

State of the Art HER2+ metastasiertes Mammakarzinom

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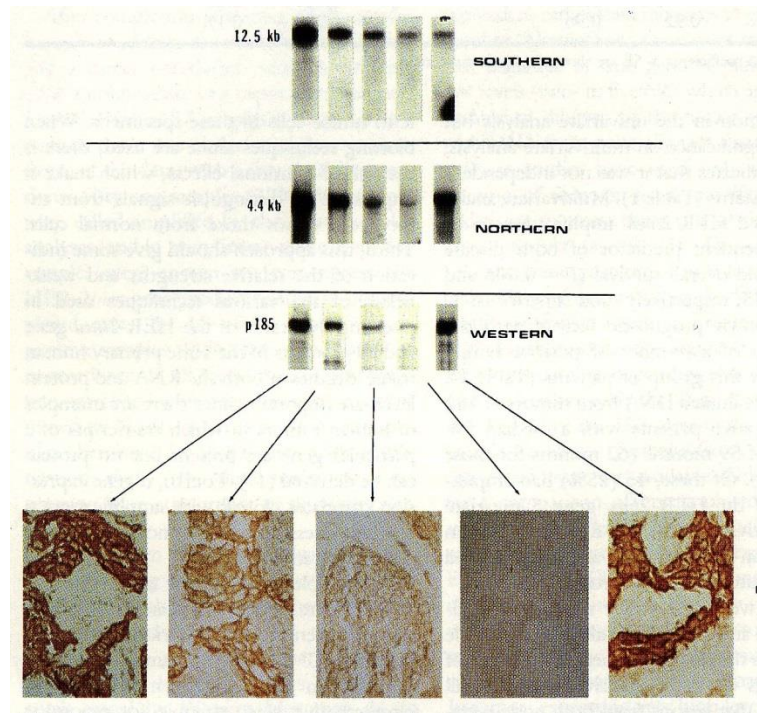
Universitäres Centrum für Tumorerkrankungen

Universitätsmedizin Mainz

Conflict of Interest (COI)

- **Forschungsunterstützung:**
 - AstraZeneca, BioNTech, Eisai, Genentech, Novartis, Pantarhei Bioscience, Pfizer, Pierre-Fabre, Roche
- **Vortragsstätigkeit:**
 - AstraZeneca, Celgene, Eisai, Novartis, Pfizer, Pierre-Fabre, Roche
- **Beratertätigkeit:**
 - AstraZeneca, Celgene, Eisai, Lilly, Novartis, Pantarhei Bioscience, Pfizer, Pierre-Fabre, Roche

HER-2 alias c-erbB-2



Southern

Northern

Western

IHC

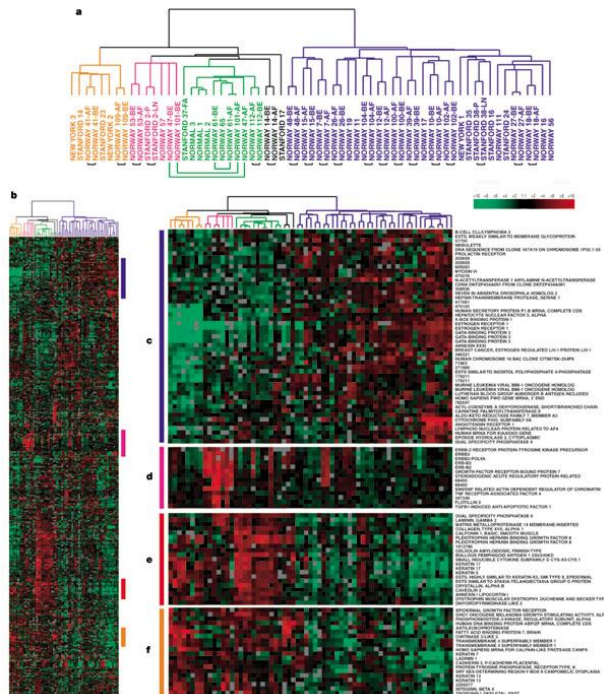
Molecular Portraits

-Basal-like

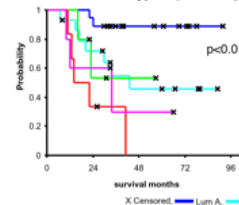
-Erb-B2

-Normal breast-like

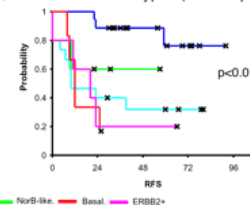
-Luminal / ER+



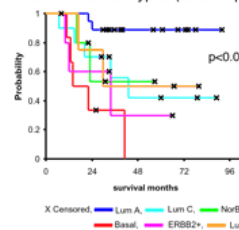
A 5 tumor subtypes (based upon Fig 1)



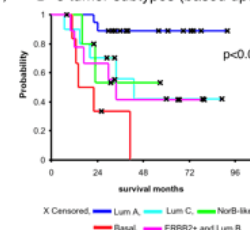
B 5 tumor subtypes (based upon Fig 1)

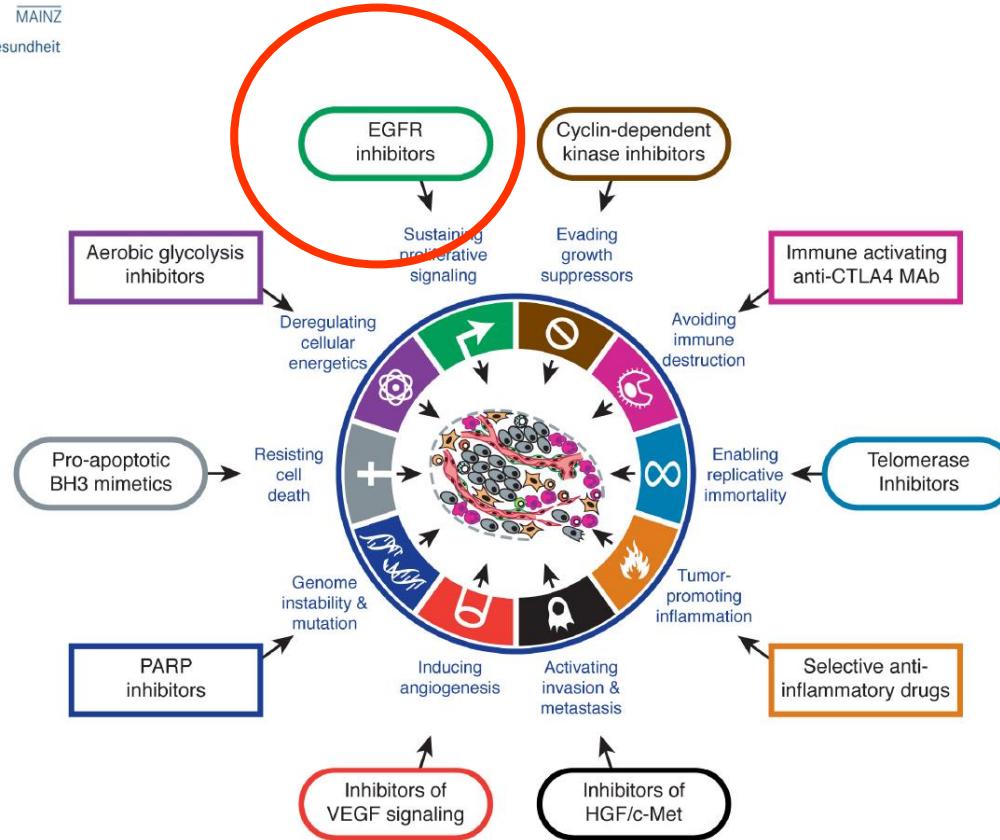


C 6 tumor subtypes (based upon Fig 1)



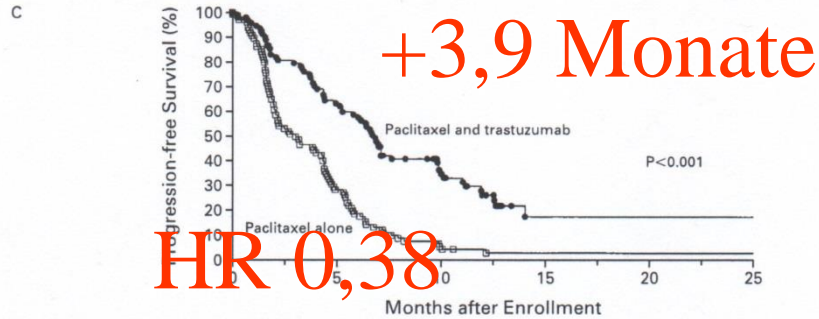
D 5 tumor subtypes (based upon Fig 5)





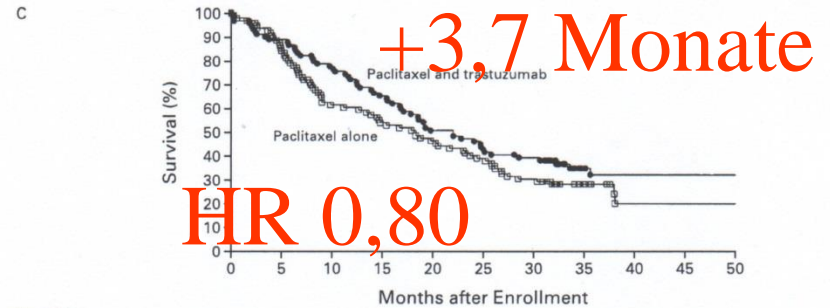
Hanahan and Weinberg, 2011

Paclitaxel / Trastuzumab



HR 0,38

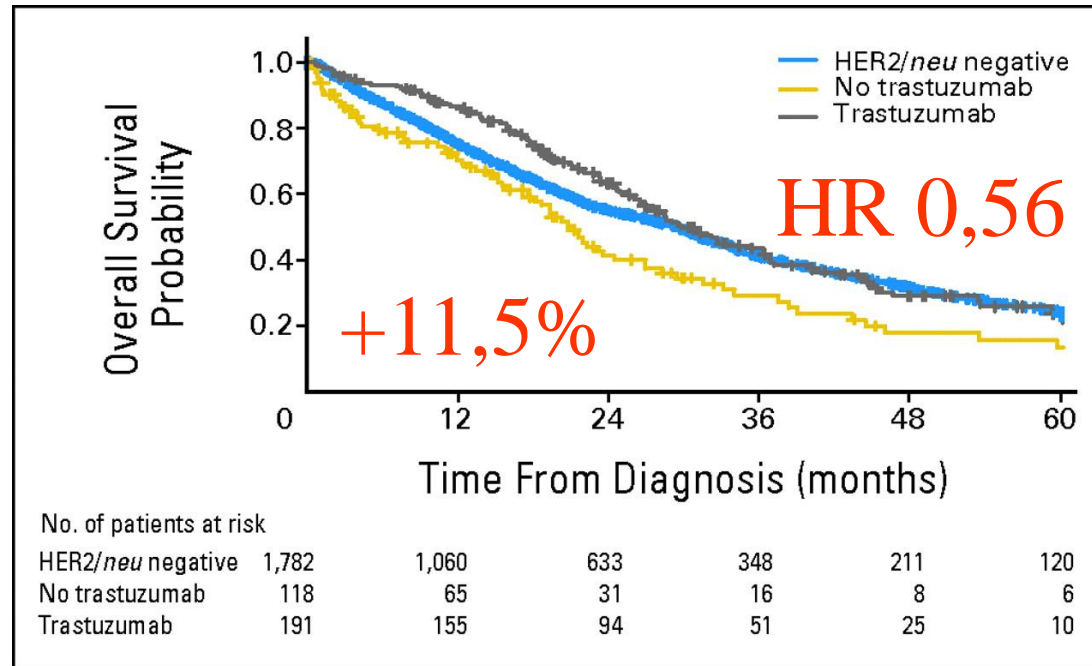
| No. AT RISK | 0 | 5 | 10 |
|----------------------------|----|----|----|
| Paclitaxel and trastuzumab | 92 | 54 | 23 |
| Paclitaxel alone | 96 | 26 | 5 |



HR 0,80

| No. AT RISK | 0 | 5 | 10 | 15 | 20 | 25 | 30 | 35 | 40 |
|----------------------------|----|----|----|----|----|----|----|----|----|
| Paclitaxel and trastuzumab | 92 | 80 | 69 | 58 | 45 | 39 | 34 | 15 | 2 |
| Paclitaxel alone | 96 | 81 | 58 | 51 | 44 | 37 | 28 | 14 | 2 |

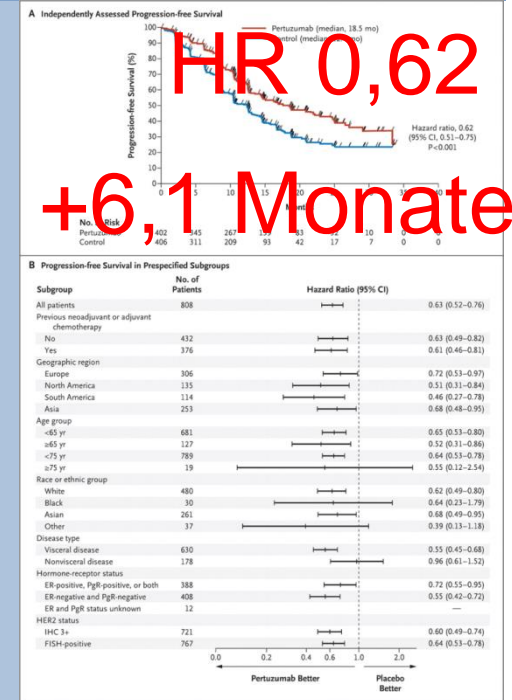
HER-2 und Trastuzumab beim metastasierten Mammakarzinom



**Jede HER2 positive Patientin
sollte eine gegen HER2
gerichtete Therapie erhalten**

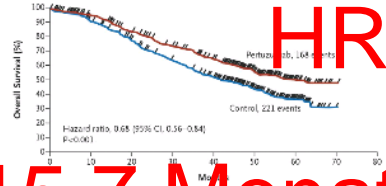
Trastuzumab +/- Pertuzumab (CLEOPATRA)

- HER2+ metastasiert (n = 808)
 - Trastuzumab +/- Pertuzumab
- PFS 18,5 vs. 12,4 Monate
 - HR 0,62
- Vergleichbares Toxizitätsprofil



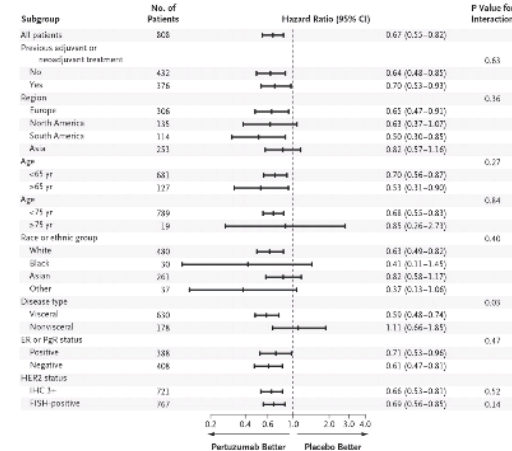
CLEOPATRA – Gesamtüberleben

A Overall Survival



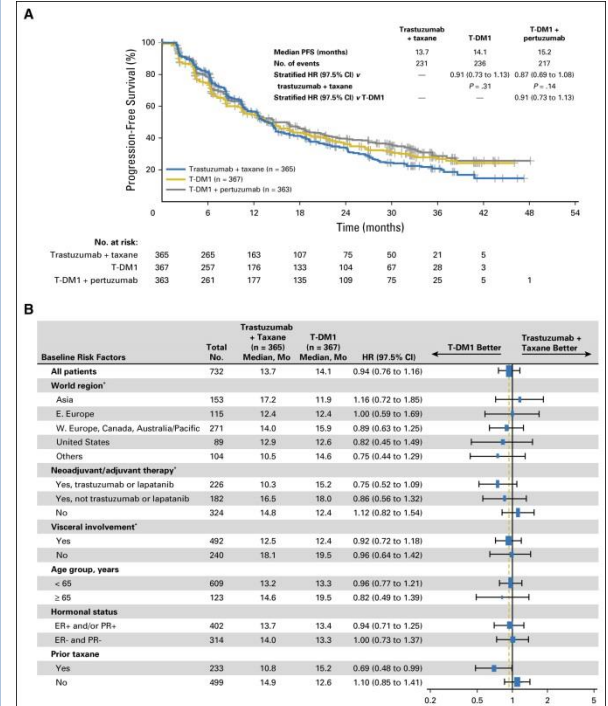
+15,7 Monate

B Subgroup Analysis of Overall Survival



MARIANNE

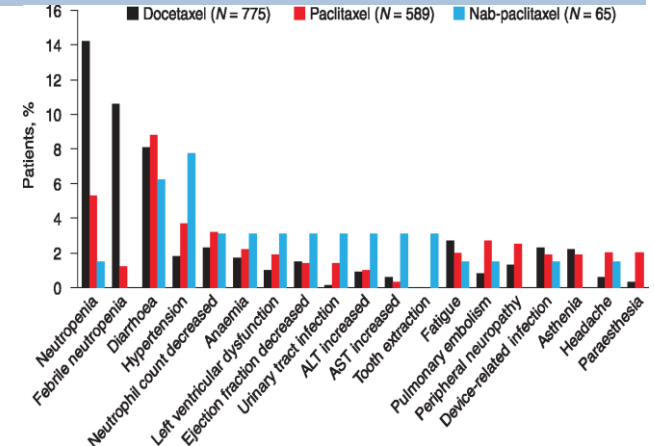
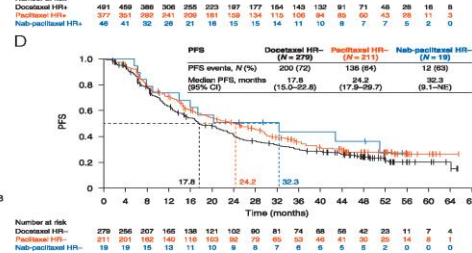
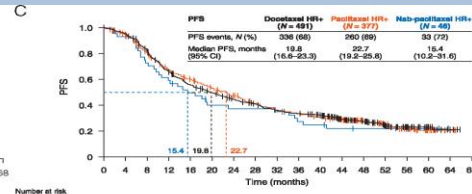
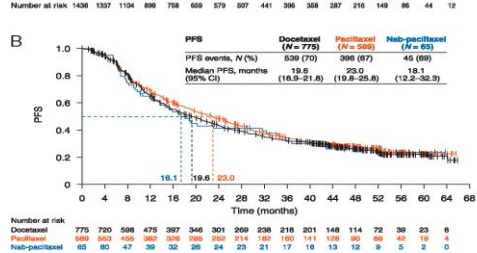
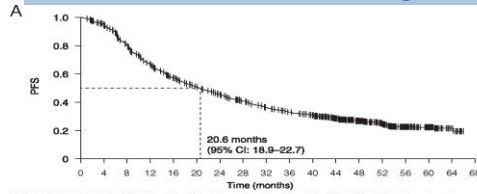
- 1st line HER2+ (n=1095)
 - Taxan/Trastuzumab vs. T-DM1 vs. T-DM1/Pertuzumab
- PFS 13,7 vs. 14,1 vs. 15,2 Monate
- Grad 3/4 Toxizitäten
 - 54% vs. 45% vs. 46%



Welches Taxan bei dualer Blockade?

PERUSE

- HER2+ metastasiert (n=1436)
 - duale Blockade + (Docetaxel vs. Paclitaxel vs. nab-Paclitaxel)
- PFS vergleichbar (20,6 Monate)
- Nebenwirkungsprofil unterschiedlich



Erstlinientherapie beim HER2-pos. metastasierten Mammakarzinom



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| | Oxford | | |
|--|-----------------|----|-------|
| | LoE | GR | AGO |
| ■ Docetaxel + Trastuzumab + Pertuzumab | 1b | A | ++ |
| ■ Paclitaxel (wk) + Trastuzumab + Pertuzumab | 2b | B | ++ |
| ■ nab-Paclitaxel + Trastuzumab + Pertuzumab | 3b ^a | C | + |
| ■ Vinorelbin + Trastuzumab + Pertuzumab | 3b | B | + |
| ■ T-DM 1 (Rückfall innerhalb von 6 Monaten und nach Taxan und Trastuzumab) | 2b | B | + |
| ■ 1 st line Chemotherapie* + Trastuzumab | 1b | B | + |
| ■ Trastuzumab mono | 2b | B | +/- |
| ■ Taxan + Lapatinib | 1b | B | +/- |
| ■ Taxan + Trastuzumab + Everolimus | 1b | B | - |
| ■ Trastuzumab + Aromatase-Inhibitoren (ER+) | 2b | B | +/-** |
| ■ Lapatinib + Aromatase-Inhibitoren (ER+) | 2b | B | +/-** |

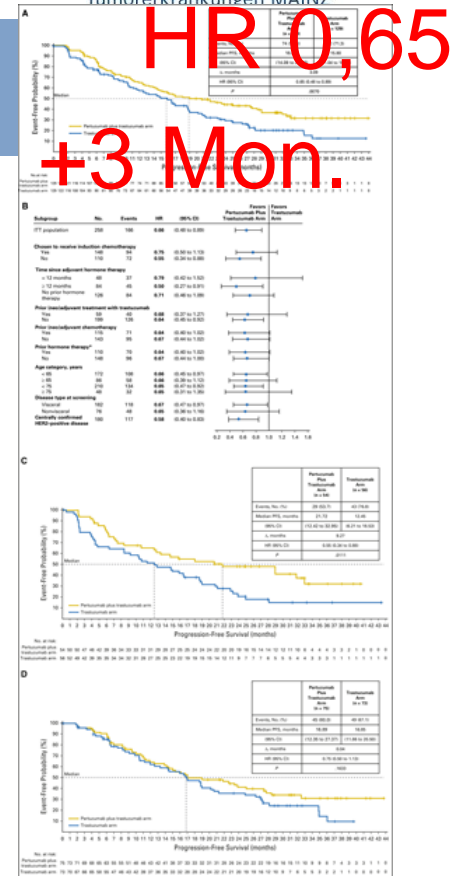
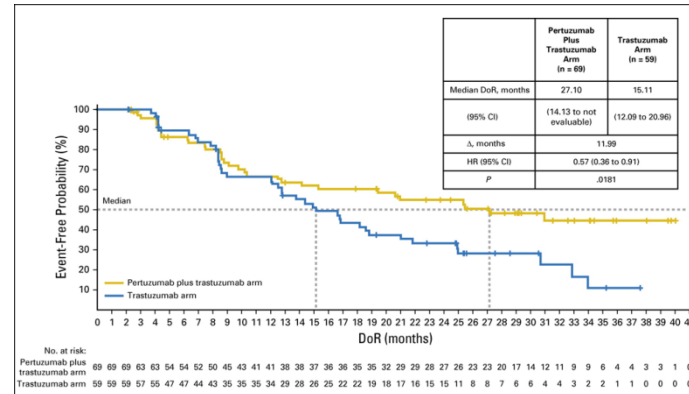
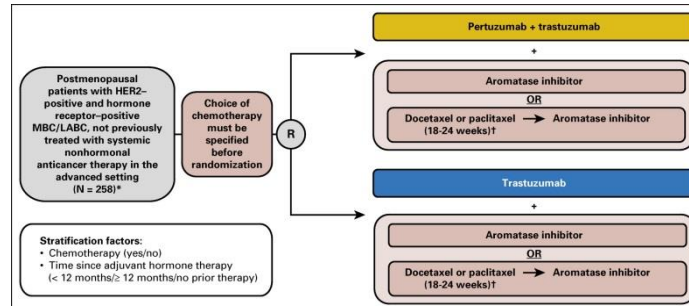
* Taxane; Vinorelbine; Paclitaxel/Carboplatin; Capecitabine/Docetaxel,

** siehe Kapitel „Endokrine +/- targeted Therapie“

**Muss es bei HER2+ / ER+ immer
Chemotherapie sein?**

PERTAIN

- 1st line metastasiert ER+ / HER2+
- AI + T vs. AI + duale Blockade
- PFS 19 vs. 16 Monate
- HR 0,65



Endokrine Therapie der postmenopausalen HER2-positiven metastasierten Mammakarzinompatientin



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- Anastrozol und Trastuzumab
- Letrozol und Trastuzumab
- Letrozol und Lapatinib
- Fulvestrant und Lapatinib
- Aromataseinhibitor und Trastuzumab / Pertuzumab*

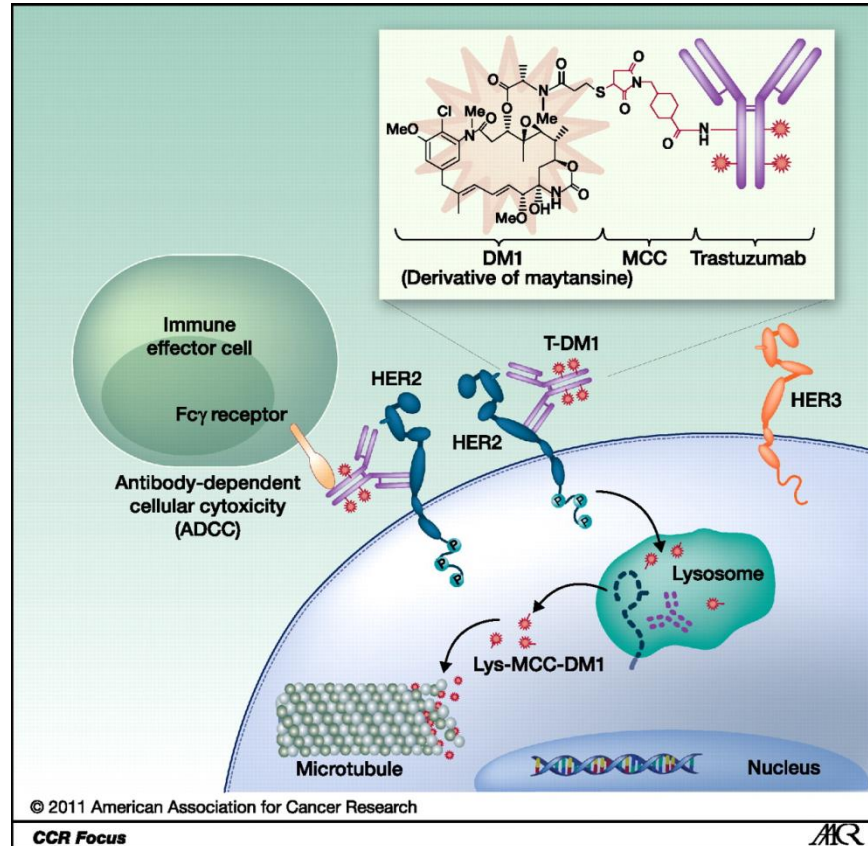
| Oxford | | |
|-----------------|----|-----|
| LoE | GR | AGO |
| 1b | B | +/- |
| 2b | B | +/- |
| 1b | B | +/- |
| 1b | B | +/- |
| 2b ^a | B | +/- |

Geringe Wirksamkeit einer alleinigen endokrinen Therapie.

Eine Induktions-Chemotherapie zusammen mit einer anti-HER2-Therapie (gefolgt von endokriner plus anti-HER2-Erhaltungstherapie) sollte in Erwägung gezogen werden!

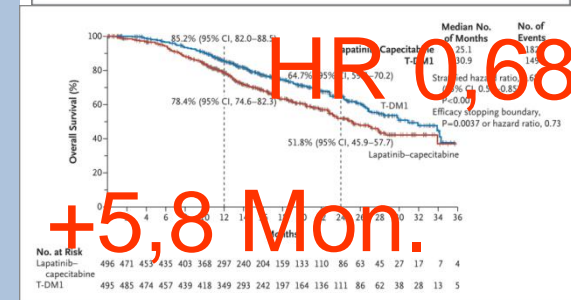
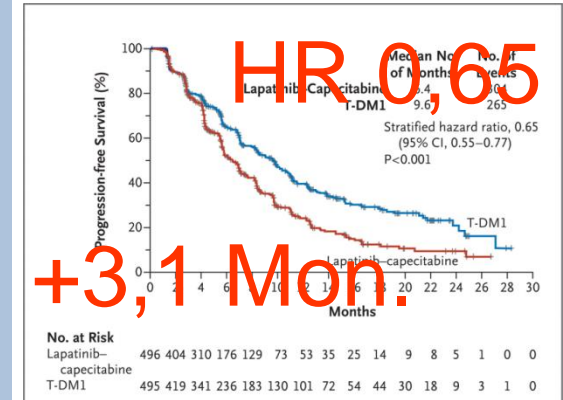
* **Studienteilnahme empfohlen**

Was kommt nach Trastuzumab / Pertuzumab?



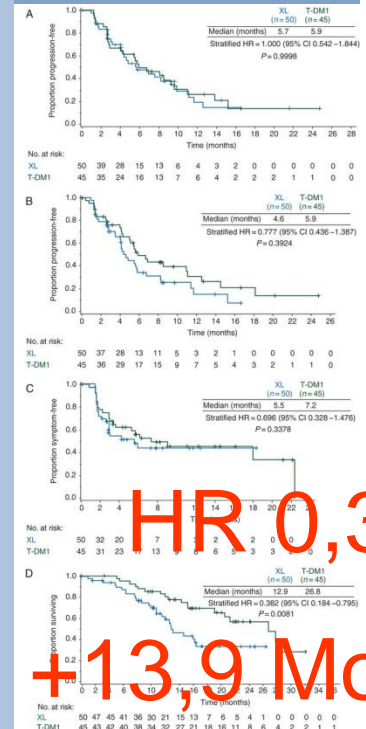
EMILIA

- HER2+ nach Trastuzumab (n=991)
 - T-DM1 vs. Lapatinib / Capecitabine
- PFS
 - 9,6 vs. 6,4 Monate; HR 0,65
- OS
 - 30,9 vs. 25,1 Monate; HR 0,68
- Grad 3/4 Toxizitäten
 - 41% vs. 57%



EMILIA - zerebrale Metastasen

- Behandelte asymptomatische ZNS Metastasen zu Studienbeginn (n=95)
 - T-DM1 vs. Lapatinib / Capecitabine
- PFS 5,9 vs. 5,7 Monate; HR 1,00
- OS 26,8 vs. 12,9 Monate; HR 0,38
- „...treated, asymptomatic CNS metastases at baseline, T-DM1 was associated with significantly improved OS...”



2nd line Therapie bei HER2-pos. mBC (nach Vorbehandlung mit Trastuzumab)



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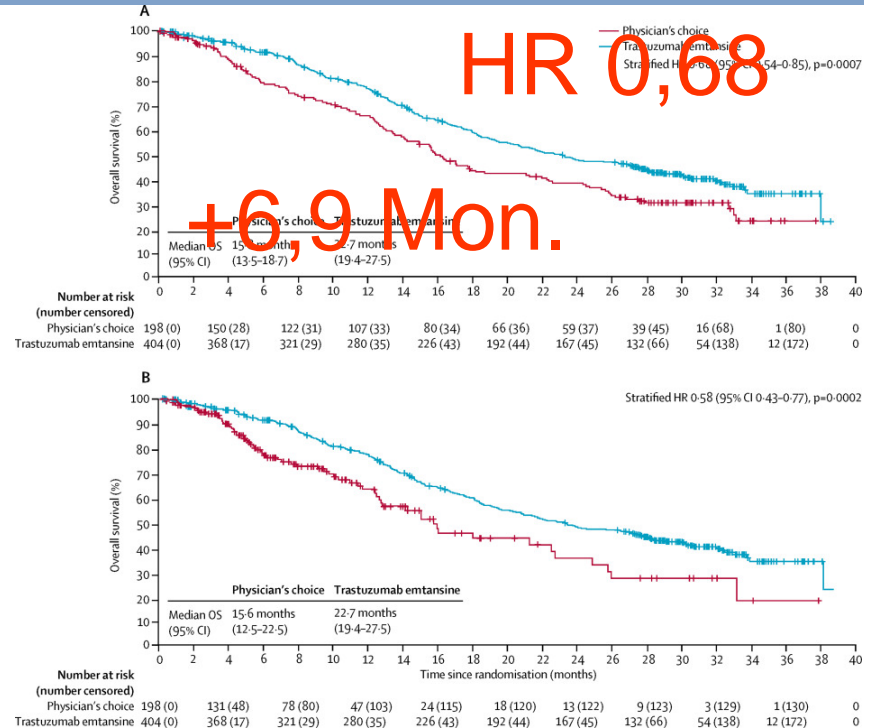
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|---|-----------------------|----------|------------|
| | LoE | GR | AGO |
| ■ T-DM 1 | 1b | A | ++ |
| ■ TBP: 2nd line Chemotherapie + Trastuzumab | 2b | B | + |
| ■ BP: 2nd line Chemotherapie + Trastuzumab + Pertuzumab | 5 | D | +/- |
| ■ 2nd line Chemotherapie* + Trastuzumab + Pertuzumab (falls noch nicht gegeben) | 5 | D | +/- |
| ■ Taxane + Trastuzumab + Pertuzumab | 5 | D | + |
| ■ Capecitabin + Trastuzumab + Pertuzumab | 1b^a | B | +/- |
| ■ Capecitabine + Lapatinib | 1b | B | + |
| ■ Trastuzumab + Lapatinib (HR neg. tumor) | 2b | B | + |

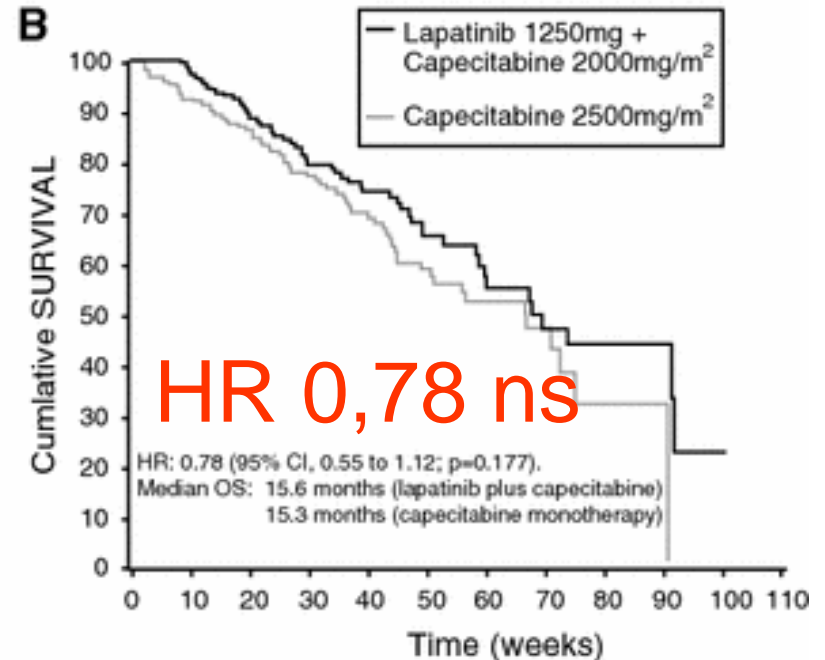
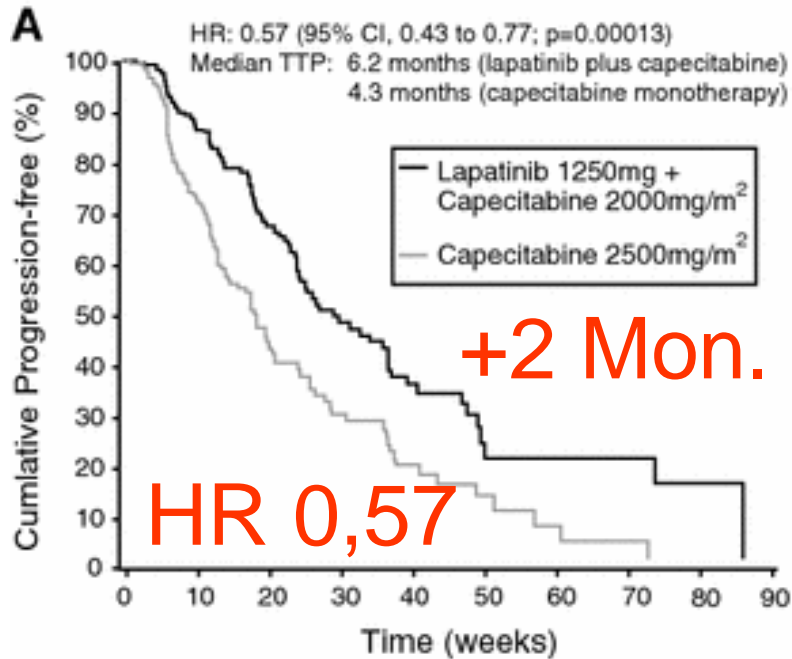
* e.g. Vinorelbine; Taxane/Carboplatin; Capecitabin/Docetaxel (Toxizität!)

TH3RESA

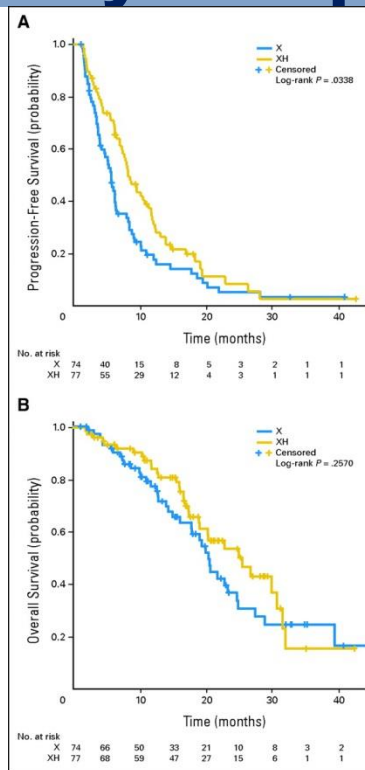
- HER2+ vorbehandelt (≥ 2 Linien) (n=602)
 - T-DM1 vs. physicians choice
- OS 22,7 vs. 15,8 Monate
 - HR 0,68
- Grad 3/4 Toxizitäten
 - 40% vs. 47%



Update Lapatinib



Treatment beyond progression



+2,6 Monate

HR 0,66

+5,1 Monate

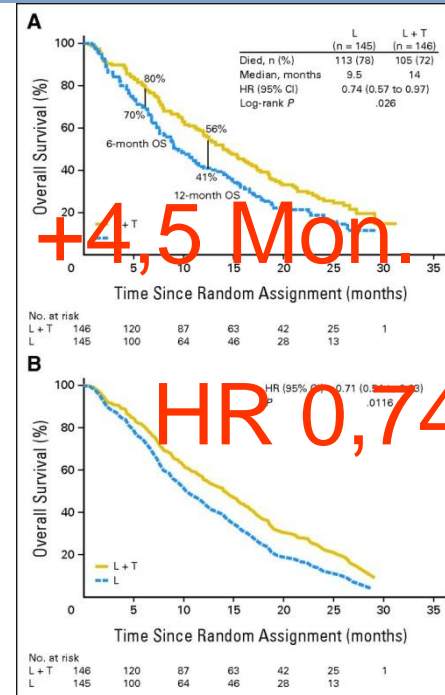
HR 0,76 ns

EGF 104900 - Trastuzumab / Lapatinib

- HER2+ metastasiert (n=291)
 - Trastuzumab/Lapatinib vs. Lapatinib

- OS 0,74
 - +15% nach 12 Monaten
 - +4,5 Monate

- **Duale Blockade effektiv** bei stark vorbehandelten HER2+ Patientinnen



Weitere Therapielinien bei HER2-pos. metastasiertem Mammakarzinom

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FORSCHEN
LEHREN
HEILEN

| | Oxford | | |
|--|---|--|---|
| | LoE | GR | AGO |
| <ul style="list-style-type: none"> ■ Vorbehandlung mit Trastuzumab <ul style="list-style-type: none"> ■ T-DM 1 ■ Capecitabin + Lapatinib ■ Vinorelbin + Lapatinib ■ Trastuzumab + Lapatinib (HR neg. Pat.) ■ Chemotherapie + Trastuzumab („<i>treatment beyond progression</i>“) ■ Pertuzumab + Trastuzumab ■ Vinorelbin + Trastuzumab + Everolimus (<i>Trastuzumab resistent, Taxan vorbehandelt</i>) ■ Daten nach Vorbehandlung mit Trastuzumab und Pertuzumab und für TBP mit Pertuzumab sind bislang nicht verfügbar. <ul style="list-style-type: none"> ■ Experimentelle Anti-HER2-Regime ■ Für Patienten nach Trastuzumab und Pertuzumab Vorbehandlung, Therapie gemäß obenstehender Empfehlungen | <p>1b</p> <p>1b</p> <p>2b</p> <p>2b</p> <p>2b</p> <p>2b</p> <p>2b</p> <p>1b</p> <p>5</p> <p>5</p> | <p>A</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>D</p> <p>D</p> | <p>++</p> <p>+</p> <p>+/-</p> <p>+</p> <p>+</p> <p>+</p> <p>+/-</p> <p>+</p> <p>+</p> |

State of the Art HER2+ metastasiertes Mammakarzinom?

**Auf jeden Fall *anti-HER2-
Therapie!***

Vielen Dank!

