

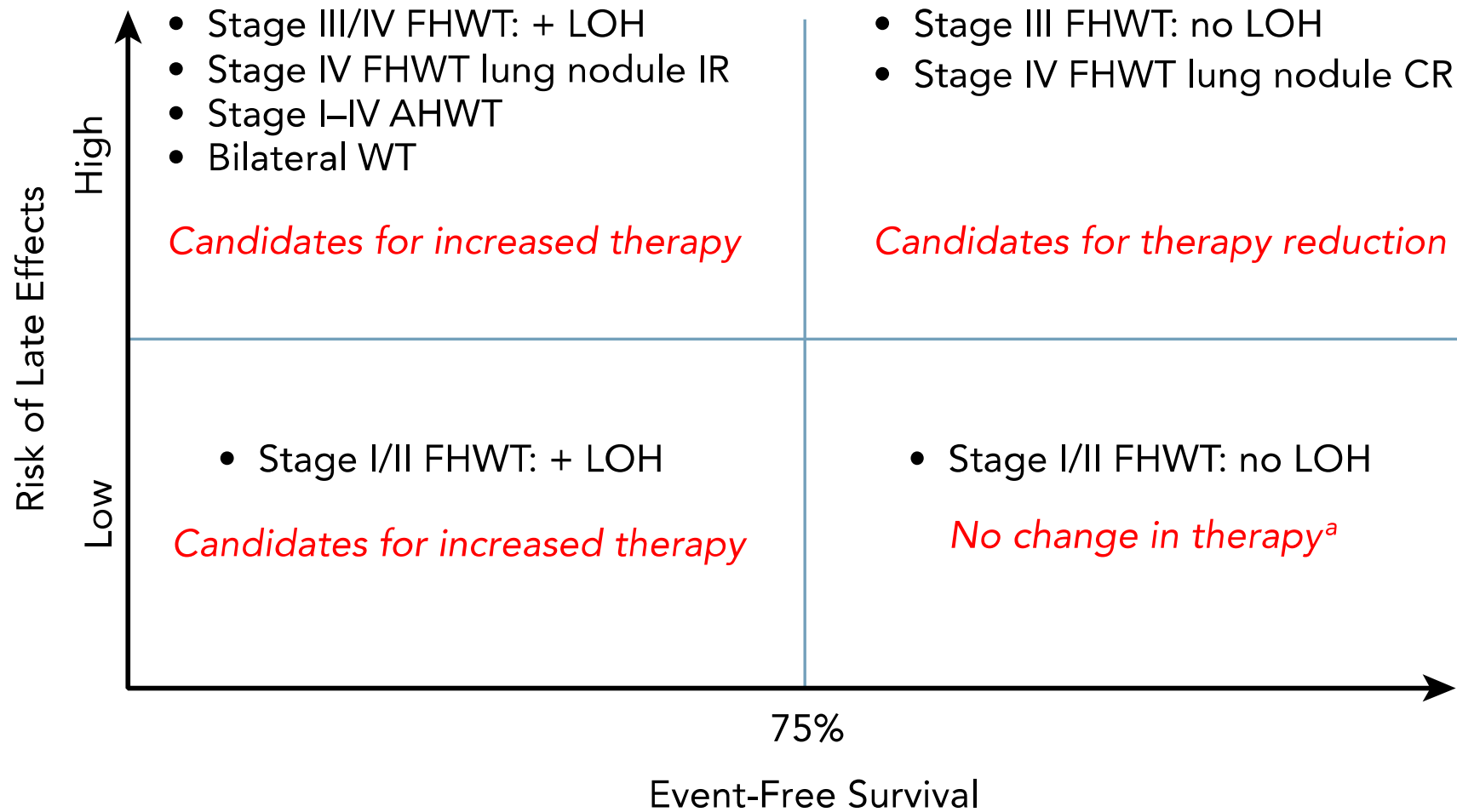
Results of recent COG trials for renal tumors (AREN studies)

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All Renal Tumors
(& Extra-renal Wilms or Extra-renal/Extra-CNS Rhabdoid)

SURGERY

**Very Low
Risk
Standard**

Regimen EE4A
Vincristine
Dactinomycin

Regimen DD4A
Vincristine
Dactinomycin
Doxorubicin

**Higher Risk
FHWT**

Regimen M
Vincristine
Dactinomycin
Doxorubicin
Cyclophosphamide
Etoposide

**Bilateral
and Bilaterally
Predisposed**

AREN0534

Tumor Bank

High Risk
UHWT, CCSK,
RTK, RCC

Regimen UH1
Cyclophosphamide
Carboplatin
Etoposide
Vincristine
Doxorubicin
Cyclophosphamide
Radiation therapy

Other
Low Risk WT
CMN, CN, etc

AREN03B2

Very low risk FH WT (AREN0532)

Age < 2 years
Tumor weight < 500g
NO predisposition syndrome
Stage I only
* Had LN sampled

Treated with nephrectomy alone

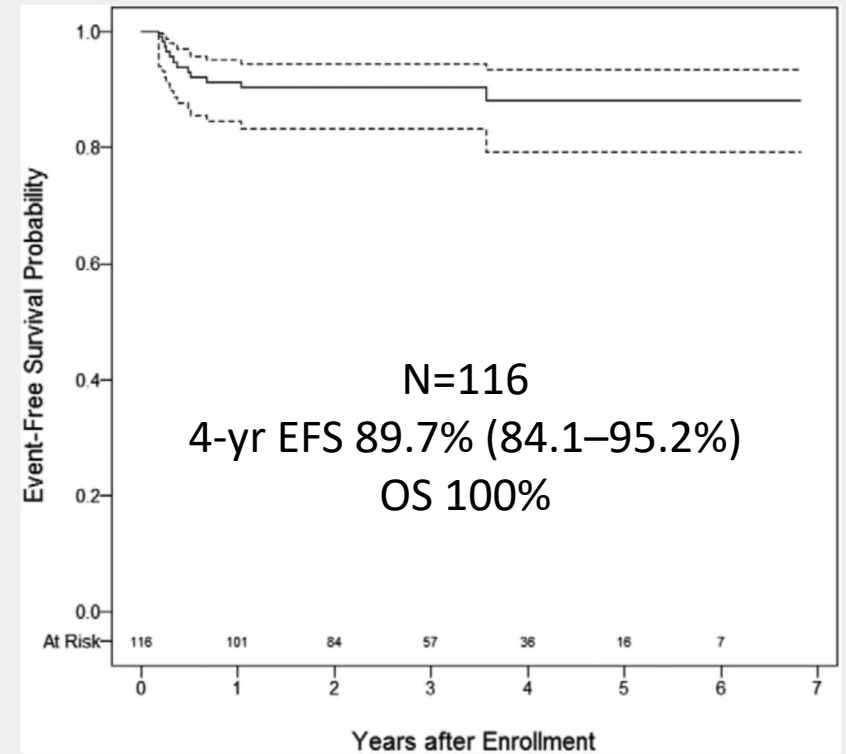


FIGURE 1. Event free survival for very low-risk Wilms tumor patients managed by observation alone after nephrectomy (solid line; dashed lines 95% confidence intervals).

AREN 0533
Higher risk

***Stage IV FH WT
(lung mets only)***

No LOH 1p/16q

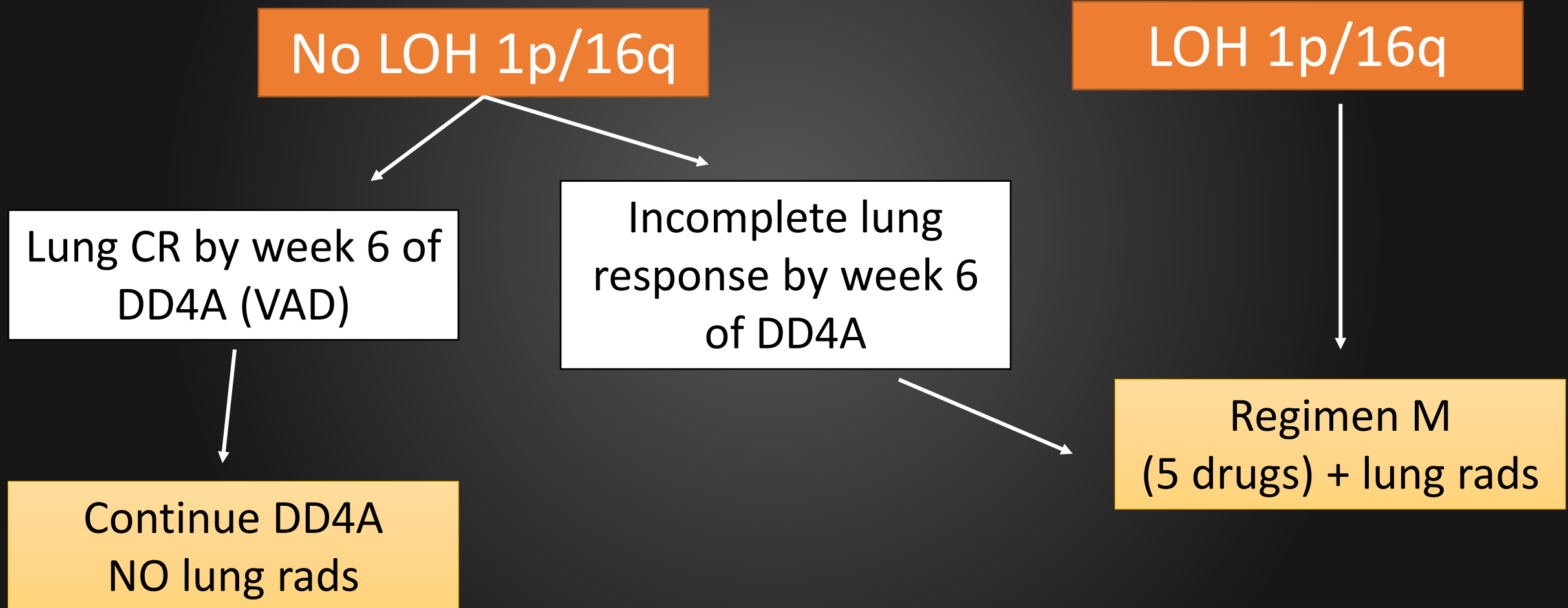
LOH 1p/16q

Lung CR by week 6 of
DD4A (VAD)

Incomplete lung
response by week 6
of DD4A

Continue DD4A
NO lung rads

Regimen M
(5 drugs) + lung rads



Treatment of Stage IV Favorable Histology Wilms Tumor With Lung Metastases: A Report From the Children's Oncology Group AREN0533 Study

JCO 2018

David B. Dix, Nita L. Seibel, Yueh-Yun Chi, Geetika Khanna, Eric Gratas, James R. Anderson, Elizabeth A. Mullen, James I. Geller, John A. Kalapurakal, Arnold C. Paulino, Elizabeth J. Perlman, Peter F. Ehrlich, Marcio Malogolowkin, Julie M. Gastier-Foster, Elizabeth Wagner, Paul E. Grundy, Conrad V. Fernandez, and Jeffrey S. Dome

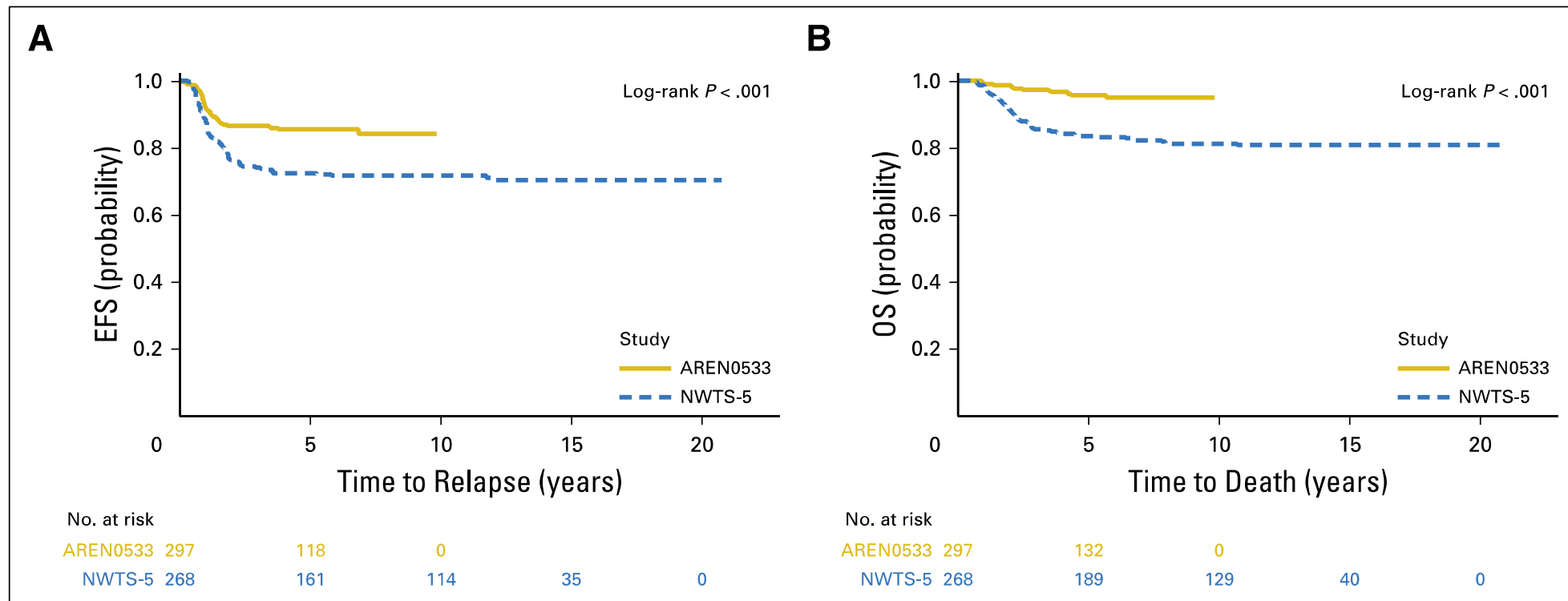


Fig 5. (A) Event-free survival (EFS) and (B) overall survival (OS) for patients with isolated pulmonary metastases in AREN0533 compared with NWT5-5.

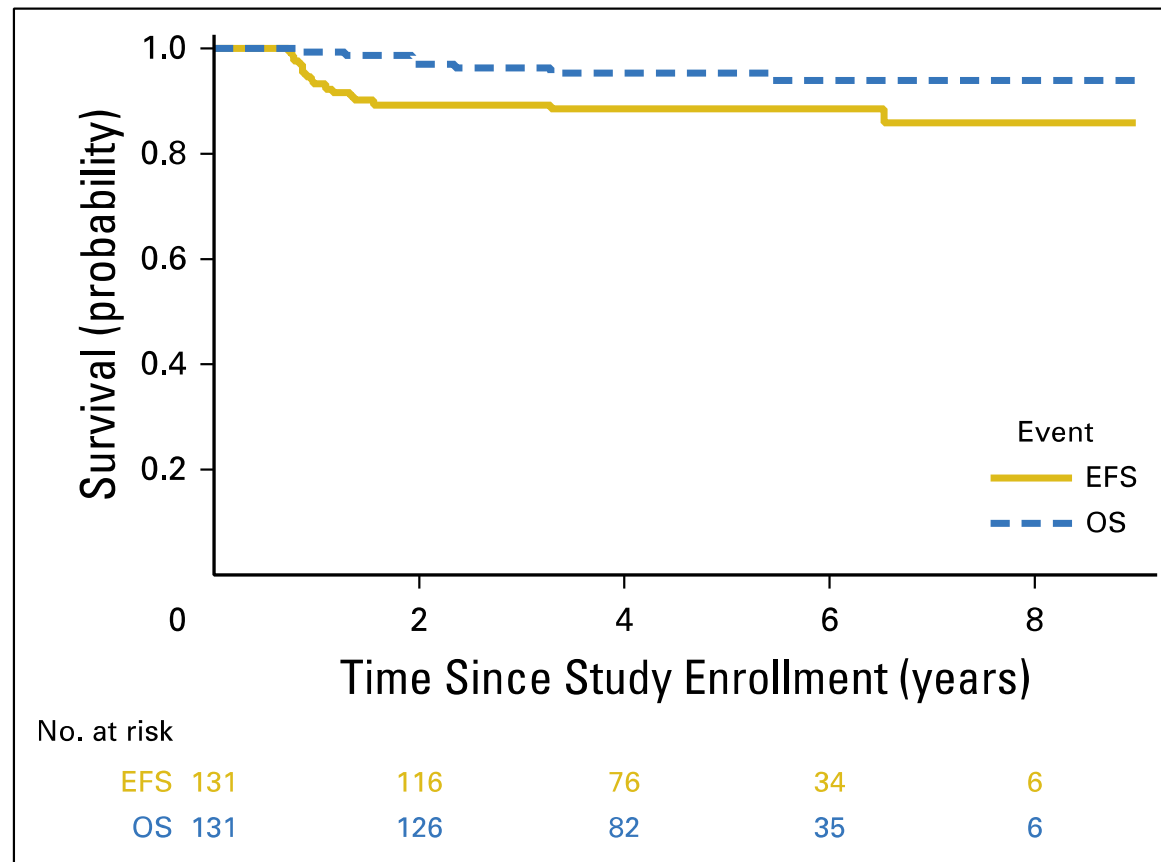
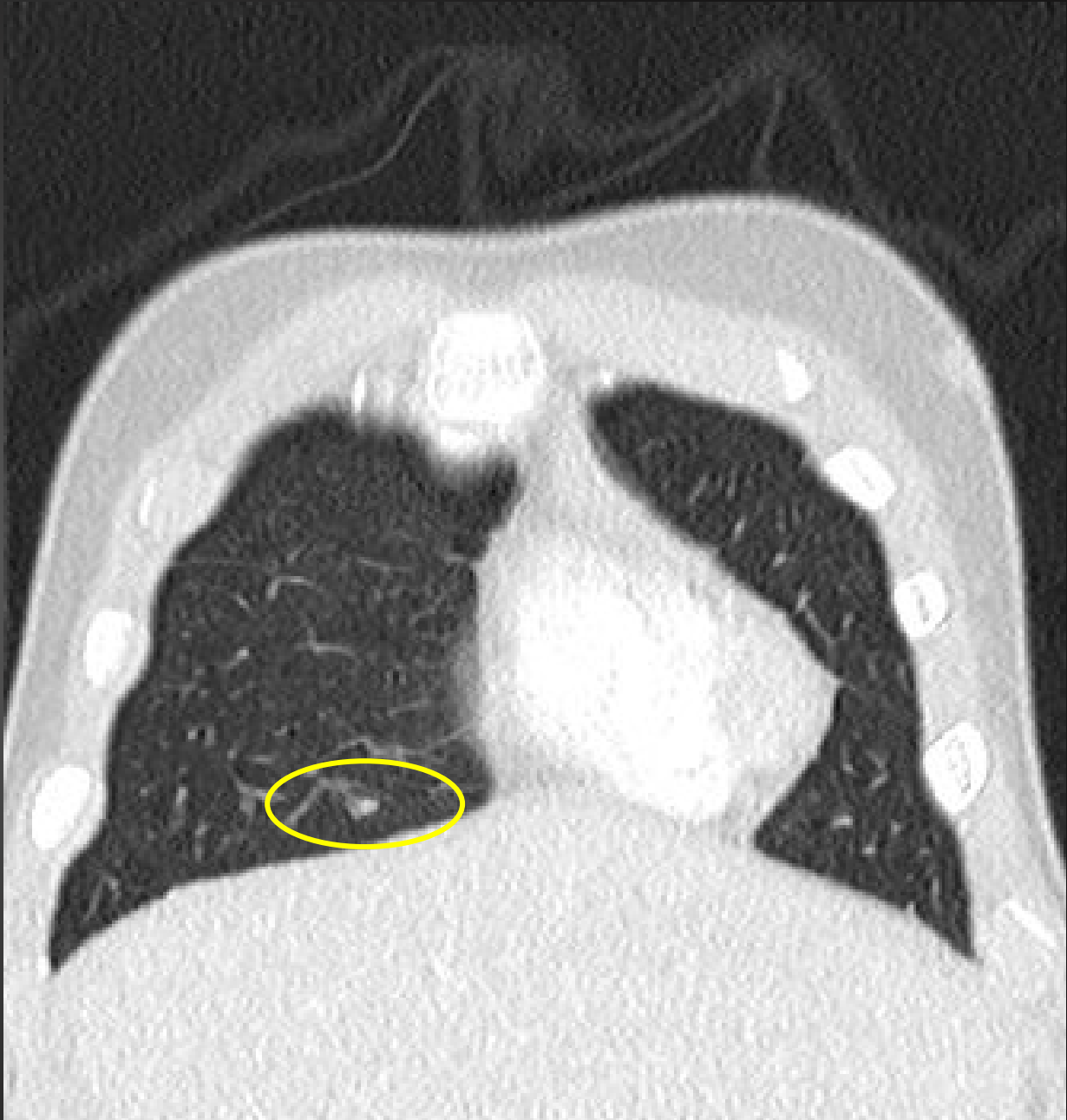


Fig 4. Event-free survival (EFS) and overall survival (OS) for patients with incomplete lung nodule response without loss of heterozygosity who completed treatment with lung radiation therapy and four cycles of cyclophosphamide/etoposide in addition to vincristine/dactinomycin/doxorubicin.

Table 1. Outcomes According to 1q Gain Status

Group	No. (%)	4-year EFS, % (95% CI)	<i>P</i>	4-year OS, % (95% CI)	<i>P</i>
Incomplete lung nodule response					
1q gain+	42 (36.2)	86 (72.2 to 99.3)	.15	93 (83.1 to 100)	.45
1q gain-	74 (63.8)	92 (84.4 to 99.8)		96 (90.4 to 100)	
Complete lung nodule response					
1q gain+	21 (21.9)	57 (73.4 to 100)	.001	89 (73.4 to 100)	.16
1q gain-	75 (78.1)	86 (73.4 to 100)		97 (73.4 to 100)	

Abbreviations: EFS, event-free survival; OS, overall survival.



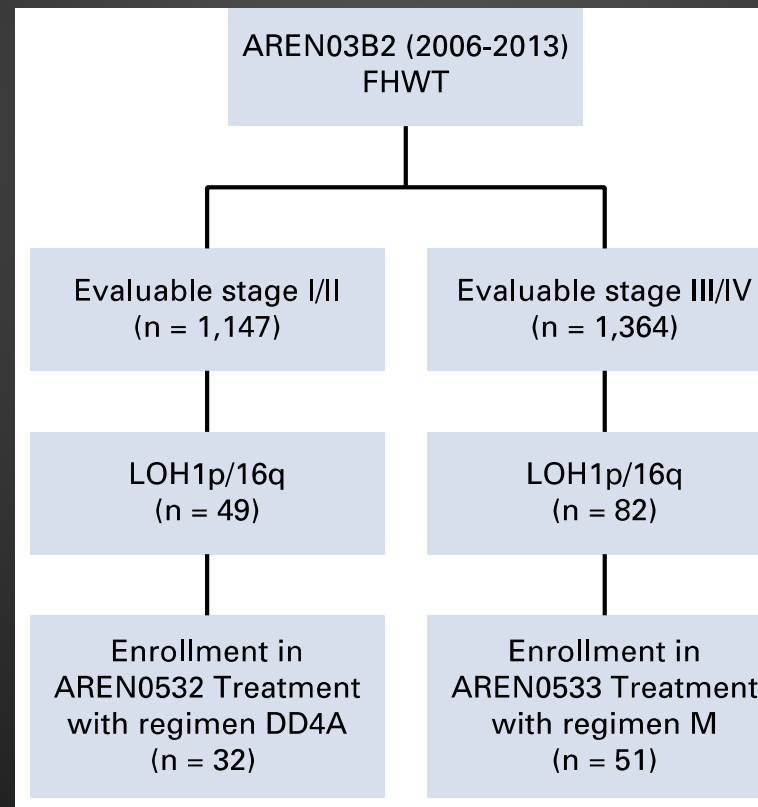
Augmentation of Therapy for Combined Loss of Heterozygosity 1p and 16q in Favorable Histology Wilms Tumor: A Children's Oncology Group AREN0532 and AREN0533 Study Report

David B. Dix, MBChB¹; Conrad V. Fernandez, MD²; Yueh-Yun Chi, PhD³; Elizabeth A. Mullen, MD⁴; James I. Geller, MD⁵; Eric J. Gratas, MD⁶; Geetika Khanna, MD⁷; John A. Kalapurakal, MD⁸; Elizabeth J. Perlman, MD⁹; Nita L. Seibel, MD¹⁰; Peter F. Ehrlich, MD, MSc¹¹; Marcio Malogolowkin, MD¹²; James Anderson, PhD¹³; Julie Gastier-Foster, PhD¹⁴; Robert C. Shamberger, MD¹⁵; Yeonil Kim, MS³; Paul E. Grundy, MD¹⁶; and Jeffrey S. Dome, MD, PhD¹⁷ on behalf of the AREN0532 and AREN0533 study committees.

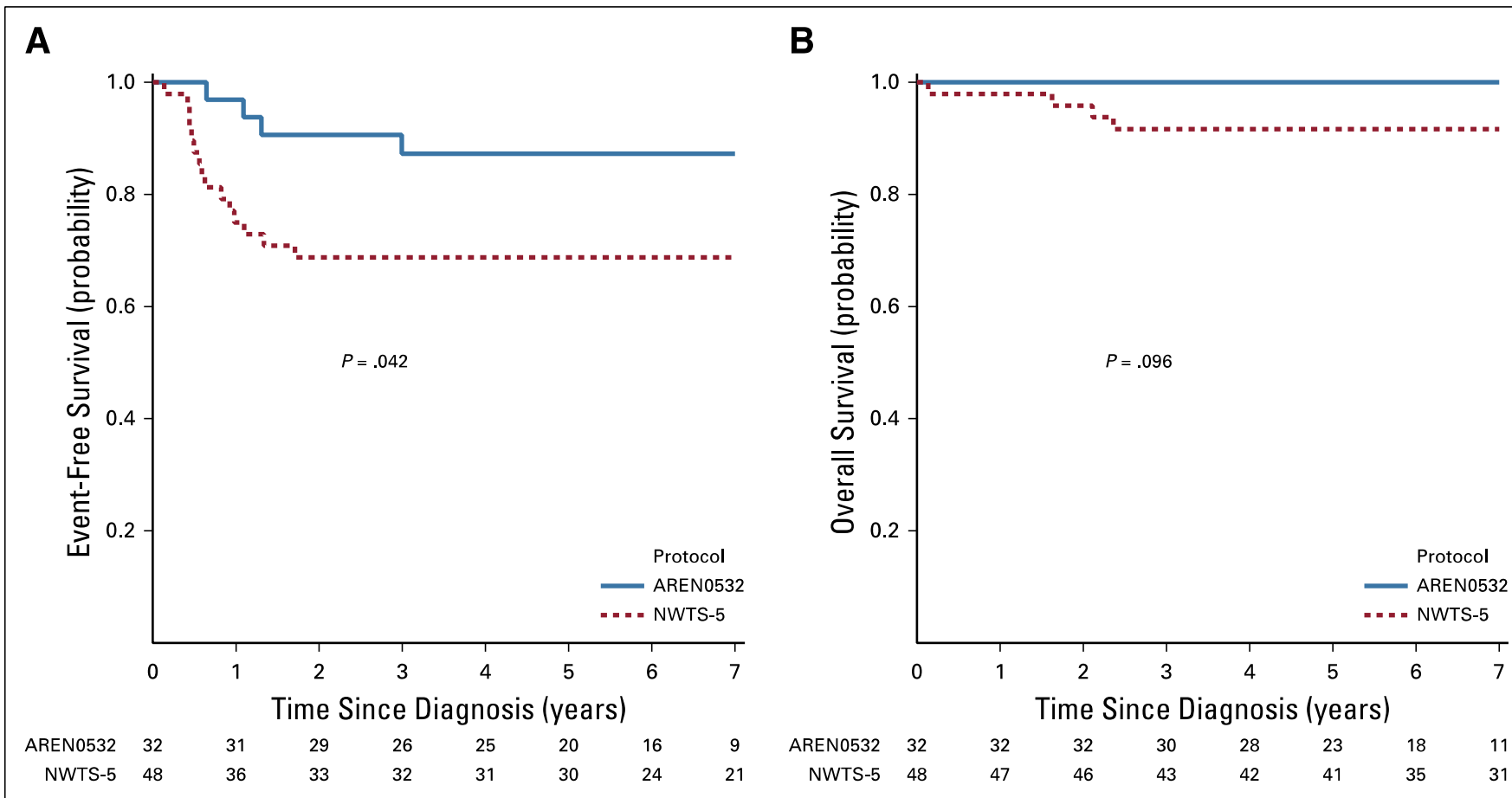
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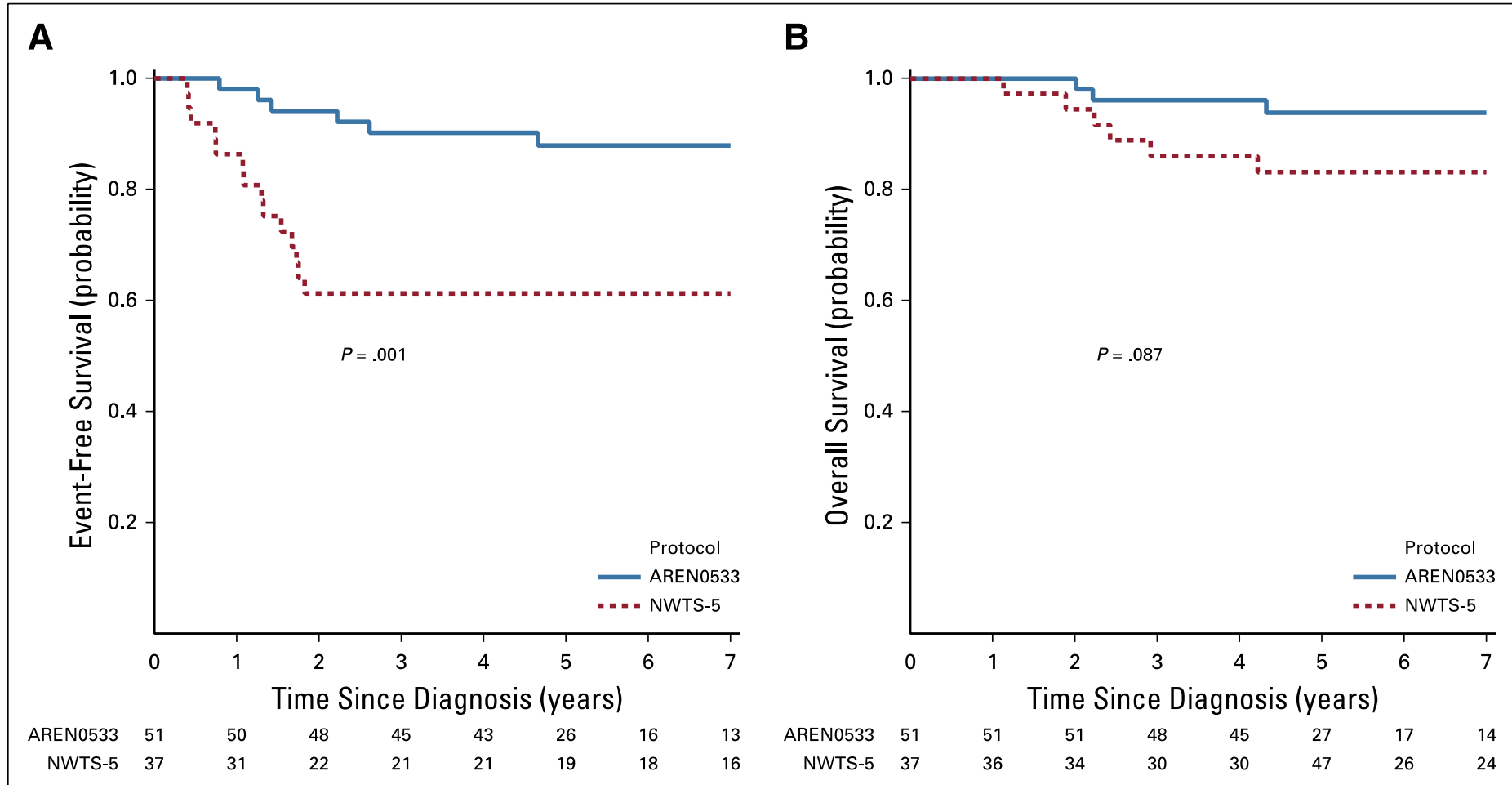
2019



STAGES I / II



STAGES III / IV



Results of the First Prospective Multi-institutional Treatment Study in Children With Bilateral Wilms Tumor (AREN0534)

A Report From the Children's Oncology Group

Peter Ehrlich, MD, MSC, Yuen Y. Chi, PhD,† Murali M. Chintagumpala, MD,‡ Fred A. Hoffer, MD,§
Elizabeth J. Perlman, MD,¶ John A. Kalapurakal, MD,|| Ann Warwick, MD,** Robert C. Shamberger, MD,††
Geetika Khanna, MD,‡‡ Tom E. Hamilton, MD,†† Ken W. Gow, MD,§§ Arnold C. Paulino, MD,¶¶
Eric J. Gratias, MD,||| Elizabeth A. Mullen, MD,†† James I. Geller, MD,*** Paul E. Grundy, MD,†††
Conrad V. Fernandez, MD,‡‡‡ Michael L. Ritchey, MD,§§§ and James S. Dome, MD, PhD¶¶¶*

Annals of Surgery • Volume 266, Number 3, September 2017

Bilateral synchronous renal masses > 1cm

To improve 4-year EFS for bilateral WT

To have at least 75% of patients receive surgical treatment by 12 weeks after initiation of chemo

To prevent complete removal of at least 1 kidney in 50% of patients by administering neoadjuvant 3-drug chemo

Primary aim n=189 BWT patients

Study	4-year EFS	4-year OS
NWTS-5	56%	81%
AREN0534	82%	94%

Central review imaging, surgery and pathology in real-time



NWTS-4 – 38/188 BWT patients

Non-responsive or progressive disease
after initial chemo

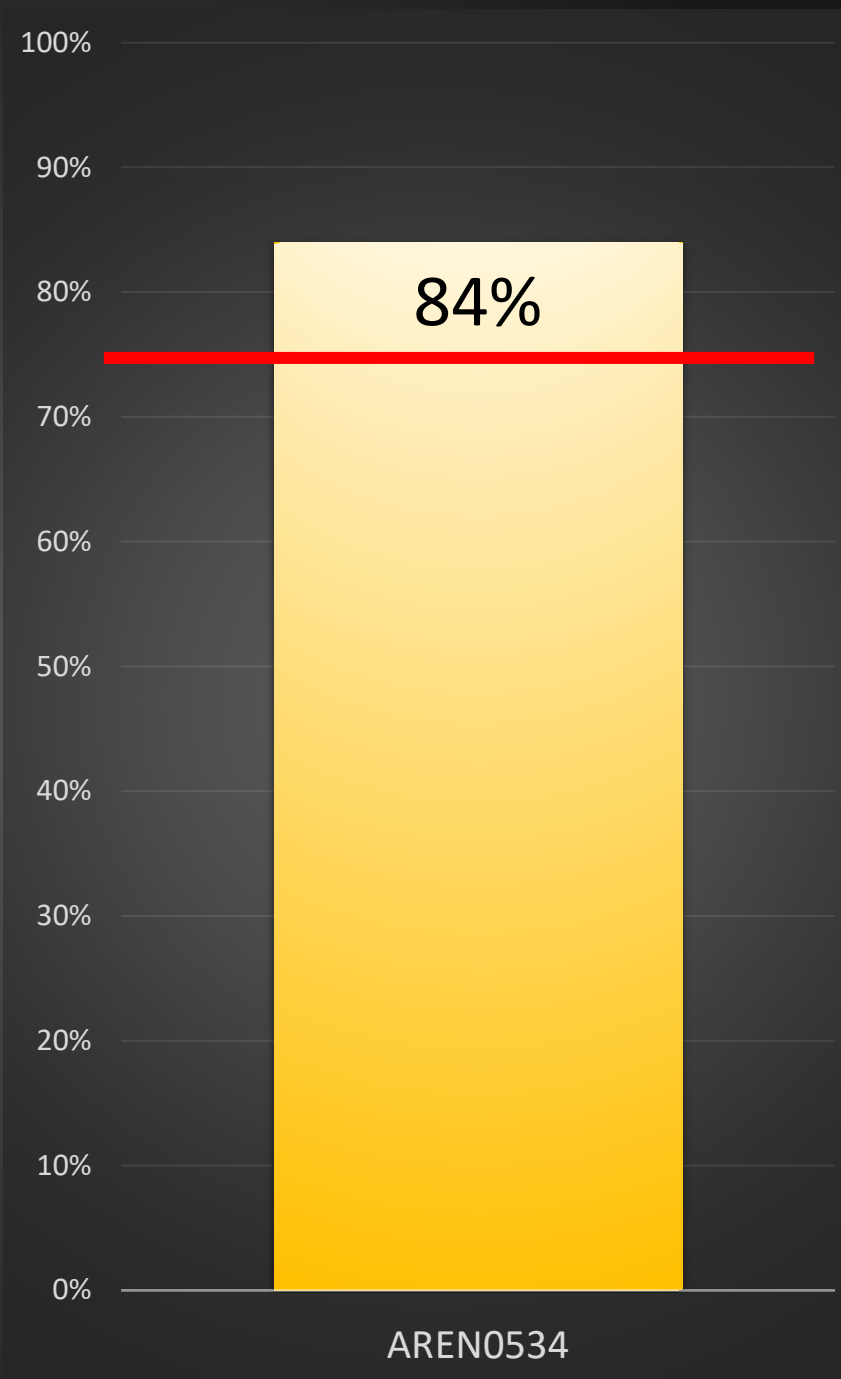
- 36 patients – 2nd regimen of chemo
- 25 patients – 3rd regimen of chemo
- 11 patients – XRT before surgery

Median time before
definitive resection
7 months (2-29)!!

Timing of surgical treatment

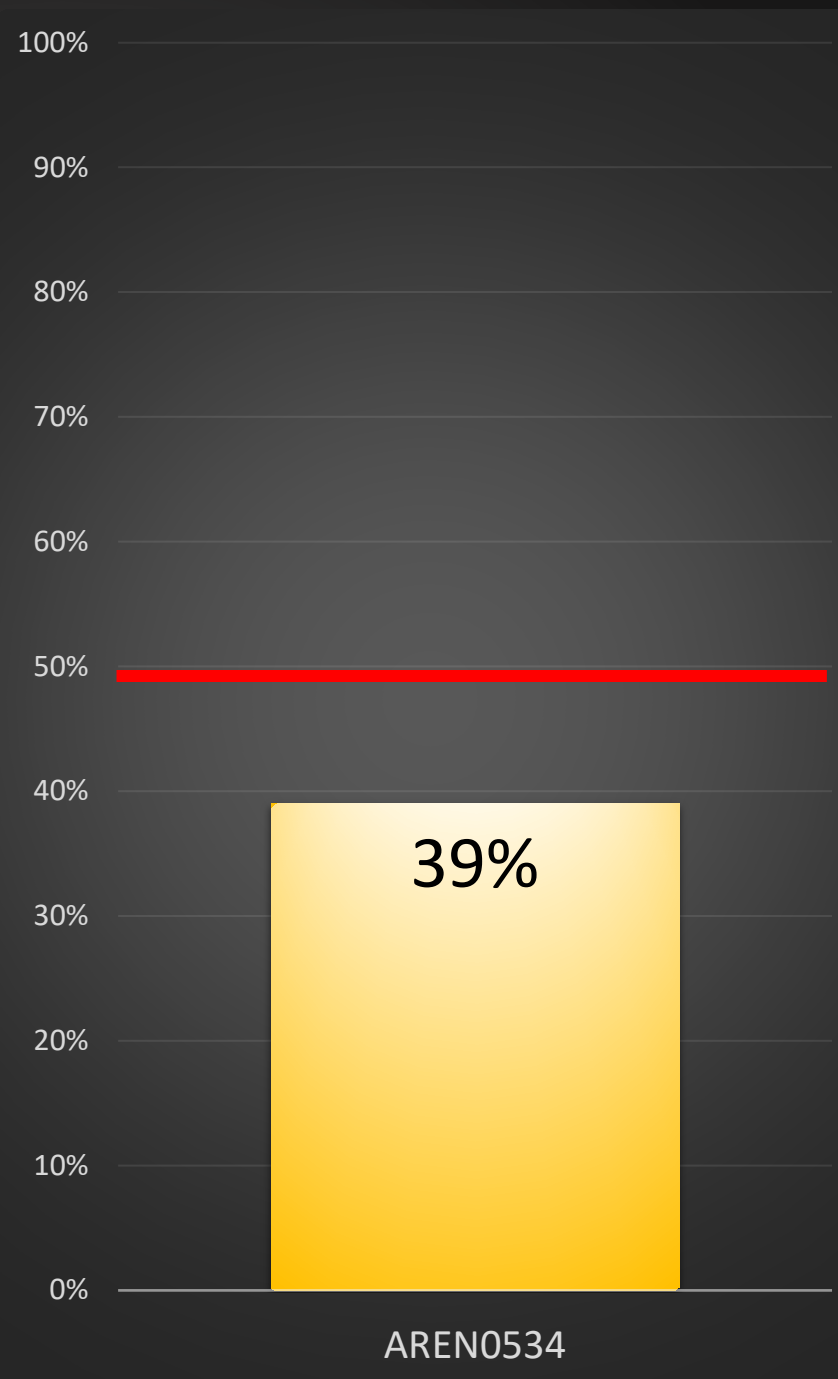
1/3 surgery at
6 weeks

Ehrlich et al. *Ann Surg* 2017



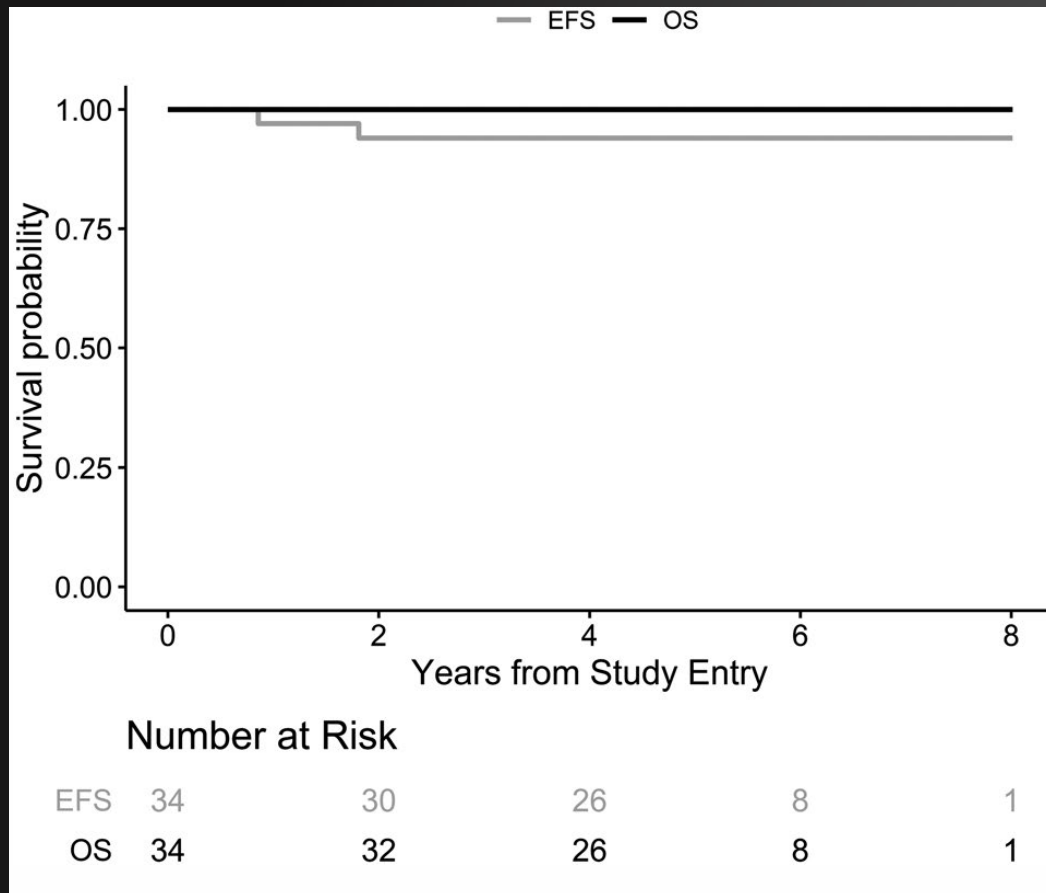
Rate of bilateral NSS

Ehrlich et al. *Ann Surg*, 2017



AREN0534 – bilaterally predisposed tumors

N=34

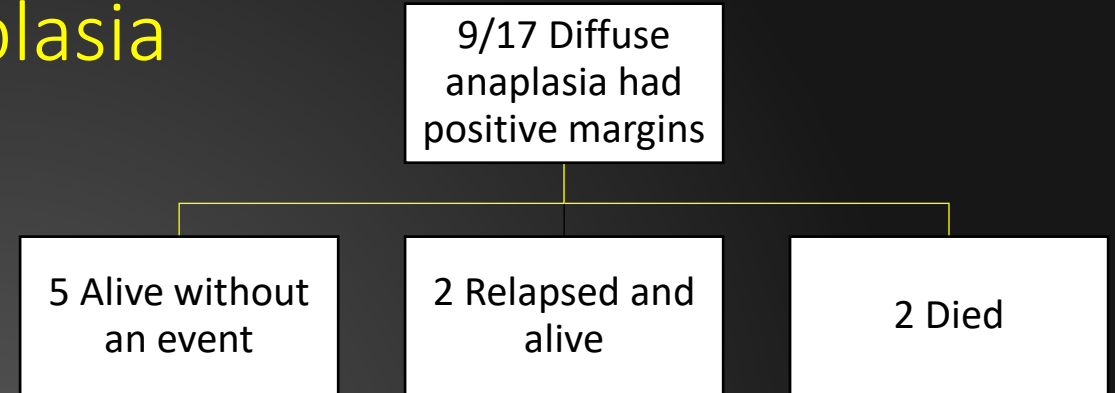


Eligibility	Surgical Procedure
Beckwith-Wiedemann syndrome, N = 9	Partial nephrectomies, n = 8
	Total nephrectomy, n = 1
Hemihypertrophy, N = 9	Complete resolution, n = 2
	Partial nephrectomies, n = 4
	Total nephrectomies, n = 3
Multicentric, N = 10	Partial nephrectomies, n = 4
	Total nephrectomies, n = 6
WAGR, N = 2	Partial nephrectomy, n = 1
	Total nephrectomy, n = 1
Solitary kidney, N = 2	Partial nephrectomies, n = 2
Denys-Drash syndrome, N = 1	Total nephrectomy, n = 1
Simpson-Golabi-Behmel syndrome, N = 1	Partial nephrectomy, n = 1

Abbreviation: WAGR, Wilms tumor/aniridia/genitourinary anomalies/range of developmental delays.

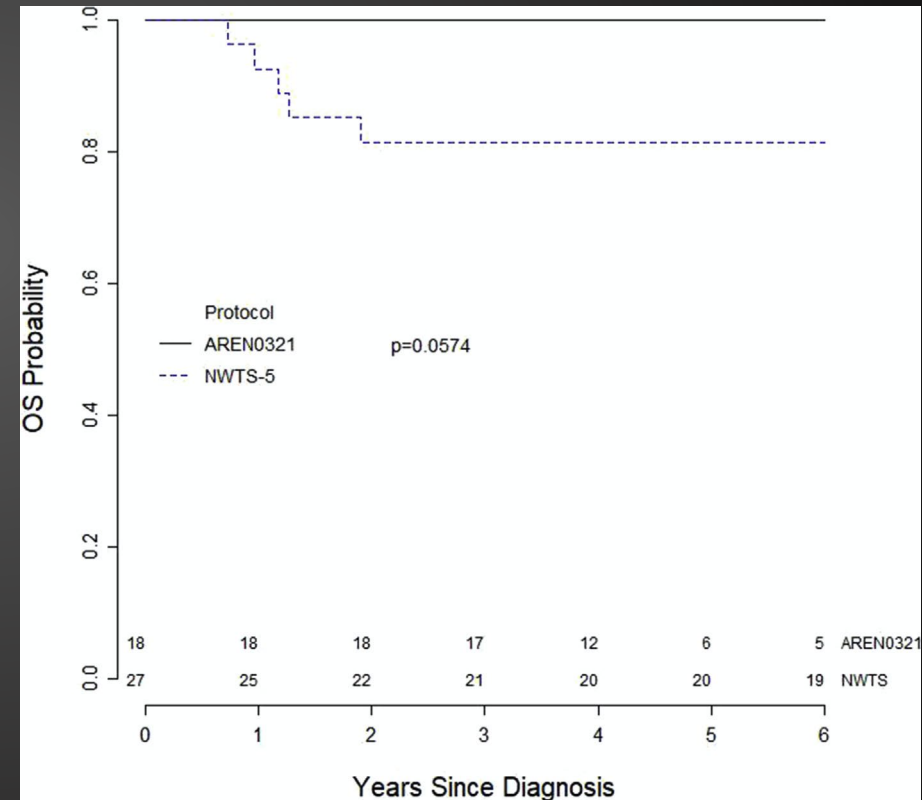
AREN0534 – Bilateral with anaplasia

- 17 diffuse anaplasia (4/17 bilateral)
 - 4 relapses
 - 5 deaths
- 8 focal anaplasia (1/8 bilateral)
 - 1 death
- Late events were uncommon



Histology	NWTS 5 4-yr EFS % (95% CI)	AREN0534 4-yr EFS % (95% CI)
All Stage V	56% (44.8-66.6)	82.1%(73.5-90.8)
Favorable Histology	65% (38.7-98.1)	84.1% (75.2 –93.1)
Focal Anaplasia	76% (33.2-93.5)	87.5%(57.2 – 100)
Diffuse Anaplasia	25% (5.88-51.0)	58.2% (15.65 – 100)

AREN0321 – Stage I Anaplastic – 3-drug chemo + flank radiation



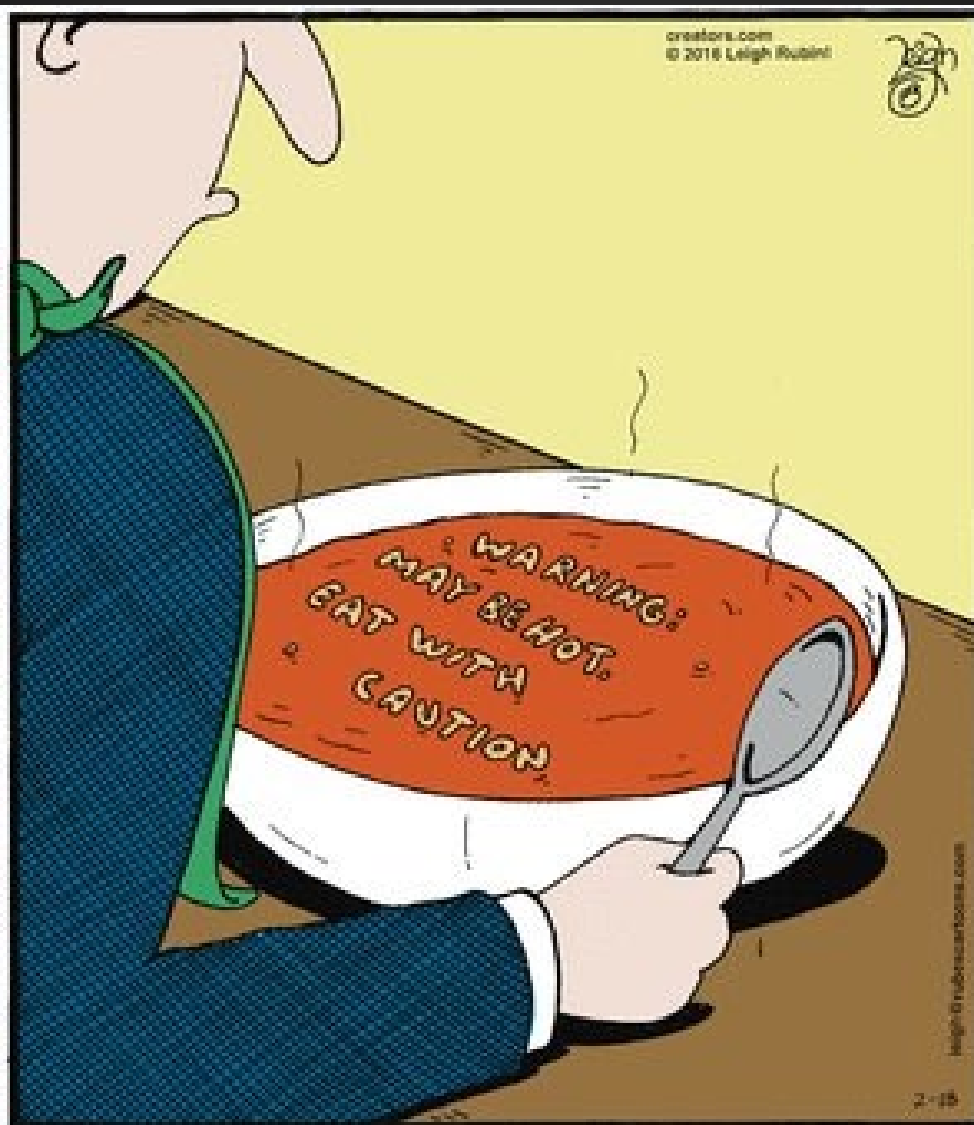
Activity of Vincristine and Irinotecan in Diffuse Anaplastic Wilms Tumor and Therapy Outcomes of Stage II to IV Disease: Results of the Children's Oncology Group AREN0321 Study

Najat C. Daw, MD¹; Yueh-Yun Chi, PhD²; John A. Kalapurakal, MD³; Yeonil Kim, PhD²; Fredric A. Hoffer, MD⁴; James I. Geller, MD⁵; Elizabeth J. Perlman, MD⁶; Peter F. Ehrlich, MSc, MD⁷; Elizabeth A. Mullen, MD⁸; Anne B. Warwick, MPH, MD⁹; Paul E. Grundy, MD¹⁰; Arnold C. Paulino, MD¹¹; Eric Gratias, MD¹²; Deborah Ward, PharmD¹³; James R. Anderson, PhD¹⁴; Geetika Khanna, MD¹⁵; Brett Tornwall, PhD²; Conrad V. Fernandez, MD¹⁶; and Jeffrey S. Dome, MD, PhD¹⁷ on behalf of the AREN0321 Study Committee

JCO 2020

TABLE 5. Four-Year OS for Patients With Stage II to V DAWT Treated in NWTS-3 and NWTS-4, NWTS-5, AREN0321, or AREN0534 According to Stage

Stage	NWTS-3 and NWTS-4		NWTS-5	AREN0321
	Regimen DD-RT: VDA/XRT (%) ^{1a} (n = 29)	Regimen J: VDACy/XRT (%) ^{1a} (n = 30)	Regimen I: VDCyE/XRT (%) Unilateral (n = 110) Bilateral (n = 20) ^b	Regimen UH1/2: VDCy/CyCE/XRT (%) Unilateral (n = 66) Bilateral (n = 17) ^c
II	46.9	70.1	78.4 (60.0 to 96.9)	86.2 (68.0 to 100)
III	20.8	56.3	64.7 (51.6 to 77.8)	88.6 (76.4 to 100)
IV	0	16.7	32.1 (14.8 to 49.4)	49.2 (27.5 to 71.0) ^d
V	—	—	41.6 (19.7 to 62.2)	68.4 (24.9 to 100)



Alphabet soup once the legal department gets involved

Thank you!



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