# Neue zielgerichtete Therapien in der Brustkrebsforschung – was wir von diesen Therapien erwarten

Dr. Johannes Holtschmidt

GBG

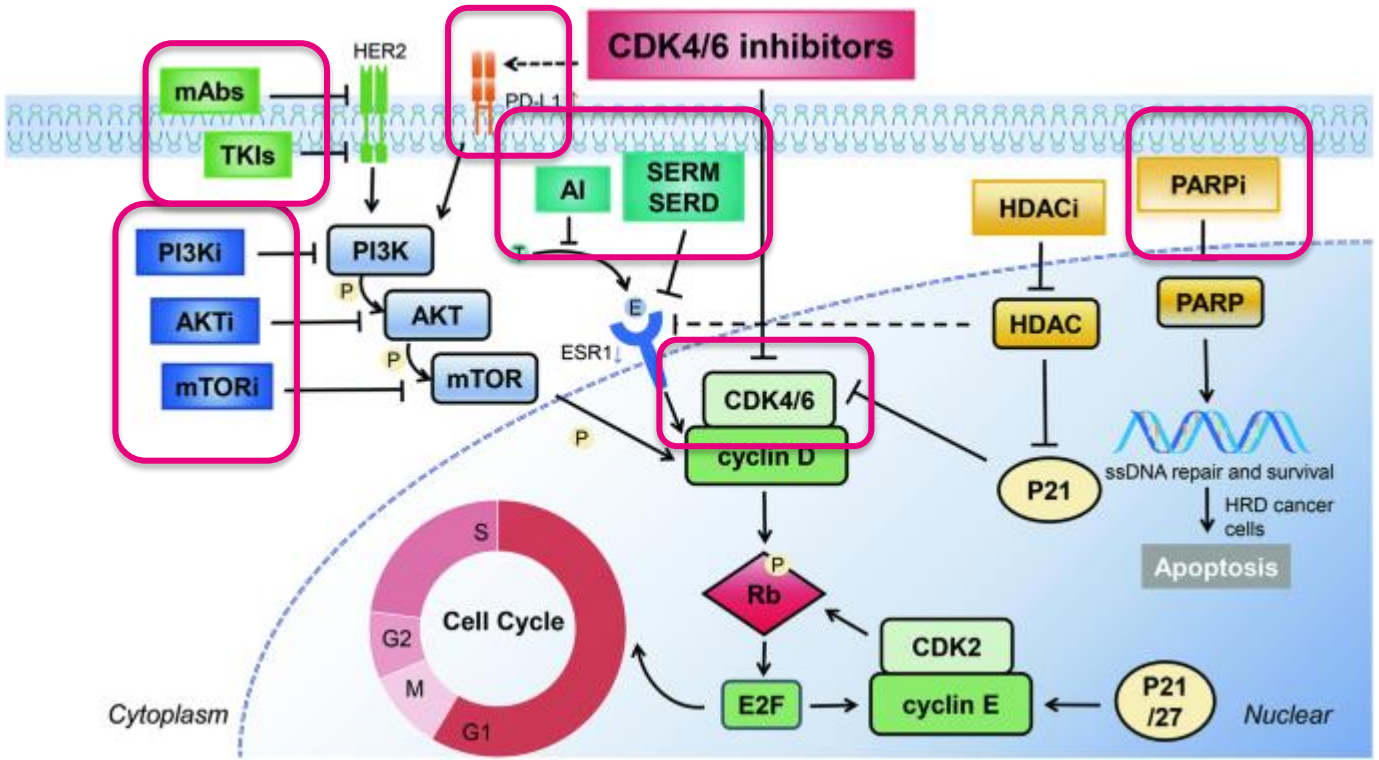
# Conflict of Interest

22. ASM
FRANKFURT /MAIN

- Employee of: German Breast Group (GBG) Forschungs GmbH, Neu-Isenburg, Germany.
- Consulting or Advisory Role: Pfizer, Roche, Novartis, Seattle Genetics, Lilly, AstraZeneca/MedImmune, Bristol-Myers Squibb, Abbvie, Amgen, Diiachi Sankyo, GlaxoSmithKline, Eisai Europe, Relay Therapeutics, Sanofi, Olema Pharmaceuticals, Menarini Group, MSD Oncology, BeiGene, Bicycle Therapeutics, BMS, Jazz Pharmaceuticals (paid to institution).
- Speakers' Bureau: AstraZeneca, Daiichi Sankyo Europe GmbH, Novartis, Pfizer, Roche, Gilead Sciences, Seattle Genetics, Menarini Group, Agendia, Bayer, Medscape, MSD, Stemline Therapeutics, Streamedup! (paid to institution).
- Research Funding: Abbvie, AstraZeneca, Celgene, Novartis, Pfizer, Daiichi Sankyo, Gilead, MolecularHealth, Menarini Group, Greenwich LifeSciences (paid to institution).
- Patents, Royalties, Other Intellectual Property: Patent Pending EP14153692.0, Patent Pending EP21152186.9, Patent Issued EP15702464.7, Patent Pending EP19808852.8, Digital Ki67 Evaluator, VM Scope GmbH (paid to institution).
- Personal disclosures: personal fees and non-financial support from Daiichi Sankyo, non-financial support from Hologic, personal fees from MSD Oncology, personal fees from Novartis, personal fees from Palleos Health Care, personal fees from Pfizer, personal fees from Roche Pharma, personal fees from Seagen and personal fees from Bayer AG.

# Molekulare Ziele für Therapien bei Brustkrebs

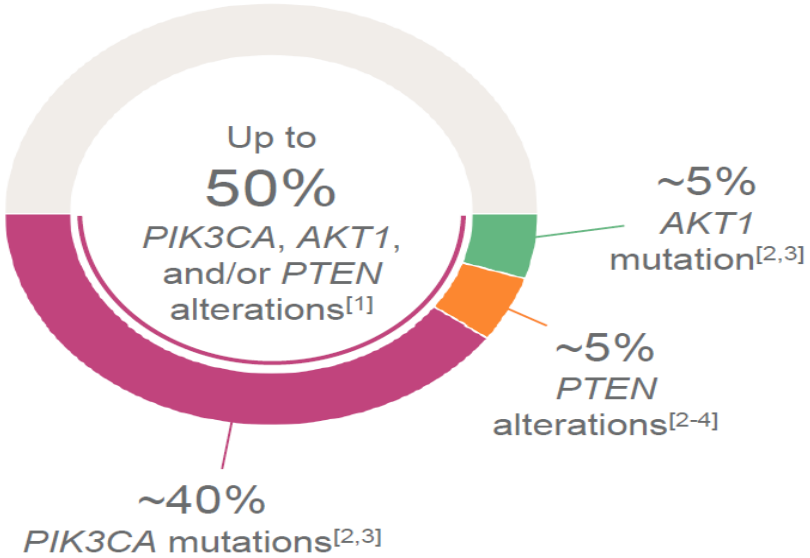





Wang et al. Cancer Gene Therapy 2024

# Neue endokrine Therapien (Auszug)

# PI3K Pathway Alterationen



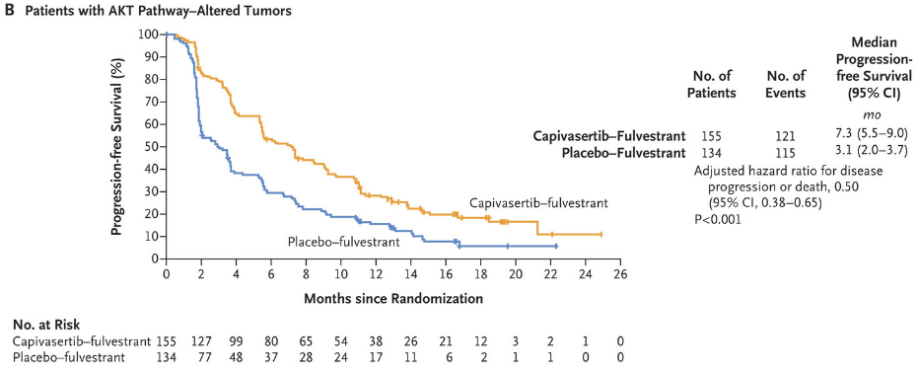

| Gene | Key Genetic Alterations | Consequence |
|---|---|---|
| *PIK3CA*[2] | Point mutations of *PIK3CA* | Gain of function of PI3K |
| *AKT1*[3] | Point mutations of *AKT1* | Gain of function of AKT protein |
| *PTEN*[4] | Point mutations, large deletions, and genomic rearrangements involving *PTEN* | Loss of function of PTEN protein |

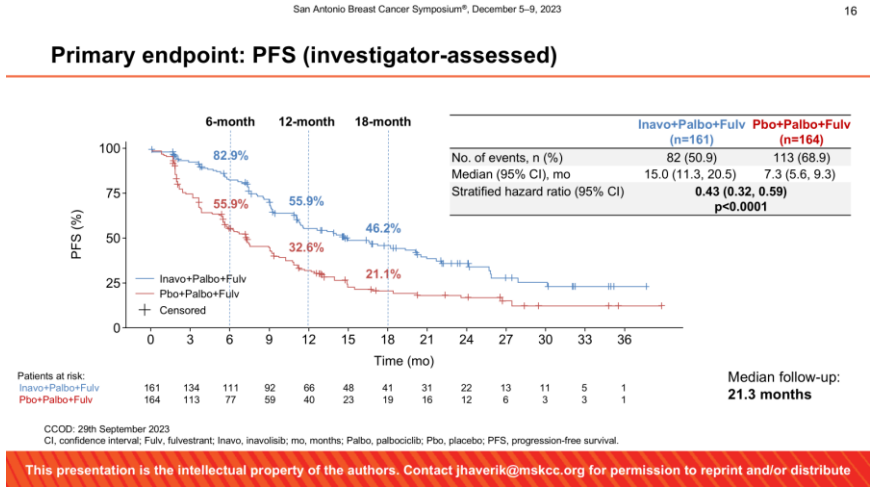
1. Martorana F, et al. Front Pharmacol. 2021;12:662232; 2. MiricescuD, et al. Int J Mol Sci. 2020;22:173; 3. Smyth LM, et al. Cancer Discov. 2020;10:526-535; 4. Chen J, et al. Front Oncol. 2022;12:825484

# Inavolisib und Capivasertib



- Inavolisib (Inavo120) und Capivasertib (CAPItello291) haben ihre Wirksamkeit bei Vorhandensein von *PIK3CA* bzw. *PIK3CA/PTEN/AKT1 Alterationen* bei metastasierten HRpos/HER2neg Mammakarzinom bewiesen.



# Inavolisib und Capivasertib



- Neben der Zulassung in dieser Situation mit Fulvestrant +/- Palbociclib wird die Kombination mit modernen endokrinen Therapien klinisch relevant

- ADC sind auf dem Vormarsch in frühe Linien
- Orale Therapien sind oftmals besser für die QoL

- T-DXd oder moderne kombinierte ET bestehend aus moderner ET + PIK3 gerichteter Theapie in der 2nd line HRpos/HER2neg?
- Adjuvanter Einsatz bestehend aus moderner ET + PIK3 gerichteter Theapie?

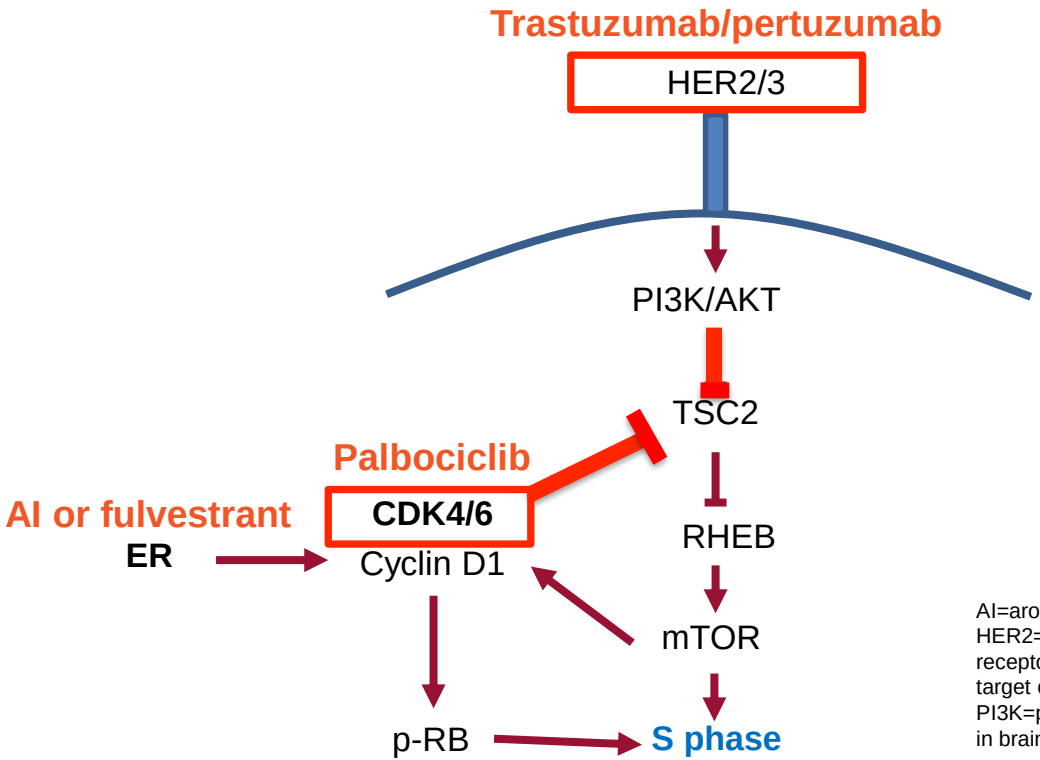


1. Jhaveri et al. SABCS 2023



2. Turner NC et al. N Engl J Med 2023

# ET und Kombinationspartner bei HRpos/HER2pos




**The HER2 and CDK4/6 pathways converge at the tumor suppressor protein TSC2**

**When CDK4/6 and HER2 inhibitors are combined, potent suppression of RB phosphorylation and mTORC1 activity, enhancing anti-proliferative effects in tumor cells**

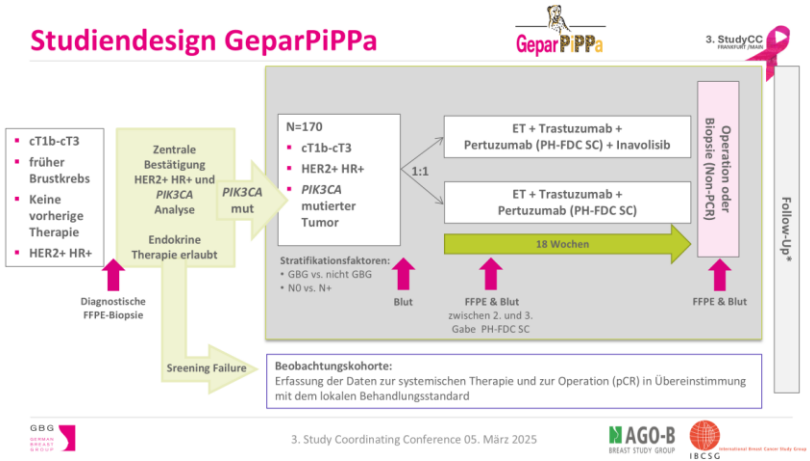
AI=aromatase inhibitor; AKT=protein kinase B; CDK4/6=cyclin-dependent kinase 4/6; HER2=human epidermal growth factor receptor 2; HER3=human epidermal growth factor receptor 3; CDK4/6=cyclin-dependent kinase 4/6; ER=estrogen receptor; mTOR=mammalian target of rapamycin; mTORC1=mammalian target of rapamycin complex 1; PI3K=phosphoinositide 3-kinase; p-RB=retinoblastoma protein; RHEB=ras homolog enriched in brain; S phase=synthesis phase; TSC2=tuberous sclerosis complex 2.

# ET und Kombinationspartner bei HRpos/HER2pos

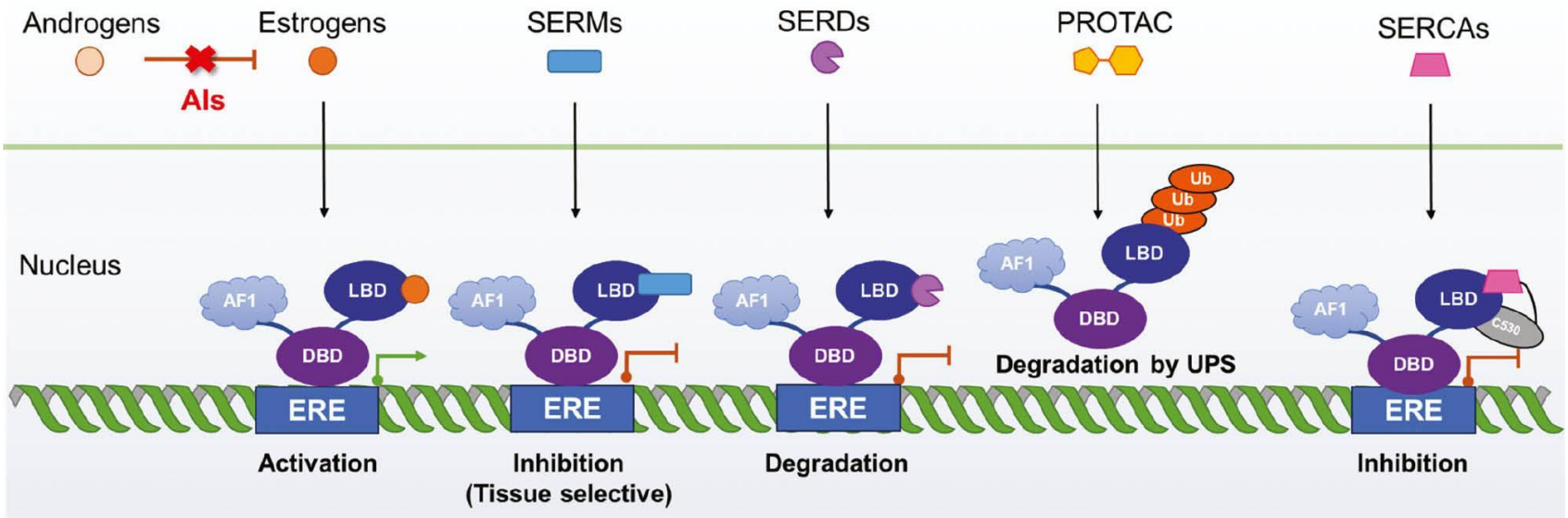


- Der endokrine Backbone in einer Erhaltungstherapie mit Trastuzumab/Pertuzumab spielt eine Rolle beim HRpos/HER2pos Mammakarzinom
- Auch potentielle Kombinationspartner der ET spielen eine Rolle
- In der PATINA Studie wurde ein klinisch relevanter Vorteil für die Addition von Palbociclib zu ET+T+P berichtet[1]

- Einsatz von CDK4/6i mit ET+T+P bei frühem HRpos/HER2pos Mammakarzinom
- Einsatz von PIK3 gerichteten Therapien mit ET+T+P bei frühem HRpos/HER2pos Mammakarzinom

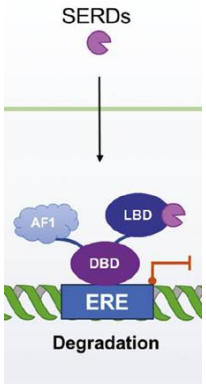


# ER gerichtete Medikamenten Klassen




Jian Min et al. *Acta Materia Medica.* 2024

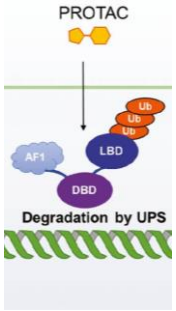
# SERDs

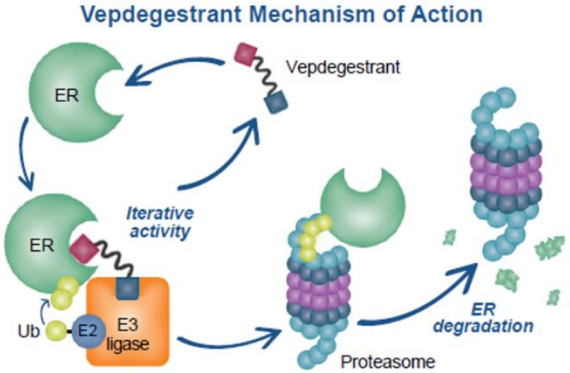



| | EMERALD[1] | SERENA-2[2] | EMBER-3[3] | AMEERA-3[4,5] | acelERA[6-8] |
|---|---|---|---|---|---|
| **Treatment** | **Elacestrant** | **Camizestrant** | **Imlunestrant ± abemaciclib** | **Amcenestrant** | **Giredestrant** |
| **Control arm** | FUL-AIs | FUL | FUL-exemestane | FUL-AIs-tamoxifen | FUL-AIs |
| **Phase** | 3 | 2 | 3 | 2 | 2 |
| **N** | 478 | 240 | 874 | 367 | 303 |
| **Patients** | Men or postmenopausal women | Postmenopausal women | Men or postmenopausal women | Men or women (any menopausal status) | Men or women (any menopausal status) |
| **Prior CDK 4/6 inhibitor** | Required (100%) | Permitted (69%) | Permitted | Permitted (79.7%) | Permitted (42%) |
| **Allowed prior FUL** | YES | NO | NO | YES | YES |
| **Allowed prior CT in MBC** | YES | YES | NO | YES | YES |
| **Data readout** | Positive | Positive | Positive | Negative | Negative |

1. Bidard FC, et al. J Clin Oncol. 2022; 2. Oliviera M et al. Lancet Oncol 2024 3. Jhaveri K et al. NEJM; 2024; 5. Tolaney SM, et al. Ann Oncol. 2022; 7. Martin M, et al. J Clin Oncol. 2021; 8. Martin Jiminez M, et al. Ann Oncol. 2022; Jian Min et al. *Acta Materia Medica.* 2024

# PROTACs




- PROteolysis TArgeting Chimera (PROTAC) heterobifunktionelle Moleküle, mit einem Liganden für das Target und (bei Vepdegestrant das ER) und einem weiteren Liganden für das Substrat (E3-Ubiquitin-Ligase-Komplex)
- Nach der Bindung an ER rekrutiert der PROTAC-Vepdegestrant einen E3-Ubiquitin-Ligase-Komplex, der ER mit Ubiquitin-Tags für den proteasomalen Abbau markiert.



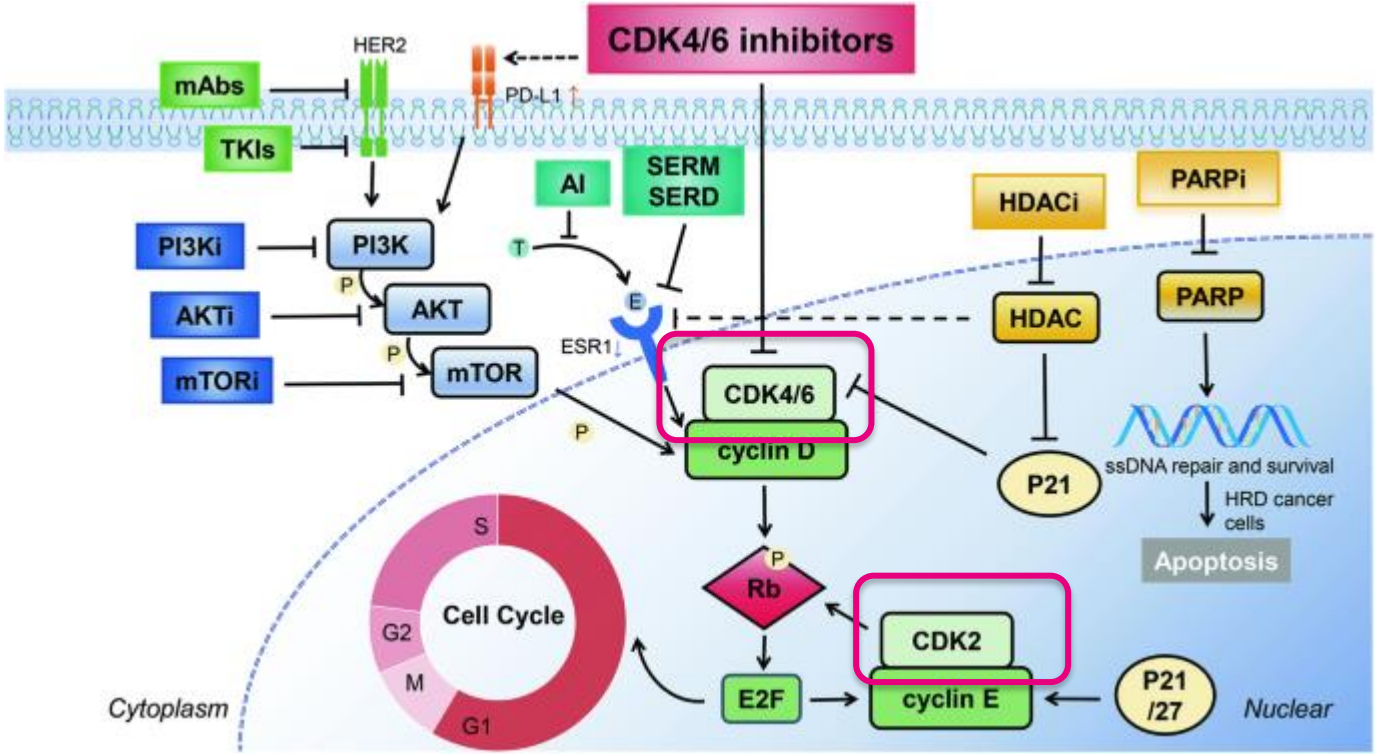
Pfizer Oncology

Jian Min et al. *Acta Materia Medica.* 2024

# Neue Kombinationspartner für endokrine Therapien

# Molekulare Ziele bei Brustkrebs



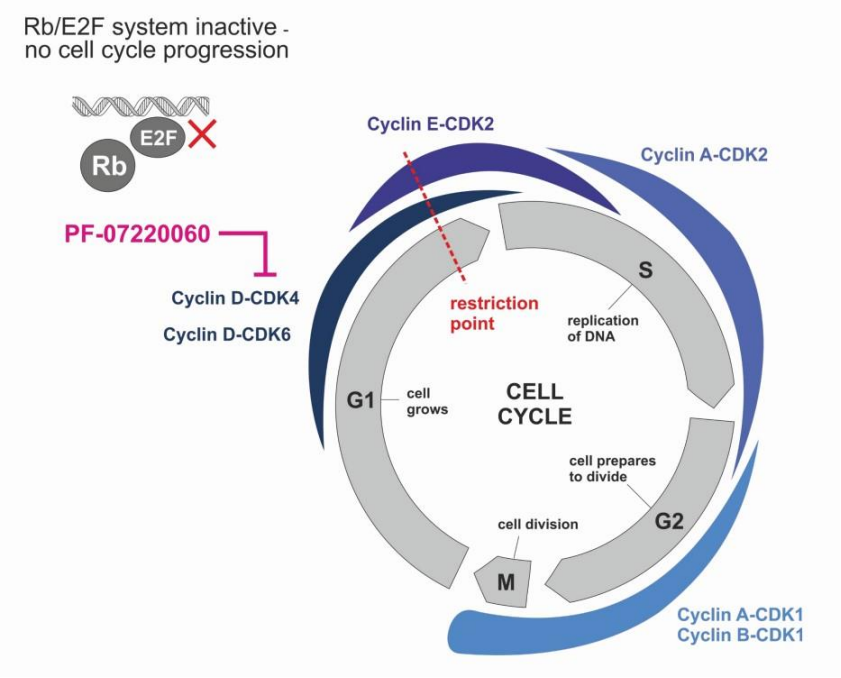



Wang et al. Cancer Gene Therapy 2024

# CDK4i Atirmociclib PF-07220060



- Atirmociclib is an oral, highly potent, selective, next generation inhibitor of CDK4 with sparing of CDK6
- Phase III trial Atirmociclib + Fulvestrant vs TPC in HR+/HER2- mBC with progression on CDK4/6i+AI (NCT06105632)
- About 500 patients will be randomized 1:1
- One additional line including ESR1, PIK3CA, AKT1, PTEN, or BRCA directed treatment is allowed
- Diverse CDK4i, CDK2i, CDK2/9i bei multiplen Firmen in Entwicklung



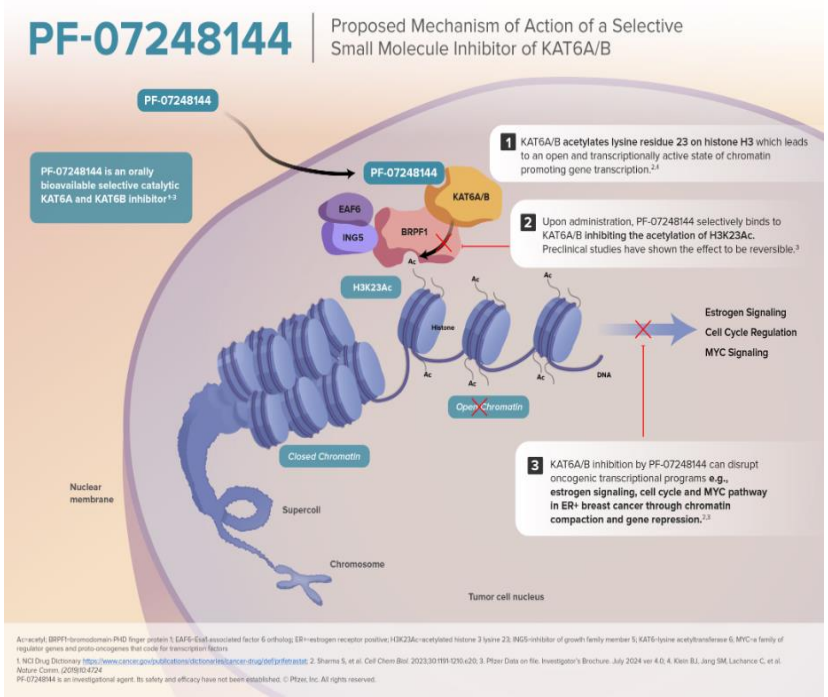



Pfizer Oncology
Giordano et al. ASCO 20204

# Prifetrastat (PF-07248144) KAT6i



- Prifetrastat ist ein potenter und selektiver Inhibitor der Lysin-Acetyltransferasen KAT6A und KAT6B
- KAT6A Acetylierung führt zu einem entspannten Chromatinzustand, der die Gentranskription erleichtert.
- Durch die Hemmung von KAT6A und KAT6B wird die Acetylierung von H3K23 reduziert, was zu einer Chromatinkondensation und Unterdrückung der Gentranskription führt.
- Mehrere Substanzen in Entwicklung in BC



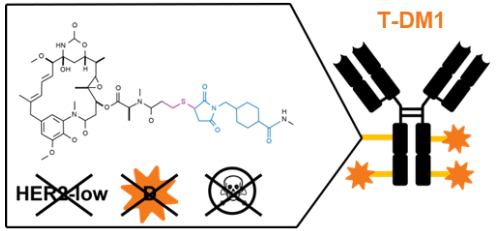
# ADC Therapien (Auszug)

# Zugelassene ADC Therapien



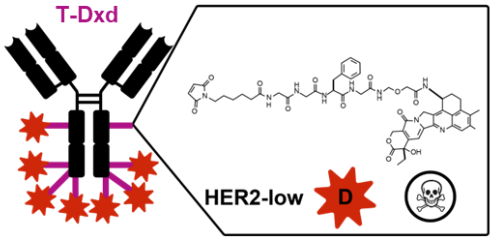
**2. Generation ADC**

**Target Antigen:** HER2 (Trastuzumab vehicle)
**mAb isotype:** IgG1
**Linker type:** non-cleavable
**Payload (class):** DM1 (Maytansinoid)
**Payload action:** Microtubule inhibitor
**DAR:** 3.5 (mean)




**3. Generation ADC**

**Target Antigen:** HER2 (Trastuzumab vehicle)
**mAb isotype:** IgG1
**Linker type:** cleavable
**Payload (class):** Dxd (Camptothecin)
**Payload action:** Topoisomerase-1 inhibitor
**DAR:** 8




**3. Generation ADC**

**Target Antigen:** TROP2
**mAb isotype:** IgG1
**Linker type:** cleavable
**Payload (class):** SN-38, active metabolite of irinotecan (Camptothecin)
**Payload action:** Topoisomerase-1 inhibitor
**DAR:** 8

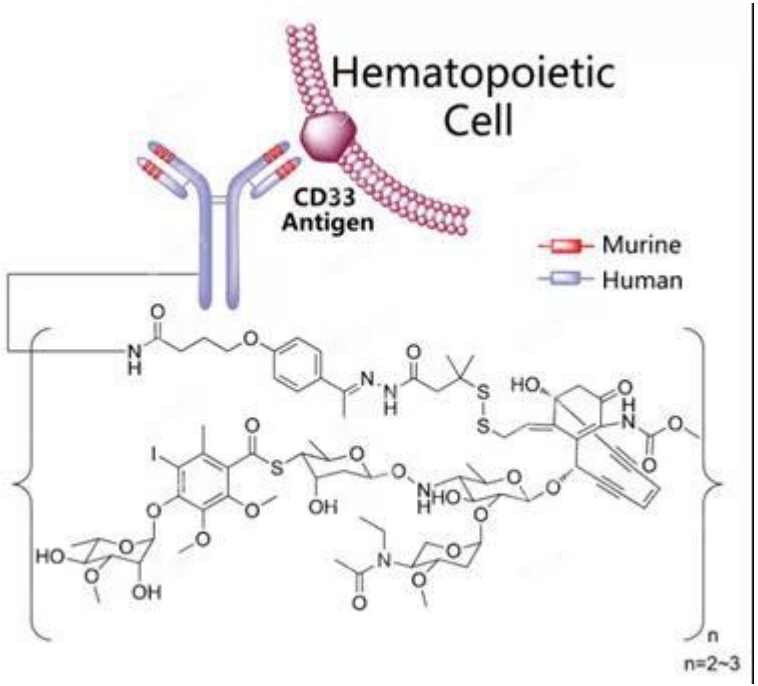

Legend: **HER2-low** Targets HER2-low tumours | D Diffusible cytotoxic moiety | Bystander killing effect



Corti C, et al Cancers 13:2898, 2021.

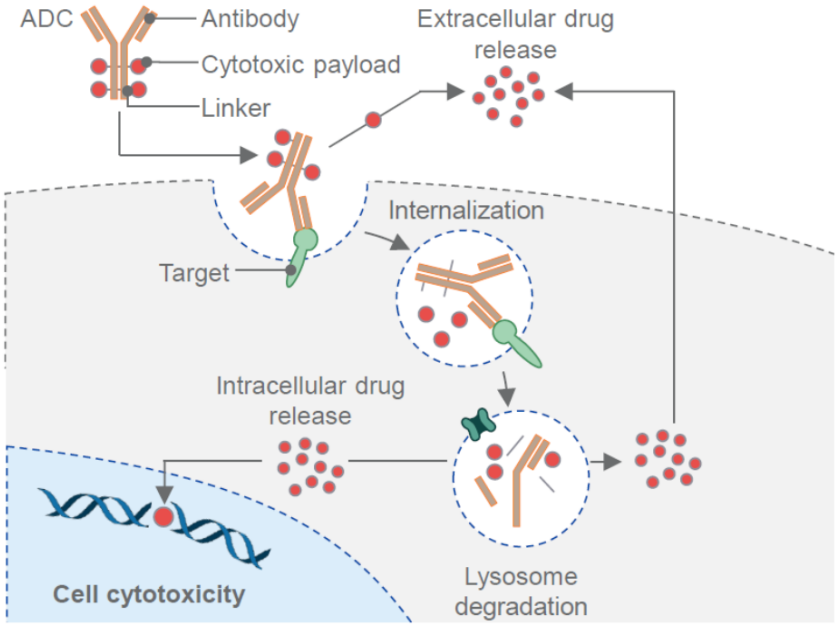
# Erste ADC Therapie Gemtuzumab Ozogamicin

- In **2000**, the first antibody conjugate Gemtuzumab Ozogamicin was approved by FDA, the target is CD33.
- Endocytosed by the target cell, it will release calicheamicin by hydrolyzing linker, which induces double-stranded DNA breaks
- This drug is used to treat CD33-positive acute myeloid leukemia

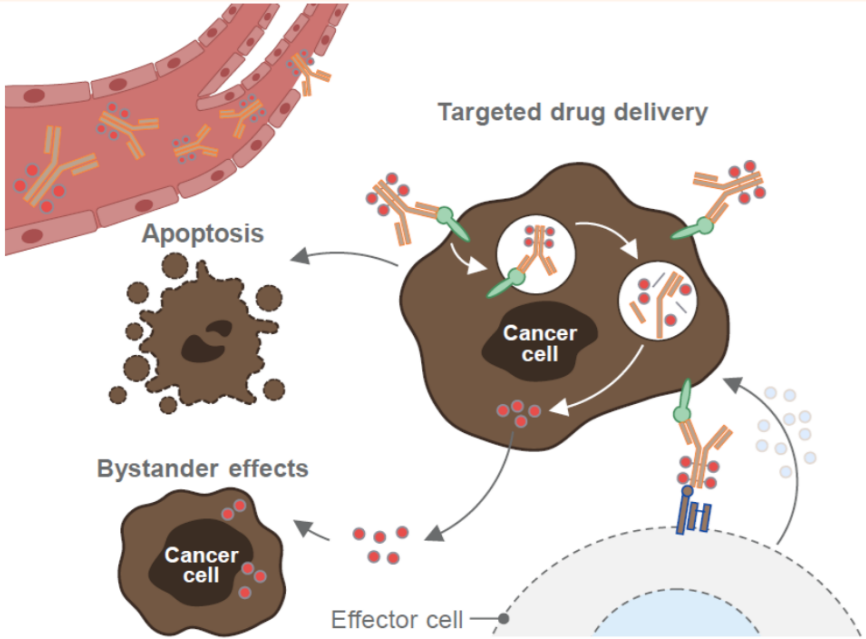


# Wirkweise ADC Therapien

**Bystander Effect:**
Killing of antigen-negative cells due to payload release before internalization or membrane permeability




**Additional ADC Effects:**
- Antibody driven (ADCC, CDC, ADCP)
- Target-driven effects




ADC, antibody-drug conjugate; ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cell-mediated phagocytosis; CDC, complement-dependent cytotoxicity.

Chau CH, et al. Lancet. 2019;394:793-804; Fu Z, et al. Signal Transduct Target Ther. 2022;7:93; Tarantino P, et al. Nat Rev Clin Oncol. 2023;20:558-576.

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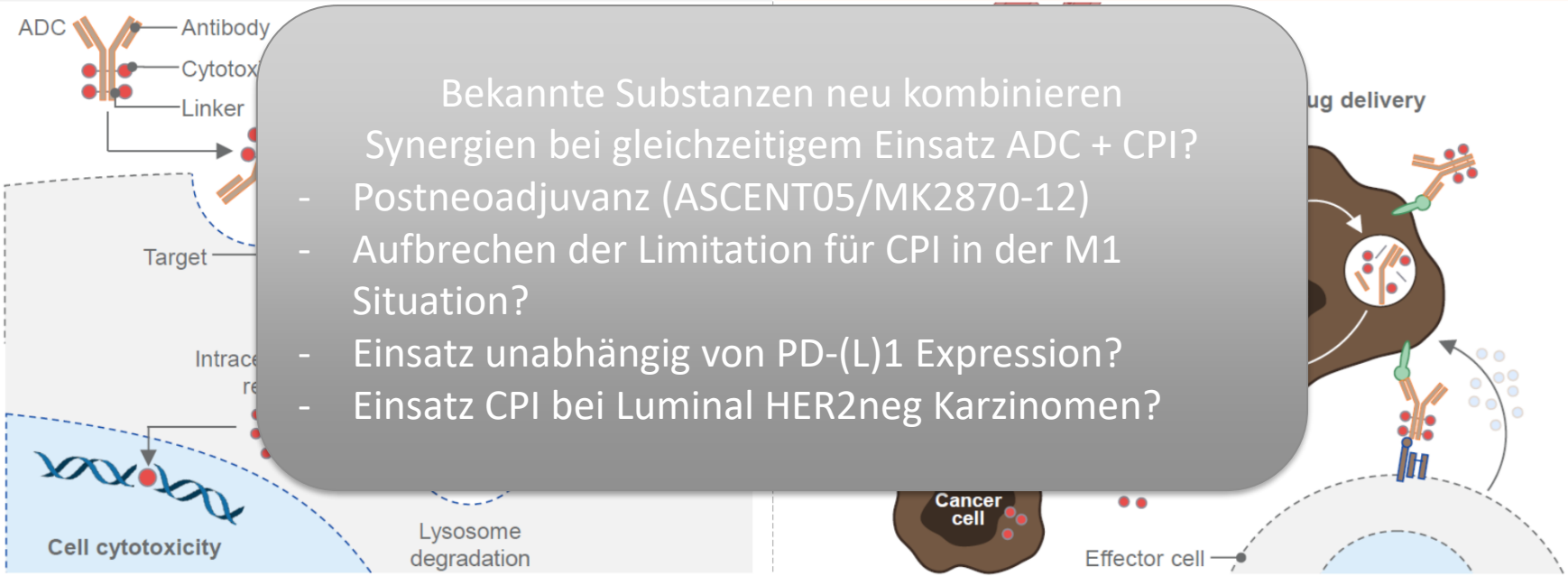


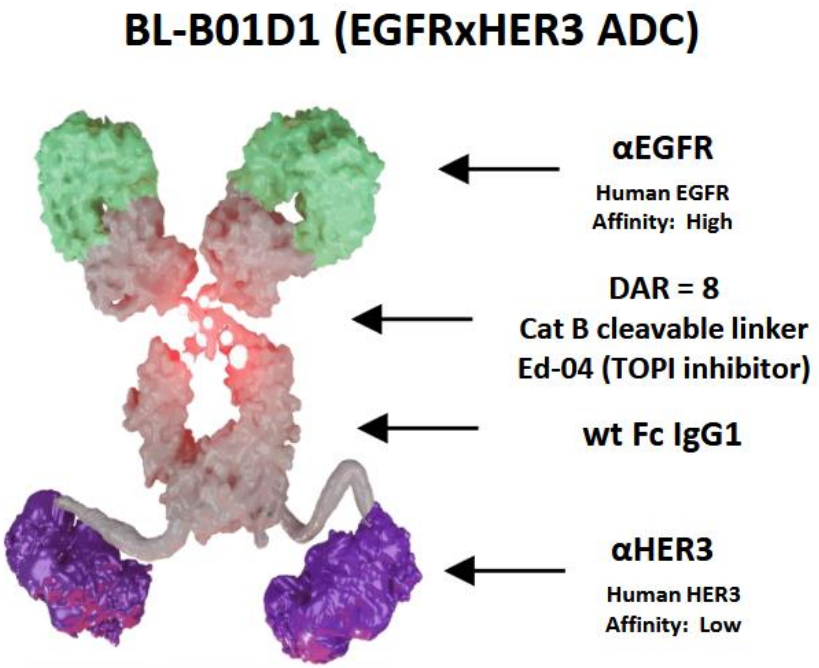

Bekannte Substanzen neu kombinieren
Synergien bei gleichzeitigem Einsatz ADC + CPI?
- Postneoadjuvanz (ASCENT05/MK2870-12)
- Aufbrechen der Limitation für CPI in der M1 Situation?
- Einsatz unabhängig von PD-(L)1 Expression?
- Einsatz CPI bei Luminal HER2neg Karzinomen?

ADC, antibody-drug conjugate; ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cell-mediated phagocytosis; CDC, complement-dependent cytotoxicity.

Chau CH, et al. Lancet. 2019;394:793-804; Fu Z, et al. Signal Transduct Target Ther. 2022;7:93; Tarantino P, et al. Nat Rev Clin Oncol. 2023;20:558-576.

# Neue ADC-Therapien (Auszug)

# Izalontamab brengitecan BL-B01D1



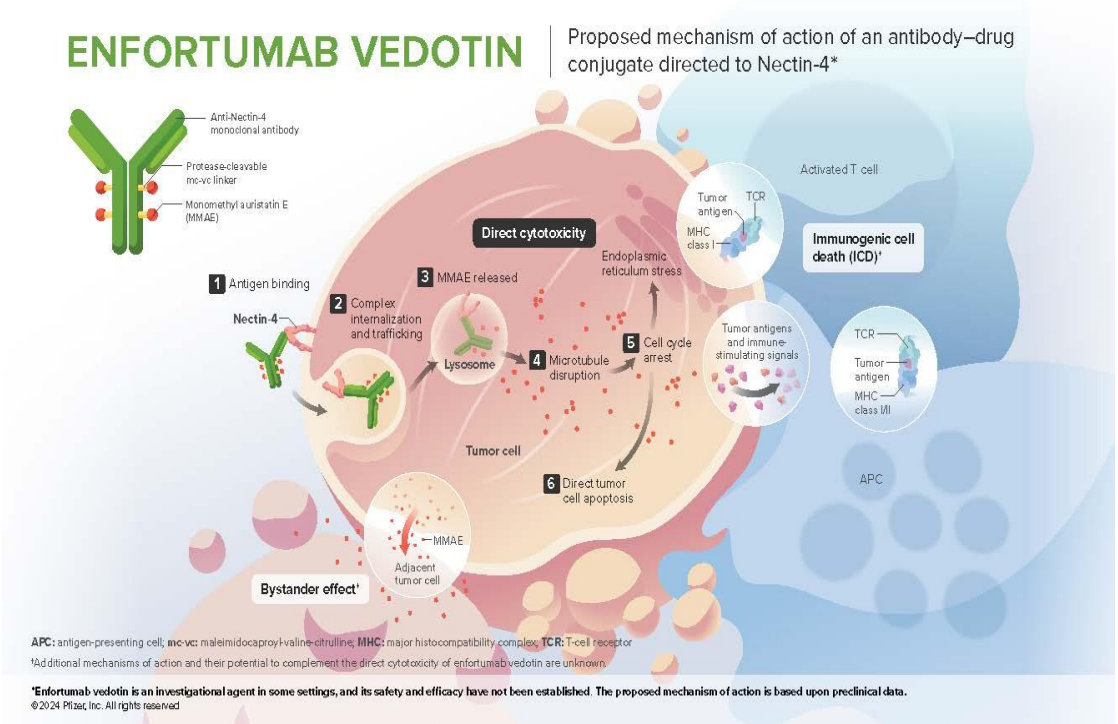

- First in class bispezifischer Anti-HER3/EGFR ADC
- 2 new targets in the field of BC
- Topoisomerase-I-Inhibitor payload
- Cleavable
- DAR 8

Ye, et al. ESMO 2024

# Enfortumab vedotin



- NECTIN4 gerichteter ADC
- Monomethylauristatin E Payload
- Neues Target und neue Payload im Bereich BC
- Mikrotubuli Inhibitor
- DAR 3.8
- Enfortumab Vedotin ist beim metast. Urothel-CA zugelassen



# Enfortumab vedotin

| Trial | Regime | Phase | Indikation | (Vorläufige) Ergebnisse |
|---|---|---|---|---|
| NCT04225117 | Enfortumab vedotin | Phase 2 | mBC:<br>HR+ HER2- (cohort 1),<br>TNBC (cohort 2) | Safety in both cohorts was manageable and consistent with previous reports[1] |

TNBC cohort (N=42)
64% had ≥2L systemic tx for metastatic BC
33% had prior sacituzumab govitecan

HR+/HER2- BC cohort (N=45)
73% had ≥3L systemic tx for metastatic BC

| Efficacy Parameters | TNBC N=42 | HR+/HER2- N=45 |
|---|---|---|
| Confirmed ORR, n (%) | 8 (19.0) | 7 (15.6) |
| Confirmed DCR, n (%) | 24 (57.1) | 23 (51.1) |
| Time to response, mo, median (range) | 1.8 (1.6, 3.6) | 3.5 (1.7, 5.5) |
| DOR | 3.8 (1.9, 3.9) | 7.2 (3.5, 7.2) |
| PFS | 3.5 (2.1, 4.6) | 5.4 (3.4, 5.7) |
| OS | 12.9 (10.3, NE) | 19.8 (12.8, NE) |

Values are median (95% CI) in mo unless otherwise noted.
+ indicates censoring. NE, not estimable.

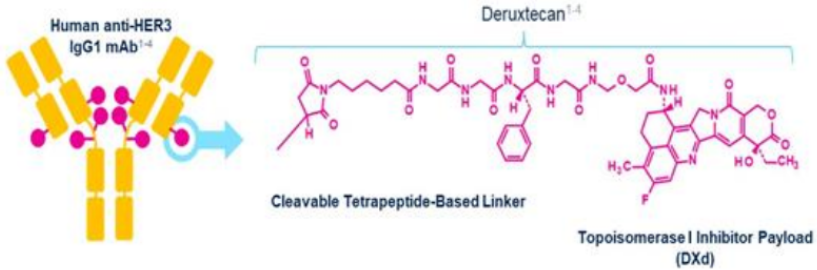
[1]Giordano A, et al. 2024 ASCO

# Patritumab deruxtecan (HER3-DXd)



## Background

- Despite the improved clinical outcomes achieved with endocrine therapy + CDK4/6 inh in HR+/HER2- advanced breast cancer, effective therapeutic options are limited after disease progression[1-3]
- **High expression of Human Epidermal Growth Factor Receptor-3 (HER3)** is associated with **poor prognosis** and plays a key role in **resistance to PI3K/AKT/mTOR inh, HER2-targeting therapies and endocrine therapy**[4-12]
- **HER3-DXd** is an antibody-drug conjugate composed of an anti-HER3 monoclonal antibody conjugated to a topoisomerase-I inh by a cleavable peptide linker[13-16]
- Prior phase I and II studies showed **promising activity of HER3-DXd** across breast cancer subtypes and across a range of HER3 membrane expression[17-20]




Pistilli ESMO 2024

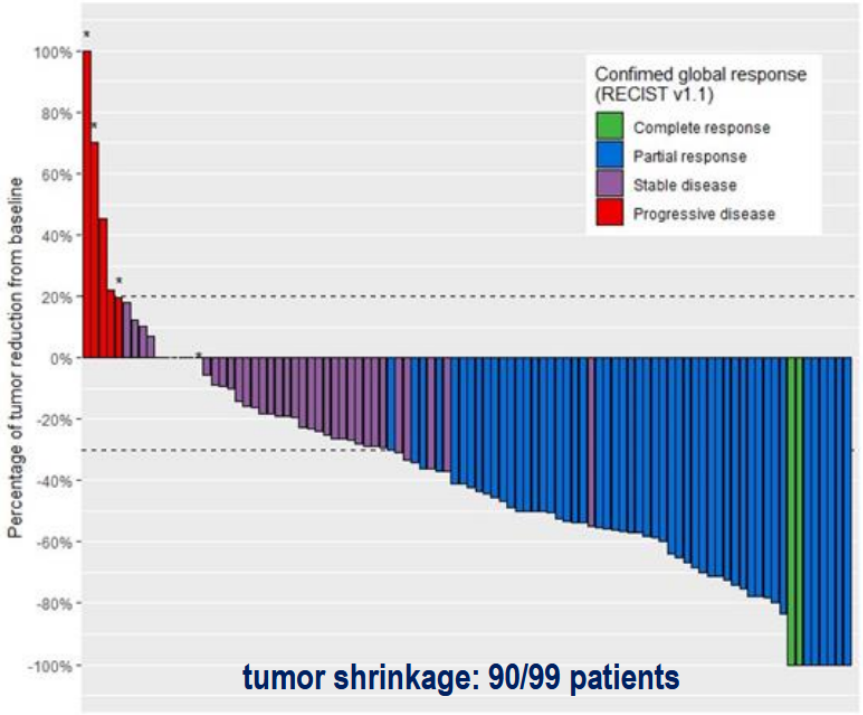


1. Gennari A, et al. *Ann Oncol* 2021;32:1475-1495; 2. Wolff AC, et al. *J Clin Oncol* 2023;41:3867–72;3. Moy B, et al. *J Clin Oncol* 2023;41:1318–20; 4. Jura N, et al, Proc Natl Acad Sci USA 2009, 106:21608-13; 5.Hynes NE et al, Nat Rev Cancer 2005, 5(5): 341-354; 6.Ocana et al, J Natl Cancer Inst 2013, 105:266–273; 7.Chandarlapaty S et al, Cancer Cell, 2011, 19:58-71; 8. Rodrik-Outmezguine VS et al, Cancer Discov 2011, 1:248-59; 9.Chakrabarty A et al, Proc Natl Acad Sci U S A 2012;109: 2718–23; 10. Huang X et al, Cancer Res 2010, 70:1204-14; 11.Liu B et al, Int J Cancer 2007;120:1874-82.; 12. Morrison MM et al, Oncogene (2016) 35, 1143–1152; 13.Hashimoto Y, et al. Clin Cancer Res. 2019;25(23):7151-7161; 14. Nakada T, et al. Chem Pharm Bull (Tokyo). 2019;67(3):173-185; 15. OgitaniY, et al. Clin Cancer Res. 2016;22(20):5097-5108; 16. KoganemaruS, et al. Mol Cancer Ther. 2019;18(11):2043-2050. 17; Krop I et al, JCO 2023, 18.Hamilton E et al, ASCO 2023.; 19 Oliveira M et al, Ann Oncol 2023; 20. Braso-Maristany et al, Nature Communications 2024

# ICARUS-BREAST01 (HER3-DXd)

94% ERpos; HER2neg 99%






| | N=99 | |
|---|---|---|
| | n | % [95%CI][a] |
| **Confirmed ORR[b]** | **53** | **53.5** [43.2; 63.6] |
| CR | 2 | 2.0 [0.2;7.1] |
| PR | 51 | 51.5 [41.3; 61.7] |
| SD | 37 | 37.4 [27.8; 47.7] |
| PD | 7 | 7.1 [2.9; 14.0] |
| NE[c] | 2 | 2.0 [0.2;7.1] |
| **CBR[d]** | **62** | **62.6** [52.3;72.1] |

**No significant association between HER2 expression and ORR (*p-value 0.8*)[e]**

BARCELONA 2024 ESMO congress

a. Clopper-Pearson (Exact) method was used for confidence interval; b. Confirmation of response must be demonstrated with a new tumor assessment 4 weeks or later from the initial response; c. 2 patients were not evaluable for ORR: one patient had only one tumor assessment with PR and then treatment discontinued due to clinical progression, a second patient had not evaluable as global response of target lesions. d. CBR is defined as the presence of at least a confirmed PR or CR, or a stable disease (SD) >6 months; e. logistic regression model was performed to estimate association between HER2 expression and ORR

# ICARUS-BREAST01 (HER3-DXd)

## Conclusion and perspectives

- HER3-DXd showed clinically meaningful activity and manageable safety profile in patients with HR+/HER2- ABC progressing after 2 or more lines of therapy, including CDK4/6inh:
  ***ORR 53.5% [95%CI, 43.2; 63.6]; mDoR 8.7 [8.1; 12.5]; mPFS 9.4 mos [95%CI 8.1; 13.4]***

- Activity of HER3-DXd was observed **across a range of tumor HER3 and HER2 membrane expression by IHC**

- Although with the limitations of the small sample size, exploratory biomarker analysis suggest that:
  -distribution of HER3-DXd in the tumor may play a role in determining a better treatment response
  -up-regulation of genes involved in immune response, particularly interferon alpha and gamma were significantly enriched in the entire cohort and among responders

- **Efficacy and safety profile of HER3-DXd make this ADC an optimal candidate for further larger trials in patients with HR+/HER2- ABC after failure of CDK4/6 inhibitors**

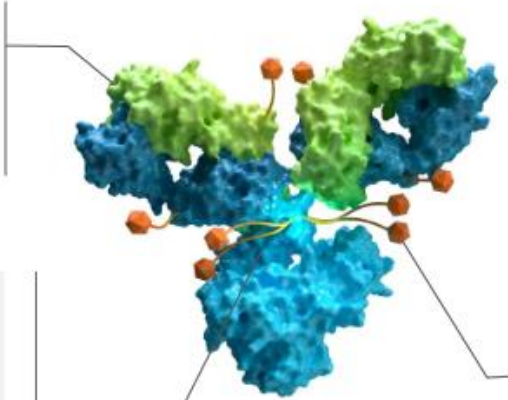
# Sacituzumab tirumotecan (TROP2)



**Figure 1. Structure of sac-TMT**

## Antibody

- hRS7, a recombinant humanized anti-TROP2 antibody with high affinity



## Linker

- **Kthiol conjugation:** irreversible coupling to improve stability of ADC
- **Payload release:** intracellular cleavage and extracellular hydrolysis in TME
- **Balanced stability:** balance between efficacy and safety to expand therapeutic window

## Payload

- **Novel topo I inhibitor** (a belotecan derivative), highly active
- Average **DAR: 7.4** (range: 7–8)
- **Bystander effect**
- Methylsulfonyl derivatization enhances linker stability and toxin permeability

TME: tumor microenvironment DAR:drug-to-antibody ratio

Yin et al. ESMO 2024

# Sacituzumab tirumotecan (TROP2)



- OptiTROP-Breast01: phase III sacituzumab tirumotecan vs TPC (eribulin, vinorelbine, capecitabine, or gemcitabine) bei mTNBC
- 2 oder mehr vorangegangene Linien
- medianes PFS 5.7 mo (95% CI, 4.3 to 7.2) mit ST vs 2.3 months (95% CI, 1.6 to 2.7) mit Chemo
- Statistisch signifikanter OS Vorteil (HR 0.53; 95% CI, 0.36 to 0.78; P=0.0005; median not reached)

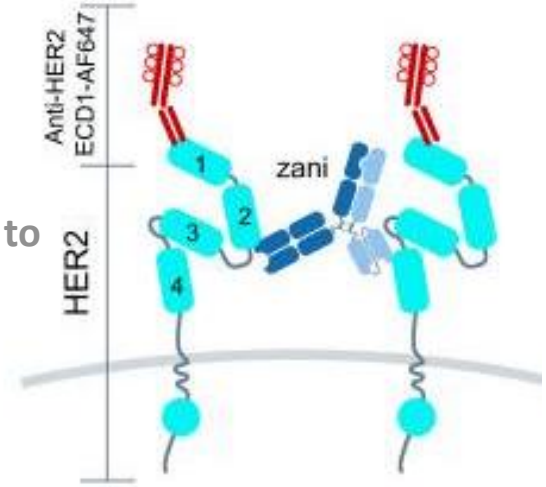
| Event，N (%) | Sac-TMT (N=130) | | TPC (N=132) | |
|---|---|---|---|---|
| | With prior PD-(L)1 inhibitors (N=32 ) | Without prior PD-(L)1 inhibitors (N=98) | With prior PD-(L)1 inhibitors (N=36) | Without prior PD-(L)1 inhibitors (N=96) |
| **Any TRAE** | 32 (100.0) | 98 (100.0) | 34 (94.4) | 93 (96.9) |
| **Grade ≥3** | 20 (62.5) | 62 (63.3) | 21 (58.3) | 54 (56.3) |
| **Serious** | 6 (18.8) | 21 (21.4) | 3 (8.3) | 15 (15.6) |
| **Leading to dose reduction** | 9 (28.1) | 31 (31.6) | 8 (22.2) | 13 (13.5) |
| **Leading to dose interruption** | 18 (56.3) | 55 (56.1) | 16 (44.4) | 38 (39.6) |
| **Leading to treatment discontinuation** | 0 | 2 (2.0) | 0 | 2 (2.1) |
| **Leading to death** | 0 | 1 (1.0) | 0 | 0 |

Xu et al. ASCO 2024
Yin et al. ESMO 2024

# Neue Antikörper Therapien (Auszug)

# Zanidatamab biparatopisch Anti-HER2

- Zanidatamab: biparatopischer IgG1-like Ab directed against ECD4 (trastuzumab) and ECD2 (pertuzumab) of HER2.
- Multiple mechanisms of action including induction of HER2 clustering to trigger complement dependent cytotoxicity, signal inhibition, antibody dependent cellular cytotoxicity and phagocytosis.
- HER2+ mBC: median PFS of 12 mo with zanzidatamab + fulvestrant + palbociclib in pts with median 4 prior lines of treatment for mBC.[2]
- HER2+ eBC: neoadj. zanidatamab +/- ET as chemo-free treatment showed a preliminary pCR rate of 36%, which is promising compared to other trials (24% for T+P+ET) (15% for T+ET).[3,4,5]
- FDA approval for met. HER2pos biliary tract carcinoma in 2024

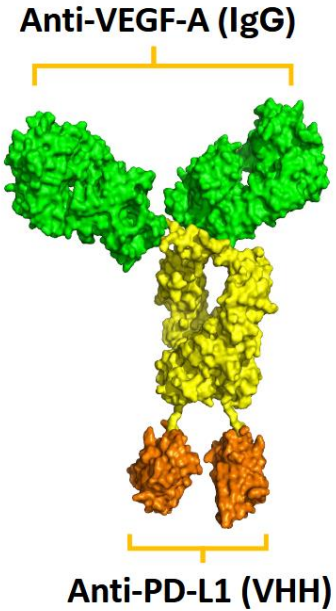



1. Weisser Nat Commun 2023, 2. Escrivá-de-Romani SABCS 2023
3. Valero ESMO open 2023 4.Gluz JAMA Oncol 2023, 5. Harbeck JCO 2017

# BNT327



- Bispezifischer Antikörper PD-L1/VEGF-A
- VEGF-A zielt darauf ab, die immunsuppressive Wirkung des Tumor-Mirco-Environements zu modulieren
- Nicht geeignete Tumore für ein CPI zugänglich machen?
- Open-label, single-arm, multi-center, Phase Ib/II study of PM8002/BNT327 + nab-paclitaxel for 1L TNBC (NCT05918133) in China
- Response Rates und PFS wurden auf ESMO uns SABCS 2024 präsentiert (leider einarmig)




1. Wu et al. ESMO 2024
2. Wu et al. SABCS 2024

# Efficacy - NCT05918133



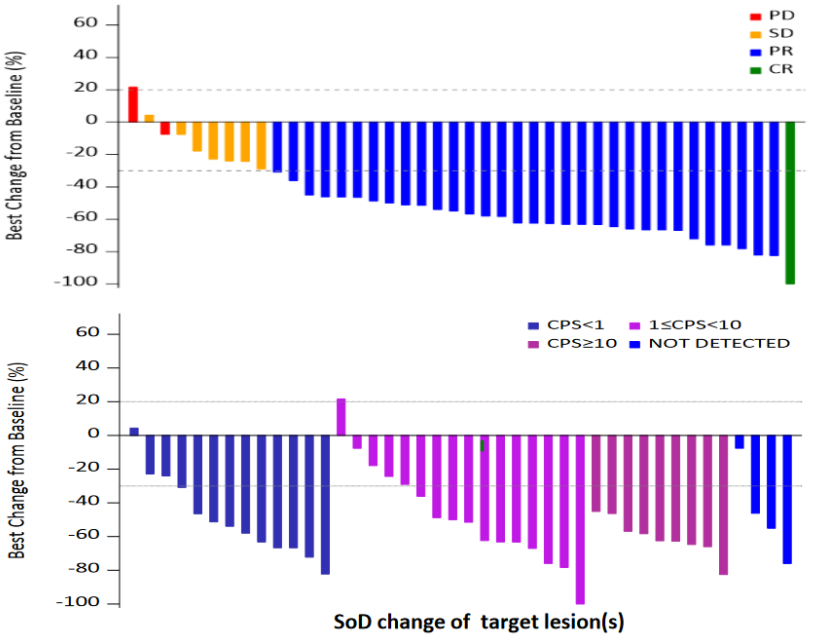
## Efficacy in the Overall Population and by PD-L1 expression

- PM8002/BNT327 showed clinically meaningful efficacy irrespective of PD-L1 status (assessed by means of the PD-L1 IHC E1L3N assay)

| Variable | ITT | PD-L1 CPS<1 | PD-L1 1≤CPS<10 | PD-L1 CPS≥10 | NOT DETECTED |
|---|---|---|---|---|---|
| Population (n) | 42 | 13 | 16 | 9 | 4 |
| CR | 1 (2.4) | 0 (0.0) | 1 (6.3) | 0 (0.0) | 0 (0.0) |
| PR | 32 (76.2) | 10 (76.9) | 10 (62.5) | 9 (100.0) | 3 (75.0) |
| SD | 7 (16.7) | 3 (23.1) | 4 (25.0) | 0 (0.0) | 0 (0.0) |
| PD | 2 (4.8) | 0 (0.0) | 1 (6.3) | 0 (0.0) | 1 (25.0) |
| ORR % (95% CI) | 78.6 (63.2, 89.7) | 76.9 (46.2, 95.0) | 68.8 (41.3, 89.0) | 100.0 (66.4, 100.0) | 75.0 (19.4, 99.4) |
| cORR % (95% CI) | 73.8 (58.0, 86.1) | 76.9 (46.2, 95.0) | 56.3 (29.9, 80.3) | 100.0 (66.4, 100.0) | 75.0 (19.4, 99.4) |
| DCR % (95% CI) | 95.2 (83.8, 99.4) | 100.0 (75.3, 100.0) | 93.8 (69.8, 99.8) | 100.0 (66.4, 100.0) | 75.0 (19.4, 99.4) |
| mPFS (Mo), (95%CI) | 13.5 (9.4, --) | NR (5.7, --) | 14.0 (7.2, --) | 10.8 (5.5, 13.5) | 14.0 (1.8, --) |

ORR 74%

- For the ITT population, mTTR was 1.9 mo and mDoR 11.7 mo; mOS was not reached

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CPS, combined positive score; CR, complete response; cORR, confirmed ORR; DCR, disease control rate; IHC, immunohistochemistry; mDoR, median duration of response; mPFS, median progress-free survival; mTTR, median time to response; Mo, month; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameters

# Zusammenfassung



- Viele Substanzen sind neu verfügbar
- Viele Einsatz-Situationen und alle mögliche Kombinationen von bereits verfügbaren Substanzen sind noch nicht untersucht
- Noch mehr Substanzen sind in Entwicklung, so dass die Übersicht schwer fällt
- Rasche Veränderungen der Therapiestandards erschwert den Vergleich zusätzlich

- ADC sind auf dem Vormarsch in frühe Linien und ggfs in die frühe Erkrankungssituation
- Zielgerichtete endokrine Therapien wie SERDs und PIK3 gerichtete Substanzen werden mutmaßlich in die frühen Situationen rücken
- Voraussetzung ist die Targets/Mutationen zu kennen!
- Bitte frühzeitig bei Metastasierung mit HER2neg Mammakarzinom somatisch und Keimbahn testen

Heilung durch Innovation, Kompetenz und Partnerschaft – führend in der Brustkrebs-Forschung

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22. Annual Scientific Meeting 06. – 07. März 2025