

# A Phase II Study of Low-dose Protracted Irinotecan in Patients with Advanced Sarcomas

Sarah N. Dumont<sup>1, 2</sup>, Jonathan C. Trent<sup>1</sup>, Jason A. Salganick<sup>1</sup>, S.R. Patel<sup>1</sup>, D.S Araujo<sup>1</sup>, A.G. Dumont<sup>1</sup>, R.S. Benjamin<sup>1</sup>

<sup>1</sup> Department of Sarcoma Medical Oncology and <sup>2</sup> Leukemia, University of Texas MD Anderson Cancer Center

## Objectives

- Objective response rate according to RECIST, defined as complete or partial response at 6 weeks or stable disease lasting at least 12 weeks.
- Median overall survival and progression-free survival
- Toxicity evaluation of protracted administration

## Treatment Plan: Irinotecan

16 mg/m<sup>2</sup> of daily, intravenously over one hour, for 5 days x 2 weeks, with a 2-day rest, repeated in 21-day cycles.

## Patients Eligibility

- Locally advanced or metastatic sarcoma
- Must have received or refused standard chemotherapy
- Life expectancy  $\geq$  3 months, performance status  $\geq$  2
- Informed consent signed

Table 1. Patient Characteristics

<b>Number evaluated for toxicity:</b>	<b>38</b>
Good histology (small cell sarcoma)	13 (34%)
Intermediate (other)	22 (58%)
Poor (Chondrosarcoma)	3 (8%)
<b>Number evaluated for efficacy:</b>	<b>36*</b>
<b>Median age</b>	48 (21-71)
<b>Gender</b>	
Male	25 (66%)
Female	13 (34%)
<b>Prior Therapy</b>	
None	1 (2%)
Chemotherapy	33 (91%)
Radiotherapy	18 (50%)
Surgery	32 (88.9%)

\*1 early death, 1 inevaluable

Predictive Histology	Number of patients (%)	Best Response			Response Rate (%)	Early discontinuation due to toxicity (%)
		Progressive disease (%)	Stable disease (%)	Partial response (%)		
<b>Good response</b>						
Rhabdomyosarcoma	4 (10)	1 (3)	3 (8)	-	0	1 (3)
Ewing's sarcoma/PNET	7 (18)	1 (3)	2 (5)	3 (8)	71	2 (5)
Small cell unclassified sarcoma	2 (5)	2 (5)	-	-	0	-
<b>Intermediate</b>						
Synovial sarcoma	2 (5)	1 (3)	-	1 (3)	50	-
Angiosarcoma	1 (3)	-	-	1 (3)	100	-
Dedifferentiated	4 (10)	2 (5)	2 (5)	-	0	1 (3)
Pleomorphic	1 (3)	-	-	-	0	1 (3)
Myxoid liposarcoma	1 (3)	1 (3)	-	-	0	-
Leiomyosarcoma	5 (13)	3 (8)	1 (3)	-	0	2 (5)
Unclassified sarcoma	5 (13)	3 (8)	1 (3)	1 (3)	20	-
Malignant fibrous histiocytoma	3 (8)	1 (3)	1 (3)	-	0	1 (3)
<b>Poor prognostic</b>						
Chondrosarcoma	2 (5)	-	1 (3)	-	50	1 (3)
Chordoma	1 (3)	1 (3)	-	-	0	-
<b>Total</b>	<b>38</b>	<b>16 (44)</b>	<b>11 (30)</b>	<b>6 (16)</b>	<b>24</b>	<b>9 (23)</b>

Table 2. Response according to histology

Table 3. Toxicity Data

Median number of cycles: 2 (1-10)

Grade Toxicity 0=none, 5=death	Number of patients	Percentage of patients
0	2	5%
1	5	13%
2	14	37%
3	12	31%
4	4	11%
5	1	3%

Toxicity Grade 3 and 4	Number of patients	Percentage of patients
Diarrhea	11	30%
Fatigue	10	27%
Nausea / vomiting	10	27%
Abdominal pain	6	16%
Granulocytopenia	3	8%
Myalgia	3	8%
Dehydration	2	5%
Thrombocytopenia	2	5%

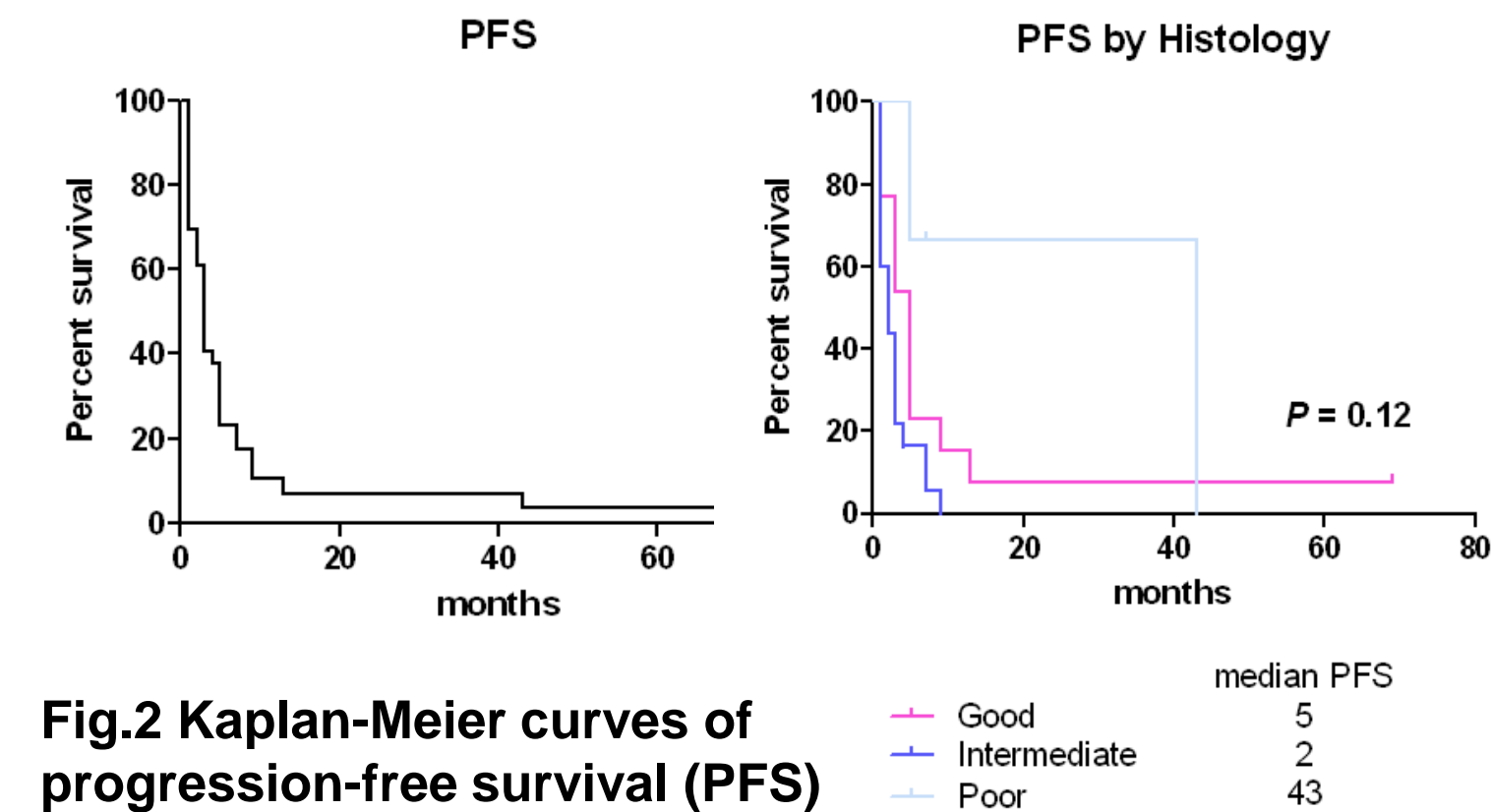


Fig.2 Kaplan-Meier curves of progression-free survival (PFS)

## Results

- The median OS was 9 months from inclusion
- The median PFS was 3 months
- The objective response rate was 24 %
- The objective response rate of Ewing's sarcoma family of tumors (ESFT) was 71%
- The main adverse effects were diarrhea and fatigue.

## Conclusion

Irinotecan has a high activity in ESFT with some lesser activity in other histologies. Despite a low dose protracted-schedule delivery, this regimen remained poorly tolerated.

## References

- Bisogno G, Riccardi R, Ruggiero A, Arcamone G, Prete A, Surico G, et al. Phase II study of a protracted irinotecan schedule in children with refractory or recurrent soft tissue sarcoma. *Cancer*. 2006 Feb 1;106(3):703-7.
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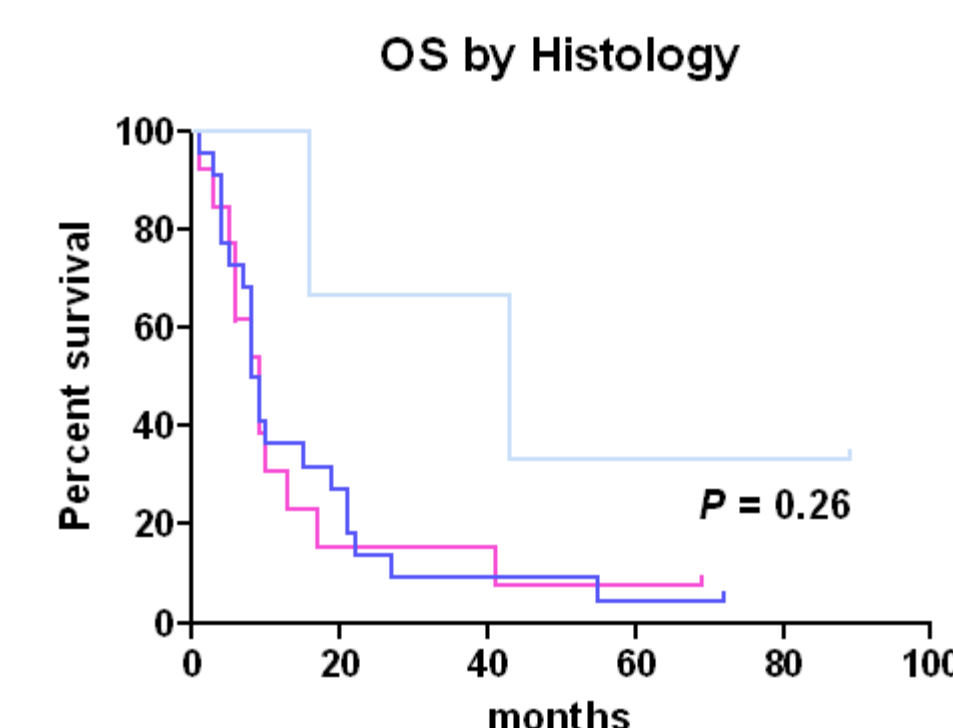
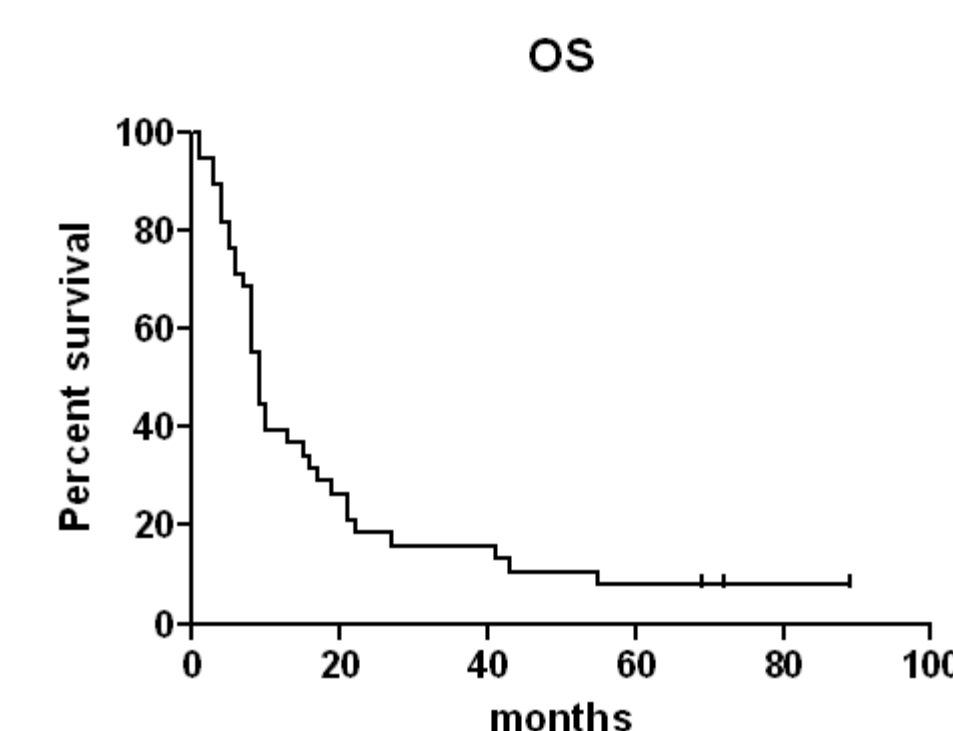


Fig. 3 Kaplan-Meier curves of overall survival (OS) and OS by histology



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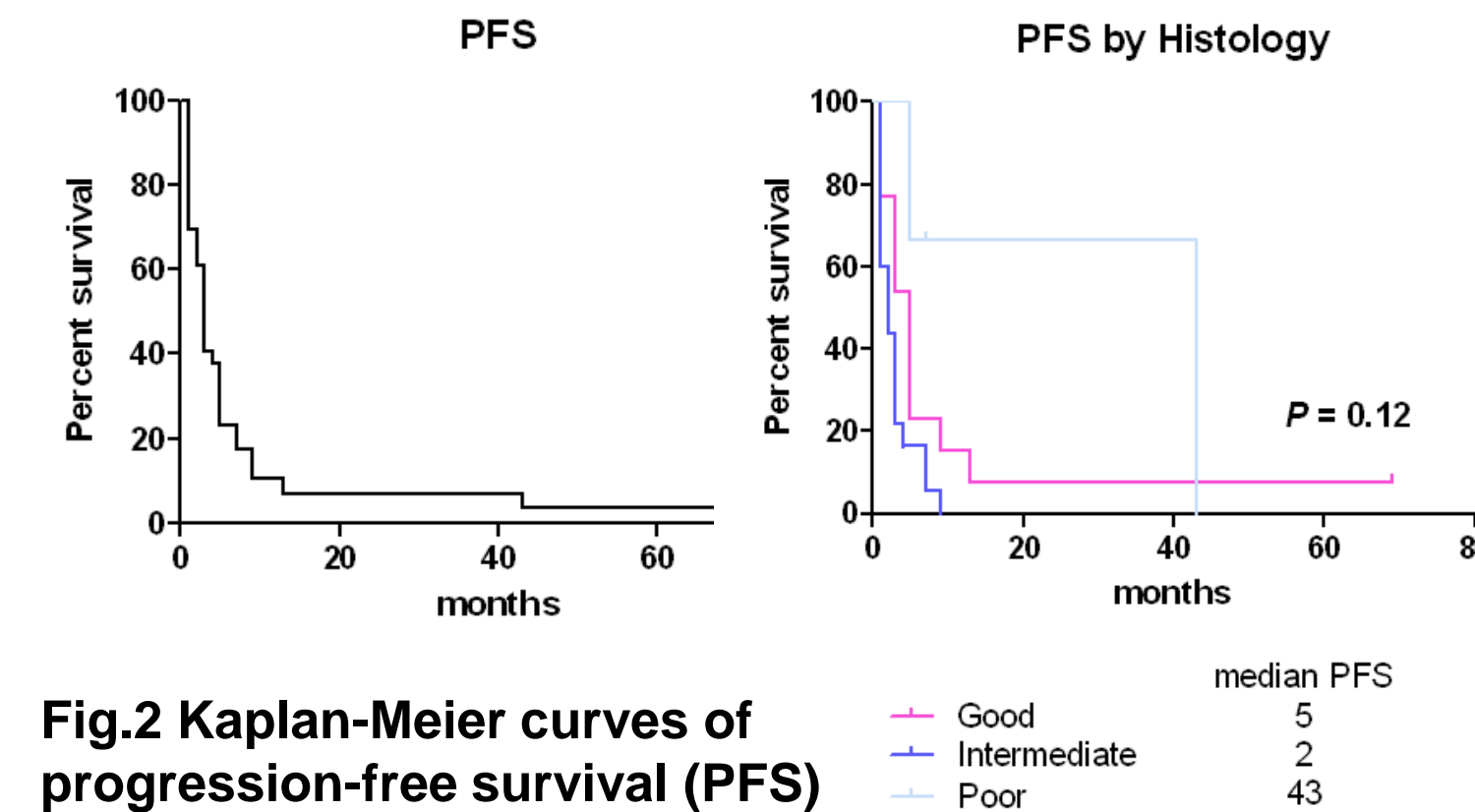


Fig.2 Kaplan-Meier curves of progression-free survival (PFS)

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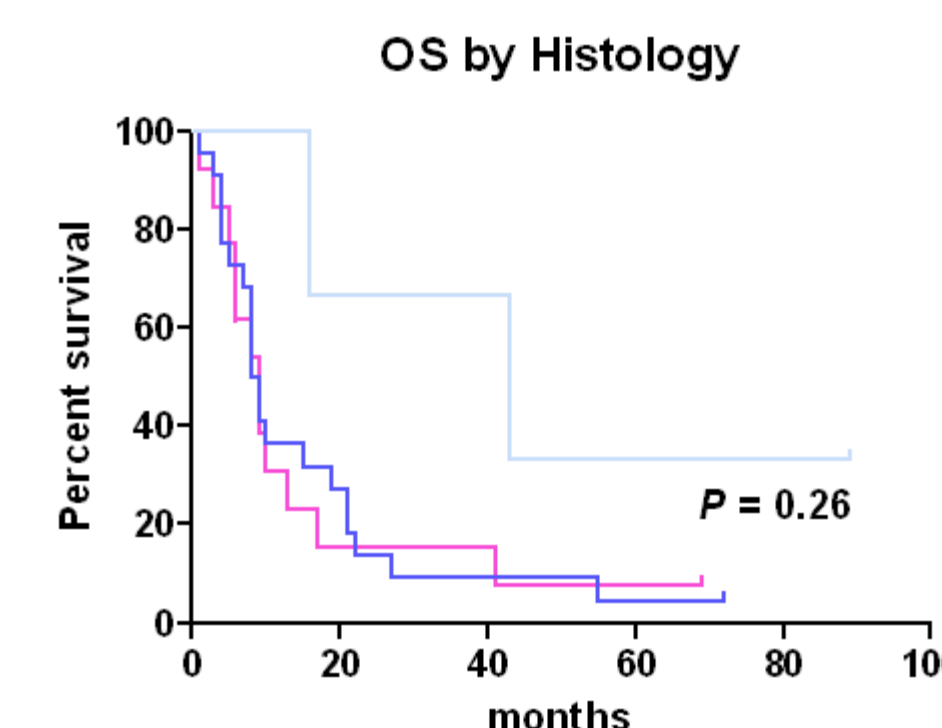
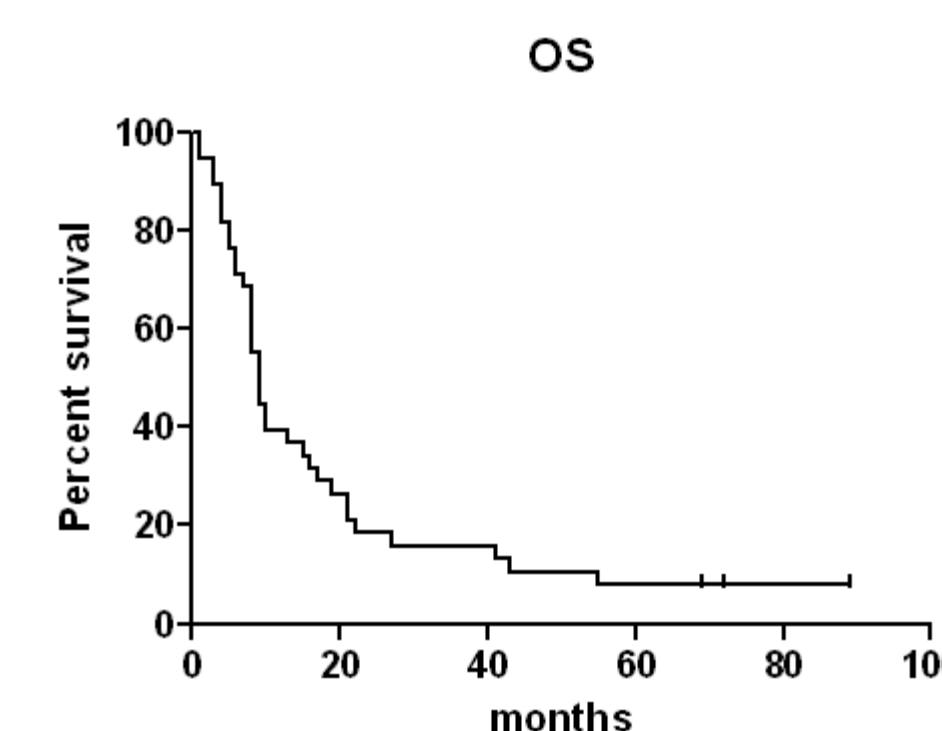
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