elcc European Lung Cancer Conference

PD-L1 expression and its association with survival in malignant pleural mesothelioma

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Organisers

IASLC International Association for the Study of Lung Cancer

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European Society for Medical Oncology

Disclosure slide

- Presenter has no disclosures

PD-L1 (B7-H1)

- PD-L1 is a co-inhibitory immune checkpoint molecule
- PD-L1 is expressed by many malignancies and is associated with advanced disease and poor survival in most of these

Hypothesis

- PD-L1 is expressed in malignant pleural mesothelioma and is associated with poor survival

Study Design

- Archived samples of malignant pleural mesothelioma were identified and evaluated for adequacy
- Despite clinical diagnosis of malignant pleural mesothelioma, cases that did not have appropriate IHC profile were excluded

Study Design

IHC criteria

- Specimens must have been positive for at least two mesothelioma markers: WT-1, calretinin, CK5/6, D2-40
- Specimens must have been positive for at least two carcinoma markers: MOC31, pCEA, TTF-1, BerEP4

Study Design

- Tissue blocks were sectioned at 5 microns
- IHC performed with anti-human B7-H1 clone 5H1-A3 as described previously (Frigola et al Clin Cancer Res 2011; 17:1915-23)

Study Design

- Extent and location of positively-stained malignant cells were determined by a pathologist
- Specimens with 5% or more positively-stained cells were considered positive (Thompson et al Cancer Res 2006;66:3381-5)
- Patient records were abstracted for clinicopathologic information, treatment and survival

Study Design

- X^2 test used to compare clinicopathologic differences between PD-L1 positive and negative groups
- Survival modeled with Kaplan-Meier method and groups compared by log-rank test
- Cox proportional hazards model used for multivariate analysis

Results

- 224 cases with sufficient tissue were identified from 1986-2006
- 106 cases included after IHC review by a thoracic pathologist

Table

* Univariate analysis

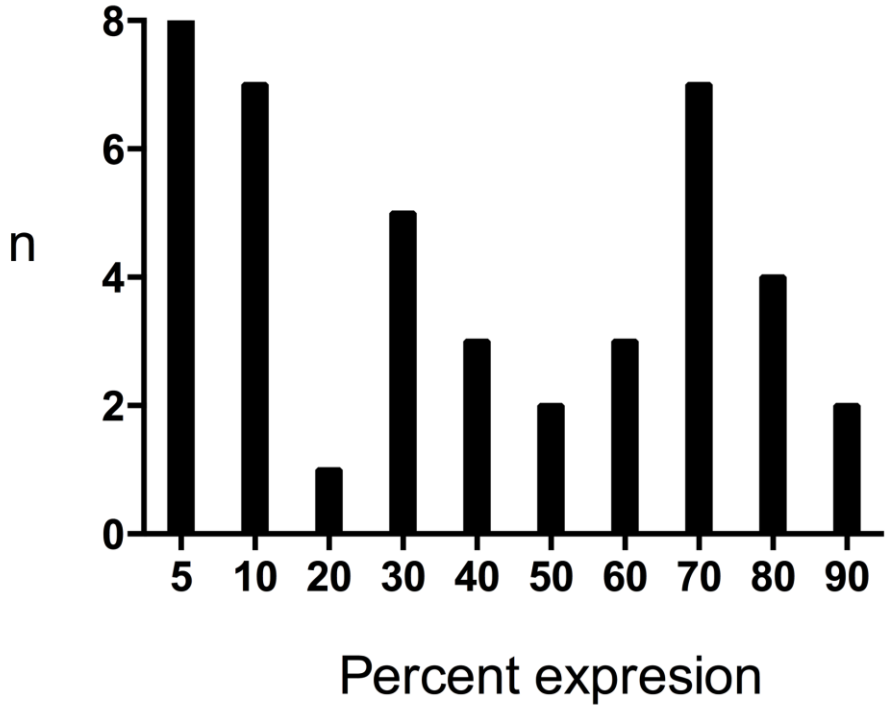
	PD-L1 positive	PD-L1 negative	P-value*
n (%)	42 (40%)	64 (60%)	
Gender			0.72
Male	35 (83%)	55 (86%)	
Female	7 (17%)	9 (14%)	
Age y (median, IQR)	68 (59-75)	65 (58-73)	0.19
Decade of Dx			0.57
1980's	0 (0%)	1 (2%)	
1990's	22 (52%)	35 (55%)	
2000's	20 (48%)	28 (43%)	

Table continued

* Univariate analysis

	PD-L1 +	PD-L1 -	P-value*
Subtype			<0.0001
Epithelioid	14 (33%)	54 (84%)	
Sarcomatoid	16 (38%)	1 (2%)	
Biphasic	12 (29%)	9 (14%)	
Surgical treatment offered			0.03
Yes	7 (17%)	23 (36%)	
No	35 (83%)	41 (64%)	
Lymphocytic infiltration			0.36
Yes	38 (90%)	54 (84%)	
No	4 (10%)	10 (16%)	

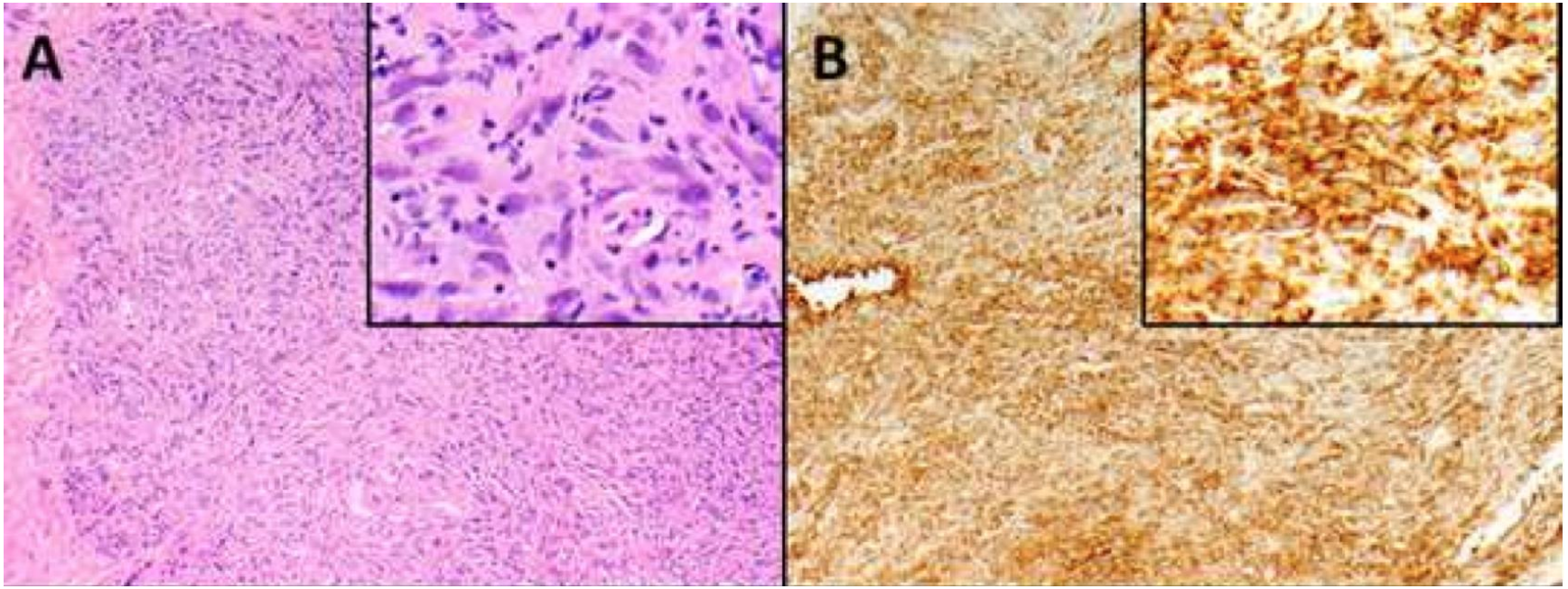
Distribution of expression



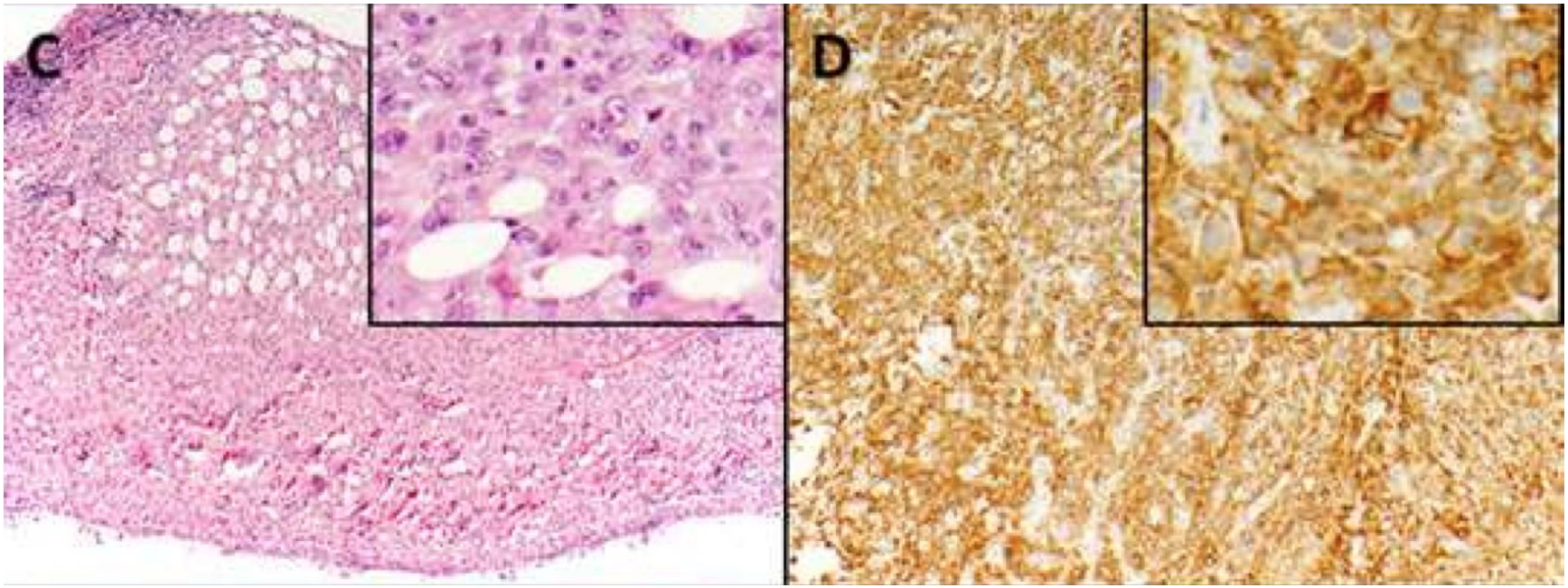
Localization of PD-L1

- Cytoplasmic: 18 (43%)
- Membranous: 10 (24%)
- Cytoplasmic and membranous: 14 (33%)

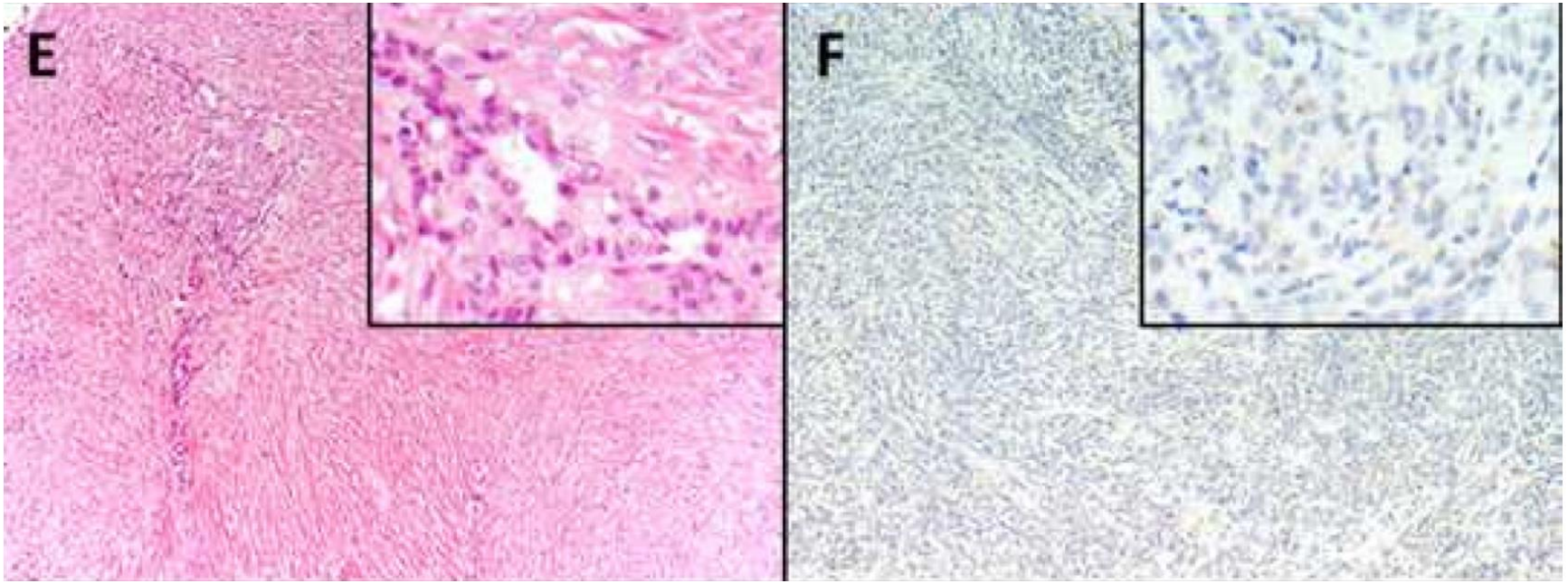
Sarcomatoid



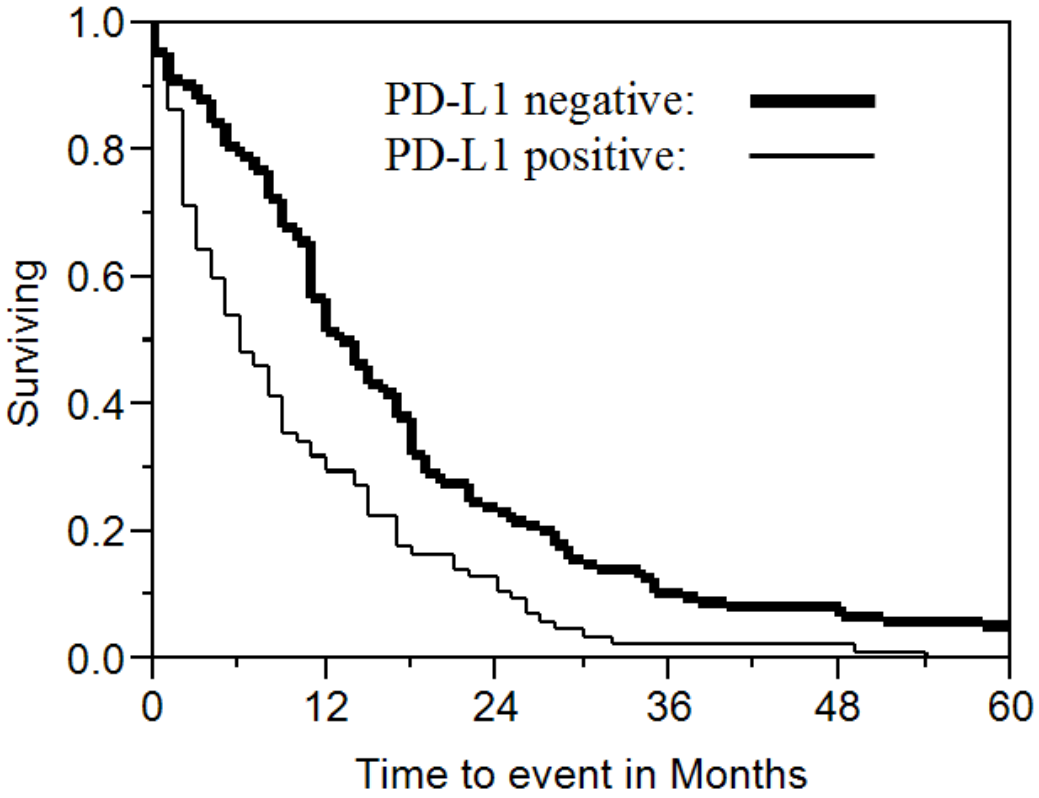
Epithelioid



Biphasic



Overall Survival



PD-L1 negative:
14.5 months (IQR 9-19)

PD-L1 positive:
5 months (IQR 2-9.5)

p<0.0001

Multivariate analysis

- PD-L1 expression remained significantly associated with worse survival after adjusting for age, histology and therapy

  (risk ratio 1.71, 1.03-2.78, p=0.04)
- Sarcomatoid histology also remained significantly associated with worse survival

  (risk ratio 2.18, 1.08-4.23, p=0.03)

Conclusions

- PD-L1 expression was detected in 40% of specimens of malignant pleural mesothelioma
- Almost all sarcomatoid subtypes expressed PD-L1
- PD-L1 expression is associated with poor survival in malignant pleural mesothelioma

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Thank you

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