Advances in PPGL

Wednesday, 28 January 2026, 18:00 – 19:10 CET

Disclosure Statement

Ashley GROSSMAN (Moderator) has no potential conflicts of interest to report.

The Aim and Concept

- ✓ Transferring research to education and teaching is a major goal at ENETS.
- ✓ Webinars are free of charge and can be accessed by all.
- ✓ All webinars will be recorded and made available on the ENETS website after the event.
- ✓ **This webinar is intended for HCPs qualified by law to prescribe medicine.**

CME Accreditation by UEMS-EACCME®

- ✓ This webinar is accredited by UEMS-EACCME® with **1.0 European CME Credits (ECMEC®).**
- ✓ To receive CME credit, participants must **attend the live webinar** and complete a **feedback form**.
- ✓ Responses are anonymous.
- ✓ To obtain your **certificate with the European CME credits** for this webinar, please contact the ENETS Office at office@enets.org.

Live poll question: Getting to know the audience

In which medical discipline are you trained or currently working?

Tonight's faculty

Ashley GROSSMAN

Royal Free Hospital
London, UK
Endocrinology

Jaydira DEL RIVERO

National Cancer Institute /
National Institutes of Health
Bethesda, Maryland, USA
Oncology

Camilo JIMENEZ

University of Texas
MD Anderson Cancer Center
Houston, Texas, USA
Endocrinology

Svenja NÖLTING

University Hospital Zürich,
Switzerland
Endocrinology

Tonight's agenda

18:00 – 18:05	**Opening comments** *Ashley GROSSMAN, GBR*
18:05 – 18:20	**Update in the genetics and diagnostic approach of PPGL: what the clinician should know** *Jaydira DEL RIVERO, USA*
18:20 – 18:35	**Treatment of advanced PPGL** *Camilo JIMENEZ, USA*
18:35 – 18:50	**Bench-bedside-back - patient tissue as key for personalised medicine** *Svenja NÖLTING, SUI*
18:50 – 19:05	**Discussion**
19:05 – 19:10	**Closing comments** *Ashley GROSSMAN, GBR*

Update in the Genetics and Diagnostic Approach of PPGL: What the Clinicians Should Know

Jaydira Del Rivero, MD

Associate Research Physician

Developmental Therapeutics Branch

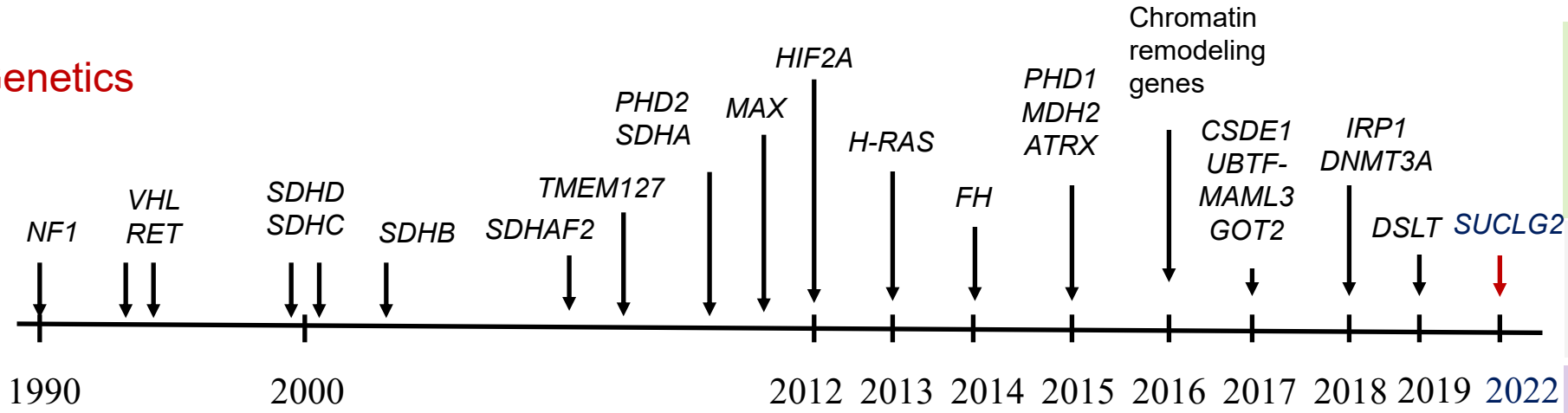
National Cancer Institute/National Institutes of Health

Disclosure Information

- I have no personal or professional conflicts of interests.
- I have no financial disclosures

PPGL: Continuing Progress

Genetics



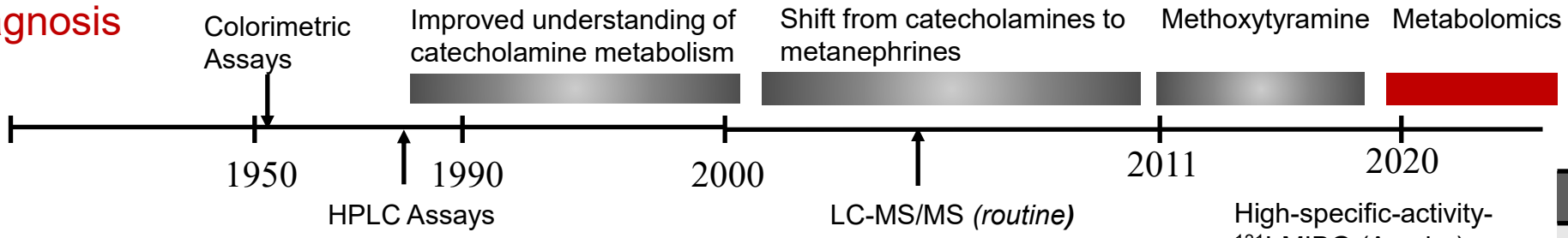
Cluster I: Pseudohypoxia group
DHA, SDHB, SDHC, SDHD, SDHAF2, FH, VHL, IDH1/2, MHD2, PHD1/2, and *HIF2/EPAS1*

Cluster II: Kinase signaling group
RET, *NF1*, *TMEM127*, *MAX*, and *HRAS*

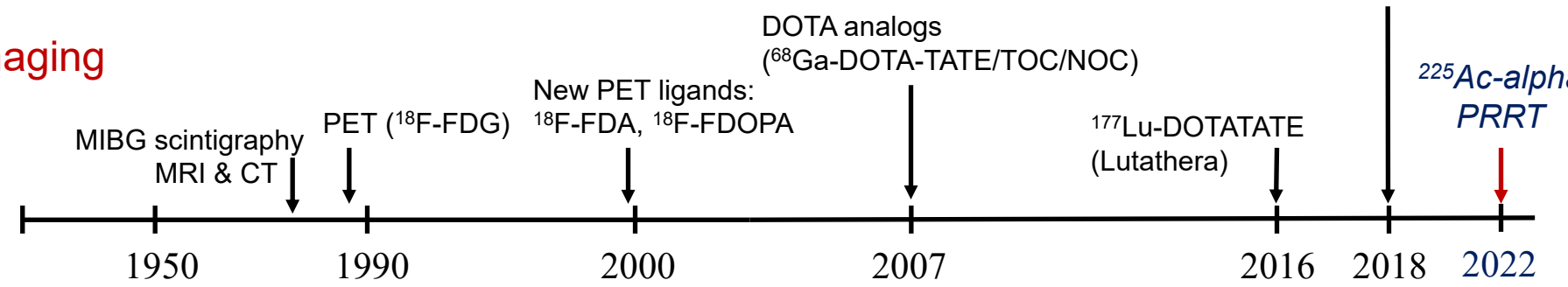
Cluster III: Wnt signaling group
CSDE1 and *MAML3*

40%-45% PPGL → germline pathogenic variant
> 40% SDHB for metastatic PPGL

Biochemical Diagnosis



Imaging

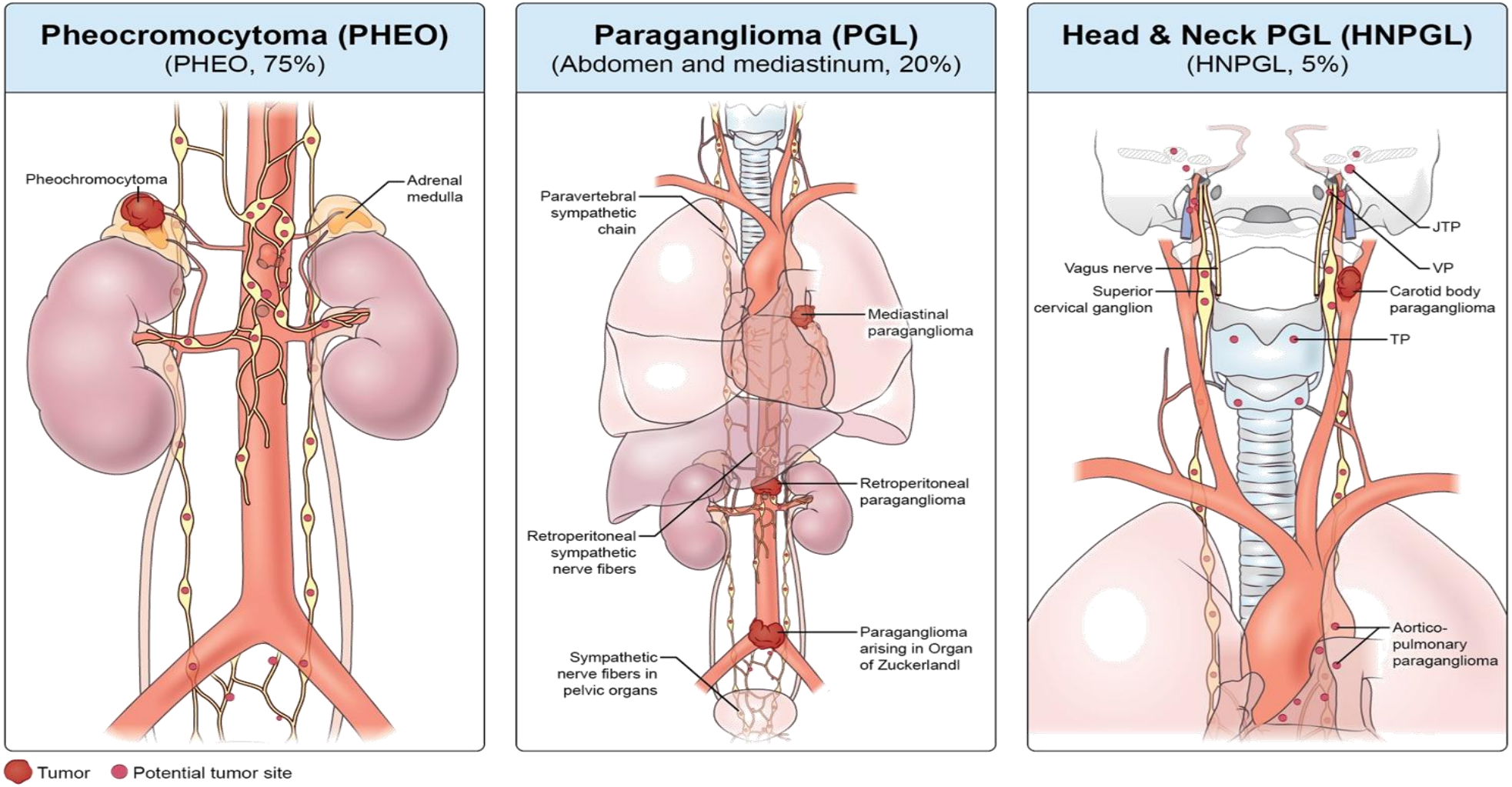


Sensitivities mPPGL	
^{123}I-MIBG	50-60%
^{68}Ga-Dotatate	98-99%
^{18}F-FDG	68-92%

Hadrava Vanova JNCI 2021; in press
Pacak et al. Nat. Rev. Endocrinol. 2020; 16:621
Ghayee et al. Metabolism 2020; 110:154297
Dahia et al. Endocr. Relat. Cancer 2020; 27:T41
Jimenez et al. Cancers 2019; 11:1018
Fishbein et al. Cancer Cell 2017; 31:181

Adapted Courtesy of K. Pacak and G Eisenhofer

Pheochromocytoma/Paraganglioma (PPGL)



Lenders et al. *Clin Endocrinol Metab.* 2014;99(6):1915-1942.

PPGLs Genetics

Cluster I: Pseudohypoxia group
DHA, SDHB, SDHC, SDHD, SDHAF2, FH, VHL
IDH1/2, MHD2, PHD1/2, and ***HIF2/EPAS1***

Cluster II: Kinase signaling group
RET, ***NF1***, ***TMEM127***, ***MAX***, and ***HRAS***

Cluster III: Wnt signaling group
CSDE1 and ***MAML3***

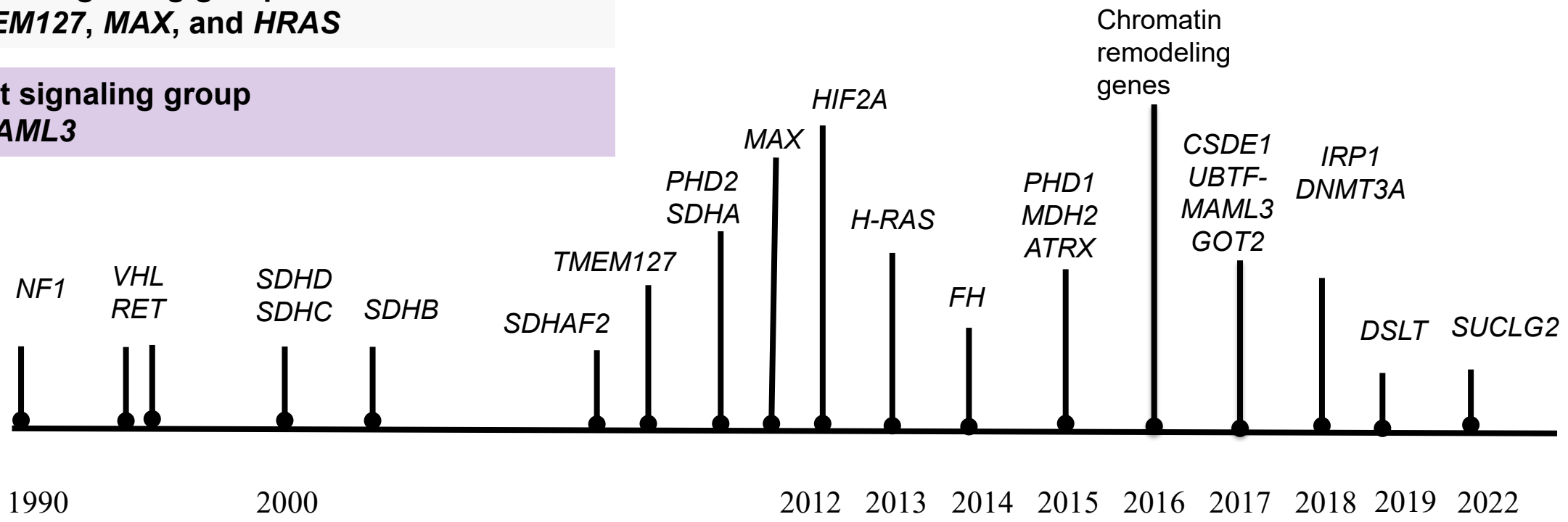
SDHx-mutated tumors → PARP inhibitors with TMZ

Cluster I PPGLs → HIF2-alpha inhibitors

Cluster II PPGLs → Tyrosine Kinase Inhibitors

SSTR expression → 177Lu DOTATATE

NE transporter system expression → ^{131}I-MIBG therapy



- **35%-40% PPGL → germline pathogenic variant**
- **About 40% of metastatic PPGL has *SDHx* pathogenic variant**

Adapted. Courtesy of K. Pacak
Fishbein et al. Cancer Cell 2017; 31:181
Crona et al. Endocr. Rev. 2017; 38:489
Dahia et al. Nat. Rev. Cancer 2014; 14:108
Fischbein, Del Rivero…Jimenez, NANETS Consensus Guidelines 2021

Parasympathetic paragangliomas:
Most often found in the head and neck

95% casos: non-functional/non-secreting

Sympathetic paragangliomas:
Located in the sympathetic paravertebral ganglia of thorax, abdomen, and pelvis

Functional/secreting

Pheochormocytomas
Adrenal medulla

Functional/secreting

Paraganglioma

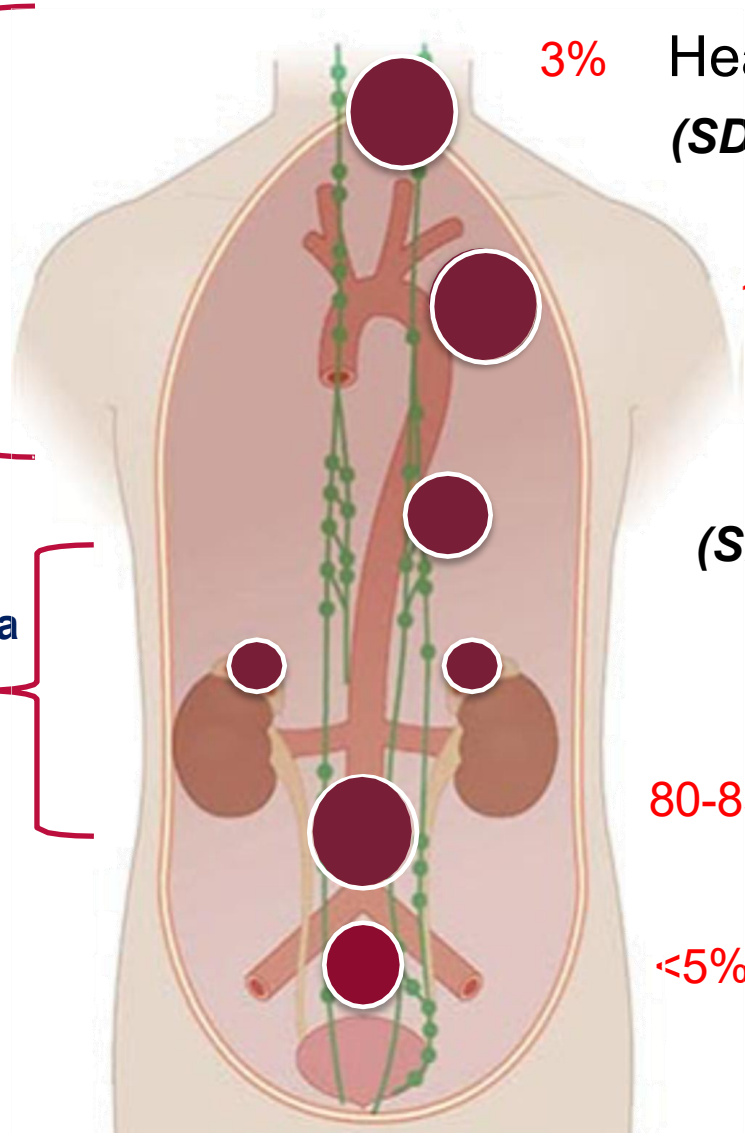
Extra-adrenal

15-20% of cases

Pheochromocytoma

Adrenal

80-85% of cases



3% Head and neck

(SDHx → SDHD)

12% Thorax

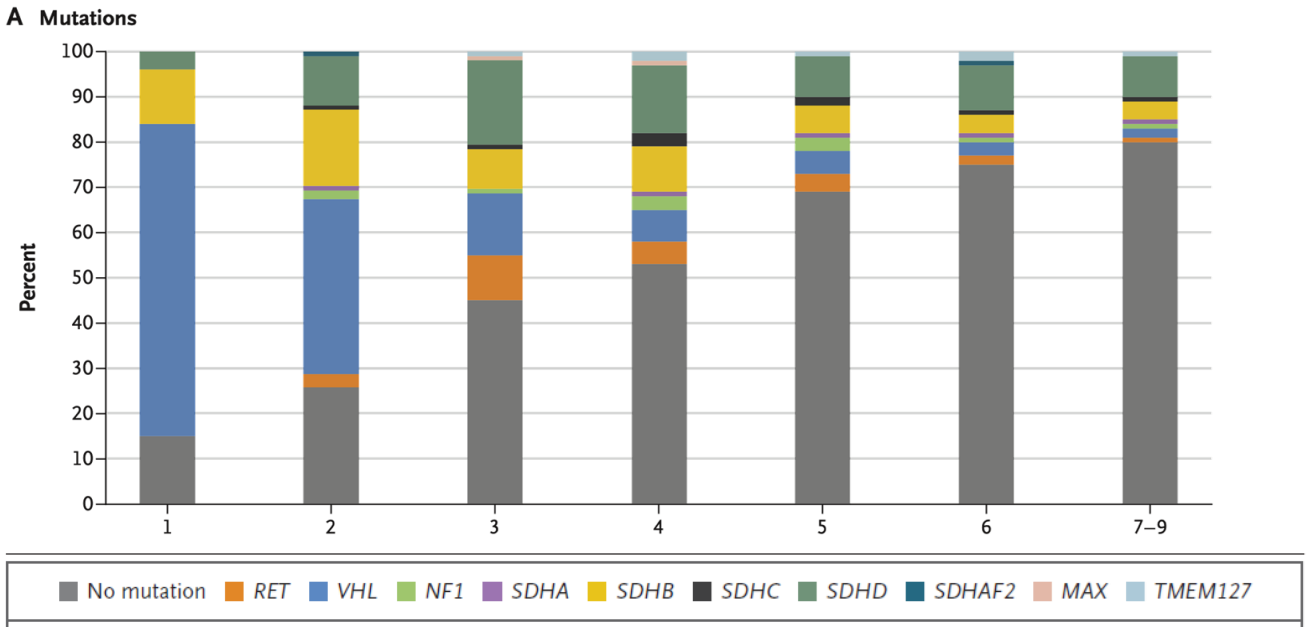
(SDHx → SDHB)

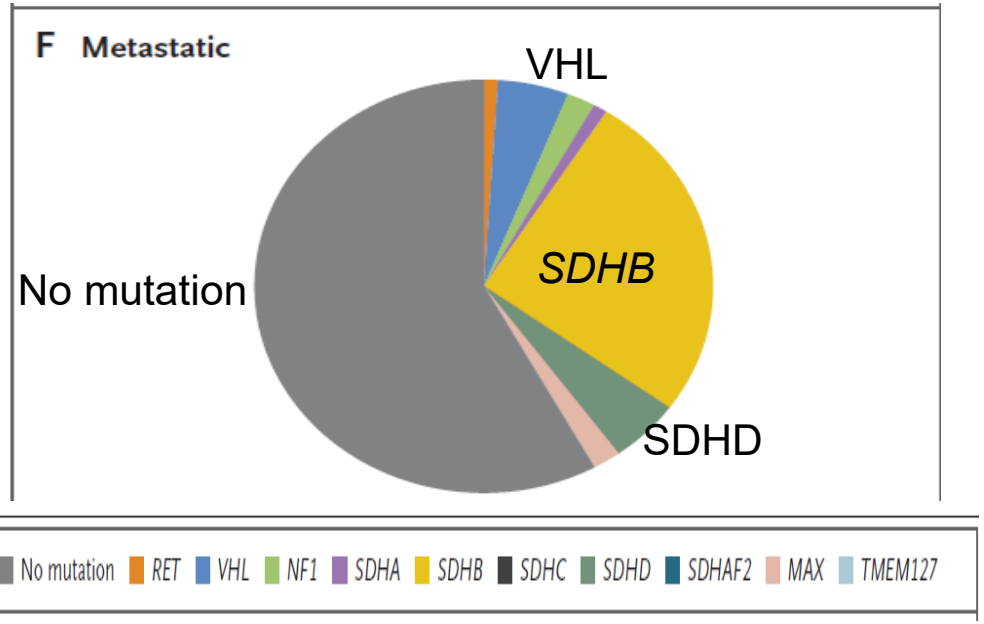
80-85% Abdomen

<5% Pelvis

(bladder, prostate)

Genetic Counseling and Testing





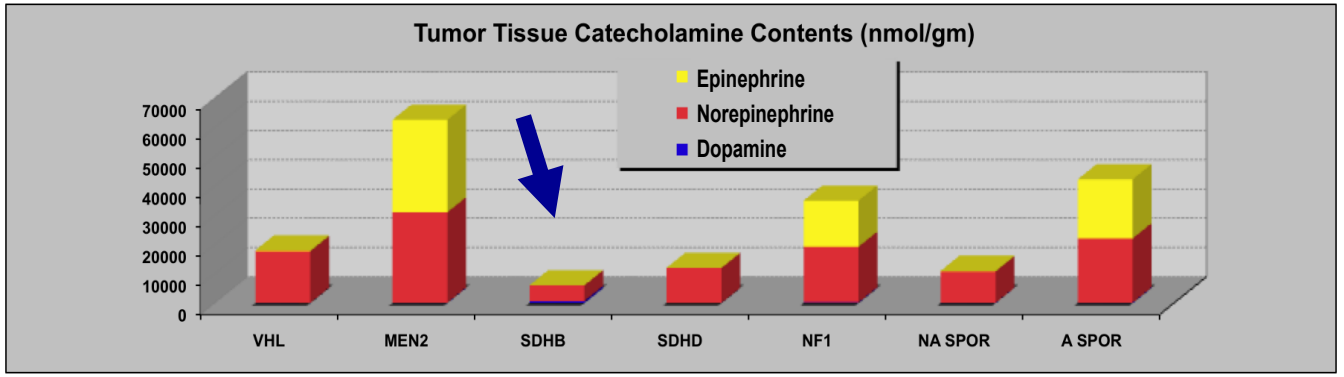
Recommendation

We recommend that all patients patients with primary PPGL or metastatic PPGL have clinical germline genetic and recommend family cascade testing if the patient carriers a susceptibility gene pathogenic variant.

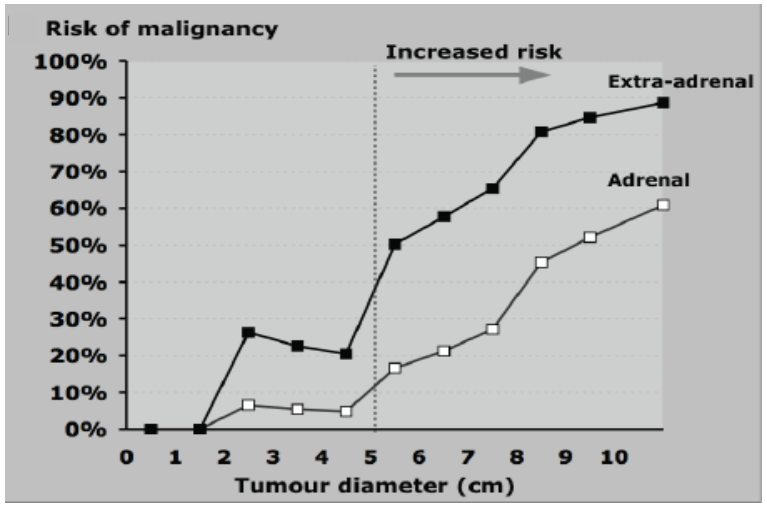
Fischbein, Del Rivero…Jimenez, NANETS Consensus Guidelines 2021
N Engl J Med 2019;381:552-65. DOI: 10.1056/NEJMra1806651

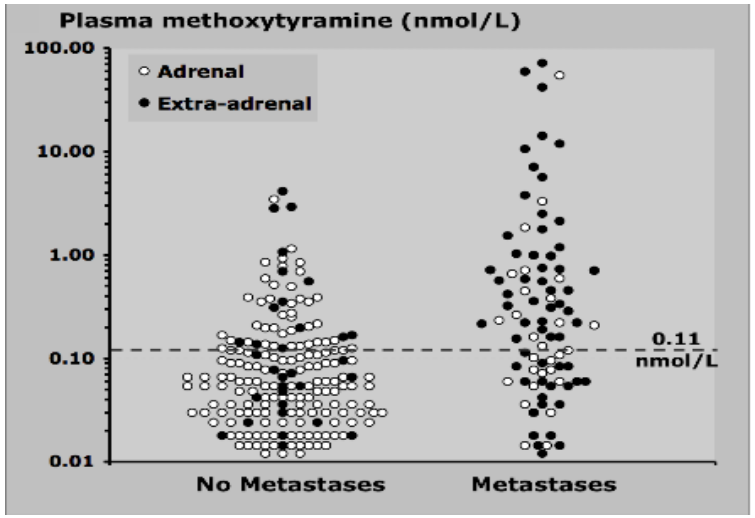
Predictors of Hereditary Disease

- Family history of PPGL
- Age <40 years at diagnosis
- Multiple or bilateral tumors
- Extra-adrenal location (especially head-and-neck paragangliomas)
- Metastatic disease
- Associated syndromic features



Eisenhofer et al. Endocr. Relat. Cancer 2011; 18:97
Fischbein, Del Rivero…Jimenez, NANETS Consensus Guidelines 2021





Zelinka et al. Eur.J. Clin. Invest.; 2011; 41:1121
Eisenhofer et al. Eur. J. Cancer; 2012; 48:1739

Genotype-Phenotype Correlations in Hereditary PPGL

Gene	Typical Tumor Location & Pattern	Metastatic Risk / Penetrance	Key Phenotypic Features	Inheritance / Surveillance
SDHD	Predominantly head-and-neck paragangliomas; often multifocal	Low–moderate metastatic risk; high penetrance	Multiple tumors common	**Paternal inheritance**; screen only if variant inherited from father
SDHB	Extra-adrenal paragangliomas (abdomen, thorax, pelvis)	**Highest metastatic risk (~30–70%)**	Aggressive behavior, dopamine secretion	**Early, intensive lifelong surveillance** (start ~6–10 years)
SDHC	Mainly head-and-neck paragangliomas	Low penetrance; low metastatic risk	Usually solitary tumors	Later onset; less intensive surveillance
SDHA	Abdominal paragangliomas ± pheochromocytoma	Moderate metastatic risk	Variable phenotype	Lower penetrance but **surveillance required**
SDHAF2	Head-and-neck paragangliomas, often multiple	Very low metastatic risk	Early onset	**Paternal inheritance**, similar to SDHD

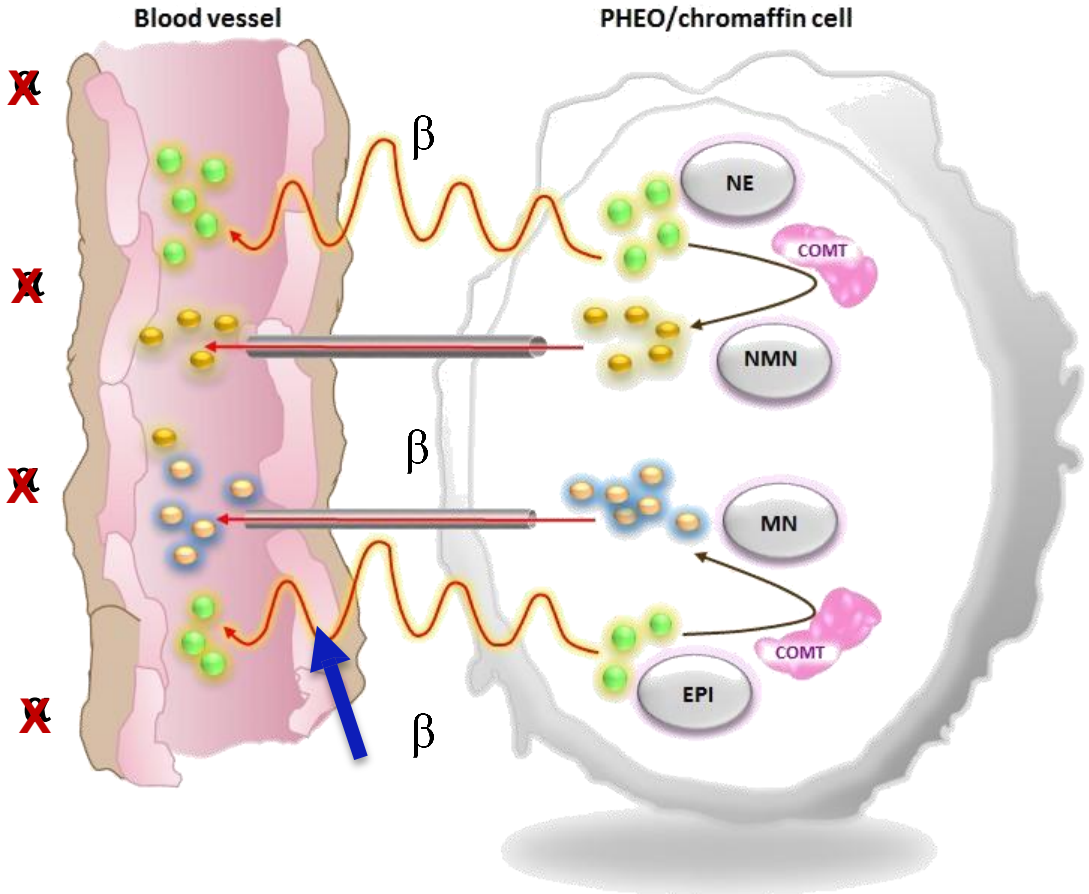
Amar L et al. Nat Rev Endocrinol. 2021 Jul;17(7):435-444
Casey, RT et al. *Nat Rev Endocrinol* 20, 729–748 (2024)
Lussey-Lepoutre C. Best Pract Res Clin Endocrinol Metab. 2025 Jan;39(1):101938.

Genotype-Phenotype Correlations in Hereditary PPGL

Gene / Syndrome	Typical Tumor Location & Pattern	Metastatic Risk	Key Associated Features	Surveillance
VHL disease	Bilateral adrenal pheochromocytomas (type 2)	Low	Renal cell carcinoma, CNS hemangioblastomas, pancreatic NETs	**Youngest age at diagnosis**; multisystem surveillance essential
MEN2 (RET mutations)	Bilateral adrenal pheochromocytomas (up to 50%)	Low	Medullary thyroid carcinoma (≤98%), hyperparathyroidism (MEN2A)	PCC screening guided by **RET risk category**
NF1	Usually unilateral pheochromocytoma (~3%)	Low	Café-au-lait spots, neurofibromas, Lisch nodules	Diagnosis often clinical; PPGL screening symptom-driven

Amar L et al. Nat Rev Endocrinol. 2021 Jul;17(7):435-444
Casey, RT et al. *Nat Rev Endocrinol* 20, 729–748 (2024)
Lussey-Lepoutre C. Best Pract Res Clin Endocrinol Metab. 2025 Jan;39(1):101938.

Clinical Features: "The Great Mimic"



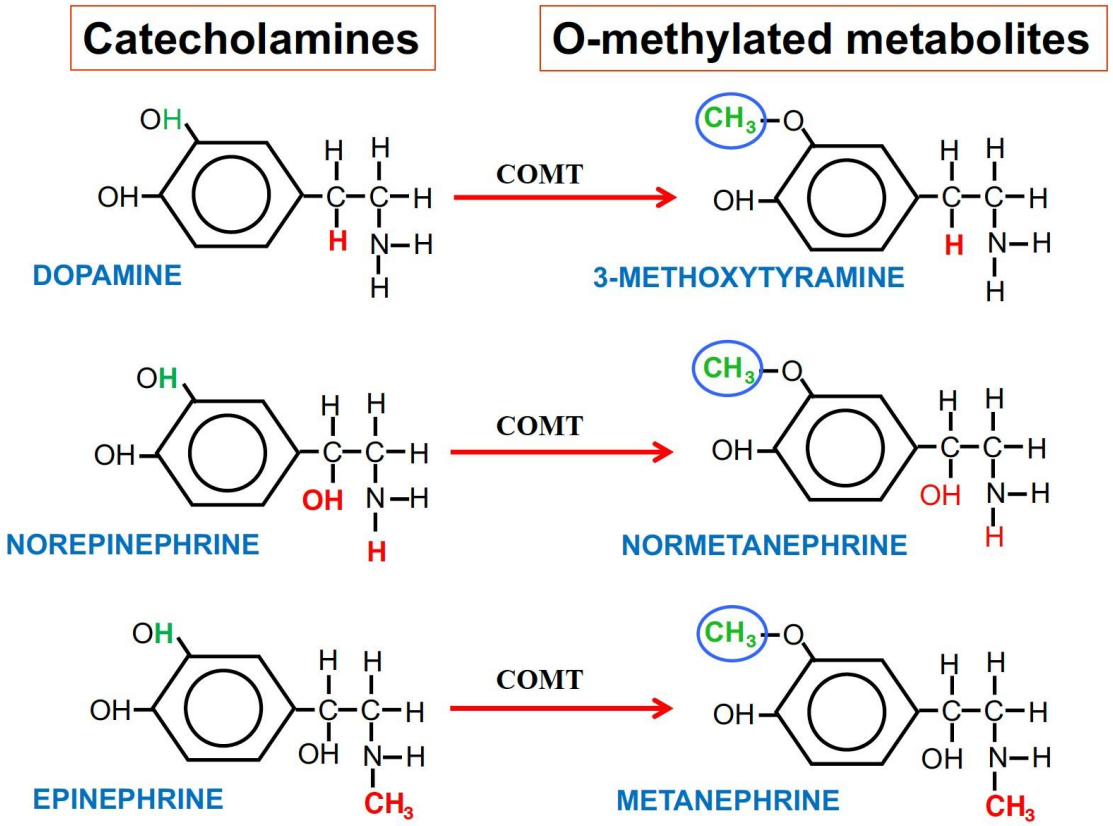
α blockers: doxazosin, phenoxybenzamine
prazosin, terazosin

*α blockers is recommended before any procedure, ablative or systemic therapies

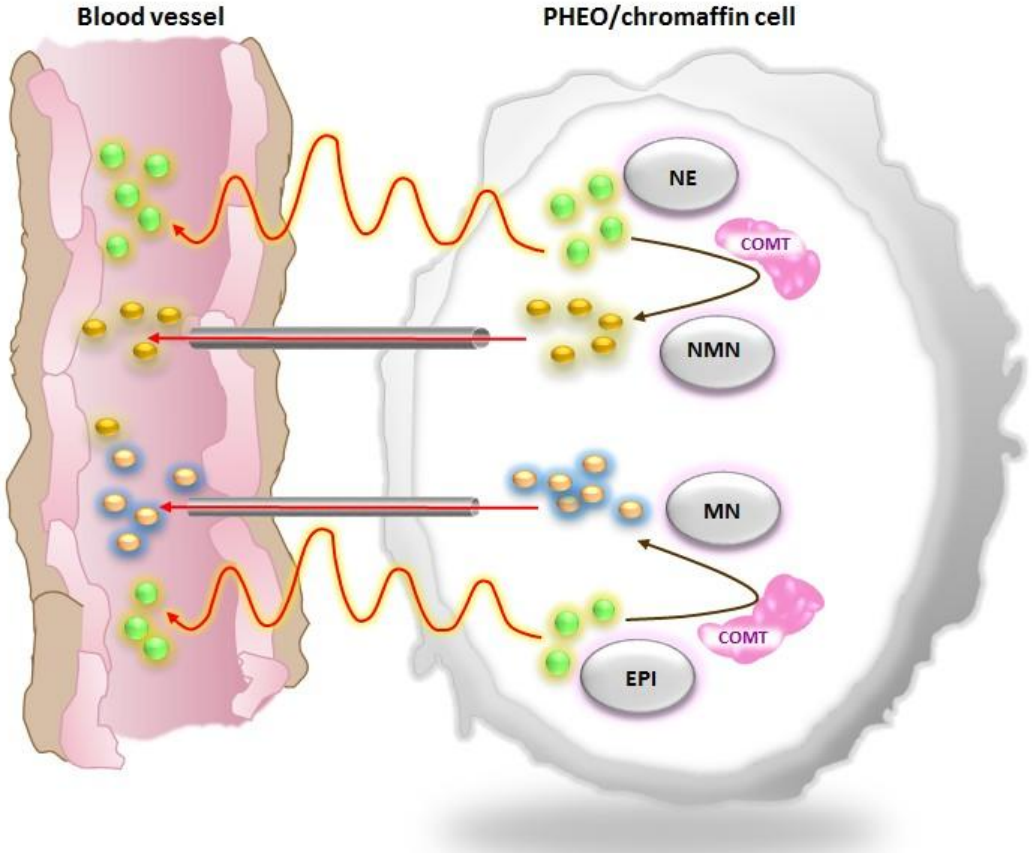
Symptoms	Incidence	Signs	Incidence
Headaches	++	**Hypertension**	++++
Palpitations	+++	Tachycardia or reflex bradycardia	+++
Diaphoresis	+++	Postural hypotension	++
Anxiety/nervousness	++	Hypertension, paroxysmal	++
Tremulousness	++		
Nausea/emesis	++	Weight loss	++
Pain in chest/abdomen	++	Pallor	++
		Hypermetabolism	++
Weakness/fatigue	+++	Fasting hyperglycemia	++
Dizziness	+	Tremor	++
Heat intolerance	+	Increased respiratory rate	++
Paresthesias	+	Decreased gastrointestinal motility	++
Constipation	++	Psychosis (rare)	very rare
Dyspnea	+	Flushing, paroxysmal (rare)	+
Visual disturbances	+		
Seizures, grand mal	very rare		

Fischbein, Del Rivero…Jimenez, NANETS Consensus Guidelines 2021
Pacak et al. DeGroot Endocrinology Textbook, 2021
Lenders et al. J. Hypertens. 2020; 38:1443 Eisenhofer et al. Eur. J. Cancer 2012; 48:1739

Diagnostic Approach: Biochemical Testing



- **Plasma free metanephrines or 24-hour urine fractionated metanephrines** are the cornerstone of biochemical diagnosis, with **97% sensitivity and 93% specificity**
- Elevations **>3 times the upper limit of normal are diagnostic**.

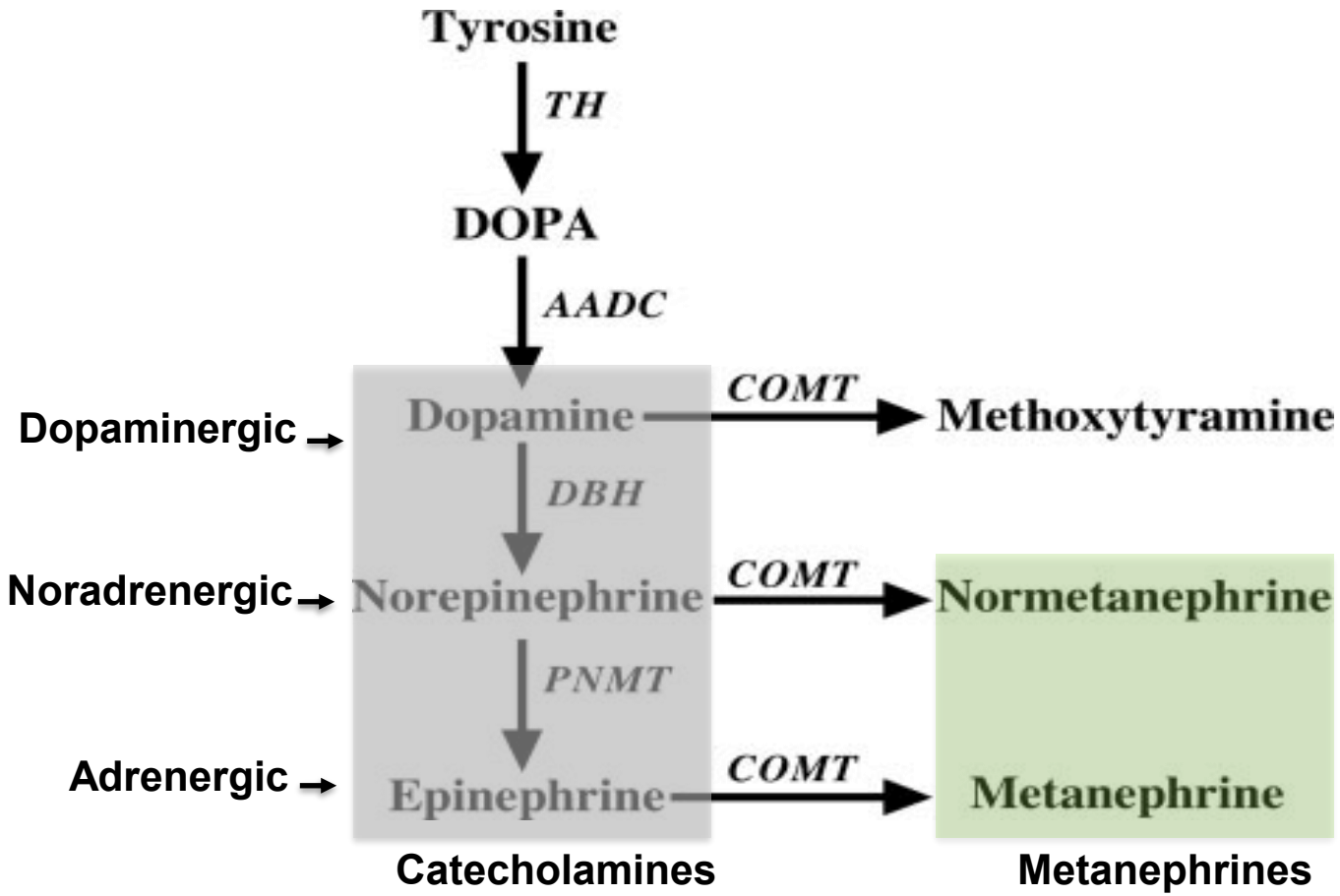


Metanephrines are produced and released continuously independent of pulsatile catecholamine secretion

COMT: catechol-O-methyl transferase

Lenders et al. JAMA 2002; 287:1427
Darr et al. Endocrine 2017; 56:495
Eisenhofer et al. Eur. J. Cancer 2012; 48:1739
& adapted from Lenders and Eisenhofer

Biochemical Diagnosis of PPGL



PHENOTYPE: Adrenergic: produces MN or EPI

MEN, NF-1 → **Always adrenergic (assess syndromic and familial presentation)**

PHENOTYPE: Noradrenergic: produces NMN or NE

VHL, SDHx → **Assess syndromic and familial presentation**

PHENOTYPE: Noradrenergic & dopaminergic: produces also DA or MTY

SDHx → **See location: e.g. head/neck: SDHD**

Lenders et al. JAMA 2002; 287:1427
Darr et al. Endocrine 2017; 56:495
Eisenhofer et al. Eur. J. Cancer 2012; 48:1739
& adapted from Lenders and Eisenhofer

Important Preanalytical Considerations

- Discontinue interfering medications (tricyclic antidepressants, psychoactive agents) →2 weeks before testing
- Plasma samples should be drawn in the supine position
- Clinical circumstances (acute illness) can cause false positives

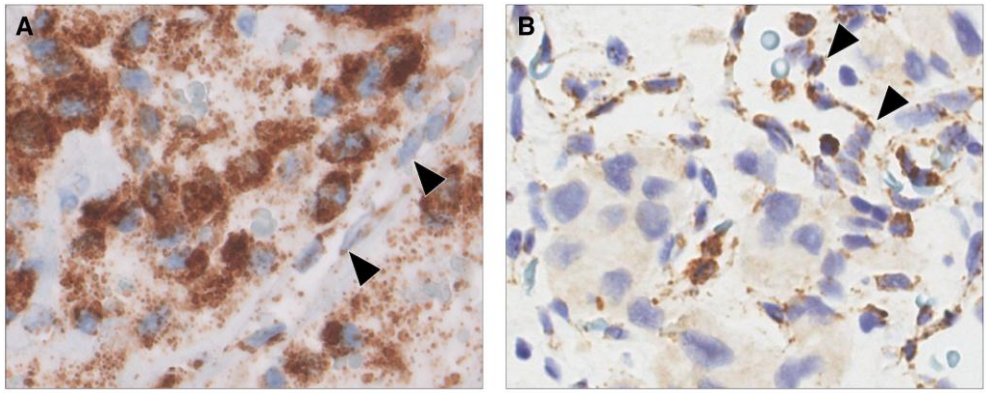
	Plasma		Urine	
	NMN	MN	NMN	MN
Acetaminophen	++	-	++	-
Labetalol	-	-	++	++
Sotalol	-	-	++	++
Buspirone	-	++	-	++
TCA	++	-	++	-
Phenoxybenzamine	++	-	++	-
Sulphasalazine	++	-	++	-
Levodopa	+	+	++	+

Acetaminophen: stop: 3-5 days; interferes with HPLC method

Eisenhofer & Pacak, Harrison's Textbook online, 2004
Lenders et al. Endocrine Society Guideline. JCEM 2014, 99(6):1915-1942

Role of SDHB Immunohistochemistry

- Sensitivity: ~95% for detection of SDHx-related tumors
- Specificity: ~82–92%, depending on tumor type and clinical setting
- Positive predictive value (PPV):
  - Head-and-neck paragangliomas: ~100%
  - Pheochromocytomas: ~25%



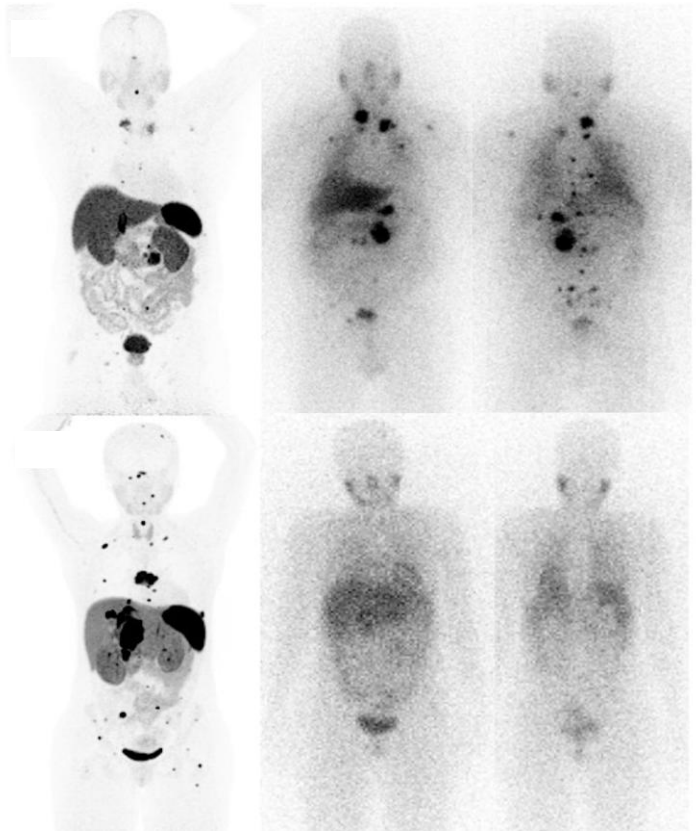
Loss of SDHB by IHC

Clinical Utility

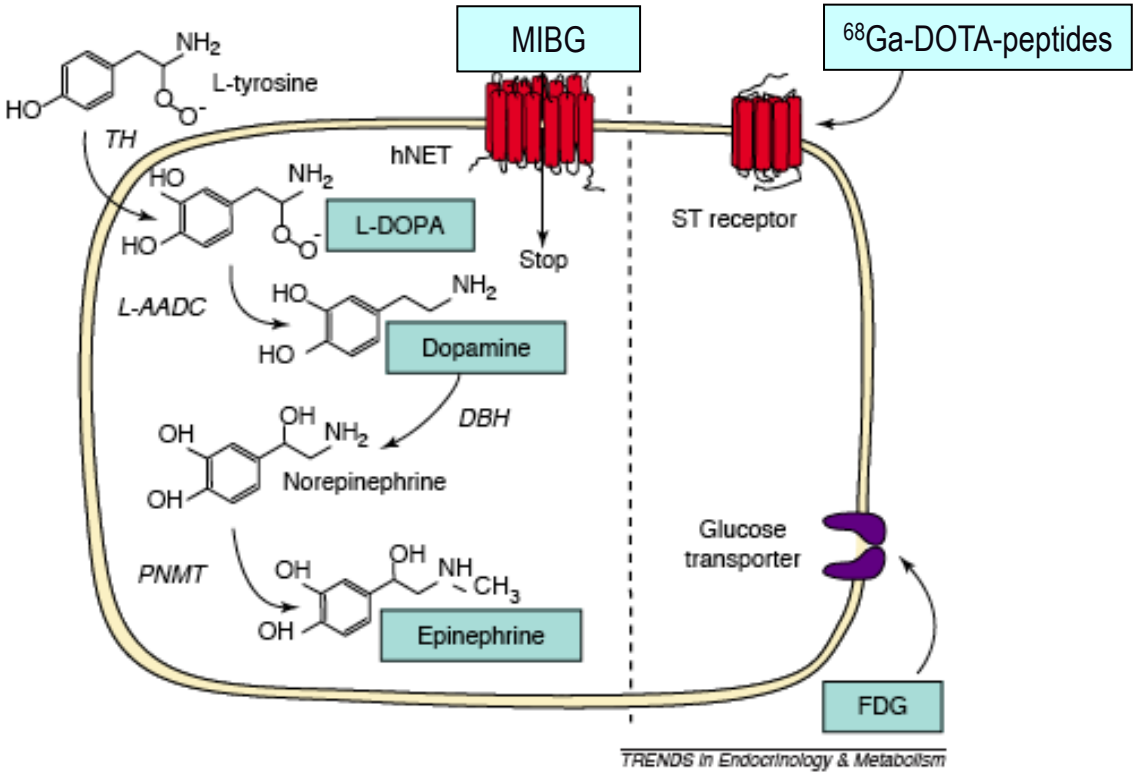
- Guides genetic testing
  - SDHB loss → prioritize SDHx germline testing
- Prognostic information
  - Independent association with shorter disease-free survival and higher metastatic risk, especially relevant in SDHB-related disease
- Context-dependent interpretation
  - Must be integrated with tumor site, biochemistry, and family

Molecular Imaging PPGL → Theranostics

- Diagnosis, staging, follow up of PPGL
- Selection for targeted molecular radiotherapy



^{68}Ga-Dotatate ^{123}I-MIBG

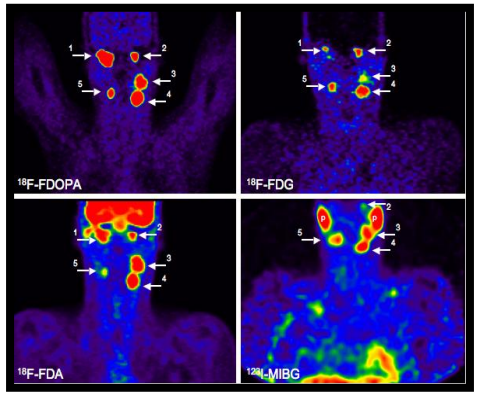


Sensitivities mPPGL	
^{123}I-MIBG	50-60%
^{68}Ga-Dotatate	98-99%
^{18}F-FDG	68-92%

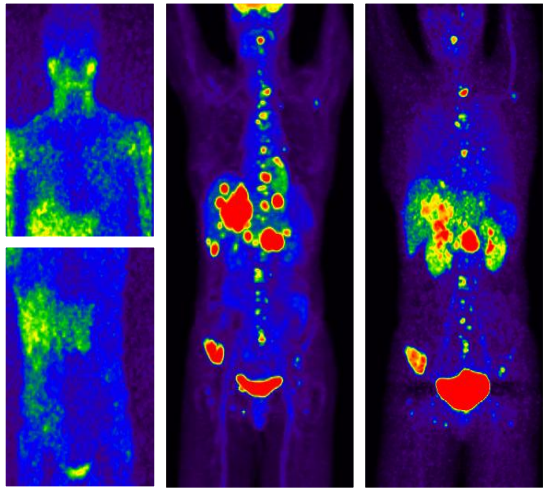
Taieb et al. J. Nucl. Med. 2012; 53:264

PET Imaging Algorithm for PPGLs

Head and neck PGLs:
^{18}F-FDOPA: 100% (9 pts)



Kign et al. JCEM 2010; 95:481
King et al. JCEM 2011; 96:2779



^{123}I- MIBG | ^{18}F-FDG PET | ^{18}F-DA

Nuclear Imaging Algorithm for Pheochromocytoma / Paraganglioma (PPGL)

Radiotracer selection guided by tumor location, genotype, and metastatic status.

Sporadic localized PHEO (adrenal, non-metastatic)	**Cluster 1 or 2 Genotype** (NF1, RET/MEN2, VHL, EPAS/HIF2A, MAX):	**Cluster 1 Genotype:** Parasympathetic HNPGL (head & neck)	**Cluster 1 Genotype:** Sympathetic extra-adrenal, multifocall and /or metastatic	**Any Genotype and Sporadic:** Metastatic
Recommended: ^{18}F-FDOPA PET/CT or ^{123}I-MIBG SPECT/CT **Alternative:** SSTR PET/CT or ^{18}F-FDG PET/CT	**Recommended:** ^{18}F-FDOPA PET/CT **Alternative:** SSTR PET/CT or ^{18}F-FDG PET/CT consider ^{123}I-MIBG SPECT/CT if planning ^{131}I-MIBG therapy.	**Recommended:** SSTR PET/CT **Alternative:** ^{18}F-FDOPA PET/CT or ^{18}F-FDG PET/CT	**Recommended:** SSTR PET/CT **Alternative:** ^{18}F-FDG PET/CT consider ^{123}I-MIBG SPECT/CT if planning ^{131}I-MIBG therapy.	**Recommended:** SSTR PET/CT **Alternative:** • ^{18}F-FDG PET/CT (biology/aggressiveness) • ^{123}I-MIBG SPECT/CT (if planning ^{131}I-MIBG) • ^{18}F-FDOPA PET/CT (if cluster-2 biology is suspected)

Taïeb D et al. Eur J Nucl Med Mol Imaging. 2019 Sep;46(10):2112-2137
Hernandez et al. Radioligand Therpaies for PPGL. *Submitted for publication*

Cluster-Based and General Systemic Therapies for Metastatic PPGL

Clinical Context	Preferred Therapeutic Options	Rationale
Cluster 1 – Pseudohypoxia(SDHx, VHL, EPAS1)	**Belzutifan** (VHL / EPAS1) **Temozolomide or CVD** (especially SDHB)	HIF stabilization, angiogenesis, and DNA repair vulnerability dominate biology
Cluster 2 – Kinase signaling(RET, NF1, TMEM127, MAX)	**Anti-angiogenic TKIs** (sunitinib, cabozantinib) **Selpercatinib** (RET-driven disease)	Kinase pathway activation; targetable oncogenic drivers
SSTR-positive disease	**PRRT (^{177}Lu-DOTATATE)**	High somatostatin receptor expression on functional imaging
MIBG-avid disease (any cluster)	**High-specific-activity ^{131}I-MIBG**	NET expression enables targeted radiotherapy

Conclusions

- ✓ PPGLs have the highest heritability of all tumors, with approximately 40% of cases harboring germline mutations in over 20 susceptibility genes
- ✓ All patients with PPGL should receive genetic counseling and testing
- ✓ SDHB mutations confer the highest metastatic risk and require the most intensive surveillance starting in childhood
- ✓ Lifelong surveillance is required for all PPGL patients due to risk of recurrence and metastasis
- ✓ Plasma metanephrines are the preferred biochemical test with high sensitivity and specificity
- ✓ SDHB immunohistochemistry can guide genetic testing and provides independent prognostic information
- ✓ Functional imaging → recommended to be cluster-specific
- ✓ Three main molecular clusters: Cluster 1 (Pseudohypoxia/Krebs Cycle), Cluster 2 (Kinase signaling), Cluster 3 (Wnt Signaling)
- ✓ Molecular cluster classification guides biochemical testing, imaging selection, surveillance intensity, and therapeutic options
- ✓ Multidisciplinary management with tumor boards is essential for optimal outcomes

Thank You for Your Attention!

jaydira.delrivero@nih.gov

Office: 240-858-3851

Direct: 240-805-2888

@JaydiDelRivero

Treatment of Advanced Pheochromocytoma and Paraganglioma

Camilo Jimenez, MD
Professor
Department of Endocrine Neoplasia and Hormonal Disorders
The University of Texas MD Anderson Cancer Center
Houston, Texas, USA

DISCLOSURE INFORMATION

Research support provided by MERCK, EXELIXIS, LANTHEUS PHARMACEUTICALS, PROGENICS

DISCLOSURE SLIDE

- *Advisory Board: MERCK*

- *The University of Texas MD Anderson Cancer Center has received research financial support from MERCK, EXELIXIS, LANTHEUS PHARMACEUTICALS, PROGENICS*

Outline

- ✓ Introduction
  - ✓ Pheochromocytomas and Paragangliomas are tumors with heterogeneous behavior

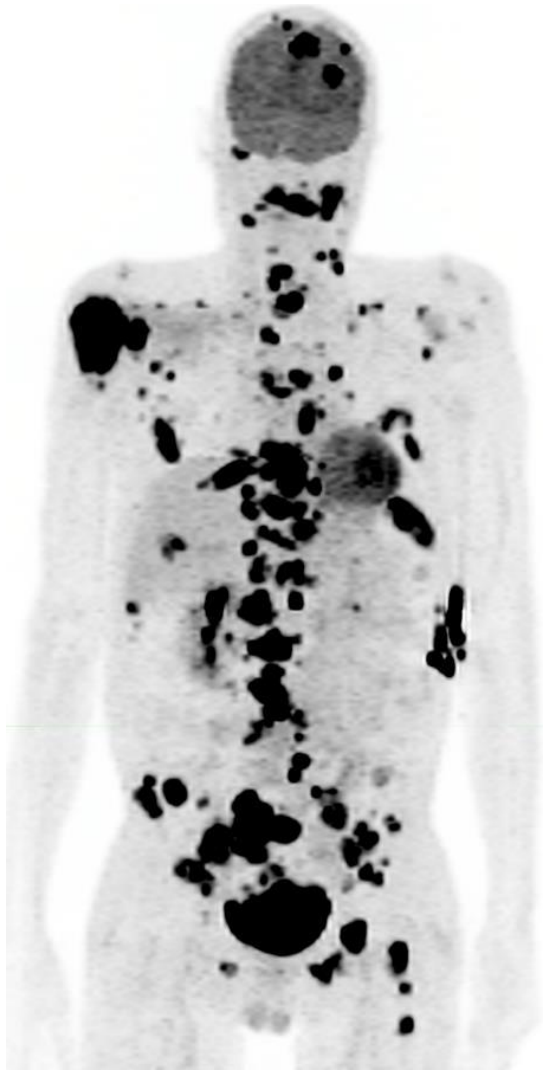
- ✓ Clinical Trials with Definitive Results:

- ✓ Active and/or effective systemic therapies that target hallmarks of cancer irrespective of genotype
  - ✓ Cabozantinib
  - ✓ Sunitinib

- ✓ Systemic therapies that represent examples of precision medicine
  - ✓ Belzutifan

Metastatic Pheochromocytomas and Paragangliomas

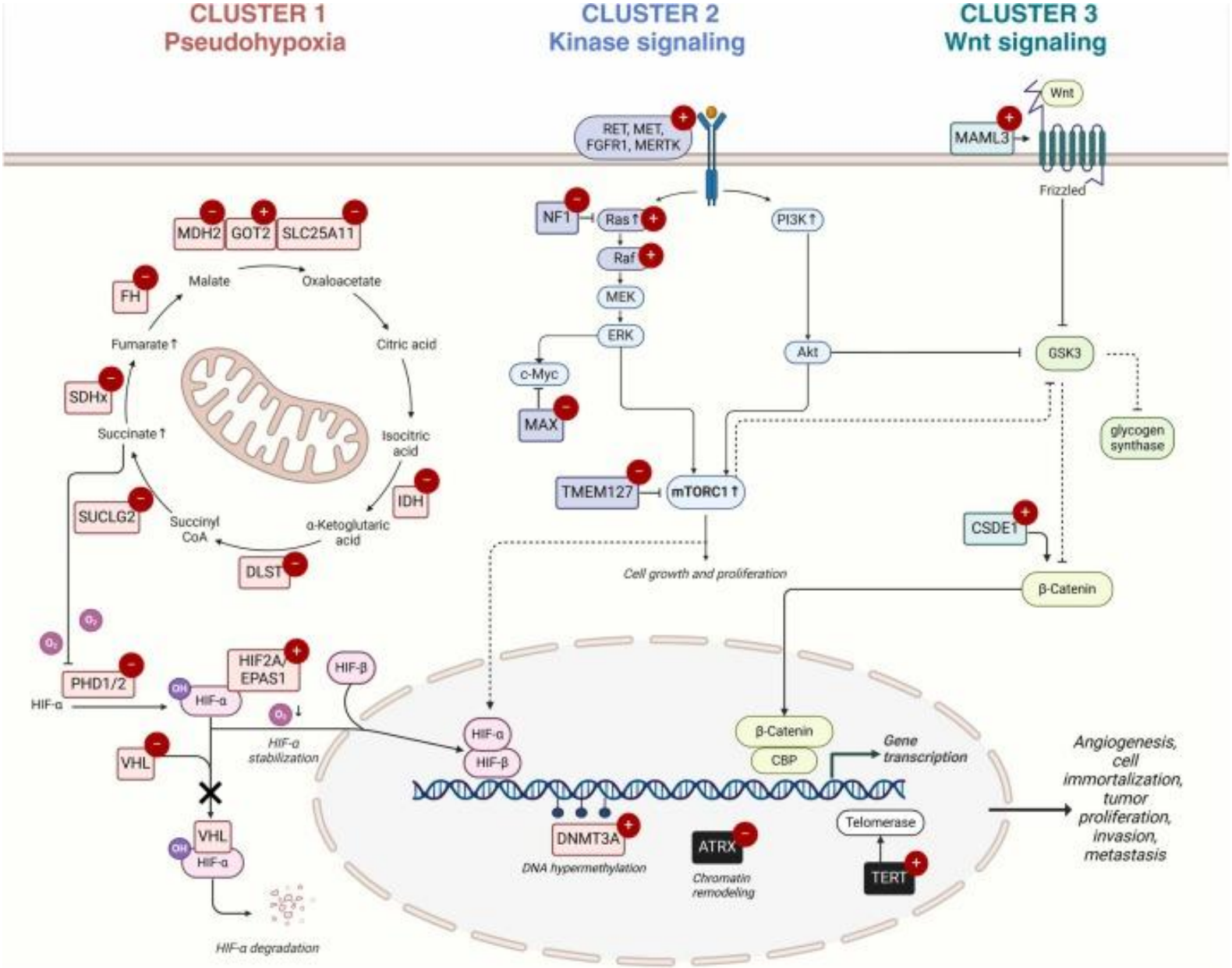
Up to 25% of pheochromocytomas and paragangliomas are metastatic (MPPGLs)



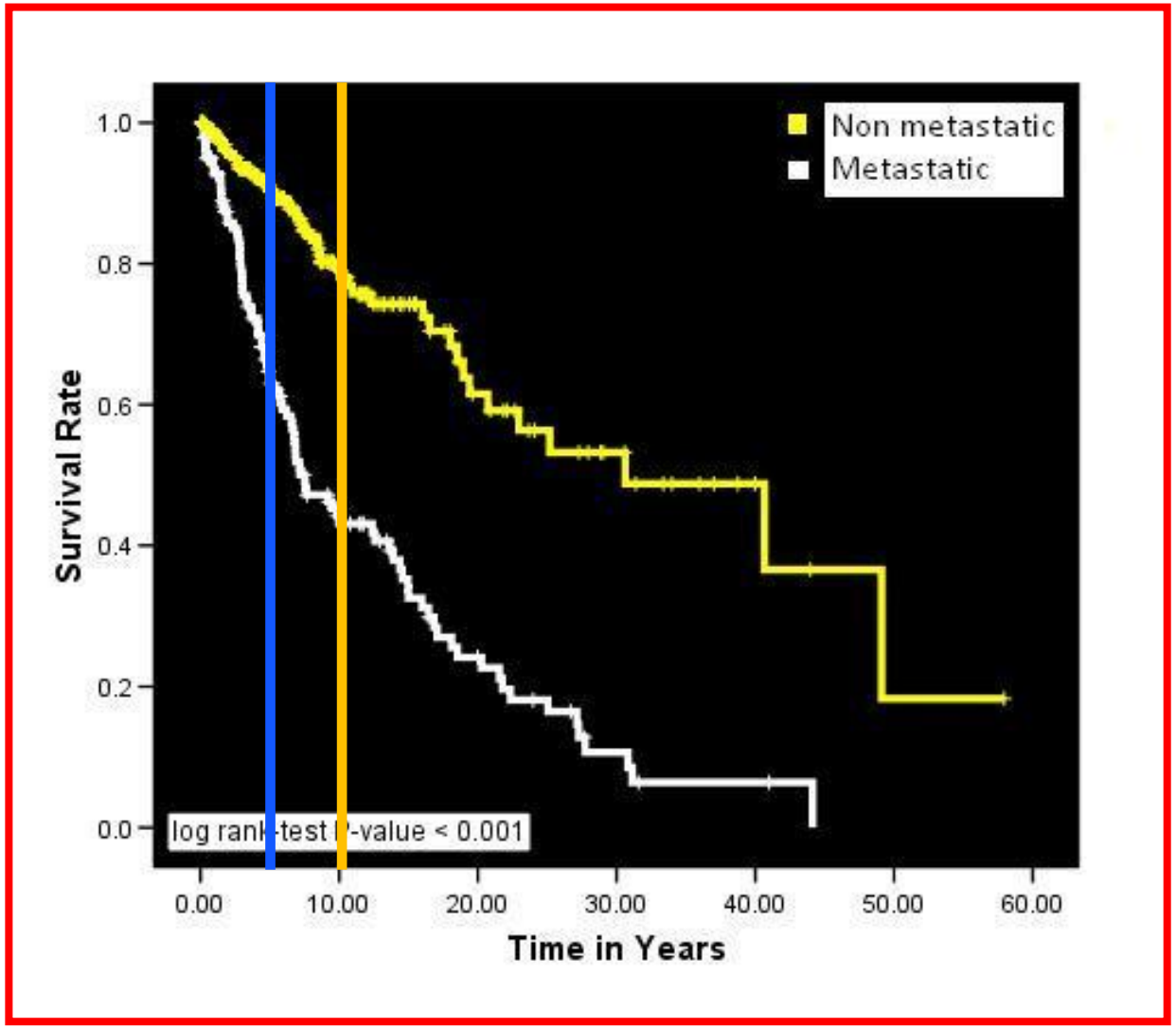
- ✓ MPPGLs may or may not be hormonally active
- ✓ Up to 50% of MPPGLs are associated with germline *SDHB* pathogenic variants (Cluster 1-Pseudohypoxia)
- ✓ Metastases happen more commonly in lymph nodes, bones, liver, and lungs
- ✓ 50% are synchronous, 50% are metachronous
- ✓ 50-60% express the noradrenaline transporter and are MIBG-avid and >90% express the somatostatin receptors (DOTATATE positive)

Molecular phenotype of Metastatic pheochromocytomas and paragangliomas:

Cluster 1: 80-85%
Cluster 2: 5-10%
Cluster 3: 5-7%



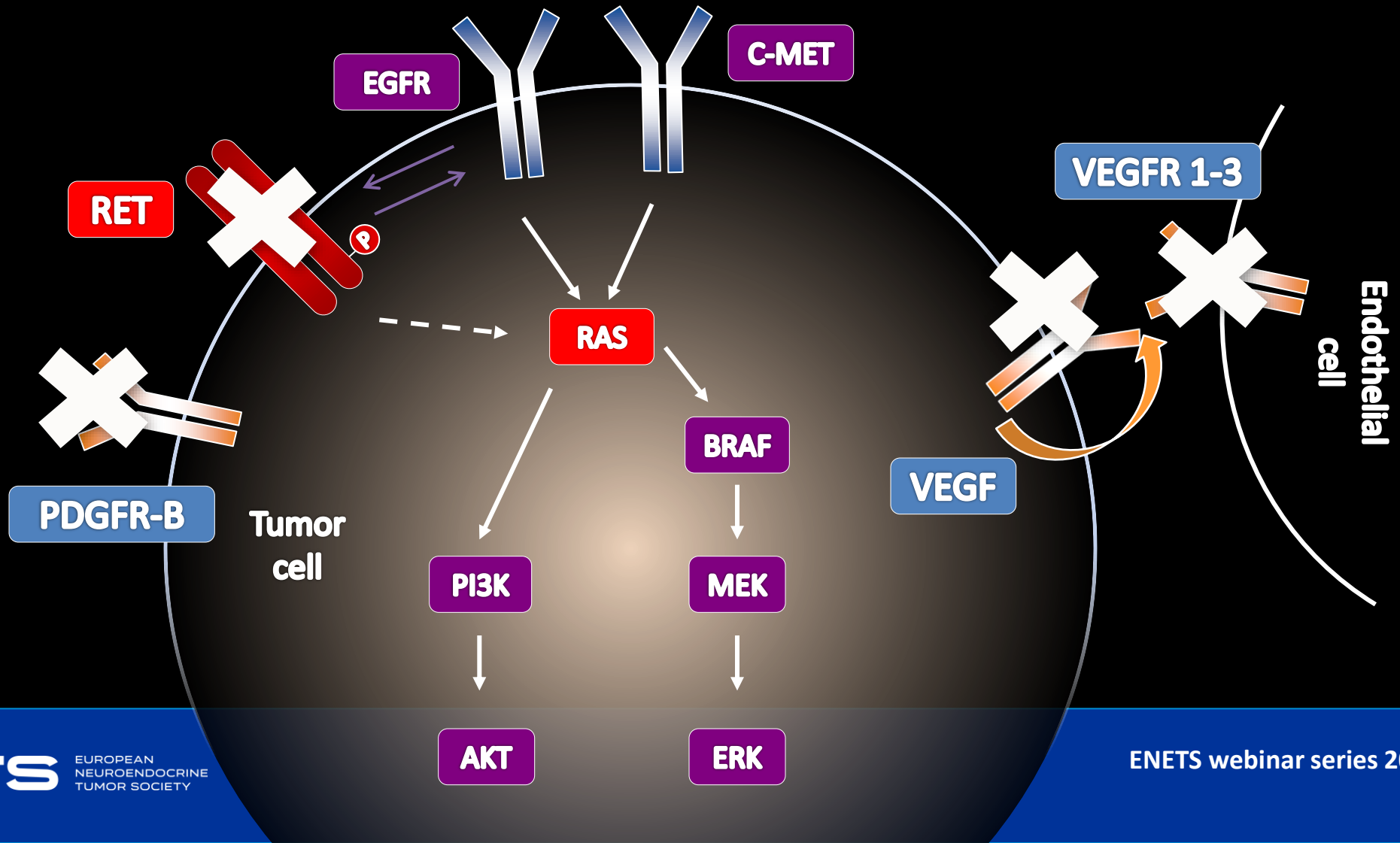
Overall Survival MPPGLs vs. Non-metastatic PPGLs



Morbidity and survival are determined by:

1. Hormonal activity
2. Tumor burden
3. Speed of progression

Sunitinib


EGFR
C-MET
RET
VEGFR 1-3
RAS
BRAF
PDGFR-B
VEGF
Tumor cell
Endothelial cell
PI3K
MEK
AKT
ERK

Sunitinib for metastatic progressive phaeochromocytomas and paragangliomas: results from FIRSTMAPPP, an academic, multicentre, international, randomised, placebo-controlled, double-blind, phase 2 trial

Eric Baudin, Bernard Goichot, Alfredo Berruti, Julien Hadoux, Salma Moalla, Sandrine Laboureau, Svenja Nölting, Christelle de la Fouchardière, Tina Kienitz, Timo Deutschbein, Stefania Zovato, Laurence Amar, Magalie Haissaguerre, Henri Timmers, Patricia Niccoli, Antongiulio Faggiano, Moussa Angokai, Livia Lamartina, Florina Luca, Deborah Cosentini, Stefanie Hahner, Felix Beuschlein, Marie Attard, Matthieu Texier, Martin Fassnacht*; on behalf of the ENDOCAN-COMETE and ENSAT Networks*

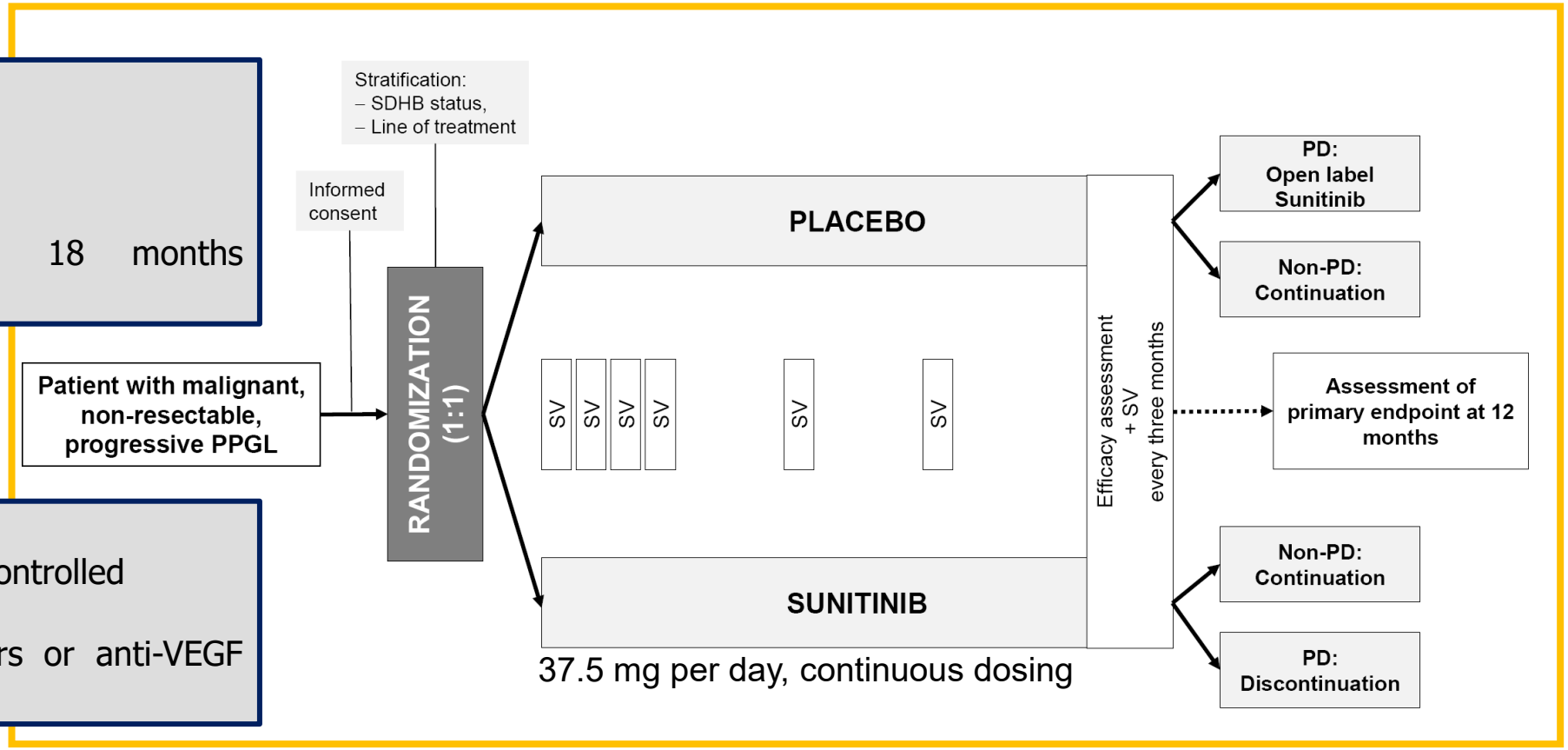
THE LANCET

Baudin E, et al. Lancet. 2024 Mar 16;403(10431):1061-1070.

FIRSTMAPPP: Double-blind Randomized Phase II Trial

Main inclusion criteria
- Metastatic disease
- Pre-treated or not
- Evaluable, RECIST 1.1 criteria
- Progressive disease within 18 months according to RECIST

Main exclusion criteria
- Hypertension that cannot be controlled
- Abnormal cardiac function
- Prior tyrosine kinase inhibitors or anti-VEGF inhibitors.

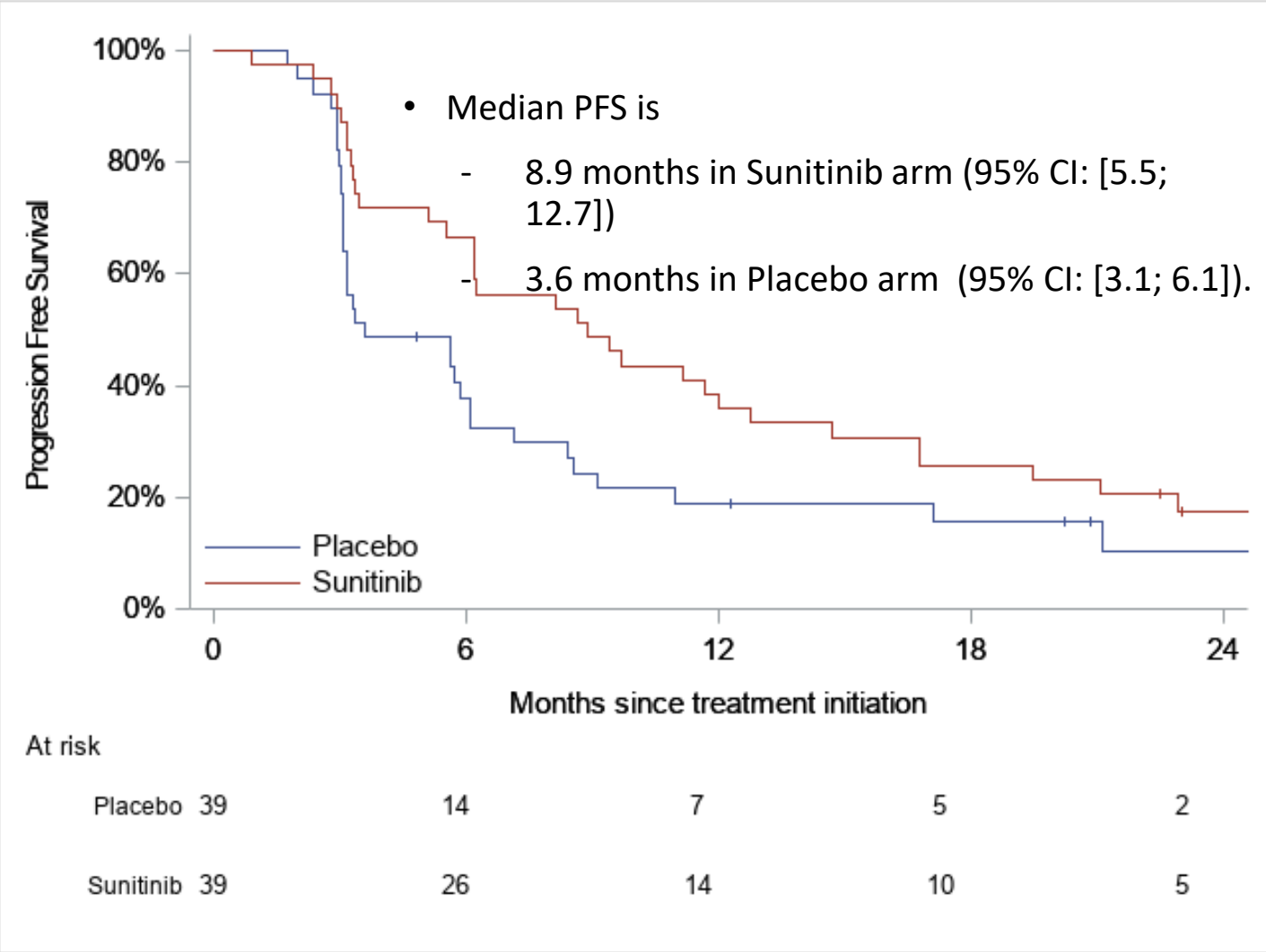


RECIST 1.1/12 weeks
Real time central review

Sunitinib dose 37.5 mg daily (continuous dosing)

Baudin E, et al. Lancet. 2024 Mar 16;403(10431):1061-1070.

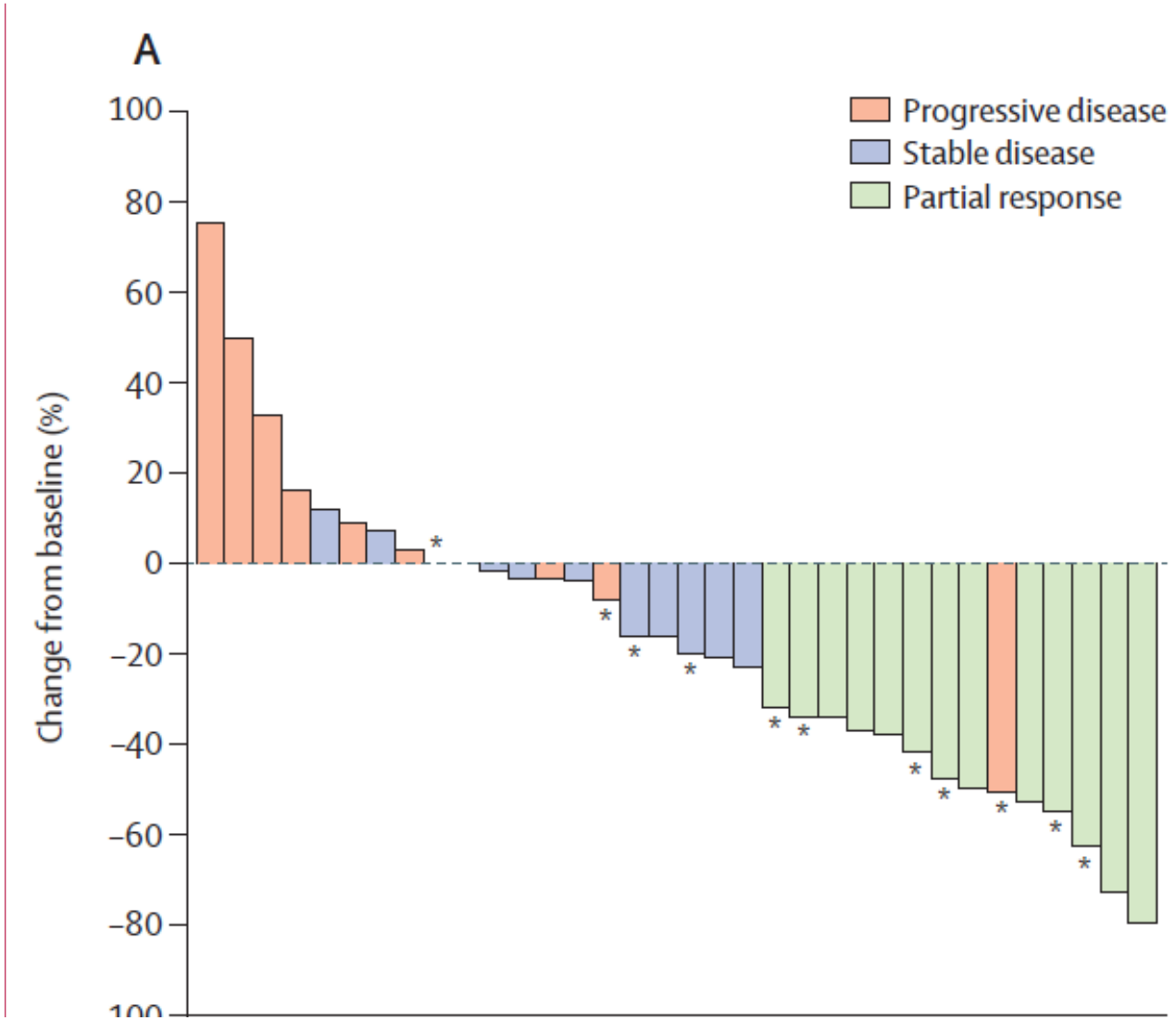
Progression Free Survival



- Median PFS is
  - 8.9 months in Sunitinib arm (95% CI: [5.5; 12.7])
  - 3.6 months in Placebo arm (95% CI: [3.1; 6.1]).

Baudin E, et al. Lancet. 2024 Mar 16;403(10431):1061-1070.

FIRSTMAPPP: Objective Response Rate 36%

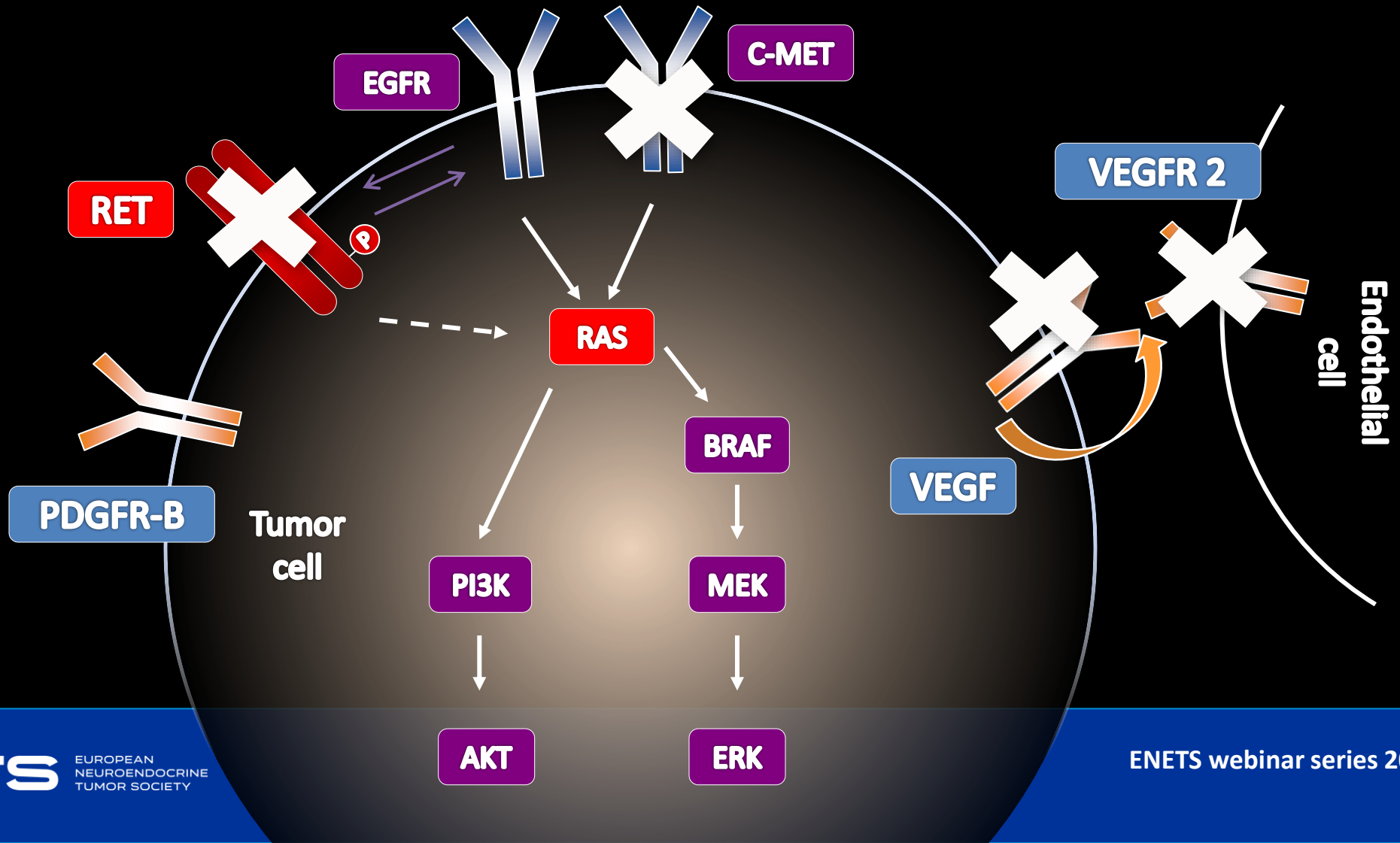


ORR 36%
DCR 72%

SDHB (+)
ORR 50%

Baudin et al, Lancet, 2024

Cabozantinib



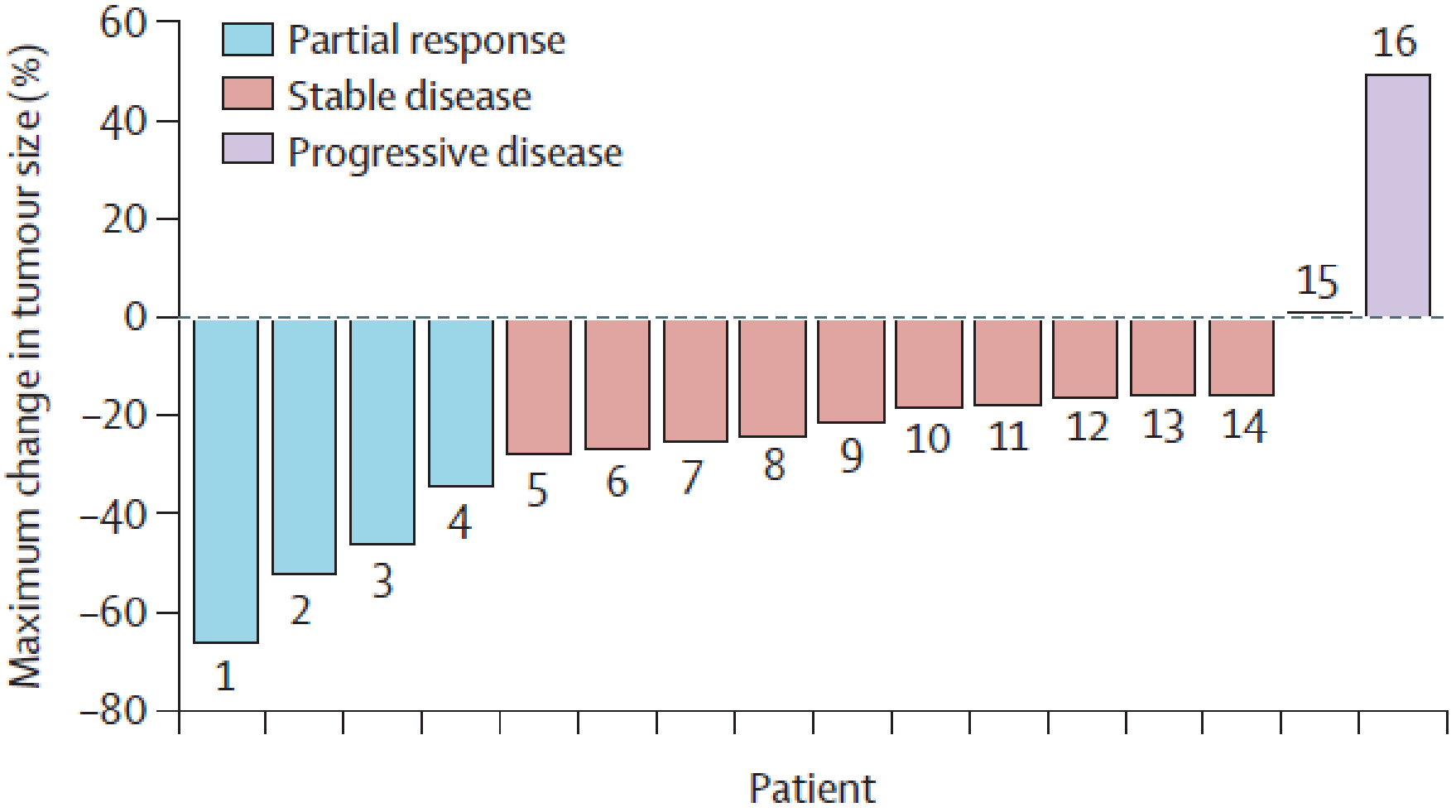
Cabozantinib in patients with unresectable and progressive metastatic phaeochromocytoma or paraganglioma (the Natalie Trial): a single-arm, phase 2 trial

Camilo Jimenez, Mouhammed Amir Habra, Matthew T Campbell, Gina Tamsen, Damaris Cruz-Goldberg, James Long, Roland Bassett, Robert Dantzer, Vania Balderrama-Brondani, Jeena Varghese, Yang Lu

THE LANCET
Oncology

Jimenez C et al. Lancet Oncol. 2024 Apr 9:S1470-2045(24)00133-5.

NATALIE: Objective Response Rate 25%

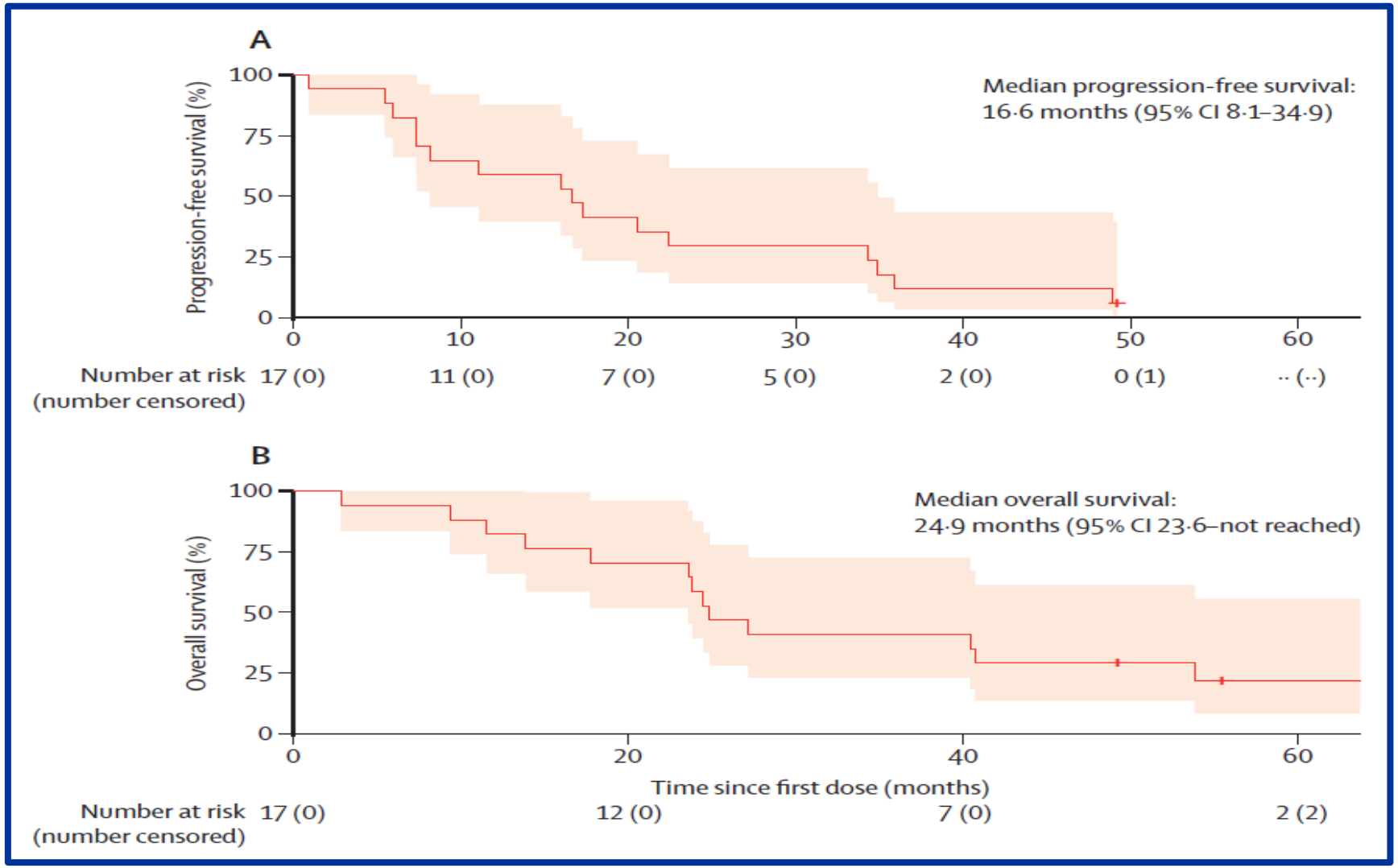


ORR 25%
DCR 93%

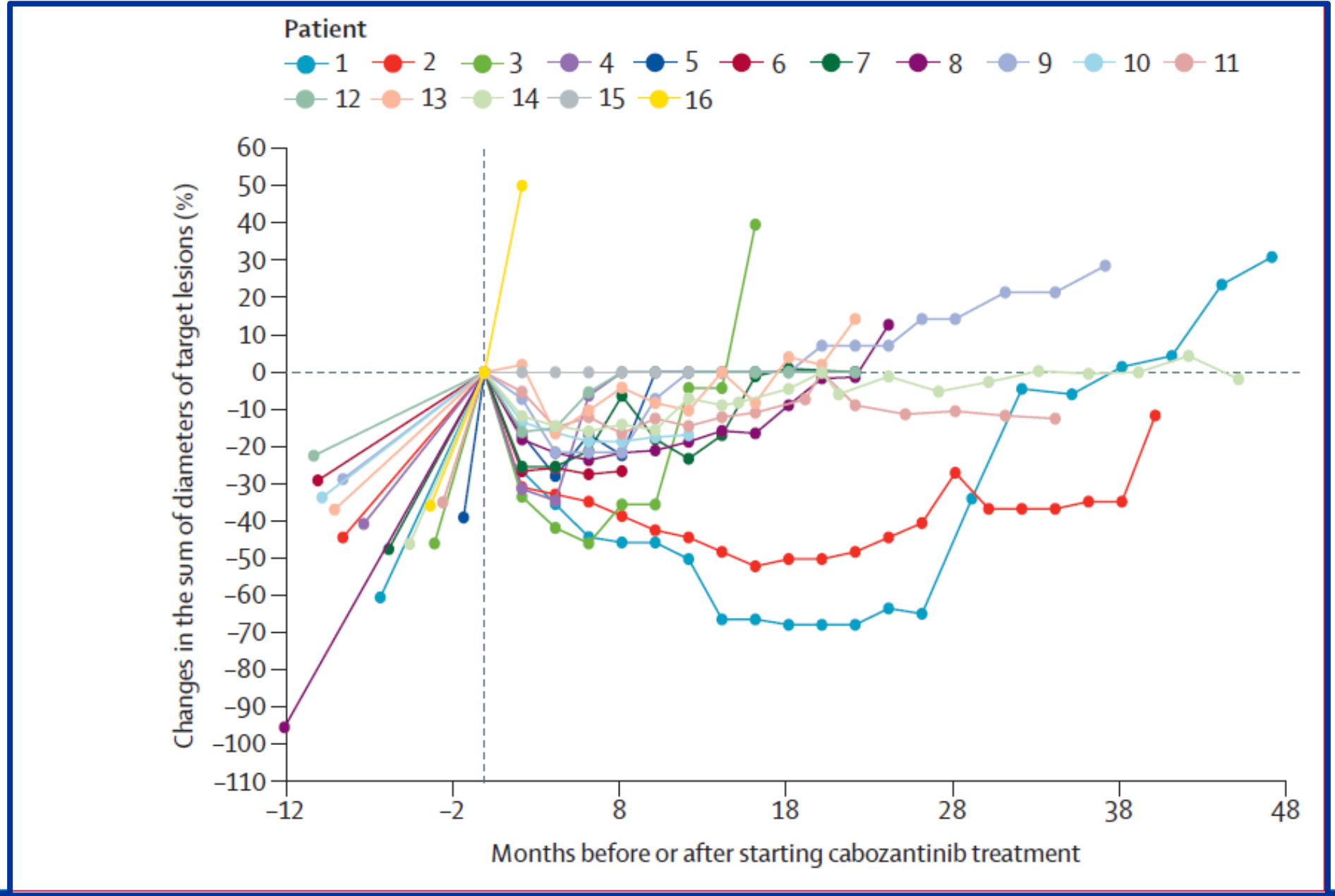
SDHB (+):
ORR 60%
DCR 100%

Jimenez C et al. Lancet Oncol. 2024 Apr 9:S1470-2045(24)00133-5.

Median Progression Free Survival and Median Overall Survival



Jimenez C et al. Lancet Oncol. 2024 Apr 9:S1470-2045(24)00133-5.



Jimenez C et al. Lancet Oncol. 2024 Apr 9:S1470-2045(24)00133-5.

Adverse events

	Grade 1	Grade 2	Grade 3
Laboratory abnormalities			
Increased ALT or AST	15 (88%)	0	0
Increased alkaline phosphatase	7 (41%)	2 (12%)	0
Increased amylase or lipase	2 (12%)	1 (6%)	2 (12%)
Increased creatinine	6 (35%)	1 (6%)	0
Hypomagnesaemia	3 (18%)	0	1 (6%)
General disorders			
Dysgeusia	12 (71%)	0	0
Hand-and-foot syndrome	7 (41%)	3 (18%)	1 (6%)
Mucositis	8 (47%)	2 (12%)	0
Fatigue	7 (41%)	9 (53%)	0
Weight loss	8 (47%)	2 (12%)	0
Hypertension	4 (24%)	11 (65%)	1 (6%)
Diarrhoea	7 (41%)	0	0
Nausea	8 (47%)	0	0
Arthralgia or myalgia	6 (35%)	0	0
Primary hypothyroidism	4 (24%)	8 (47%)	0
Anorexia	7 (41%)	4 (24%)	0
Hoarseness	4 (24%)	0	0
Rectal fistula	0	0	1 (6%)
QT interval prolongation	0	0	1 (6%)
Grey hair or skin hypopigmentation	7 (41%)	0	0
Peripheral oedema	2 (12%)	0	0

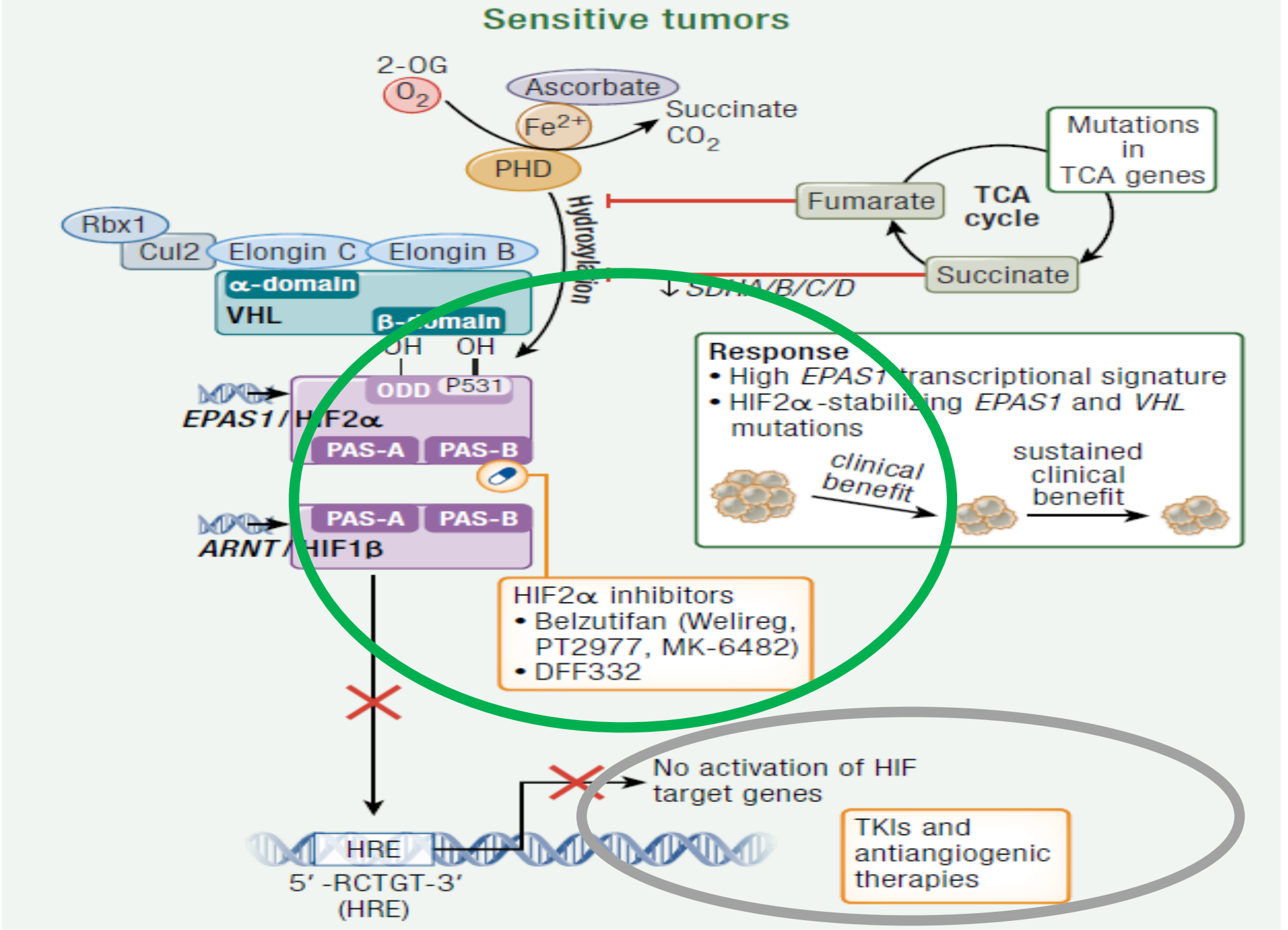
Jimenez C et al. Lancet Oncol. 2024 Apr 9:S1470-2045(24)00133-5.

NATALIE Trial: Oncomine Analysis

Solid Tumor Genomic Assay-DNA Report

- ✓ A next-generation sequencing (NGS)–based analysis was performed to detect somatic mutations in the coding sequence of 136 genes and selected copy number variations (amplifications) in 47 genes in the DNA extracted from the sample
- ✓ There were no c-met pathogenic variants/amplifications
- ✓ There were 5 cases with paraganglioma syndrome type 4.
- ✓ There were no somatic pathogenic variants.
- ✓ Oncomine did not test for cluster 3 pathogenic variants

Jimenez C et al. Lancet Oncol. 2024 Apr 9:S1470-2045(24)00133-5.


Sensitive tumors
2-OG
O_2
Ascorbate
Fe^{2+}
Succinate
CO_2
PHD
Hydroxylation
Mutations in TCA genes
Fumarate
TCA cycle
Succinate
↓SDHA/B/C/D
Rbx1
Cul2
Elongin C
Elongin B
α-domain
VHL
β-domain
OH
OH
ODD
P531
EPAS1/HIF2α
PAS-A
PAS-B
ARNT/HIF1β
PAS-A
PAS-B
Response
• High EPAS1 transcriptional signature
• HIF2α-stabilizing EPAS1 and VHL mutations
clinical benefit
sustained clinical benefit
HIF2α inhibitors
• Belzutifan (Welireg, PT2977, MK-6482)
• DFF332
No activation of HIF target genes
TKIs and antiangiogenic therapies
HRE
5′ -RCTGT-3′
(HRE)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Belzutifan for Advanced Pheochromocytoma or Paraganglioma

Camilo Jimenez, M.D.,[1] Mikkel Andreassen, M.D., Ph.D.,[2] Alice Durand, M.D.,[3] Sophie Moog, M.D., Ph.D.,[4] Andrew Hendifar, M.D.,[5] Staffan Welin, M.D.,[6] Francesca Spada, M.D., Ph.D.,[7,8] Rohini Sharma, M.B., B.S., Ph.D.,[9] Edward Wolin, M.D.,[10] Joseph Ruether, M.D.,[11] Rocio Garcia-Carbonero, M.D.,[12] Martin Fassnacht, M.D.,[13,14] Jaume Capdevila, M.D., Ph.D.,[15] Jaydira Del Rivero, M.D.,[16] Othon Iliopoulos, M.D.,[17] Olivier Huillard, M.D.,[18] Raymond Jang, M.D.,[19] Knut Mai, M.D.,[20,21] Elena Artamonova, M.D., Ph.D.,[22] Andreas Hallqvist, M.D.,[23] Tobias Else, M.D.,[24] Amos Odeleye-Ajakaye, M.S.,[25] Alexander Gozman, M.D.,[25] Girish S. Naik, M.D., M.M.Sc.,[25] and Alfredo Berruti, M.D.,[26] for the LITESPARK-015 Investigators*

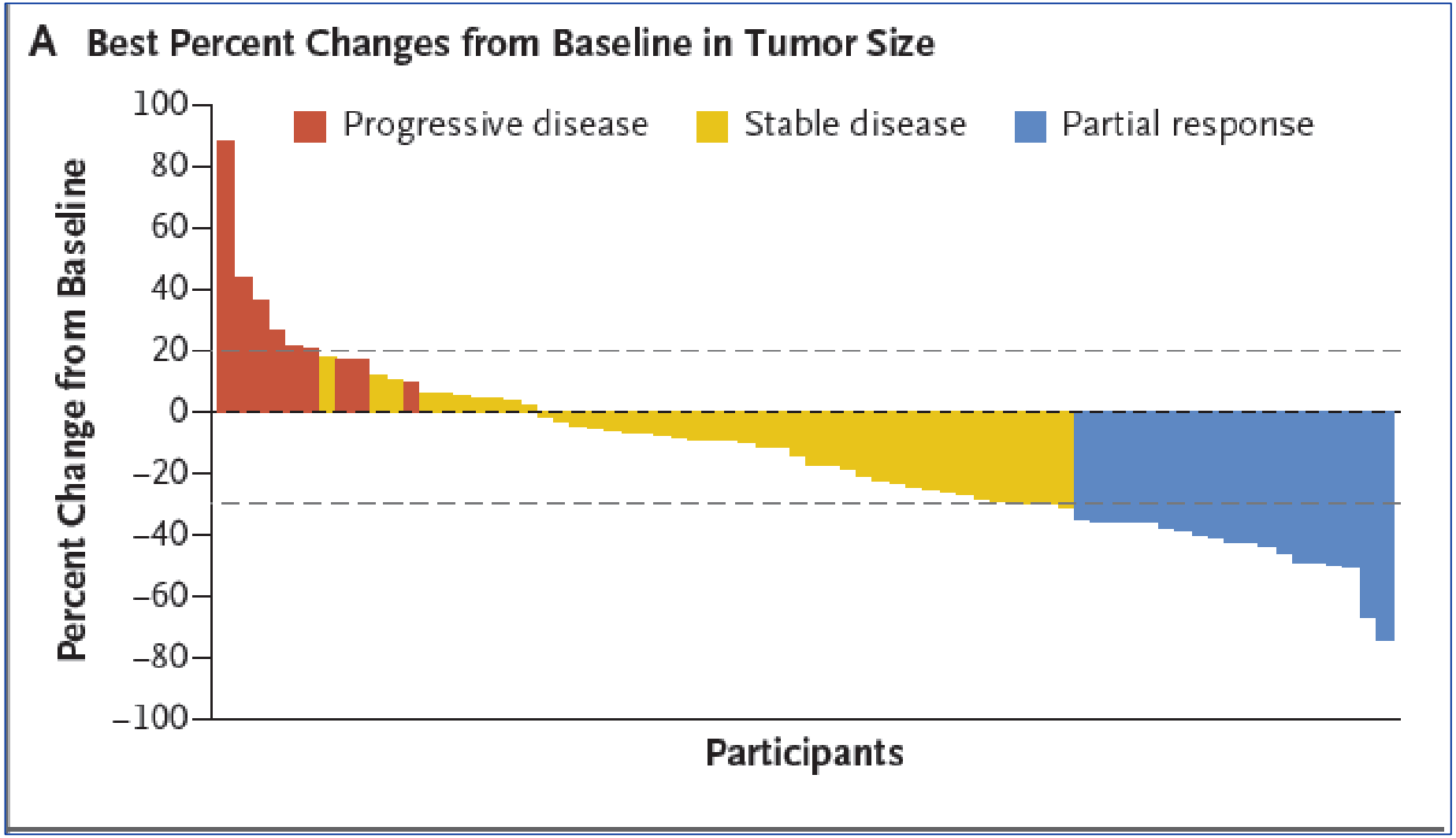
Baseline Characteristics

Demographic or characteristic	PPGL N = 72
Median age, (range)	51.5 (22-77)
≥ 65	9 (13%)
Sex	
Male	42 (58%)
Female	30 (42%)
Geographical region	
North America	21 (29%)
Western Europe	46 (64%)
Rest of the World	5 (7%)
ECOG performance status	
0	39 (54%)
1	33 (46%)
Prior lines of therapy[a]	
Median (range)	1 (0[a],5)
≥1 prior line of systemic therapy	54 (75%)
Prior therapy	
Chemotherapy	36 (50%)
Radiopharmaceutical	32 (44%)
VEGF tyrosine kinase inhibitor	18 (25%)
Other anti-cancer therapy	5 (7%)
Somatostatin analog	10 (14%)
Disease presentation type	
Locally advanced	2 (3%)
Metastatic	70 (97%)

Demographic or characteristic	PPGL N = 72
Medical history of hypertension	
Yes	60 (83%)
No	2 (17%)
Genetic syndrome history	
Yes	28 (39%)
SDHA-related tumor predisposition syndrome	2 (3%)
SDHB-related tumor predisposition syndrome	24 (33%)
SDHD-related tumor predisposition syndrome	2 (3%)
No	20 (28%)
Unknown	24 (33%)
Diagnosis	
Pheochromocytoma	24 (33%)
Paraganglioma	45 (63%)
Both	3 (4%)
Baseline tumor burden (mm)	
Median (range)	84.5 (10-261)
Baseline site of disease or metastasis	
Lymph node	48 (67%)
Bone	41 (57%)
Liver	23 (32%)
Lung	19 (26%)
Peritoneum	10 (14%)
Other	57 (79%)

Jimenez C et al. NEJM, 2025, Nov. 20, 2012-2022

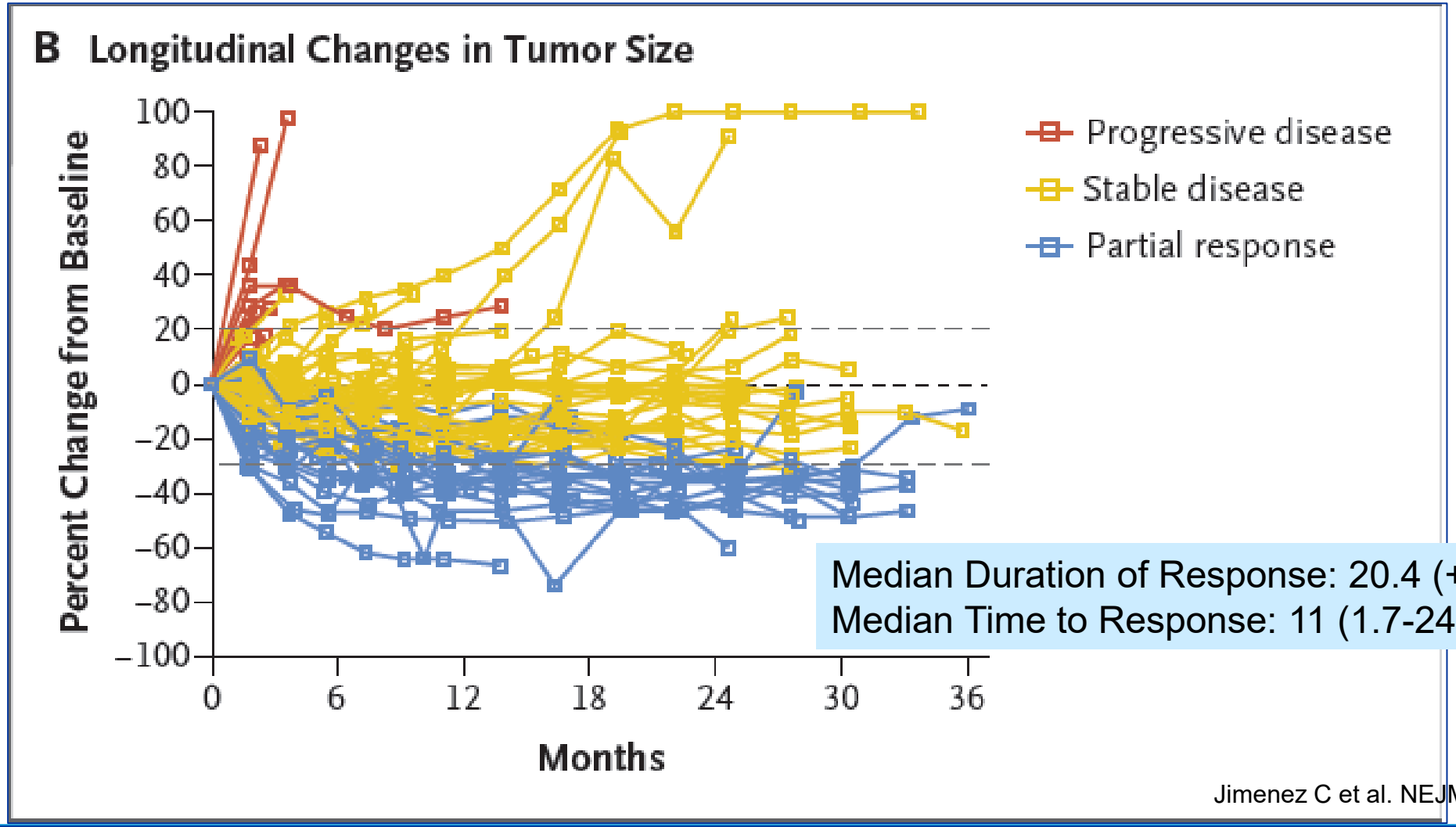
LITESPARK 015: ORR



ORR: 19 (26%)
DCR: 61 (85%)
CR: 0
PR: 19 (26.4%)
SD: 42 (58.3%)

Jimenez C et al. NEJM, 2025, Nov. 20, 2012-2022

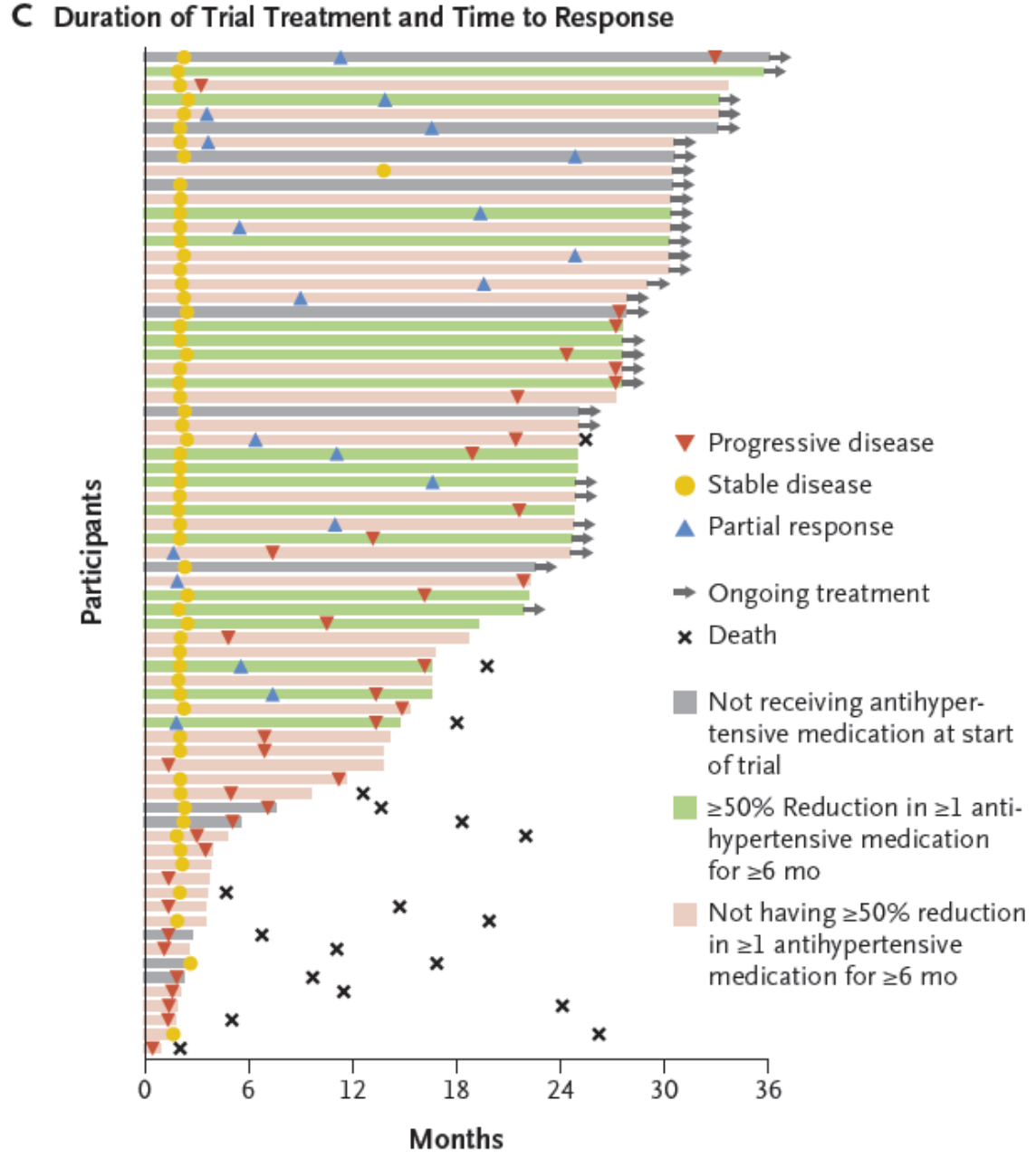
LITESPARK 015: Duration of Response



Median Duration of Response: 20.4 (+5.6-+26.6) months
Median Time to Response: 11 (1.7-24.8) months

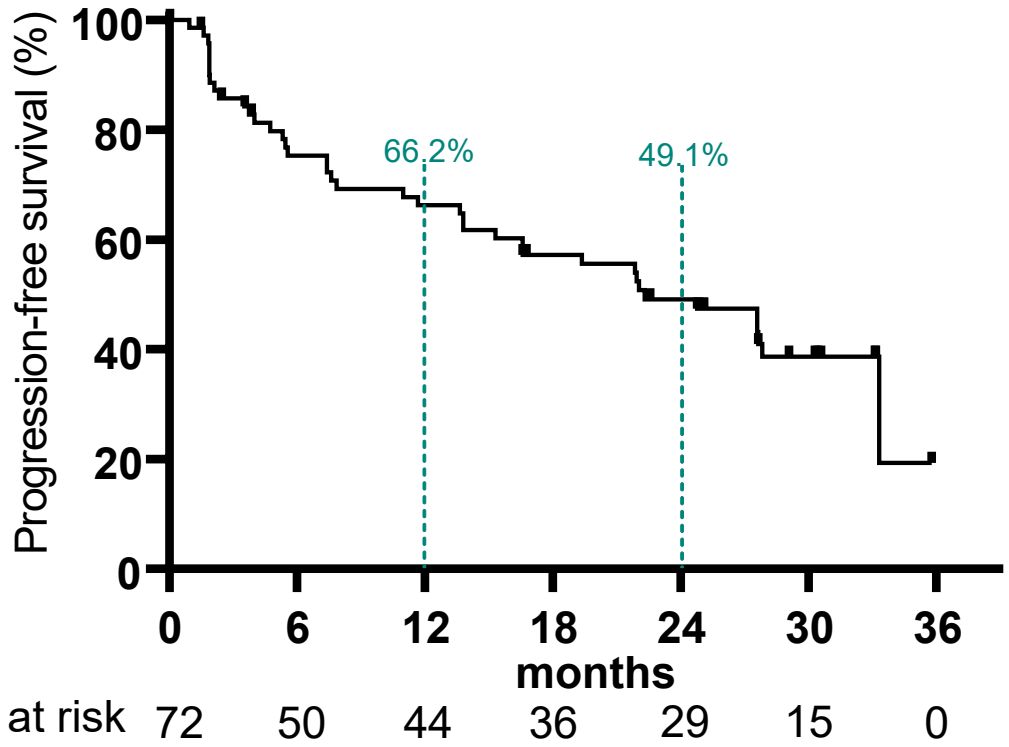
Jimenez C et al. NEJM, 2025, Nov.20, 2012-2022

LITESPARK 015: Duration of Trial Treatment and Time to Response

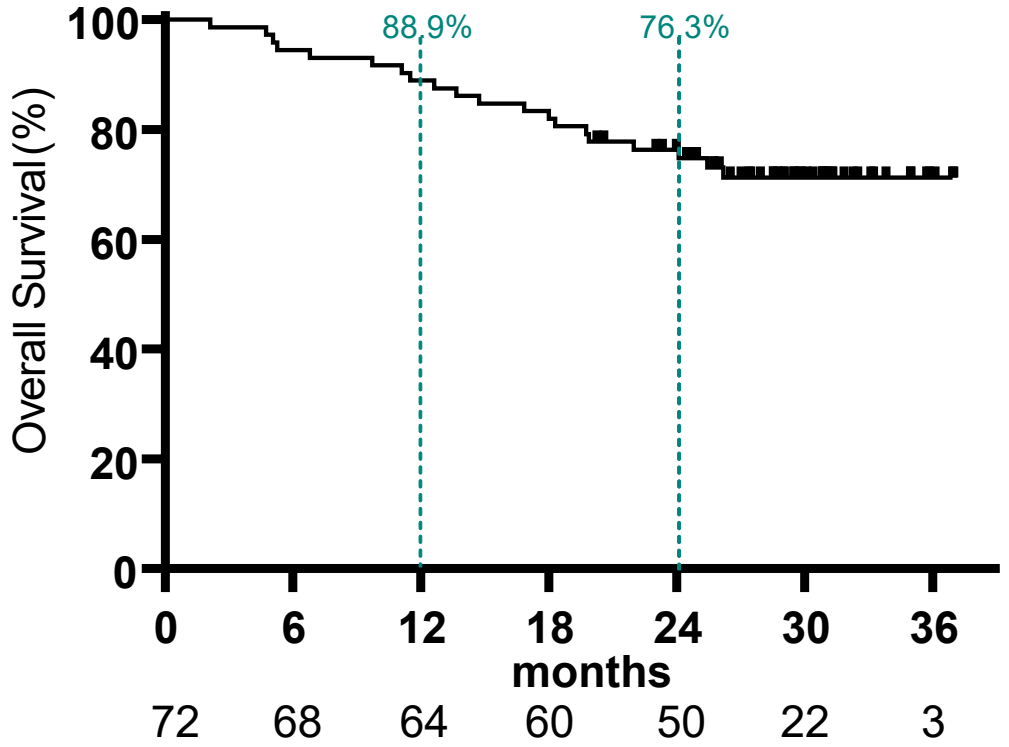


Jimenez C et al. NEJM, 2025, Nov. 20, 2012-2022

Survival Outcomes



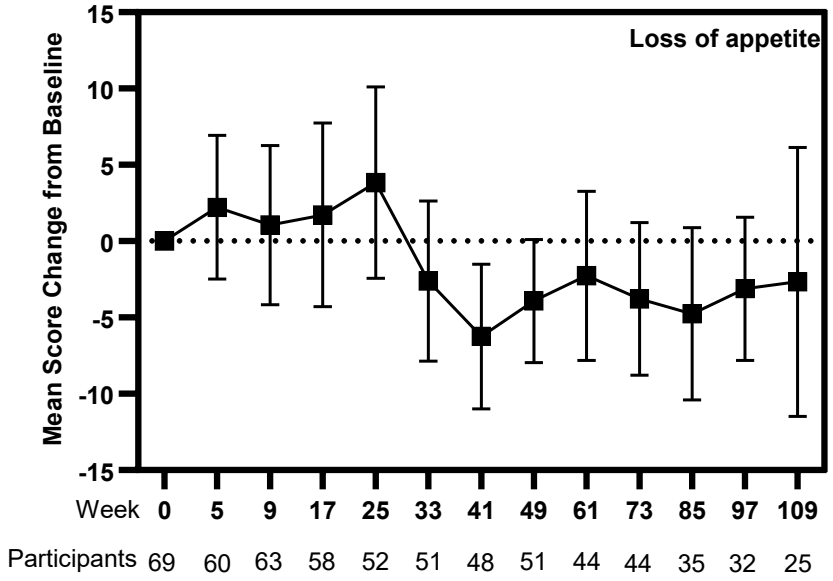
Median PFS, mo (95% CI)	22.3 (13.8- NR)

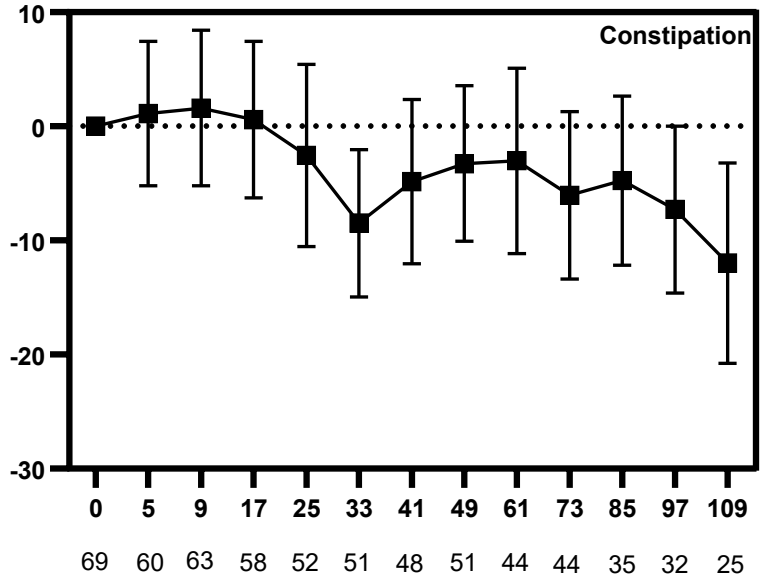


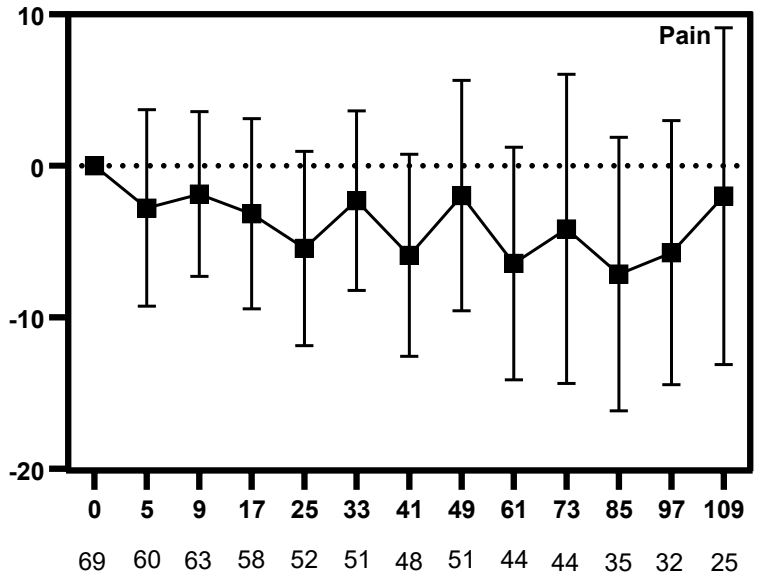
Median OS, mo (95% CI)	NR (NR- NR)

Jimenez C et al. NEJM, 2025, Nov. 20, 2012-2022

Global Health Status and Quality of Life







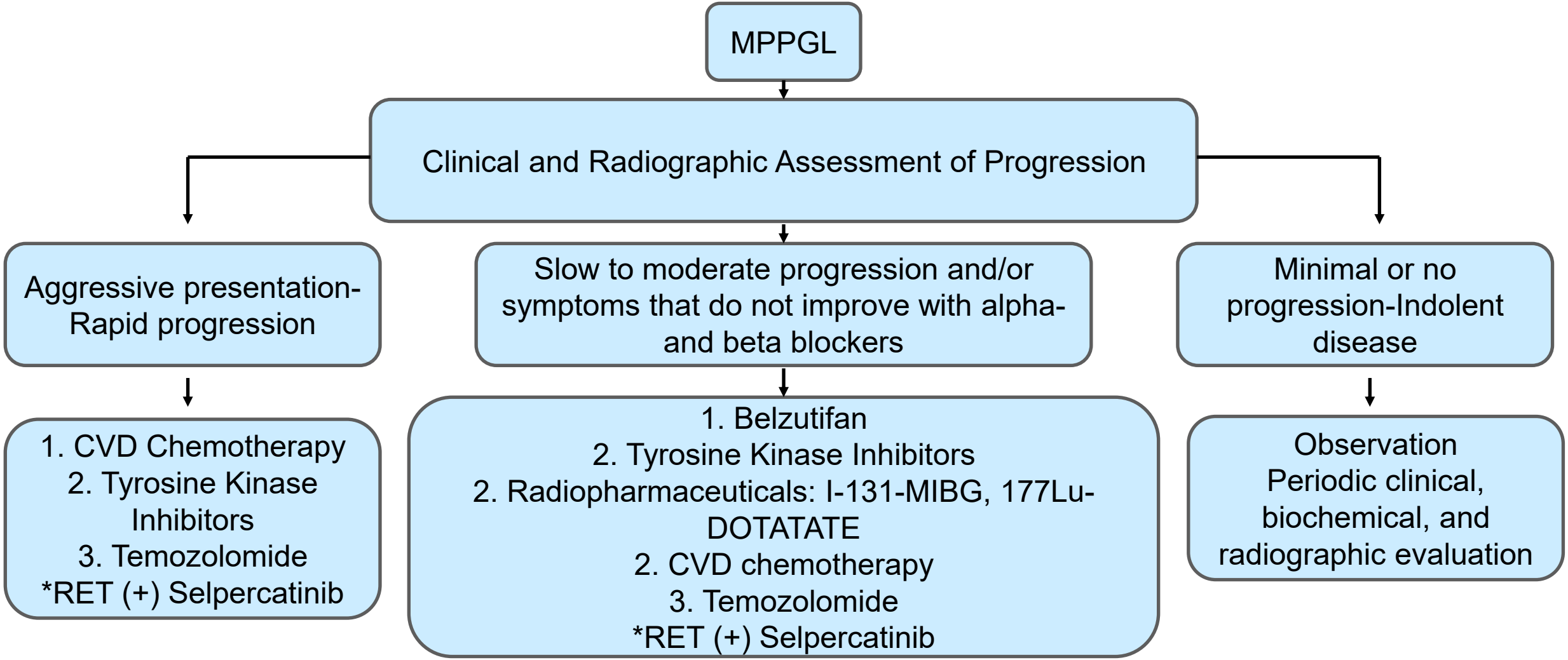
	PPGL PRO population N = 69	
	Global Health Status/QoL	Physical functioning
Improved, n (%) [95% CI]	15 (21.7) [12.7 - 33.3]	14 (20.3) [11.6 - 31.7]
Stable	36 (52.2) [39.8 - 64.4]	40 (58.0) [45.5 - 69.8]
Improved + Stable	51 (73.9) [61.9 - 83.7]	54 (78.3) [66.7 - 87.3]
Deteriorated	17 (24.6) [15.1 - 36.5]	12 (17.4) [9.3 - 28.4]
Unconfirmed	1 (1.4) [0 - 7.8]	3 (4.3) [0.9 - 12.2]

Jimenez C et al. NEJM, 2025, Nov. 20 2012-2022

Treatment Related Adverse Events

Adverse Events, n (%)	PPGL N = 72	
Any grade	71 (99)	
Grade 3-4	33 (46)	
Serious adverse events	8 (11)	
Led to death (Grade 5)	0	
Led to discontinuation	2 (3)	
Led to dose reduction	9 (13%)	
Treatment-related AEs occurring in ≥ 10% of participants	**Any**	**Grade ≥3**
Anemia	63 (88)	16 (22)
Fatigue	23 (32)	3 (4)
Dyspnea	15 (21)	0
Hypoxia	10 (14)	7 (10)
Asthenia	10 (14)	0
Nausea	9 (13)	1 (1)
Edema peripheral	9 (13)	0
Headache	8 (11)	0

Jimenez C et al. NEJM, 2025, Nov. 2012-2022



Combination with Belzutifan?? Clinical Trials?

cjimenez@mdanderson.org

Bench-Bedside-Back – patient tissue as key for personalised medicine

Prof. Dr. Svenja Nölting

University Hospital Zurich, USZ, University of Zurich, UZH

DISCLOSURE SLIDE

I have no conflicts/disclosures to declare

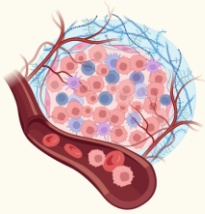
Overview

- Background: Genetics
- (Personalized) Therapy overview
- Research rational
- Patient-derived PPGL platform for next-generation personalized drug testing
- Patient-derived PPGL platform for next-generation personalized risk assessment
- Transferability to GEP-NET
- Summary

Background: Genetics and Overview

CLUSTER 1
Pseudohypoxia

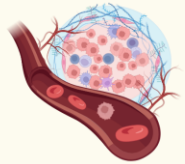
Cluster 1A: ***SDHx,*** *FH, MDH2, GOT2, SLC25A11, IDH, DLST*
Cluster 1B: ***VHL****, EPAS1 (HIF2A), PHD1/2, IRP1*



- Mostly extra-adrenal (PGL)
- Metastatic risk up to 75%
- Norepinephrine, dopamine

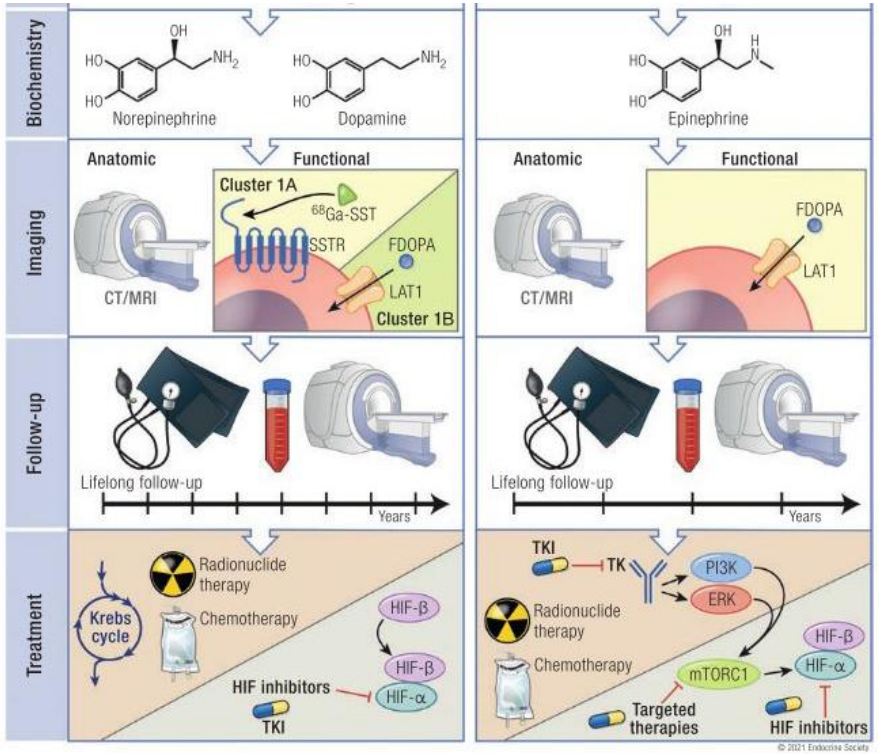
CLUSTER 2
Kinase signaling

Cluster 2: ***NF1, RET,*** *MAX, TMEM127, HRAS, BRAF, MET, MERTK, FGFR1, NGFR*



- Mostly adrenal (PCC)
- Metastatic risk 2-12%
- Epinephrine

CLUSTER 3
Wnt signaling



Nölting, *Syllabus 28. Intensivkurs Endokrinologie der DGE* 2025;
Nölting et al., *Endocrine Reviews* 2021

- PPGLs highest heritability among all cancers
- 65-80% of PPGLs assigned to one of 3 molecular clusters
- Consensus: Germline testing of *all* patients
- Diagnostics: Biochemistry: Plasma(nor)metanephrines (LC-MS/MS)
- Diagnostics: Personalized functional imaging
- Personalized follow-up

- (Personalized genetically tailored) therapy?

Background: *SDHB* & *SDHD* PPGL consensus statements

nature reviews endocrinology

https://doi.org/10.1038/s41574-023-00926-0

Consensus statement

Check for updates

Management of phaeochromocytoma and paraganglioma in patients with germline *SDHB* pathogenic variants: an international expert Consensus statement

David Taïeb[1], Svenja Nölting[2,3], Nancy D. Perrier[4], Martin Fassnacht[5], Jorge A. Carrasquillo[6], Ashley B. Grossman[7,8], Roderick Clifton-Bligh[9], George B. Wanna[10], Zachary G. Schwam[10], Laurence Amar[11,12], Isabelle Bourdeau[13], Ruth T. Casey[14], Joakim Crona[15], Cheri L. Deal[16], Jaydira Del Rivero[17], Quan-Yang Duh[18], Graeme Eisenhofer[19], Tito Fojo[20,21], Hans K. Ghayee[22,23], Anne-Paule Gimenez-Roqueplo[11,24], Antony J. Gill[25,26], Rodney Hicks[27], Alessio Imperiale[28], Abhishek Jha[29], Michiel N. Kerstens[30], Ronald R. de Krijger[31,32], André Lacroix[33], Ivica Lazurova[34], Frank I. Lin[35], Charlotte Lussey-Lepoutre[11,36], Eamonn R. Maher[14], Ozgur Mete[37], Mitsuhide Naruse[38,39], Naris Nilubol[40], Mercedes Robledo[41,42], Frédéric Sebag[43], Nalini S. Shah[44], Akiyo Tanabe[45], Geoffrey B. Thompson[46], Henri J. L. M. Timmers[47], Jiri Widimsky[48], William J. Young Jr[49], Leah Meuter[50], Jacques W. M. Lenders[47] & Karel Pacak[29]

Novel PPGL guideline in preparation

Nature Reviews Endocrinology 2024

THE LANCET
Diabetes & Endocrinology

Volume 11, Issue 5, May 2023, Pages 345-361

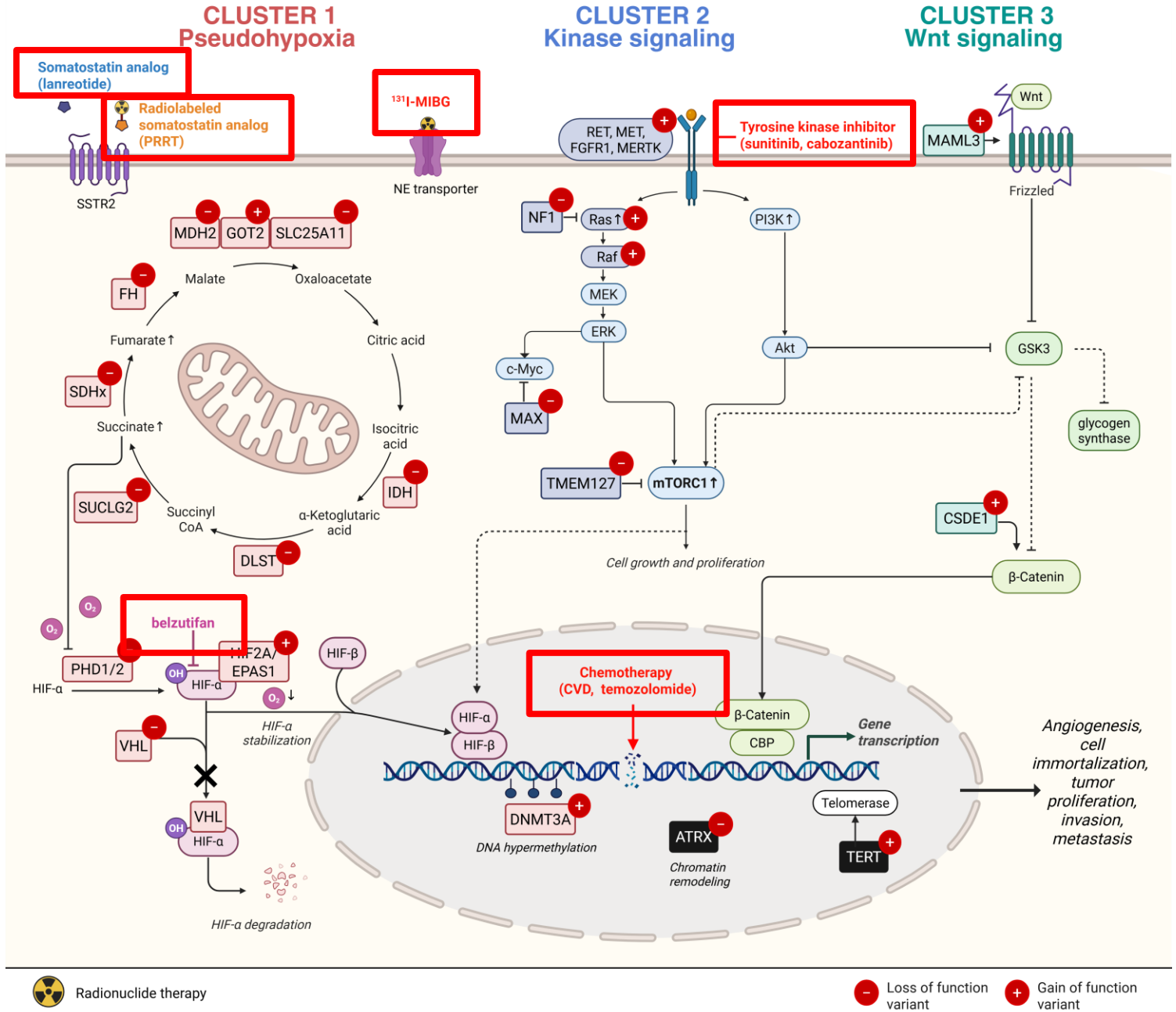
Review

Clinical consensus guideline on the management of phaeochromocytoma and paraganglioma in patients harbouring germline *SDHD* pathogenic variants

Prof David Taïeb MD [ap], Prof George B Wanna MD [ar], Maleeha Ahmad MD [a], Prof Charlotte Lussey-Lepoutre MD [d ad], Prof Nancy D Perrier MD [ak], Prof Svenja Nölting MD [aj], Prof Laurence Amar MD [d e], Prof Henri J L M Timmers MD [aa], Zachary G Schwam MD [ar], Prof Anthony L Estrera MD [t], Prof Michael Lim MD [a], Erqi Liu Pollom MD [c], Lucas Vitzthum MD [c], Prof Isabelle Bourdeau MD [g], Ruth T Casey PhD [h], Prof Frédéric Castinetti MD [am ao], Prof Roderick Clifton-Bligh PhD [i j], Eleonora P M Corssmit MD [k], Ronald R de Krijger MD [m n], Jaydira Del Rivero MD [o], Prof Graeme Eisenhofer PhD [r], Hans K Ghayee DO [u], Prof Anne-Paule Gimenez-Roqueplo MD [d f], Prof Ashley Grossman FmedSci [v w], Prof Alessio Imperiale MD [x], Prof Jeroen C Jansen MD [l], Abhishek Jha MBBS [p], Michiel N Kerstens MD [y], Prof Henricus P M Kunst MD [z ab], Prof James K Liu MD [ac], Prof Eamonn R Maher MD [h], Prof Daniele Marchioni MD [ae], Prof Leilani B Mercado-Asis MD [af], Prof Ozgur Mete MD [ag ah], Mitsuhide Naruse MD [ai], Naris Nilubol MD [q], Prof Neeta Pandit-Taskar MD [al], Prof Frédéric Sebag MD [an], Akiyo Tanabe MD [aq], Prof Jiri Widimsky MD [as], Leah Meuter BS [b], Prof Jacques W M Lenders MD [s aa], Prof Karel Pacak MD [p]

Lancet Diabetes Endocrinol. 2023

(Personalized genetically tailored) Therapy Overview



Fischer*, Del Rivero*,…Nölting*, Jimenez*,
*contributed equally,
Best Pract Res Clin Endocrinol Metab 2025

(Personalized genetically tailored) Therapy Overview: Phase 2 Studies

What`s new (including genetics)?

Prospective Phase 2 studies 2024 & 2025:

- Only one FDA-approved drug (May 2025) HIF-2α inh. belzutifan (LITESPARK-015, molecular-genetic analysis pending, *SDHB*>sporadic), n=72
- TKI sunitinib (FIRSTMAPPP, first and only RCT, Objective Response Rate (ORR) *SDHB*>others), n=78
- TKI cabozantinib (NATALIE, ORR *SDHB*>others), n=17
- PRRT (long Progression Free Survivall (PFS)/Overall Survival (OS) sporadic>*SDHX*), n=36
- Ctx high tumor burden, fast-growing, *SDHB* maybe better response
- LAMPARA (lanreotid) ongoing (ASCO 2025: PFS > 2J, disease stabilising) (n=14/18 *SDHX*)

Fischer*, Del Rivero*,…,Nölting*, Jimenez*, *contributed equally, *Best Pract Res Clin Endocrinol Metab* 2025
Baudinet al., *Lancet* 2024
Jimenez et al., *Lancet Oncol* 2024
Jimenez et al., *N Engl J Med* 2025
FDA (www.fda.gov) approval for belzutifan (May 2025)
Lin et al., *J Clin Oncol* 2025

Rational for my translational research

Rarity of disease: Lack of prospective randomized placebo-controlled therapy studies (RCT) (only one RCT: FIRSTMAPPP (sunitinib))

Performance of randomized prospective clinical trials exceptionally challenging

Baudin et al.,
Lancet. 2024

Solution?

Aims

Personalized therapies

Genetically tailored therapies

Problem: No reliable human cell lines available

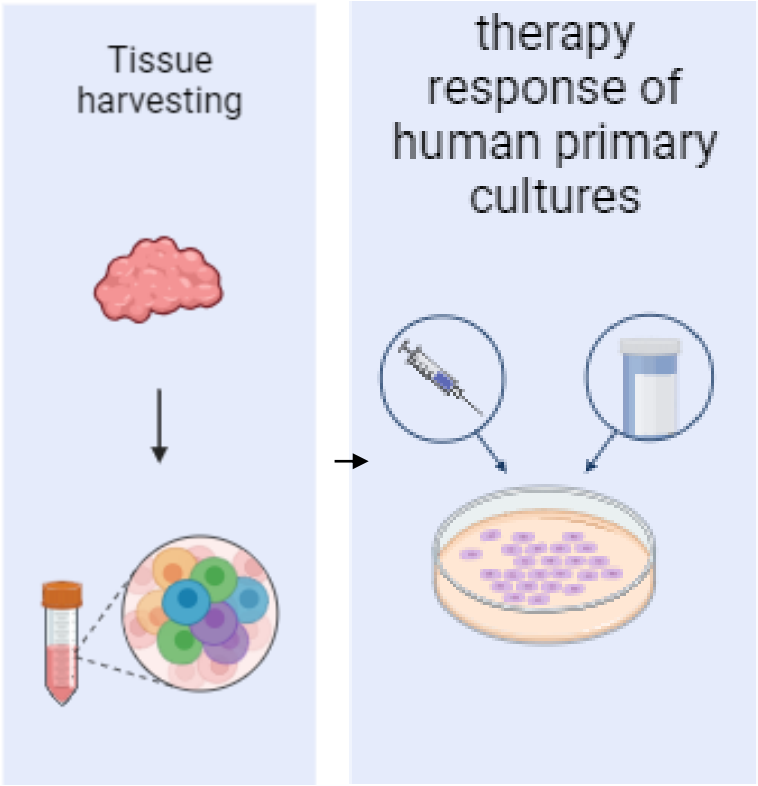
Patient-derived PPGL platform for next-generation personalized drug testing

Endocrine-Related Cancer | K Wang, I Schütze *et al.* | Human pheochromocytoma primary cultures | **29**:6 | **285**–306

RESEARCH

Personalized drug testing in human pheochromocytoma/paraganglioma primary cultures

Katharina Wang[1,*], Ina Schütze[2,*], Sebastian Gulde[3], Nicole Bechmann[4,5], Susan Richter[4], Jana Helm[5], Michael Lauseker[6], Julian Maurer[1], Astrid Reul[2], Gerald Spoettl[1], Barbara Klink[7,8,9], Doreen William[9], Thomas Knösel[10], Juliane Friemel[11], Michel Bihl[11], Achim Weber[11], Maria Fankhauser[1], Laura Schober[1], Diana Vetter[12], Martina Broglie Däppen[13], Christian G Ziegler[5], Martin Ullrich[14], Jens Pietzsch[14,15], Stefan R Bornstein[5], Christian Lottspeich[1], Matthias Kroiss[1,16], Martin Fassnacht[16], Vera Ursula Julia Wenter[17], Roland Ladurner[18], Constanze Hantel[2,5], Martin Reincke[1], Graeme Eisenhofer[4,5], Ashley B Grossman[19,20], Karel Pacak[21], Felix Beuschlein[1,2], Christoph J Auernhammer[1], Natalia S Pellegata[3] and Svenja Nölting[1,2]



Wang,…, Nölting,
Endocr Relat Cancer 2022

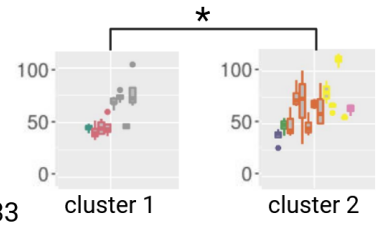
Created by BioRender

Patient-derived PPGL platform – personalized drug testing & risk assessment

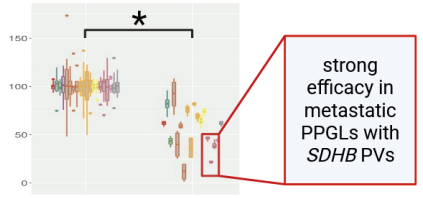
NATALIE trial cabozantinib: ORR overall 25% vs. *SDHB* 60% (Jimenez, Lancet Oncol 2024)

Case report: Complete response of a *SDHB* mPPGL to zolendronic acid (Schutte, BMJ Case Rep 2024)

Cluster-related differences in tumour response to cabozantinib:

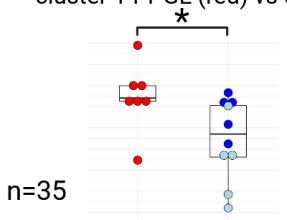


72h mean cell viability (%) with 40 µM zoledronic acid vs control



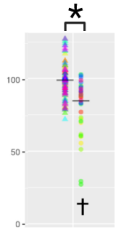
Wang et al... Nölting, ERC 2022

Cluster-related differences in tumour response to cannabidiol: cluster 1 PPGL (red) vs cluster 2 PPGL (blue)



Wang et al... Nölting, JCEM 2024

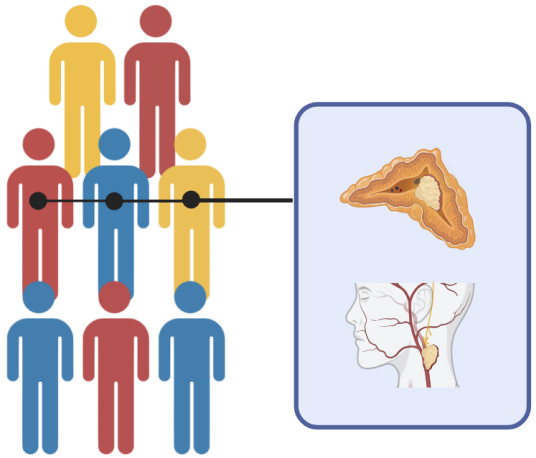
72h mean cell viability (%) with 1 µM estradiol: no *NF1* PV vs *NF1* PV



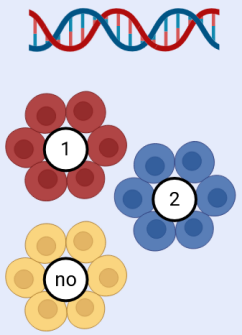
-> significantly higher anti-tumour effects in PPGLs with *NF1* PVs

Wang et al... Nölting, EJE 2025

Patient-derived PPGL (n=15-20 per year)

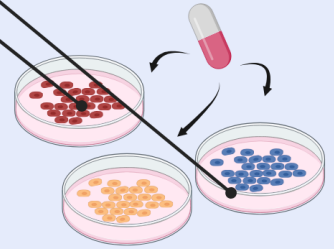


Genetic testing + cluster designation

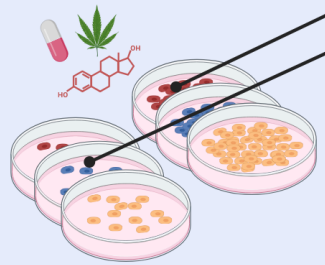


Correlation with clinical parameters

Drug screening in 2D/3D patient primary cultures



Risk assessment (e.g., cannabinoids, sex hormones): Anti-tumour/tumour-promoting effects depending on the genetic background



>110 fresh surgery-derived PPGL
>50 drugs

Wang,..., Nölting, *Endocr Relat Cancer* 2022

Wang,...Zitzmann*, Nölting*, *JCEM* 2024

*contributed equally

Wang,..., Nölting, *Eur J Endocrinol.* 2025

Wang,..., Nölting *Best Pract Res Clin Endocrinol Metab* 2025

Tumour composition and hormone receptor expression analysis

Predictive kinase signalling activation patterns (Automated Western Blotting, Jess®, and IHC)

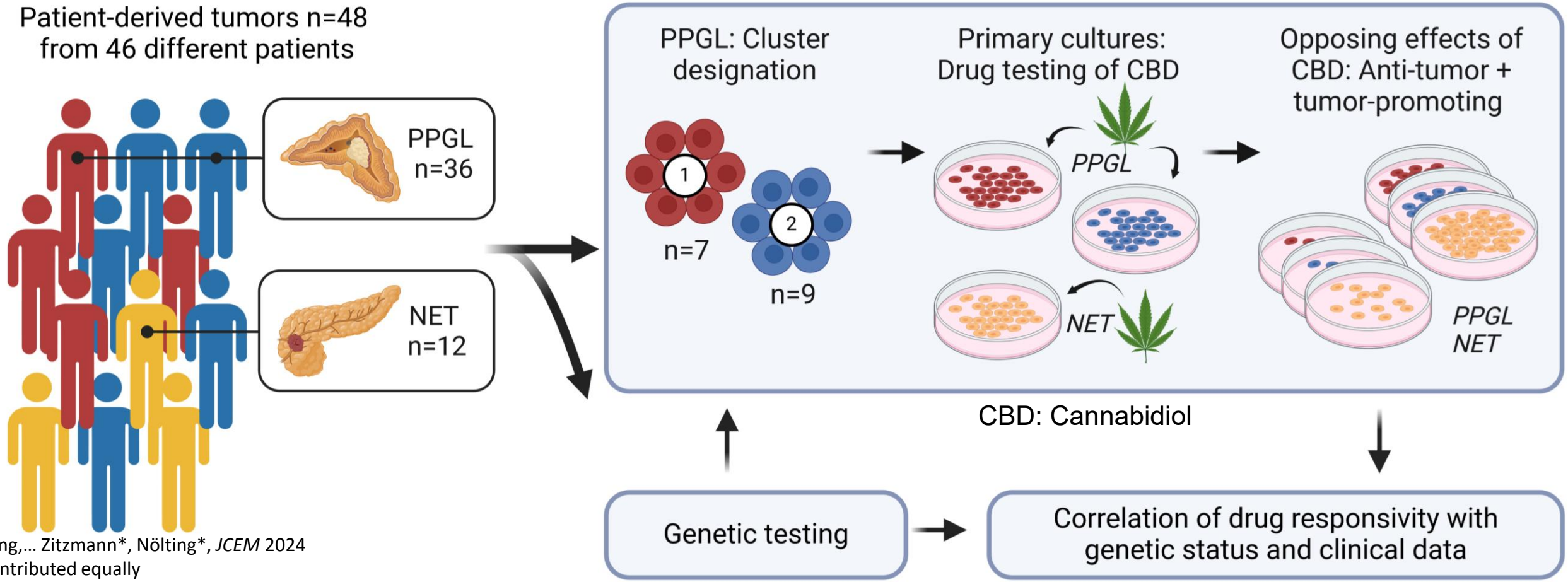
Efficacy and risk: Cannabidiol (CBD) in PPGL & GEP-NET

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

LEGALIZATION OF CANNABIS IN GERMANY

Opposing Effects of Cannabidiol in Patient-derived Neuroendocrine Tumor, Pheochromocytoma/ Paraganglioma Primary Cultures

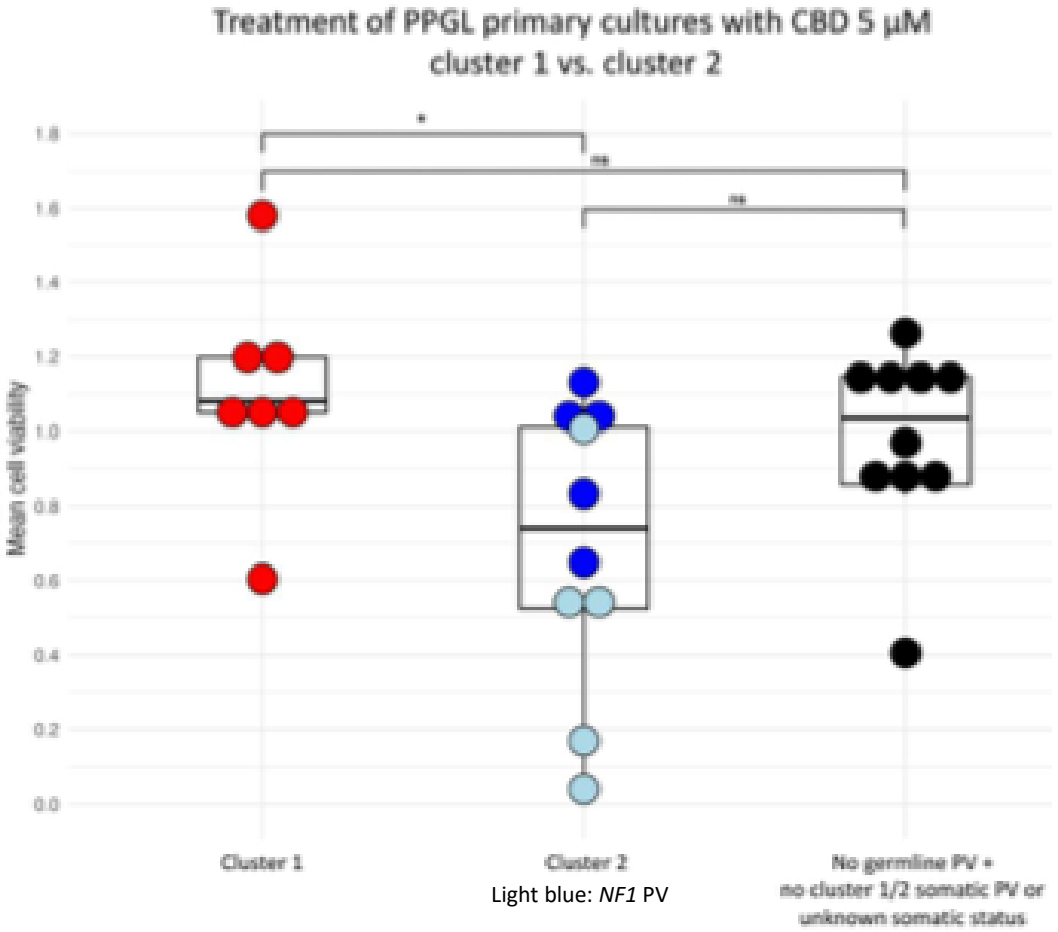
Katharina Wang ✉, Laura Schober, Alessa Fischer, Nicole Bechmann, Julian Maurer, Lea Peischer, Astrid Reul, Constanze Hantel, Martin Reincke, Felix Beuschlein, Mercedes Robledo, Hermine Mohr, Natalia S Pellegata, Katharina Schilbach, Thomas Knösel, Matthias Ilmer, Martin Angele, Matthias Kroiss, Umberto Maccio, Martina Broglie-Däppen, Diana Vetter, Kuno Lehmann, Karel Pacak, Ashley B Grossman, Christoph J Auernhammer, Kathrin Zitzmann, Svenja Nölting



Wang,… Zitzmann*, Nölting*, *JCEM* 2024
*contributed equally

Efficacy and risk: Cannabidiol (CBD) in PPGL & GEP-NET: Opposing effects

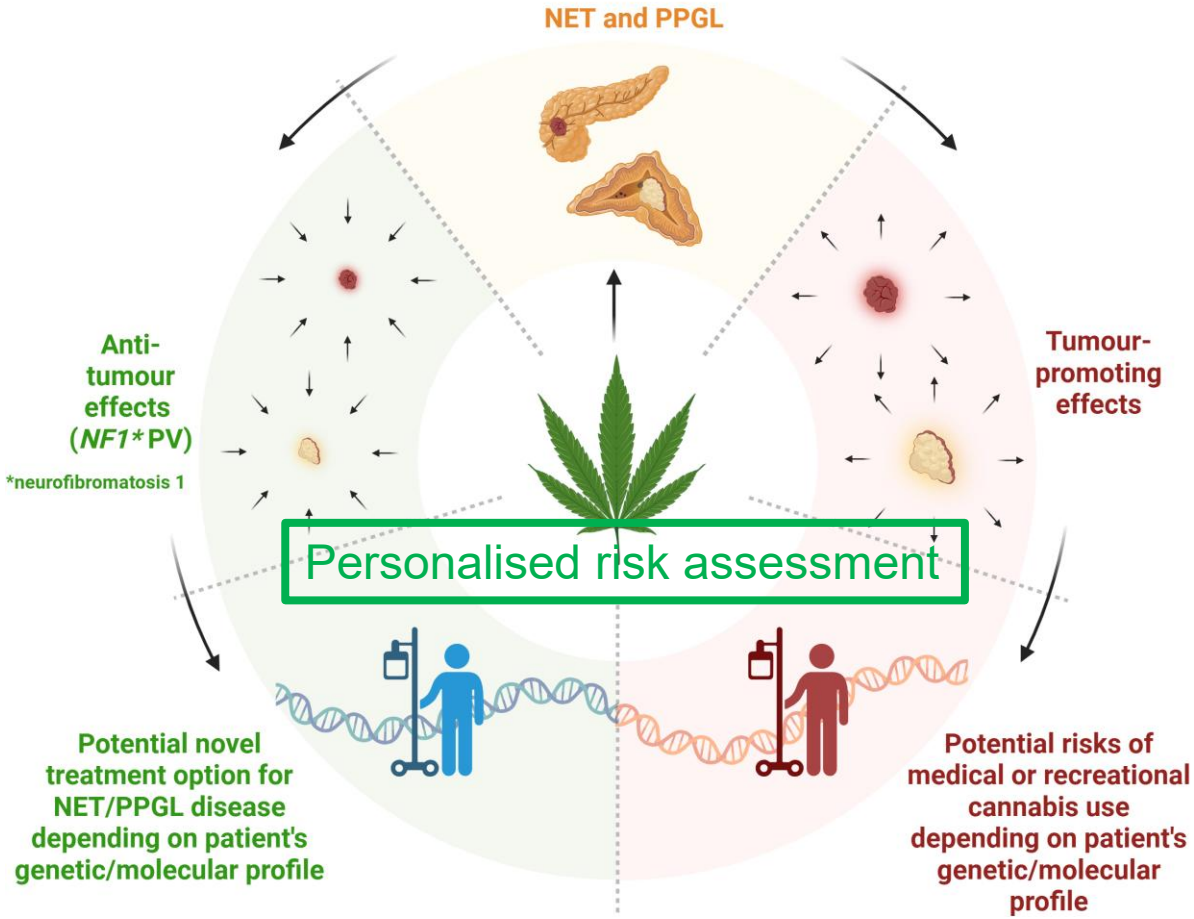
JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM



Light blue: *NF1* PV

Wang,… Zitzmann*, Nölting*, *JCEM* 2024
*contributed equally

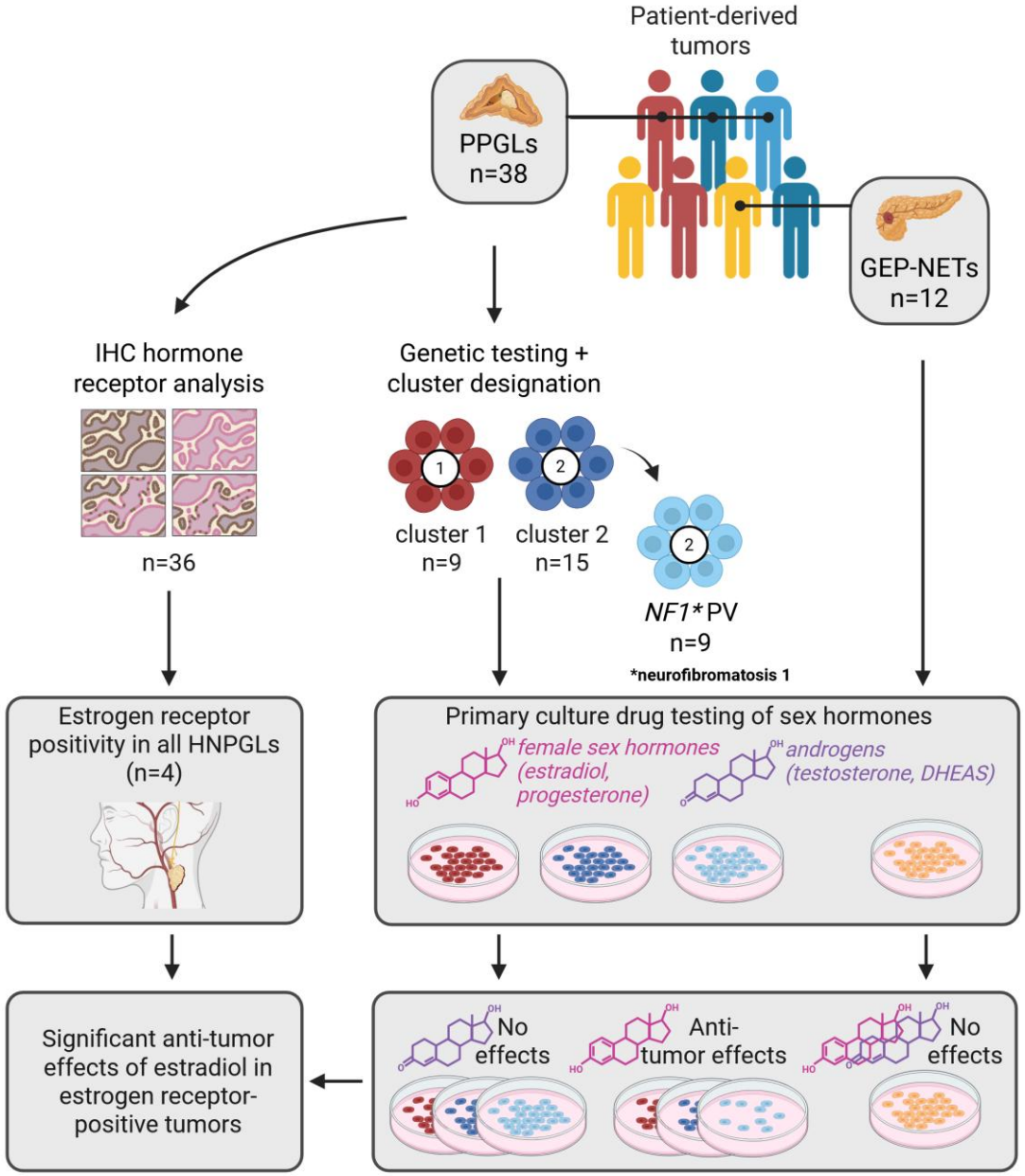
Potential effects of cannabinoids on neuroendocrine tumours and phaeochromocytomas/paragangliomas

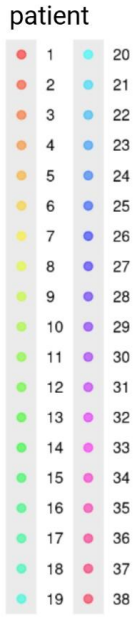


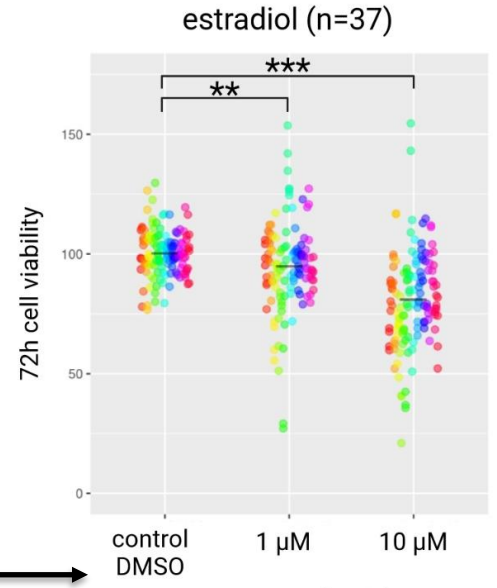
Efficacy or risk? Sex hormones in PPGL & GEP-NET: Female sex hormones anti-tumor effects

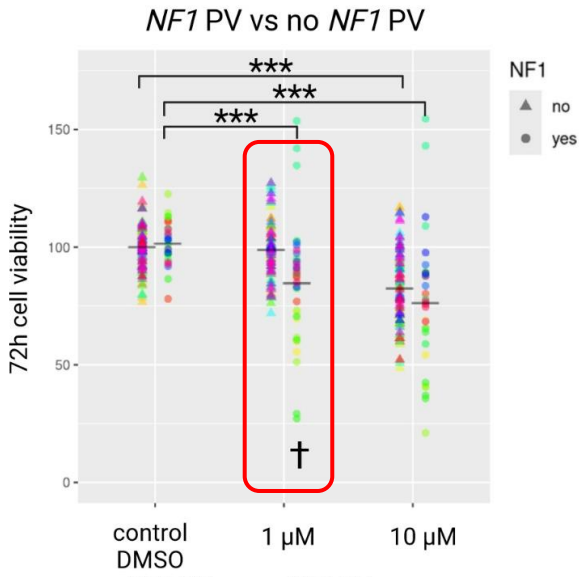
EJE
Impact of sex hormones on pheochromocytomas, paragangliomas, and gastroenteropancreatic neuroendocrine tumors

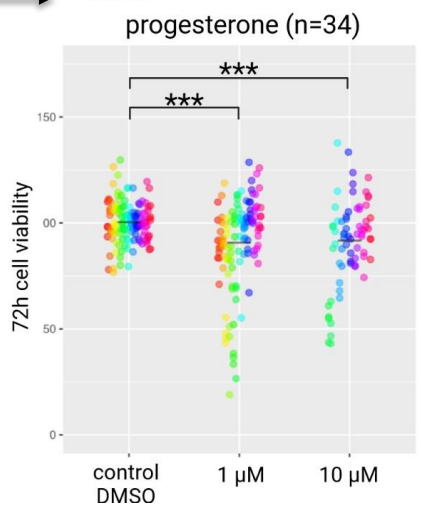
Katharina Wang, Alessa Fischer, Umberto Maccio, Kathrin Zitzmann, Mercedes Robledo, Michael Lauseker, Jana Bauer, Nicole Bechmann, Simon Gahr, Julian Maurer, Lea Peischer, Astrid Reul, Hanno Nieß, Petra Zimmermann, Matthias Ilmer, Katharina Schilbach, Thomas Knösel, Matthias Kroiss, Martin Fassnacht, Simon A Müller, Gregoire B Morand, Alexander Huber, Diana Vetter, Kuno Lehmann, Zsolt Kulcsar, Hermine Mohr, Natalia S Pellegata, Constanze Hantel, Martin Reincke, Felix Beuschlein, Karel Pacak, Ashley B Grossman, Christoph J Auernhammer, Svenja Nölting ✉

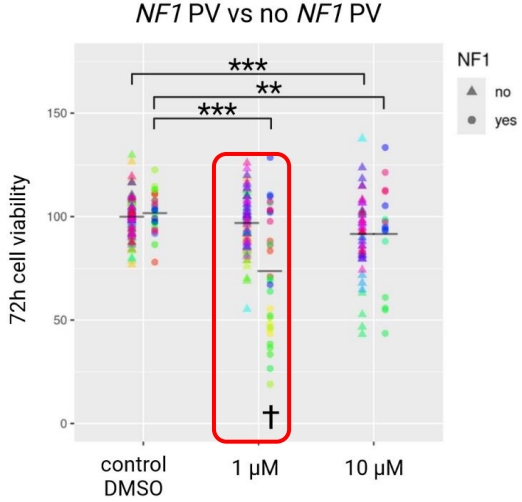








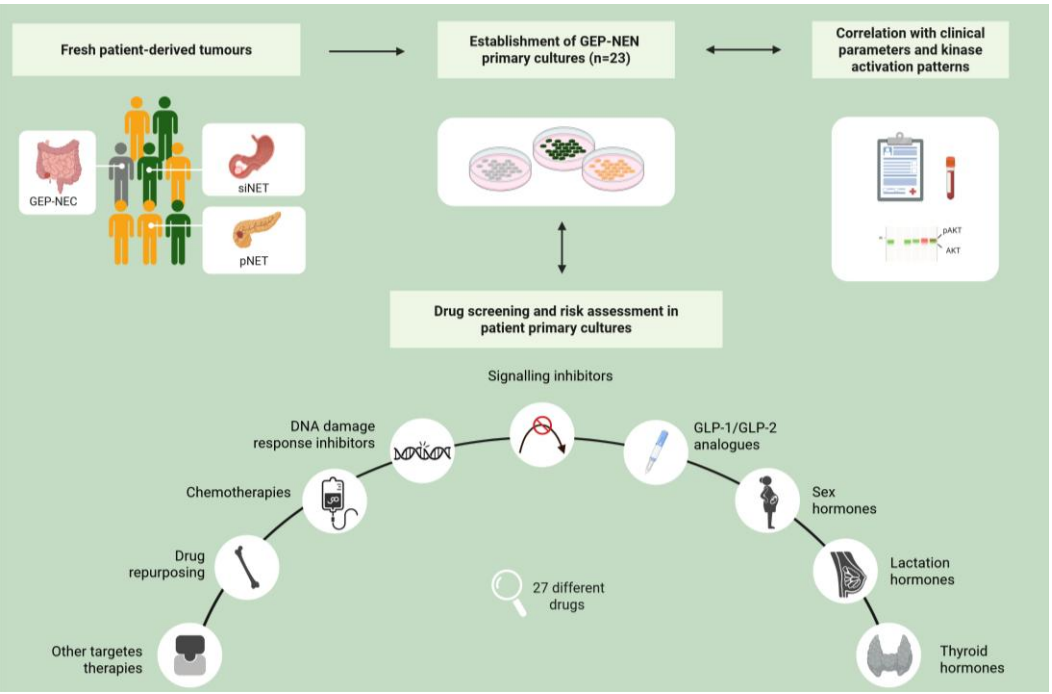




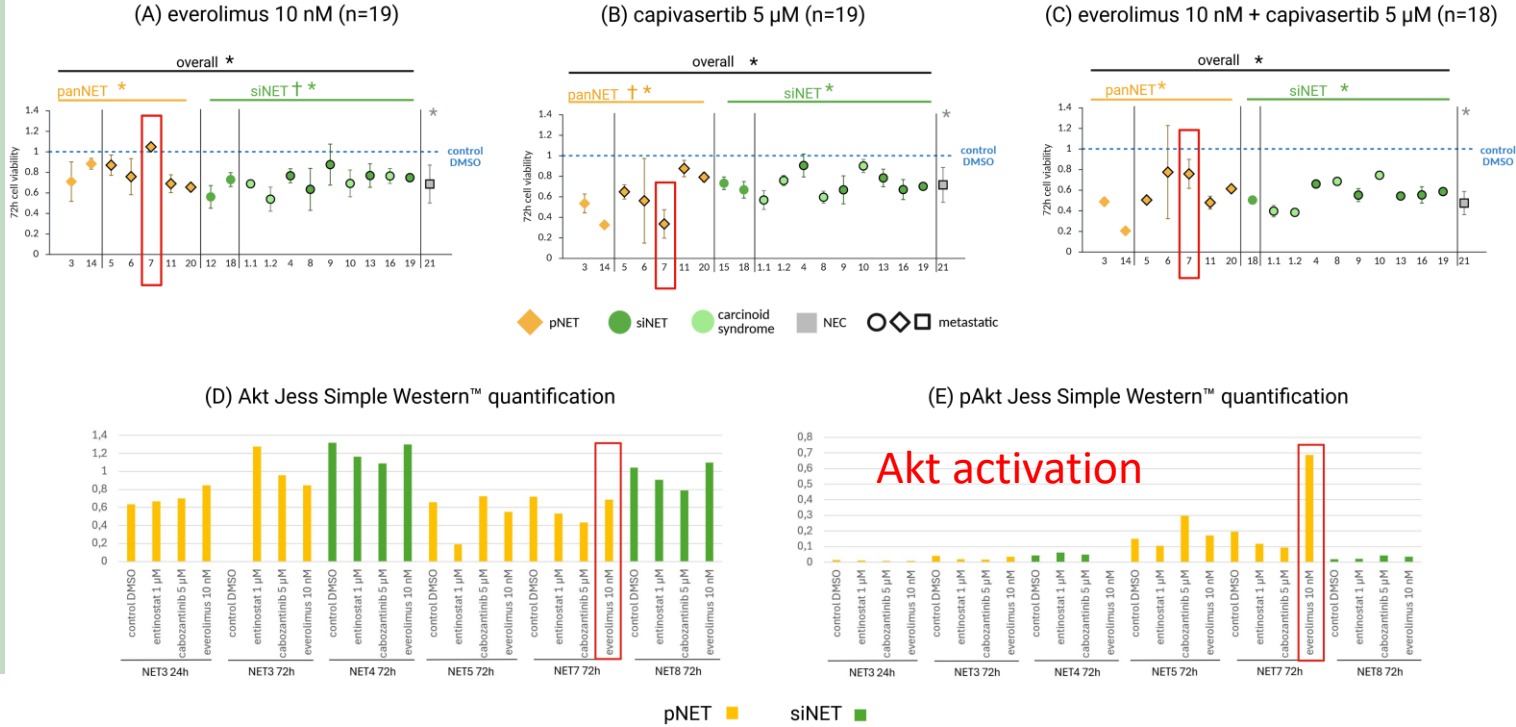
Wang,,…Nölting, *Eur J Endocrinol.* 2025

Transferability: Patient-derived GEP-NET platform – personalized drug testing

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM



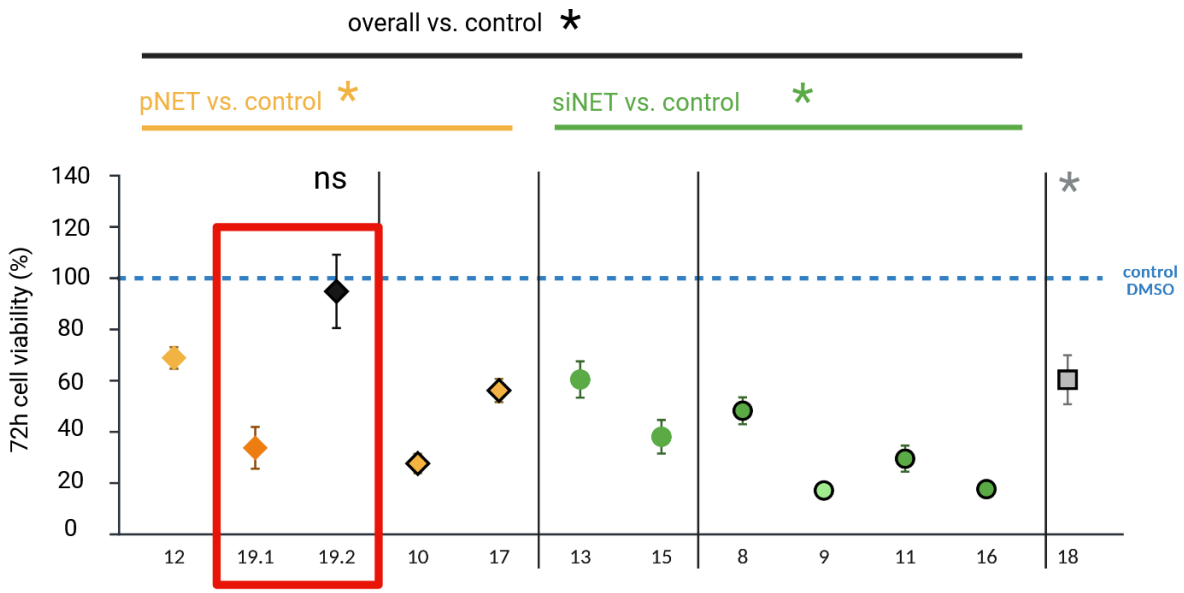
Targeted (combination) therapies: mTORi everolimus and AKTi capivasertib



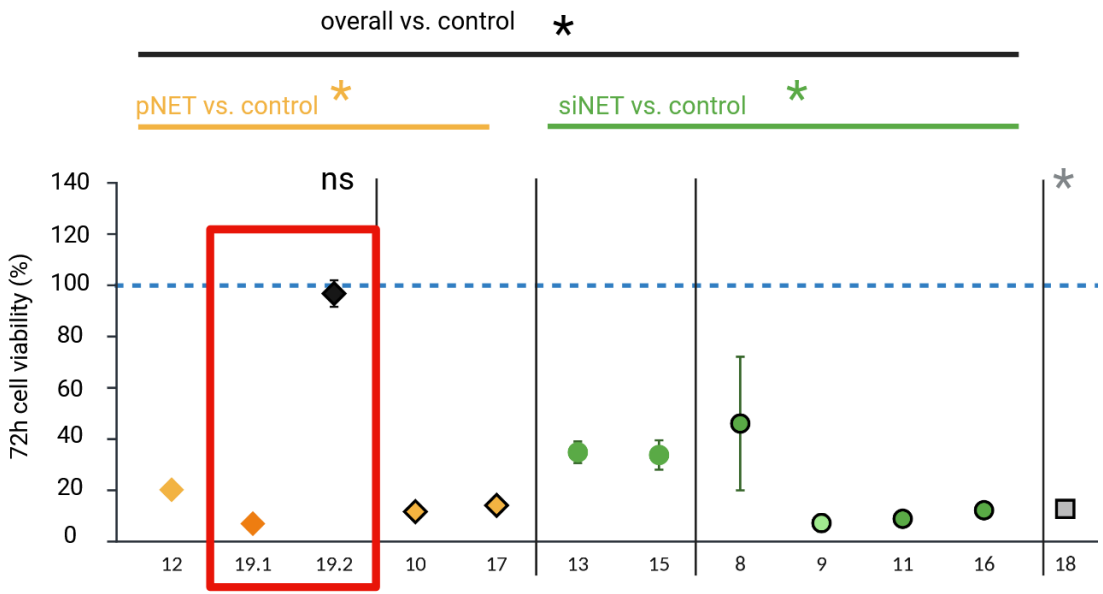
Auernhammer*, Wang*…Nölting,
*contributed equally,
JCEM 2026

Transferability: Patient-derived GEP-NET platform and 3D spheroids

(C) metformin 10 mM (n=12)



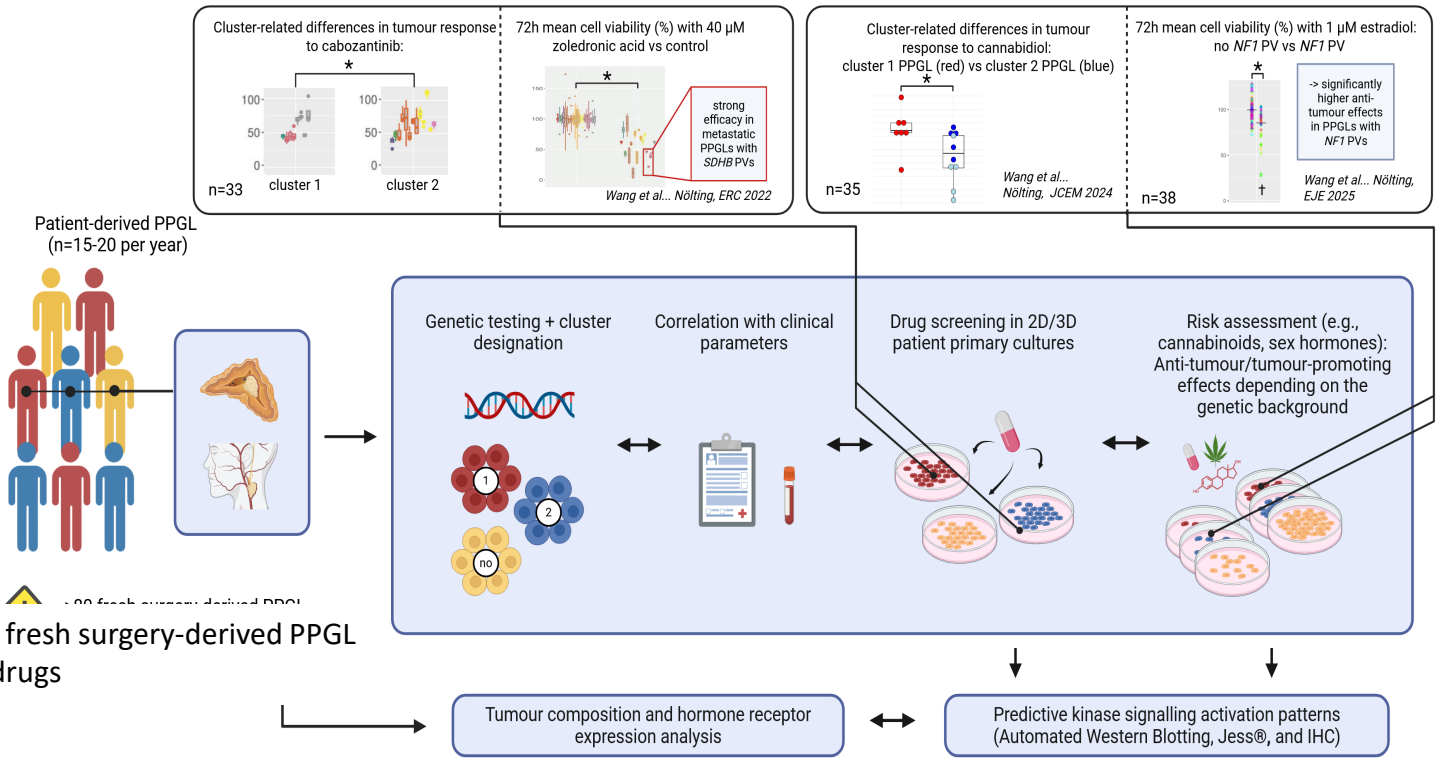
(D) metformin 50 mM (n=12)



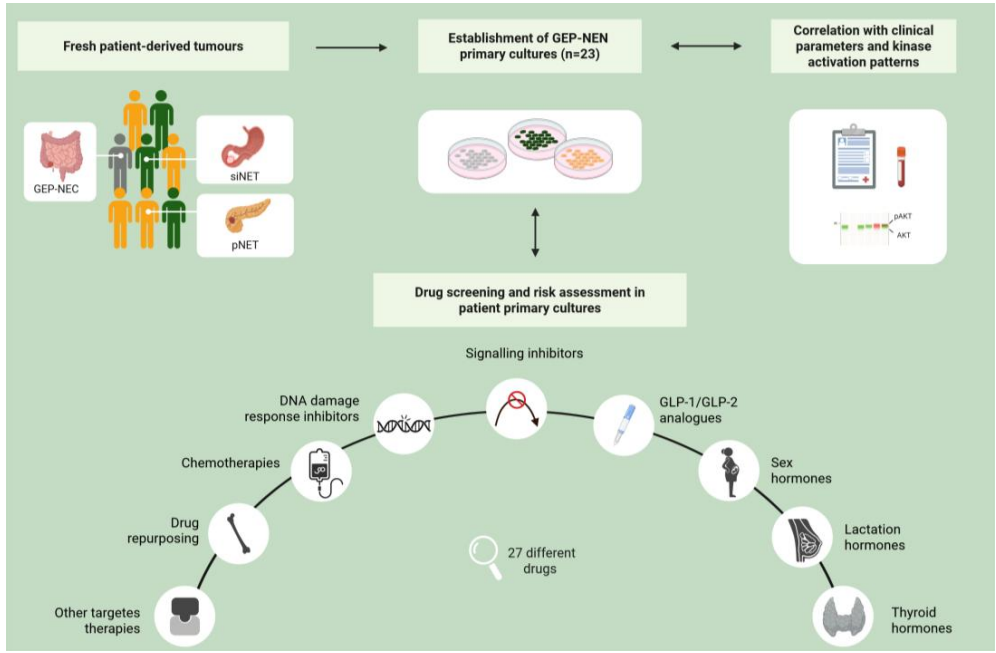
Nölting*, Luca*,…Hantel,
*contributed equally,
Endocr Relat Cancer 2025

Summary

- Rational: Prospective clinical studies extremely challenging in PPGL, no reliable human cell lines
- Patient-derived PPGL platform for next-generation personalized drug testing & risk assessment
- Direct clinical relevance for the individual patient
- Identification of genetically tailored therapies or risk factors for tumor-promoting effects
- Transferabilty of the PPGL patient-derived tumor platform to other (neuro)endocrine tumors



>110 fresh surgery-derived PPGL
>50 drugs



Auernhammer…Nölting, *JCEM,* 2026

Wang,…Nölting, *Endocr Relat Cancer* 2022; Wang,…Zitzmann*, Nölting*, *JCEM* 2024; Wang,…Nölting, *Eur J Endocrinol.* 2025; Wang,…Nölting, *Best Pract Res Clin Endocrinol Metab* 2025; Auernhammer*, Wang*,…Nölting, *JCEM* 2026, *contributed equally

Prof. Dr. med. Svenja Nölting
Senior Consultant

Lead Clinician for Endocrine Tumor Diseases
Department of Endocrinology, Diabetology and Clinical Nutrition
University Hospital of Zurich (USZ), University of Zurich (UZH)

Co-Head of the Neuroendocrine Tumor Board
Co-Head of the Endocrine and Neuroendocrine Tumor Center
ENETS Center of Excellence Zürich
Comprehensive Cancer Center Zürich

Discussion

Closing comments

Take-home messages

- Germline genetic analysis is essential for all phaeochromocytomas and especially paragangliomas.
- Targeted therapies now play a significant role in treatment.
- Molecular agents such as TKIs, belzutifan and PRRT need individualisation.
- Patient-derived tumour platforms may help personalise therapy.
- Therapy sequencing remains unclear: guideline assist, MDTs essential.

A BIG "Thank You" to

- ✓ Our speakers and moderators
- ✓ The ENETS Office team: Martina FLESCHEN, Ulrike KNELL, Anna MALDRYK & Leah MATTHEWS
- ✓ The ENETS Education Group
- ✓ YOU, our valued participants

The ENETS Education Group

- **Simona GLASBERG (Lead)** | Endocrinology | Israel
- **Mairéad McNAMARA (Lead)** | Oncology | United Kingdom
- Eric BAUDIN | Endocrinology | France
- Emanuel CHRIST | Endocrinology | Switzerland
- Timm DENECKE | Radiology | Germany
- Antongiulio FAGGIANO | Endocrinology | Italy
- Gregory KALTSAS | Endocrinology | Greece
- Anna KOUMARIANOU | Oncology | Greece
- Francesco PANZUTO | Gastroenterology | Italy
- Margot TESSELAAR | Oncology | The Netherlands

PLEASE SAVE THE DATE!

23rd Annual ENETS Conference

4 – 6 March 2026 in Krakow, Poland

Register now!

https://enetsconference.org

Connect with ENETS
→ Follow us on social media!

www.linkedin.com/company/european-neuroendocrine-tumor-society-ev/

www.facebook.com/european.neuroendocrine.tumor.society

@enets.bsky.social
https://bsky.app/profile/enets.bsky.social

Join us online!

Sponsor acknowledgements

The ENETS Webinar Series 2026 is supported by Bioscientifica, Camurus, IPSEN, ITM, Novartis, Sanofi and SERB SAS with unrestricted educational grants.

Thank you for attending this webinar!

We'd love to hear your thoughts!

Please take a moment to complete the **feedback form** when you leave the Zoom room.

To obtain your **certificate with the European CME credits** for this webinar, please contact the ENETS Office at office@enets.org.

Curious about our next webinars?

Visit the ENETS website for all the details!