Clinicopathologic Predictors of Outcomes in Children with Stage I Germ Cell Tumors: A Pooled *Post Hoc* Analysis of Trials from the Children's Oncology Group

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INTRODUCTION

- Patients with clinical stage I (CS I: cN0M0) germ cell tumors (GCT) exhibit favorable oncologic outcomes
- While prognostic features can help inform treatment in adults with CS I GCT, we lack reliable means to predict relapse among pediatric patients
- **Objective:** To identify predictors of relapse in children with CS I GCT using pooled prospective clinical trial data from the Children's Oncology Group (COG)

METHODS

- Pooled *post hoc* analysis on pediatric CS I GCT patients enrolled in 3 prospective trials:
  - **INT-0097:** An intergroup study of the treatment of children with localized malignant germ cell tumors – A phase II study
  - **INT-0106:** An intergroup study of high-risk malignant germ cell tumors in children – A phase III study
  - **AGCT0132:** A phase III study of reduced therapy in the treatment of children with low and intermediate risk extracranial germ cell tumors
- **Variables of interest**:
  - Age
  - pT stage
  - Histology (central review)
  - LVI (present/absent)
  - Tumor markers
  - Complete resection
- **Primary outcome**: Event-free survival (EFS)
  - Time from enrollment to relapse, subsequent malignant neoplasm (SMN), death, or last F/U
  - EFS assessed using Kaplan-Meier methods and proportional hazards regression modeling with models selected using backwards stepwise regression (conditional removal for p>0.05)

RESULTS

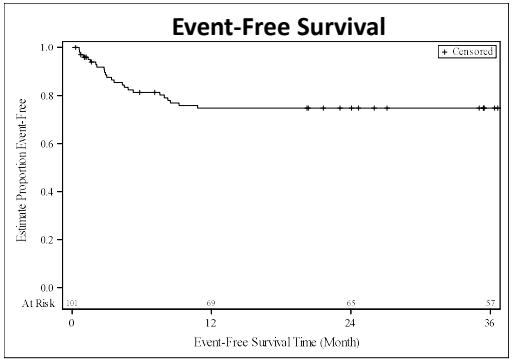
- 119 patients identified – **101 records reviewed:**

Age (years)	Number of patients
<1	30
1	35
2	15
3	5
4	1
12	1
13	1
14	12
15	1

pT stage distribution	Number of patients (%)
pT1	38 (37%)
pT2	36 (36%)
pT3	3 (3%)
Not reported	24 (24%)

Pathologic Characteristic	Yes	No	Not reported
Choriocarcinoma present	9 (9%)	70 (69%)	22 (22%)
Seminoma present	5 (5%)	74 (74%)	22 (22%)
Embryonal carcinoma present	15 (15%)	64 (63%)	22 (22%)
Immature teratoma present	13 (13%)	66 (66%)	22 (22%)
Mature teratoma present	9 (9%)	70 (69%)	22 (22%)
Any teratoma present	15 (15%)	64 (63%)	22 (22%)
Yolk sac tumor present	79 (78%)	0 (0%)	22 (22%)
Lymphovascular invasion (LVI)	36 (35%)	30 (30%)	35 (35%)

- **88 patients** with outcomes data available:



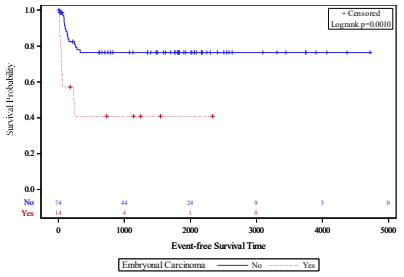
-Median f/u: 5.0 years
-EFS: 75% at 1, 2, 3 years
-Median EFS not reached
-Overall survival: 100%

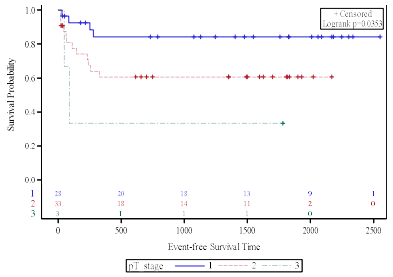
- Predictors of relapse:

Predictor	Univariable Analysis HR (95% CI)	P-value	Multivariable Analysis HR (95% CI)	P-value
Age ≥12 years	3.3 (1.4-8.0)	**0.005**	*	
pT stage:				
pT1	Ref.	**0.007**	Ref.	**<0.0001**
pT2	3.8 (1.2-11.7)		8.0 (2.3-28.2)	
pT3	9.7 (1.8-53.0)		14.3 (2.3-87.9)	
Choriocarcinoma present	4.2 (1.5-11.7)	**0.003**	*	
Embryonal carcinoma present	4.4 (1.8-11.0)	**0.002**	11.6 (3.9-34.9)	**0.0022**
Immature teratoma present	4.0 (1.6-10.3)	**0.003**	--	
Mature teratoma present	6.7 (2.5-18.0)	**0.0002**	--	
Any teratoma present	4.6 (1.9-11.6)	**0.0003**	*	
LVI	2.8 (1.1-7.4)	**0.03**	*	

**Variables removed from MVA after stepwise selection process. Age was removed given collinearity with the other variables*

No significant impact on relapse:
- AFP levels
- HCG levels
- Presence of seminoma
- Presence of yolk sac tumor





Limitations:
- Retrospective analysis
- Missing data for certain variables of interest
- Relative paucity of events

CONCLUSIONS

- Using combined data from multiple prospective trials, our study identifies clinicopathologic features that predict relapse in pediatric CS I GCT patients
- Further investigation is required to incorporate these features into personalized treatment recommendations for these patients