GIOVEDÌ 16 MAGGIO 2019

12:00 - 13:00 WELCOME LUNCH

13:00 - 13:15 **INTRODUZIONE** - N. Fazio

13:15 - 14:15 **Diagnosi, classificazione e terminologia dei GEP NET**
- Il Patologo — M. Milione

Approccio diagnostico-terapeutico al paziente con NET pancreatico
- Il Radiologo — L. Funicelli
- Il Medico nucleare — A. Filice
- L'Endocrinologo — A. Lania
- L'Oncologo — C. Carnaghi
- Il Gastroenterologo — D. Ravizza

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HISTOLOGICAL REPORT

MORPHOLOGY

1)Well Differentiated

vs

2) Poorly Differentiated

Immunohistochemestry (IHC)

General Neuroendocrine markers:

1) Synaptophisyn

2) Chromogranin-a

Proliferation

1) Ki-67

2) Mitotic Index

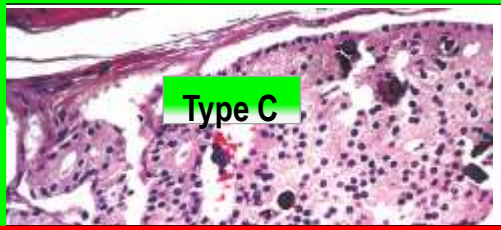
Morphology: Well Differentiated *vs* Poorly Differentiated

Insular or nested growth pattern

- ✓ large nests nomorphous, polygonal
- ✓ NO mitoses
- ✓ NO atypia
- ✓ Peripheral palisading
- ✓ Stipped nuclear cromatin

Trabecular- Ribbon growth pattern

- ✓ long trabeculae
- ✓ loops
- ✓ separated by fine vascular stroma



Glandular or Acinar growth pattern

- ✓ Small, polygonal cells
- ✓ glandlike lumina
- ✓ secretions or even psammomatous calcifications

W D N N
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l f u o
l f r p
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WD-NENS

Poorly differentiated growth pattern

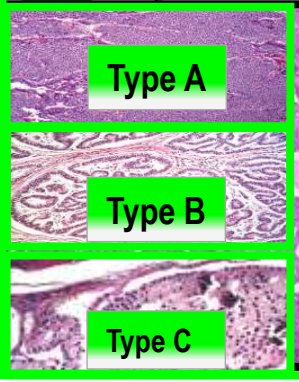
- ✓ High tumor cells nucleus-to-cytoplasm ratio
- ✓ Hypercromatism
- ✓ Poor defined nest and trabeculae.

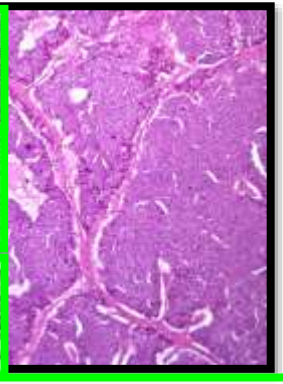
PD-NEC*
or simply
NEC

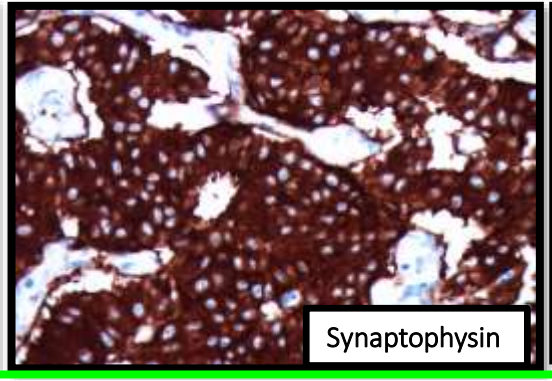
*Poorly Differentiated Neuroendocrine Carcinomas

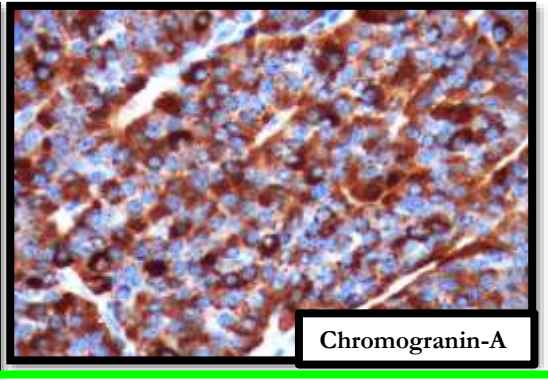
Morphology and Immunohistochemestry

Well Differentiated Neuroendocrine Tumour (NET)

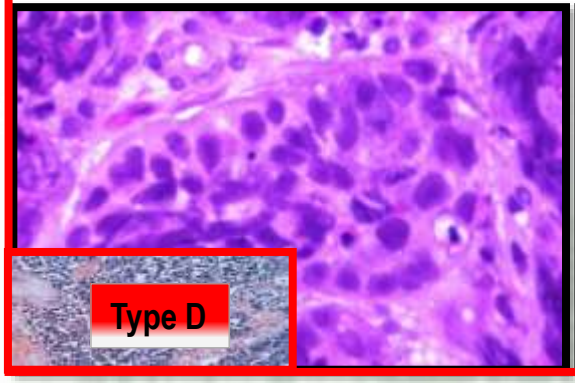


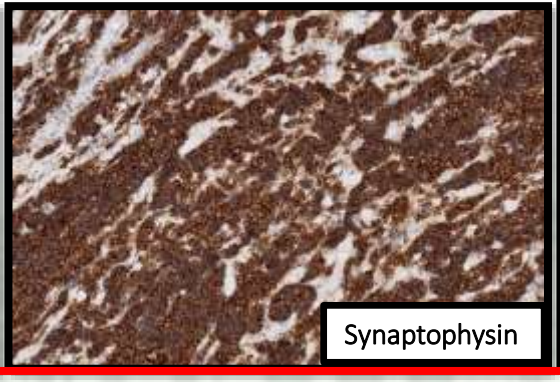


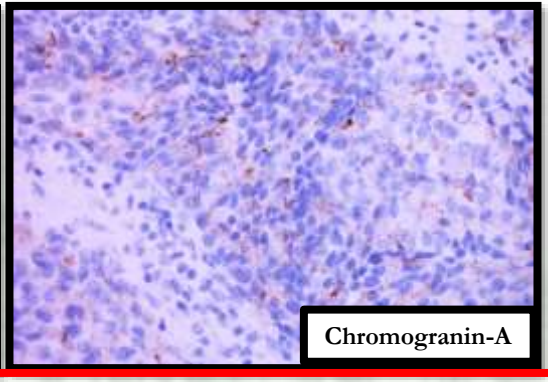




Poorly Differentiated Neuroendocrine Carcinoma(NEC)







Proliferation…. Ki-67 as Prognostic Pillar

G non è grado istologico ma classe prognostica

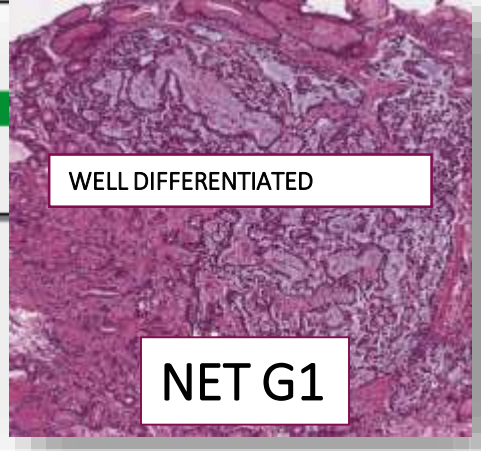
NETG1

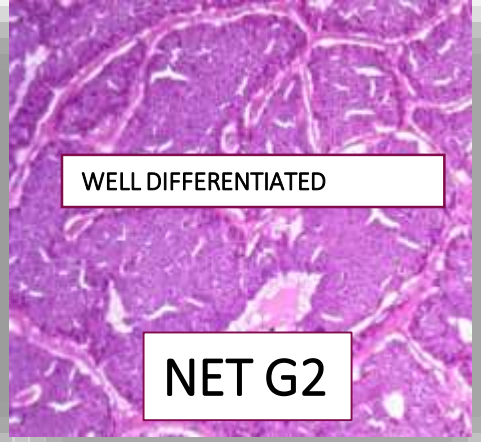
Ki-67 < 2%

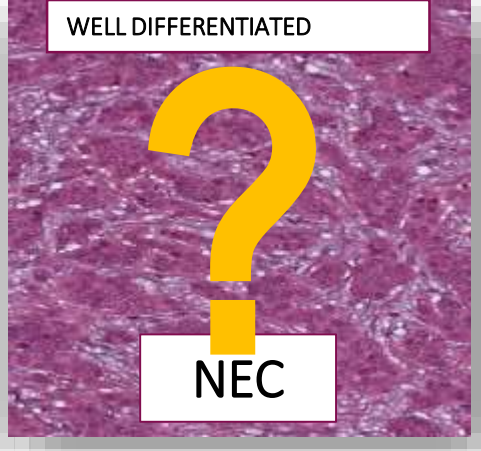
NETG2

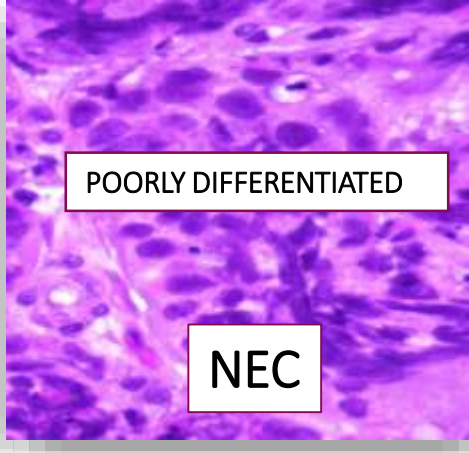
NEC

Ki-67 > 20%



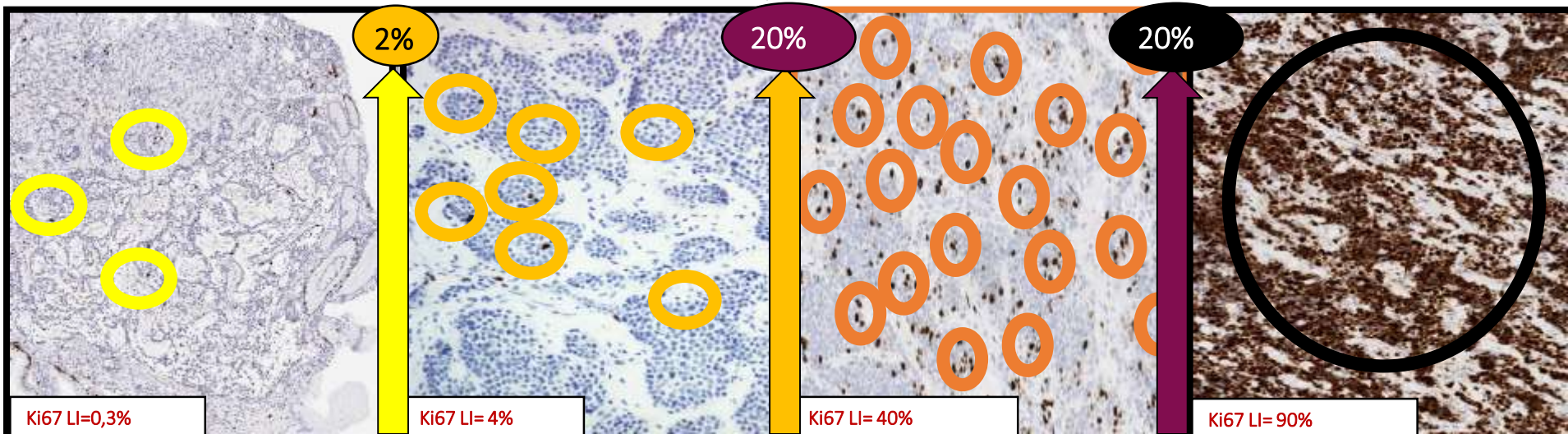






Ki-67= N°positive nuclei per 2 mm²

$$\frac{\text{N°positive nuclei}}{\text{2000 nuclei}} \% = \text{Ki-67 LI}$$



NEC according WHO 2010

NET G3 (WHO 2017)
WD morphology
Ki67>20%

La Rosa, Hum Pathol 2011
Velayoudom-Cephise, ERC 2013
Basturk, Mod Pathol 2013
Agaimy, Mod Pathol 2013
Hijioka, J Gastroenterol 2014
Basturk, Am J Surg Pathol 2015
Heetfeld, Endocrine Related Cancer 2015
Milione, Neuroendocrinology 2016

NEC (WHO 2017)
PD morphology
Ki67>20%

Good prognosis	Intermediate prognosis	Worse prognosis
NO RESPONSE to **Platinum Based Chemoterrapy**	NO OR POOR RESPONSE to Platinum Based Chemoterrapy	RESPONSE **to Platinum Based Chemoterrapy**

Table 6.01 2017 WHO classification and grading of pancreatic neuroendocrine neoplasms (PanNENs)

Classification/grade	Ki-67 proliferation index[a]	Mitotic index[a]
Well-differentiated PanNENs: pancreatic neuroendocrine tumours (PanNETs)		
PanNET G1	< 3%	< 2
PanNET G2	3–20%	2–20
PanNET G3	> 20%	> 20
Poorly differentiated PanNENs: pancreatic neuroendocrine carcinomas (PanNECs)		
PanNEC (G3)	> 20%	> 20
Small cell type		
Large cell type		
Mixed neuroendocrine–non-neuroendocrine neoplasm		

[a] The Ki-67 proliferation index is based on the evaluation of ≥ 500 cells in areas of higher nuclear labelling (so-called hotspots). The mitotic index is based on the evaluation of mitoses in 50 high-power fields (HPF; 0.2 mm^2 each) in areas of higher density, and is expressed as mitoses per 10 high-power fields (2.0 mm^2). The final grade is determined based on whichever index (Ki-67 or mitotic) places the tumour in the highest grade category. For assessing Ki-67, casual visual estimation (eyeballing) is not recommended; manual counting using printed images is advocated [2257].

Good Prognosis

Bad Prognosis

Gastro Entero Pancreatic (GEP) 2010

WD

PD

Pancreas 2017

WD

PD

Neuroendocrinology. 2018 Oct 9. doi: 10.1159/000494355. [Epub ahead of print]

COMPETITIVE TESTING THE WHO 2010 VS THE WHO 2017 GRADING OF PANCREAS NEUROENDOCRINE NEOPLASIA: DATA FROM A LARGE INTERNATIONAL COHORT STUDY.

Rindi G, Klersy C, Albarello L, Baudin E, Bianchi A, Büchler MW, Caplin M, Couvelard A, Cros J, de Herder WW, Delle Fave G, Doglioni C, Federspiel B, Fischer L, Fusai G, Gavazzi F, Hansen C, Inzani F, Jann H, Komminoth P, Knigge U, Landoni L, La Rosa S, Lawlor R, Luong T, Marinoni I, Panzuto F, Pape UF, Partelli S, Perren A, Rinzivillo M, Rubini C, Ruszniewski P, Scarpa A, Schmitt AM, Schinzari G, Scoazec JY, Sessa F, Solcia E, Spaggiari P, Toumpanakis C, Vanoli A, Wiedenmann B, Zamboni G, Zandee W, Zerbi A, Falconi M.

Abstract

Background: the World Health Organization (WHO) and the American Joint Cancer Committee (AJCC) modified the grading of pancreatic neuroendocrine neoplasms from a three-tiers (WHO-AJCC 2010) to a four-tiers system by introducing the novel category of NET G3 (WHO-AJCC 2017).

OBJECTIVES: This study aims at validating the WHO-AJCC 2017 and identifying the most effective grading system.

METHOD: 2102 patients were enrolled; entry criteria were i) performed surgery; ii) at least two years of follow-up; iii) observation time up to 2015. Data from 34 variables were collected; grading was assessed and compared for efficacy by statistical means including Kaplan Meier method, Cox regression analysis, Harrell's C statistics and Royston's explained variation in univariable and multivariable analyses.

RESULTS: At descriptive analysis, the two grading systems demonstrated statistically significant differences for the major category sex but not for age groups. At Cox regression analysis, both grading systems showed statistically significant differences between grades for OS and EFS, however no statistically significant difference was observed between the two G3 classes of WHO-AJCC 2017. At multivariable analysis for the two models fitted to compare efficacy, the two grading systems performed equally well with substantially similar optimal discrimination and well-explained variation for both OS and EFS. The WHO-AJCC 2017 grading system retained statistically significant difference between the two G3 classes for OS but not for EFS.

CONCLUSIONS: the WHO-AJCC 2017 grading is at least equally performing as the WHO-AJCC 2010 but allows the successful identification of the most aggressive PanNET subgroup. Grading is confirmed as probably the most powerful tool for patient survival prediction.

WHO 2019 GEP

?

WHO 2017 Pancreas

NET G1/G2/G3 (well-differentiated NEN)

NEC (G3), large cell or small cell type (poorly differentiated NEN)

Mixed neuroendocrine–non-neuroendocrine neoplasm

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grazie

VIII EDIZIONE

NEN PRECEPTORSHIP

LA PRATICA CLINICA NELLE NEOPLASIE NEUROENDOCRINE

16/17 Maggio 2019 | IEO, Istituto Europeo di Oncologia - Milano

NEN Preceptorship

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