

# 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

Shyamli Singla, Justin Wong, Nirmish Singla, Mark Krailo, Li Huang, Furqan Shaikh, Deborah Billmire, Frederick Rescorla, Jonathan Ross, Bryan Dicken, James Amatruda, A. Lindsay Frazier, Aditya Bagrodia

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### INTRODUCTION

- Patients with clinical stage I (CS I: cNOMO) 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 15 5 1 1 1 1 1 12 1			
2				
3				
4				
12				
13				
14				
15				

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%) 22 (22%) 22 (22%) 22 (22%) 22 (22%)	
Embryonal carcinoma present	15 (15%)	64 (63%)		
Immature teratoma present	13 (13%)	66 (66%)		
Mature teratoma present	9 (9%)	70 (69%)		
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%)	



#### -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		Multivariable Analysis		
	HR (95% CI)	P-value	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)		No significant impact on relapse
pT3	9.7 (1.8-53.0)		14.3 (2.3-87.9)		AFP levels
Choriocarcinoma present	4.2 (1.5-11.7)	0.003	*		HCG levels Dresenses of semineme
Embryonal carcinoma	4.4 (1.8-11.0)	0.002	11.6 (3.9-34.9)	0.0022	Presence of seminoma Presence of yelk see tumor
present					· Fresence of york sac turnor
Immature teratoma	4.0 (1.6-10.3)	0.003			
present					
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



# 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