



Induction Chemoradiotherapy Followed by Surgical Resection for Locally Advanced Thymoma and Thymic Carcinoma:

Initial Results from a Phase II, Multi-institutional
Clinical trial

Robert J. Korst, Andrea Bezjak, Shanda H.
Blackmon, Noah Choi, Panos Fidias, Geoffrey
Liu, Cameron D. Wright, Shaf Keshavjee



Disclosures

- The authors have no relationships to disclose



Background

- Thymic epithelial tumors (TET) are best cured by complete surgical resection
- Approximately 50% of locally advanced TET (stage III) are completely resected
- Induction chemotherapy may enhance resectability of locally advanced TET
- TET are radiosensitive



Hypothesis

- Induction chemoradiotherapy will provide benefits over chemotherapy alone
 - Pathologic response
 - Complete resection rate
 - Recurrence and survival

Methods

- A phase II prospective clinical trial at 4 institutions
 - Induction cisplatin/etoposide plus 4500cGY IMRT or 3-D conformal
 - Surgical resection
 - Postoperative chemo(radio)therapy dependent on:
 - Completeness of resection
 - Masaoka stage
 - WHO histologic type

Inclusion criteria

- Mediastinal thymoma or thymic carcinoma
 - Tumor >8 cm, or
 - Tumor 5-8 cm, plus
 - Irregular or scalloped borders
 - Heterogeneous
 - Ectopic calcification
 - Obvious great vessel/adjacent organ invasion/encirclement
 - Tumor <5 cm
 - Obvious great vessel/adjacent organ invasion/encirclement

Endpoints

- **Primary: Pathologic response**
 - Complete: No tumor in specimen
 - Near complete: <10% viable tumor
- **Secondary:**
 - Ability of CT criteria and SUV_{max} in predicting Masaoka stage and WHO histologic type
 - Assessment of radiographic response using CT and FDG-PET
 - Toxicity and surgical complications
 - Recurrence rates, failure patterns, survival

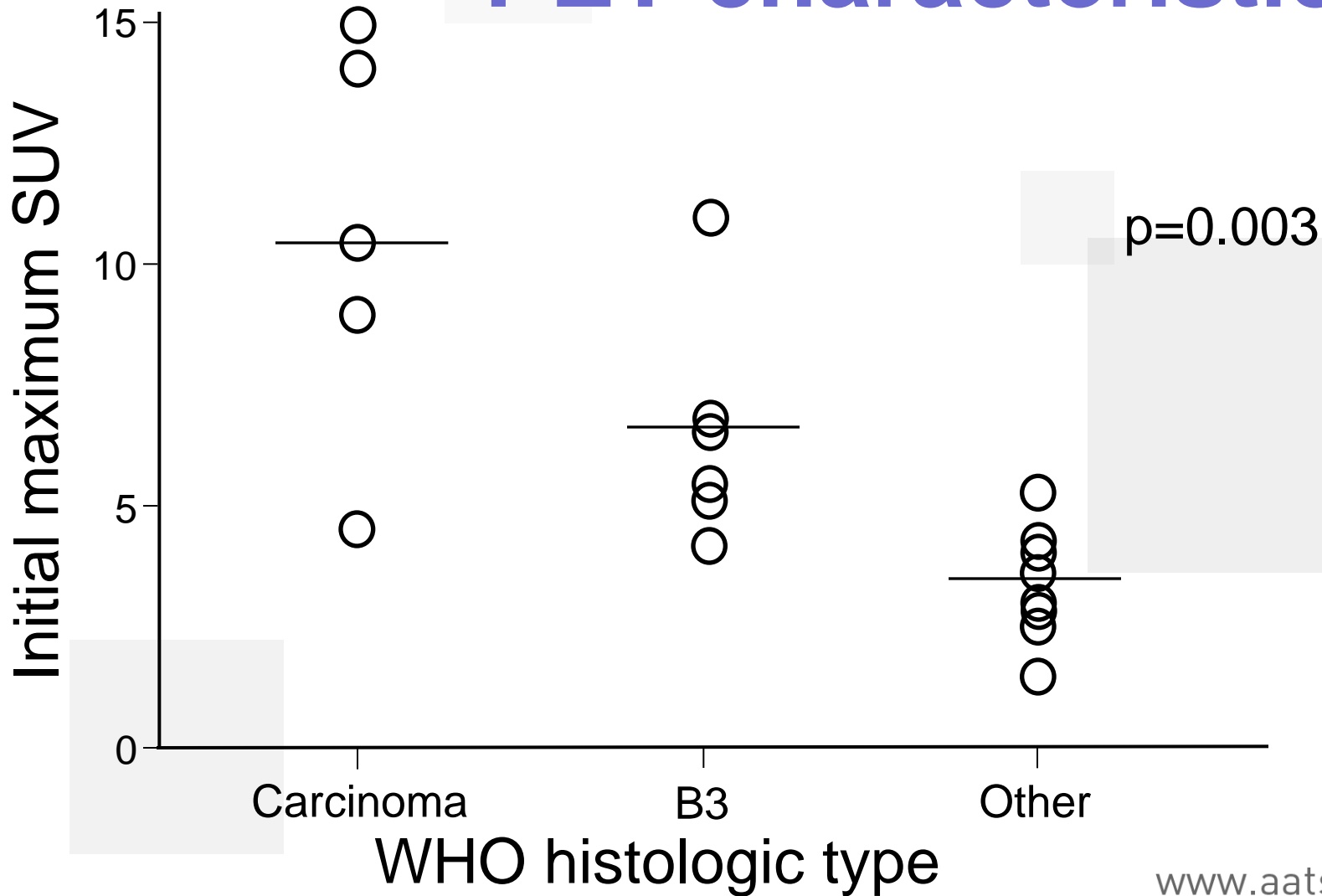
Patient population

- 22 patients signed consent
 - 1 withdrew prior to treatment
- 17 males (80%); median age: 51
- Paraneoplastic syndromes
 - 5 (24%) myasthenia gravis
 - 1 (5%) pure red cell aplasia

CT characteristics

<u>CT characteristic</u>	<u># patients (%)</u>	
>8 cm	6	(29)
5-8 cm	15	(71)
<5 cm	0	
Lobulated/scalloped border	15	(71)
Heterogeneous	15	(71)
Ectopic calcification	6	(29)
Obvious vessel/organ invasion or encirclement	7	(33)

PET characteristics



Induction protocol

- Completed in 20 of 21 patients
 - Second chemo cycle refused by 1 patient
- All 21 patients completed RT (4000-4500 cGY)
 - 3D conformal: 6 (29%)
 - IMRT: 15 (71%)
 - 4500 cGY: 17 (81%)
- Grade 3 or 4 toxicity in 9 patients (41%)

Induction protocol toxicity

Toxicity	# patients (%)	
Grade 3		
Tinnitus	1	(5)
Allergic reaction	1	(5)
Dehydration	1	(5)
Myasthenia exacerbation	1	(5)
Esophagitis	1	(5)
Nausea/vomiting	1	(5)
Febrile neutropenia	2	(9)
Grade 4		
Thrombocytopenia	1	(5)
Cardiac arrest	1	(5)

Radiographic response (CT)

- RECIST response assessment
 - 10 partial responses
 - 11 stable disease
 - 0 complete responses
 - 0 progressive disease
- Trend toward higher % size reduction in carcinoma patients versus “low risk” thymoma (A, AB, B1, B2, metaplastic)
 - -28% versus -15%; $p=0.09$

Surgical resection

- Attempted in all 21 patients
- Complete resection: 17 (77%)
- R1: 3 (14%)
- R2: 1 (5%)
- Complications: 8 patients (36%)



Surgical complications

Complication	# patients (%)	
Pneumonia	1	(5)
Pulmonary infiltrate	1	(5)
Hemothorax	1	(5)
Mucous plugging	1	(5)
Aspiration	1	(5)
Pleural effusion	1	(5)
Intraoperative cardiac arrest	1	(5)
Multiple organ failure	1	(5)
Neutropenia	1	(5)
Dressler's syndrome	2	(9)
Death	2	(9)
Atrial fibrillation	3	(14)

Post-surgical Masaoka stage

<u>Masaoka stage</u>	<u># patients (%)</u>	
I	2	(10)
II	4	(19)
III	12	(57)
IVA	1	(5)
IVB	2	(10)

Post-surgical WHO histologic type

<u>WHO histologic type</u>	<u># patients (%)</u>	
Metaplastic	1	(5)
A	2	(10)
AB	1	(5)
B1	1	(5)
B2	3	(14)
B3	6	(29)
Carcinoma	7	(33)

Pathologic response

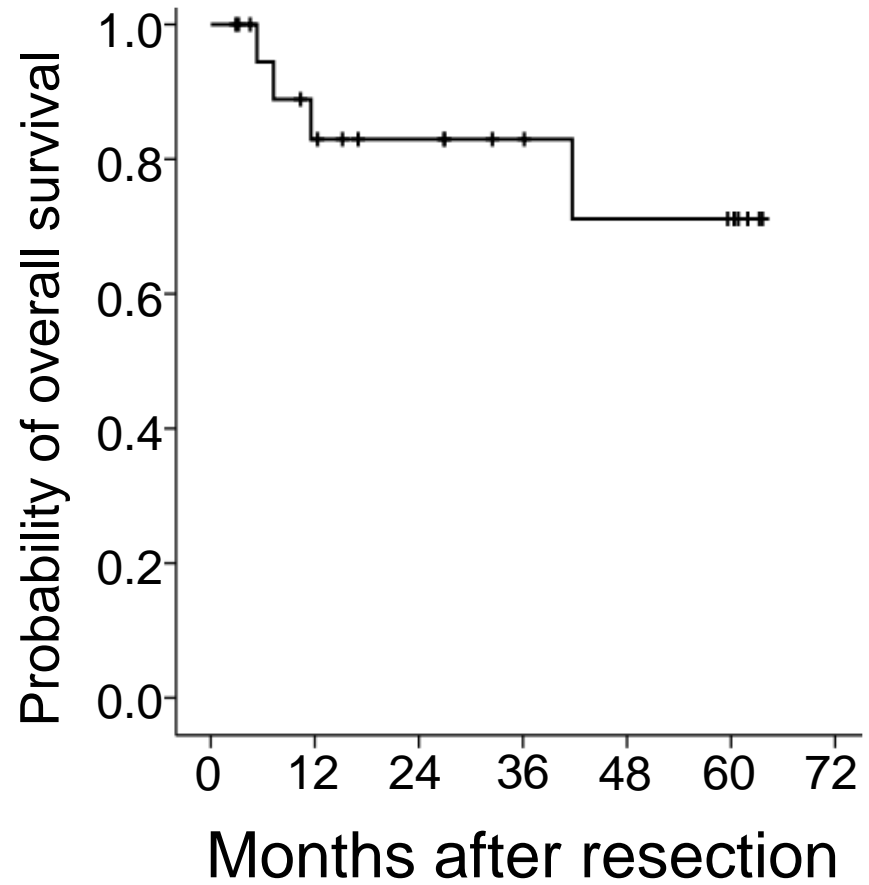
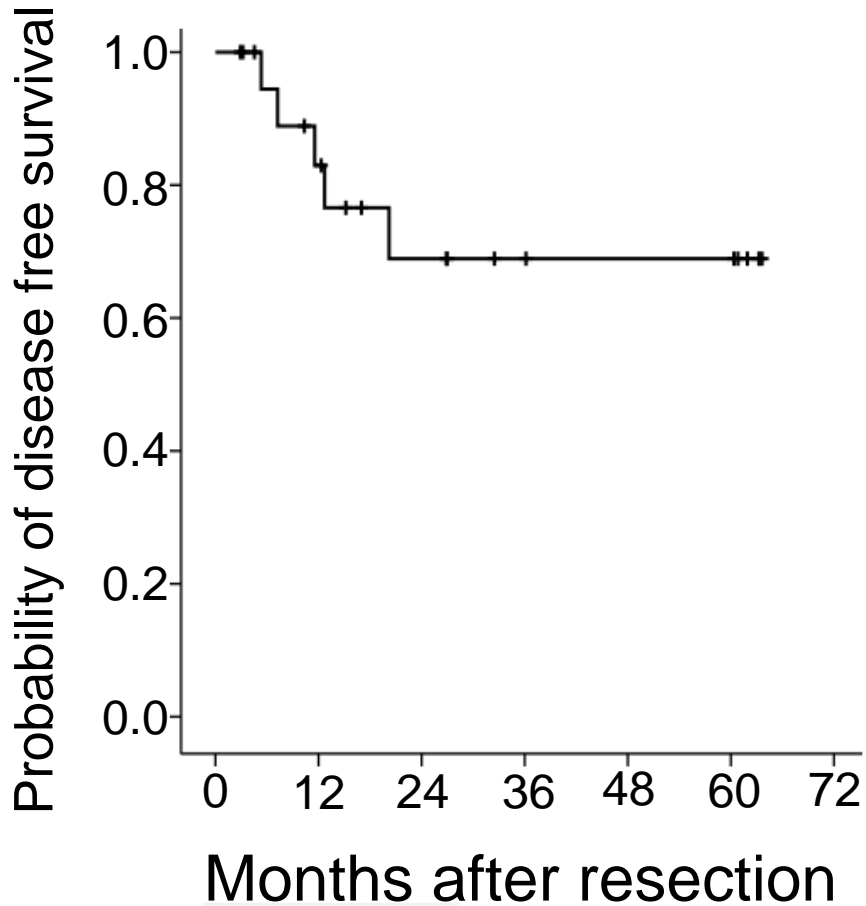
- No complete pathologic responses
- 5 patients (24%) had a near complete pathologic response
 - 4 carcinomas
 - 1 B3



Recurrence

- Median followup: 27 months (0-64)
- No recurrence in completely resected patients
- 19 patients survived into followup period
 - 15 NED
 - 1 AWD
 - 1 DOD
 - 1 DOC
 - 1 lost to followup

Survival



Conclusions

- CT and PET can identify patients with higher risk TET
 - More advanced Masaoka stage
 - More aggressive histologic type
- Induction chemoradiotherapy is associated with a high rate of complete resection for locally advanced TET
 - Near complete pathologic response in 24%
- Thymic carcinoma may respond the best to induction chemoradiotherapy