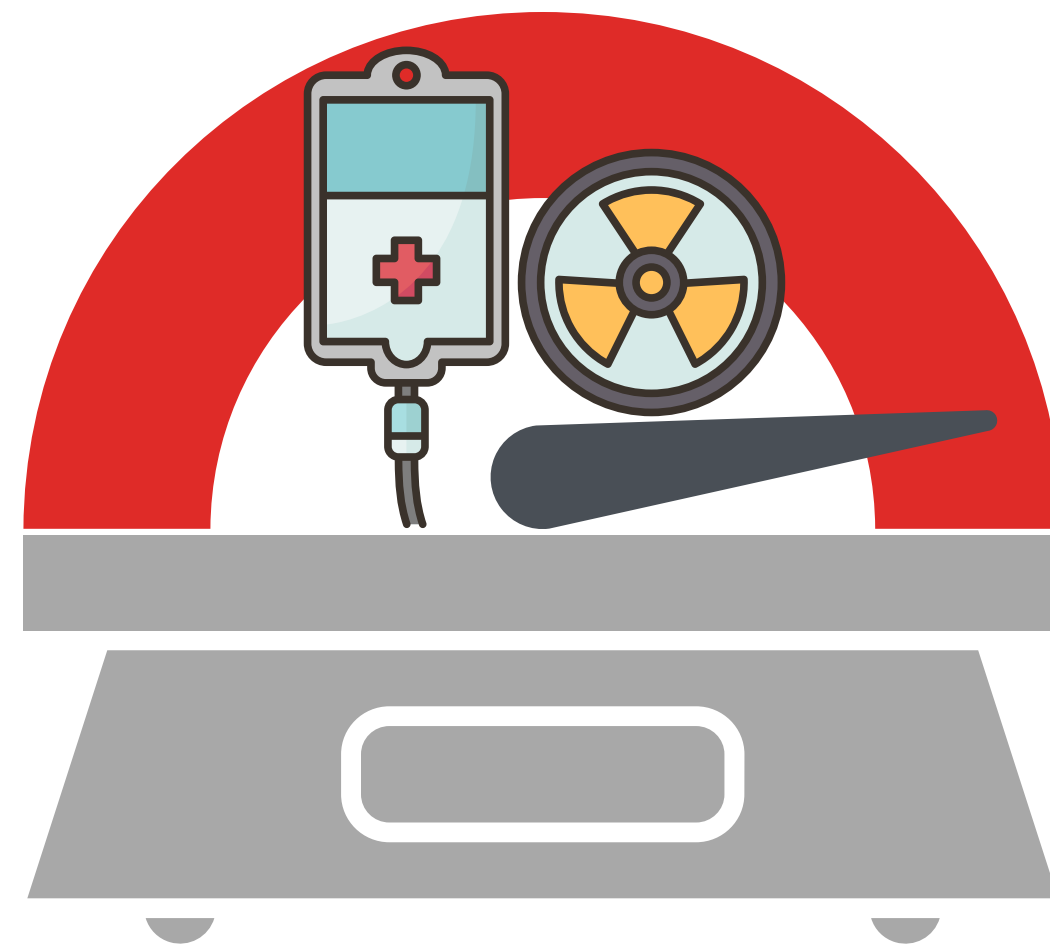


Adjuvant Chemoradiation Therapy



Stage 1/2

Non-blastemal
predominant



Stage III

Blastemal predominant

*Molecular biomarkers NOT

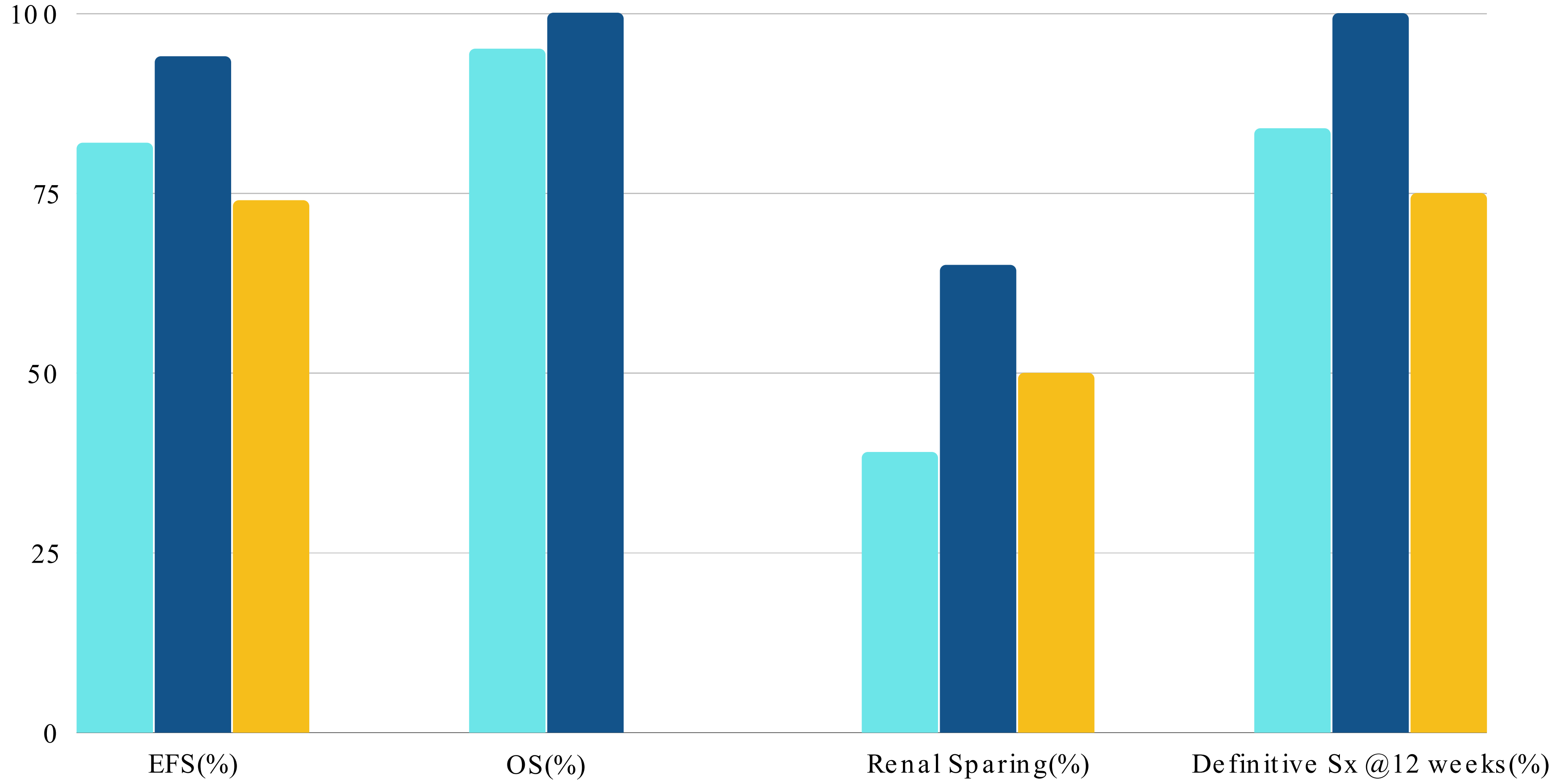


Chemoradiation Therapy Regimens

Name	Regimen	Duration
Induction	Vincristine, dactinomycin, +/- doxorubicin (VA/VAD)	6 - 12 weeks
EE-4A	Vincristine, dactinomycin (VA)	19 weeks
DD-4A	Vincristine, dactinomycin, doxorubicin, radiation	25 weeks
Regimen-1	Vincristine, doxorubicin, cyclophosphamide, etoposide, radiation	28 weeks
Revised UH-1	Vincristine, doxorubicin, cyclophosphamide, carboplatin, etoposide, radiation	31 weeks

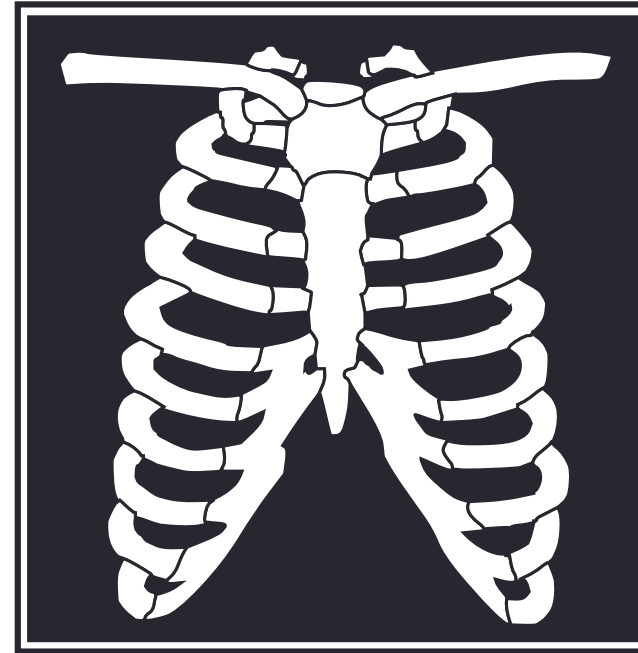
AREN0534 Results

■ BWT ■ Predisposition ■ Study Goal





Surveillance



Years	Frequency
1-2	q3 months
3-4	q6 months



Atrium Health
Levine Children's

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