

HER2-positief uitgezaaide borstkanker in Zuidoost Nederland: wat we hebben geleerd van het SONABRE register

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SONABRE Registry
SOtheast Netherlands Advanced BREast cancer

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SONABRE Registry

SOUtheast Netherlands Advanced BREast cancer



- **11** ziekenhuizen in Zuidoost Nederland
- **5000** patiënten met diagnose uitgezaaide borstkanker sinds 2007
- **100** patiënten: 3-maandelijkse kwaliteit van leven vragenlijst (EQ-5D)

De waarde van het SONABRE register

Spiegelinformatie:

- Behandelpatronen in de dagelijkse praktijk
- Implementatie nieuwe geneesmiddelen
- Patiëntuitkomsten in de dagelijkse praktijk



The initial hormone receptor/HER2 subtype is the main determinator of subtype discordance in advanced breast cancer: a study of the SONABRE registry

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Discordantie in subtype primaire tumor versus subtype van metastase

guiding systemic treatment choices in breast cancer, but can change during the disease course. This study aims to evaluate the biopsy rate and receptor subtype discordance rate in patients diagnosed with advanced breast cancer (ABC).

Methods Patients diagnosed with ABC in seven hospitals in 2007–2018 were selected from the SOtheast Netherlands Advanced BREast cancer (SONABRE) registry. Multivariable logistic regression analyses were performed to identify factors influencing biopsy and discordance rates.

Results Overall, 60% of 2854 patients had a biopsy of a metastatic site at diagnosis. One of the factors associated with a reduced biopsy rate was the HR +/HER2 + primary tumor subtype (versus HR +/HER2- subtype; OR = 0.68; 95% CI: 0.51–0.90). Among the 748 patients with a biopsy of the primary tumor and a metastatic site, the overall receptor discordance rate was 18%. This was the highest for the HR +/HER2 + primary tumor subtype, with 55%. In 624 patients with metachronous metastases, the HR +/HER2 + subtype remained the only predictor significantly related to a higher discordance rate, irrespective of prior (neo-)adjuvant therapies (OR = 7.49; 95% CI: 3.69–15.20).

Conclusion The HR +/HER2 + subtype has the highest discordance rate, but the lowest biopsy rate of all four receptor subtypes. Prior systemic therapy was not independently related to subtype discordance. This study highlights the importance of obtaining a biopsy of metastatic disease, especially in the HR +/HER2 + subtype to determine the most optimal treatment strategy.

Keywords Breast cancer · Metastatic disease · Hormone receptor · HER2 receptor · Subtype · Biopsy



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Invloed van implementatie van pertuzumab en T-DM1 op de overleving van patiënten met HER2+ MBC

Receptor subtype

Patients and methods We included 493 systemically treated patients consecutively diagnosed with HER2 + ABC in 2008–2017 from the SOtheast Netherlands Advanced BREast cancer (SONABRE) Registry. Median OS was obtained using the Kaplan–Meier method and differences between periods (2008–2012 versus 2013–2017) were tested using multivariable Cox proportional hazards regression modeling. The 3-year implementation rates were estimated for any HER2-targeted therapy, pertuzumab, and T-DM1 by using the competing risk method and calculated from the date of diagnosis of ABC to start of HER2-targeted therapy of interest.

Results The median OS in 2008–2012 versus 2013–2017 was 28.3 versus 39.7 months in all patients (adjusted hazard ratio (adjHR) 0.85, 95%CI 0.66–1.08), 29.9 versus 36.3 months in patients with HR +/HER2 + disease (adjHR 0.97, 95%CI 0.72–1.32), and 22.7 versus 40.9 months in patients with HR-/HER2 + disease (adjHR 0.59, 95%CI 0.38–0.92). Any HER2-targeted therapy was used in 79% of patients in 2008–2012 and in 84% in 2013–2017. The use of pertuzumab and T-DM1 in 2013–2017 was 48% and 29%, respectively. For patients diagnosed with HR +/HER2 + and HR-/HER2 + disease, implementation rates in 2013–2017 were, respectively, 77% and 99% for any HER2-targeted therapy, 38% and 69% for pertuzumab, and 24% and 40% for T-DM1.

Conclusion The survival of patients with HER2 + ABC improved since the introduction of pertuzumab and T-DM1. There is

Receptor discordantie

Achtergrond (1)

- Het subtype uitgezaaide borstkanker bepaalt grotendeels de behandelopties
- Conversie primaire tumor – metastase individuele receptoren

	ER	PR	HER2
- → +	22%	16%	10%
+ → -	23%	49%	21%

(Review Schrijver et al, JNCI,2018;110(6))

- Conversie op niveau van subtype onbekend

Receptor discordantie

Achtergrond (2)



- NABON richtlijn 2012

Niveau 3

Histologische bevestiging van de diagnose gemetastaseerd mammacarcinoom is gewenst ook voor bepaling van hormoonreceptoren en HER2 overexpressie, en ter uitsluiting van een benigne afwijking of een andere primaire tumor.

C [NCCN guidelines, 2010; ESMO guidelines, 2010]

- Hoe vaak wordt een biopsie van de metastase afgenomen?

Receptor discordantie

Onderzoeksvragen

1. Hoe vaak wordt er een biopt genomen van de metastase, en welke factoren hebben hier invloed op?
2. Hoe vaak verschilt het subtype van de metastase van die van de primaire tumor, en welke factoren hangen hiermee samen?

Receptor discordantie Patiënten

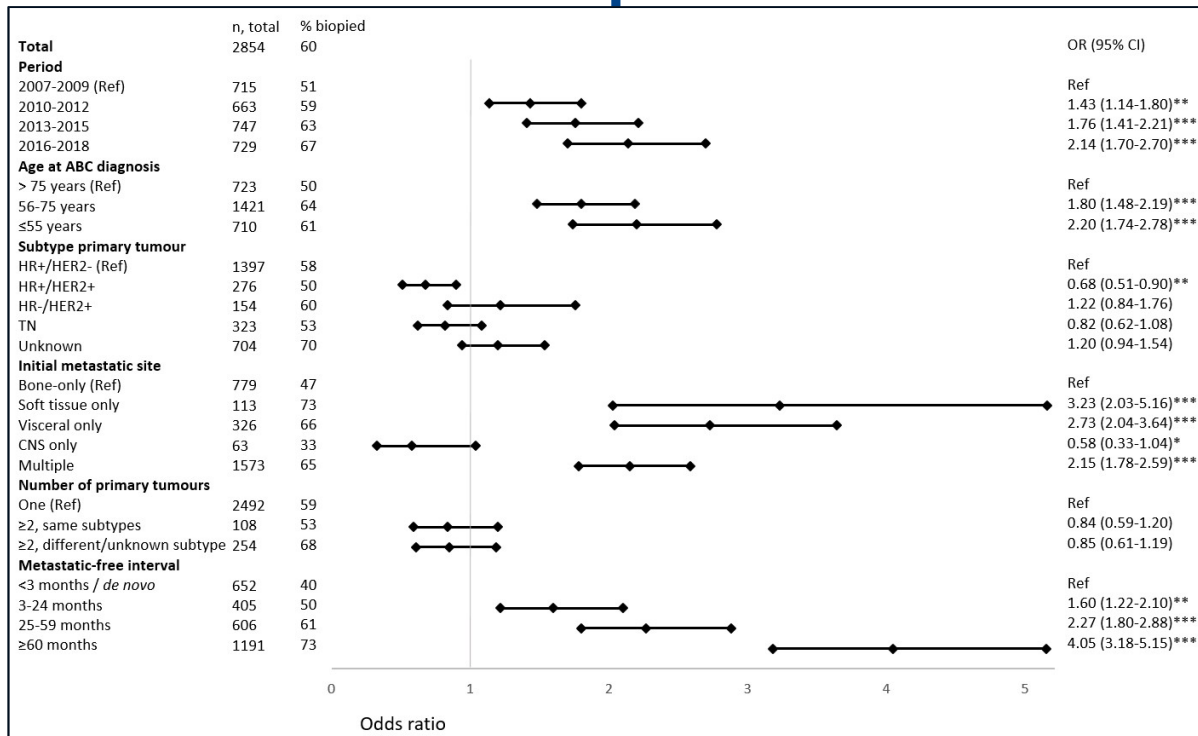


RQ1: **2854** patiënten met een diagnose MBC in 2007-2018 in 7 deelnemende ziekenhuizen

RQ2: **748** patiënten met informatie over subtype primaire tumor en metastase

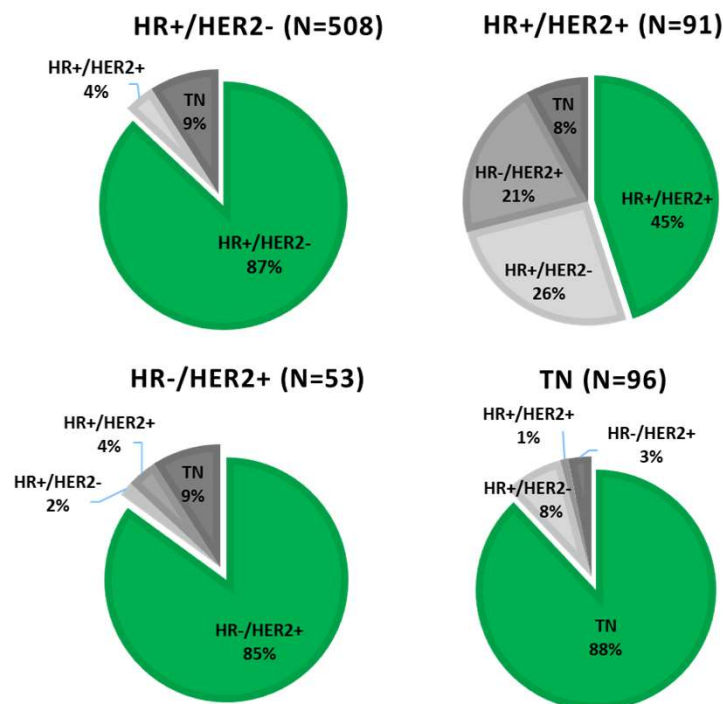
Receptor discordantie

Resultaat: 60% biopst metastase

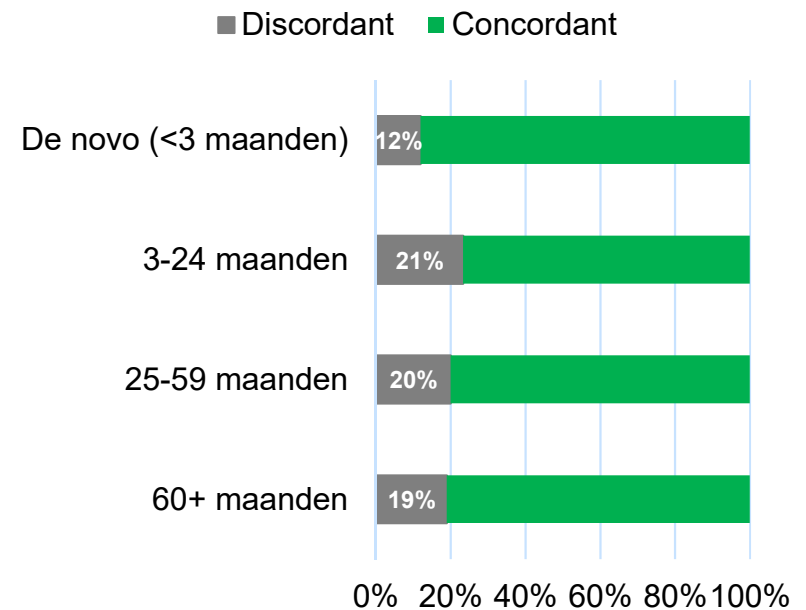


Receptor discordantie

Resultaat: 18% subtype discordantie



Metastase-vrij interval



Receptor discordantie

Discussie

Hypothese ontstaan discordantie:

1. Meetfout
2. Tumor heterogeniteit
3. Conversie, t.g.v. mutaties, systemische behandeling

Receptor discordantie

Conclusie

1. 60% biopt, 18% subtype discordantie
2. HR+/HER2+ subtype hoogste discordantie, minder vaak biopt
3. Biopt % neemt toe met MFI, maar % discordantie verschilt nauwelijks

Aanbeveling: Volg de NABON richtlijn en biopteer de metastase waar mogelijk



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HER2+ MBC

Patiënten en methoden

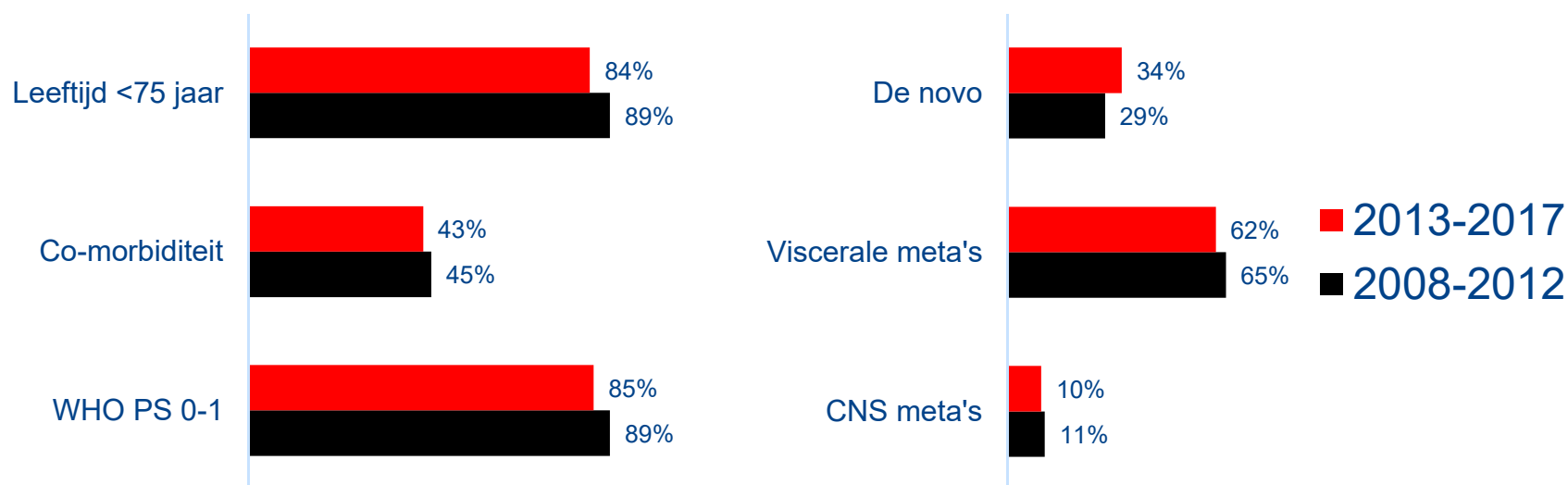
- Pertuzumab (1L) en T-DM1 (2L+) sinds 2013 beschikbaar
- Diagnose 2008-2012 versus 2013-2017:
 - Overall survival (OS)
 - Gebruik pertuzumab en T-DM1
- Follow-up in 2019
- Stratificatie van hormoon receptor status

HER2+ MBC



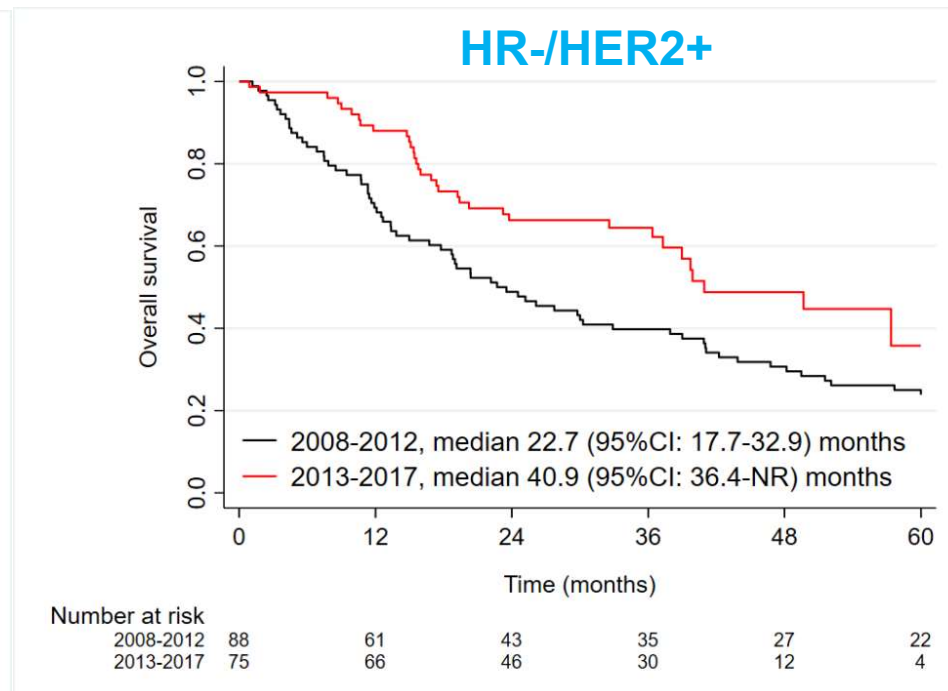
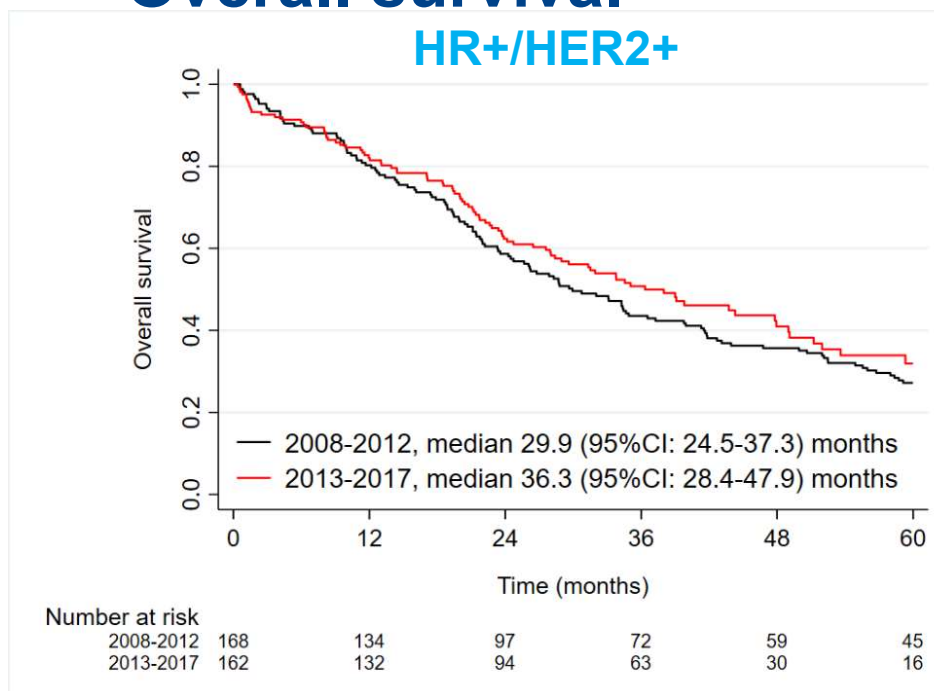
SONABRE
Registry

Kenmerken bij diagnose uitzaaiingen (n=493)



HER2+ MBC

Overall survival



HER2+ MBC

Gebruik pertuzumab en T-DM1



SONABRE
Registry

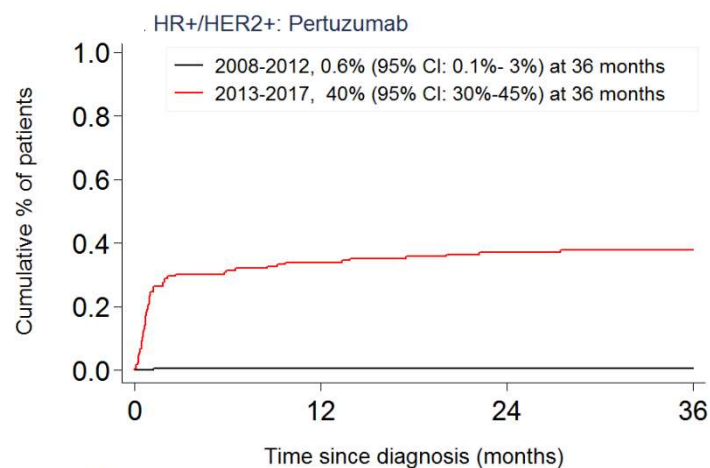
3-year use of pertuzumab and T-DM1

Pertuzumab, HR+/HER2+



0% 20% 40% 60% 80%

■ 2008-2012 ■ 2013-2018



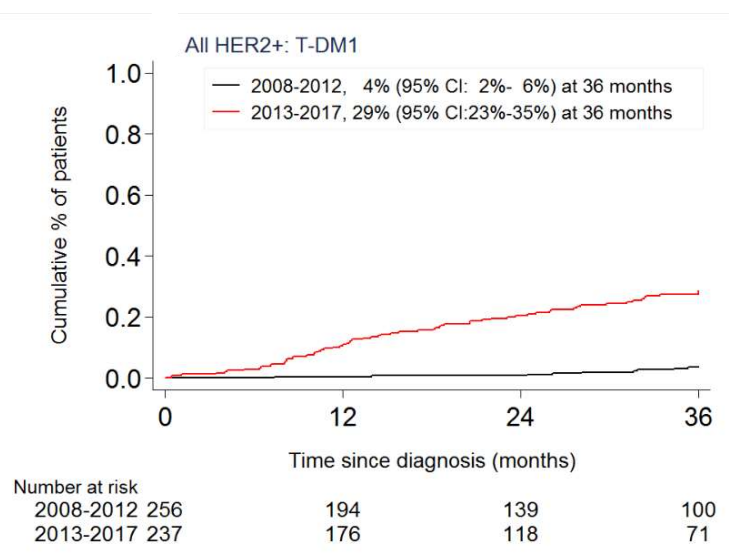
Number at risk				
2008-2012	168	39	25	17
2013-2017	162	37	16	11

HER2+ MBC

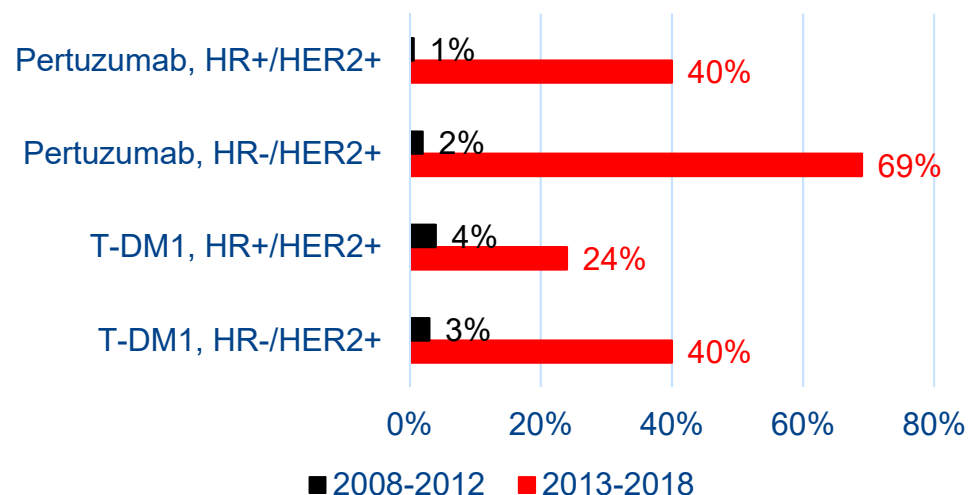
Gebruik pertuzumab en T-DM1



SONABRE
Registry



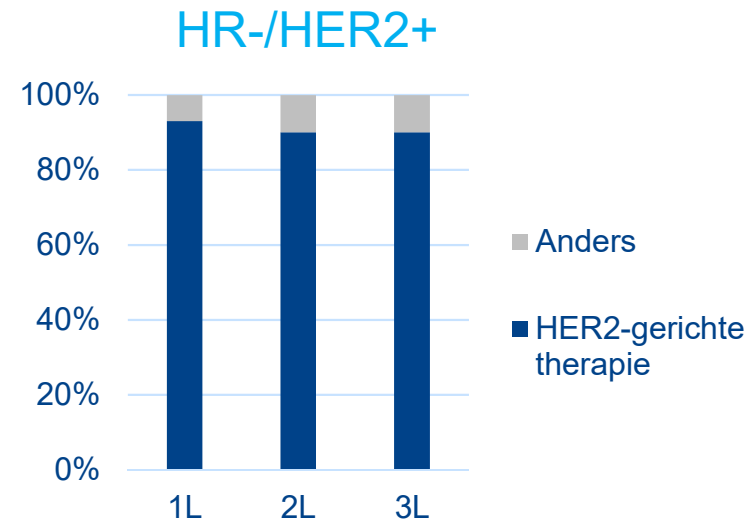
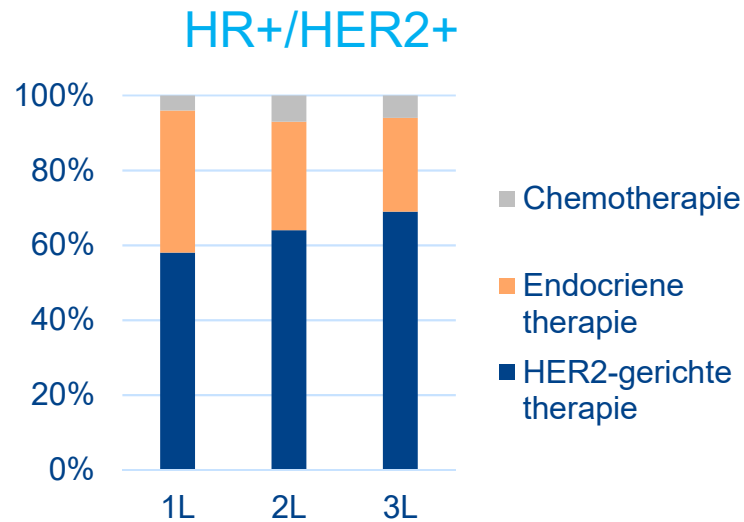
3-year use of pertuzumab and T-DM1



HER2+ MBC

Behandelpatronen sinds 2013

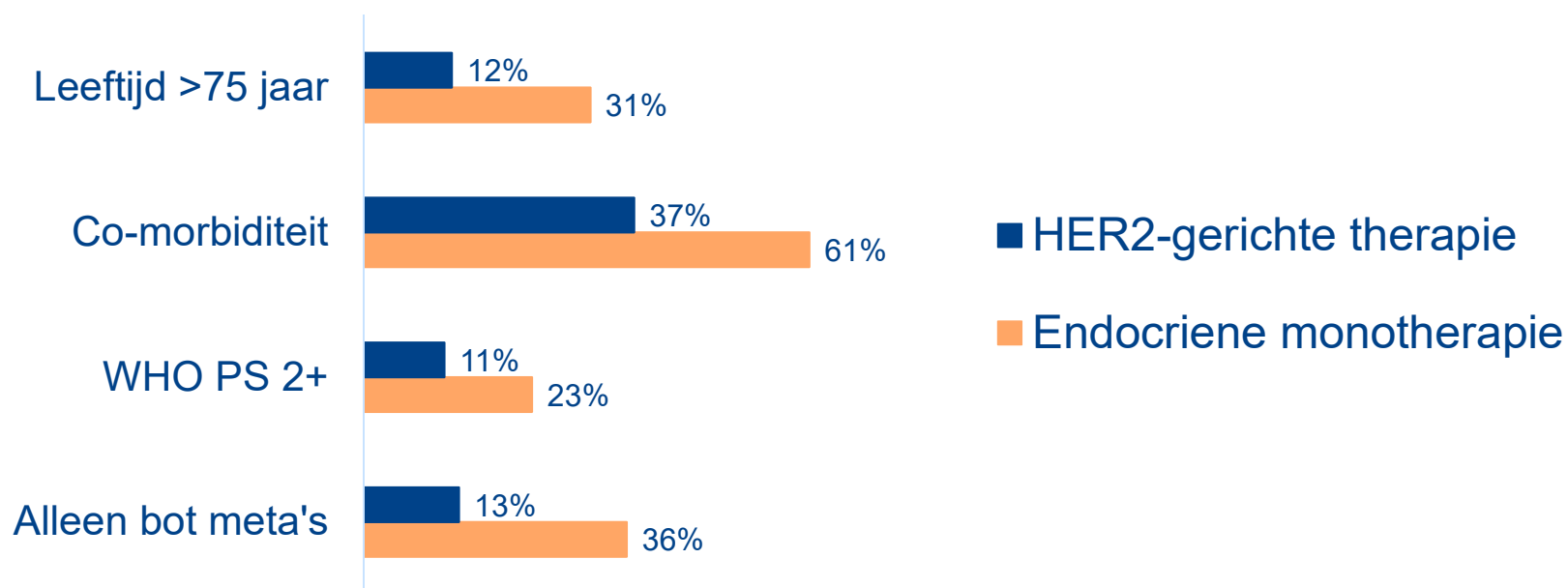
Minder HER2-gerichte therapie voor HR+/HER2+ MBC



HER2+ MBC

Behandelpatronen sinds 2013

Karakteristieken bij start 1^e lijn HR+/HER2+ MBC



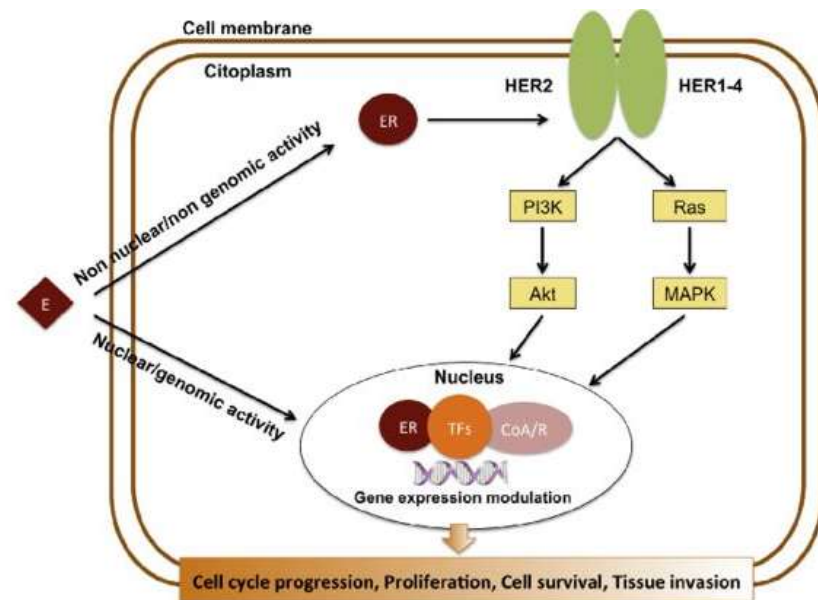
HER2+ MBC

Discussie

HR+/HER2+

Cross-talk tussen ER en HER2

Belang HER2-gerichte plus
endocrine (onderhouds-)
behandeling (ASCO 2022)



Schettini, Cancer Treat Rev. 2016;46:20-6.

HER2+ MBC

Samenvattend



HR+/HER2+

- Nauwelijks verbetering in OS
- Veelvuldig gebruik endocriene monotherapie

HR-/HER2+

- OS toename in lijn met CLEOPATRA (pertuzumab)
- Goede implementatie pertuzumab en T-DM1

Aanbeveling HR+/HER2+ (ASCO 2022):

Gebruik 1^e lijn HER2-gerichte therapie indien mogelijk, ook bij een mild beloop.
Gevolgd door HER2-gerichte plus endocrine onderhoudsbehandeling.

Wat hebben we geleerd

1. Receptor bepaling metastase belangrijk
2. Voorzichtig met gebruik nieuwe geneesmiddelen
3. HR+/HER2+: start waar mogelijk met pertuzumab, trastuzumab plus taxaan, gevolgd door onderhoudsbehandeling middels endocrien, pertuzumab en trastuzumab. Optimale behandelduur van pertuzumab en trastuzumab onduidelijk (aandachtspunt BOOG).

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Patiënten

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