

**Randomized phase 2b trial comparing
first-line treatment with aldoxorubicin
versus doxorubicin in patients with
advanced soft tissue sarcomas**

Sant Chawla, M.D.
Principal Investigator

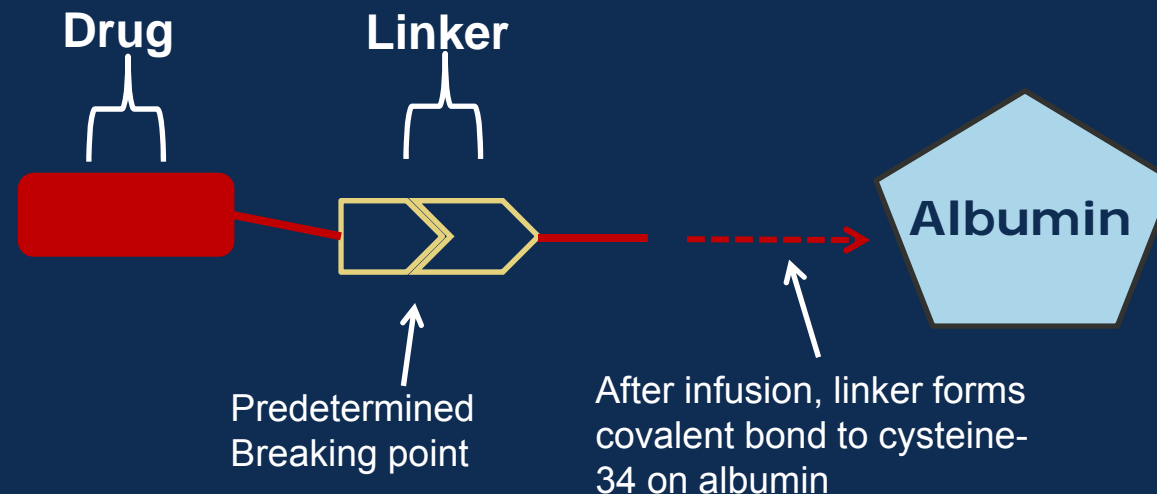
Director, Sarcoma Oncology Center
Santa Monica, California

PRESENTED AT THE 2014 ASCO ANNUAL MEETING. PRESENTED DATA IS THE PROPERTY OF THE AUTHOR.



Targeting Tumors Using Endogenous Albumin

Acid-sensitive linker coupled to doxorubicin binds covalently to circulating albumin in < 5 minutes

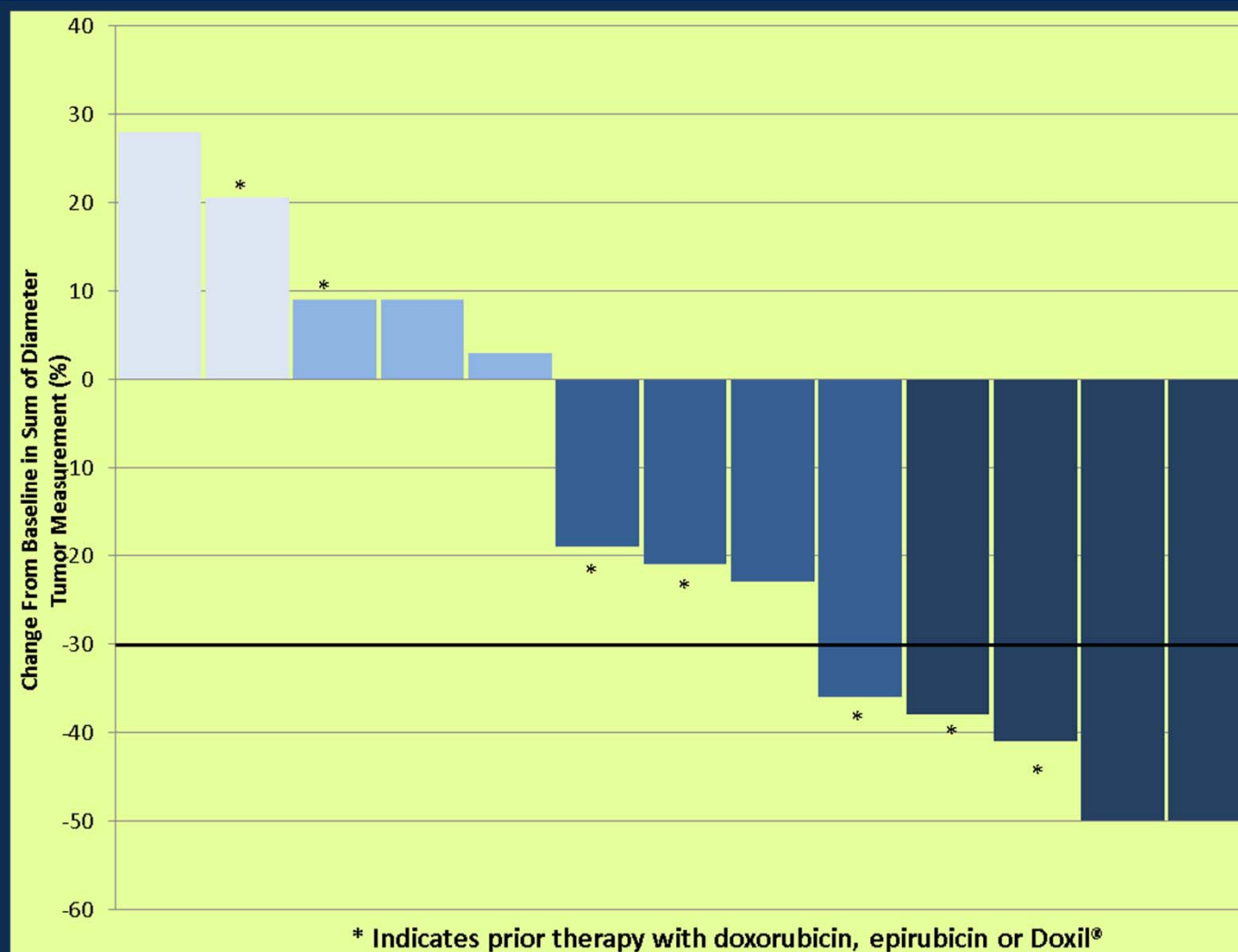


- Able to deliver several times more drug because drug is inactive until released at the tumor
- **Linker** can be used with many types of cancer drugs: anthracyclines, taxanes, camptothecins, platinum, etc.

Pharmacokinetics

- Aldoxorubicin has a relatively long circulating half-life (20 hr), narrow volume of distribution and slow clearance.
- Dose-proportional increases in maximum concentration and AUC were observed.
- Circulating free doxorubicin was $< 2\%$ of total doxorubicin measured.
- Only trace amounts of doxorubicinol could be detected.
- No drug accumulation over multiple cycles occurred.
- Less than 5% of doxorubicin is excreted in the urine primarily as the unmetabolized drug

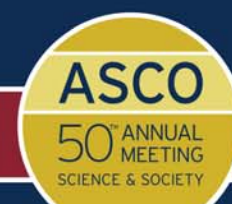
Phase 1b/2 Study Results



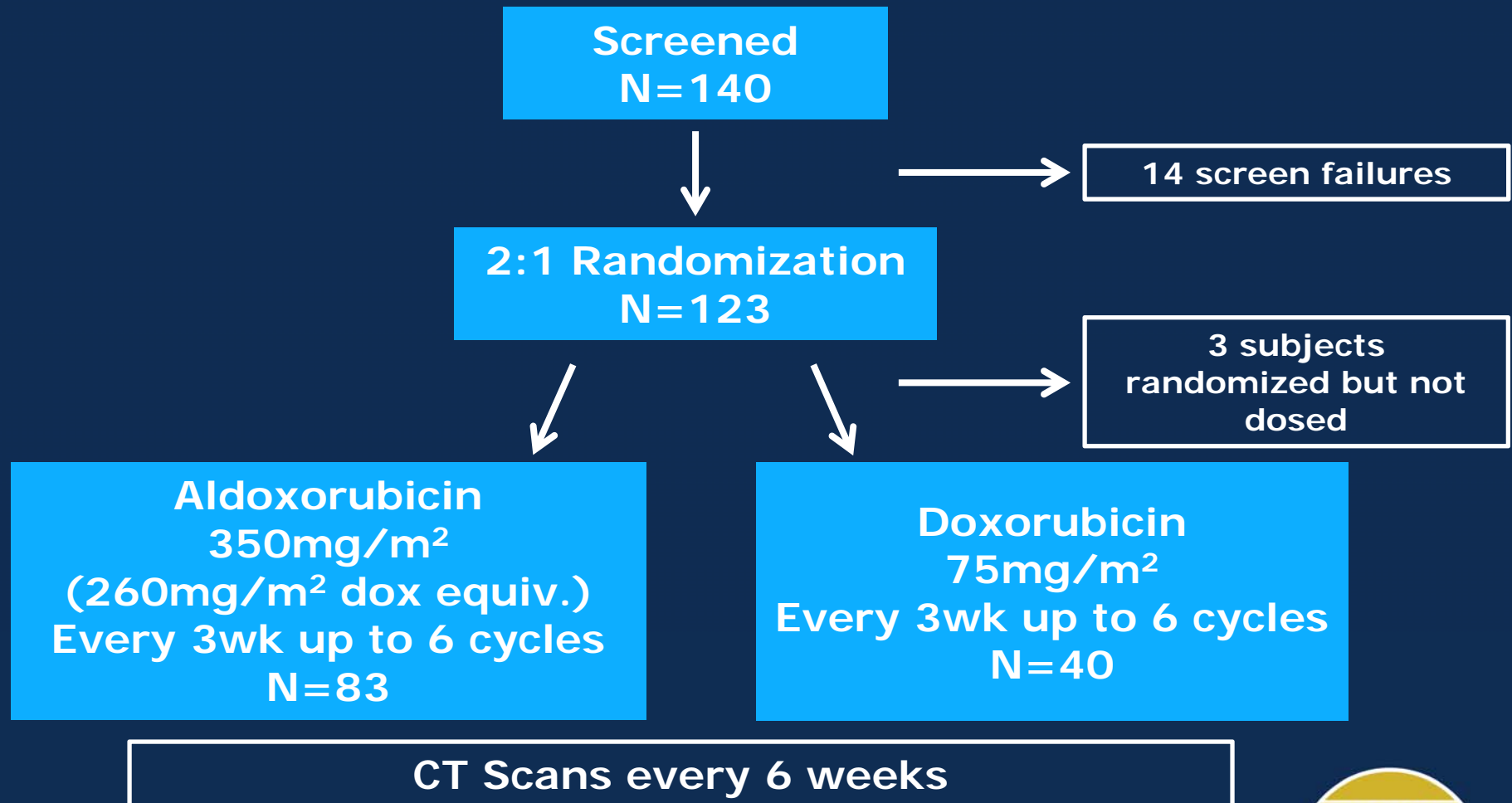
PFS = 11.3 months
OS = 21.7 months
ORR = 38%

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Phase 2b Trial Design



Subject Characteristics

Characteristics	Aldoxorubicin	Doxorubicin
N	83	40
Age, median (range)	54.0 (21-77)	54.0 (23-77)
Male / Female (%)	46 / 54	45 / 55
Race, (%)		
Caucasian	74	80
Black or African American	1	2.5
Asian	19	15
Other	6	2.5
ECOG, (%)		
0-1	96	92
2	4	8
Completed Cycles, median (range)	6 (1-8)	4 (1-6)

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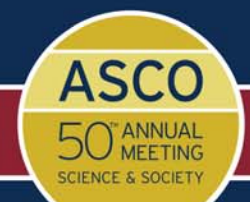


Disease Characteristics

Histopathology (as determined by investigator)	Aldoxorubicin N = 83	Doxorubicin N = 40
Leiomyosarcoma, (%)	34	35
Liposarcoma, (%)	16	15
Fibrosarcoma, (%)	14	10
Synovial sarcoma, (%)	6	10
Others, (%)	30	30

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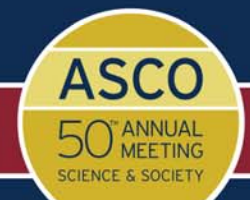


PFS Results

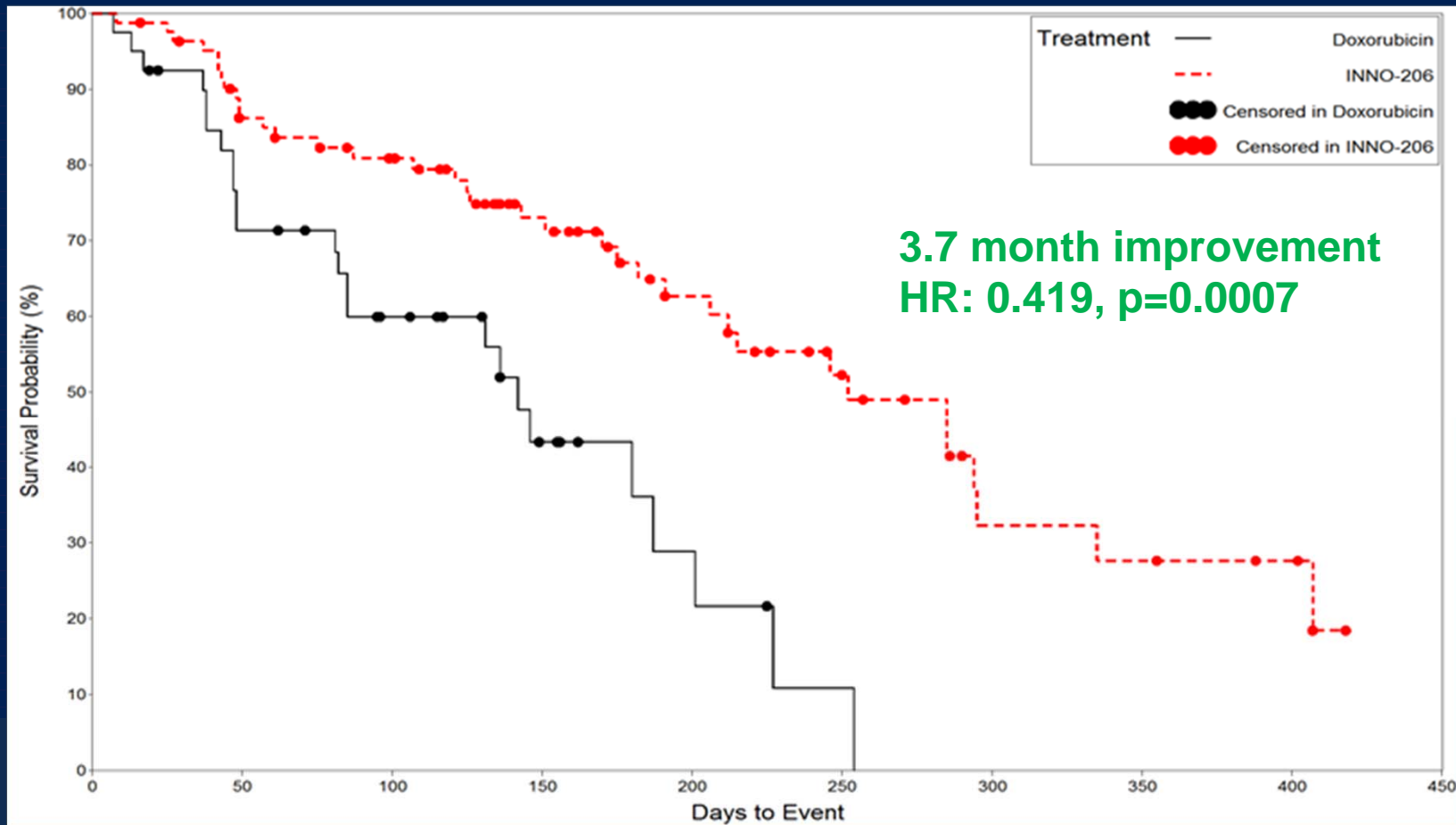
	All Subjects Intent-to-treat	P Value
Scans Read by Investigator		
Aldoxorubicin	8.4 months	P=0.0004
Doxorubicin	4.7 months	
Improvement over dox	3.7 mos. (79%)	
Hazard ratio	0.419 (0.25-0.69)	P=0.0007
Scans Read by Blinded Central Lab		
Aldoxorubicin	5.7 months	P=0.014
Doxorubicin	2.8 months	
Improvement over dox	2.9 mos. (104%)	
Hazard ratio	0.584 (0.37-0.93)	P=0.024

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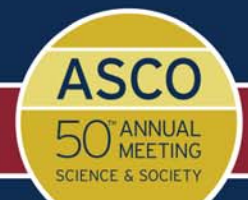


K-M Curve – Investigator

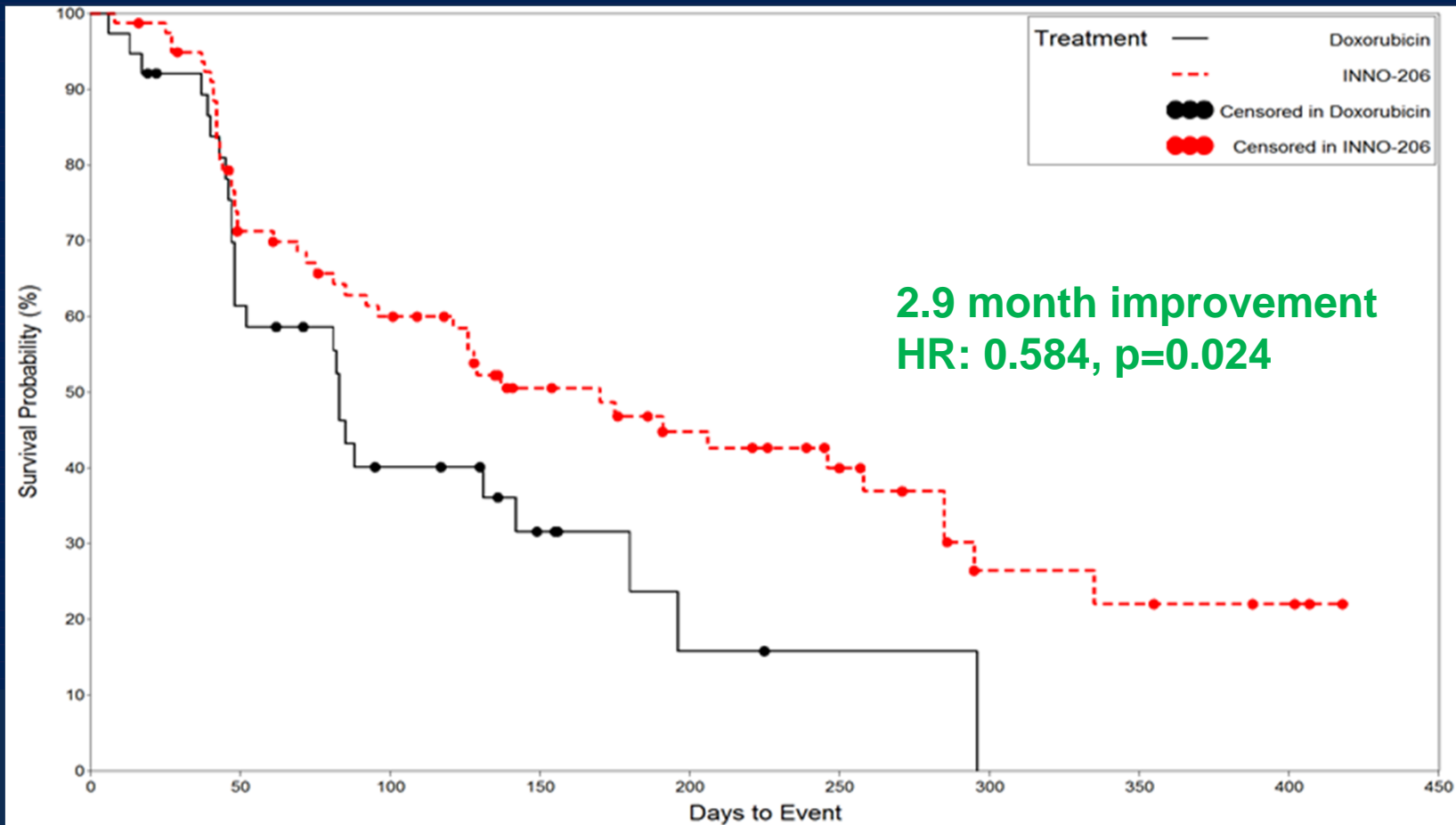


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K-M Curve – Central Lab



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PFS at 6 Months

	All Subjects Intent-to-Treat	P Value
Scans Read by Investigator		
Aldoxorubicin	68.1%	P=0.002
Doxorubicin	36.6%	
Improvement over dox	86.1%	
Scans Read by Blinded Central Lab		
Aldoxorubicin	45.7%	P=0.02
Doxorubicin	22.9%	
Improvement over dox	99.6%	

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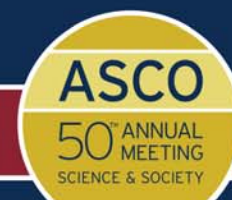


Overall Response Rate

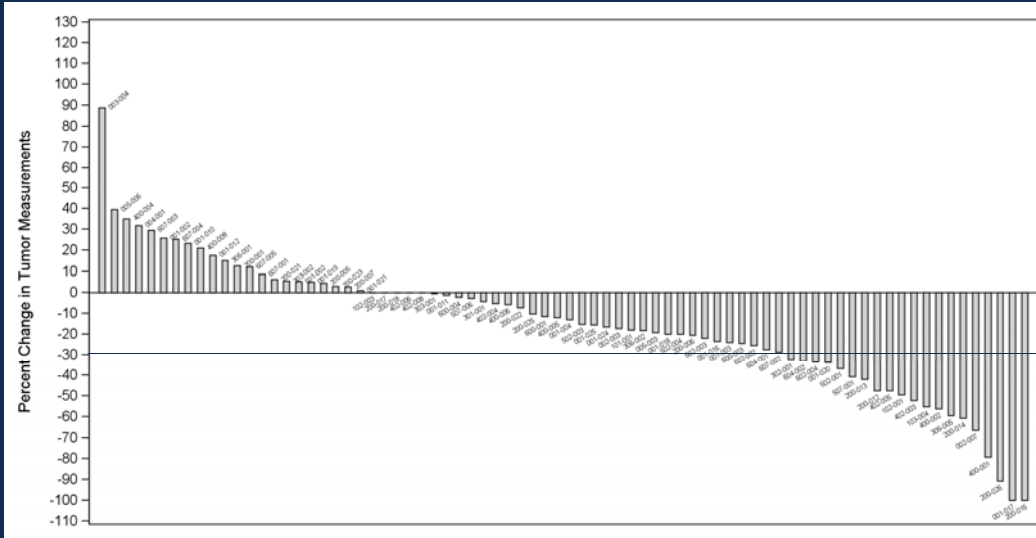
	Aldoxorubicin	Doxorubicin
Scans Read by Investigator		
Complete Response	2.4%	0%
Partial Response	19.3%	5.0%
Overall Response Rate	21.70%	5.0%
Scans Read by Blinded Central Lab		
Complete Response	0%	0%
Partial Response	23.8%	0%
Overall Response Rate	23.8%	0%

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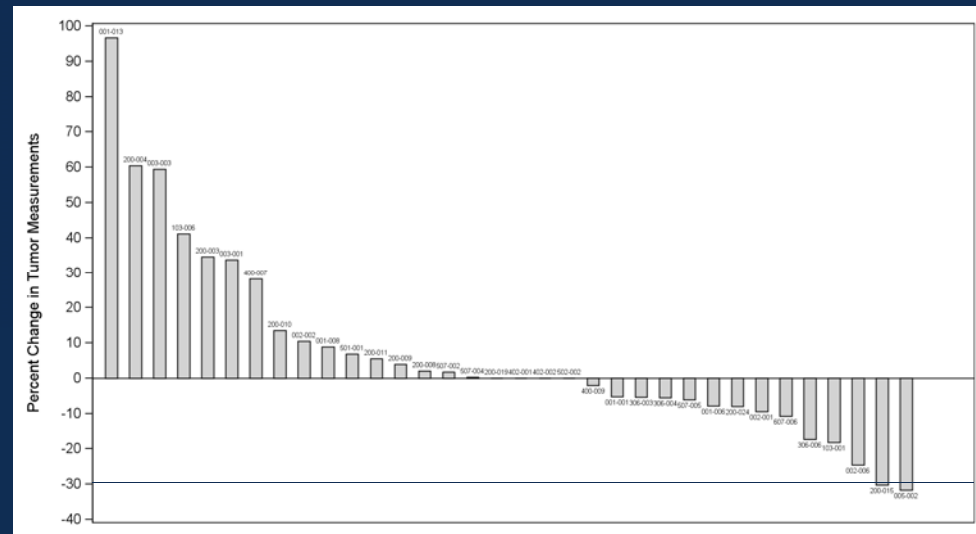


Waterfall Plot - Investigator

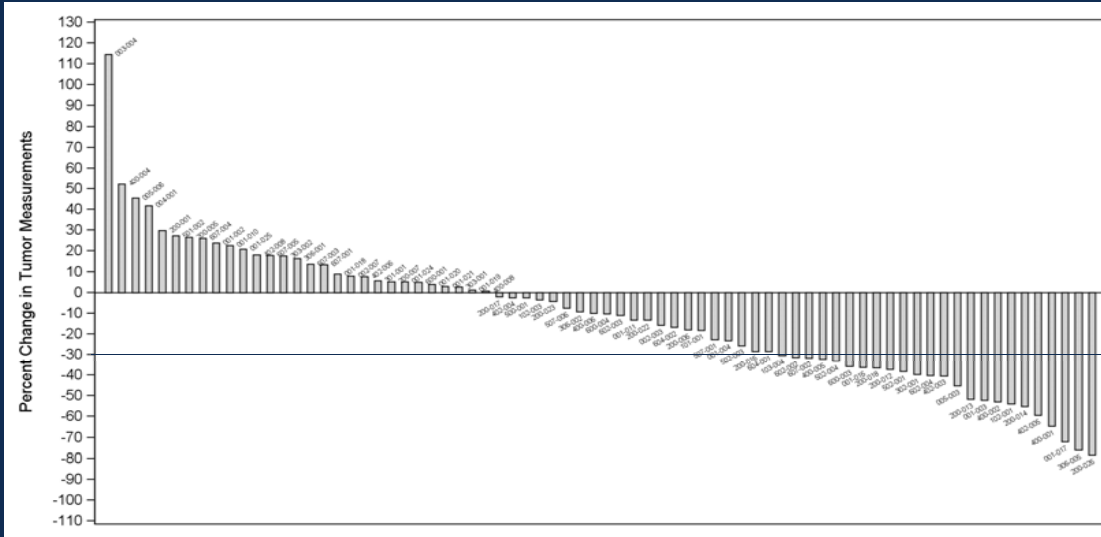


← **Aldoxorubicin**
64.5% had tumor shrinkage

Doxorubicin →
41.2% had tumor shrinkage

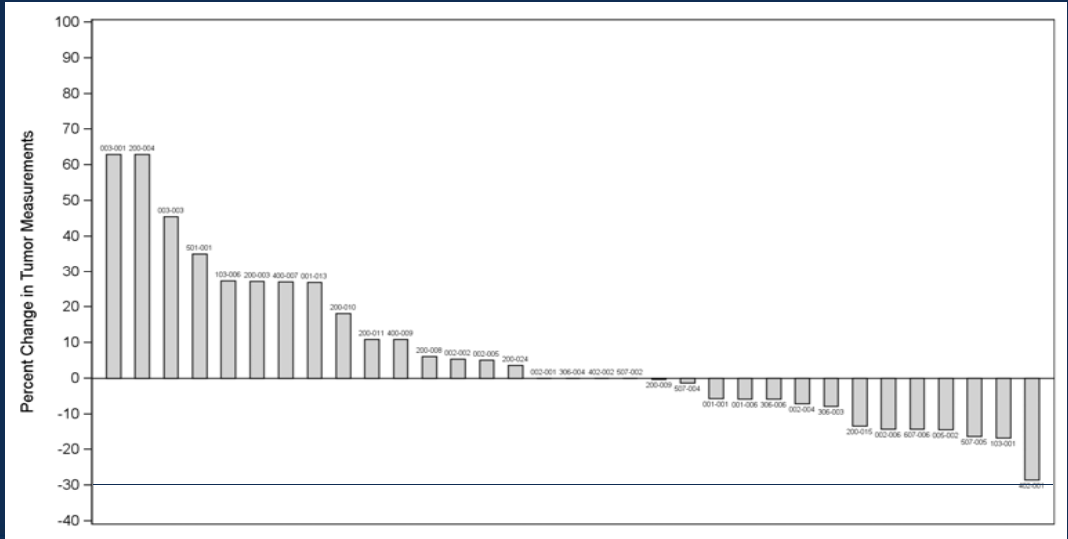


Waterfall Plot – Blinded Central Lab



← **Aldoxorubicin**
60.8% had tumor shrinkage

Doxorubicin →
39.4% had tumor shrinkage

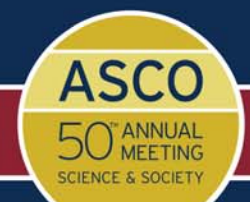


Comparison to Current STS Treatments

	CytRx Phase 2b Investigator assessed		EORTC Phase 3 Dox vs. dox+ ifosfamide	
	Aldox	Dox	Dox+ ifos	Dox
N	83	40	215	217
PFS	8.4	4.7	7.4	4.6
P value	0.0004		0.003	
ORR	21.7%	5.0%	26.5%	13.6%

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Grade 3/4 TEAEs

	Aldoxorubicin	Doxorubicin
	N=83	N=40
Event	(%)	(%)
Neutropenia	40	20
Neutropenic fever	15.7	17.5
Thrombocytopenia	6	5
Anemia	13.2	20
Nausea/vomiting	7.2	0
Mucositis	10.8	2.5
Fatigue/weakness	6.0	5.0

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Cardiac Evaluation

	Aldoxorubicin	Doxorubicin
% subjects with $\geq 10\%$ decrease in LVEF	24%	33%
% subjects with $\geq 15\%$ decrease in LVEF	10%	24%
% subjects with $\leq 50\%$ of expected institutional normal	0%	6%

Conclusions

- Aldoxorubicin significantly increases PFS, PFS at 6 months and ORR compared to doxorubicin therapy for first line STS.
- Grade 3 or 4 neutropenia, mucositis and nausea/vomiting are higher in aldoxorubicin-treated patients but are not treatment limiting.
- The aldoxorubicin patients received more than 5 times the cumulative amount of doxorubicin in this study than the doxorubicin patients without any evidence of clinically relevant decreased LVEF, and in more instances an increase in LVEF, either by MUGA or echocardiogram.
- A phase 3 pivotal trial under a SPA is ongoing for relapsed/refractory STS.