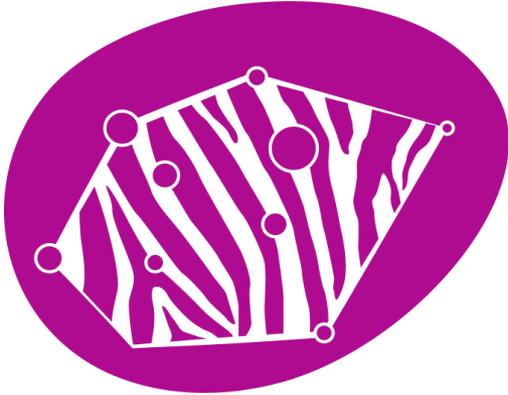# NET
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MEETING SUMMARY
UPDATE FROM ENETS 2019
Barcelona, Spain

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CLINICAL IMPACT OF THE WHO
CLASSIFICATION 2017

DISCLAIMER

Please note: The views expressed within this presentation are the personal opinion of the author. They do not necessarily represent the views of the author's academic institution or the rest of the NET CONNECT group.

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NEW WHO CLASSIFICATION
PERREN, A. ORAL PRESENTATION, ENETS 2019
&
CONSEQUENCES FOR TREATMENT
SORBYE, H. ORAL PRESENTATION, ENETS 2019

Lloyd, RV et al. WHO Classification of Tumours of Endocrine Organs, IARC Press, Lyon, 2017

BACKGROUND

- GEP NEN are classified into three groups based on **mitotic activity and Ki-67 index** in the **WHO 2010 classification.**[1] It included three distinct groups:
    - **well-differentiated NET** (G1 or G2)
    - **poorly-differentiated NEC G3**
    - mixed adenoneuroendocrine carcinomas **(MANEC)**

- New observations and publications provided new understanding into PanNEN, which prompted the new **WHO update in 2017**[2]
    - key changes and clinical implications are presented
    - publication of the fifth edition of the WHO Classification of Tumours of the Digestive System is expected in April 2019

GEP, gastroenteropancreatic; NEC, neuroendocrine carcinomas; NEN, neuroendocrine neoplasm; NET, neuroendocrine tumours; PanNEN, pancreatic neuroendocrine neoplasm; WHO, world health organisation.

1. Klimstra, DS et al. WHO Classification of Tumours of the Digestive System, IARC Press, Lyon, 2010.
2. Lloyd, RV et al. WHO Classification of Tumours of Endocrine Organs, IARC Press, Lyon, 2017.

COMPARISON OF RECENT WHO CLASSIFICATIONS

WHO classification 2010 | WHO classification 2017

For pancreatic NENs

	Ki-67 index	Mitotic index		Ki-67 index	Mitotic index
Well differentiated NETs			**Well differentiated NETs**		
NET G1	≤2%	< 2/10 HPF	NET G1	<3%	<2/10 HPF
NET G2	3%-20%	2-20/10 HPF	NET G2	3%-20%	2-20/10 HPF
			NET G3	>20%	>20/10 HPF
Poorly differentiated NECs			**Poorly differentiated NECs**		
NEC G3	>20%	>20/10 HPF	NEC G3 - Small cell type - Large cell type	>20%	>20/10 HPF
Mixed adenoneuroendocrine carcinoma (MANEC)			**Mixed neuroendocrine-nonneuroendocrine neoplasm (MiNEN)**		

HPF, high power fields; NEC, neuroendocrine carcinomas; NEN, neuroendocrine neoplasm; NET, neuroendocrine tumours; PanNEN, pancreatic neuroendocrine neoplasm; WHO, world health organisation

1. Klimstra, DS et al. WHO Classification of Tumours of the Digestive System, IARC Press, Lyon, 2010.
2. Lloyd, RV et al. WHO Classification of Tumours of Endocrine Organs, IARC Press, Lyon, 2017.
Perren, A. Summary of oral presentation at ENETS 2019.

KEY CHANGES IN WHO CLASSIFICATION 2017

- Grade 1 to 2 Ki-67 cut-off moved from ≤ 2% to < 3%

- Two groups of patients within G3 category are defined:-
    - **NET G3** – well differentiated morphology
    - **NEC G3** – poorly differentiated morphology

- Naming of mixed cell tumours changed from MANEC to **MiNEN**

MANEC, mixed adenoneuroendocrine carcinoma; MiNEN, mixed neuroendocrine non-neuroendocrine neoplasms; NEC, neuroendocrine carcinomas; NET, neuroendocrine tumours; WHO, world health organisation

Lloyd, RV et al. WHO Classification of Tumours of Endocrine Organs, IARC Press, Lyon, 2017.
Perren, A. Summary of oral presentation at ENETS 2019

THEREAPEUTIC OPTIONS

NET G3

- Somatostatin-based therapy (when receptors expressed)
- Targeted therapies
- Non-platinum-based chemotherapy (i.e. TEMCAP)
- Role of surgery and immunotherapy to be defined

NEC G3

- Platinum-based chemotherapy
- Second-line therapy to be defined
- Role of surgery and immunotherapy to be defined

Morphology is not the only important feature!

- NET G3 with very high Ki-67:
  - may benefit from platinum-based chemotherapy

- NEC G3 with not very high Ki-67:
  - other options such as NET G3 (e.g. TEMCAP or targeted therapies)

SUMMARY

- Previously defined G3 group divided based on tumour morphology into **NET G3 and NEC G3**

- Anticipate that future updates will propose a similar classification also for other **tumour primary sites.** Waiting for the new WHO classification for other digestive NENs to be released
  - expected April 2019

NEC, neuroendocrine carcinomas; NEN, neuroendocrine neoplasm; NET, neuroendocrine tumours; WHO, world health organisation

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