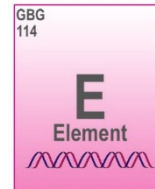


Lieber früh als nie – Warum frühes molekulares Testen so wichtig ist

Prof. Dr. med. Thomas Decker
Medizinischer Geschäftsführer
MVZ für Hämatologie und Onkologie
Ravensburg GmbH Studienzentrum



Case report-1

56 jährige Patientin

Schmerzen BWS, Thoraxwand li., zunehmend seit mehreren Monaten

Z.n. Mamma Ca Mitte 2021

cT1c, cN+, ER100%, PR 100%, Her2 neu 0, KI67 50%, G3

4 x EC, Paclitaxel x 12 neoadjuvant

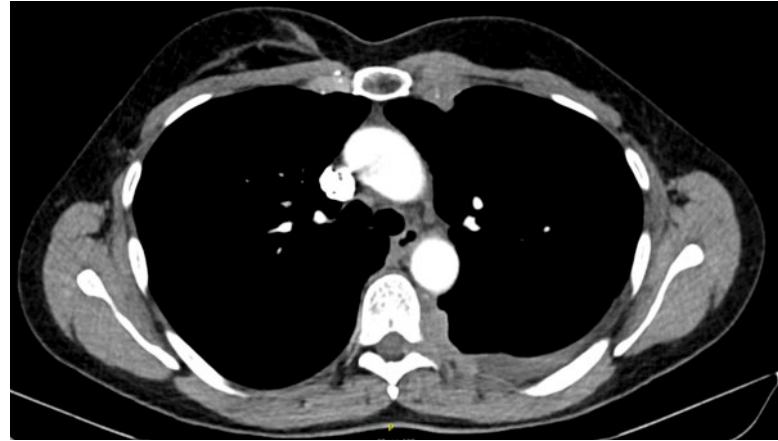
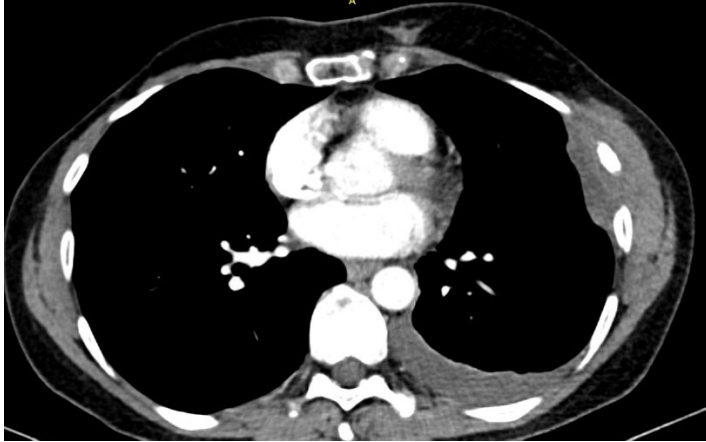
BET, ALND

ypT1c,ypN1a (mi), L1

Zoladex, Letrozol , Abemaciclib (2 Jahre)

bis Anfang 25, endokrine Therapie wegen Nebenwirkungen beendet

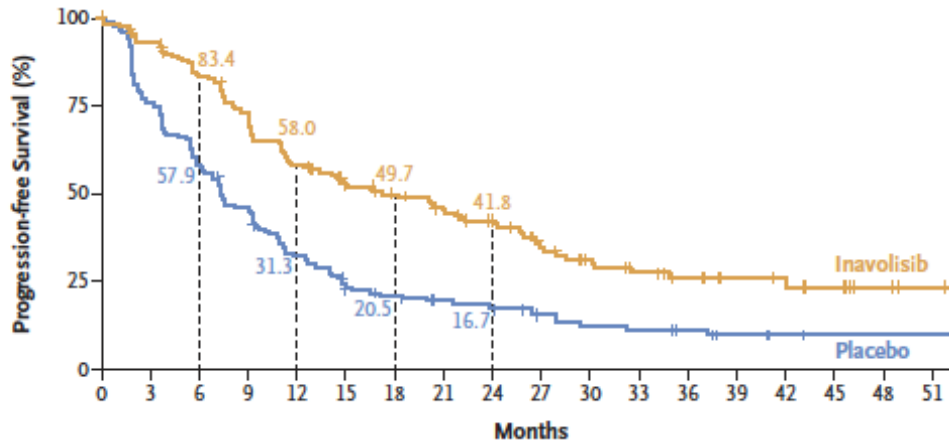
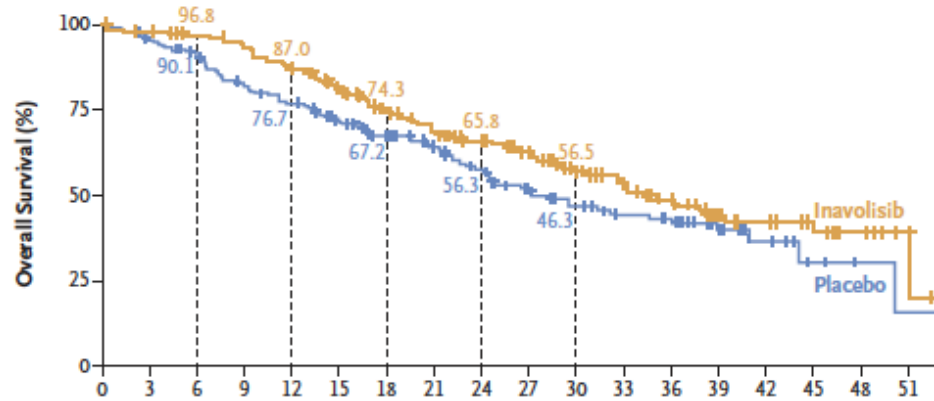
Case report-1



Histo: NST Mamma Ca, ER 90%, PR 0%, Her2: 0, G3, Ki67 60%

**Liquid Biopsy: keine ESR1- Mutation, keine PIK3CA Mutation
BRCA-2 Mutation**

Rationale PIK-3CA

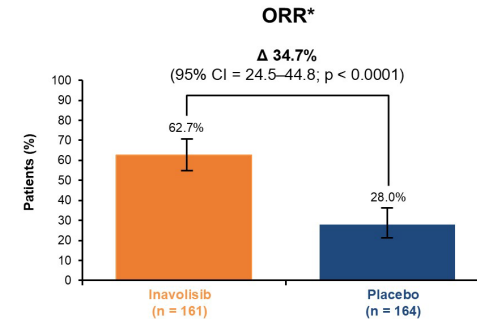


ORIGINAL ARTICLE

Overall Survival with Inavolisib in *PIK3CA*-Mutated Advanced Breast Cancer

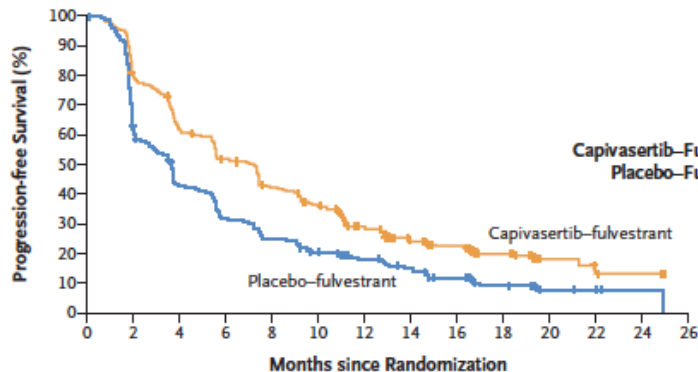
Endokrine Resistenz

Jhaveri et al, NEJM 2025; 392



Rationale PIK-3CA/PTEN/AKT

A Overall Population



	No. of Patients	No. of Events	Median Progression-free Survival (95% CI) <i>mo</i>
Capivasertib + fulvestrant	355	258	7.2 (5.5–7.4)
Placebo + fulvestrant	353	293	3.6 (2.8–3.7)

Adjusted hazard ratio for disease progression or death, 0.60 (95% CI, 0.51–0.71)

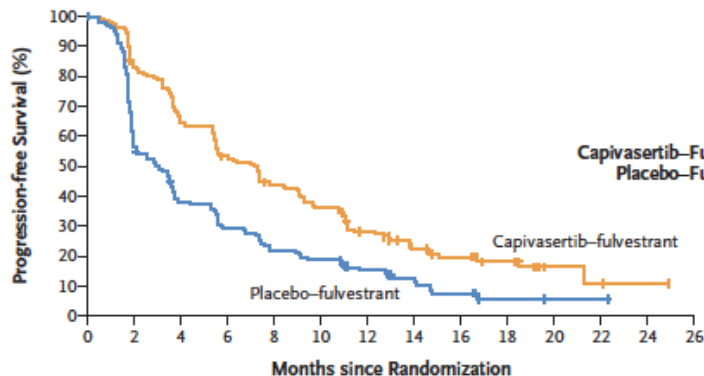
P<0.001

ORIGINAL ARTICLE

Capiasertib in Hormone Receptor-Positive Advanced Breast Cancer

N.C. Turner, M. Oliveira, S.J. Howell, F. Dalenc, J. Cortes, H.L. Gomez Moreno, X. Hu, K. Jhaveri, P. Krivorotko, S. Loibl, S. Morales Murillo, M. Oker, Y.H. Park, J. Sohn, M. Toi, E. Tokunaga, S. Yousef, L. Zhukova, E.C. de Bruin, L. Grinstead, G. Schiavon, A. Foxley, and H.S. Rugo, for the CAPitello-291 Study Group*

B Patients with AKT Pathway-Altered Tumors



	No. of Patients	No. of Events	Median Progression-free Survival (95% CI) <i>mo</i>
Capivasertib + fulvestrant	155	121	7.3 (5.5–9.0)
Placebo + fulvestrant	134	115	3.1 (2.0–3.7)

Adjusted hazard ratio for disease progression or death, 0.50 (95% CI, 0.38–0.65)

P<0.001

Rationale ESR-1: EMERALD Studie

Inclusion:

- Advanced/metastatic ER+/HER2- breast cancer
- Progressed or relapsed on 1 or 2 lines of endocrine therapy, which was given in combination with CDK4/6 Inhibitor for advanced disease
- ECOG 0/1

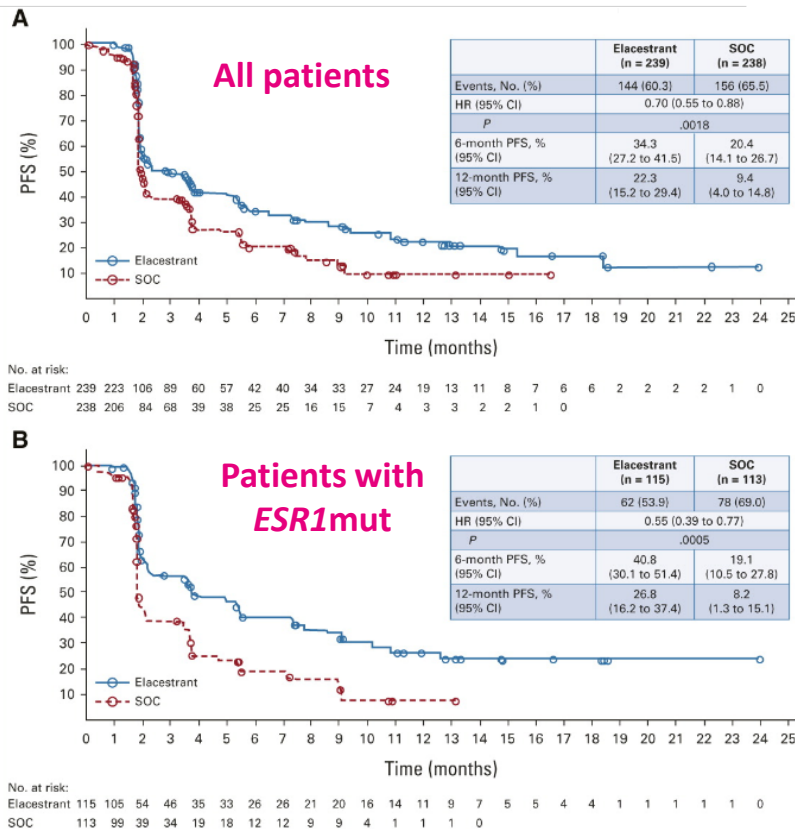
R 1:1
N=239

Elacestrant
400 mg qd

SOC:
Fulvestrant
Exemestan
Anastrozol
Letrozol

Stratification:

- *ESR1* Mutation
- Prior treatment with fulvestrant
- Presence of visceral metastases



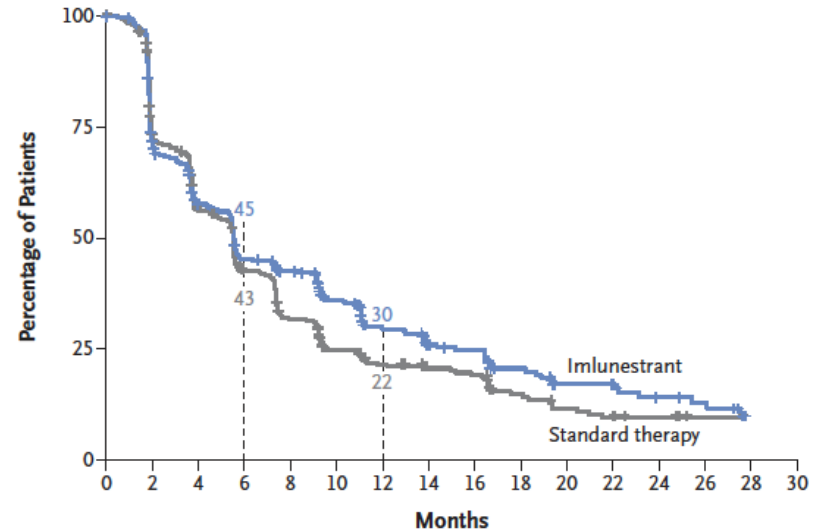
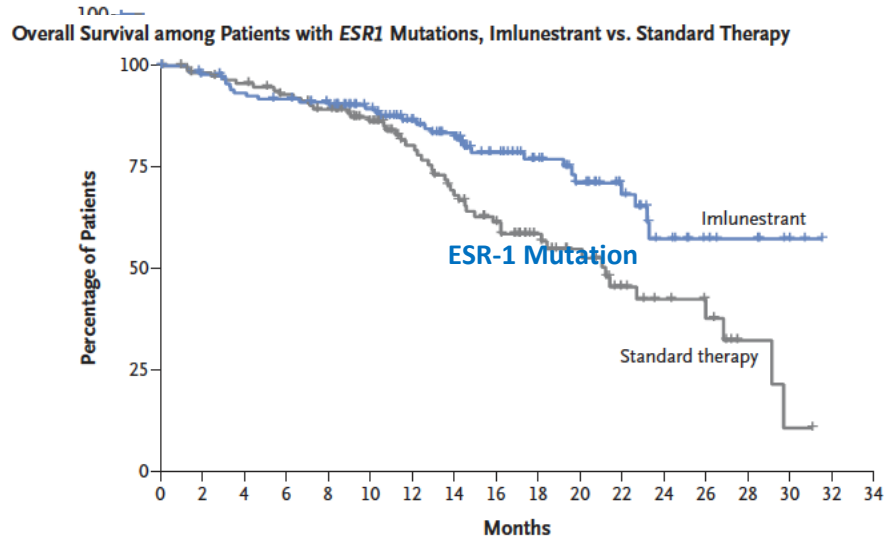
Rationale ESR-1: Ember3 Studie

...und Giredestrant, Camizestrant, Vepdegestrant...

ORIGINAL ARTICLE

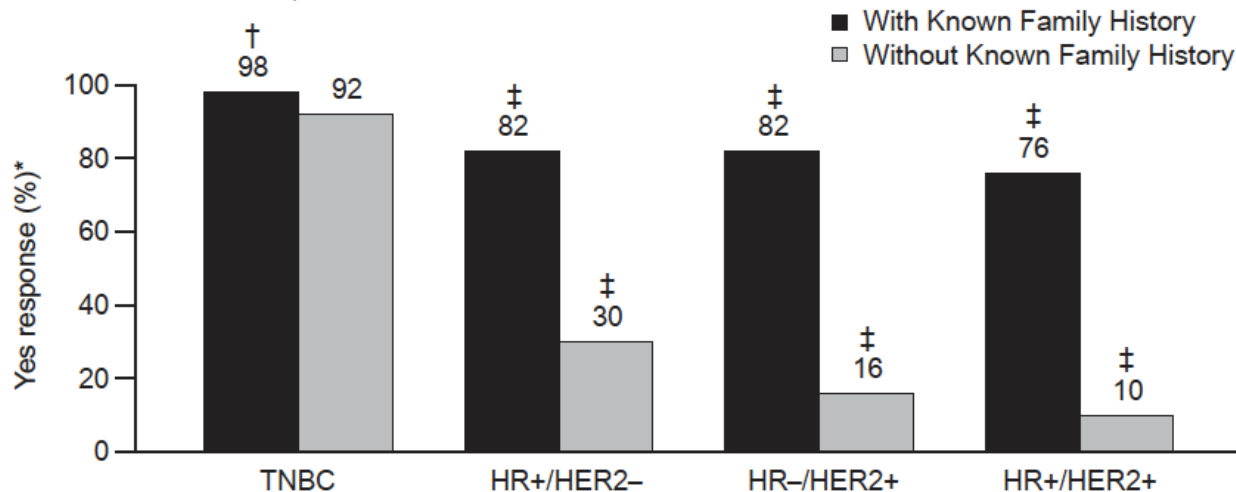
Imlunestrant with or without Abemaciclib in Advanced Breast Cancer

NEJM 2024
EMA Zulassung 01/2026



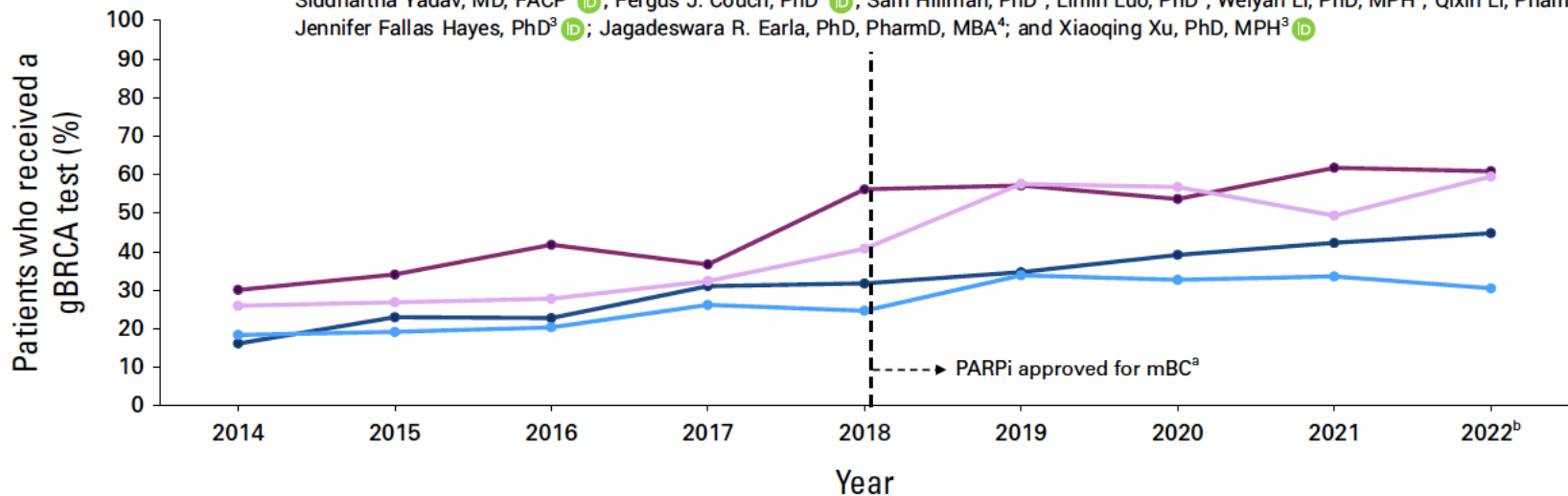
Awareness and Availability of Routine Germline *BRCA1/2* Mutation Testing in Patients with Advanced Breast Cancer in Germany

Michael P. Lux^{a,b,c} Thomas Decker^d Eva Diana Runkel^e Alexander Niyazov^f
Ruben G.W. Quek^g Norbert Marschner^h Nadia Harbeckⁱ



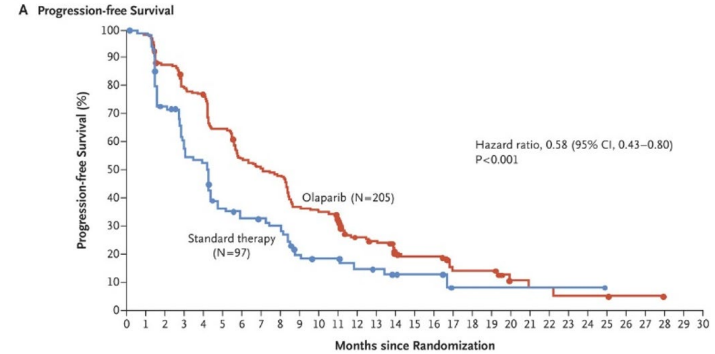
Real-World Germline BRCA Testing, Poly(ADP-ribose) Polymerase Inhibitor Utilization, and Survival Outcomes in Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer

Siddhartha Yadav, MD, FACP¹ ; Fergus J. Couch, PhD¹ ; Sam Hillman, PhD²; Linlin Luo, PhD³; Weiyan Li, PhD, MPH³; Qixin Li, PharmD, MS³; Jennifer Fallas Hayes, PhD³ ; Jagadeswara R. Earla, PhD, PharmD, MBA⁴; and Xiaoqing Xu, PhD, MPH³ 



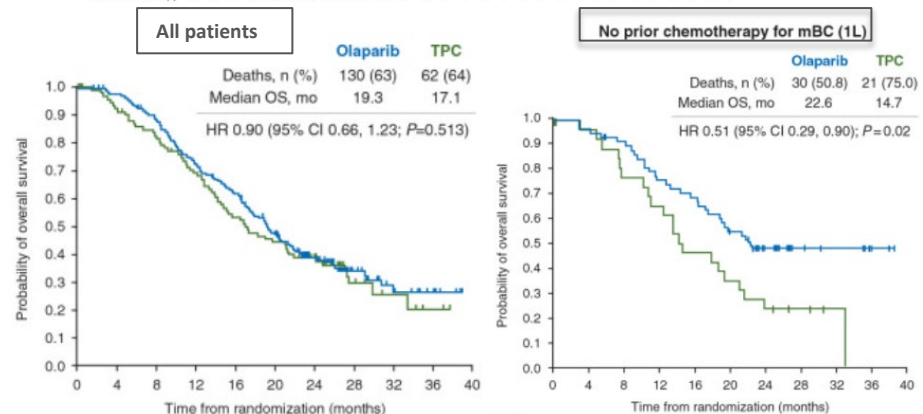
Rationale II – BRCA Testung

- OlympiAD Studie: Olaparib zeigt bei Patientinnen mit HER2- MBC und *gBRCA1/2 Mutation* ein verbessertes medianes PFS, höhere Ansprechraten und eine geringere Toxizität im Vergleich zu SOC.¹
- Potenzielle Verbesserung im OS bei Patientinnen ohne vorherige CTX in der M1 Situation und insgesamt gute Langzeitverträglichkeit.²



No. at Risk

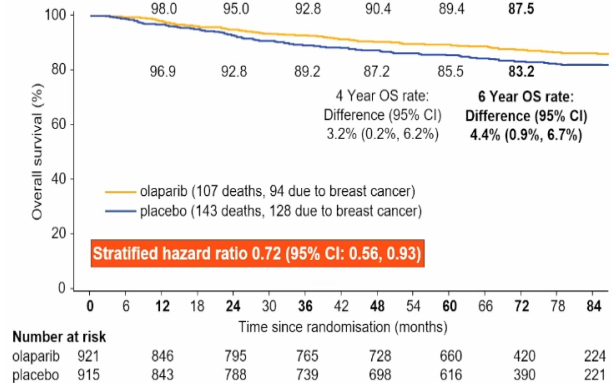
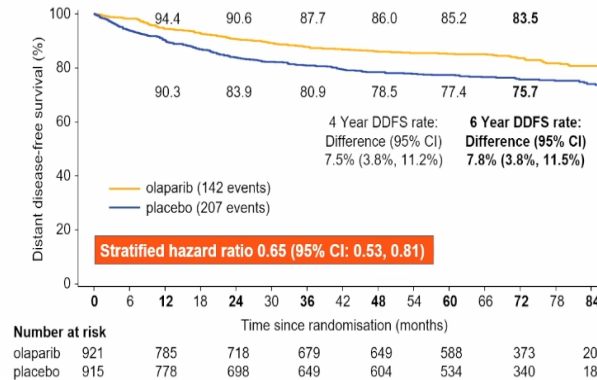
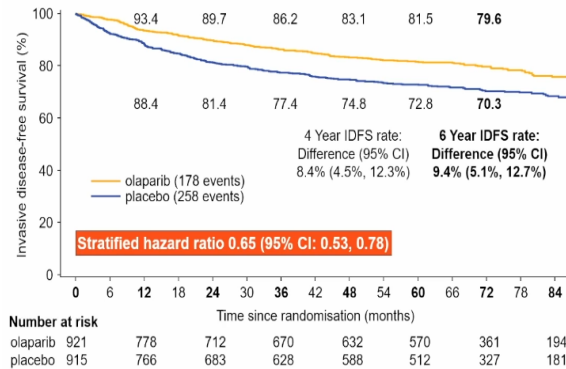
	205	201	177	159	154	129	107	100	94	73	69	61	40	36	23	21	21	11	11	11	4	3	3	2	2	1	1	1	0
Olaparib	205	177	159	154	129	107	100	94	73	69	61	40	36	23	21	21	11	11	11	4	3	3	2	2	1	1	1	1	0
Standard therapy	97	88	63	46	44	29	25	24	21	13	11	11	8	7	4	4	4	1	1	1	1	1	1	1	0	0	0	0	0



1. Robson. N Engl J Med. 2017; 2. Robson. Ann Oncol. 2019

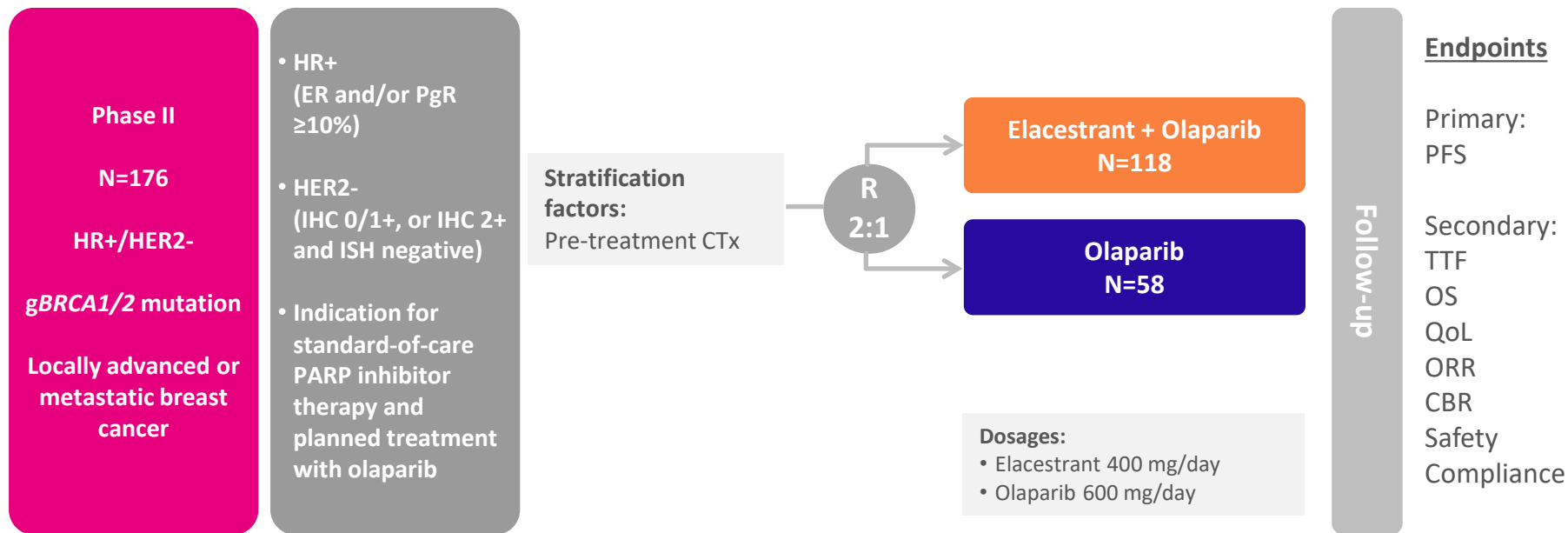
Rationale – BRCA

- Die adjuvante Therapie mit Olaparib kombiniert mit ET in der OlympiA Studie ist effektiv und sicher.¹
- Nach längerem FU (10 Jahre) zeigt sich eine klinische bedeutsame Verbesserung in iDFS, DDFS und OS.^{2,3}



1. Tutt. N Engl J Med. 2021; 2. Geyer. Ann Oncol. 2022; 3. Garber. SABCS. 2024

ELEMENT Study Design



Einschluss-/ Ausschlusskriterien

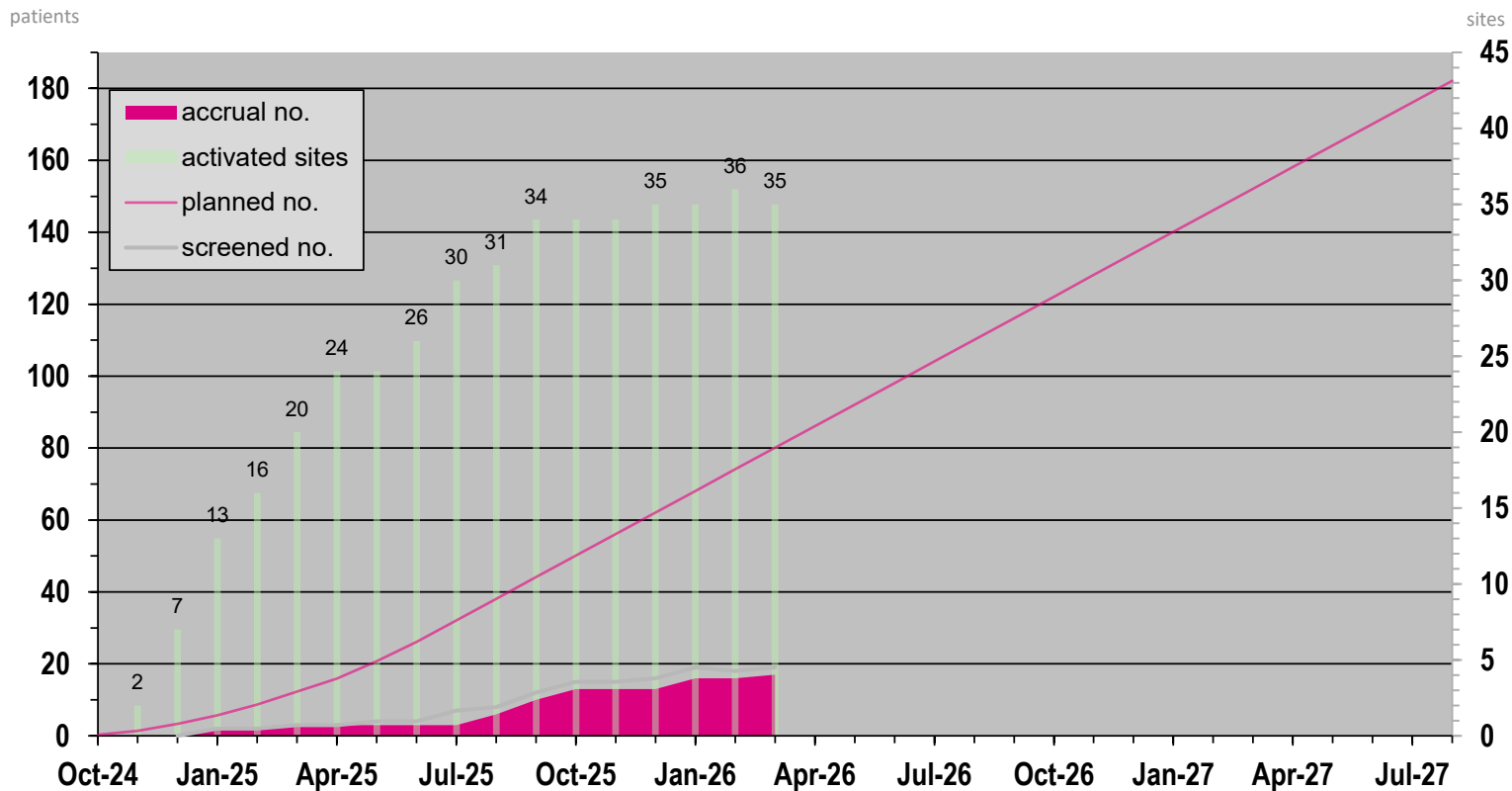
Einschlusskriterien (Auswahl)

- HR+ (ER und/oder PgR $\geq 10\%$) und HER2- (IHC 0/1+, oder 2+ ohne ISH-Amplifikation) MBC – lokale Bestätigung
- gBRCA1/2-Mutationen – lokale Testung
- Indikation für die Standardtherapie mit PARP-Inhibitoren und geplante Behandlung mit Olaparib
- ECOG PS 0-2
- Lebenserwartung >6 Monate

Ausschlusskriterien (Auswahl)

- Symptomatische viszerale Metastasierung
- Vorherige Behandlung mit PARP-Inhibitoren
- Unkontrollierter Bluthochdruck (SBP > 140 mmHg oder DBP > 90 mmHg)
- Thromboembolisches Ereignis in den letzten 6 Monaten (z.B. TVT, LAE)
- Unkontrollierte signifikante aktive Infektionen

Rekrutierung (Stand 01.03.2026) n = 17



Rekrutierer

Zentrum	Hauptprüfer/in	Patienten pro Zentrum
0003 National Center for Tumor Diseases (NCT)	PD Dr. Michel	5
0069 Klinik der J. W. Goethe Universität	Prof. Dr. med Solbach	2
0411 Marien Hospital Witten	PD Dr. Graeser	2
0743 MVZ für Hämatologie und Onkologie Ravensburg GmbH	Prof. Dr. Decker	2
0216 Kli. Essen-Mitte Ev. Huyssens-Stift./Knapps.GmbH, Kl. f. Senologie/Brustz.	Dr. Frindte	1
0268 Klinikum Bayreuth GmbH	Prof. Dr. Mundhenke	1
0274 Universitätsklinikum Tübingen, Department für Frauengesundheit	Prof. Dr. Hartkopf	1
0365 Universitätsklinikum des Saarlandes Homburg	Prof.Dr. Radosa	1
0400 Universitätsklinikum Essen	Prof. Dr. Bittner	1
0459 Haematologie-Onkologie im Zenrtum MVZ GmbH	Dr. Heinrich	1

Zeitplan

Planung	
Anzahl der Zentren	Ca. 40 Zentren für eine Rekrutierung von 6 Patienten pro Monat
First Patient In (FPI):	Q4/2024
Rekrutierungszeitraum	Ca. 36 Monate (Q4/2024 – Q4/2027)
Studiendauer	Ca. 48 Monate (36 Monate Rekrutierung + 12 Monate Follow-up)
Region	Deutschland

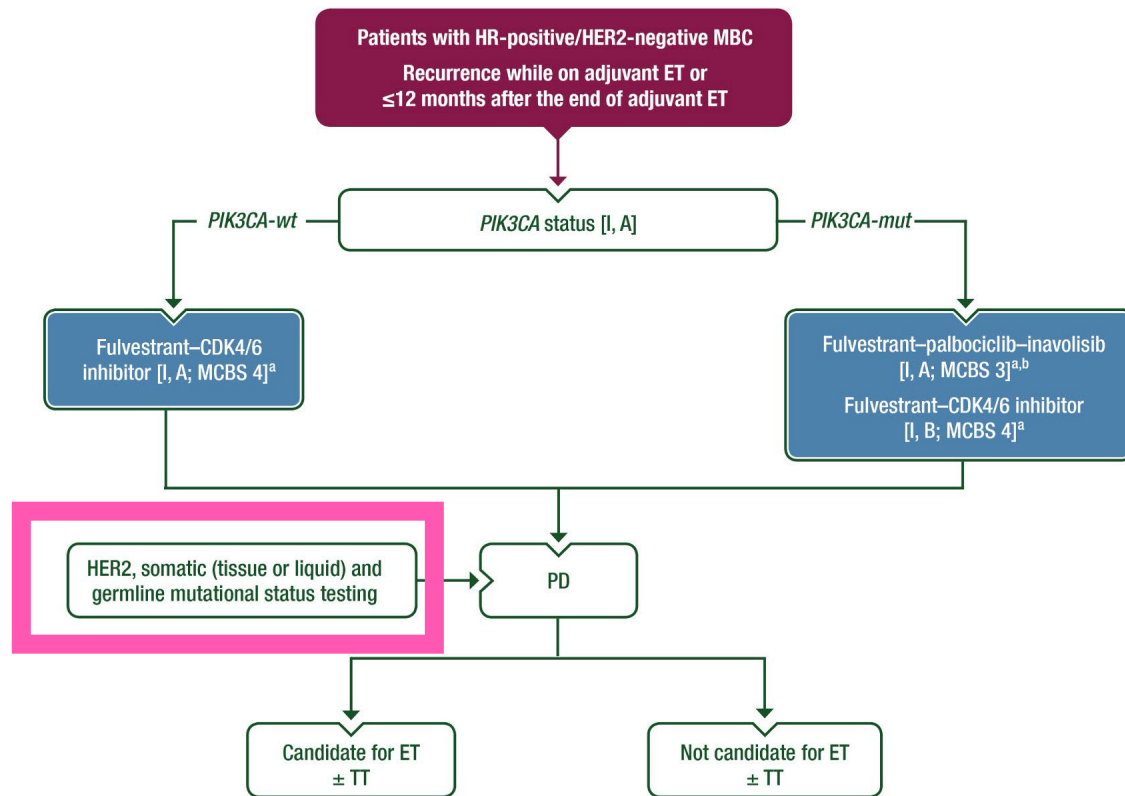
CLINICAL PRACTICE GUIDELINES

ESMO Metastatic Breast Cancer Living Guideline
v1.2 April 2025

HR-positive/HER2-negative MBC: Recurrence While on Adjuvant ET or ≤12 Months After the End of Adjuvant ET

^aOFS if the patient is menopausal

^bFDA approved, not EMA approved



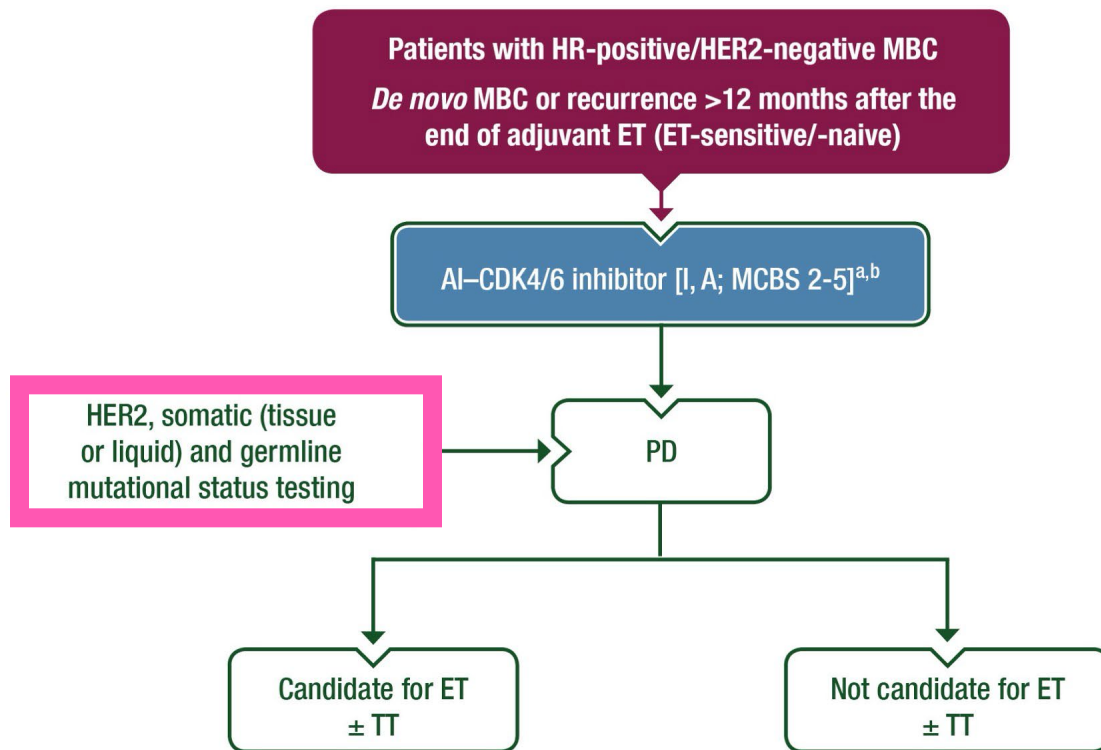
CLINICAL PRACTICE GUIDELINES

ESMO Metastatic Breast Cancer Living Guideline
v1.2 April 2025

HR-positive/HER2-negative: **De Novo MBC or Recurrence >12 Months After the End of Adjuvant ET (ET-sensitive/-naive)**

^aOFS if the patient is premenopausal

^bIn exceptional cases (e.g. CDK4/6 inhibitor is not available in first-line), endocrine therapy alone in followed by fulvestrant combined with CDK4/6 inhibitor upon disease progression may be an option for MBC *de novo* or recurring >12 months after the end of adjuvant endocrine therapy [I, C] (Sonke, 2024)

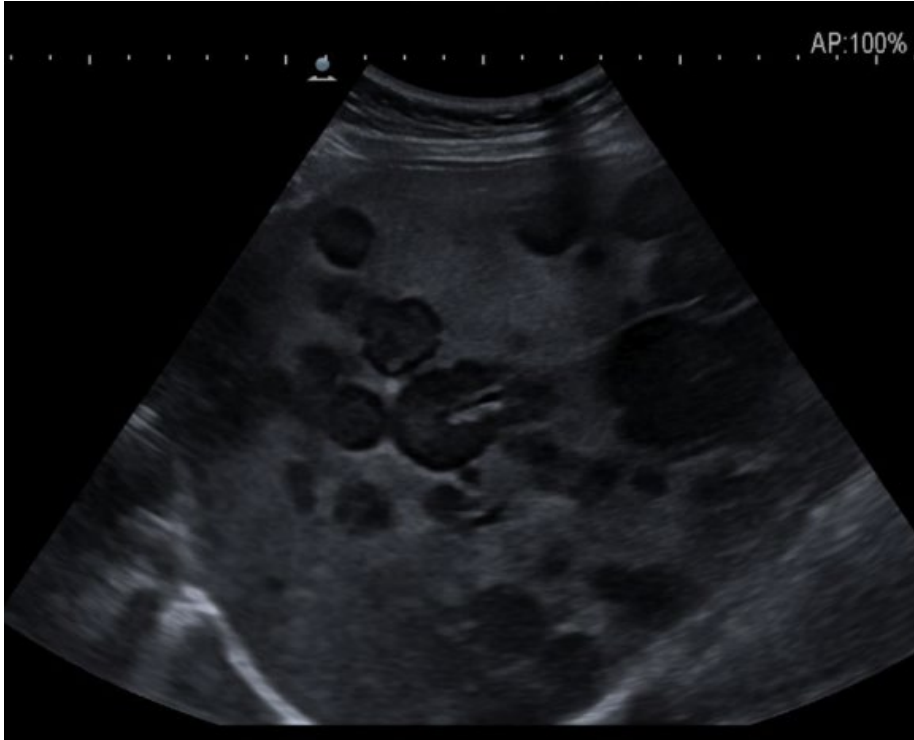


NGS statt Einzeltestung?

Table 3. List of genomic alterations level I/II according to ESCAT in advanced breast cancer

Gene	Alteration	Estimated prevalence	ESCAT score	Drug class matched	References
ERBB2	Amplifications	15%-20%	IA	Anti-HER2 monoclonal antibodies HER2 TKIs Anti-HER2 ADCs	Baselga et al., <i>N Engl J Med</i> 2012 ⁵⁵ Krop et al., <i>Lancet Oncol</i> 2014 ⁵⁶ Lin et al., <i>J Clin Oncol</i> 2020 ⁵⁷ Saura et al., <i>J Clin Oncol</i> 2020 ⁵⁸ Rugo et al., <i>JAMA Oncol</i> 2021 ⁵⁹
	Hotspot mutations	4%	IIB	Pan-HER TKIs Anti-HER2 ADCs	Hyman et al., <i>Nature</i> 2018 ⁵¹ Smyth et al., <i>Cancer Discov</i> 2020 ⁶⁰ Li et al., <i>Ann Oncol</i> 2023 ⁶¹
PIK3CA	Hotspot mutations	30%-40%	IA (ER-positive HER2-negative ABC)	α -specific PI3K inhibitors*	André et al., <i>N Engl J Med</i> 2019 ⁶² Rugo et al., <i>Lancet Oncol</i> 2021 ⁶³ Turner et al., <i>N Engl J Med</i> 2023 ⁷⁰
ESR1	Mutations	30%-40%	IA (ER-positive HER2-negative ABC resistant to AI)	SERDs	Bidard et al., <i>J Clin Oncol</i> 2022 ⁶⁴ Bardia et al., <i>Cancer Res</i> 2023 ⁶⁵
BRCA1/2	Germline pathogenic/likely pathogenic variants	4%	IA	PARP inhibitors	Litton et al., <i>N Engl J Med</i> 2018 ⁶⁶ Robson et al., <i>Eur J Cancer</i> 2023 ⁶⁷
	Somatic mutations	3%	IIB	PARP inhibitors	Tung et al., <i>J Clin Oncol</i> 2020 ⁶⁸
PTEN	Mutations/deletions	7%	I/II	AKT inhibitors	Schmid et al., <i>J Clin Oncol</i> 2020 ⁶⁹ Turner et al., <i>N Engl J Med</i> 2023 ⁷⁰
AKT1	Mutations (p. E17K)	5%	I/II	AKT inhibitors	Kalinsky et al., <i>JAMA Oncol</i> 2021 ⁷¹ Turner et al., <i>N Engl J Med</i> 2023 ⁷⁰
PALB2	Germline pathogenic/likely pathogenic variants	1%	IIB	PARP inhibitors	Tung et al., <i>J Clin Oncol</i> 2020 ⁶⁸ Gruber et al., <i>Nat Cancer</i> 2022 ⁷²

Besser früh als spät testen: Rationale...



Kontakt

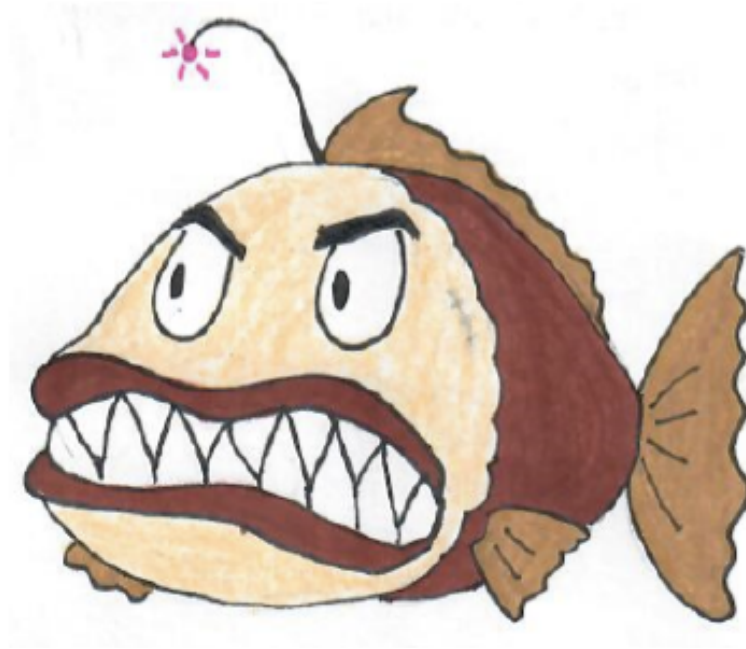
Leiter der Klinischen Prüfung:

Prof. Dr. Thomas Decker
Studienzentrum Onkologie Ravensburg

Projektmanagement:

Dr. Laura Steinmann
GBG Forschungs GmbH, Neu-Isenburg
E-Mail: ELEMENT@gbg.de

Ihr Vetter, der
Furzfischfressfischfischfressfeindfangfischforellenfamilien-
fechtfischfriseurenvetter war jedoch sehr feige und der Feind
aller Fische.



Früh testen...

Wer ein PDF vom Furfischforlesebuch haben möchte:

Email an:

Alle anderen:

Besser früh als spät testen
Besser spät als nie!!