Supplementary Materials

New prognostic frontiers for lung neuroendocrine tumors

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Short title: New prognostic frontiers for lung N

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Supplementary results. Associations with age, peripheral versus central location of the primary tumor and necrosis

1. AGE

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Age * Smoke yes 1 no 0	165	55,0%	135	45,0%	300	100,0%
Age* Central 1 vs Periferic 0 primary lesion	200	66,7%	100	33,3%	300	100,0%
Age * 18 FDG PET scan Not done Positive 1 Negative 0	103	34,3%	197	65,7%	300	100,0%
Age* Octreoscan/68GalliumPET Not done NA Positive 1 Negative 0	63	21,0%	237	79,0%	300	100,0%
Age * Tcat	192	64,0%	108	36,0%	300	100,0%
Age * Npos1neg0	190	63,3%	110	36,7%	300	100,0%
Age * Stage	196	65,3%	104	34,7%	300	100,0%
Age * Ki67	165	55,0%	135	45,0%	300	100,0%
Age* Necrosis Not done NA Positive 1 Negative 0	199	66,3%	101	33,7%	300	100,0%
Age* Diagnosis Typical carcinoid 0 Atypical carcinoid 1	200	66,7%	100	33,3%	300	100,0%
Age * Typesurgery	178	59,3%	122	40,7%	300	100,0%

Count

		Smoke yes 1 no 0		
		0	1	Total
Age	< = MED	47	37	84
	>MED	55	26	81
Total		102	63	165

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2,494[a]	1	0,114		
Continuity Correction[b]	2,014	1	0,156		
Likelihood Ratio	2,504	1	0,114		
Fisher's Exact Test				0,149	0,078
Linear-by-Linear Association	2,479	1	0,115		
N of Valid Cases	165				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 30,93.

b. Computed only for a 2x2 table

Crosstab

Count

		Central 1 vs Periferic 0 primary lesion		
		0	1	Total
Age	< = MED	27	76	103
	>MED	44	53	97
Total		71	129	200

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	7,998[a]	1	0,005		
Continuity Correction[b]	7,184	1	0,007		
Likelihood Ratio	8,053	1	0,005		
Fisher's Exact Test				0,005	0,004
Linear-by-Linear Association	7,958	1	0,005		
N of Valid Cases	200				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 34,43.

b. Computed only for a 2x2 table

Crosstab

Count

		18 FDG PET scan Not done Positive 1 Negative 0		
		0	1	Total
Age	< = MED	12	36	48
	>MED	14	41	55
Total		26	77	103

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0,003[a]	1	0,958		
Continuity Correction[b]	0,000	1	1,000		
Likelihood Ratio	0,003	1	0,958		
Fisher's Exact Test				1,000	0,570
Linear-by-Linear Association	0,003	1	0,958		
N of Valid Cases	103				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 12,12.

b. Computed only for a 2x2 table

Crosstab

Count

		Octreoscan/68GalliumPET Not done NA Positive 1 Negative 0		
		0	1	Total
Age	< = MED	14	24	38
	>MED	8	17	25
Total		22	41	63

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0,156[a]	1	0,693		
Continuity Correction[b]	0,015	1	0,901		
Likelihood Ratio	0,156	1	0,693		
Fisher's Exact Test				0,790	0,453
Linear-by-Linear Association	0,153	1	0,696		
N of Valid Cases	63				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 8,73.

b. Computed only for a 2x2 table

Crosstab

Count

		Tcat				
		1	2	3	4	Total
Age	< = MED	53	33	10	3	99
	>MED	63	23	4	3	93
Total		116	56	14	6	192

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	5,037[a]	3	0,169
Likelihood Ratio	5,128	3	0,163
Linear-by-Linear Association	3,152	1	0,076
N of Valid Cases	192		

a. 2 cells (25,0%) have expected count less than 5. The minimum expected count is 2,91.

Crosstab

Count

		Npos1neg0		
		0	1	Total
Age	< = MED	68	31	99
	>MED	72	19	91
Total		140	50	190

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2,662[a]	1	0,103		
Continuity Correction[b]	2,151	1	0,142		
Likelihood Ratio	2,686	1	0,101		
Fisher's Exact Test				0,137	0,071
Linear-by-Linear Association	2,648	1	0,104		
N of Valid Cases	190				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 23,95.

b. Computed only for a 2x2 table

Crosstab

Count

		Stage				
		1	2	3	4	Total
Age	< = MED	51	33	8	7	99
	>MED	60	23	9	5	97
Total		111	56	17	12	196

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	2,887[a]	3	0,409
Likelihood Ratio	2,899	3	0,407
Linear-by-Linear Association	1,065	1	0,302
N of Valid Cases	196		

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 5,94.

Crosstab

Count

		Ki67			
		1	2	3	Total
Age	< = MED	49	35	4	88
	>MED	34	39	4	77
Total		83	74	8	165

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	2,204[a]	2	0,332
Likelihood Ratio	2,208	2	0,332
Linear-by-Linear Association	1,754	1	0,185
N of Valid Cases	165		

a. 2 cells (33,3%) have expected count less than 5. The minimum expected count is 3,73.

Crosstab

Count

		Necrosis Not done NA Positive 1 Negative 0		
		0	1	Total
Age	< = MED	83	20	103
	>MED	82	14	96
Total		165	34	199

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0,820[a]	1	0,365		
Continuity Correction[b]	0,514	1	0,473		
Likelihood Ratio	0,824	1	0,364		
Fisher's Exact Test				0,452	0,237
Linear-by-Linear Association	0,816	1	0,366		
N of Valid Cases	199				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 16,40.

b. Computed only for a 2x2 table

Crosstab

Count

		Diagnosis Typical carcinoid 0 Atypical carcinoid 1		
		0	1	Total
Age	< = MED	67	36	103
	>MED	72	25	97
Total		139	61	200

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1,985[a]	1	0,159		
Continuity Correction[b]	1,576	1	0,209		
Likelihood Ratio	1,994	1	0,158		
Fisher's Exact Test				0,170	0,105
Linear-by-Linear Association	1,975	1	0,160		
N of Valid Cases	200				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 29,59.

b. Computed only for a 2x2 table

Count

		Typesurgery								
		pneumonectomy	bilobectomy	lobectomy	sleeve resection	segmental resection	wedge resection	extended resection	other	Total
Age	< = MED	7	8	62	2	3	5	4	1	92
	>MED	4	2	67	0	2	9	2	0	86
Total		11	10	129	2	5	14	6	1	178

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	9,430[a]	7	0,223
Likelihood Ratio	10,874	7	0,144
Linear-by-Linear Association	0,245	1	0,620
N of Valid Cases	178		

a. 9 cells (56,3%) have expected count less than 5. The minimum expected count is 0,48.

2. TUMOR LOCATION: PERIPHERAL VERSUS CENTRAL

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Per cent	N	Per cent	N	Percent
Central 1 vs Periferic 0 primary lesion * Smoke yes 1 no 0	246	82,0%	54	18,0%	300	100,0%
Central 1 vs Periferic 0 primary lesion * 18 FDG PET scan Not done Positive 1 Negative 0	200	66,7%	100	33,3%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Octreoscan/68Gallium PET Not done NA Positive 1 Negative 0	64	21,3%	236	78,7%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Tcat	276	92,0%	24	8,0%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Npos1neg0	265	88,3%	35	11,7%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Stage	274	91,3%	26	8,7%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Ki67	231	77,0%	69	23,0%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Necrosis Not done NA Positive 1 Negative 0	293	97,7%	7	2,3%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Diagnosis Typical carcinoid 0 Atypical carcinoid 1	298	99,3%	2	0,7%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Typesurgery	276	92,0%	24	8,0%	300	100,0%
Central 1 vs Periferic 0 primary lesion * Age	200	66,7%	100	33,3%	300	100,0%

Crosstab

Count

		Smoke yes 1 no 0		Total
		0	1	
Central 1 vs Periferic 0 primary lesion	0	65	37	102
	1	77	67	144
Total		142	104	246

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2,572[a]	1	0,109		
Continuity Correction[b]	2,169	1	0,141		
Likelihood Ratio	2,587	1	0,108		
Fisher's Exact Test				0,118	0,070
Linear-by-Linear Association	2,562	1	0,109		
N of Valid Cases	246				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 43,12.

b. Computed only for a 2x2 table

Crosstab

Count

		18 FDG PET scan Not done Positive 1 Negative 0		Total
		0	1	
Central 1 vs Periferic 0 primary lesion	0	21	62	83
	1	51	66	117
Total		72	128	200

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	7,049[a]	1	0,008		
Continuity Correction[b]	6,277	1	0,012		
Likelihood Ratio	7,206	1	0,007		
Fisher's Exact Test				0,011	0,006
Linear-by-Linear Association	7,013	1	0,008		
N of Valid Cases	200				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 29,88.

b. Computed only for a 2x2 table

Count

		Octreoscan/68GalliumPET Not done NA Positive 1 Negative 0		Total
		0	1	
Central 1 vs Periferic 0 primary lesion	0	9	13	22
	1	13	29	42
Total		22	42	64

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0,634[a]	1	0,426		
Continuity Correction[b]	0,270	1	0,603		
Likelihood Ratio	0,627	1	0,428		
Fisher's Exact Test				0,580	0,300
Linear-by-Linear Association	0,625	1	0,429		
N of Valid Cases	64				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 7,56.

b. Computed only for a 2x2 table

Crosstab

Count

		Tcat				Total
		1	2	3	4	
Central 1 vs Periferic 0 primary lesion	0	72	22	7	2	103
	1	103	56	9	5	173
Total		175	78	16	7	276

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	**4,375[a]**	**3**	**0,224**
Likelihood Ratio	**4,480**	**3**	**0,214**
Linear-by-Linear Association	**1,415**	**1**	**0,234**
N of Valid Cases	**276**		

a. 2 cells (25,0%) have expected count less than 5. The minimum expected count is 2,61.

Crosstab

Count

		Npos1neg0		Total
		0	1	
Central 1 vs Periferic 0 primary lesion	**0**	**70**	**27**	**97**
	1	**130**	**38**	**168**
Total		**200**	**65**	**265**

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0,904[a]	1	0,342		
Continuity Correction[b]	0,644	1	0,422		
Likelihood Ratio	0,894	1	0,344		
Fisher's Exact Test				0,375	0,210
Linear-by-Linear Association	0,900	1	0,343		
N of Valid Cases	265				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 23,79.

b. Computed only for a 2x2 table

Crosstab

Count

		Stage				Total
		1	2	3	4	
Central 1 vs Periferic 0 primary lesion	0	62	21	10	6	99
	1	108	49	12	6	175
Total		170	70	22	12	274

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	**2,978[a]**	**3**	**0,395**
Likelihood Ratio	**2,946**	**3**	**0,400**
Linear-by-Linear Association	**0,542**	**1**	**0,462**
N of Valid Cases	**274**		

a. 1 cells (12,5%) have expected count less than 5. The minimum expected count is 4,34.

Crosstab

Count

		Ki67			Total
		1	2	3	
Central 1 vs Periferic 0 primary lesion	**0**	**59**	**23**	**2**	**84**
	1	**83**	**57**	**7**	**147**
Total		**142**	**80**	**9**	**231**

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	**4,432[a]**	**2**	**0,109**
Likelihood Ratio	**4,536**	**2**	**0,104**
Linear-by-Linear Association	**4,312**	**1**	**0,038**
N of Valid Cases	**231**		

a. 1 cells (16,7%) have expected count less than 5. The minimum expected count is 3,27.

Crosstab

Count

		Necrosis Not done NA Positive 1 Negative 0		Total
		0	1	
Central 1 vs Periferic 0 primary lesion	0	97	12	109
	1	157	27	184
Total		254	39	293

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0,797[a]	1	0,372		
Continuity Correction[b]	0,511	1	0,475		
Likelihood Ratio	0,815	1	0,367		
Fisher's Exact Test				0,477	0,239
Linear-by-Linear Association	0,794	1	0,373		
N of Valid Cases	293				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 14,51.

b. Computed only for a 2x2 table

Crosstab

Count

		Diagnosis Typical carcinoid 0 Atypical carcinoid 1		Total
		0	1	
Central 1 vs Periferic 0 primary lesion	0	87	25	112
	1	136	50	186
Total		223	75	298

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0,772[a]	1	0,380		
Continuity Correction[b]	0,549	1	0,459		
Likelihood Ratio	0,781	1	0,377		
Fisher's Exact Test				0,411	0,230
Linear-by-Linear Association	0,769	1	0,380		
N of Valid Cases	298				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 28,19.

b. Computed only for a 2x2 table

3. NECROSIS

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Necrosis Not done NA Positive 1 Negative 0 * Smoke yes 1 no 0	245	81,7%	55	18,3%	300	100,0%
Necrosis Not done NA Positive 1 Negative 0 * 18 FDG PET scan Not done Positive 1 Negative 0	198	66,0%	102	34,0%	300	100,0%
Necrosis Not done NA Positive 1 Negative 0 * Octreoscan/68GalliumPET Not done NA Positive 1 Negative 0	64	21,3%	236	78,7%	300	100,0%
Necrosis Not done NA Positive 1 Negative 0 * Tcat	274	91,3%	26	8,7%	300	100,0%
Necrosis Not done NA Positive 1 Negative 0 * Npos1neg0	264	88,0%	36	12,0%	300	100,0%
Necrosis Not done NA Positive 1 Negative 0 * Stage at diagnosis	295	98,3%	5	1,7%	300	100,0%
Necrosis Not done NA Positive 1 Negative 0 * Gruppoki67	229	76,3%	71	23,7%	300	100,0%

Crosstab

Count

		Smoke yes 1 no 0		Total
		0	1	
Necrosis Not done NA Positive 1 Negative 0	0	126	81	207
	1	16	22	38
Total		142	103	245

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4,639[a]	1	0,031		
Continuity Correction[b]	3,901	1	0,048		
Likelihood Ratio	4,578	1	0,032		
Fisher's Exact Test				0,048	0,025
Linear-by-Linear Association	4,620	1	0,032		
N of Valid Cases	245				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 15,98.

b. Computed only for a 2x2 table

Crosstab

Count

		18 FDG PET scan Not done Positive 1 Negative 0		Total
		0	1	
Necrosis Not done NA Positive 1 Negative 0	0	56	116	172
	1	12	14	26
Total		68	130	198

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1,851[a]	1	0,174		
Continuity Correction[b]	1,298	1	0,255		
Likelihood Ratio	1,786	1	0,181		
Fisher's Exact Test				0,189	0,128
Linear-by-Linear Association	1,842	1	0,175		
N of Valid Cases	198				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 8,93.

b. Computed only for a 2x2 table

Crosstab

Count

		Octreoscan/68GalliumPET Not done NA Positive 1 Negative 0		Total
		0	1	
Necrosis Not done NA Positive 1 Negative 0	0	18	32	50
	1	4	10	14
Total		22	42	64

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	0,268[a]	1	0,605		
Continuity Correction[b]	0,040	1	0,842		
Likelihood Ratio	0,274	1	0,601		
Fisher's Exact Test				0,755	0,429
Linear-by-Linear Association	0,263	1	0,608		
N of Valid Cases	64				

a. 1 cells (25,0%) have expected count less than 5. The minimum expected count is 4,81.

b. Computed only for a 2x2 table

Crosstab

Count

		Tcat				Total
		1	2	3	4	
Necrosis Not done NA Positive 1 Negative 0	0	168	56	9	3	236
	1	7	20	7	4	38
Total		175	76	16	7	274

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	47,059[a]	3	0,000
Likelihood Ratio	42,735	3	0,000
Linear-by-Linear Association	46,326	1	0,000
N of Valid Cases	274		

a. 2 cells (25,0%) have expected count less than 5. The minimum expected count is ,97.

Crosstab

Count

		Npos1neg0		Total
		0	1	
Necrosis Not done NA Positive 1 Negative 0	0	180	47	227
	1	19	18	37
Total		199	65	264

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	13,386[a]	1	,000		
Continuity Correction[b]	11,922	1	,001		
Likelihood Ratio	11,881	1	,001		
Fisher's Exact Test				,001	,001
Linear-by-Linear Association	13,335	1	,000		
N of Valid Cases	264				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 9,11.

b. Computed only for a 2x2 table

Crosstab

Count

		Gruppoki67			Total
		1	2	3	
Necrosis Not done NA Positive 1 Negative 0	0	135	54	5	194
	1	7	25	3	35
Total		142	79	8	229

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	31,141[a]	2	,000
Likelihood Ratio	30,850	2	,000
Linear-by-Linear Association	29,173	1	,000
N of Valid Cases	229		

a. 1 cells (16,7%) have expected count less than 5. The minimum expected count is 1,22.

Crosstab

Count

		Diagnosis Typical carcinoid 0 Atypical carcinoid 1		Total
		0	1	
Necrosis Not done NA Positive 1 Negative 0	0	225	31	256
	1	0	39	39
Total		225	70	295

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	144,455[a]	1	0,000		
Continuity Correction[b]	139,639	1	0,000		
Likelihood Ratio	134,302	1	0,000		
Fisher's Exact Test				0,000	0,000
Linear-by-Linear Association	143,965	1	0,000		
N of Valid Cases	295				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 9,25.

b. Computed only for a 2x2 table

Kaplan-Meier survival curves of: high mitotic count (> 10 per 10 HPF) versus mitotic count ≤ than 10 per 10 HPF in terms of PFS and OS (upper part of the figure, left and right side, respectively); and of high Ki67 value (> 20%) versus Ki67 lower than 20% in terms of both PFS and OS (lower part of the figure, left and right side, respectively). P-values have been considered as significant if < 0.05 and are reported according to the corresponding univariant COX regression analysis.