A Danish and a Turkish cohort of patients with pleural mesothelioma treated with pemetrexed-based chemotherapy: differences, similarities and prognostic factors

P0-102

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Objectives

We investigated a Danish and a Turkish cohort of pleural mesothelioma patients treated with pemetrexed-based chemotherapy in first-line palliative setting. Our aim was to compare patient characteristics, overall survival, and prognostic factors in these two populations.

Methods

Patients diagnosed with pleural mesothelioma during 2003-2013 in Aalborg, Denmark, and during 2010-2021 in Eskişehir, Turkey, were included in the study. Patient and survival information was obtained through medical journals and records. BAP1 loss or retain in tumor cells was assessed by immunohistochemistry with BAP1 mouse monoclonal antibody. Overall survival was defined as the time from diagnosis to death. For statistical analyses, Fisher´s exact test, t-test, log-rank tests, Kaplan-Meier curves, and univariate and multivariate Cox regression analyses were performed using STATA version 17. P-values < 0.05 were considered significant.

Conclusion

Somatic BAP1 loss, good performance status, and epithelioid subtype were independently associated with improved survival, with BAP1 status being the most significant prognostic factor in both cohorts. Although the type of asbestos exposure, occupational or environmental, causes different epidemiological findings, it does not seem to affect the overall survival and BAP1 status for mesothelioma patients.

Results

A total of 127 patients, 43 from Denmark and 84 from Turkey were included in the study (Table 1). There were significant differences regarding the sex (p<0.01), age at diagnosis (p<0.01), mesothelioma subtype (p=0.01), mesothelioma stage (p<0.01), performance status (p<0.01) and type of asbestos exposure (p<0.00001) for the two populations. There was no significant difference in the overall survival and BAP1 status of the Danish and Turkish patients. BAP1 loss was prognostic for survival in the Danish, the Turkish, and the combined cohort (Figure 1). Uni- and multivariate analysis of the two cohorts combined showed that BAP1 loss (p<0.01), epithelioid subtype (p<0.01), and performance status 0-1 (p=0.059) were associated with improved survival (Table 2).

Table 1. Patient characteristics, treatment and survival information for the Danish and the Turkish cohorts.

Characteristics	Danish cohort (n=43)	Turkish cohort (n=84)	P-value
Age, y, median (min - max)	70 (42-82)	65 (30-81)	< 0.01
Sex, male, n (%)	40 (93%)	55 (66%)	< 0.01
Mesothelioma subtype			
Epithelioid, n (%)	18 (42%)	57 (68%)	0.01
Sarcomatoid, n (%)	3 (7%)	6 (7%)	
Biphasic, n (%)	22 (51%)	21 (25%)	
ECOG PS, n (%)			
0	18 (42%)	6 (7%)	
1	21 (49%)	75 (89%)	< 0.01
2	4 (9%)	3 (4%)	
TNM stage			
I	6 (14%)	15 (17.5%)	
II	9 (21%)	3 (4.5%)	
III	16 (37%)	56 (66%)	< 0.01
IV	12 (28%)	10 (12%)	
Lines of treatment, n (%)			
One	18 (42%)	27 (32%)	0.56
Two	14 (32.5%)	32 (39%)	
Three or more	11 (25.5%)	25 (29%)	
BAP1			
Retained	14 (32.5%)	32 (38%)	0.57
Lost	29 (76.5%)	52 (62%)	
Type of asbestos exposure			
Occupational	37 (86%)	2 (2.5%)	
Environmental	0	80 (95%)	< 0.01
Domestic	5 (12%)	0	
None reported	1 (2%)	2 (2.5%)	
Survival, mo, median (95% CI)	17 (11-20)	14 (10-17)	0.96

Table 2. Univariate and multivariate cox regression analysis for the 127 mesothelioma patients.

Variable	Overall survival Univariate analysis		Overall survival Multivariate analysis	
	HR (95%CI)	P-value	HR (95%CI)	P-value
Age				
≤ 65	1	0.66		
> 65	1.08 (0.76-1.54)			
Sex				
Female	1	0.66		
Male	0.91 (0.61-1.37)			
PS				
0-1	1	0.038	1	0.059
≥ 2	2.26 (1.05-4.88)		2.13 (0.97-4.67)	
Subtype				
Epithelioid	1	0.039	1	0.007
Non-epithelioid	1.47 (1.02-2.12)		1.72 (1.16-2.54)	
BAP1 status				
Loss	1	0.003	1	< 0.01
Retained	1.74 (1.21-2.52)		2.10 (1.42-3.11)	

Figure 1. Kaplan Meier (KM) curves for the Danish (DK), the Turkish (TK) and the combined cohort.

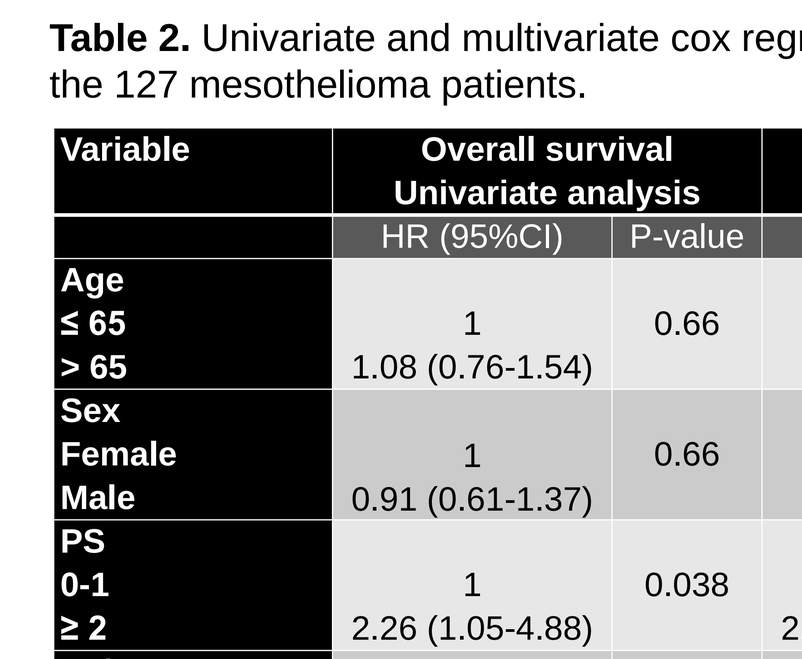

Figure 1a. KM curves for the DK and the TK patients.

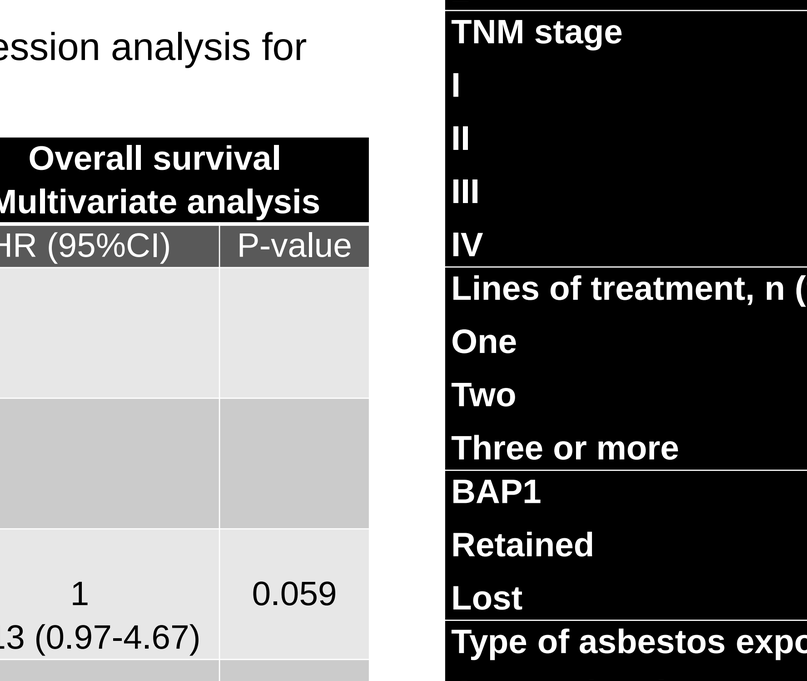

Figure 1b. KM curves for the DK and the TK patients dichotomized by BAP1 status.

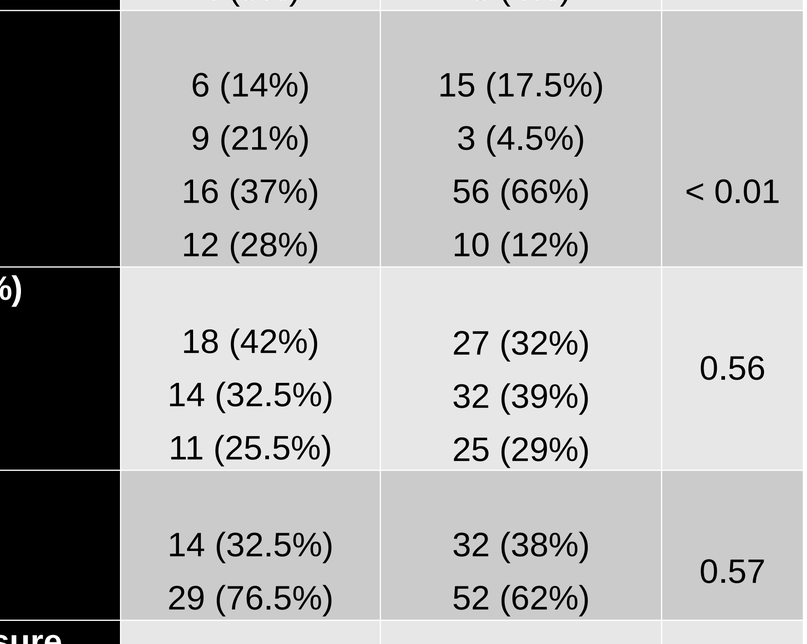

Figure 1c. KM curves for the combined cohort of the DK and TK patients dichotomized by BAP1 status.