

SARC005

Adjuvant treatment of high risk uterine
LMS with gemcitabine/docetaxel
followed by doxorubicin:
A phase II multi-center trial

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Objectives

- Determine 2-year PFS among women with uterine LMS treated with gem-doce x 4, followed by doxorubicin x4
- Determine tolerability/toxicity
- Explore predictors of PFS: age, tumor size, grade, serosal involvement, **STS-AJCC stage v. FIGO stage**, mitotic rate, ER, PR, menopausal status at dx

Schema

Gemcitabine 900 mg/m² over 90 minutes days 1, 8

Docetaxel 75 mg/m² day 8

q 3 wk x 4 cycles

Repeat CT scan

Doxorubicin 60 mg/m² q 3 w x 4

Repeat CT scan within 6 weeks after completion

CT c/a/p every 3 mo for 2 y, then every 6 mo

Eligibility

- ≥ 18 years
- FIGO stage I or II, high grade LMS s/p hysterectomy (serosal involvement IS eligible even though this is FIGO IIIA)
- < 12 weeks from surgery
- NED by CT within 3 weeks of enrollment
- Good marrow, kidneys, liver
- No other cancer within 5 years
- No prior gem, doce or dox
- No prior pelvic RT
- No current HRT or antihormone therapy
- EF $\geq 50\%$
- No hx HIV (*amendment Oct 2008*)

Correlative Studies

- Provide tumor details: size, serosal disease, mitotic rate
- Provide patient details: age, menopausal status at dx and at start of adjuvant therapy
- Send unstained slides to MSKCC
 - ER and PR
 - Institutions reimbursed \$75 when slides are received

Statistical Issues

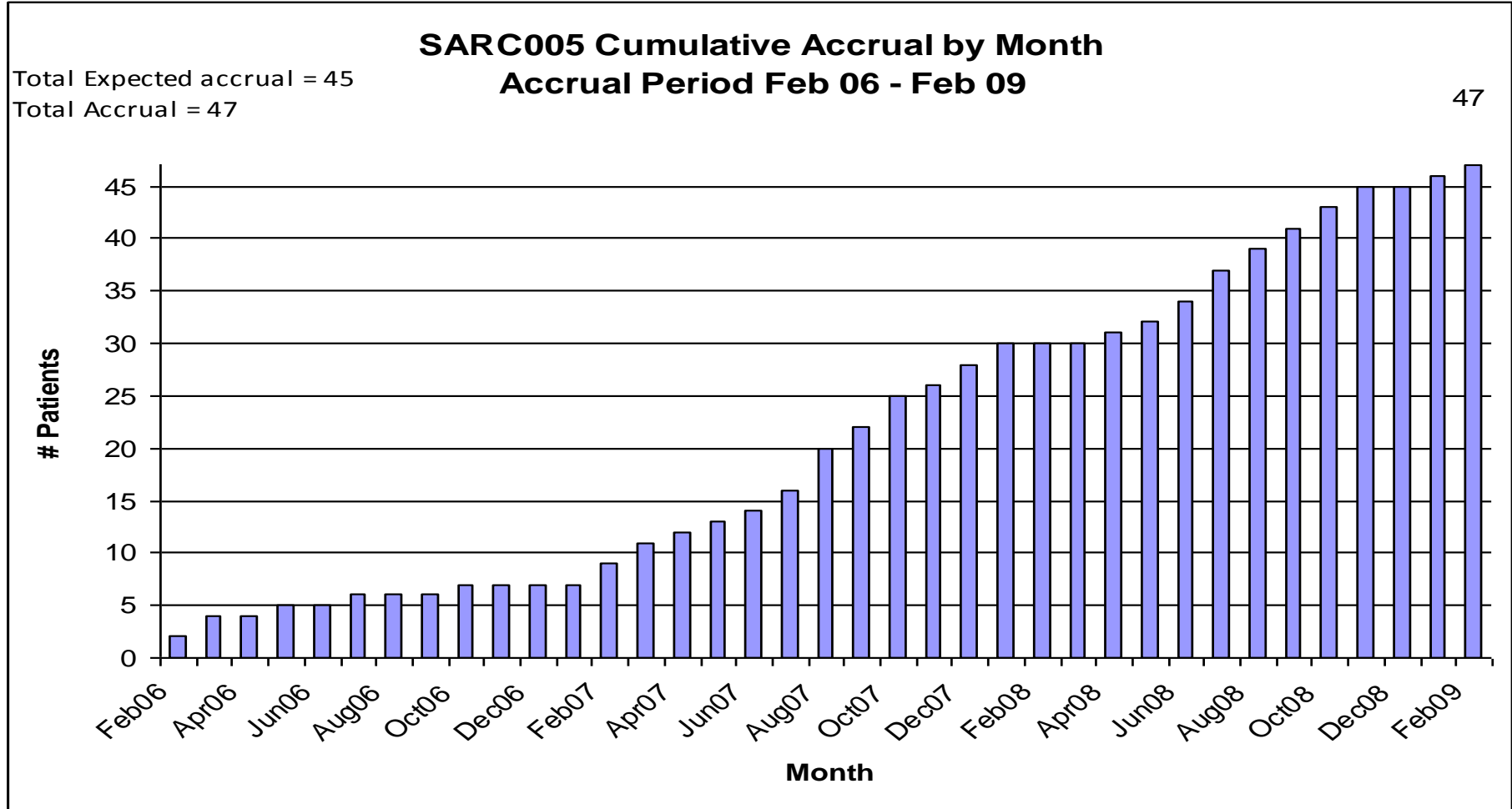
- Target accrual 45 patients
- Bayesian model for continuous assessment of PFS and safety
- Accrue at least 15 patients per year
- Stop early if data suggest 2 year PFS will be no better than 30%

Calculating Futility

- Event: death or evidence of progression
- **Stop** if number of events is too many for the total patient-disease-free-days-on study

Number of events	Minimum total time on test in days
1	0
2	0
3	408
4	920
5	1435
6	1955
7	2477
8	3003

Accrual



Results

- Recurrence events: 6
- Progression-free days = 23,757
- Median f/u = 554 days

14th Annual Meeting of the Connective Tissue Oncology Society
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Stage Specific Outcomes of Patients with Uterine Leiomyosarcoma: A Comparison of FIGO and AJCC Staging Systems

Oliver Zivanovic, Mario M. Leitao, Alexia Iasonos, Lindsay M. Jacks,
Qin Zhou, Robert A. Soslow, Margrit M. Juretzka, Dennis S. Chi,
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Background

FIGO versus AJCC

	FIGO	AJCC
Organ-based staging	✓	-
Compartment-based staging	-	✓
Involvement of uterine cervix	✓	-
Involvement of uterine serosa	✓	-
Tumor size	-	✓
Tumor grade	-	✓
Lymph node/ pelvic metastases	Stage III	Stage IV

Methods

- Patients staged based on FIGO and AJCC criteria
 - PFS and OS estimated using Kaplan-Meier method
- Predictive accuracy estimated with concordance index:
 - Analyzing all possible pairs of patients
 - Determining concordance (1.0) or discordance (0.0)
 - Overall probability: sum of the values divided by total number of data pairs

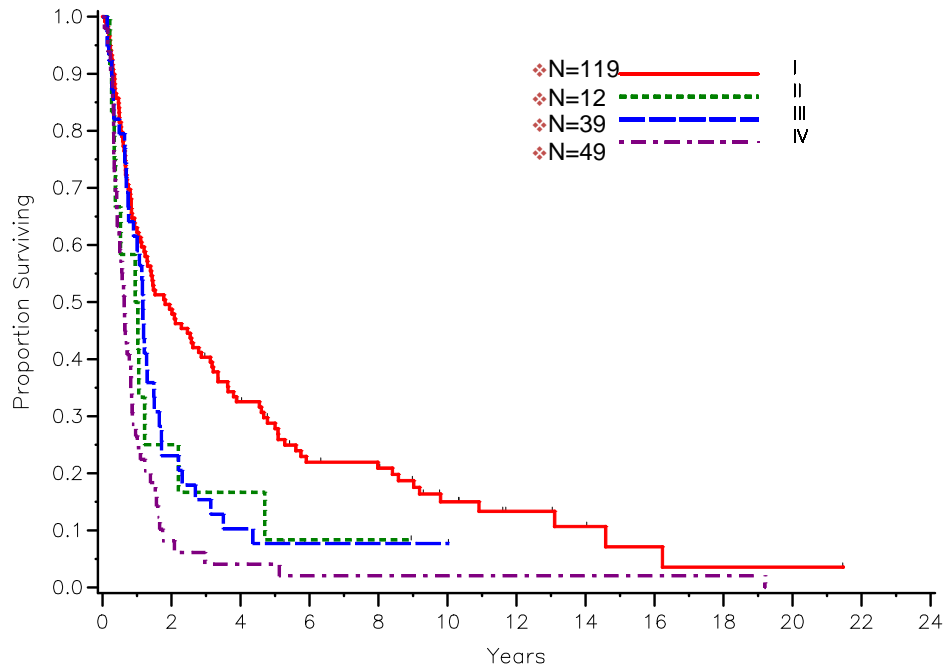
Results

Stage Specific Distribution by FIGO and AJCC

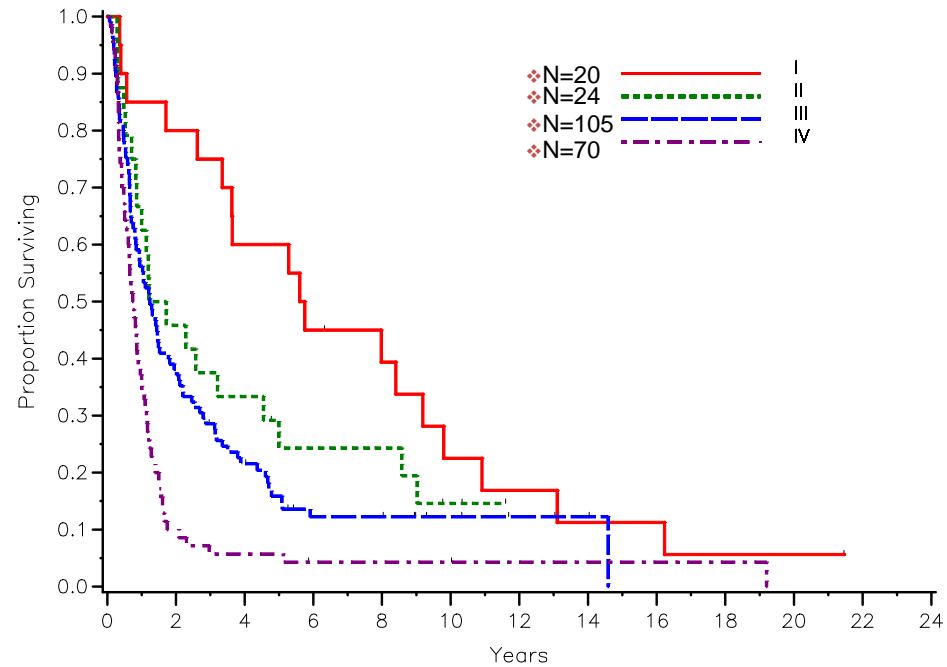
AJCC Stage	FIGO Stage				Total
	I	II	III	IV	
I	19	0	1	0	20
II	20	1	3	0	24
III	80	11	14	0	105
IV	0	0	21	49	70
Total	119	12	39	49	219

Results: PFS by FIGO and AJCC

Progression-Free Survival by FIGO Stage

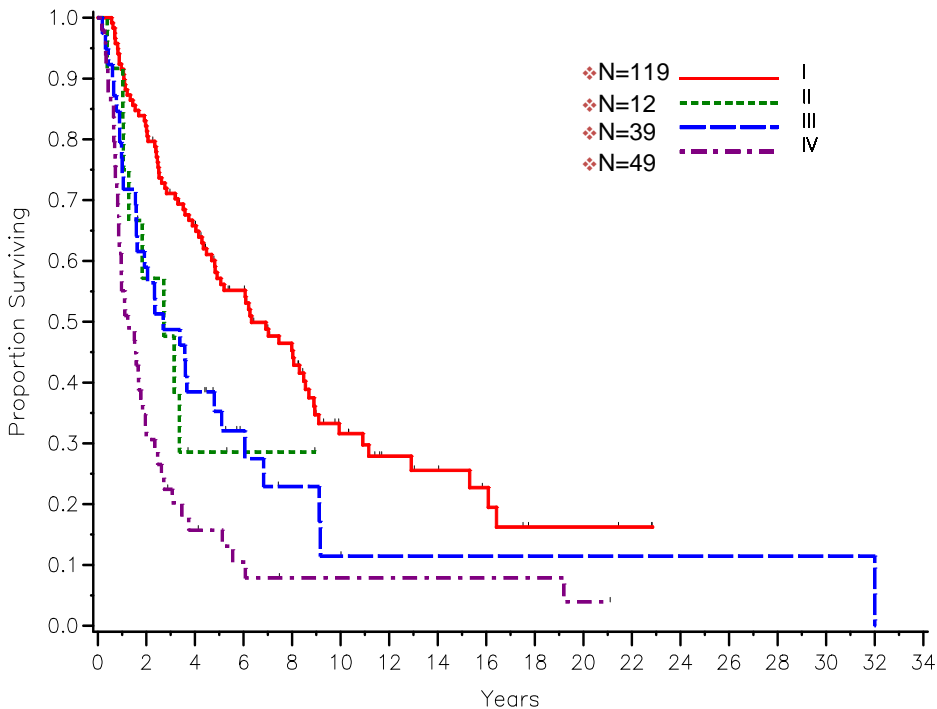


Progression-Free Survival by AJCC Stage

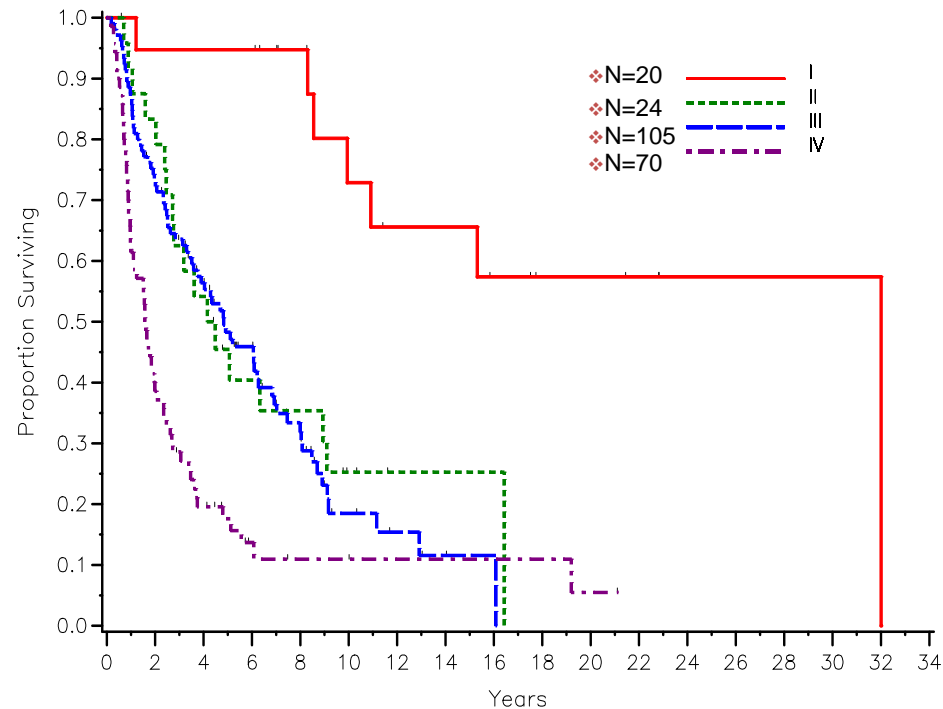


Results: OS by FIGO and AJCC

Overall Survival by FIGO Stage



Overall Survival by AJCC Stage



Results: Concordance Indices (c-index)

Endpoint	Staging-System	c-index	Bootstrap 95% CI
PFS	FIGO	0.60	0.566-0.641
	AJCC	0.60	0.560-0.639
OS	FIGO	0.62	0.586-0.660
	AJCC	0.63	0.594-0.678

Conclusions

- Stage-specific PFS and OS altered substantially when comparing AJCC versus FIGO
- Strength of AJCC: identifying patients with better prognosis
- Strength of FIGO: identifying patients with worse prognosis
- Overall predictive ability of AJCC not superior to FIGO