

Kromogranin A ved diagnose og under opfølgning
+
lidt generelt om diagnostik og usikkerhed på
undersøgelser

Mikkel Andreassen, endo RH

November 2022

Hvad står der i lærebøgerne om symptomer på neuroendokrine tumorer ?







Hvad står der i lærebøgerne om symptomer på neuroendokrine tumorer ?

Hormon producerende tumorer der giver symptomer i anfald:

- ***Flushing***
- Diarre
- Astma
- Lavt blodsukker
- Mavesår
- ***Forhøjet Kromogranin A***

Article

Incidence, Clinical Presentation and Trends in Indication for Diagnostic Work-Up of Small Intestinal and Pancreatic Neuroendocrine Tumors

Anna Bryan Stensbøl ^{1,2}, Jesper Krogh ^{1,2,3}, Pernille Holmager ^{1,2}, Marianne Klose ^{1,2}, Peter Oturai ^{1,4},
Andreas Kjaer ^{1,3,4}, Carsten Palnæs Hansen ^{1,5}, Birgitte Federspiel ^{1,6}, Seppo W. Langer ^{1,3,7}, Ulrich Knigge ^{1,2,5}
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Tyndtarms-NET 2010-11 vs. 2019-20

Table 1. Baseline characteristics of small intestinal NET patients.

Small Intestinal NET, Pre Referral		
	2010–2011	2019–2020
Number (n) of Cases	70	101
Age	65 ± 12	65 ± 12
Female, n (%)	36 (51)	44 (44)
Incidence (per 100,000)	1.39	1.84
Age adjusted incidence (pr 100,000)	1.39	1.76
Incidental findings, n (%)	19 (27)	31 (31)
Incidental finding on imaging or endoscopy, n (%)	12 (17)	24 (24)
Incidental finding after surgery, n (%)	7 (10)	7 (7)
Symptoms leading to initial investigation	51 (73)	70 (70)
GI symptoms, n (%)	28 (40)	43 (43)
GI symptoms + flushing, n (%)	5 (7)	7 (7)
Flushing, n (%)	2 (3)	2 (2)
Unspecific symptoms, n (%)	6 (9)	5 (5)
Acute surgery for ileus, n (%)	10 (14)	13 (13)
Histologic diagnosis at time of referral to NET center (%)	62 (89)	81 (80)

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Bugspytkirtel-NET 2010-11 vs. 2019-20

Pancreatic NET, Pre Referral		
	2010–2011	2019–2020
Number (n) of Cases	21	75
Age	64 ± 15	61 ± 13
Female/male	7/14	36/39
Incidence (pr 100,000)	0.42	1.39
Age adjusted incidence (pr 100,000)	0.42	1.34
Incidental findings, n (%)	4 (19)	43 (57)
Incidental finding on imaging, n (%)	4 (19)	37 (49)
Incidental finding after surgery, n (%)	0	6 (8)
Symptoms/reason leading to initial investigation	17	32
GI-symptoms, n (%)	10 (48)	9 (12)
Attack-like phenomena, n (%)	3 (14)	8 (11)
Unspecific symptoms, n (%)	4 (19)	11 (15)
MEN1 follow up, n (%)	0	4 (5)
Histologic diagnosis at time of referral to NET center (%)	13 (62)	28 (37)

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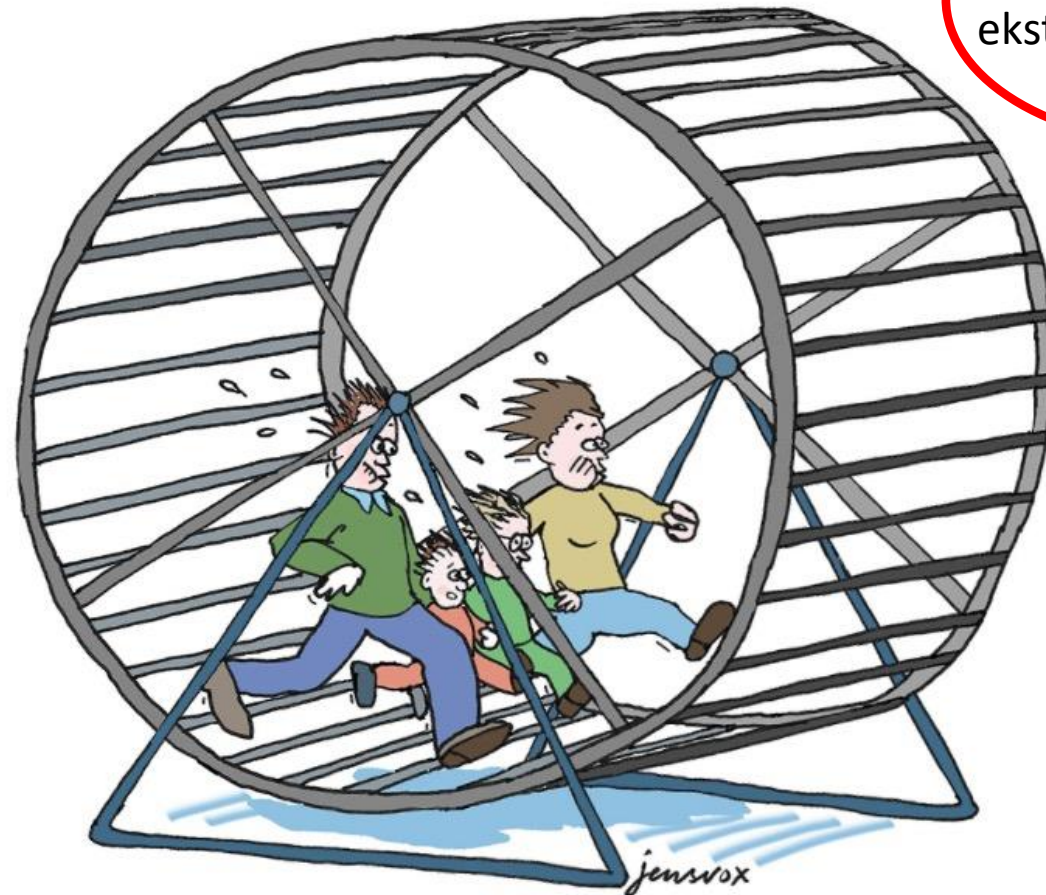
Hvorfor har det ændret sig ?

Antal CT skanninger af maveregion 2010 vs. 2020

2010: ca 260.000 skanninger (4,4% af alle danskere)

2020: ca 460.000 skanninger (8,0% af alle danskere)

Det diagnostiske hamsterhjul

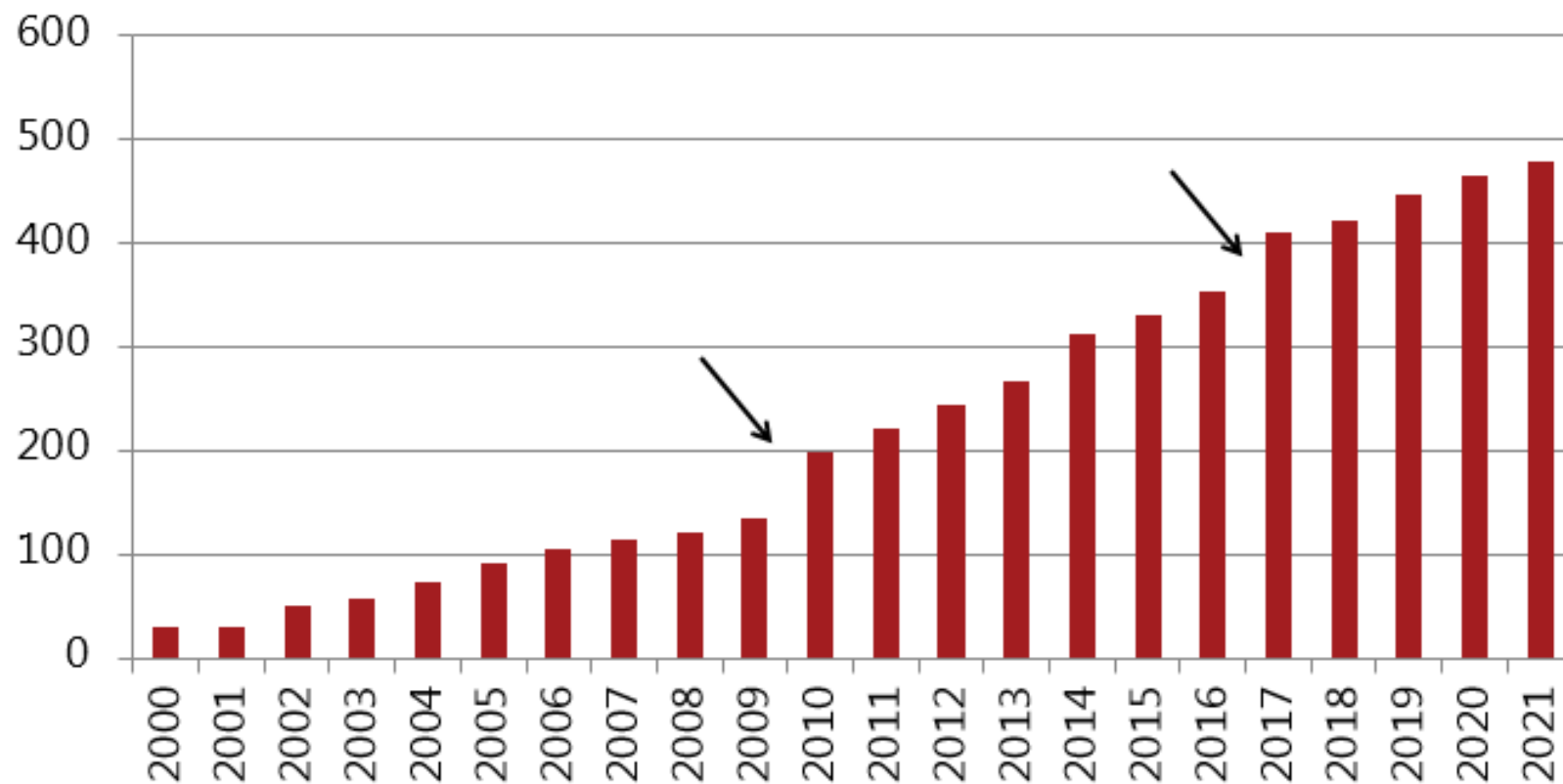


Vi må hellere lave en
ekstra undersøgelse.....



RH NET Centre

New NEN patients referred per year (GEP + BP + other)



60-årig kvinde henvist obs NET

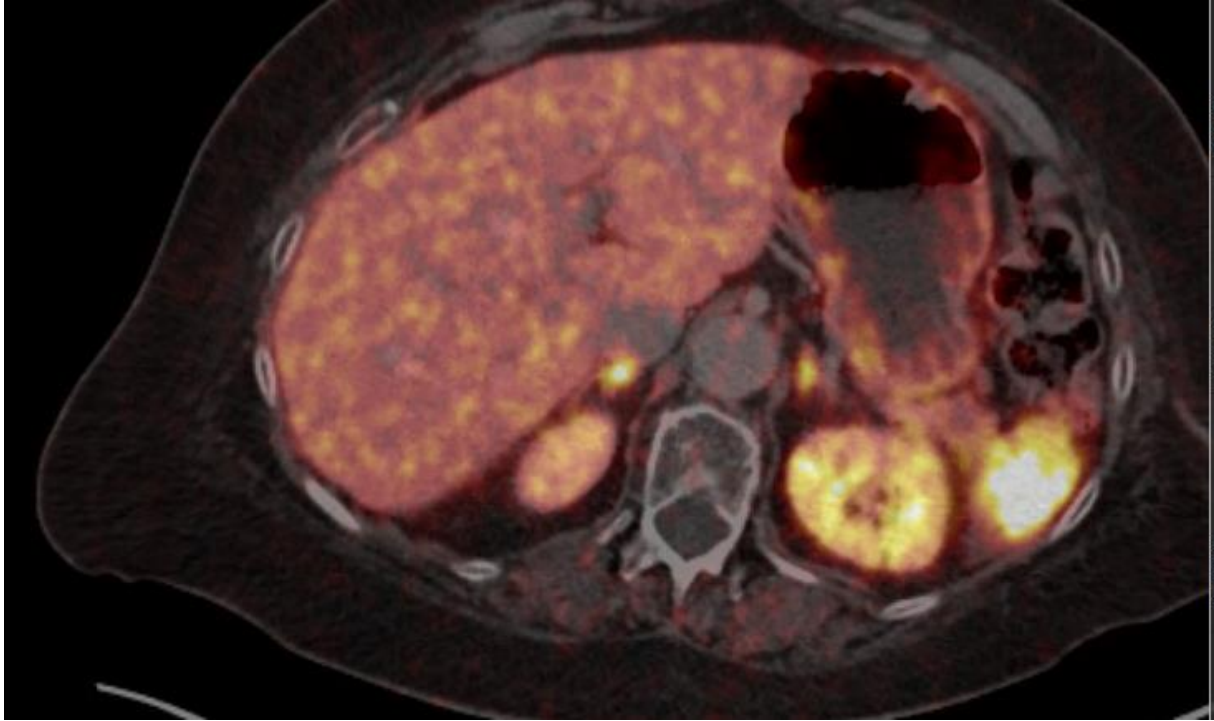
Henvisning:

Mange år tendens til diare. Kikkertundersøgelser upåfaldende. Ingen sikker flushing, dog varmefornemmelse i ansigtet. I årevis i behandling med mavesyre medicin. CT skanning upåfaldende.

Tårnhøj Kromogranin A på ca 2.500 (<130 pmol/L). Henvises obs tyndtarms NET

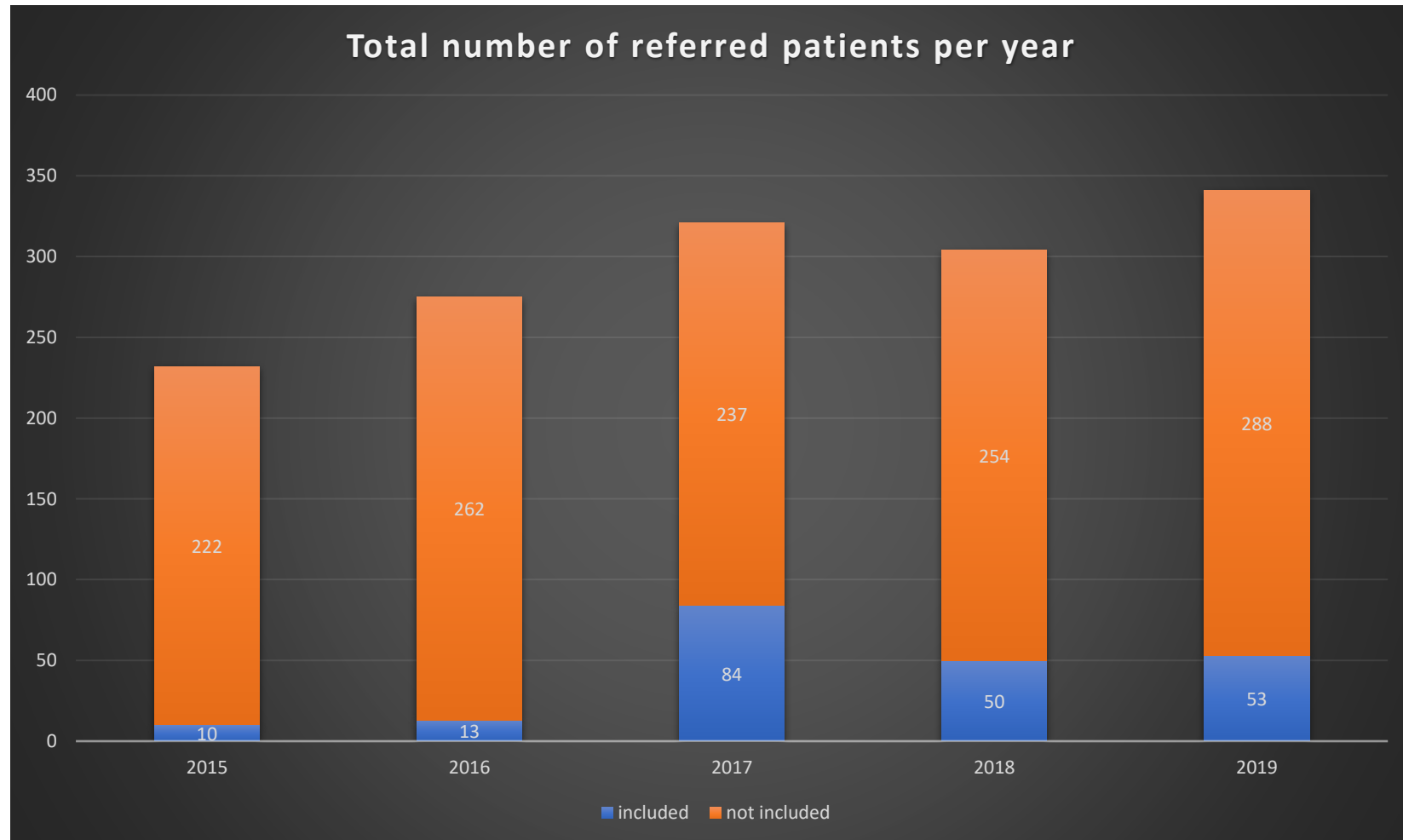
Hva' så ??

Vores patient



Konklusion:
Ingen tegn på NET.

Henviste NET pt med og uden CgA måling før henvisning

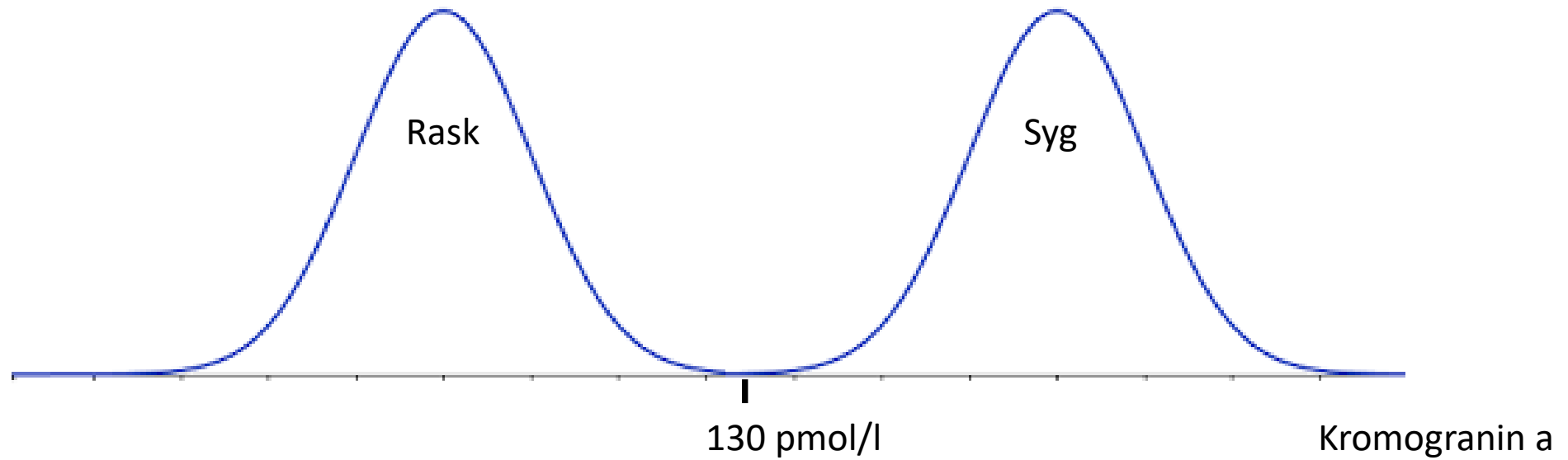


Kromogranin A (CgA)

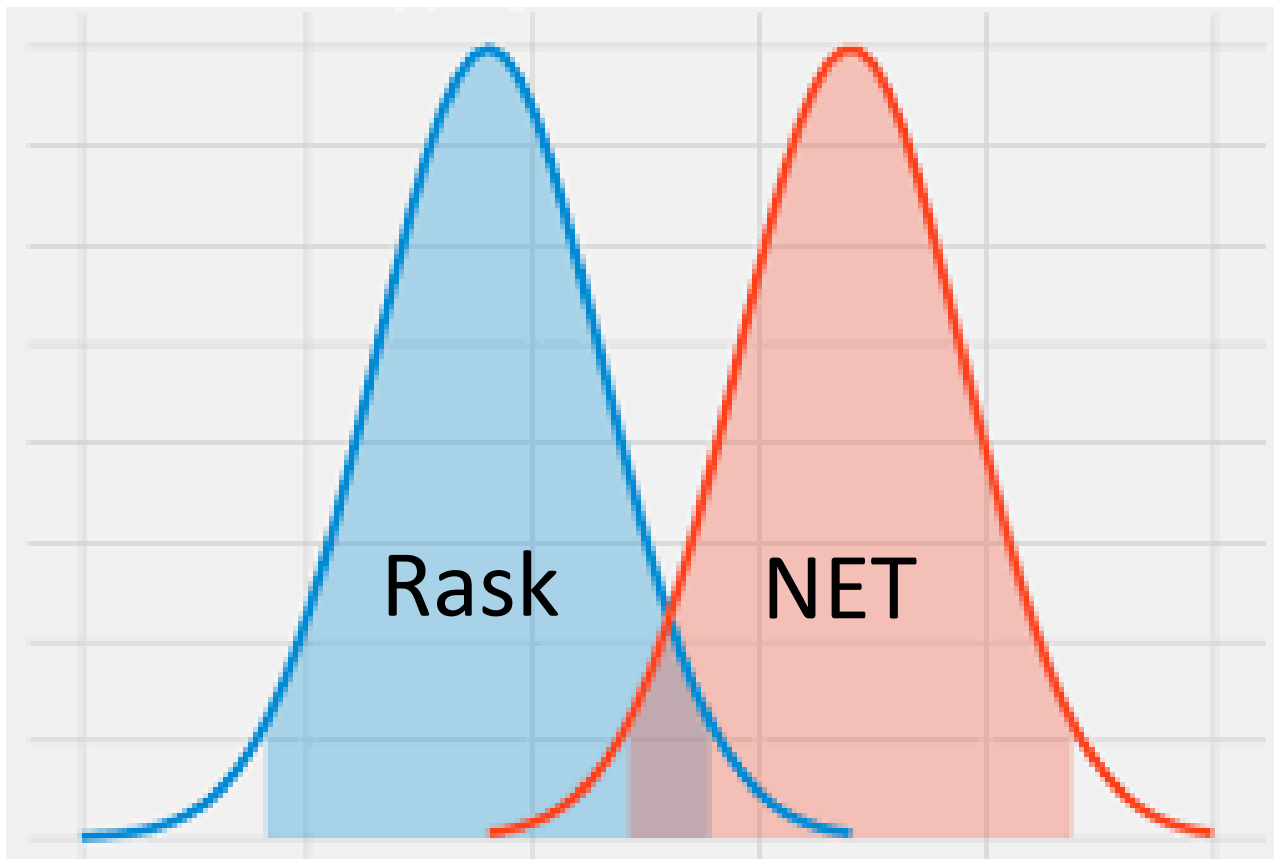
- Kommer fra Neuroendokrine celler
- Årsager til falsk forhøjede værdier
 - ***Mavesårs medicin***
 - Nyresvigt

Kan Kromogranin A bruges i den diagnostiske fase ?

Den ideelle diagnostiske situation ?





?



Article

Limited Diagnostic Utility of Chromogranin A Measurements in Workup of Neuroendocrine Tumors

Jonas Baekdal ^{1,2,*}, Jesper Krogh ^{1,2}, Marianne Klose ^{1,2}, Pernille Holmager ^{1,2},
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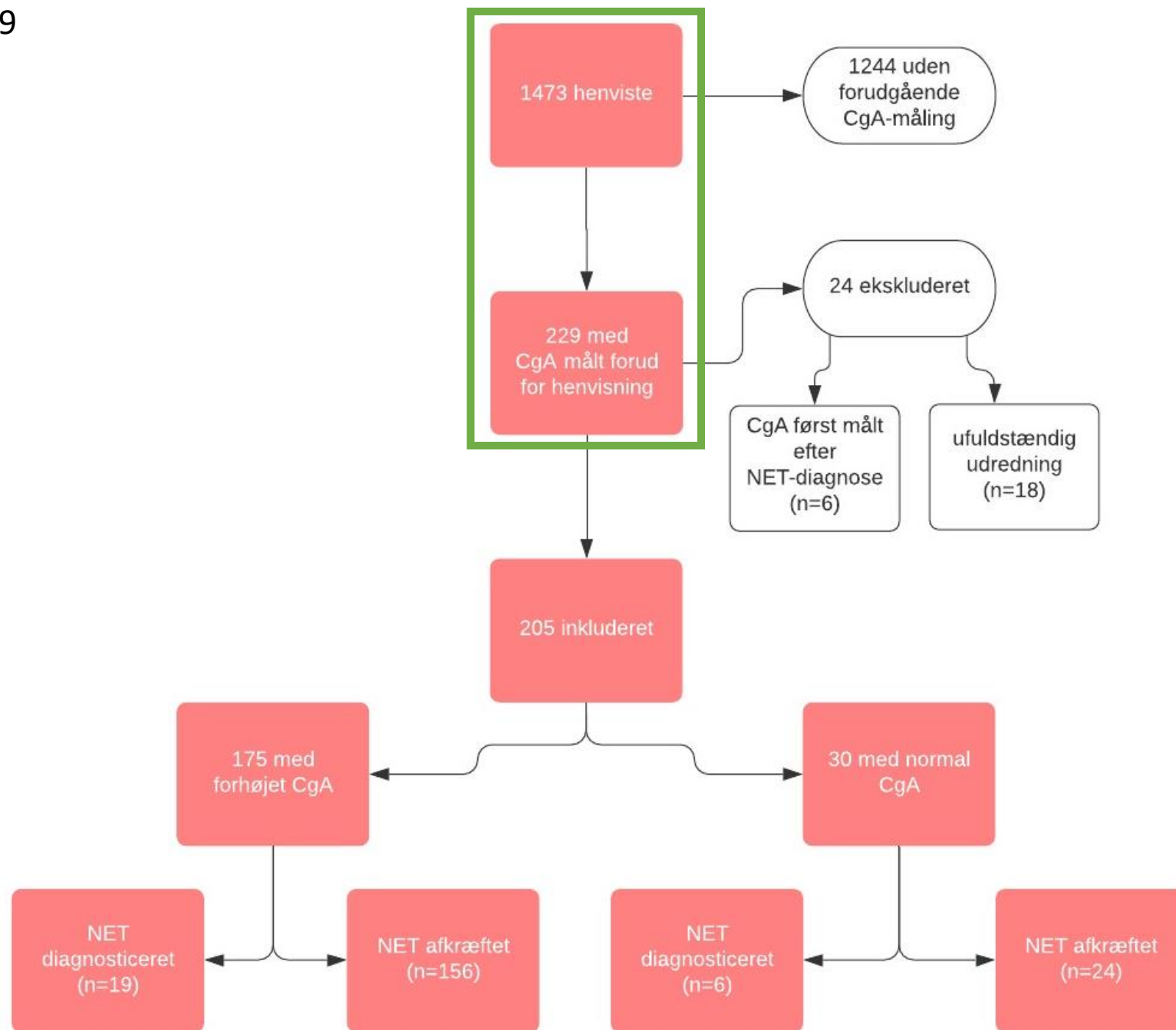
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⁷ Department of Clinical Biochemistry, Rigshospitalet, Copenhagen University Hospital, 2100 Copenhagen, Denmark

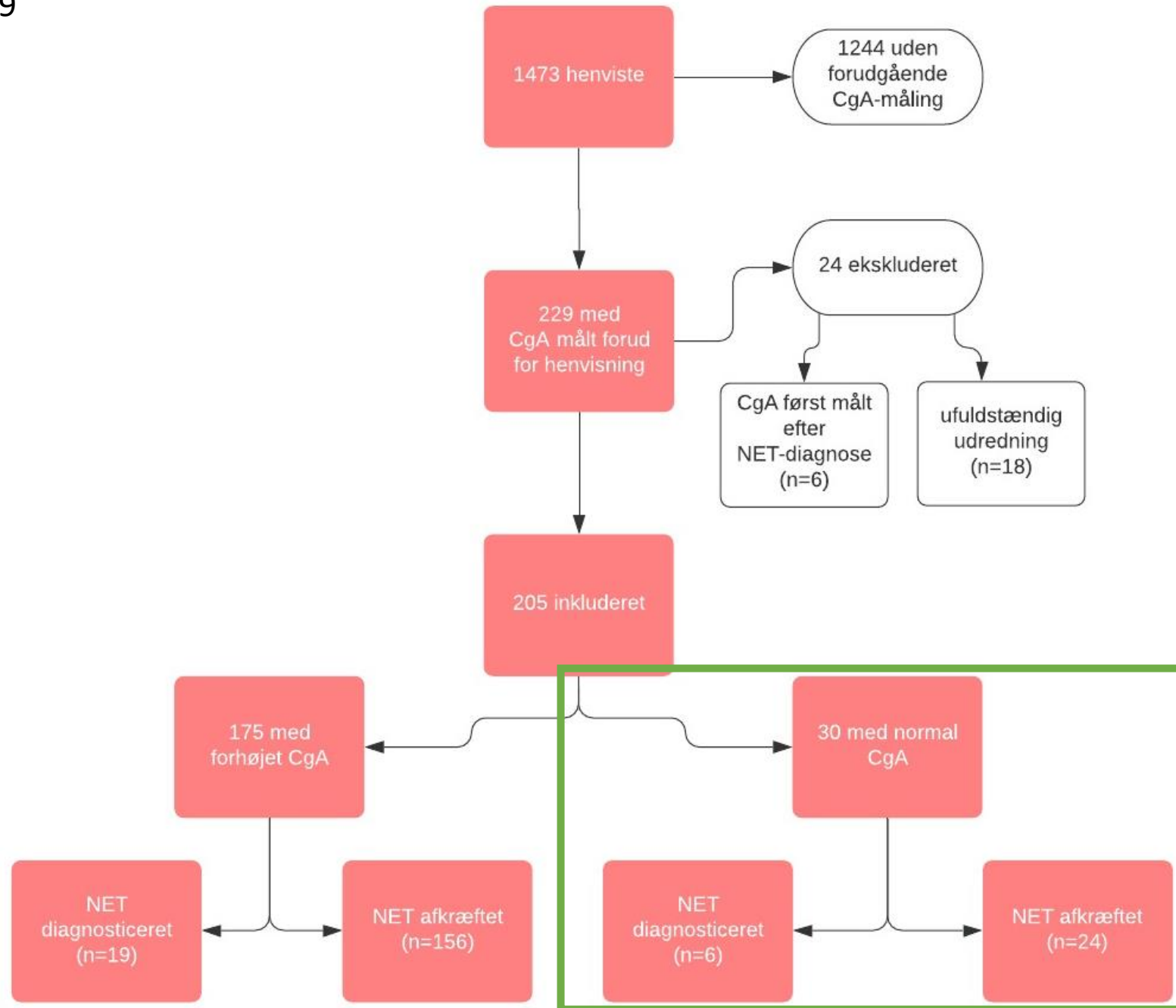
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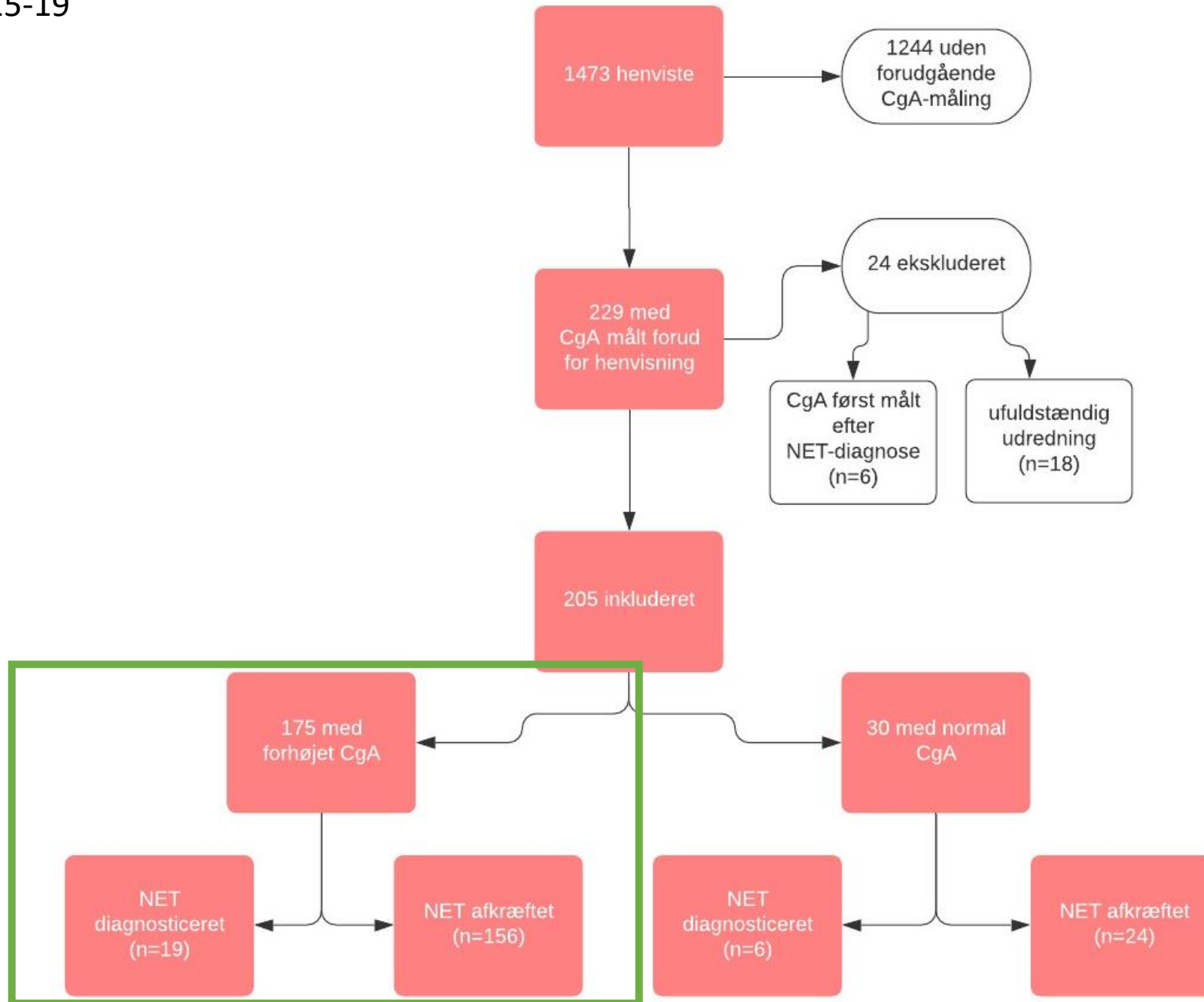
Henviste 2015-19

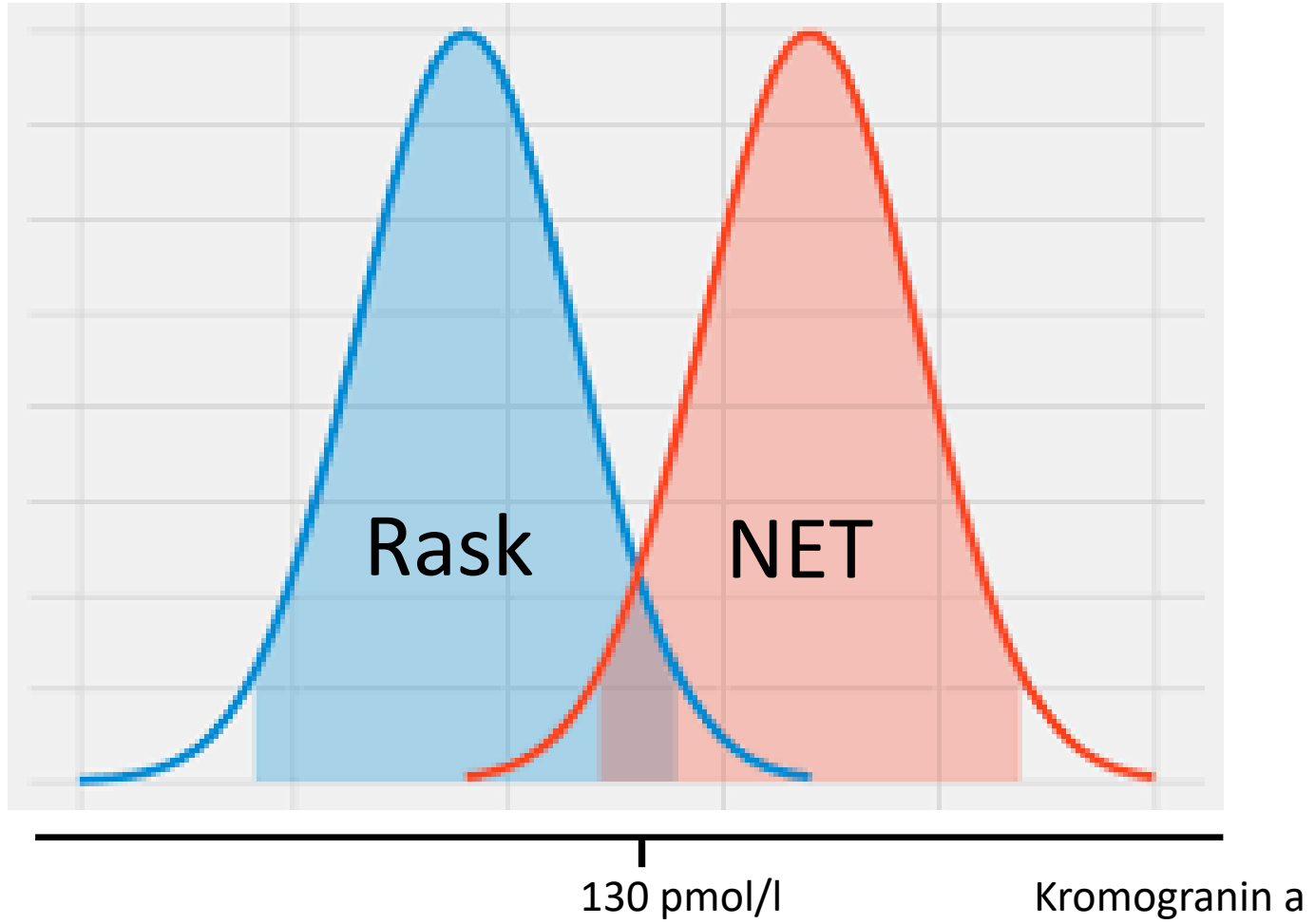


Henviste 2015-19



Henviste 2015-19





Kromogranin A under behandling.....

Prospective Study of Chromogranin A as a Predictor of Progression in Patients with Pancreatic, Small-Intestinal, and Unknown Primary Neuroendocrine Tumors

Gitte Dam^a Henning Grønbaek^a Halfdan Sorbye^b Espen Thiis Evensen^c
Björn Paulsson^d Anders Sundin^e Claus Jensen^f Dyveke Ebbesen^g
Ulrich Knigge^h Eva Tiensuu Jansonⁱ

^aDepartment of Hepatology and Gastroenterology, Neuroendocrine Tumour Centre of Excellence, Aarhus University Hospital, Aarhus, Denmark; ^bDepartment of Oncology, Haukeland University Hospital, and Clinical Science, University of Bergen, Bergen, Norway; ^cNeuroendocrine Tumor Center of Excellence, Department of Transplantation Medicine, Oslo University Hospital Rikshospitalet, Oslo, Norway; ^dNovartis Sverige AB, Kista, Sweden; ^eDepartment of Radiology, Institute of Surgical Sciences, Uppsala University, and Neuroendocrine Tumour Centre of Excellence, Uppsala University Hospital, Uppsala, Sweden; ^fDepartment of Radiology, Neuroendocrine Tumour Centre of Excellence, Rigshospitalet, Copenhagen, Denmark; ^gDepartment of Radiology, Neuroendocrine Tumour Centre of Excellence, Aarhus University Hospital, Aarhus, Denmark; ^hDepartments of Endocrinology and Surgical Gastroenterology, Neuroendocrine Tumour Centre of Excellence, Rigshospitalet, Copenhagen, Denmark; ⁱDepartment of Medical Sciences, Neuroendocrine Tumor Centre of Excellence, Uppsala University, Uppsala, Sweden

Kan Kromogranin A blive brugt til at forudsige sygdomsudvikling ?

- Patienter fra norden
- Sammenligner sygdomsudvikling på skanning med ændring i kromogranin A (ændringer > 25% anses for relevant ændring)

regression
(*n* = 18)

stable disease
(*n* = 228)

progressive disease
(*n* = 58)

regression
(*n* = 18)

CgA decrease, <i>n</i> (%)	14 (77.8)
CgA stable, <i>n</i> (%)	2 (11.1)
CgA increase, <i>n</i> (%)	2 (11.1)

	regression (<i>n</i> = 18)	stable disease (<i>n</i> = 228)
CgA decrease, <i>n</i> (%)	14 (77.8)	78 (34.2)
CgA stable, <i>n</i> (%)	2 (11.1)	107 (46.9)
CgA increase, <i>n</i> (%)	2 (11.1)	43 (18.9)

	regression (<i>n</i> = 18)	stable disease (<i>n</i> = 228)	progressive disease (<i>n</i> = 58)
CgA decrease, <i>n</i> (%)	14 (77.8)	78 (34.2)	11 (19.0)
CgA stable, <i>n</i> (%)	2 (11.1)	107 (46.9)	26 (44.8)
CgA increase, <i>n</i> (%)	2 (11.1)	43 (18.9)	21 (36.2)

Konklusion

Konklusion

- Kromogranin A kan ikke bruges til at diagnosticere NET

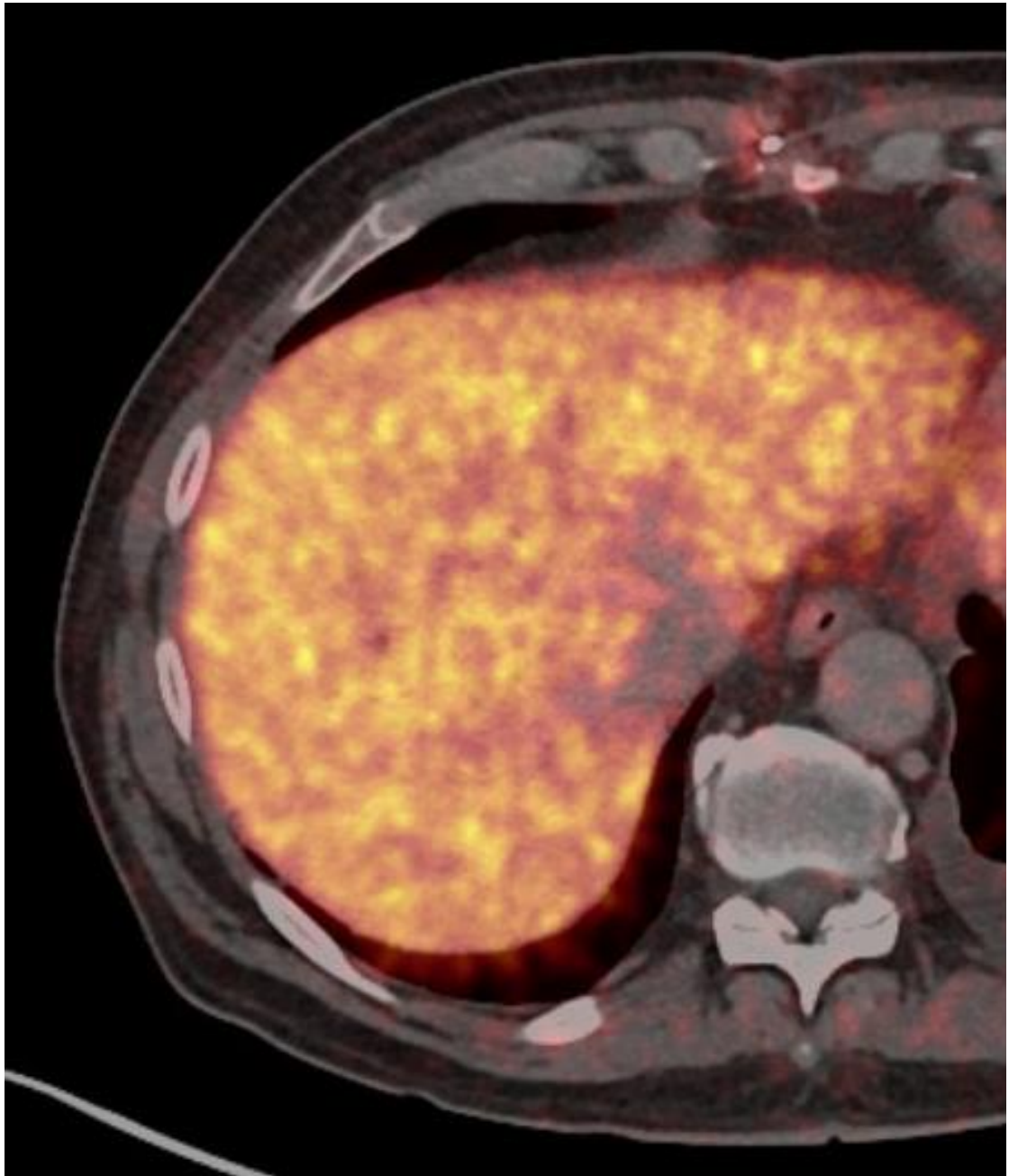
Konklusion

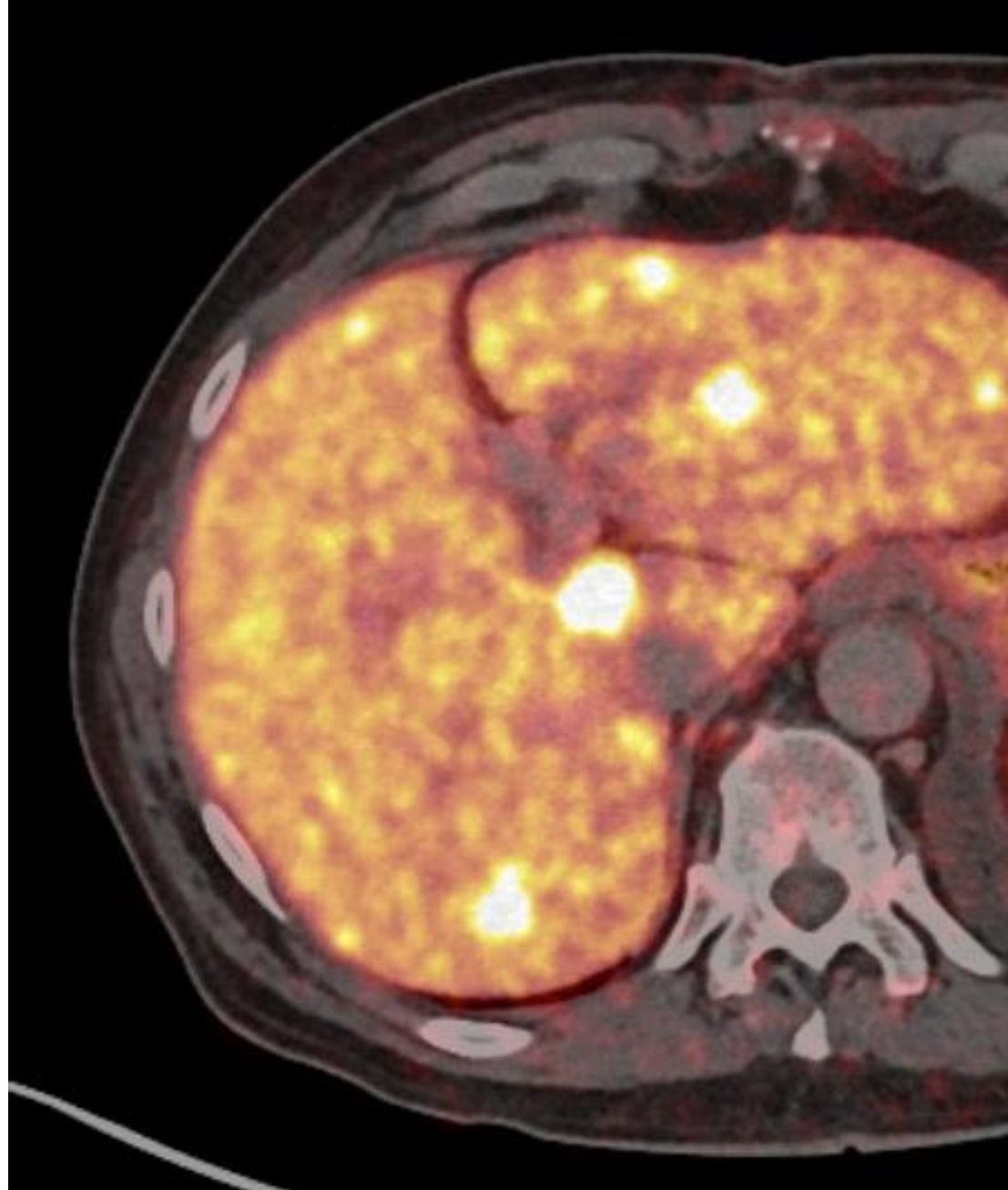
- Kromogranin A kan ikke bruges til at diagnosticere NET
- Kromogranin A kan ikke stå alene ved opfølgning af patienter

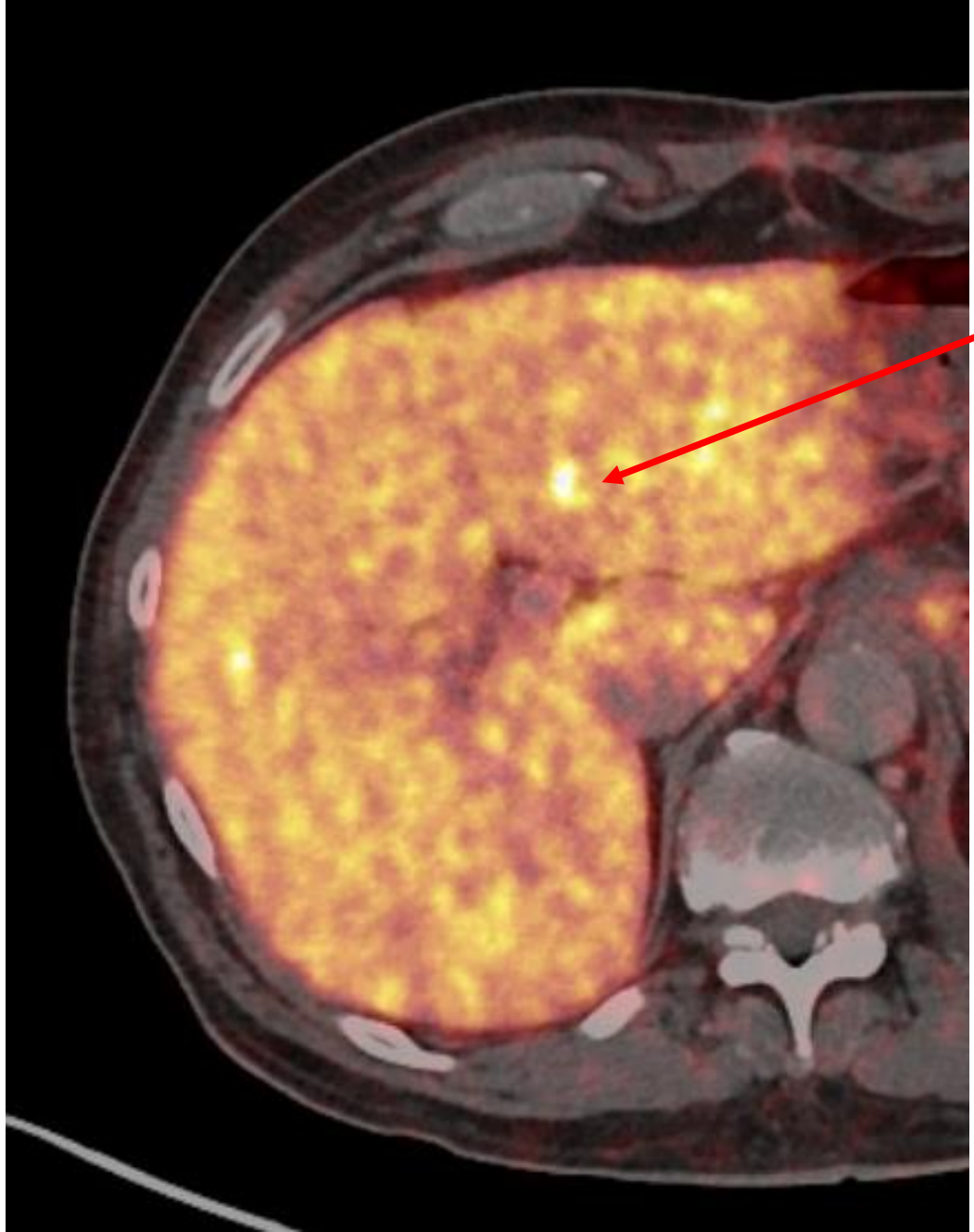
Konklusion

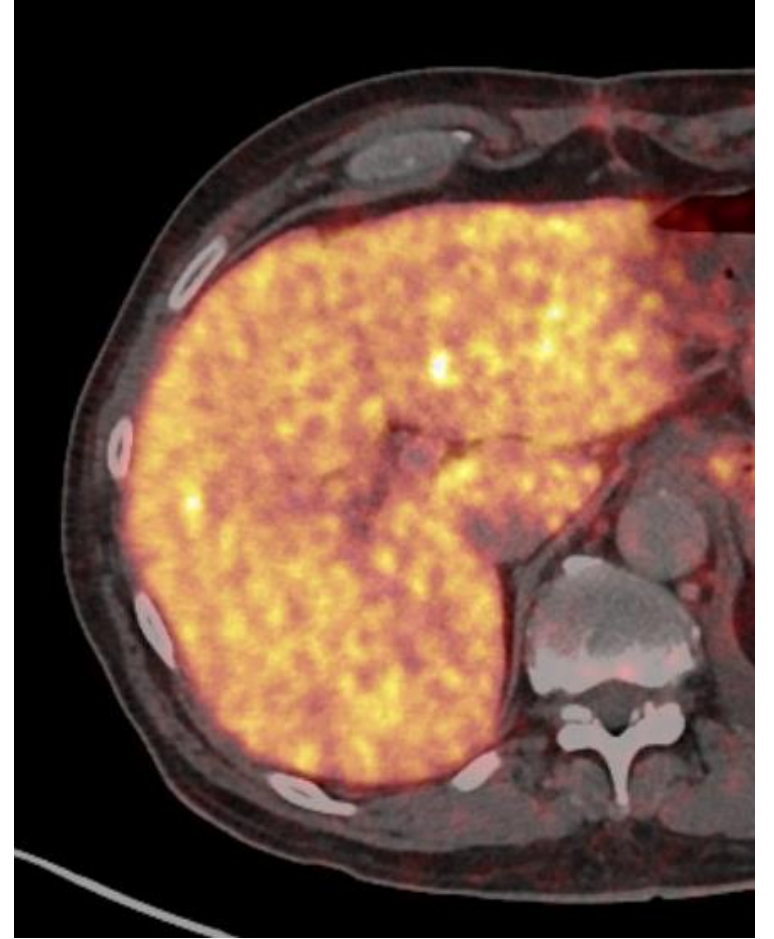
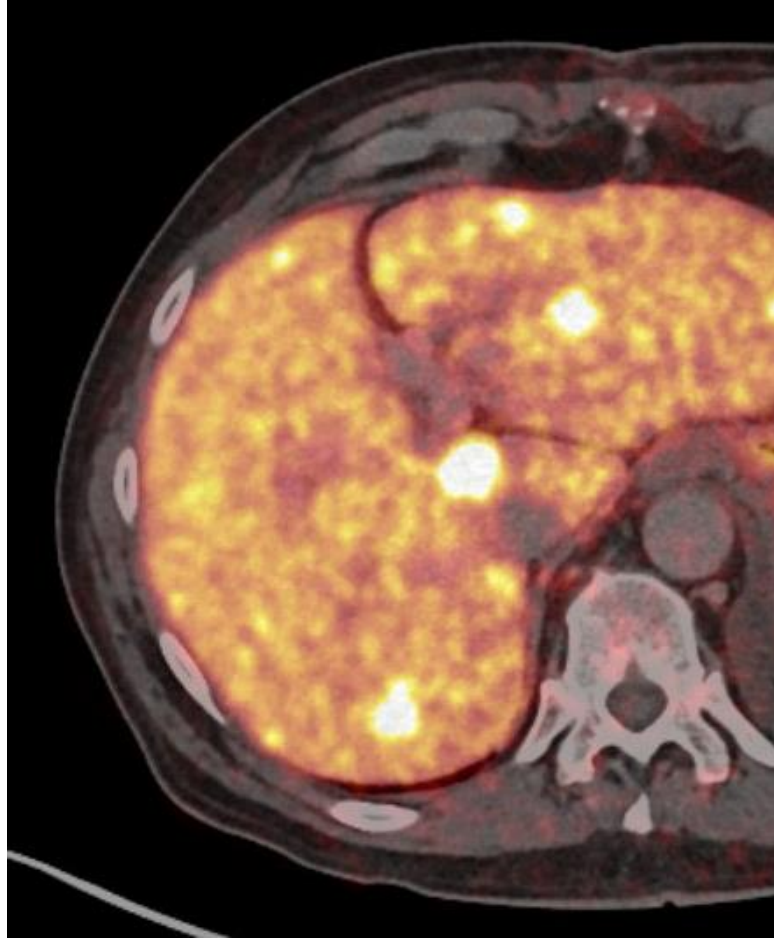
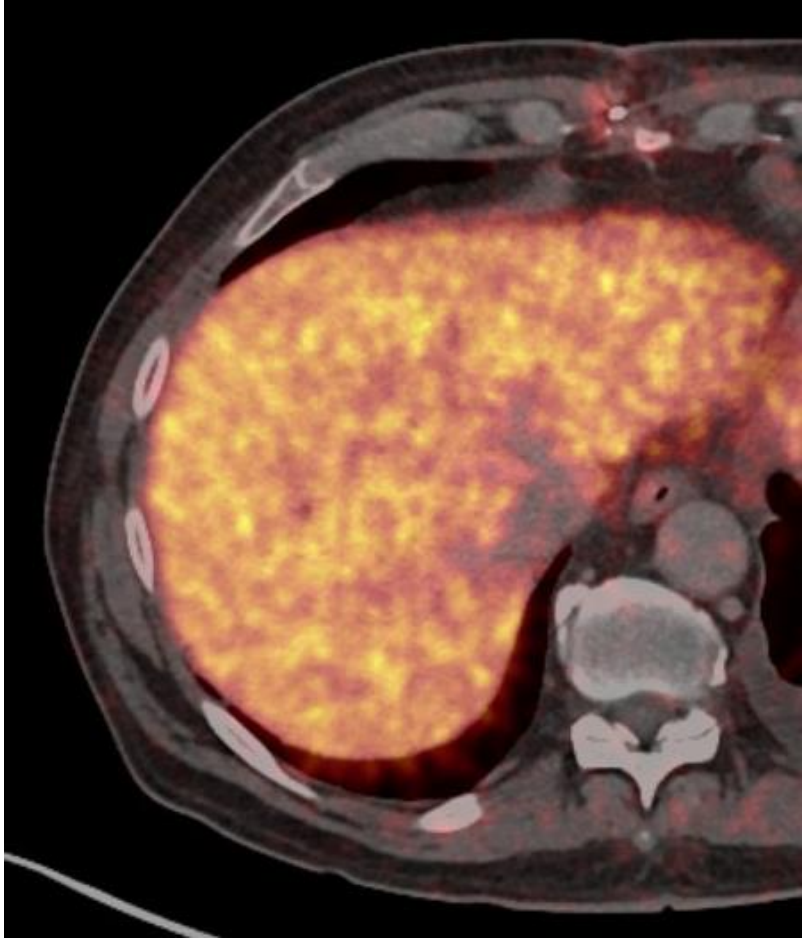
- Kromogranin A kan ikke bruges til at diagnosticere NET
- Kromogranin A kan ikke stå alene ved opfølgning af patienter
- Måske vi skal stoppe med at måle det ?

Gælder usikkerhed kun blodprøver.....

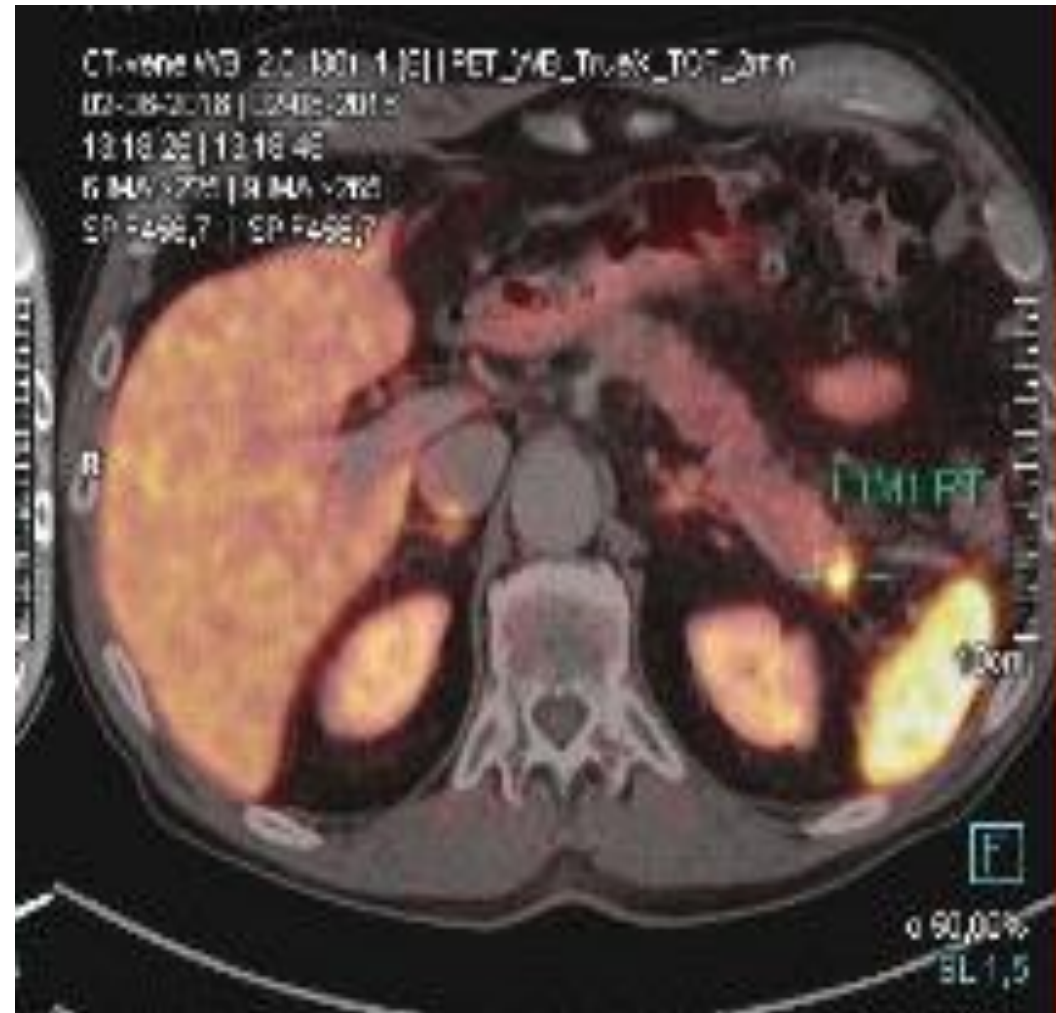








75 – årig rask mand skannes pga genetisk sygdom



Konklusion:

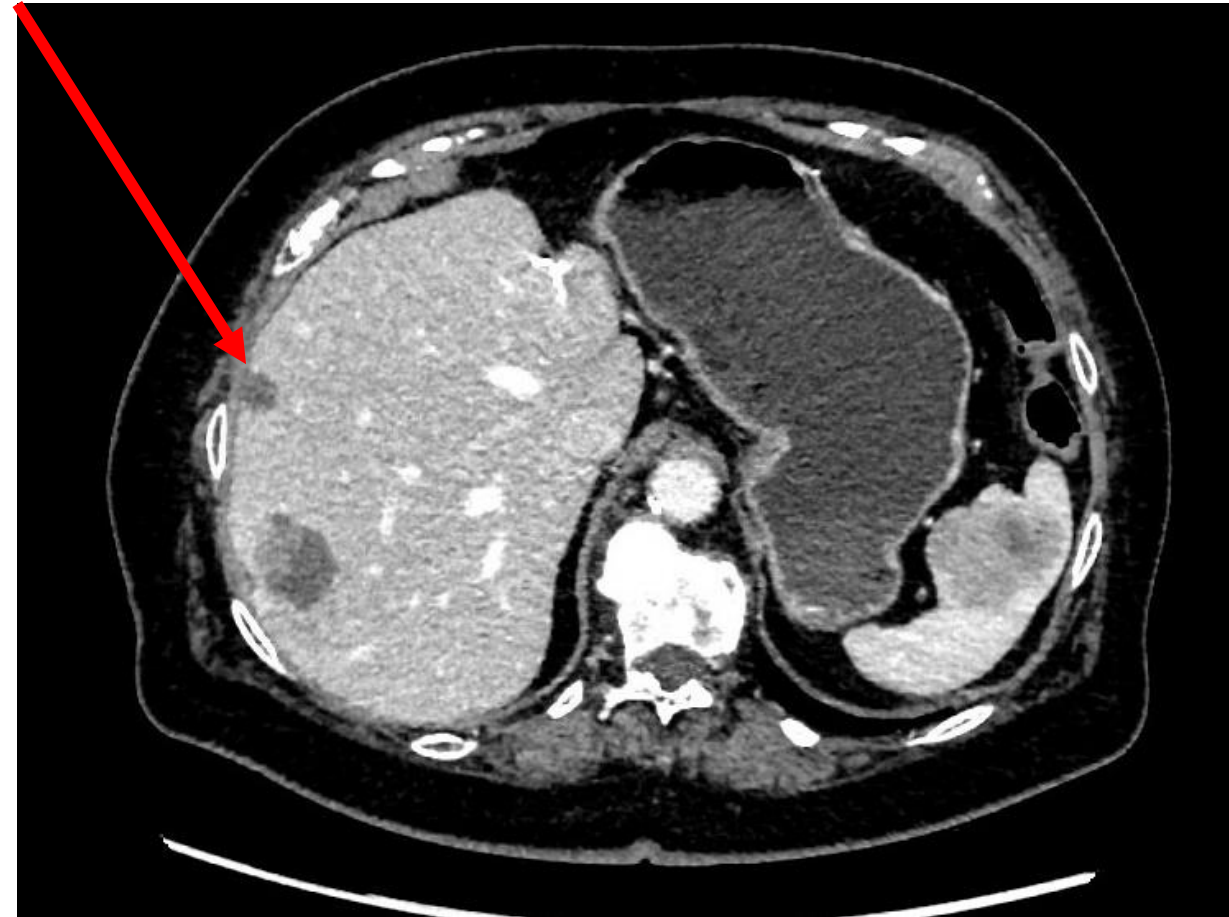
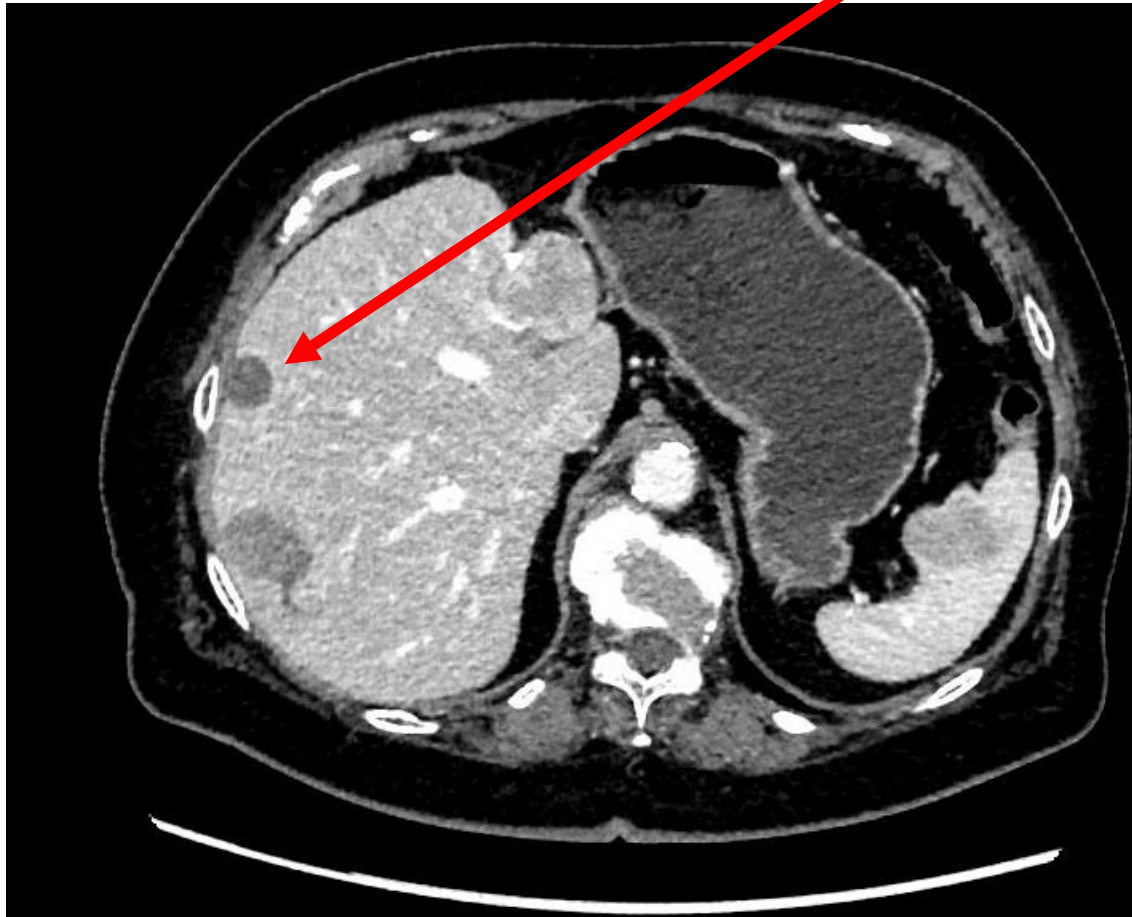
DOTATATE-optagende blandet cystisk/solid tumor i bugspytkirtlen på 2.4 cm

- **Opereres oktober 2018** (distal pancreatectomi, splenectomi, ventrikelresektion og colon resektion med anlæggelse af aflastende stomi)
- Langvarig indlæggelse
- Man fandt ikke noget
- Har det godt nu

*CT beskrivelse:
Evt let vækst af levermetastase.....*



*CT beskrivelse:
Evt let vækst af levermetastase.....*



Konklusion

- Lægevidenskab er biologi og ikke fysik

Konklusion

- Lægevidenskab er biologi og ikke fysik
- I må bære over med os

TAK