**NEUROENDOKRINE TUMOREN**
**Update Therapie**

Ina Krull
Endokrinologie / Diabetologie / Osteologie

Endokrinologie Kolloquium
13.12.23

AGENDA

- Allgemeine therapeutische Ueberlegungen
- Ausgewählte chirurgische Aspekte
- Evidenz der verschiedenen Systemtherapien
- Hormon-aktive NET: Fallbeispiele zum Management
- Ausblick

## Therapieauswahl NET

- Primarius
- Ausdehnung Lokal, Metast
- Grading / Dignität
- SSTR + / -
- Hormon-aktiv / inaktiv
- Sporadisch / hereditär MEN, VHL

## Therapieoptionen NET

- Chirurgie
- Regionale Therapie RFA, TACE, SIRT
- Somatostatin-Analoga (SSA) Peptid Radio Rez Th (PRRT) Targeted therapy Chemotherapie (INF- Alpha)

## Chirurgische Therapieoptionen NET

**Radikale Chirurgie**
- Komplette Resektion, auch von Lebermetastasen

**Debulking Chirurgie**
- Symptomkontrolle bei Hormon-aktiven NET
- Resektion Primär TU und Metastasen (70-90% des Tu Vol. resektabel, Komb. z.B. RFA)

**Palliative Chirurgie**
- z.B: Biliäre- gastrische- oder digestive Bypass-Chirurgie bei Obstruktion
- Tu bed GI Blutungen, Ileus etc

## Ausmass Chirurgie

## Appendix NET:

NET: Ca 1.5% aller Appendectomien

ENETS Guidelines 2016:

- <1cm: Appendectomie
- 1-2cm: Hemicolectomie falls
  - R1
  - Gefäss- oder Lymphgefässinvasion
  - Mesoappendix Infiltration >3mm
  - G2
- >2cm: Hemicolectomie re

Appendix NET:

Appendectomie vs Hemicolectomie re bei TU 1-2cm

Hemicolectomy versus appendectomy for patients with appendiceal neuroendocrine tumours 1-2 cm in size: a retrospective, Europe-wide, pooled cohort study

Lancet Oncol 2023; 24: 187–94

282 Appendix NET 1-2cm

163 Appendectomie

115 Hemicolect. re

| | AE | HCR | |
|---|---|---|---|
| **Histopathological features** | | | |
| Tumour location | | | |
| Tip or middle | 144 (89%) | 83 (71%) | 0·0026 |
| Base | 16 (7%) | 17 (15%) | – |
| Not available | 8 (5%) | 15 (13%) | – |
| Tumour grade | | | |
| Grade 1 | 142 (87%) | 93 (81%) | 0·56 |
| Grade 2 | 12 (7%) | 13 (11%) | – |
| Not available | 9 (5%) | 9 (8%) | – |
| Resection margin | | | |
| R0 | 155 (96%) | 96 (83%) | 0·0001 |
| R1 | 1 (1%) | 6 (10%) | – |
| Not available | 6 (4%) | 4 (3%) | – |
| Lymphovascular invasion | | | |
| Yes | 39 (27%) | 33 (39%) | 0·072 |
| No | 103 (72%) | 51 (61%) | – |
| Not available | 35 (19%) | 31 (26%) | – |
| Mesoappendix infiltration | | | |
| ≤2 mm | 42 (28%) | 28 (33%) | 0·10 |
| >2 mm | 11 (8%) | 31 (33%) | – |
| Not available | 105 (66%) | 61 (54%) | – |
| Tumour size, cm | | | |
| 1·0–1·5 | 131 (81%) | 86 (75%) | 0·10 |
| 1·6–2·0 | 28 (17%) | 29 (25%) | – |

20% regionale Mlymph bei Hemicolect Gruppe

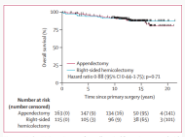
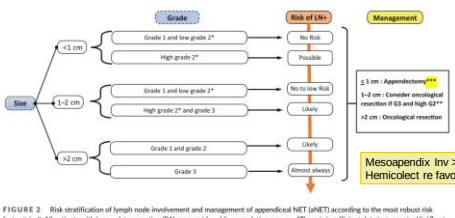



Figure 2: Kaplan-Meier estimates of overall survival for patients treated with appendectomy versus right-sided hemicolectomy

J Neuroendocrinol. 2023;1–14.

Appendix NET: ENETS Guidelines 2023




Mesoapendix Inv >3mm
Hemicolect re favorisieren

FIGURE 2 Risk stratification of lymph node involvement and management of appendiceal NET (aNET) according to the most robust risk factor "size". All patients with incomplete resection (R1) are considered for completion surgery. *There is insufficient data to suggest a Ki-67 cut off value among patients with grade 2 aNET that confers a higher risk for LN+. **No cut-off Ki-67 value has been defined ***Discuss cases in MDT if high G2. LN+, lymph node involvement; MDT, multidisciplinary team.

OPERATION
PANCREAS NET
HORMON-INAKTIV
<2CM?

PANDORA: NL multicenter, prospective Observationsstudie

ASPEN: ENETS Studie, prospective Observationsstudie

Pan-NET < 2cm, SSTR +, asymptomatisch, low-grade:
→ Sehr niedriges Risiko für maligne Progression

PANDORA: 76 Pat.
- →89% keine TU Progression über 17Mon
- →11% PD Tu >0.5cm/J

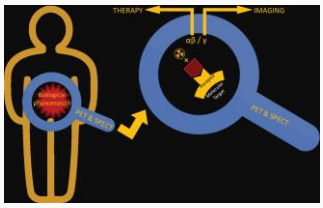
ASPEN: 1000 Pat. Interimsanalyse
- →81% watchful waiting

→ Verlaufskontrollen 6-12 Mon gerechtfertigt insb. bei MEN1, VHL

THERANOSICS:

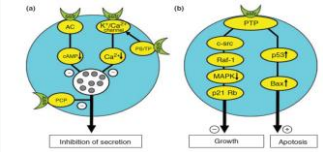
WHAT WE SEE IS
WHAT WE TREAT

**NET spez. Somatostatin Rez**




RadioGraphics 2020; 40:1715–1740

«Biotherapie» SSA:




**Octreotid, Lanreotid:**
Affinität SST Rez Subtypen sst 2, (5)

**Pasireotid:**
Multi-SST Rez Affinität sst 1;2;3;5

Kontrolle Hormonexzess

Antiproliferativ

Modlin et al, Aliment Pharmacol Ther 31, 169–188

**PROMID**

OCTREOTID LAR
VS PBO
DD NET G1

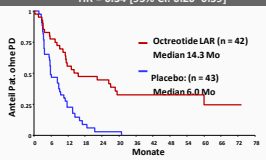
JOURNAL OF CLINICAL ONCOLOGY — ORIGINAL REPORT

Placebo-Controlled, Double-Blind, Prospective, Randomized Study on the Effect of Octreotide LAR in the Control of Tumor Growth in Patients With Metastatic Neuroendocrine Midgut Tumors: A Report From the PROMID Study Group

85 Pat.
Therapie-naiver gut diff. Dünndarm- NET
Lokal inoperabel oder metastasiert
Hormon-aktiv oder inaktiv

**TTP in Dünndarm NET**

**Octreotide LAR vs Placebo *P* = .000072**
**HR = 0.34 [95% CI: 0.20–0.59]**



## CLARINET

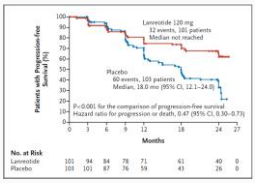
LANREOTID VS PBO
HORMON-INAKTIVE
GEP NET G1/2

ORIGINAL ARTICLE 2014

Lanreotide in Metastatic Enteropancreatic Neuroendocrine Tumors

Martyn E. Caplin, D.M., Marianne Pavel, M.D., Jaroslaw B. Ćwikła, M.D., Ph.D., Alexandra T. Phan, M.D., Markus Raderer, M.D., Eva Sedláková, M.D., Guillaume Cadiot, M.D., Ph.D., Edward M. Wolin, M.D., Jaume Capdevila, M.D., Lucy Wall, M.D., Guido Rindi, M.D., Ph.D., Alison Langley, M.Sc., Séverine Martinez, B.Sc., Joëlle Blumberg, M.D., and Philippe Ruszniewski, M.D., Ph.D., for the CLARINET Investigators*

204 Pat. Hormon-inaktiv
45% PNET
55% GI NET
KI 67: ≤10% (G1: 68%, G2:32%)




PFS nach 24Mon:
Lanreotid: 65%
Placebo:33%

## CLARINET FORTE:

PHASE II, SINGLE
ARM STUDIE

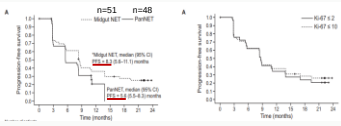
ELSEVIER ScienceDirect 2021

Original Research

Efficacy and safety of high-dose lanreotide autogel in patients with progressive pancreatic or midgut neuroendocrine tumours: CLARINET FORTE phase 2 study results

Metastasiert oder lokal fortgeschrittene
Dünndarm NET oder PanNET G1, G2
PD unter Lanreotid 120mg / 4Wo

Lanreotid 120mg / 2 Wo




PFS
8.6Mo midgut
8.0Mo PanNET

## REMINET

PHASE II-STUDIE:
LANREOTID
ERHALTUNGSTHERAPIE NACH
FIRST-LINE TH

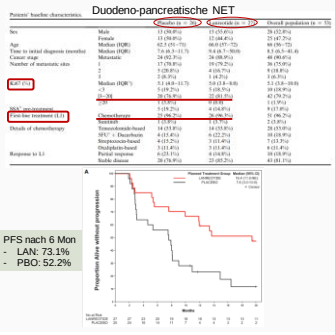
ELSEVIER ScienceDirect

Original Research

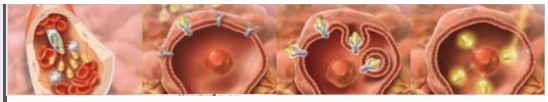
Lanreotide as maintenance therapy after first-line treatment in patients with non-resectable duodeno-pancreatic neuroendocrine tumours: An international double-blind, placebo-controlled randomised phase II trial – Prodige 31 REMINET: An FFCD study

European Journal of Cancer 175 (2022) 31e40

Duodeno-pancreatische NET




PFS nach 6 Mon
- LAN: 73.1%
- PBO: 52.2%



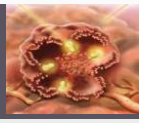
$^{177}$Lu
DOTATATE
iv. Injektion

Bindung an SSTR 2
Rez
Der NET

Internalisierung
in NET Zelle

Strahlungstherapie
In NET Zelle
↓
DNA Strangbrüche
Zelltod

PRRT



ORIGINAL ARTICLE

Phase 3 Trial of $^{177}$Lu-Dotatate for Midgut Neuroendocrine Tumors

J. Strosberg, G. El-Haddad, E. Wolin, A. Hendifar, J. Yao, B. Chasen, E. Mittra, P.L. Kunz, M.H. Kulke, H. Jacene, O. Bushnell, T.M. O'Dorisio, R.P. Baum, H.R. Kulkarni, M. Caplin, R. Lebtahi, T. Hobday, E. Delpassand, E. Van Cutsem, A. Benson, R. Srinivasankanthan, M. Pavel, J. Mora, J. Berlin, E. Grande, N. Reed, E. Seregni, K. Öberg, M. Lopera Sierra, P. Santoro, T. Thevenet, J.L. Erion, P. Ruszniewski, D. Kwekkeboom, and E. Krenning, for the NETTER-1 Trial Investigators*

## NETTER 1 Studie

N Engl J Med 2017;376:125-35

Pat mit
inoperablen
SSR + midgut
NET
PD unter
30mg Octreotde
LAR

N=116 — 4x 7.4 GBq LUTATHERA alle 8 Wo + 30mg OCTREOTID LAR alle 4 Wo

N=113 — Octreotid LAR 60mg alle 4 Wo

5J
Follow up

Progression free survival alle 3 Mon

## NETTER- 1
STUDIE

ORIGINAL ARTICLE

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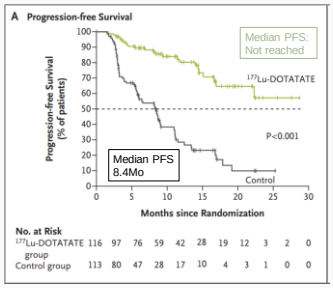

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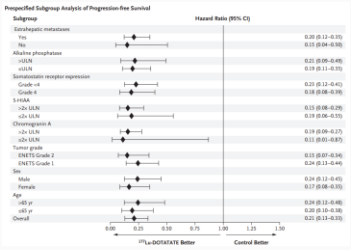


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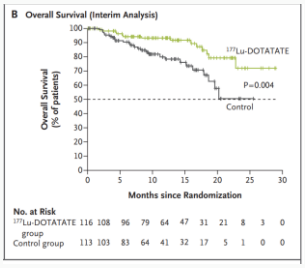
Overall survival

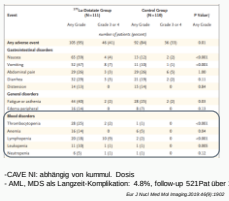



## PRRT: AE, KONTRAINDIKATIONEN

ORIGINAL ARTICLE 2017

Phase 3 Trial of $^{177}$Lu-Dotatate for Midgut Neuroendocrine Tumors

J. Strosberg, G. El-Haddad, E. Wolin, A. Hendifar, J. Yao, B. Chasen, E. Mittra, P.L. Kunz, M.H. Kulke, H. Jacene, D. Bushnell, T.M. O'Dorisio, R.P. Baum, H.R. Kulkarni, M. Caplin, R. Lebtahi, T. Hobday, E. Delpassand, E. Van Cutsem, A. Benson, R. Srirajaskanthan, M. Pavel, J. Mora, J. Berlin, E. Grande, N. Reed, E. Seregni, K. Öberg, M. Lopera Sierra, P. Santoro, T. Thevenet, J.L. Erion, P. Ruszniewski, D. Kwekkeboom, and E. Krenning, for the NETTER-1 Trial Investigators*




-CAVE NI: abhängig von kummul. Dosis
- AML, MDS als Langzeit-Komplikation: 4.8%, follow-up 521Pat über 12J

*Eur J Nucl Med Mol Imaging 2016 43(9): 1592*

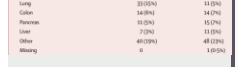
**KI:**

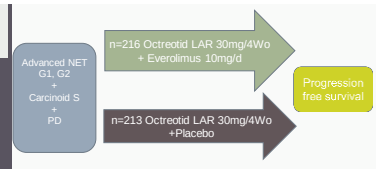
- SSTR2 neg Tumoren
- Moderate-schwere NI
- Schwere Leberinsuff
- KM Depression
- Schwer eingeschränkte cardiale Fkt.
- SS, Stillzeit

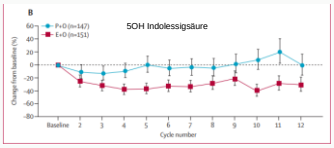
## RADIANT- 2 STUDIE

Lancet 2011

Everolimus plus octreotide long-acting repeatable for the treatment of advanced neuroendocrine tumours associated with carcinoid syndrome (RADIANT-2): a randomised, placebo-controlled, phase 3 study



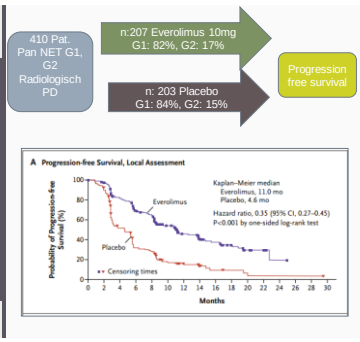




## RADIANT- 3 STUDIE

ORIGINAL ARTICLE 2011

Everolimus for Advanced Pancreatic Neuroendocrine Tumors

James C. Yao, M.D., Manisha H. Shah, M.D., Tetsuhide Ito, M.D., Ph.D., Catherine Lombard-Bohas, M.D., Edward M. Wolin, M.D., Eric Van Cutsem, M.D., Ph.D., Timothy J. Hobday, M.D., Takuji Okusaka, M.D., Jaume Capdevila, M.D., Elisabeth G.E. de Vries, M.D., Ph.D., Paolo Tomassetti, M.D., Marianne E. Pavel, M.D., Sabina Hoosen, M.D., Tomas Haas, Ph.D., Jeremie Lincy, M.Sc., David Lebwohl, M.D., and Kjell Öberg, M.D., Ph.D., for the RADO01 in Advanced Neuroendocrine Tumors, Third Trial (RADIANT-3) Study Group







## RADIANT 3 STUDIE

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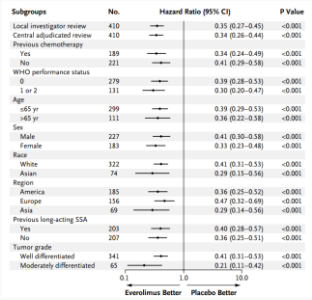
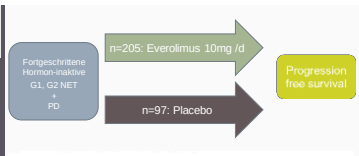


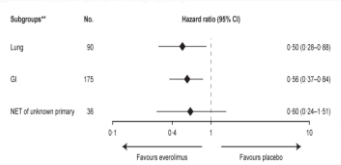
Lancet 2016

## RADIANT- 4 STUDIE

**Everolimus for the treatment of advanced, nonfunctional neuroendocrine tumours of the lung or gastrointestinal tract (RADIANT-4): a randomised, placebo-controlled, phase 3 study**

| Primary tumour site | Eve | PBO |
|---|---|---|
| Lung | 83 (35%) | 27 (28%) |
| Ileum | 47 (20%) | 24 (25%) |
| Rectum | 25 (12%) | 15 (16%) |
| NET of unknown primary site[F] | 23 (11%) | 13 (13%) |
| Jejunum | 14 (6%) | 6 (6%) |
| Stomach | 7 (3%) | 4 (4%) |
| Duodenum | 5 (4%) | 2 (2%) |
| Colon | 5 (2%) | 3 (3%) |
| Other[J] | 6 (3%) | 2 (2%) |
| Caecum | 4 (2%) | 1 (1%) |
| Appendix | 1 (1%) | 0 |

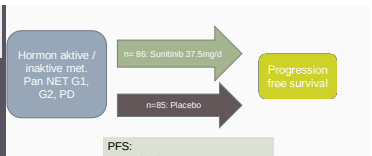


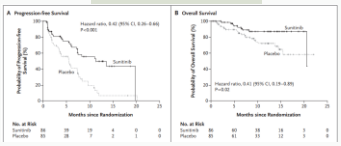

## PANCREAS NET: SUNITINIB VS PLACEBO PHASE III

The NEW ENGLAND JOURNAL of MEDICINE

Sunitinib Malate for the Treatment of Pancreatic Neuroendocrine Tumors




PFS:
- Sunitinib: 11.5Mo
- Placebo: 5.5Mo




**Sunitinib: bisher einziger registierte TKI in NET in Europa, nur in PanNET**

| | | |
|---|---|---|
| Sunitinib | Pancreas | ORR: 9.3% |
| Surufatinib | Pancreas, GI, Lung, Other | ORR: 10-19% |
| Pazopanib | Pancreas, GI, Lung, Other | ORR: 10% |
| Axitinib | GI, Lung, Other | ORR: 3% |
| Cabozantinib | Pancreas, GI, Lung, Other | ORR: 15% |
| **Lenvatinib** | Pancreas, GI | ORR: 30% (44% pNET, 16% GI NET) |

## TYROSINKINASE INHIBITOREN BEI ADVANCED WELL DIFF NEN

NEJM 2011; 364:501
Yu J 2021;13dec10.1177/17588359211042689
Front oncol 2020;10:414

Endocrine-related cancer 2016;vol23.5;411
J Clin Oncol 2017; 35;no4_suppl
JCO 2021; vol 39,20:2304

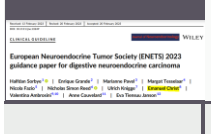
| | | |
|---|---|---|
| **Monotherapie** | Pembrolizumab in gut diff NET | ORR: 3.7% |
| | Pembrolizumab in G3 NEN | ORR: 4.7% |
| | Avelumab in G3 NEN | ORR: 7% |
| | Spartalicumab in NEN | ORR: 4-16% |
| **Kombinations-Therapie** | Ipilimumab+Nivolumab in G3 NEN | ORR: 26% |
| | Ipilimumab+Nivolumab in G3 NEN | ORR: 14.7% |
| | Durvalumab+Tremelimumab in G3 GEP-NEN | ORR: 9% |
| | Ipilimumab+Nivolumab in G1-2 NET | ORR: 0% |

## CHECKPOINT INHIBITOREN BEI NEN

Clin Cancer Res. 2020 May 01; 26(9): 2124
Br J Cancer 2020 122:1309
Ann Oncol 2018:29 (suppl 8) VIII467
Cancer 2021; 127(17): 3194

ESMO 2022;7:100364
Clin Cancer Res 2020; 26(17): 4454
ESMO Paper presentation virtual conference
Clin Cancer Res 2020;26(10):2290

## CHEMOTHERAPIE BEI NEC




| | |
|---|---|
| **Firstline bei metastasierenden GEP NEC** | Carboplatin / Etoposid<br>Irinotecan / Cisplatin alternativ |
| **Second- line bei metastasiertem GEP NEC** | FOLFIRI (5FU, Irinotecan),<br>FOLFOX (5FU, Oxaliplatin),<br>CAPOX (Capezitabin / Oxaliplatin)<br>CAPTEM (Capezitabin/Temodal) |

Pan-NET G3, KI-67 <50%

- CAPTEM
- Alternativ Streptozotozin /5FU

## CHEMOTHERAPIE BEI NEC

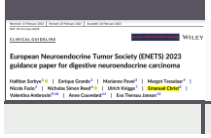



TABLE 2 Prospective and retrospective studies on first-line chemotherapy in advanced digestive neuroendocrine carcinoma.

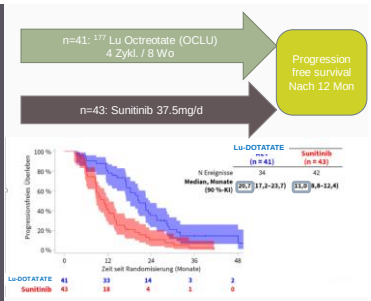
| Reference | Design | Treatment | No | Diff | RR % | PD % | PFS | OS |
|---|---|---|---|---|---|---|---|---|
| Sorbye et al. (2013)[12] | Retrospective | Etoposide + cisplatin or carboplatin | 252 | G3 | 31 | 36 | 4 m | 11 m |
| Yamaguchi et al. (2014)[13] | Retrospective | Cisplatin + etoposide or irinotecan | 258 | Poor | 28 vs. 50 | | 4 vs. 5.2 m | 7.3 vs. 13 m |
| Hentzel et al. (2015)[14] | Retrospective | Platinum + etoposide | 113 | Poor | 35 | 27 | 5 m | 16.4 m* |
| Walter et al. (2017)[15] | Retrospective | Platinum + etoposide | 152 | Poor | 30 | 27 | 6.2 m | 11.6 m |
| Morizane et al. (2022)[16] | Phase III | Cisplatin + etoposide or irinotecan | 170[7] | Poor[8] | 55 vs. 53 | 13 vs. 15 | 5.6 vs. 5.1 m | 12.5 vs. 10.9 m |
| Zhang et al. (2020)[17] | Phase II | Cisplatin + etoposide or irinotecan | 66 | Poor | 42 vs. 42 | 36 vs. 13 | 6.4 vs. 5.8 m | 11.3 vs. 10.2 m |

Note: Only retrospective studies with n > 100 and prospective studies with n > 60 were included.
Abbreviations: Diff, differentiation; OS, overall survival; PD, progressive disease at first evaluation; PFS, progression-free survival; RR, response rate.

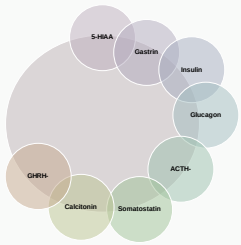
## OCLURANDOM-STUDIE PHASE II PANCREAS NET

PD bei SSR + PanNET
Ki>10%: 37%
Mhep: >25%
Hormon-aktiv:20%
> 2 Vor-System Therapien: 43%

Annals of Oncology 2022




## HORMON-ACTIVE NET




## FALL W. S. 1935

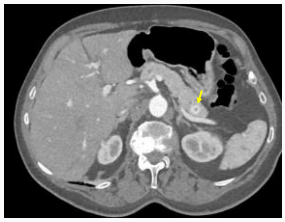
ausschliesslich morgendlich nüchtern und bei körperl. Aktivität:
- Zittern und Nausea, Gefühl wie "reisekrank«
- Unter regelmäss. ZMZ keine Symptome
- St.n. rez «Präsynkopen»
- Selbstmessung BZ: 2.4mmol/L

Fastentest:
Bei Abbruch:
- Glucose: 2.2 mmol/L
- C-Peptid: 1208 pmol/L
- Insulin: 12.6 mU/L

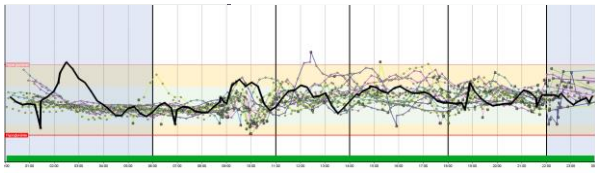
→ hyperinsulinäme Hypoglykämie

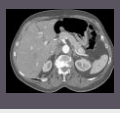
## FALL W.S. 1935

CT: 15x15mm hypervaskuläre RF mit zentraler Nekrose Pancreasschwanz,
Bereits im auswärt. MRI beschrieben
→ Gut mit Insulinom vereinbar



Aufgrund Alter, Comorbiditäten und Patientenwunsch konservativer Therapieversuch mit Proglycem, Maizena





Weitere Therapieoptionen:
- SSA
- EUS-gesteuerte RFA

## EUS-RFA IN HORMON-INAKTIVEN PANCREAS NET

medicina 2023 MDPI

Systematic Review
**Efficacy and Safety of Endoscopic Ultrasound-Guided Radiofrequency Ablation for Pancreatic Neuroendocrine Tumors: A Systematic Review and Metanalysis**

Rita Ionut Rus *, Antonia Focsineanu * and Stefan Francisc Graur *

**Table 2.** Results from studies reporting the efficacy and safety of EUS-RFA for the treatment of NF-PanNETs included in the meta-analysis **.

| Study, Year | Study Design | N of Patients/ N of NF-PanNETs | Male/ Female | Age | Tumor Size (Mean, mm) | Location | Device | N of RFA Sessions per NeTs/Pt | Efficacy * | N of Adverse Events | Follow-Up (Months) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Rossi [11], 2016 | Retrospective | 1/1 | M | 72 | 9 | T | EchoB-EUS-RFA | 1 | 100 | 0 | 34 |
| Arcidiacono [12], 2015 | Retrospective | 1/1 | M | 76 | 20 | T | EFG, Starmed | 1 | 100 | 0 | 1 |
| Fu [13], 2015 | Prospective | 2/2 | F | 69.5 | 27.5 | H | EchoB-EUS-RFA | 1.5, 1.2 | 100 | 2 | 6 |
| Chu [17], 2018 | Retrospective | 7/7 | 3M, 4F | 56.1 | 20 | H2, T5 | EFG, Starmed | 3.5, 2.5, 5.2 | 75 | 2 | 13 |
| Barthet [5], 2016 | Prospective | 12/14 | 7M, 5F | 59.9 | 15.1 | H3, T11 | EFG, Starmed | NR | 86 | 3 | 12 |
| Okuchi-no [14], 2019 | Retrospective | 11/19 | 6M, 5F | 65.9 | 16.2 | H11, T7 | EFG, Starmed | 1 | 94.5 | 2 | 8.7 |
| De Nucci [15], 2020 | Prospective | 6/6 | 3M, 3F | 77.1 | 16.2 | H4, T3 | EFG, Starmed | 1 | 100 | 1 | 12 |
| Rossini [16], 2022 | Prospective | 32/32 | 12M, 18F | 70.1 | 16.2 | H11, T21 | EFG, Starmed | 3.16, 1.7, 3.2 | 96.3 | 8 | 6 |
| Lakhtakia [24], 2023 | Retrospective | 14/14 | NR | NR | NR | NR | EFG, Starmed | NR | 85.7 | NR | 31.5 |

* Clinical efficacy was defined as complete disappearance of the lesion upon cross-sectional imaging during follow-up. ** table legend. N: number; H: pancreatic head; T: pancreatic tail; NR: not reported.

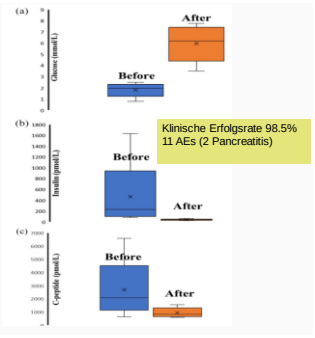
Insulinome: 90% benigne, singulär

## EUS-ETHANOL- AND RFA IN INSULINOMA

2021

**Endoscopic ultrasound-guided ethanol and radiofrequency ablation of pancreatic insulinomas: a systematic literature review**

35 case reports
75 Pat mit Insulinom: 27 RFA, 47 EA
Med. Grösse:13x10mm (2-27)




Klinische Erfolgsrate 98.5%
11 AEs (2 Pancreatitis)

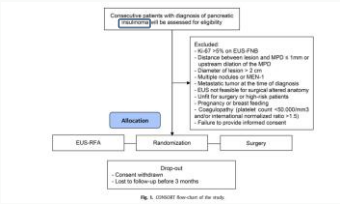
Insulinome: <2cm, KI-67 ≤5%, singulär

## RCT INSULINOM: RFA VS CHIRURGIE

Digestive and Liver Disease 2023

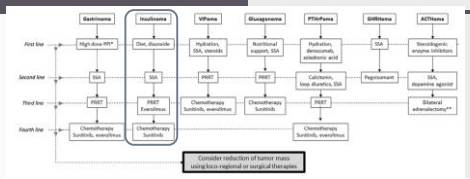
**Study protocol for a multicenter randomized controlled trial to compare radiofrequency ablation with surgical resection for treatment of pancreatic insulinoma**

**ERASIN Trial**




## HORMON-AKTIVE FORTGESCHRITTENE PAN NET

**European Neuroendocrine Tumor Society 2023 guidance paper for functioning pancreatic neuroendocrine tumour syndromes**



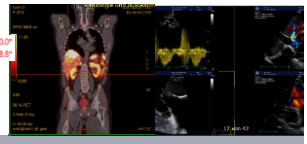

## Herr B.M. 1963

- Seit 10 J tgl. mehere Episoden von heissem roten Kopf
- Schweissausbrüche
- Wässrige Diarrhoen 5-10x/d
- Ungewollt -16kg in den letzten 2 J
- Aktuell: periphere Oedeme, Pleuraegüsse bds., Aszites

24h Urin

| | |
|---|---|
| 5-OH-Indol-Essigsäure [2-9 mg/l] | 160.0* |
| 5-OH-Indol. sre. [<10 mg/24h] | 268.8* |

Chromogranin A: 1937ug/l
Norm <102



Carcinoid- S mit Hedinger S. bei hepatisch metastasiertem Dünndarm NET

Herr M, B. 1963:

- 11/2017: Leberbiopsie: NET G1, KI-67:<1%, reichl. Expression von SSTR2
- Ga DOTATAE PET CT 1/2018: SSTR-avide 4cm Mesenteriale RF, multiple bis 6cm gr Mhep
- Echo 1/2018: LVEF 40-45%

Trikuspidalklappeninsuffizienz (systolischer Koaptationsdefekt von 15mm) bei ausgeprägter Restriktion/Immobilität aller diffus verdickter Segel, subvalvulärer Apparat relativ zart. Daraus errechneter (wha. unterschätzter) systolischer Pulmonalis-Druck um 36 mmHg (mki. ZVD geschätzt um 15 mmHg). Hochgradige Pulmonalklappeninsuffizienz bei retrahierten und verdickten Taschen. Flussbeschleunigung ohne Stenosierung

→ Somatuline Autogel 120mg/4Wo, Empfehlung Klappenersatz, im Verlauf Debulking OP
→ Wegen «NW» Somatuline von Pat. wieder gestoppt, im Verlauf Sandostatin LAR 30mg
→ Pat. weigert sich standhaft, für interdisz. Management an KSSG zu kommen

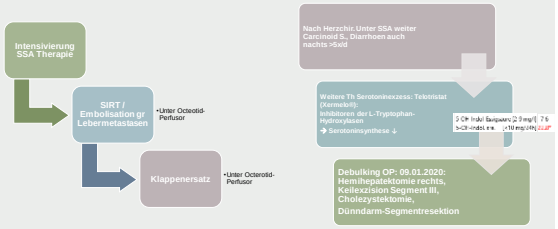
| | 12/2017 | | | | | 12/2018 |
|---|---|---|---|---|---|---|
| 5-OH-Indol-Essigsäure [2-9 mg/l] | 160.0* | 254.2* | 190.9* | sunten | 81.2* | 120.1* | 53.0* | 89.5* | 66.9* |
| 5-OH-Indol. sre. [<10 mg/24h] | 268.8* | 371.1* | 320.7* | sistiert | 196.5* | 234.2* | 108.7* | 156.6* | 152.5* |

2/2019: Re Herz-Dekompensation, rep. Pleura- und Aszitespunktionen

## Wie weiter?- In welcher Reihenfolge?

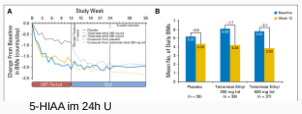
- Debulking OP
- Medikamentöse Kontrolle Serotonin-Exzess
- Lokale Lebertherapie
- Herzklappenersatz

**Wie weiter?- In welcher Reihenfolge?**

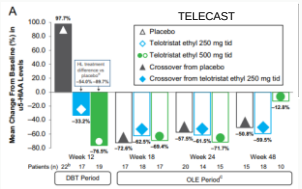



TELESTAR 2016
TELECAST 2018
PHASE III PCT TRIALS

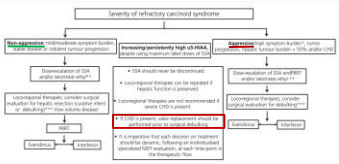
Diarrhoe / d TELESTAR



5-HIAA im 24h U

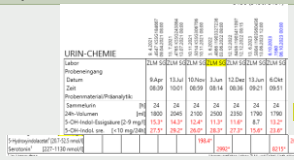



MANAGEMENT CARCINOID-S



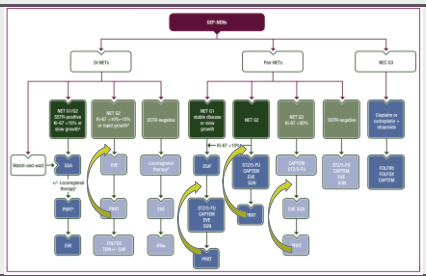

Verlauf nach Debulking OP

Anhaltend unter Lanreotid 120mg / 4 Wo
- Zunächste stabile Mhep.
- chir. Nicht behandelbare Desmoid-und ausgeprägte Lymphangiomatose / Fibromatose
- 5/2020-2/2021: 4 Zyklen $^{177}$Lu DOTATOC bei PD mesenterialer Metastase und neuem pulm Nodulus
- Aktuell:
  - MRI stabile Situation
  - Anstieg Serotonin 5OH Ind. Im Serum und Urin
  - Anstieg Chromogranin A




Diskussion RFA dominante Mhep

ESMO Guidelines 2020 GEP NET




**AUSBLICK-AUSWAHL (1)**

NETTER-2 Studie
- PRRT als First-line Th in advanced NET G2-G3

COMPOSE- Studie
- PRRT als first-oder second-line Th in GEP NETs G2-3

COMPETE trial
- Advanced GEP NET: PRRT (Lu-Edotreotide) vs Everolimus

PRRT mit Alpha Emitter

SSTR ANTAGONISTEN $^{177}$Lu Satoreotid Tetraxetan
- Phase I/II Studie in advanced midgut und PanNET

## AUSBLICK-AUSWAHL (2)

**CONTROL NET Study in NET G1-2**

- PRRT versus PRRT+Chemo (CAPTEM PRCT) in DD NET
- PRRT+Chemo (CAPTEM PRCT) vs CAPTEM

**SEQTOR trial**

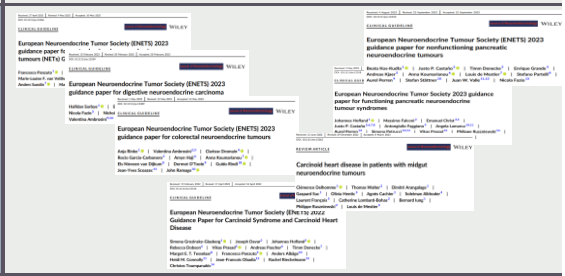
- Advanced PanNET
- Everolimus vs Chemo STZ + 5FU, bei PD Therapie-switch

**CABINET- Studie**

- Phase III Cabozantinib in advanced PanNET

**Gastrin Rez Antagonist Netazepide Phase II Studie**

## 7 Neue ENETS Guidance Papers 2022 / 2023



**DANKE!**