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A Population Based Pathology Analysis on Application of WHO-Nomenclature in Pulmonary Neuroendocrine Tumors

Jules L. Derks[1]; Robert Jan van Suylen[2]; Erik Thunnissen[3]; Michael A. den Bakker[4]; Egbert F. Smit[5]; Harry J.M. Groen[6]; PALGA: Dutch Pathology Registry[7]; Ernst-Jan. M. Speel[8]*; Anne-Marie C. Dingemans[1]*

* Authors contributed equally

[1]Department of Pulmonary Diseases, GROW school for Oncology & Developmental Biology, Maastricht University Medical Centre, Maastricht, the Netherlands
[2]Department of Pathology, Jeroen Bosch Hospital, s' Hertogenbosch, the Netherlands
[3]Department of Pathology, VU medical Center, Amsterdam, the Netherlands
[4]Department of Pathology, Maasstad Hospital, Rotterdam, the Netherlands
[5]Department of Pulmonary Diseases, VU Medical Center, Amsterdam, the Netherlands
[6]Department of Pulmonary Diseases, University of Groningen and University Medical Centre, Groningen, the Netherlands
[7]PALGA, the nationwide network and registry of histo- and cytopathology in the Netherlands, Houten, the Netherlands
[8]Department of Pathology, GROW school for Oncology & Developmental Biology, Maastricht University Medical Centre, Maastricht, the Netherlands

Background:
Pulmonary neuroendocrine tumors (pNETs) are a cluster of rare diseases that are difficult to classify. We performed a population-based analysis to investigate pNETs nomenclature application in daily pathology practice.

Methods:
Conclusions from pathology reports (2003-2012) describing carcinoids, (large cell) neuroendocrine carcinomas ((LC)NEC) or carcinomas with neuroendocrine features/differentiation were retrieved from the Dutch Pathology Registry by queries on origin/location, diagnosis and keywords, and screened for terminology. Cases with non-pulmonary/unknown origin and small cell lung cancer (SCLC) were excluded. Diagnoses were clustered into subgroups and retrieved terminology was compared to WHO 2004 diagnoses[1]. Interpretation of non-WHO nomenclature by treating physicians (N=35) and certified pathologists (N=19) was evaluated by an online questionnaire; participants were requested to cluster retrieved diagnoses into the established WHO categories[1] or as 'unknown'. Uniform interpretation was scored for diagnoses with ≥50% agreement.

Results:
7989 conclusions were retrieved. After exclusion, the final pathology conclusion of 3216 unique patients, including 55 distinctive diagnoses (in *N*=3052) and 20 uncertain diagnoses (in *N*=164), were analysed. Non-WHO nomenclature was used in 15% (*N*=448) of diagnoses and was observed more often when results of biopsy/cytology specimens were reported as compared to resections (Table 1). Diagnoses could be clustered into four groups: carcinoids (*N*=1086), NEC (*N*=1316), carcinomas with neuroendocrine features/differentiation (*N*=624) and unspecified NETs (*N*=26). Non-WHO nomenclature was found in 7% of carcinoid, 20% of NEC, 13% of carcinomas with neuroendocrine features/differentiation and 100% of unspecified NETs (Table 1). Uniform interpretation was achieved on 4/19 non-WHO nomenclature diagnoses by physicians and 10/19 non-WHO diagnoses by pathologists.

Conclusion:
In 15% of pNETs other than SCLC, a non-WHO nomenclature diagnosis was applied by certified pathologists, more often on limited tissue specimens. The interpretation was different between treating physicians and pathologists. Application of

uniform nomenclature is advocated to improve reporting of results of treatment in patients with pNET.

References:

William D. Travis, et al., *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart.* Lyon, France: IARC press, 2004.

Table 1. Characteristics of retrieved conclusions of pathology reports

Variable	Total cohort[i]			Non-WHO nomenclature cohort			
		Time period			Time period		
	Total	≤2007	≥2008	*Total*	≤2007	≥2008	vs.
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	*p**
Conclusions	3052(100)	1280 (42)	1772 (58)	448 (15)	205 (46)	243 (54)	0.076
Sampling location							
Lung	2297 (75)	890 (43)	1161 (57)	246 (55)	127 (52)	119 (48)	-
Metastasis (lymph or distant)	755 (25)	185 (34)	368 (24)	202 (45)	78 (39)	124 (61)	-
Sampling method							
Resection	1517 (50)	616 (44)	785 (56)	116 (26)	53 (46)	63 (54)	-
Non-surgical biopsy	1355 (44)	417 (39)	660 (61)	278 (62)	127 (46)	151 (54)	-
Cytology	180 (6)	42 (33)	84 (67)	54 (12)	25 (46)	29 (54)	-
Diagnosis cluster							
Carcinoid	1086 (36)	480 (44)	606 (56)	78 (7)	50 (8)	28 (6)	0.125
High-grade neuroendocrine ca.	1316 (43)	503 (38)	813 (62)	262 (20)	121 (24)	141 (17)	0.003
(LCC/NSCLC) ca. neuroendocrine diff./features	624 (20)	282 (45)	342 (55)	82 (13)	41 (15)	41 (12)	0.348
Neuroendocrine tumor n.o.s.	26 (1)	15 (58)	11 (42)	26 (100)	15 (58)	11 (42)	-

[i] *Excluding all uncertain diagnoses (N=164)*

* *Chi-square used to test if aberrant nomenclature increased/decreased significantly between time periods ≤2007 and ≥2008 (i.e. non WHO-nomenclature vs. WHO nomenclature)*

Abbreviations: vs., versus; NSCLC, non-small cell lung cancer; LCC, large cell carcinoma; n.o.s., not otherwise specified.