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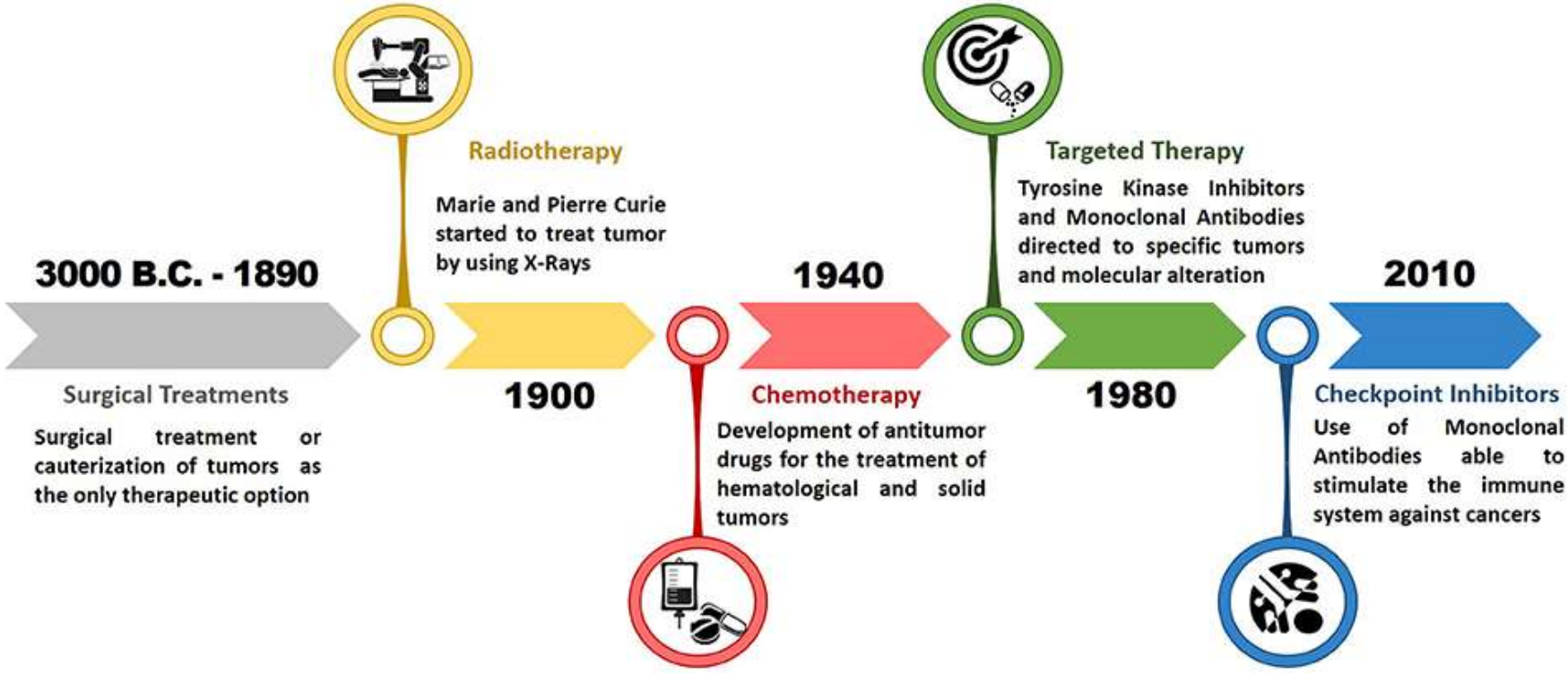
STERK IN ZORG

DE CARDIOLOOG IN HET LEVEN VAN DE ONCOLOGISCHE PATIËNT: NOODZAKELIJKE SYMBIOSE MET ALLE NIEUWE GENEESMIDDELEN?

DR. CHRISTOPHE DELENS
CARDIOLOOG

Evolutie van oncologische behandelingen.



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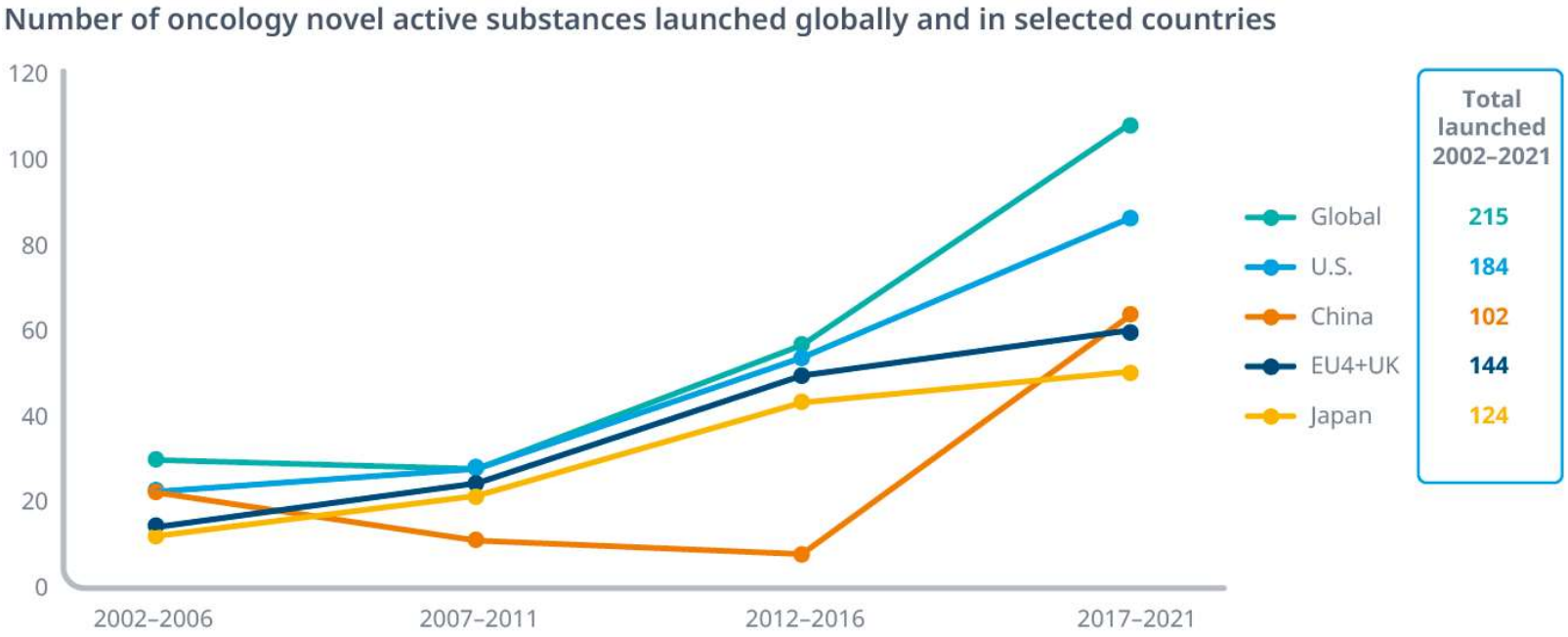
EVOLUTION OF CANCER PHARMACOLOGICAL TREATMENTS AT THE TURN OF THE THIRD MILLENNIUM. FALZONE ET AL. FRONT.PHARMACOL. 2018.

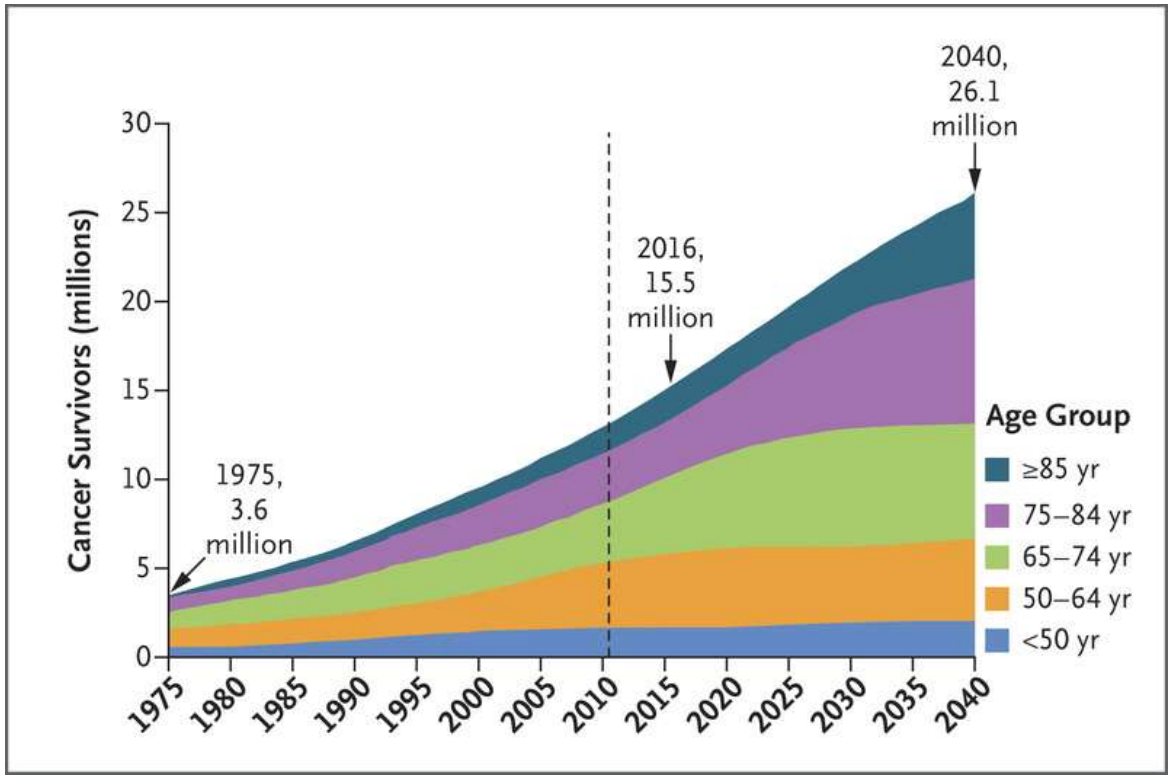
Evolutie van oncologische behandelingen.



Source: IQVIA Institute, Apr 2022.
Notes: A novel active substance (NAS) is a new molecular or biologic entity or combination where at least one element is new and is noted in the year it launches for the first time in the relevant geography. Oncology includes diagnostics.
Report: Global Oncology Trends 2022: Outlook to 2026. IQVIA Institute for Human Data Science, May 2022.

Evolutie oncologische prognose.

CHANGING DEMOGRAPHIC CHARACTERISTICS OF CANCER SURVIVORS IN THE UNITED STATES.



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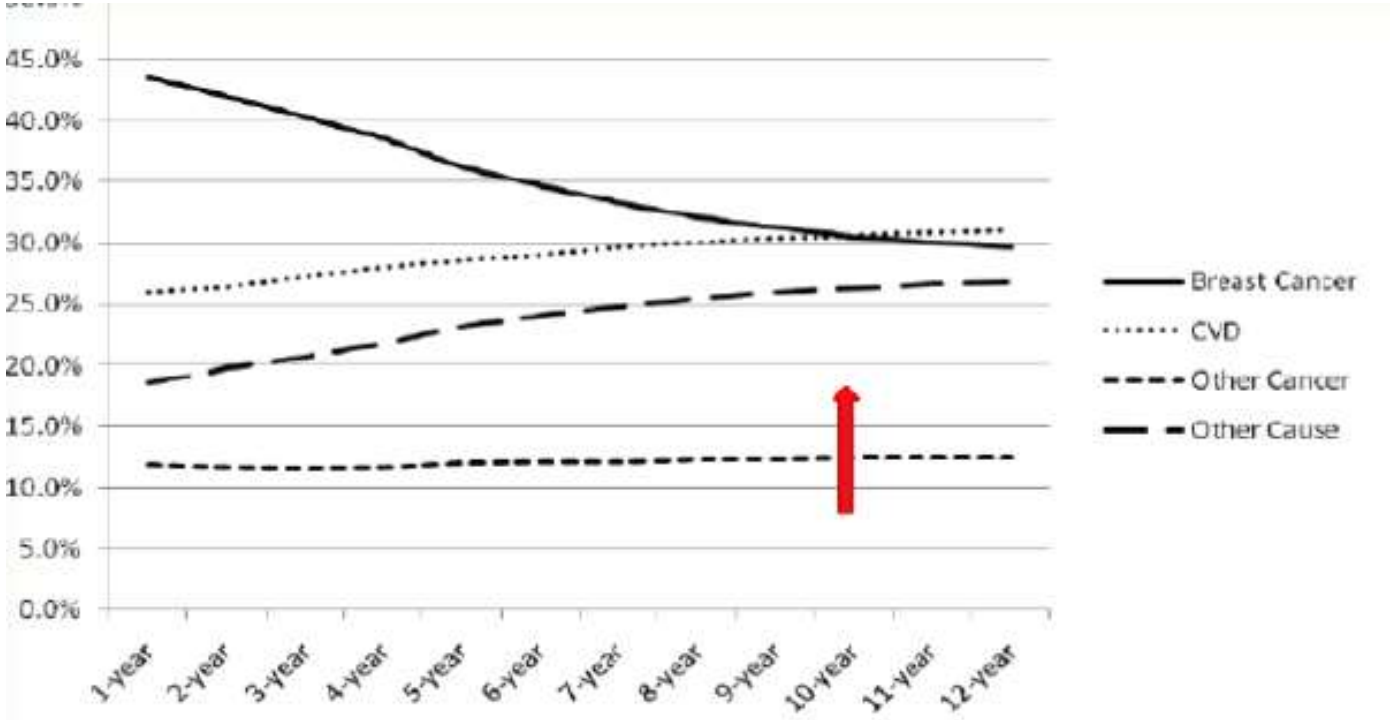
CANCER SURVIVORSHIP. CHARLES ET AL. NEJM. 2018.

Betere oncologische prognose.



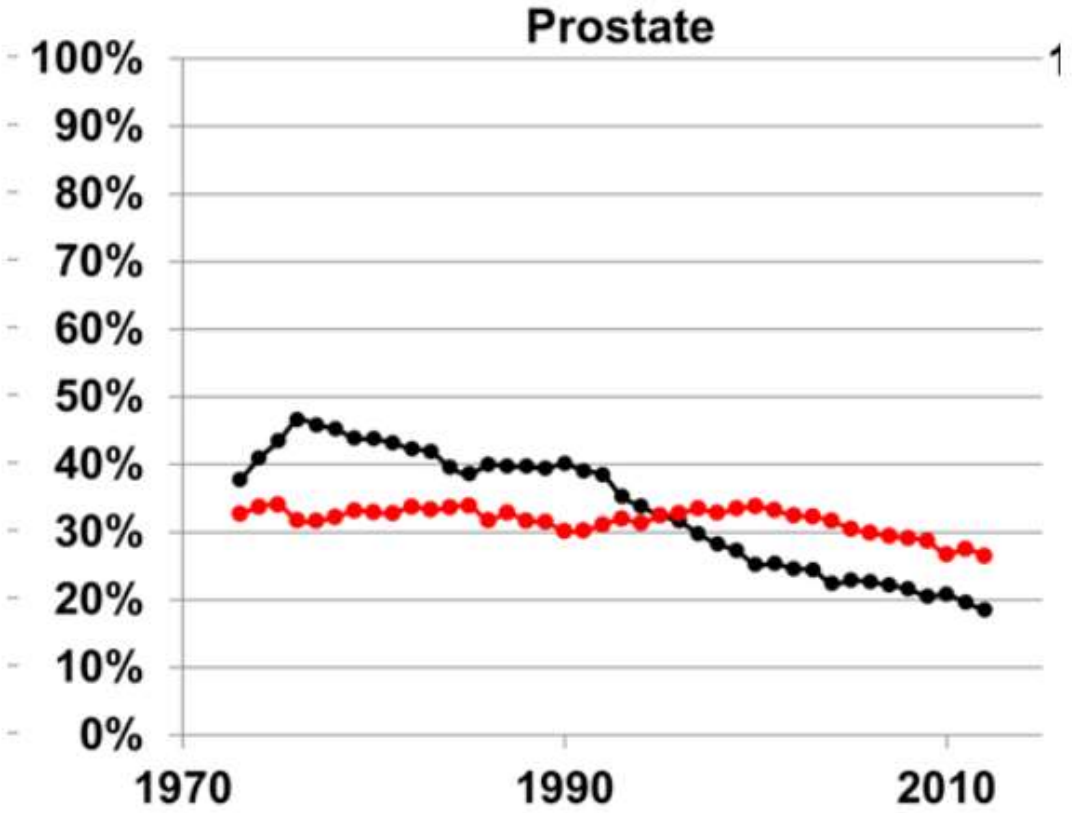
ure 2 Proportional distribution of cumulative leading causes of death by time since breast cancer diagnosis. CVD: cardiovascular ase.

OKWUOSO, JACC 2015

Betere oncologische prognose.

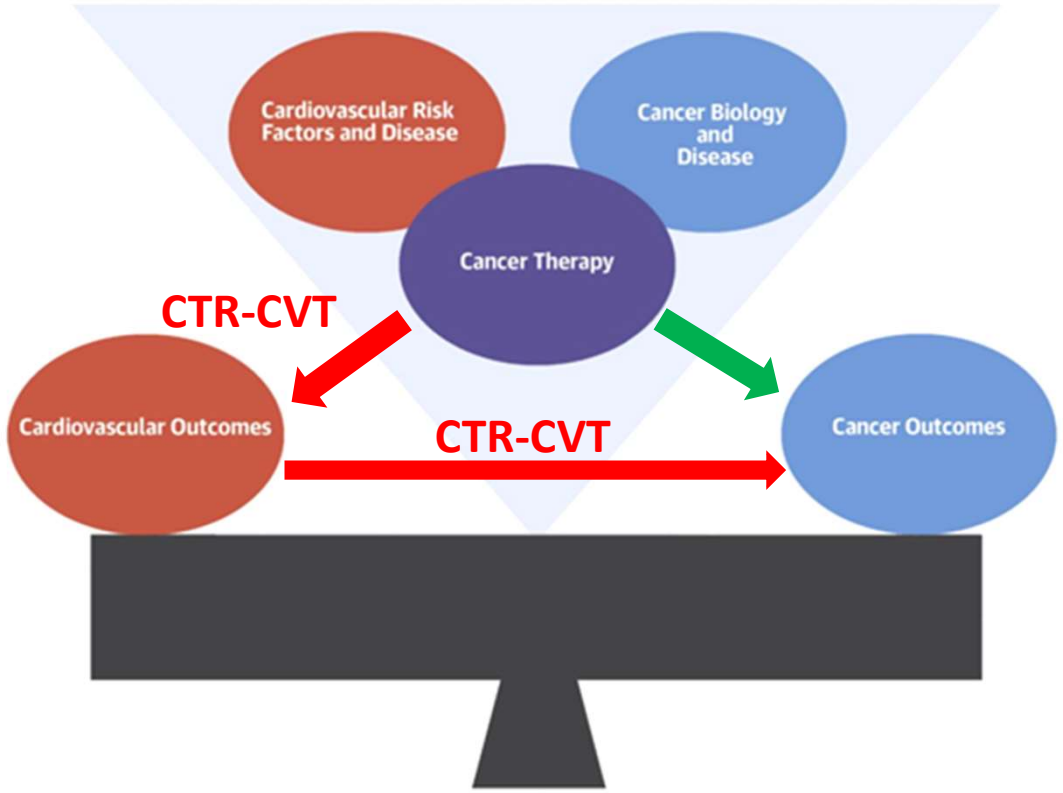
Cohorte in de VS:
509 128 patiënten met prostaatCA

Jaarlijkse overlijdenspercentages
-t.g.v. kanker
-cardiovasculaire sterfte



EUROPEAN HEART JOURNAL, EHZ766, HTTPS://DOI.ORG/10.1093/EURHEARTJ/EHZ766

Toenemend belang van CTR-CVT



Soorten CTR-CVT

Aritmieën

Myocarditis / Pericarditis

Perifeer vaatlijden

Pulmonale hypertensie

TABLE 3 Anticancer Agents Associated With Myocardial Infarction/Ischemia

Chemotherapy Agents	Frequency of Use	Incidence (%)	Prevention/ Treatment
Antimetabolites			
Capecitabine			
Flourouracil			
Monoclonal antibody-based tyrosine kinase inhibitors			
Bevacizumab	+++	0.6-8.5	
Small molecule tyrosine kinase inhibitors			
Nilotinib	++++	5.0-9.4	
Ponatinib	+		
Angiogenesis inhibitors			
Lenalidomide	+++		
Antimicrotubule agents			
Paclitaxel	++++	<1.5	

Frequency of use was determined using inpatient and outpatient doses dispensed at MD Anderson Cancer Center during the time period of January 1, 2014, through December 21, 2014. + = <1,000 doses dispensed; ++ = 1,000-5,000 doses dispensed; +++ = 5,000-10,000 doses dispensed; and ++++ = >10,000 doses dispensed (1,2,24,29).

TABLE 1 Anticancer Agents Associated With Hypertension

Chemotherapy Agents	Frequency of Use	Incidence (%)	Comments
nal antibody-based tyrosine kinase inhibitors			Pre-treatment risk asses
zumab	+++	4-35	
astuzumab	+	5.1	BP goal <140/90 mm H
			Weekly BP monitoring ir
numab			
nab			
ibitors			
imus			
olimus			
olecule tyrc			
anib			
Histone deacetylase inhibitors			
Belinostat	+	4-1	
Vorinostat	++++	3.5-6	
		26-9	
antinib			
ib			
ib			
irumab			
afenib			
tinib			
tanib			
Dabrafenib	++++	2-1	
Dasatinib	++++	<1-	
Lapatinib	++++	10-1	
Nilotinib			
Vandetani			
BRAF inhibit			
Vemurafenib	++++	3	
Trametanib	++++		
Proteasome inhibitor			
Carfilzomib	++		
Bortezomib	++		
Miscellaneous			
Tretinoin	++++		
Ziv-aflibercept			
Proteasome inhibitc			
Bortezomib			
Carfilzomib			
Antimetabolites			
Decitabine			

See Table 1 for frequency of use description (55,72).

K = potassium; Mg = magnesium; QTc = corrected QT in

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BP = blood pressure; HTN = hypertension.

Frequency of use was determined using inpatient during the time period of January 1, 201 dispensed; ++ = 1,000-5,000 doses and ++++ = >10,000 doses dispensed (1,2,24,

ACEI = angiotensin-converting enzyme inhibit longitudinal strain; HF = heart failure.

TABLE 2 Anticancer Agents Associated With Thromboembolism

Chemotherapy Agents	Frequency of Use	Incidence (%)	Comments
Alkylating agents			Risk factors: cancer types, metastatic disease, central venous catheter, heart failure, immobility, AF, previous history of thromboembolism, chemotherapy, hormonal therapy, old age, female
Cisplatin	+++	8.5-16.7	
Angiogenesis inhibitors			
Lenalidomide	+++	3-75	
Thalidomide			
Vorinostat			
Monoclonal antibody against VEGF			Diagnosis: compression ultrasonography, spiral CT, MR
Bevacizumab	+++	6.0-15.1	
mTOR inhibitors			
Everolimus	++++	1-4	Treatment options: aspirin, warfarin, LMWH
Small molecule tyrosine kinase inhibitors			
Axitinib	++++	3	
Dabrafenib	++++	7	Limited data with DOAC
Erlotinib	++++	3.9-11.0	
Sunitinib	++++	3	
Trametinib	++++	7	
Ziv-aflibercept	+	9	

See Table 1 for frequency of use description (55,72).

AF = atrial fibrillation; CT = computed tomography; DOAC = direct oral anticoagulant; LMWH = low molecular weight heparin; MR = magnetic resonance.

CHANG JACC 2017

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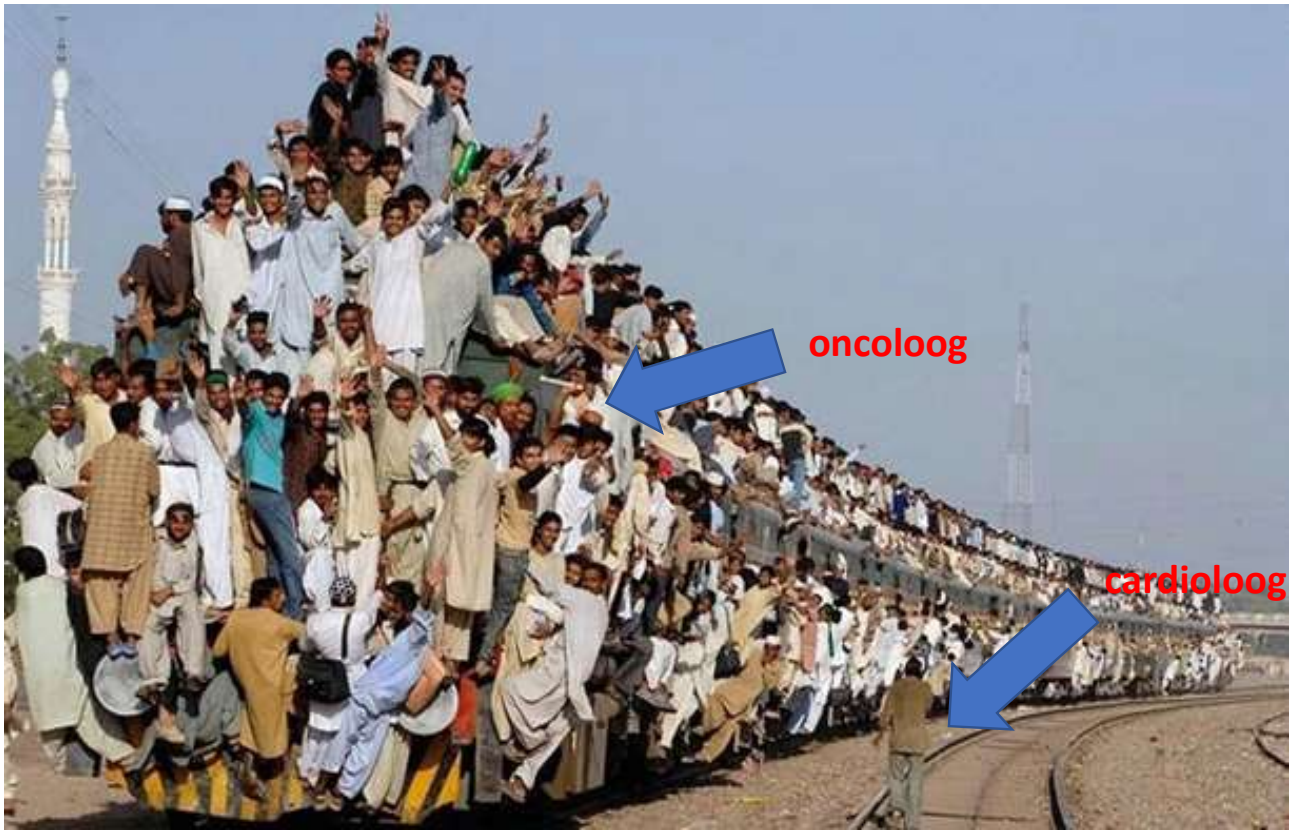
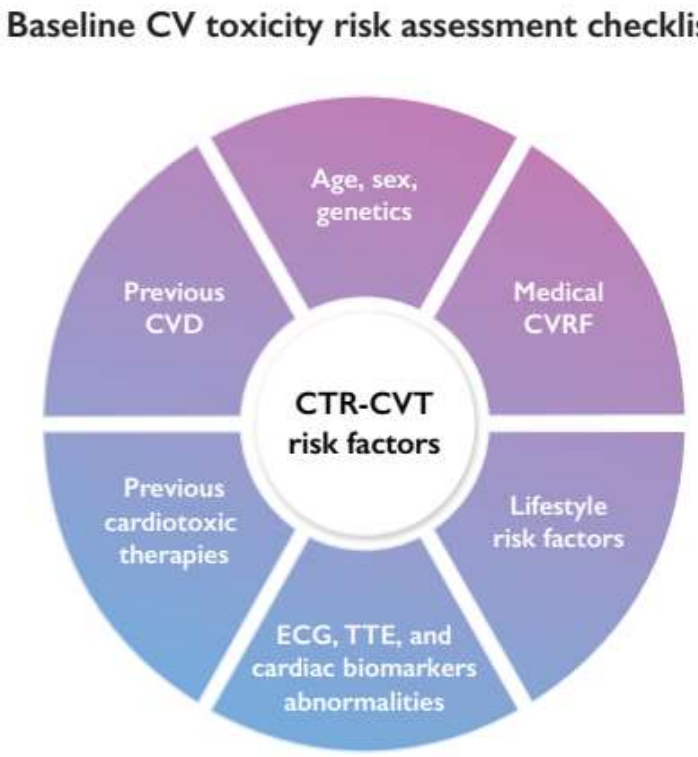
Cardio-oncologie voor 2015:



Doel van cardio-oncologie?

The overarching goal of the cardio-oncology discipline is to allow patients with cancer to receive the best possible cancer treatments safely,
minimizing CTR-CVT across the entire continuum of cancer care

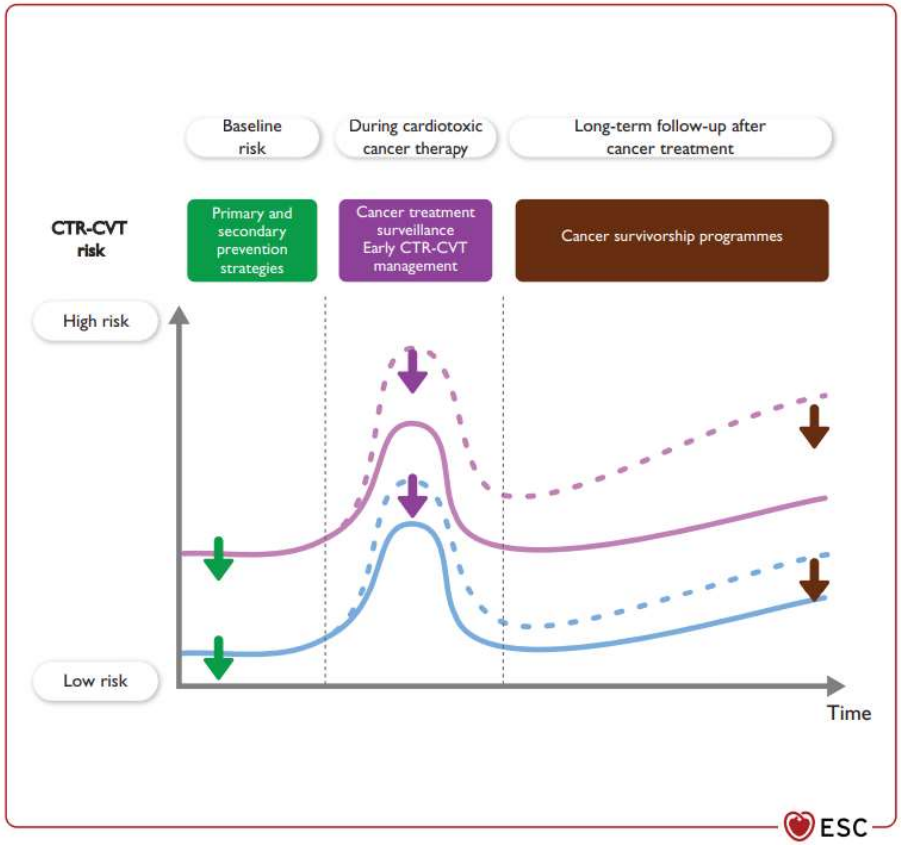
Wat is het risico op CTR-CVT.



Andere factoren :
- cancer type and prognosis
- type, duration, and intensity of cancer treatment.

ESC GUIDELINES CARDIO-ONCOLOGY 2022

Hoe risico op CTR-CVT minimaliseren?



Cardio-oncology strategy may reduce the magnitude of CTR-CVT by:

- optimizing CVD and CVRF management
- considering cardioprotective strategies in high-risk patients

- organizing cancer treatment surveillance
- introducing early cardioprotection after the detection of subclinical CTR-CVT

- identifie CS who require long-term follow-up. Cancer survivorship programmes that include annual CV risk assessment and CVRF/CVD management are recommended to minimize long-term CV adverse events

CRT-CVT: hoe screenen en behandelen?

ESC Guidelines on cardio-oncology

26 Aug 2022

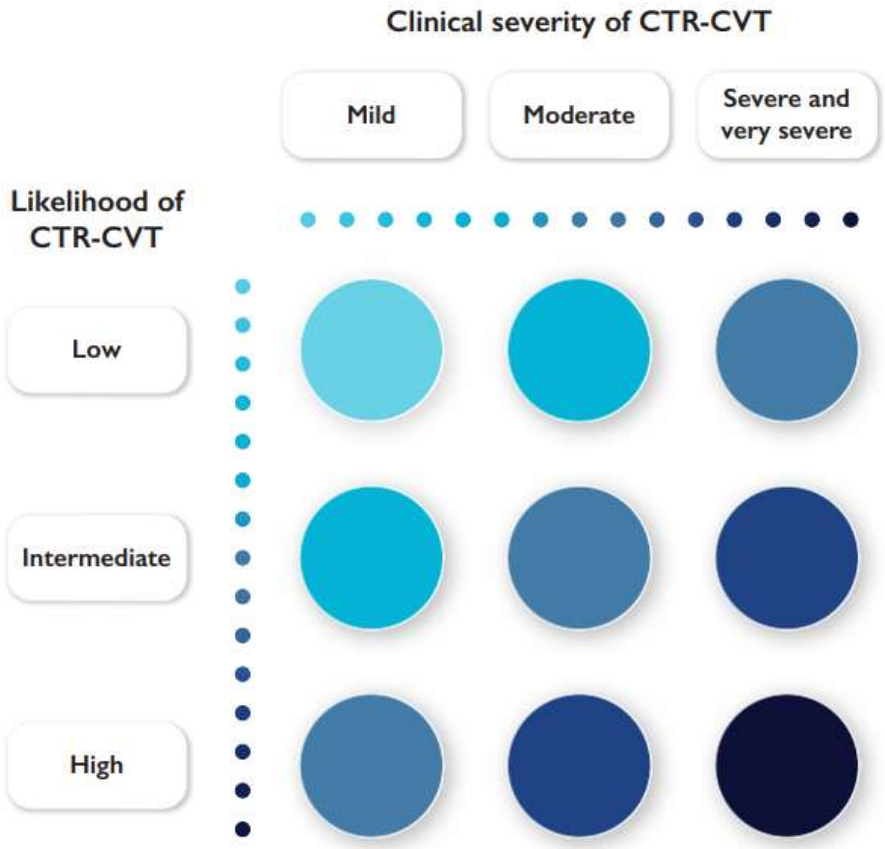
This is the first European Society of Cardiology (ESC) guideline on cardio-oncology. The aim of this guideline is to help all the healthcare professionals providing care to oncology patients before, during, and after their cancer treatments with respect to their cardiovascular health and wellness. This guideline provides guidance on the definitions, diagnosis, treatment, and prevention of cancer therapy-related CV toxicity, and the management of CV disease caused directly or indirectly by cancer. This area of medicine has limited trials and evidence to base decision making and, where evidence is limited, this guideline provides the consensus of expert opinion to guide healthcare professionals.

HTTPS://WWW.ESCARDIO.ORG/GUIDELINES/CLINICAL-PRACTICE-GUIDELINES/CARDIO-ONCOLOGY-GUIDELINES

Oncologische behandelingen

Anthracyclines	BCR-ABLi	ICI
HER 2i	Bruton-TKI	ALKi & EGFRi
CDK 4/6i	CAR-T	VEGFi
Fluoropyrimidines	Radiotherapie	RAFi & MEKi
Anti-hormonale therapie borstCa	Multipel myeloom therapie	Anti-androgeen therapie

Risicostratificatie.



Risicostratificatie:

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HTTPS://WWW.ESCARDIO.ORG/GUIDELINES/CLINICAL-PRACTICE-GUIDELINES/CARDIO-ONCOLOGY-GUIDELINES

Risicostratificatie.

Deel 1/2

Low risk patients: no risk factors OR one moderate1 risk factor

Moderate risk patients: moderate risk factors with a total of 2–4 points (Moderate 1 [M1] = 1 point; Moderate [M2] = 2 points)

High and very high risk patients: high risk (H) = moderate risk factors with a total of ≥5 points OR any high-risk factor
very-high risk (VH) = any very-high risk factor.

Table 4 Heart Failure Association–International Cardio-Oncology Society baseline cardiovascular toxicity risk stratification

Baseline CV toxicity risk factors	Anthracycline chemotherapy	HER2-targeted therapies	VEGF inhibitors	BCR-ABL inhibitors	Multiple myeloma therapies	RAF and MEK inhibitors
Previous CVD						
HF/cardiomyopathy/ CTRCD	VH	VH	VH	H	VH	VH
Severe VHD	H	H	–	–	–	H
MI or PCI or CABG	H	H	VH	–	–	H
Stable angina	H	H	VH	–	–	H
Arterial vascular disease	–	–	VH	VH	VH	–
Abnormal ankle-brachial pressure index	–	–	–	H	–	–
PH	–	–	–	H	–	–
Arterial thrombosis with TKI	–	–	–	VH	–	–
Venous thrombosis (DVT/PE)	–	–	H	M2	VH	–
Arrhythmia[a]	–	M2	M2	M2	M2	M1
QTc ≥ 480 ms	–	–	H	H	–	–
450 ≤ QTc < 480 ms (men); 460 ≤ QTc < 480 ms (women)	–	–	M2	M2	–	–
Prior PI CV toxicity	–	–	–	–	VH	–
Prior IMiD CV toxicity	–	–	–	–	H	–
Cardiac imaging						
LVEF < 50%	H	H	H	H	H	H
LVEF 50–54%	M2	M2	M2	–	M2	M2
LV hypertrophy	–	–	–	–	M1	–
Cardiac amyloidosis	–	–	–	–	VH	–
Cardiac biomarkers						
Elevated baseline cTn[b]	M1	M2	M1	–	M2	M2
Elevated baseline NP[b]	M1	M2	M1	–	H	M2

HTTPS://WWW.ESCARDIO.ORG/GUIDELINES/CLINICAL-PRACTICE-GUIDELINES/CARDIO-ONCOLOGY-GUIDELINES

Risicostratificatie.

Deel 2/2

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Age and CVRF						
Age ≥ 80 years	H	H	–	–	–	M1
Age 65–79 years	M2	M2	–	–	–	M1
Age ≥ 75 years	–	–	H	H	H	M1
Age 65–74 years	–	–	M1	M2	M1	M1
Age ≥ 60 years	–	–	–	M1	–	–
CVD 10-year risk score > 20%	–	–	–	H	–	–
Hypertension[c]	M1	M1	H	M2	M1	M2
Chronic kidney disease[d]	M1	M1	M1	M1	M1	M1
Proteinuria	–	–	M1	–	–	–
DM[e]	M1	M1	M1	M1	M1	M1
Hyperlipidaemia[f]	–	–	M1	M1	M1	–
Family history of thrombophilia	–	–	–	M1	M1	–
Current cancer treatment						
Dexamethasone > 160 mg/month	–	–	–	–	M1	–
Includes anthracycline before HER2-targeted therapy	–	M1[g]	–	–	–	–
Previous exposure to						
Anthracycline	H	M2[h]	H	–	H	H
Trastuzumab	–	VH	–	–	–	–
RT to left chest or mediastinum	H	M2	M1	–	M1	M2
Non-anthracycline chemotherapy	M1	–	–	–	–	–
Lifestyle risk factors						
Current smoker or significant smoking history	M1	M1	M1	H	M1	M1
Obesity (BMI > 30 kg/m^2)	M1	M1	M1	M1	M1	M1

HTTPS://WWW.ESCARDIO.ORG/GUIDELINES/CLINICAL-PRACTICE-GUIDELINES/CARDIO-ONCOLOGY-GUIDELINES

Casus 1

- 76 jarige vrouw – opname via spoed o.w.v. progressieve dyspnoe

- voorgeschiedenis :
  - 1990 Arteriële hypertensie
  - Hypothyroidie
  - Hypercholesterolemie
  - 2016 invasief ductulair borstCa links, graad 3 met expressie van basale cytokeratines. pT2N1. ER 0/8. PR 0/8. HER2-score 0/3. R/tumorectomie + chemo (EC DD –Taxol) + radiotherapie (15x2,67Gy en nadien boost 5x)

- Medicatie:
  - Aprovel 300mg 1dd
  - L-thyroxine 75mcg 1dd
  - Simvastatine 20mg 1dd
  - Esomeprazole 40mg 1dd
  - Zolpidem 10mg 1dd

Casus 1

- Echocardiografie:

  Niet gedilateerd LV met ernstig gedaalde systolische functie (EF 25-30%)
  diffuse hypokinesie, beste kinetiek inferolateraal
  Geen significant kleplijden
  Intravasculair overvuld.

Cordecompensatie bij de novo cardiomyopathie met ernstig gedaalde functie

Casus 1

Differentiaal diagnose:

1. Toxische cardiomyopathie
2. Ischemische cardiomyopathie
3. Idiopathische cardiomyopathie

→ *Cardiovasculaire risicofactoren:*

Nicotine –
AHT +
Hypercholesterolemie +
DM -
Familiaal –
Obesitas + (BMI 38,8)
Radiotherapie linker hemithorax +

Risicostratificatie.

Deel 1/2

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Severe VHD	H	H	–	–	–	H
MI or PCI or CABG	H	H	VH	–	–	H
Stable angina	H	H	VH	–	–	H
Arterial vascular disease	–	–	VH	VH	VH	–
Abnormal ankle-brachial pressure index	–	–	–	H	–	–
PH	–	–	–	H	–	–
Arterial thrombosis with TKI	–	–	–	VH	–	–
Venous thrombosis (DVT/PE)	–	–	H	M2	VH	–
Arrhythmia[a]	–	M2	M2	M2	M2	M1
QTc ≥ 480 ms	–	–	H	H	–	–
450 ≤ QTc < 480 ms (men); 460 ≤ QTc < 480 ms (women)	–	–	M2	M2	–	–
Prior PI CV toxicity	–	–	–	–	VH	–
Prior IMiD CV toxicity	–	–	–	–	H	–
Cardiac imaging						
LVEF < 50%	H	H	H	H	H	H
LVEF 50–54%	M2	M2	M2	–	M2	M2
LV hypertrophy	–	–	–	–	M1	–
Cardiac amyloidosis	–	–	–	–	VH	–
Cardiac biomarkers						
Elevated baseline cTn[b]	M1	M2	M1	–	M2	M2
Elevated baseline NP[b]	M1	M2	M1	–	H	M2

Risicostratificatie.

Deel 2/2

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Age ≥ 60 years	–	–	–	M1	–	–
CVD 10-year risk score > 20%	–	–	–	H	–	–
Hypertension[c]	M1	M1	H	M2	M1	M2
Chronic kidney disease[d]	M1	M1	M1	M1	M1	M1
Proteinuria	–	–	M1	–	–	–
DM[e]	M1	M1	M1	M1	M1	M1
Hyperlipidaemia[f]	–	–	M1	M1	M1	–
Family history of thrombophilia	–	–	–	M1	M1	–
Current cancer treatment						
Dexamethasone > 160 mg/month	–	–	–	–	M1	–
Includes anthracycline before HER2-targeted therapy	–	M1[g]	–	–	–	–
Previous exposure to						
Anthracycline	H	M2[h]	H	–	H	H
Trastuzumab	–	VH	–	–	–	–
RT to left chest or mediastinum	H	M2	M1	–	M1	M2
Non-anthracycline chemotherapy	M1	–	–	–	–	–
Lifestyle risk factors						
Current smoker or significant smoking history	M1	M1	M1	H	M1	M1
Obesity (BMI > 30 kg/m^2)	M1	M1	M1	M1	M1	M1

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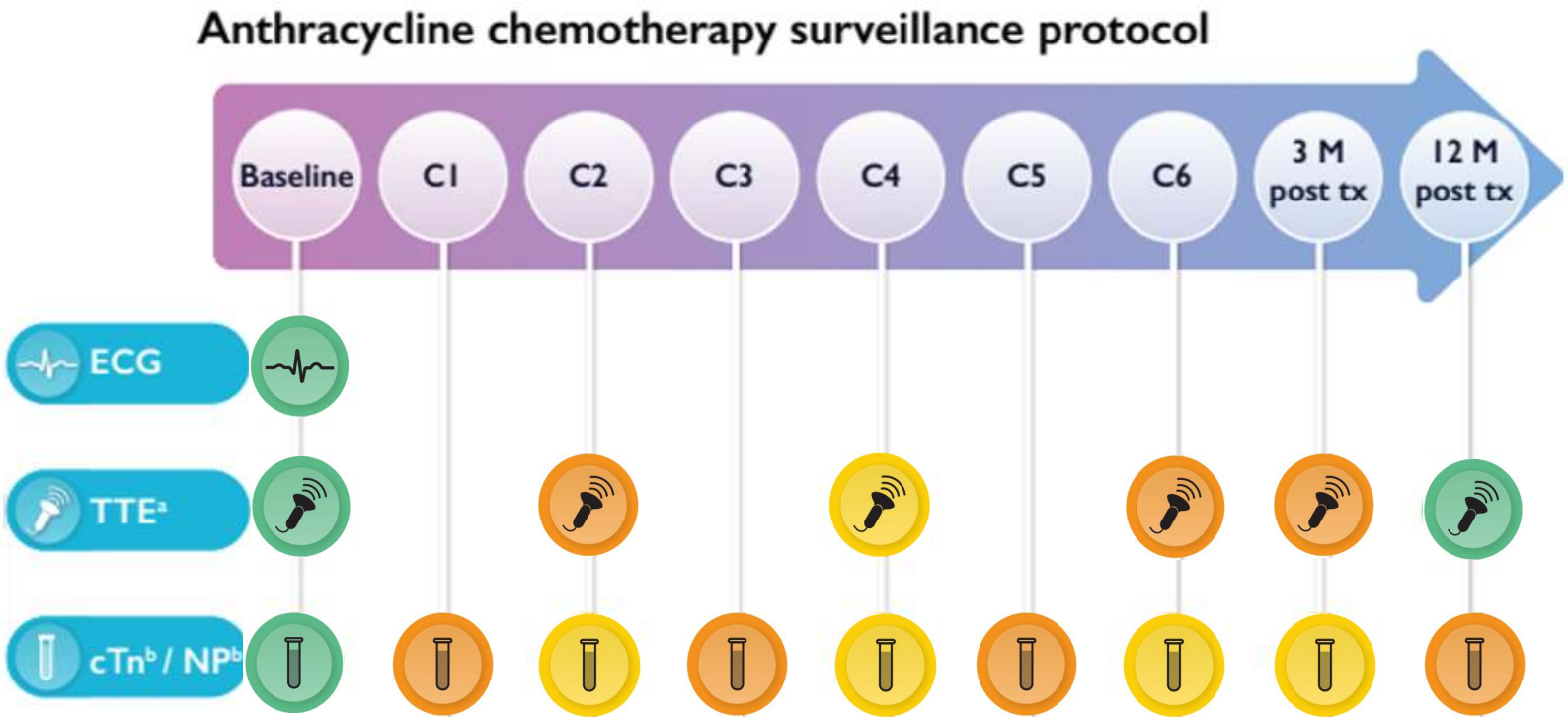
Casus 1



- Low risk patients
- Intermediate risk patients +
- High risk patients + +

VITAZ

Casus 1

La réponse dépend essentiellement de **la mise en route précoce du traitement IEC/B-**

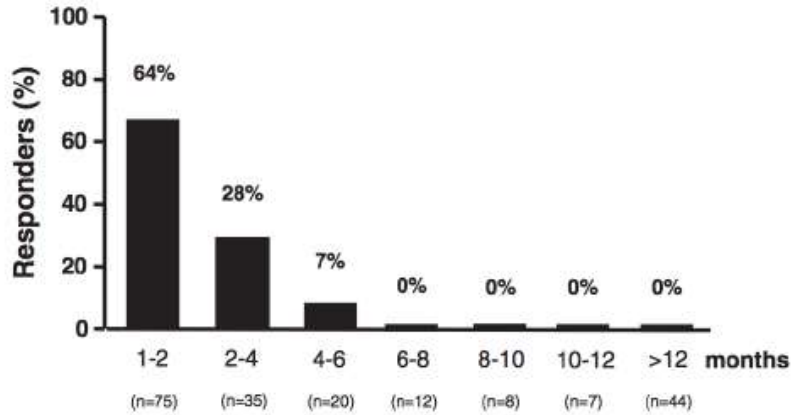


Figure 1 Percentage of Responders According to the Time Elapsed From AC Administration and Start of HF Therapy

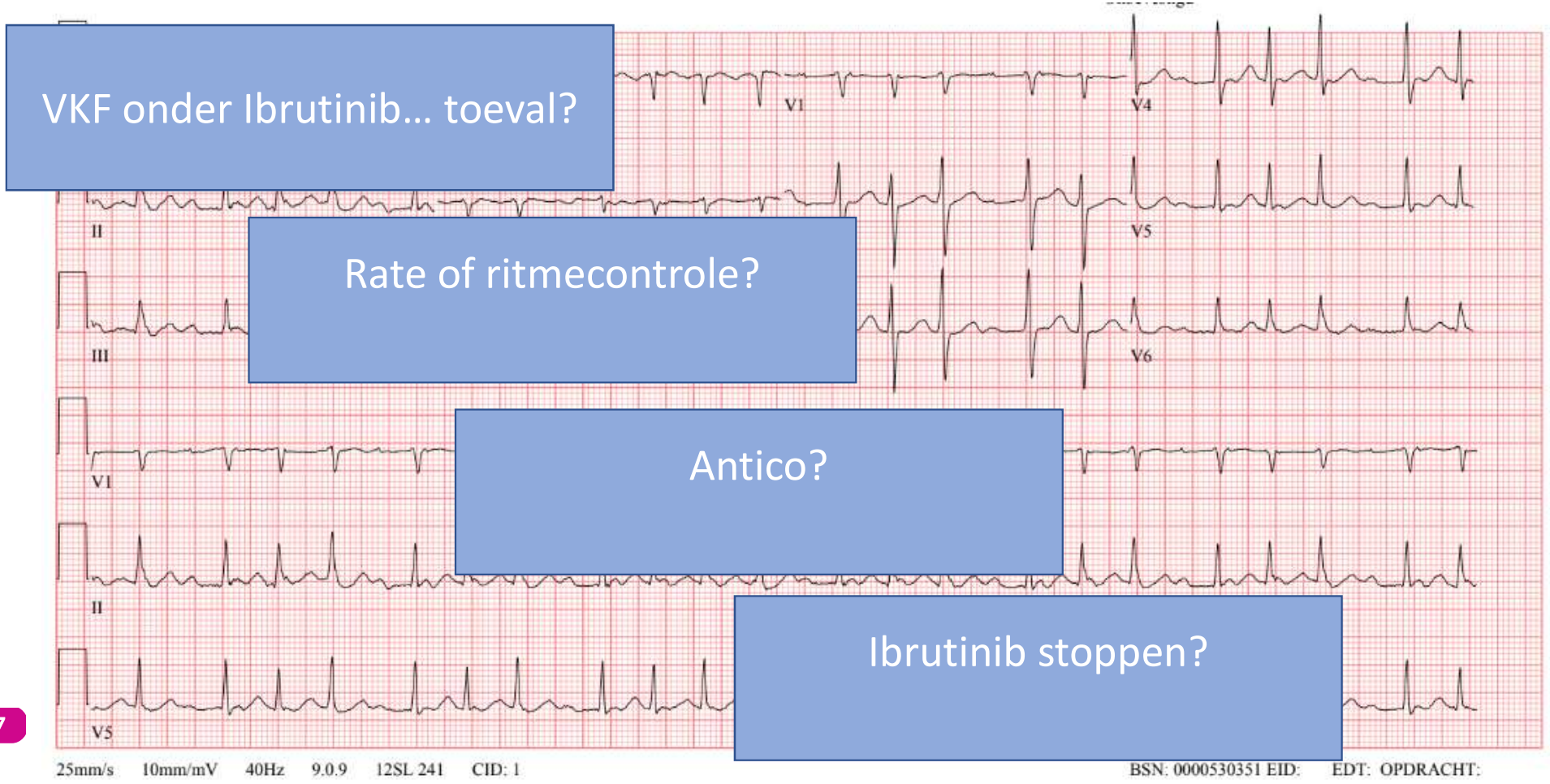
Vroege detectie is cruciaal !

Cardinale D, et al. J Am Coll Cardiol 2010; 55:213–20

Casus 2

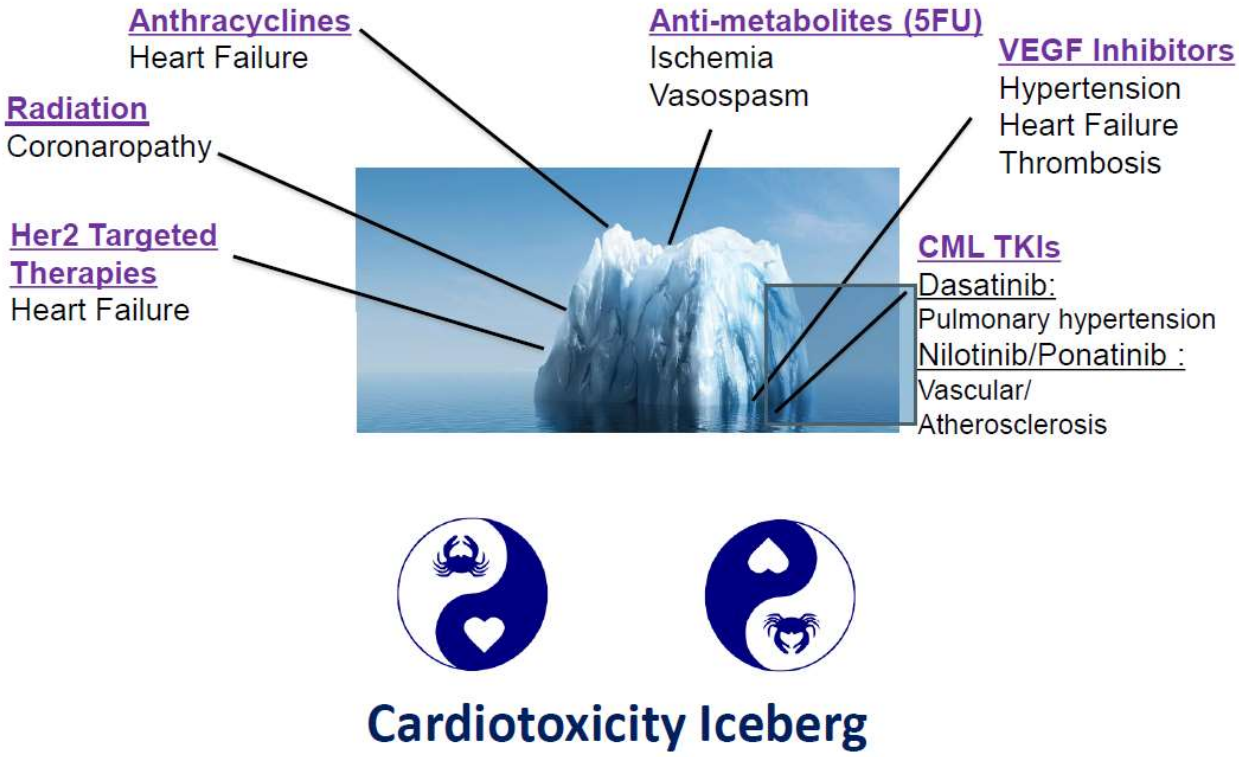
- 68 jarige man
- voorgeschiedenis :
  - 2018 PTCA RCA
  - 2021 CLL R/Bruton Tyrosine Kinase inhibitor
- Medicatie:
  - Asaflow 80mg 1dd
  - bisoprolol 2,5mg 1dd
  - Atorvastatine 80mg 1dd
  - Ibrutinib 140mg 3dd

Casus 2


VKF onder Ibrutinib… toeval?
Rate of ritmecontrole?
Antico?
Ibrutinib stoppen?
I
II
III
V1
V4
V5
V6
V1
II
V5
25mm/s 10mm/mV 40Hz 9.0.9 12SL 241 CID: 1
BSN: 0000530351 EID: EDT: OPDRACHT:

Besluit:

1. Veel oncologische behandelingen zijn potentieel cardiotoxisch



Besluit:

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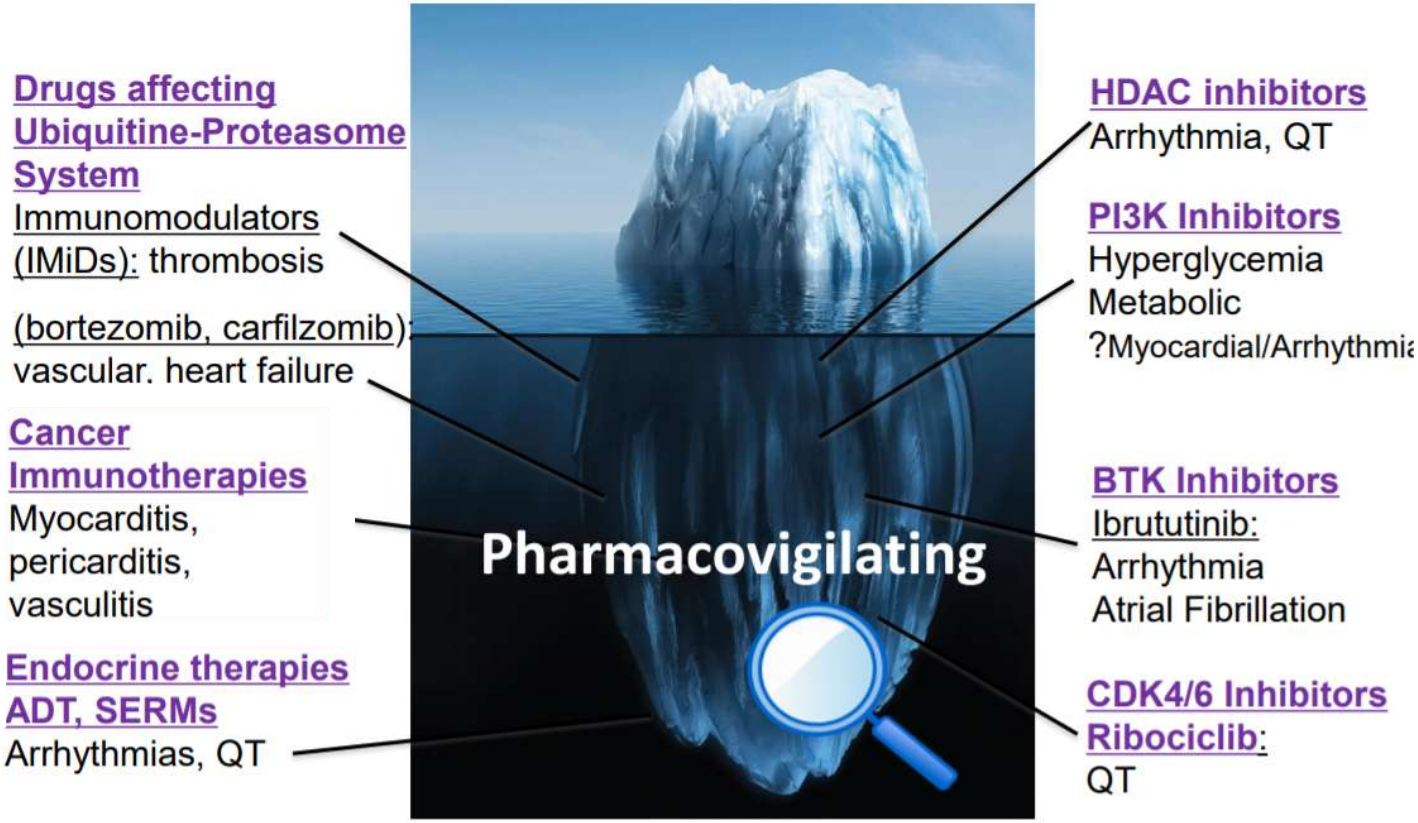


Besluit:

1. **Veel oncologische behandelingen zijn potentieel cardiotoxisch**

2. **Steeds betere prognose voor oncologische patiënten**

Besluit:

1. **Veel oncologische behandelingen zijn potentieel cardiotoxisch**

2. **Steeds betere prognose voor oncologische patiënten**

3. **Goede cardiovasculaire opvolging cruciaal**

Besluit:

1. **Veel oncologische behandelingen zijn potentieel cardiotoxisch**

2. **Steeds betere prognose voor oncologische patiënten**

3. **Goede cardiovasculaire opvolging cruciaal**

4. **Doel cardio-oncologie:**
   - **voorkomen, opsporen en snel behandelen van cardiotoxiciteit**
   - **Onderbreking van oncologische therapie trachten te voorkomen**

ZORGPAD BORSTKLINIEK IN SAMENWERKING MET DE HUISARTS

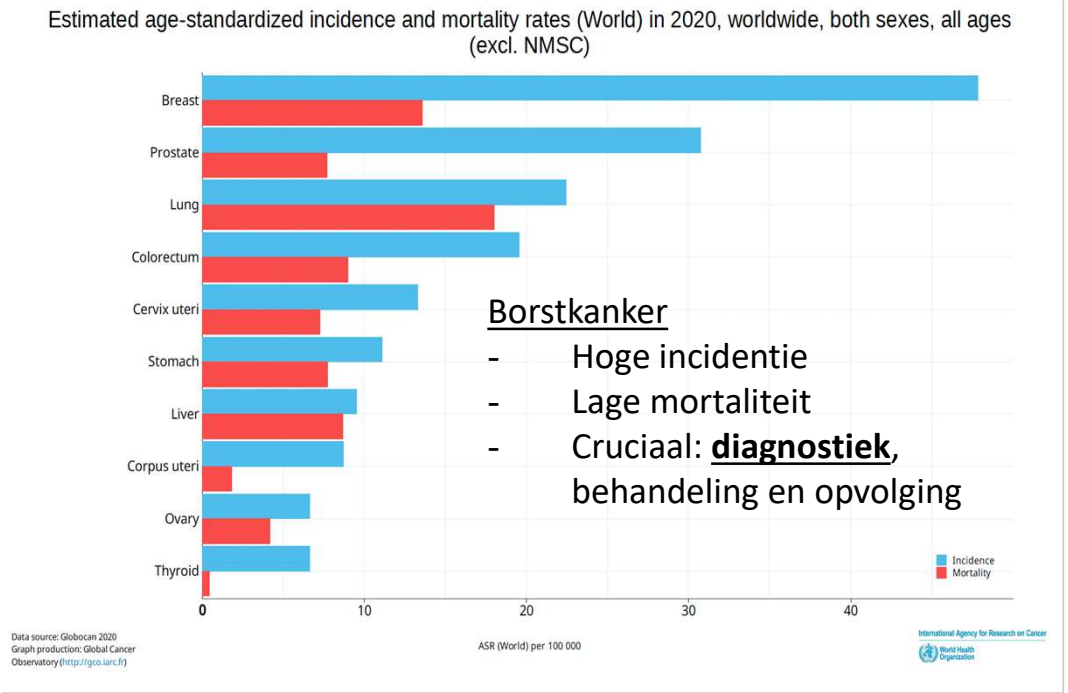
DR. CAROLINE LAMOT

Doelstelling borstkliniek Vitaz

- ❖ Behandelplan op maat van de patient:
  - snelle opvang en expertise
  - aanwezigheid van multidisciplinair ervaren team
  - beschikbaarheid van de meest moderne apparatuur en technieken: nieuw mammografietoestel met tomografie
- ❖ Maximale continuïteit van de zorg + laagdrempelig
- ❖ Continu verbeteren van informatie en communicatie, ook naar de huisarts
- ❖ Streven naar een optimale ondersteuning van patiënt
  - daling psychische morbiditeit
  - ondersteunen van de therapietrouw
  - oncorevalidatie

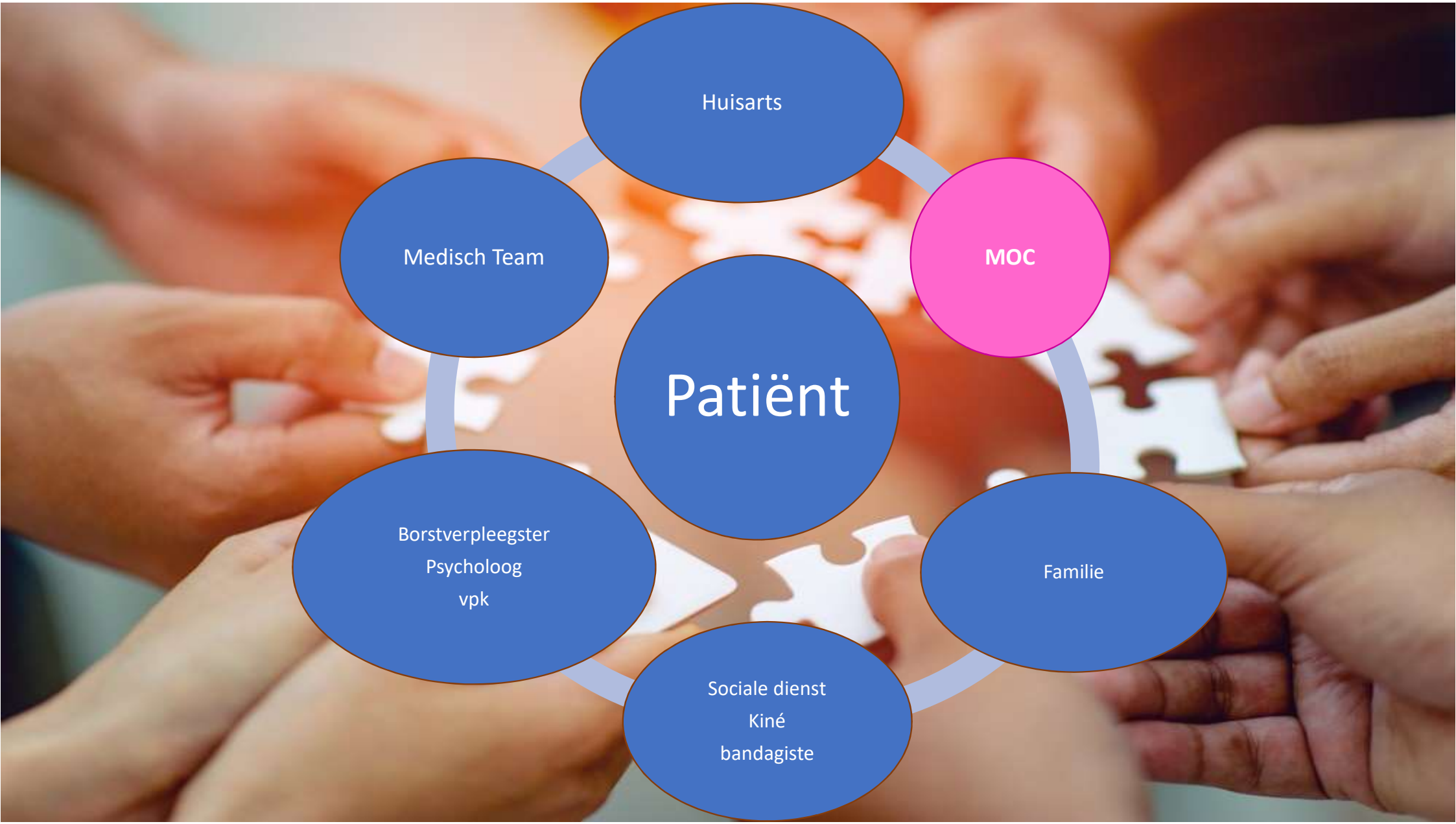
Doelstelling borstkliniek Vitaz

- Kwaliteitsnormen → genezings- en overlevingskansen groter → betere levenskwaliteit
- Uitwerken van evidence-based richtlijnen
- Stimuleren van wetenschappelijk onderzoek en deelname aan studies
- Permanente bijscholing en opleiding
- Registratie kankerregister

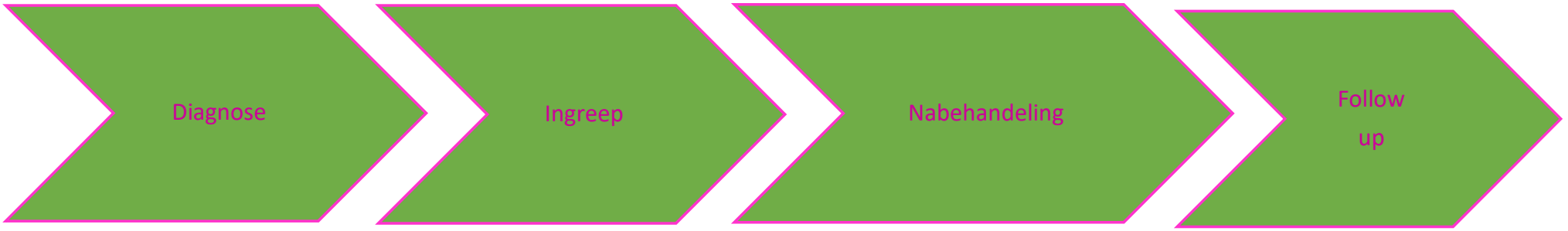


Borstkanker
- Hoge incidentie
- Lage mortaliteit
- Cruciaal: **diagnostiek**, behandeling en opvolging

VITAZ


Huisarts
Medisch Team
MOC
Patiënt
Borstverpleegster
Psycholoog
vpk
Familie
Sociale dienst
Kiné
bandagiste

Zorgpad borstkliniek



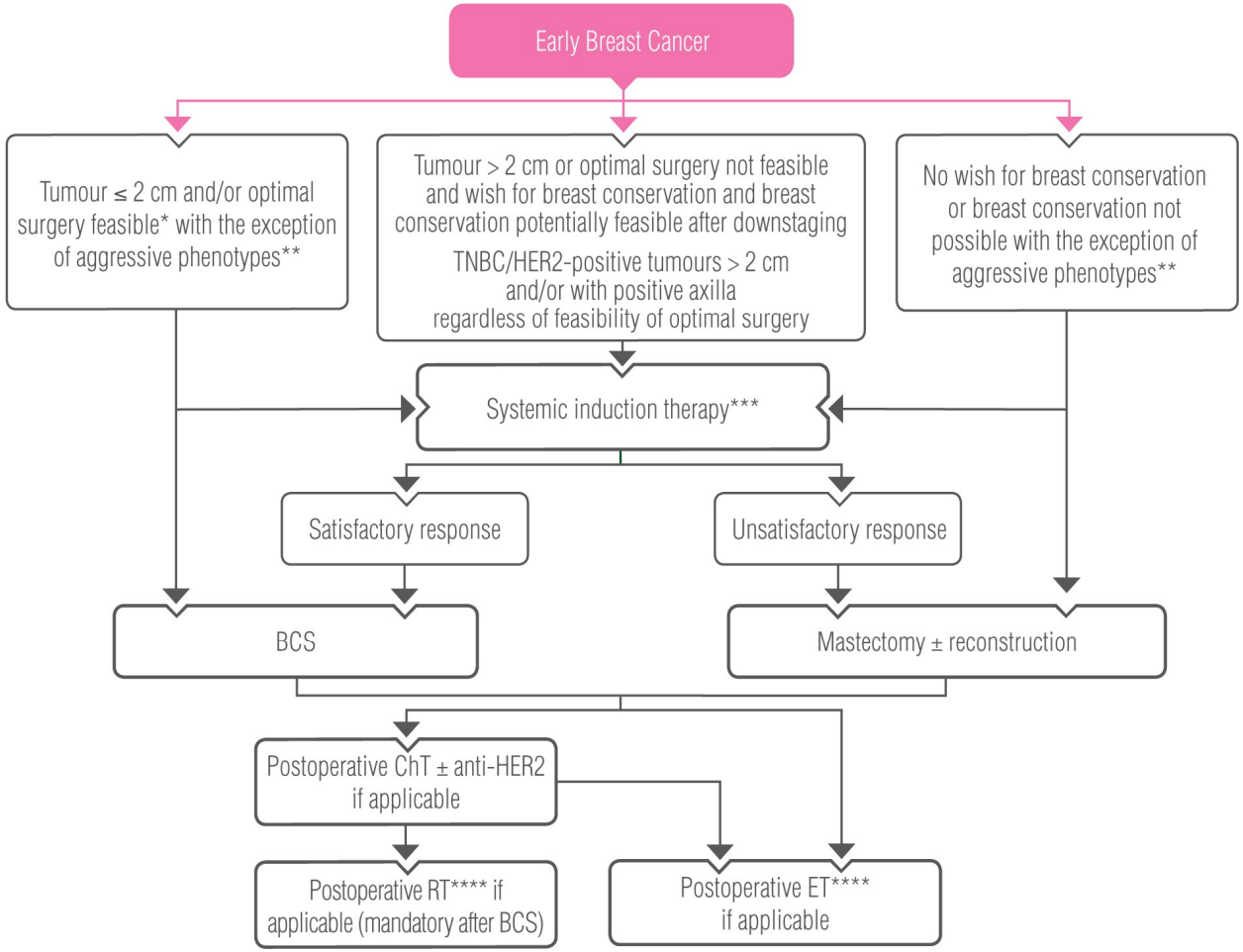
- **Aanmelding MOC**: biopsie en staging/comorbiditeit
- 1 week na ingreep: anatomopathologisch verslag
- **MOC→ behandelplan op maat**
- Afspraak oncoloog

Aanmelding MOC: elke nieuwe patiënt

1. Bespreking biopsie: **indicatie voor neo-adjuvante chemotherapie**

- Hormoongevoelig borstcarcinoom
- Her2 positief borstcarcinoom
- Triple negatief borstcarcinoom

2. Uitgebreidheid dmv TNM stadiëring



3. Comorbiditeit/ psychosociale context: interactie met huisarts via TéléMOC

UITNODIGING TÉLÉMOC:

MULTIDISCIPLINAIR ONCOLOGISCH CONSULT BORSTKLINIEK WEKELIJKS DONDERDAGMIDDAG 13U

MOC UITNODIGEN

VITAZ vzw
Dienst Kankerregistratie

Moerlandstraat 1
9100 Sint-Niklaas

E-mail: kankerregistratie@vitaz.be
www.vitaz.be

Dr. *Voornaam Achternaam*
riziv_nr *X-XXXXX-XX-XXX*

straat nr bus
postnr gemeente

Betreft volgende patiënt(en):

- *Patient_1 Voornaam Naam (°geboortedatum)*
- *Patient_2 Voornaam Naam (°geboortedatum)*
- *Patient_3 Voornaam Naam (°geboortedatum)*

Geachte Dr. *Voornaam Naam*,

Bovenstaande patiënt(en) zal/zullen worden besproken op de MOC *specialismelabel* (multidisciplinair oncologisch consult *specialismelabel*) die doorgaat op *dd-mm-yyyy hh:mi:ss* in VITAZ.

Indien u wenst online deel te nemen, vragen wij u om een mail te sturen naar kankerregistratie@vitaz.be met de vermelding van de MOC-gegevens. Op basis daarvan zullen wij tijdens de kantooruren (maandag tot vrijdag) de verdere praktische regelingen treffen, per mail of desnoods telefonisch (telefoonnummer en beschikbaarheid doorgeven).

We willen u wel waarschuwen dat de mogelijkheid altijd bestaat dat de bespreking wordt uitgesteld of maar gedeeltelijk kan worden uitgevoerd, bv. bij uitstaande onderzoeksresultaten of omwille van tijdsgebrek. Zo dit nog duidelijk wordt vóór dat de MOC doorgaat, zullen wij proberen u hiervan nog op de hoogte te stellen.

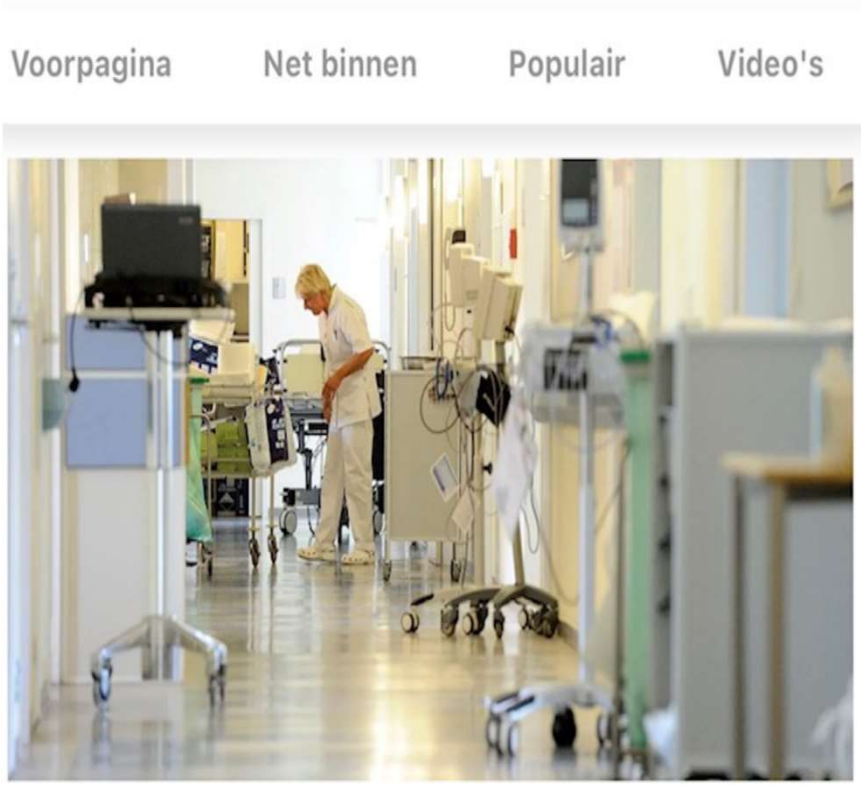
Hoogachtend,

Het kankerregistratieteam van VITAZ

Behandelplan MOC

- Obv kenmerken van tumor
  - Grootte
  - Histologisch type
  - Differentiatiegraad en Ki67 proliferatie index
  - Klieraantasting axilla
  - Receptor status: ER/PR
  - Her2 neu (FISH)
  - Snijranden

Borstkanker: meerderheid patiënten kan zonder chemotherapie



Vrouwen met borstkanker krijgen vaak onnodig chemo

Behandelplan MOC

- <u>Obv tumorprofiling:</u> mammaprint®

  - Tumor profiling bestudeert de genen in het tumorweefsel om de kans op metastasen te voorspellen
  - Mutaties in oncogenes and tumor suppressor genes: de twee belangrijkste genen waarin mutaties de kankergroei stimuleren
  - Gevalideerde genexpressieprofiel geeft informatie over de genen in de kankercel en kans op metastasen

C-High / G-Low patients (ITT population): updated outcomes		
	DMFS with CT	DMFS without CT
At 5 years (95% CI) At 8 years (95% CI)	95.7% (93.9-96.9) 92.0% (89.6-93.8)	94.8% (92.9-96.2) 89.4% (86.8-91.5)
	OS with CT	OS without CT
At 8 years (95% CI)	95.7% (93.9-97.0)	94.3% (92.2-95.8)

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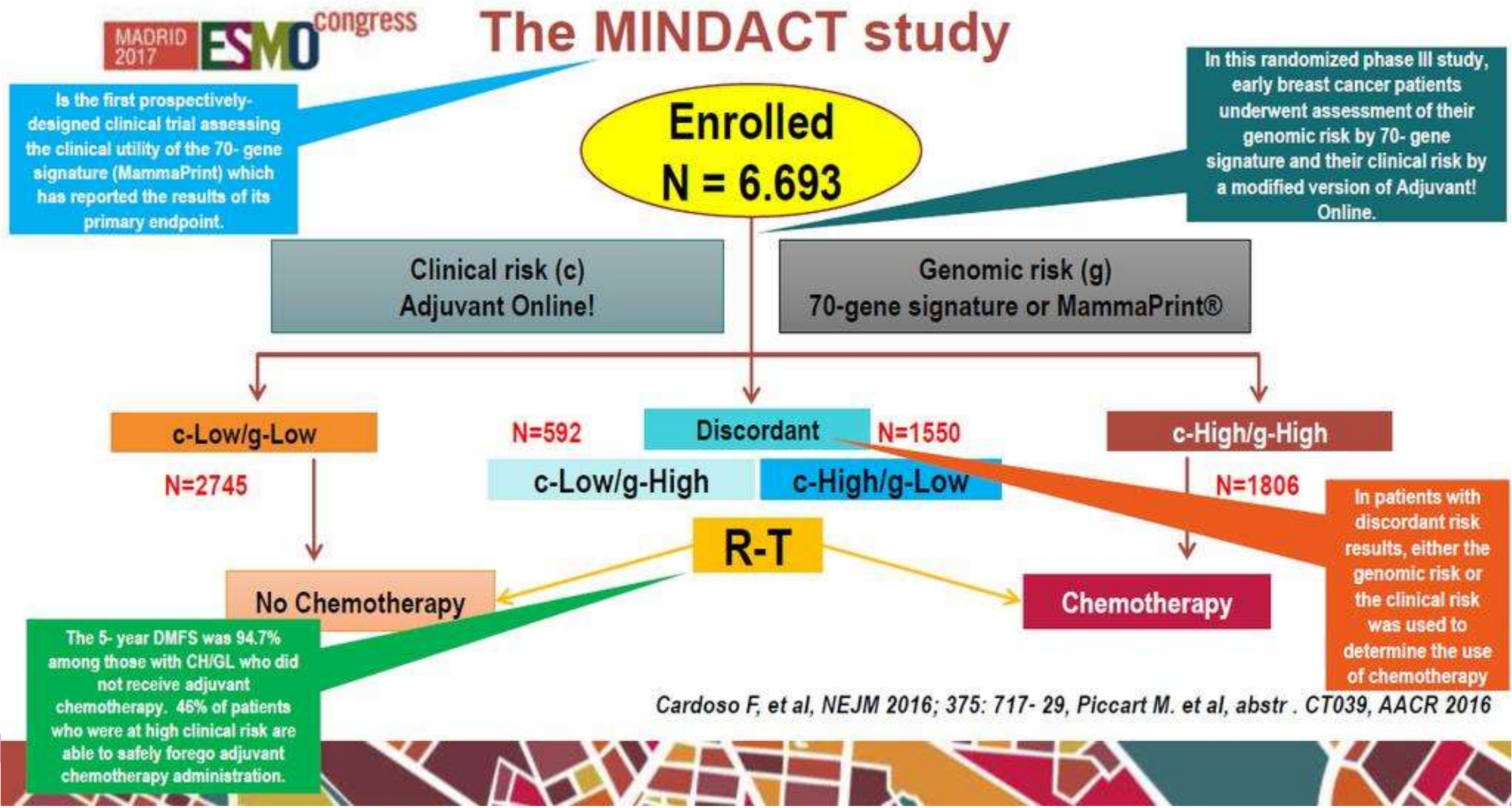

MADRID 2017 ESMO congress
The MINDACT study
Is the first prospectively-designed clinical trial assessing the clinical utility of the 70- gene signature (MammaPrint) which has reported the results of its primary endpoint.
In this randomized phase III study, early breast cancer patients underwent assessment of their genomic risk by 70- gene signature and their clinical risk by a modified version of Adjuvant! Online.
Enrolled
N = 6.693
Clinical risk (c)
Adjuvant Online!
Genomic risk (g)
70-gene signature or MammaPrint®
c-Low/g-Low
N=2745
N=592
Discordant
N=1550
c-Low/g-High
c-High/g-Low
c-High/g-High
N=1806
R-T
No Chemotherapy
Chemotherapy
In patients with discordant risk results, either the genomic risk or the clinical risk was used to determine the use of chemotherapy
The 5- year DMFS was 94.7% among those with CH/GL who did not receive adjuvant chemotherapy. 46% of patients who were at high clinical risk are able to safely forego adjuvant chemotherapy administration.
Cardoso F, et al, NEJM 2016; 375: 717- 29, Piccart M. et al, abstr . CT039, AACR 2016

MOC: To chemo or not?

To chemo or not? Grote uitdaging in adjuvant beleid van borstcarcinoom

- Multidisciplinair overleg voor **behandeling-op-maat of gepersonaliseerde geneeskunde.**
- Samenwerking en communicatie met huisarts

Overleg met huisarts: uitbouw téléMOC

- Automatische uitnodiging met patiëntgevens verstuurd via eHealth :

  deze uitnodiging bevat nog geen internetlink om deel te nemen

- Huisartsen die willen deelnemen moeten een mail sturen naar kankerregistratie@vitaz.be:

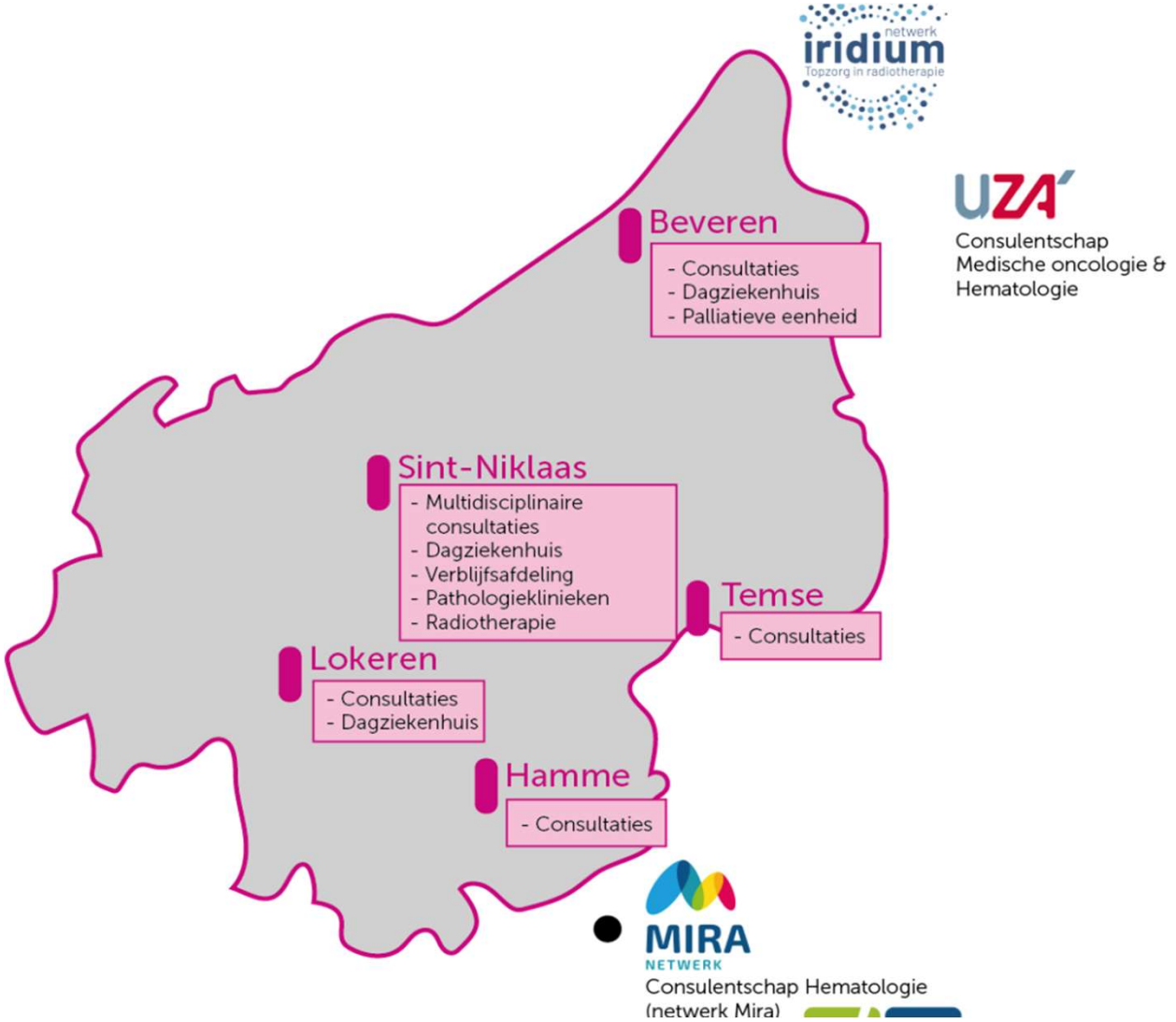
  tijdstip en link worden per kerende mail naar de huisarts verstuurd

- Kankerregistrant laat huisarts toe in Teams:

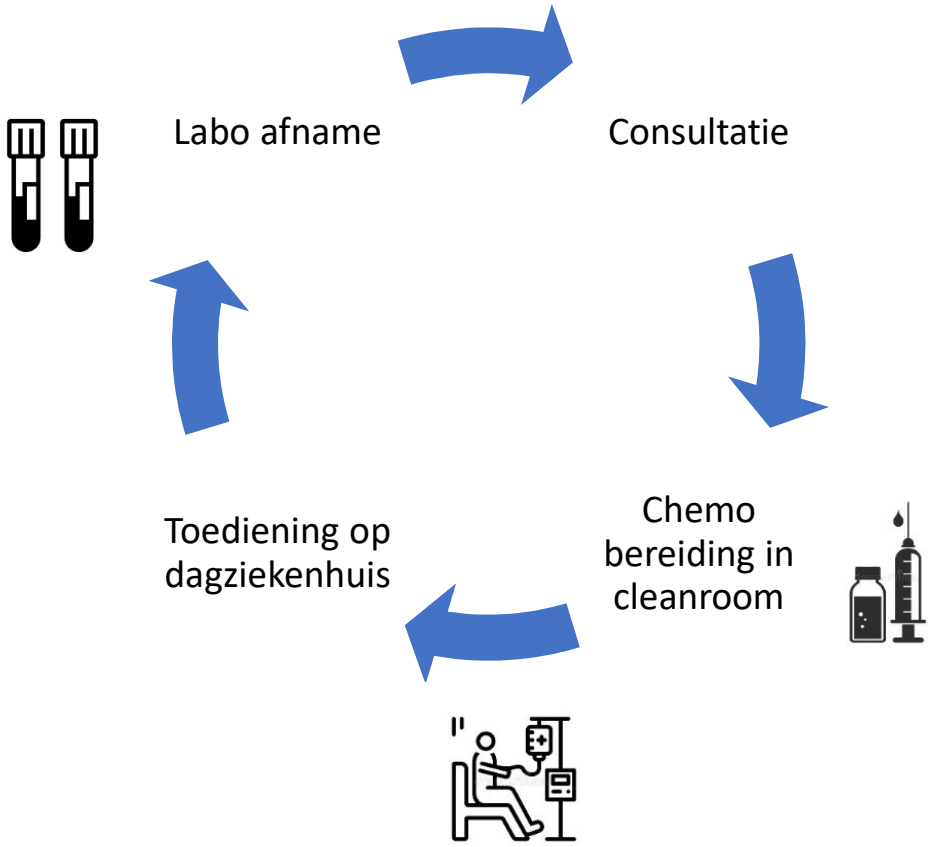
  huisarts kan deelnemen en zal na de bespreking uit de Teams sessie worden verwijderd

Zorgpad in perifere campus Beveren/ Lokeren

- Behandeling dichtbij huis
- Laagdrempelig en kleinschalige zorg
- Gestandardiseerd werken over alle campussen heen
- Bereikbaarheid van oncocoach/borstverpleegster in Beveren
- Oncologisch spreekuur voor start behandeling in Lokeren
- Multidisciplinaire bespreking op gemeen-schappelijke MOC
- Deelname aan wetenschappenlijke studies
- Radiotherapie in campus Sint-Niklaas
- Hospitalisatie campus Sint -Niklaas
- Mogelijkheid tot deelname aan onco-revalidatie



Klassieke dagziekenhuis



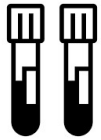
Dagziekenhuis oncologie-hematologie
werkwijze campus Beveren

CONCEPT dag -1

Wachttijden tot minimum reduceren

Dagziekenhuis zo comfortabel en aangenaam mogelijk maken

CONCEPT Dag -1



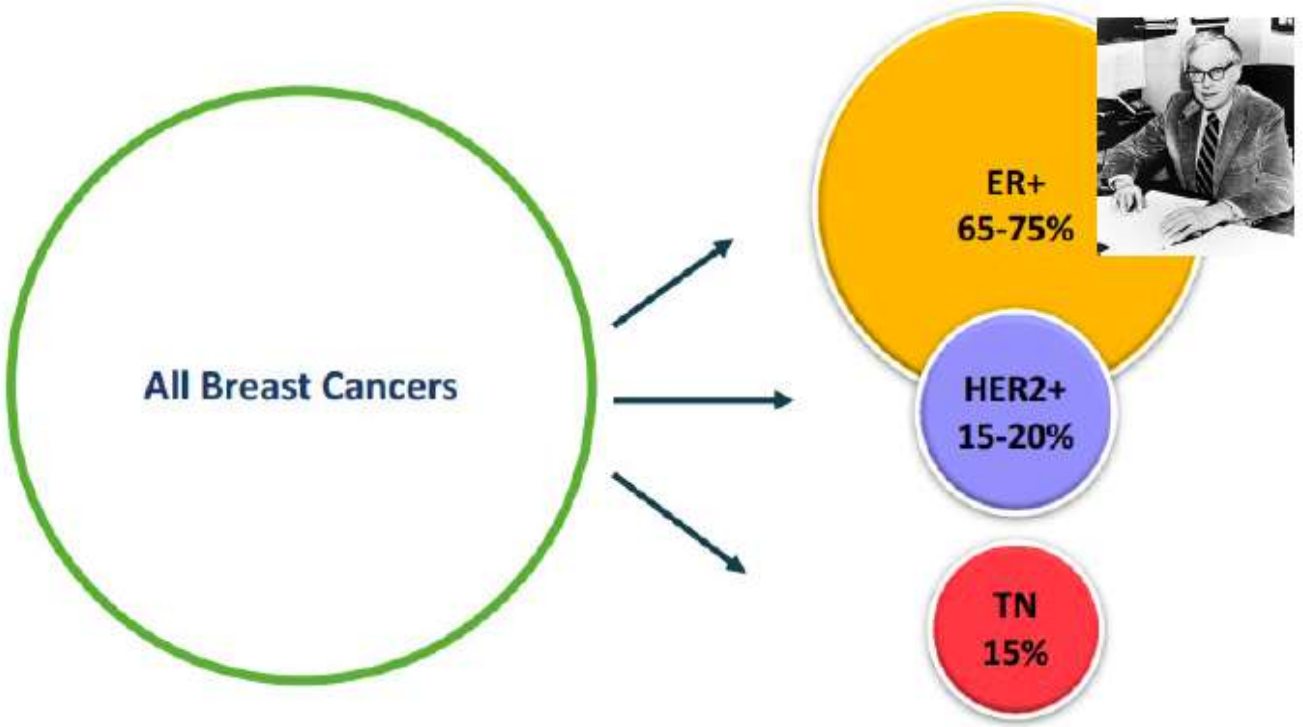
Dag -1	Dag 0
Labo	Onmiddellijk naar DZH voor start therapie
Consultatie	Geen wachttijden

Teamwork makes the dream work

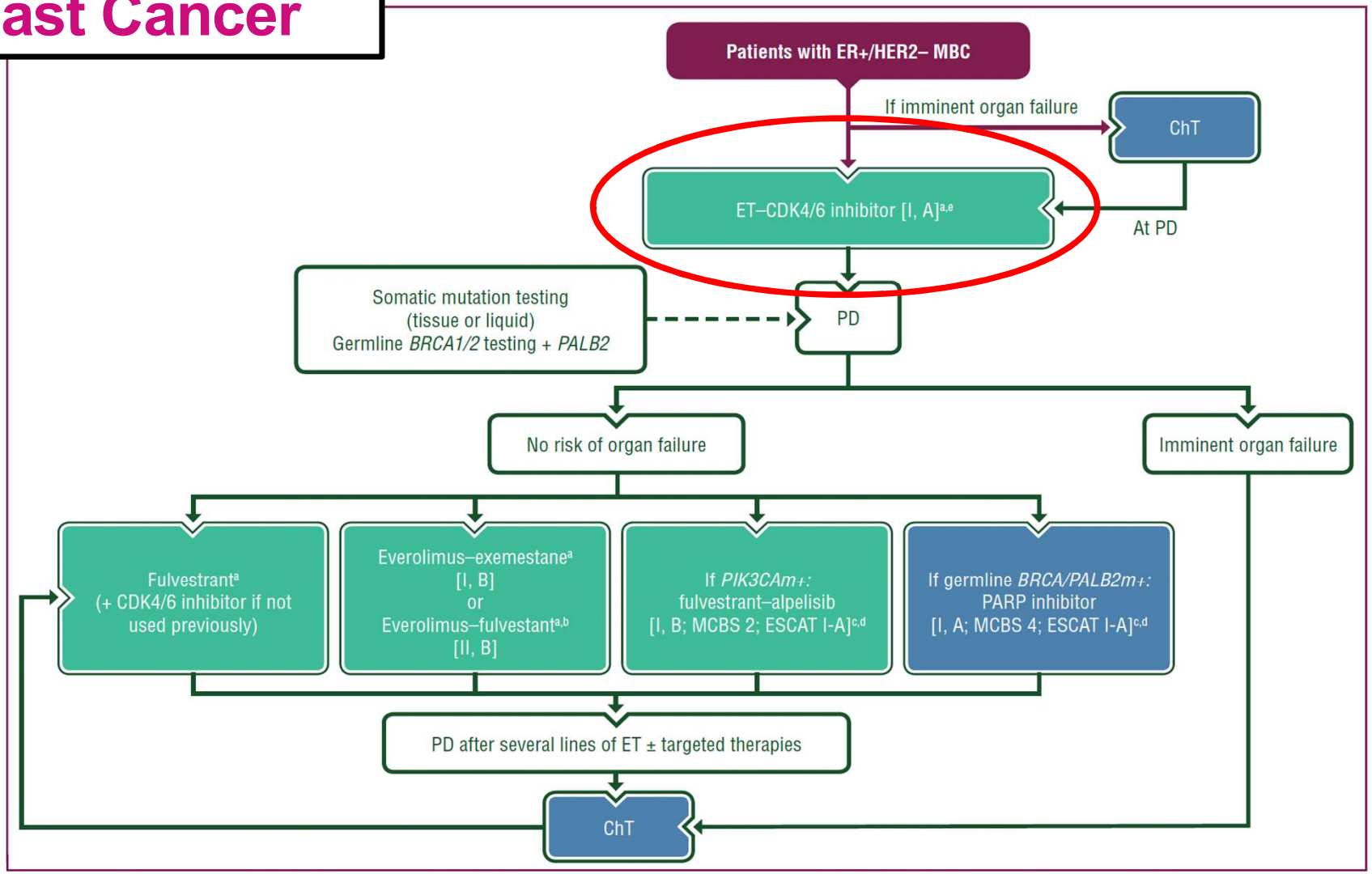
NIEUWE HORMONALE AANWINSTEN BIJ GEMETASTASEERDE BORSTKANKER

DR. MIEKE VAN DE WALLE

Breast cancer subtypes



Luminal Breast Cancer



ESMO guidelines https://www.esmo.org/guidelines/guidelines-by-topic/breast-cancer/metastatic-breast-cancer

CDK4/6 inhibitoren

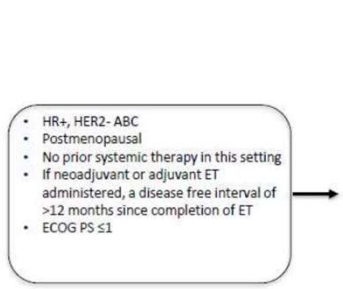
+ aromatase inhibitor (p.o.) OF fulvestrant (i.m.)

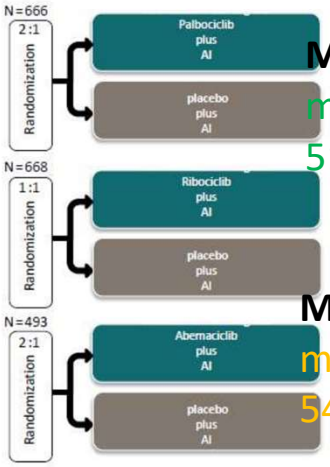
Bij premenopauzale vrouwen: + LHRH agonist om de 4 weken

ER+/HER2 – MBC: ET + CDK4/6 inhibitor => OS = + 1yr

PALOMA-2
No mOS benefit
mOS benefit yes if DFI > 12m
47,4m vs 66,3m

First line ER+/HER2- metastatic breast cancer

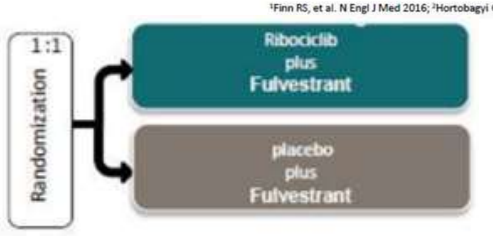




MONALEESA-2
mOS benefit
51,4m vs 63,9m

MONARCH-3
mOS benefit (int analysis)
54,5m vs 67,1m

[1]Finn RS, et al. N Engl J Med 2016; [2]Hortobagyi G, et al. N Engl J Med 2016; [3]di Leo A, et al. J Clin Oncol 2017



MONALEESA-3 1ste line
mOS benefit **1,5jr CT-delay**
51,8m vs 67,6m

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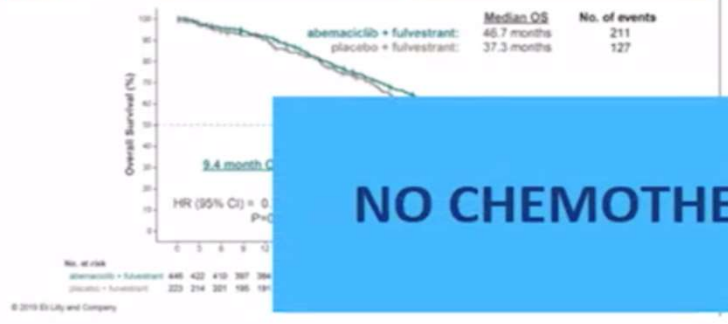
2nd Line CDK 4/6 INHIBITORS: EFFICACY

Consistent 30% RELATIVE REDUCTION IN RISK OF DEATH (OS BENEFIT)

Overall Survival **MONARCH 2**

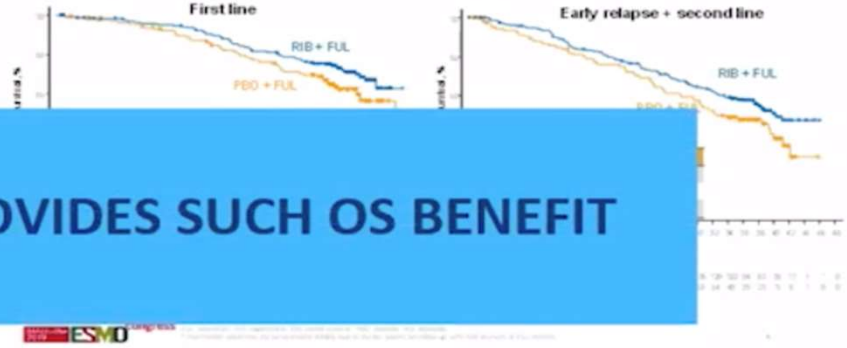


Sledge et al, ESMO 2019

MONALEESA-3 Trial

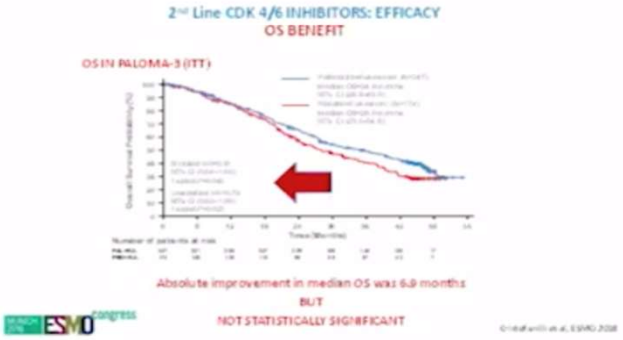
Overall Survival by Line of Therapy

OS by line of therapy was consistent with overall population



NO CHEMOTHERAPY PROVIDES SUCH OS BENEFIT

9 ms benefit in OS



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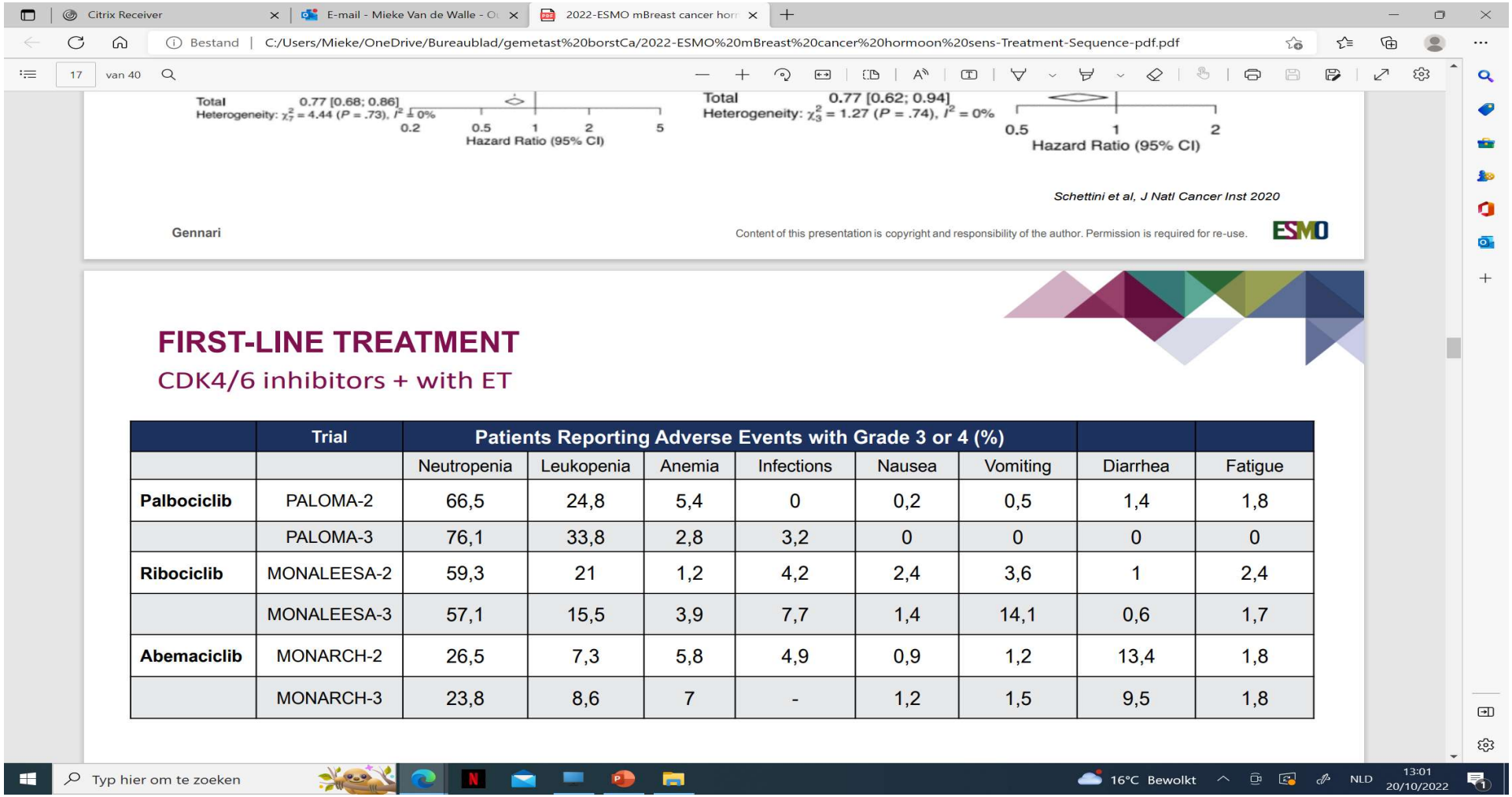
Adapted from F. Cadoso Esmo Preceptorship Breast 2021



	Trial	Patients Reporting Adverse Events with Grade 3 or 4 (%)							
		Neutropenia	Leukopenia	Anemia	Infections	Nausea	Vomiting	Diarrhea	Fatigue
Palbociclib	PALOMA-2	66,5	24,8	5,4	0	0,2	0,5	1,4	1,8
	PALOMA-3	76,1	33,8	2,8	3,2	0	0	0	0
Ribociclib	MONALEESA-2	59,3	21	1,2	4,2	2,4	3,6	1	2,4
	MONALEESA-3	57,1	15,5	3,9	7,7	1,4	14,1	0,6	1,7
Abemaciclib	MONARCH-2	26,5	7,3	5,8	4,9	0,9	1,2	13,4	1,8
	MONARCH-3	23,8	8,6	7	-	1,2	1,5	9,5	1,8

DRUG-DRUG interacties

- CDK 4/6 inhibitoren:

  CYP3A4 inhibitoren => toxiciteit ⬆

  (clarithromycine, itraconazole, ...)

  CYP3A4 inducers => efficaciteit ⬇

  en pompelmoes

- Ribociclib niet te samen met QTc verlengende medicatie (vb. anti-aritmica: amiodarone, sotalol of haloperidol, moxifloxacine,...)

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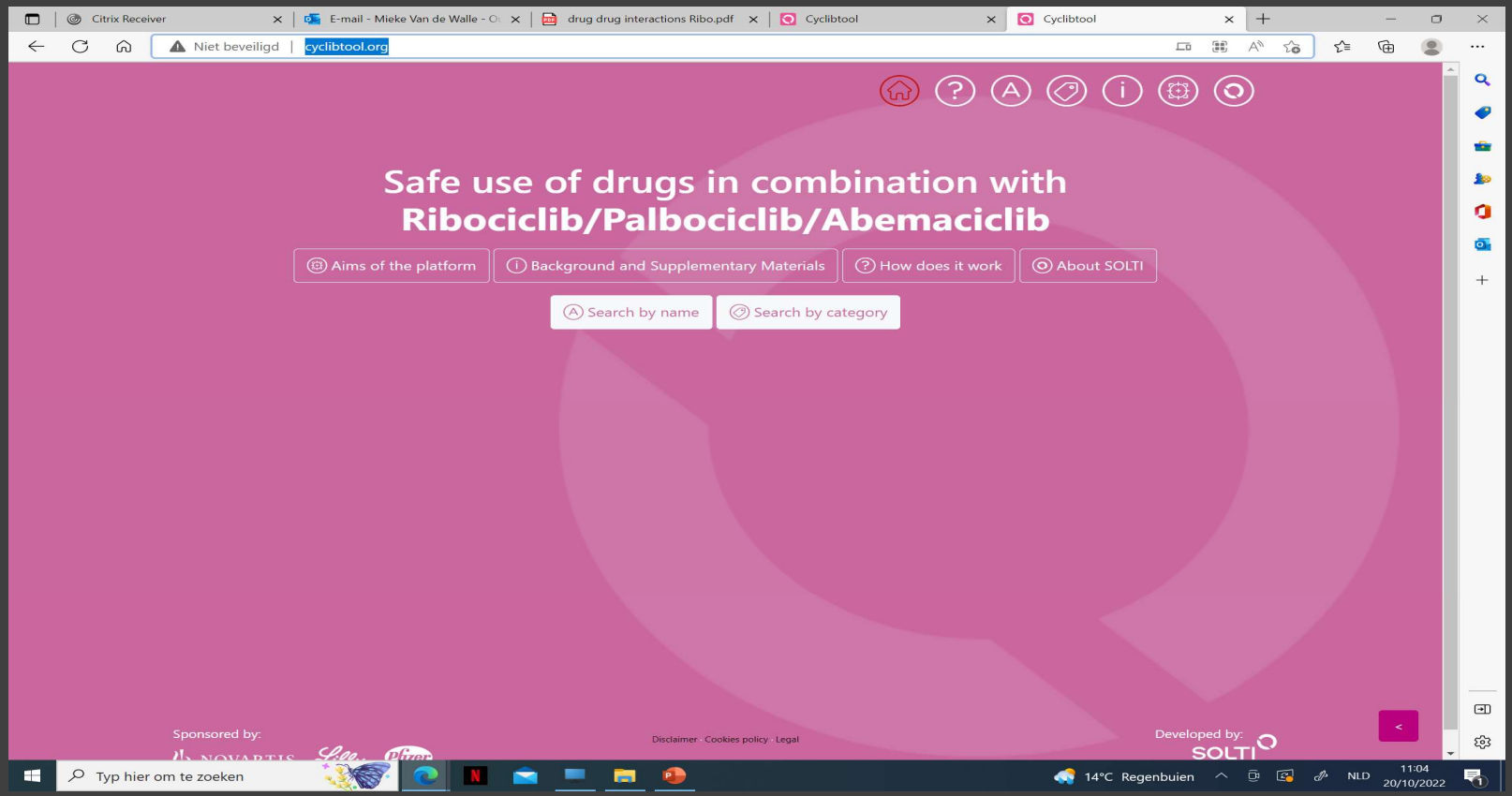
Drug- drug interacties!

- Cave: CYP3A4 inducer/inhibitor en QTc verlengende medicatie



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Conclusie: 1ste lijn ER +, HER 2- MBC

Biopt van meta zo mogelijk (exclusie discordantie primaire tumor)

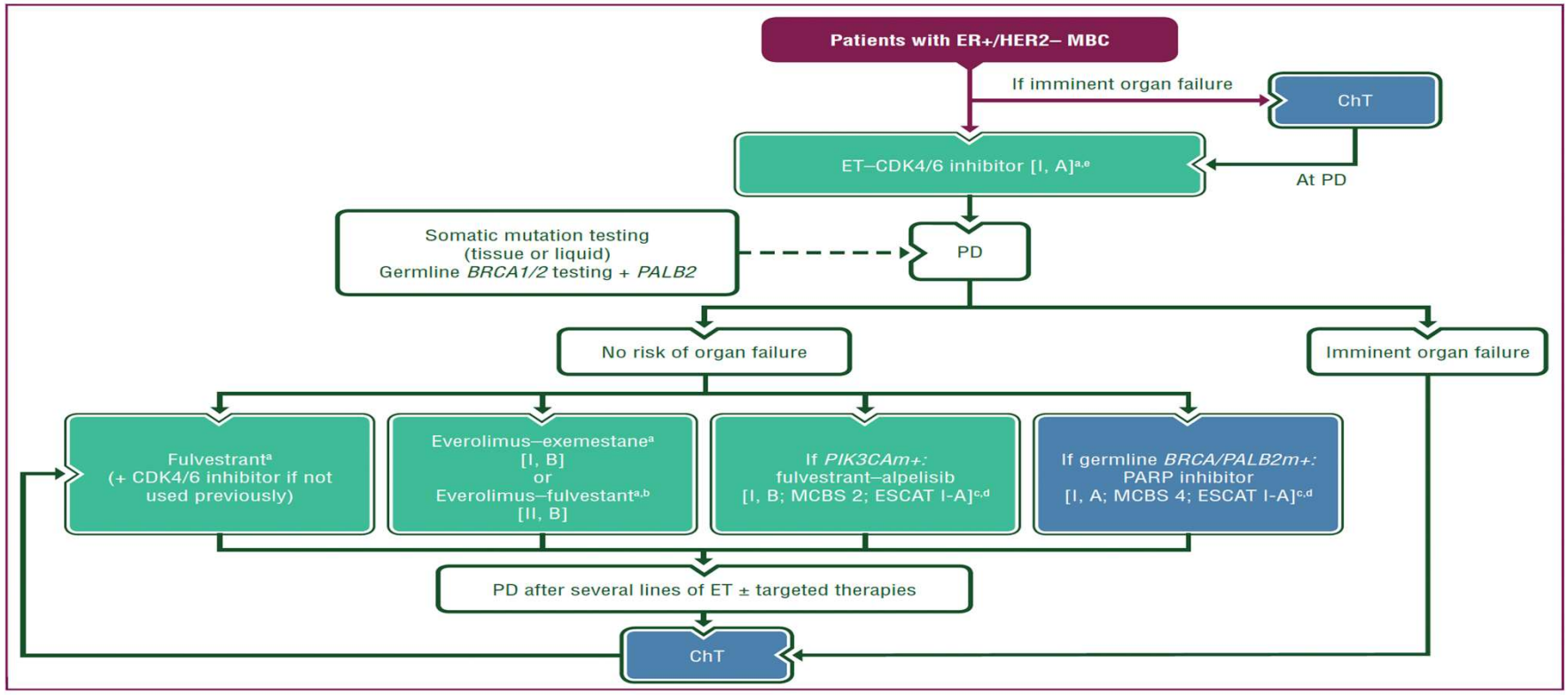
Hormonale therapie voor chemotherapie tenzij viscerale crisis

CDK4/6 inhibitoren zowel vr menopauzale als premenopauzale personen

3 soorten CDK4/6 inhibitoren met verschillend tolerantieprofiel

CAVE: drug-drug interacties (CYP3A4 inhibitors/inducers en QTc verlengende medicatie)

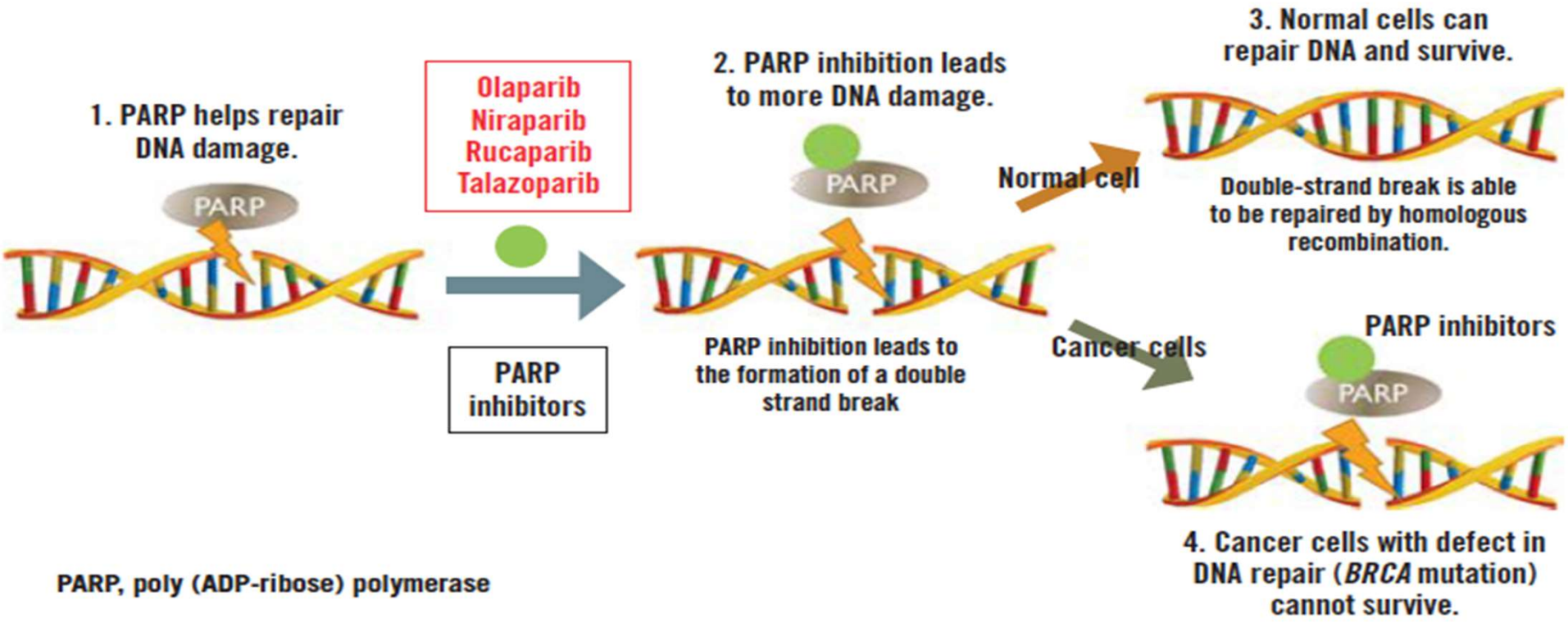
Tweede lijn bij ER+, HER2 - MBC



ESMO guidelines https://www.esmo.org/guidelines/guidelines-by-topic/breast-cancer/metastatic-breast-cancer

PARP inhibitoren bij gBRCA/PALB2 mutatie

FIGURE 1. Mechanism of Action of PARP Inhibitors



PARP, poly (ADP-ribose) polymerase

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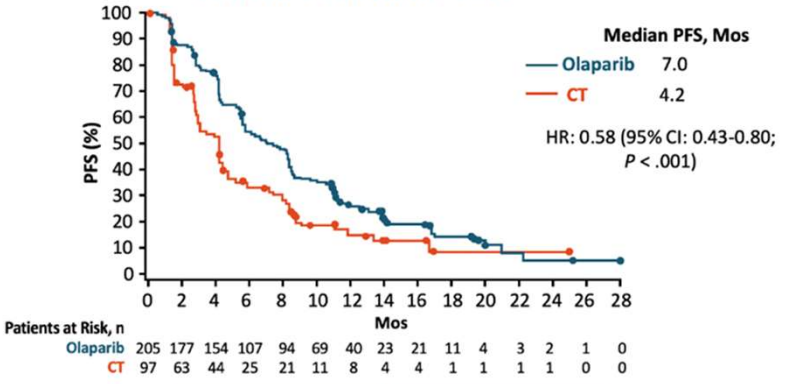
Jakob et al. **Urology Times Urologists in Cancer Care**, UCC December 2020, Volume 09, Issue 04

PARP-inhibitoren bij gBRCA/PALB2 mutatie

OlympiAD: PFS by BICR (Primary Endpoint)

Robson et al. NEJM 2017



	Olaparib 300 mg bd	Chemotherapy TPC
Events (%)	163 (79.5)	71 (73.2)
Median PFS, months	7.0	4.2

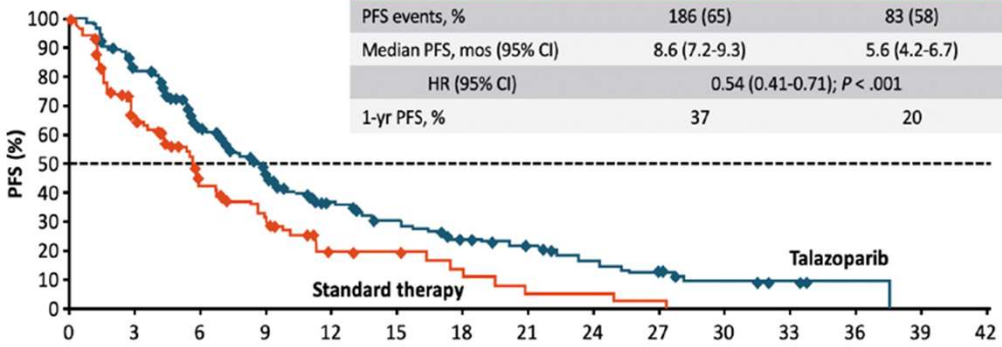
HR 0.58 95% CI 0.43 to 0.80; *P*=0.0009

PARP inhibitor: Olaparib (=Lynparza) 300mg 2x/dag

EMBRACA: PFS by BICR (Primary Endpoint)

- Median follow-up time: 11.2 mos

PFS Outcome	Talazoparib (n = 287)	Standard CT (n = 144)
PFS events, %	186 (65)	83 (58)
Median PFS, mos (95% CI)	8.6 (7.2-9.3)	5.6 (4.2-6.7)
HR (95% CI)	0.54 (0.41-0.71); *P* < .001	
1-yr PFS, %	37	20



Litton. NEJM. 2018;379:753

PARP inhibitor: Talazoparib (=Talzenna) 1mg 1x/dag

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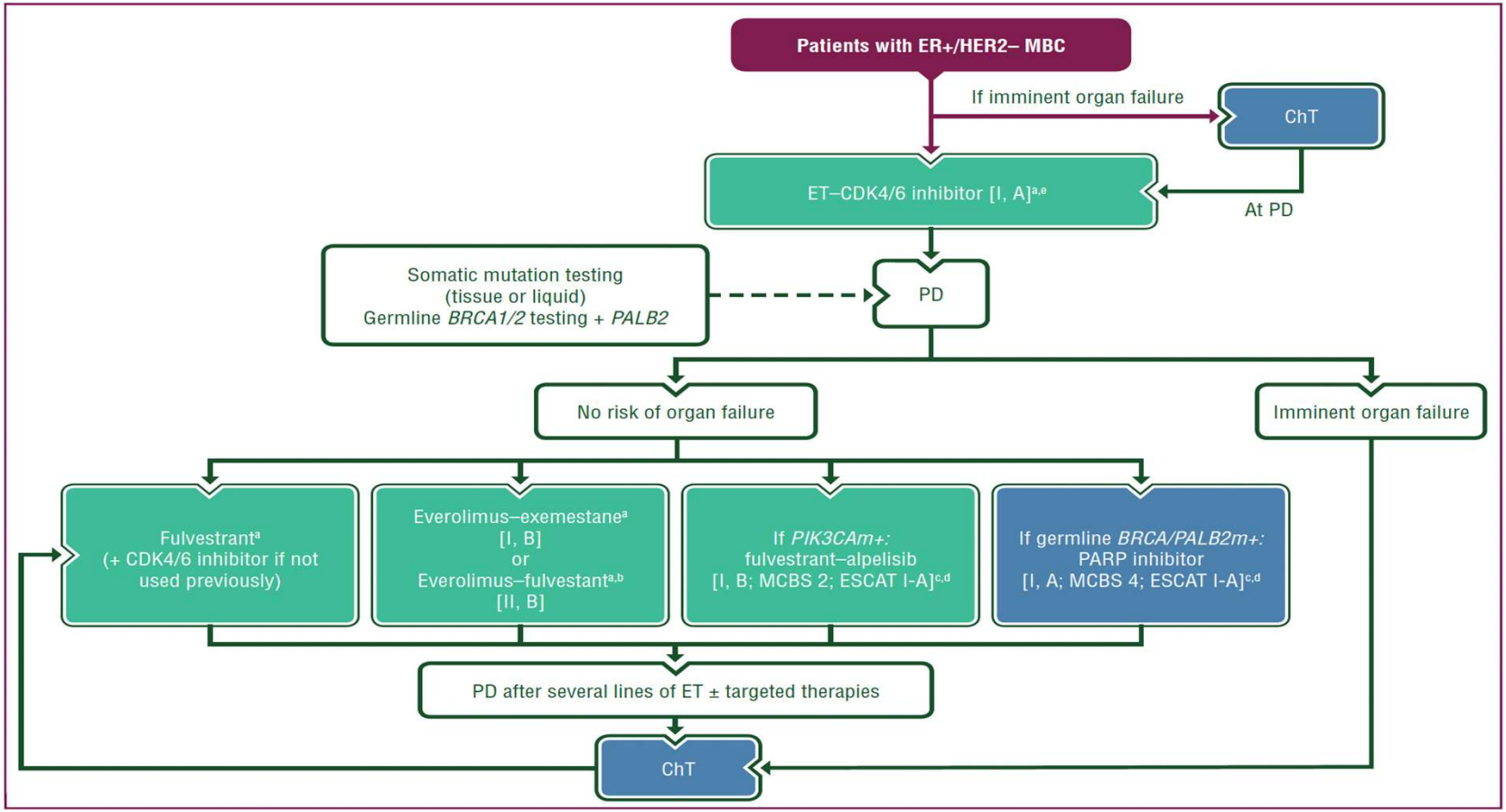
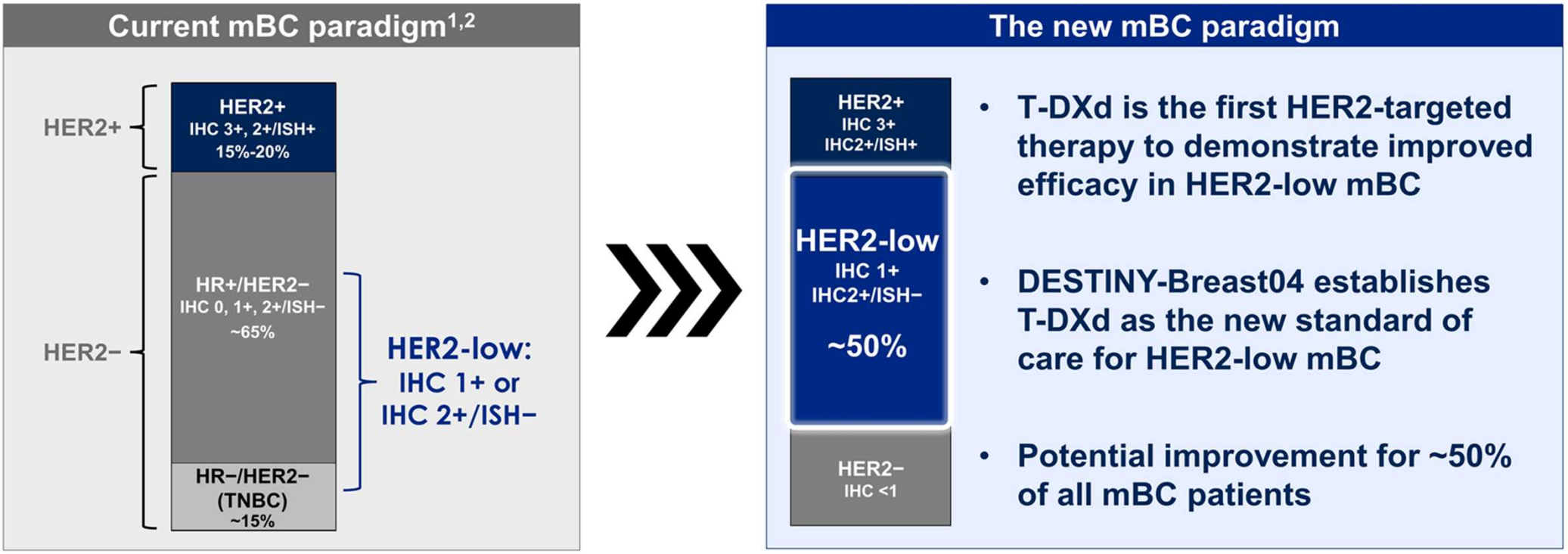
Tweede lijn bij ER+, HER2 - MBC



ER+, HER 2 FISH neg maar wel Her 2- low (=IHC 1-2)
Extra behandeloptie binnenkort:
Trastuzumab-deruxtecan

Trastuzumab-deruxtecan bij HER2 low mBC



HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; T-DXd, trastuzumab deruxtecan; TNBC, triple-negative breast cancer; TPC, treatment of physician's choice.

1. Schettini F, et al. *NPJ Breast Cancer*. 2021;7(1):1. 2. Tarantino P, et al. *J Clin Oncol*. 2020;38(17):1951-1962.

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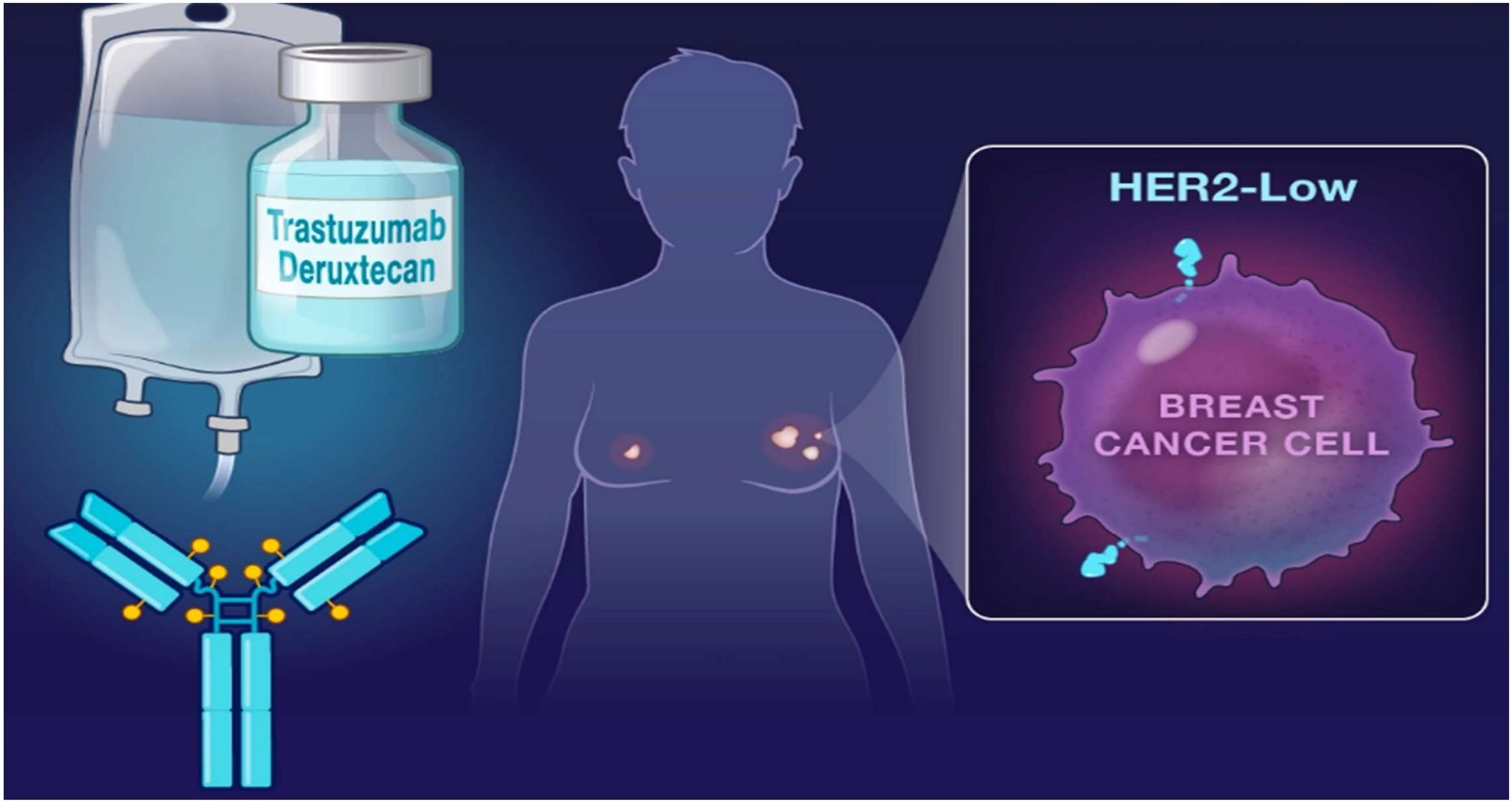
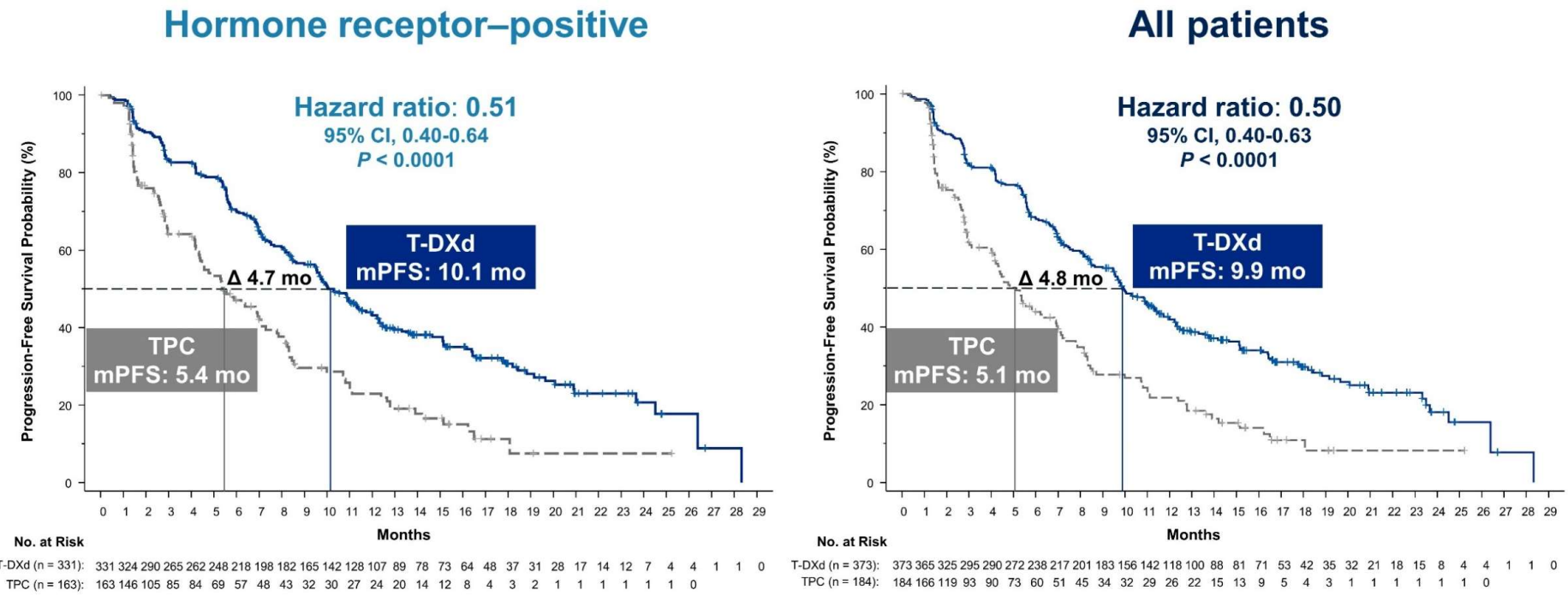

Trastuzumab
Deruxtecan
HER2-Low
BREAST
CANCER CELL

DESTINY-BREAST 04 study

PFS: trastuzumab – deruxtecan beter dan chemo

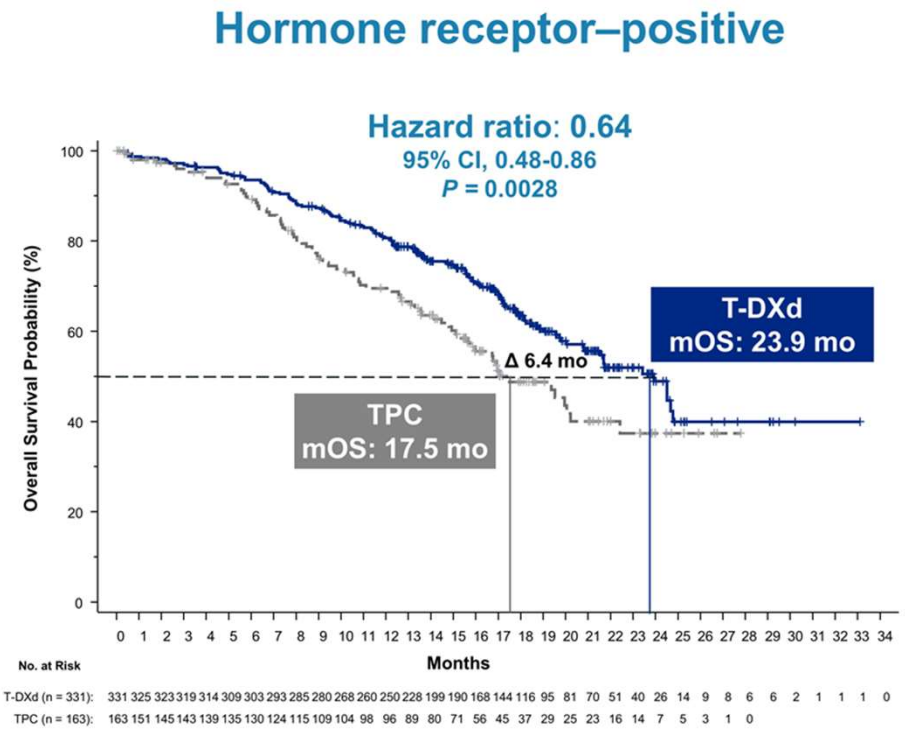


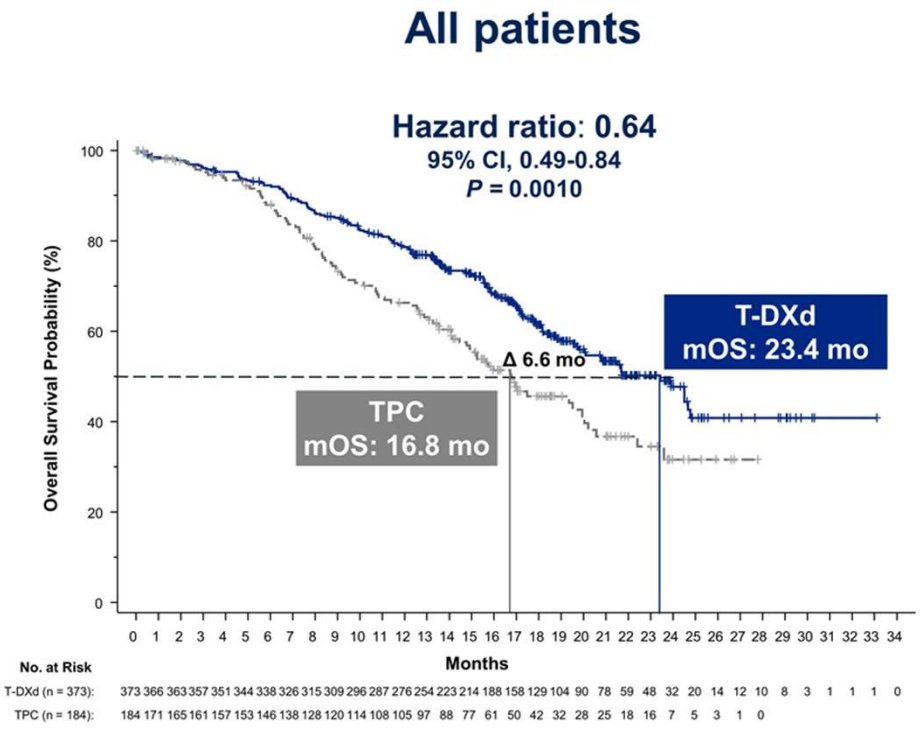
PFS by blinded independent central review.
HR, hormone receptor; mPFS, median progression-free survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

VITAZ

DESTINY-BREAST 04 study

OS: trastuzumab – deruxtecan beter dan chemo





HR, hormone receptor; mOS, median overall survival; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

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Take home message: ER+, HER 2 - MBC

1ste **lijn**: CDK 4/6 inhibitor + endocriene therapie tenzij viscerale crisis

2de **lijn**: verschillende antihormonale therapieën mogelijk, chemo bij risico op orgaan falen

Nieuwe entiteit: ER+, **HER2 low** MBC => extra behandeloptie:
trastuzumab-deruxtecan IV

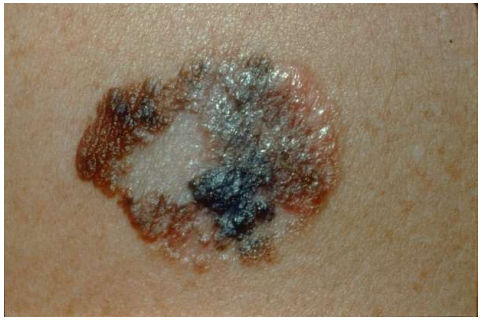
Bijwerkingen hangen af van soort geneesmiddel, zeer divers!

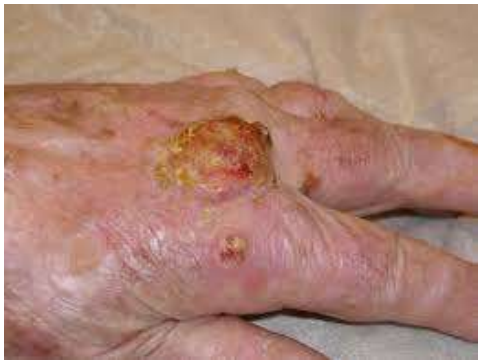
NIEUWS IN DE BEHANDELING VAN HUIDKANKER: WAT IS RELEVANT VOOR DE HUISARTS?

PROF. DR. VIBEKE KRUSE MD PHD
MEDISCHE ONCOLOGIE
VITAZ – UZA

Huidkanker

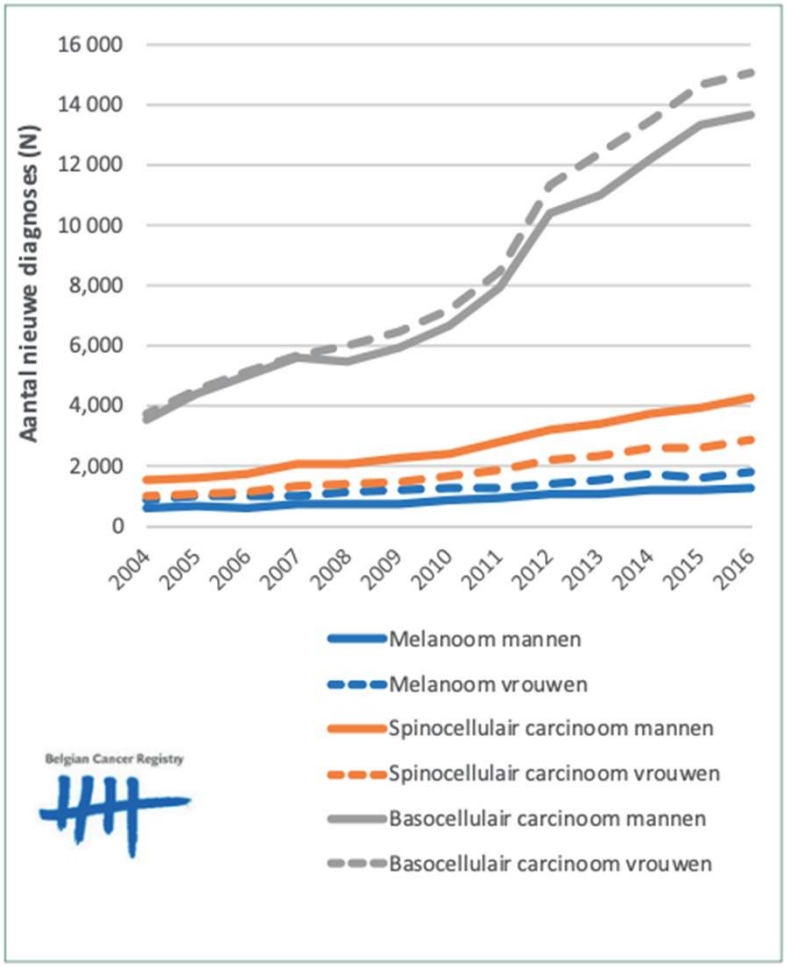
- melanoom
- non-melanoma huidkanker (NMSC)
  - spinocellulair carcinoom
  - basocellulair carcinoom
  - ...





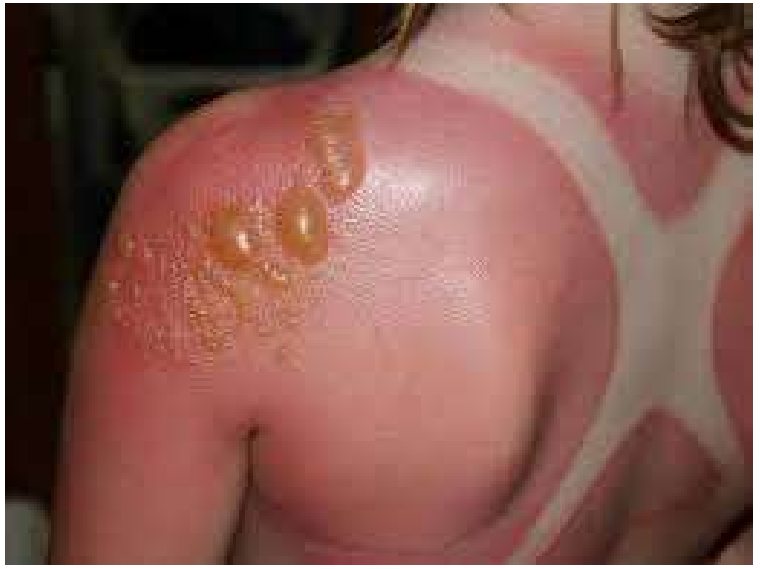
Huidkanker

Figuur 1: Evolutie van de incidentie van kwaadaardige huidtumoren, België, 2004-2016.



Gemeenschappelijke risicofactor

ZONLICHT



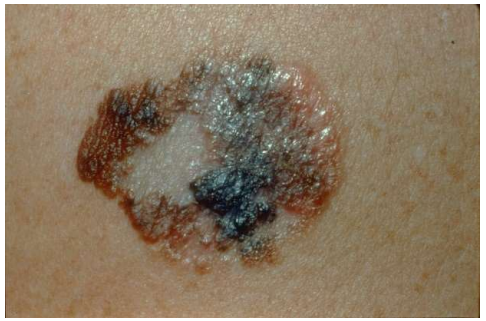
Preventie

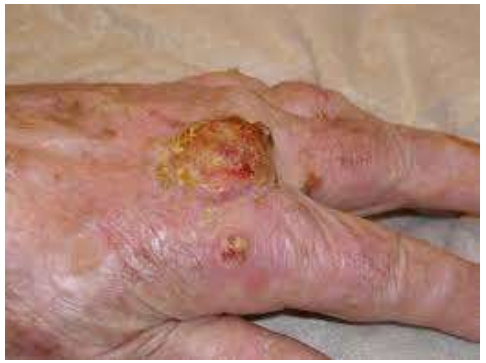

SPF 30 of meer op niet-bedekte huid
Iedere 2-3 uur
Voldoende rijkelijk aanbrengen
KLEDIJ


Ook al “zie” je de zon niet: ze is er!

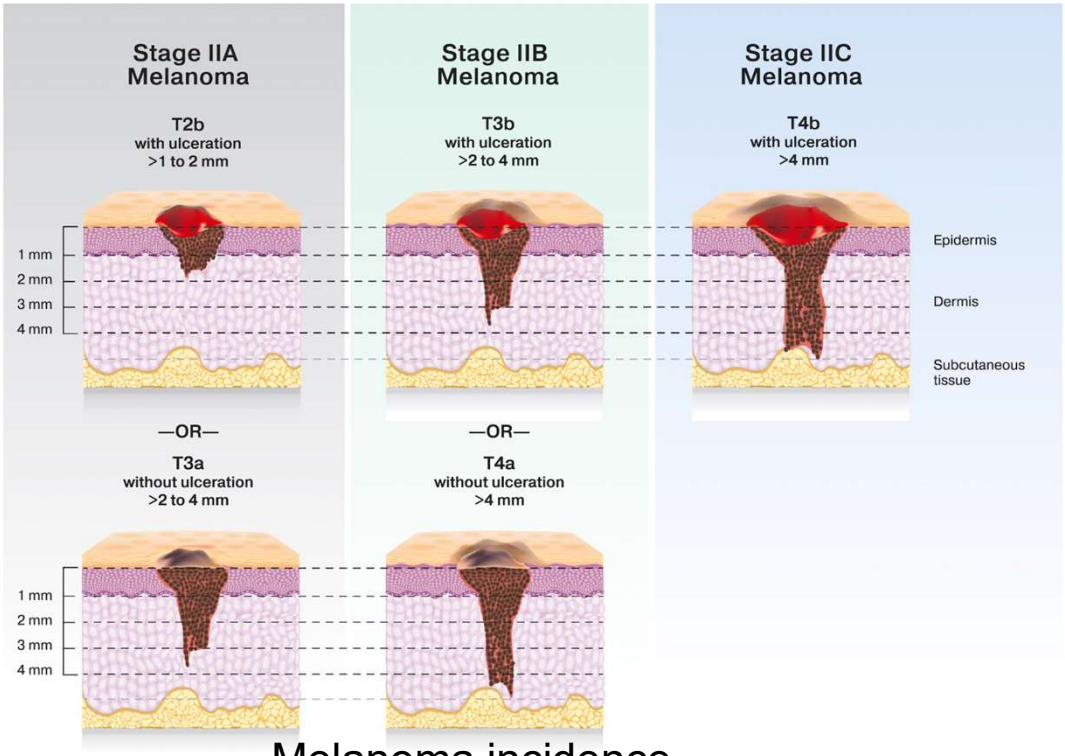
Huidkanker

- melanoom
- non-melanoma huidkanker (NMSC)
  - spinocellulair carcinoom
  - basocellulair carcinoom
  - ...





Stagering melanoom



Melanoma incidence

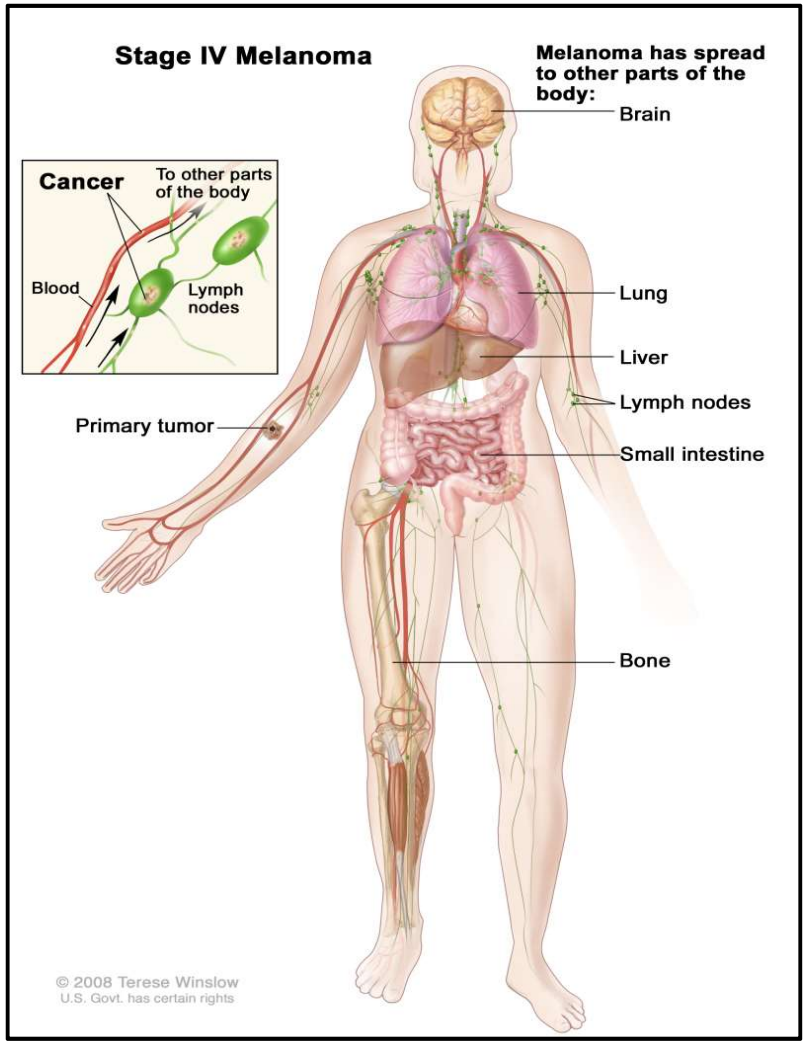
Figure 1. Schematic of stage II melanoma according to the 8th edition of the American Joint Cancer Classification.

- **T =** **tumorgrootte**
- **N =** **aantal ingenomen lymfeklieren**
- **M =** **aanwezigheid van metastasen**

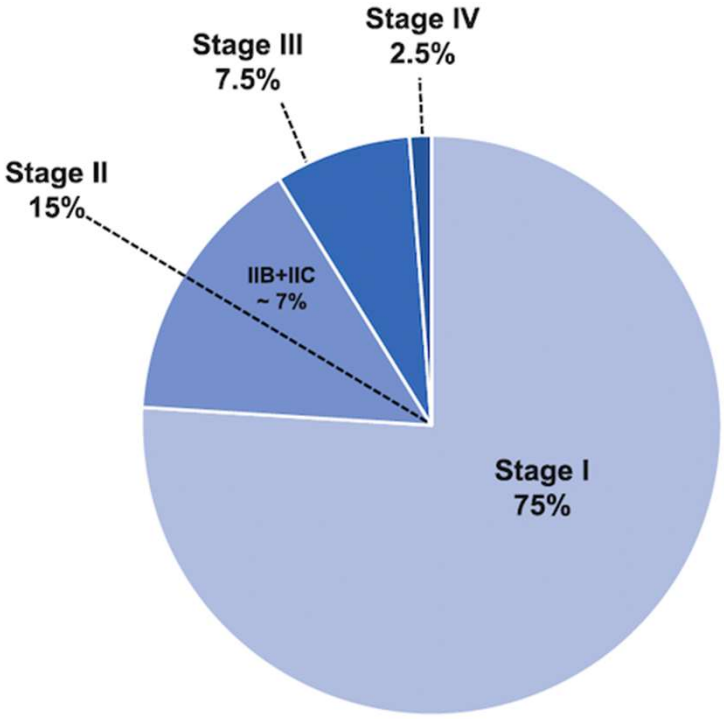
Stadium I en II:	**N0**
Stadium III:	**N + (regionale klieren)**
Stadium IV:	**meta's op afstand**

Poklepovic el al.Cancer 2019, DOI: 10.1002/cncr.32585

Stagering melanoom



Bij diagnose



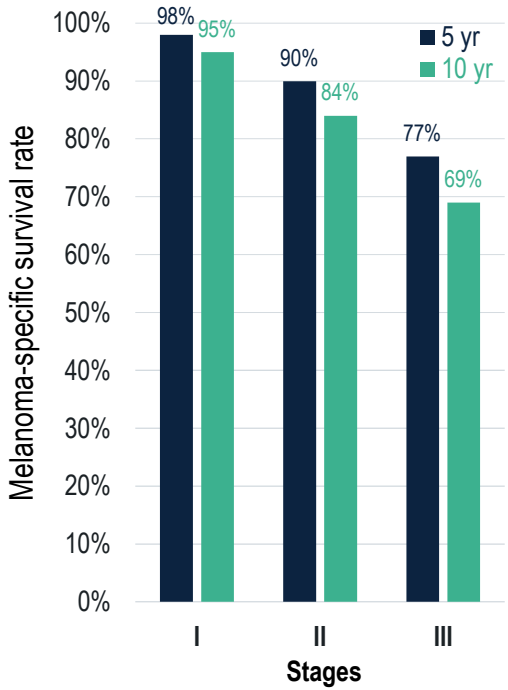
Poklepovic el al.Cancer 2019, DOI: 10.1002/cncr.32585

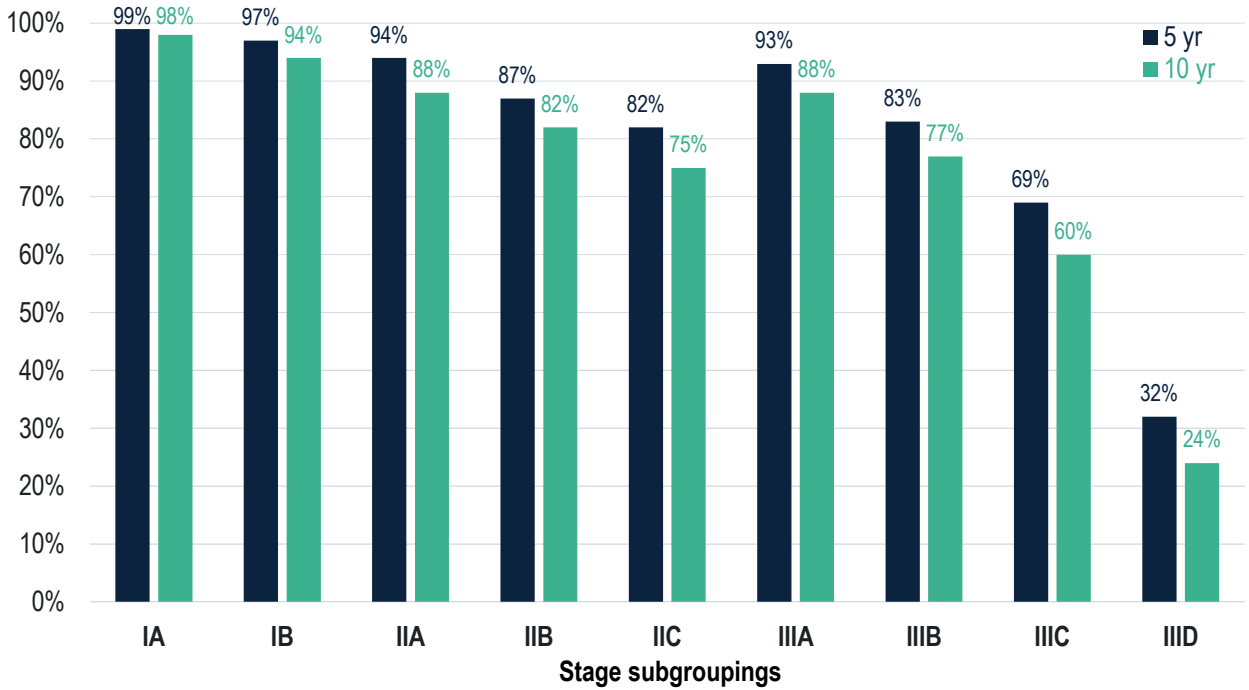
VITAZ

Global: Epidemiology (1 of 2)

De overleving is afhankelijk van stadium bij diagnose

International 5-year and 10-year Melanoma-specific Survival Rates for Melanoma, by Skin Cancer Stage





Gershenwald JE, et al. *CA Cancer J Clin*. 2017;67(6):472–492.

Global: Epidemiology (1 of 2)

De overleving is afhankelijk van stadium bij diagnose

International 5-year and 10-year Melanoma-specific Survival Rates for Melanoma, by Skin Cancer Stage

Gershenwald JE, et al. *CA Cancer J Clin*. 2017;67(6):472–492.

MSD

Adjuvante therapie mogelijk bij

(Dikke) primaire melanomen zonder klieraantasting (IIb en IIc)

- 2,1mm met ulceratie (pT3b) of
- >4mm ongeacht ulceratie (pT4a en pT4b)
- Geen kliermeta's

Primair melanomen (ongeacht Breslow) met kliermeta's (III)

- Alle T stadia
- N+

Gemetastaseerde ziekte na complete resectie

Adjuvante therapie mogelijk bij

(Dikke) primaire melanomen zonder klieraantasting (IIb en IIc)

- 2,1mm met ulceratie (pT3b) of
- >4mm ongeacht ulceratie (pT4a en pT4b)
- Geen kliermeta's

IV toediening

Primair melanomen (ongeacht Breslow) met kliermeta's (III)

- Alle T stadia
- N+

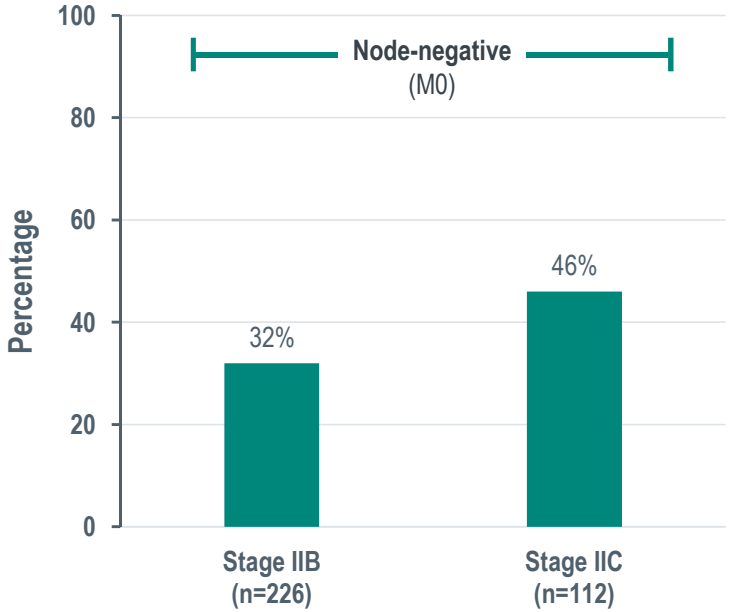
IV en PO toediening

Gemetastaseerde ziekre na complete resectie

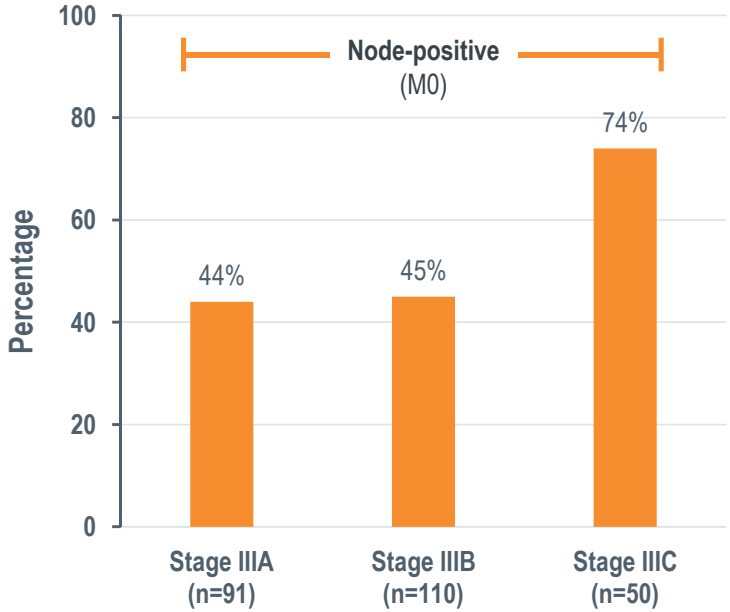
Recurrence Rates for Resected High-risk Melanoma

Risico op herval

Stage IIB/IIC Melanoma Recurrence Rates[1,a]



Stage III Melanoma Recurrence Rates[2,b]



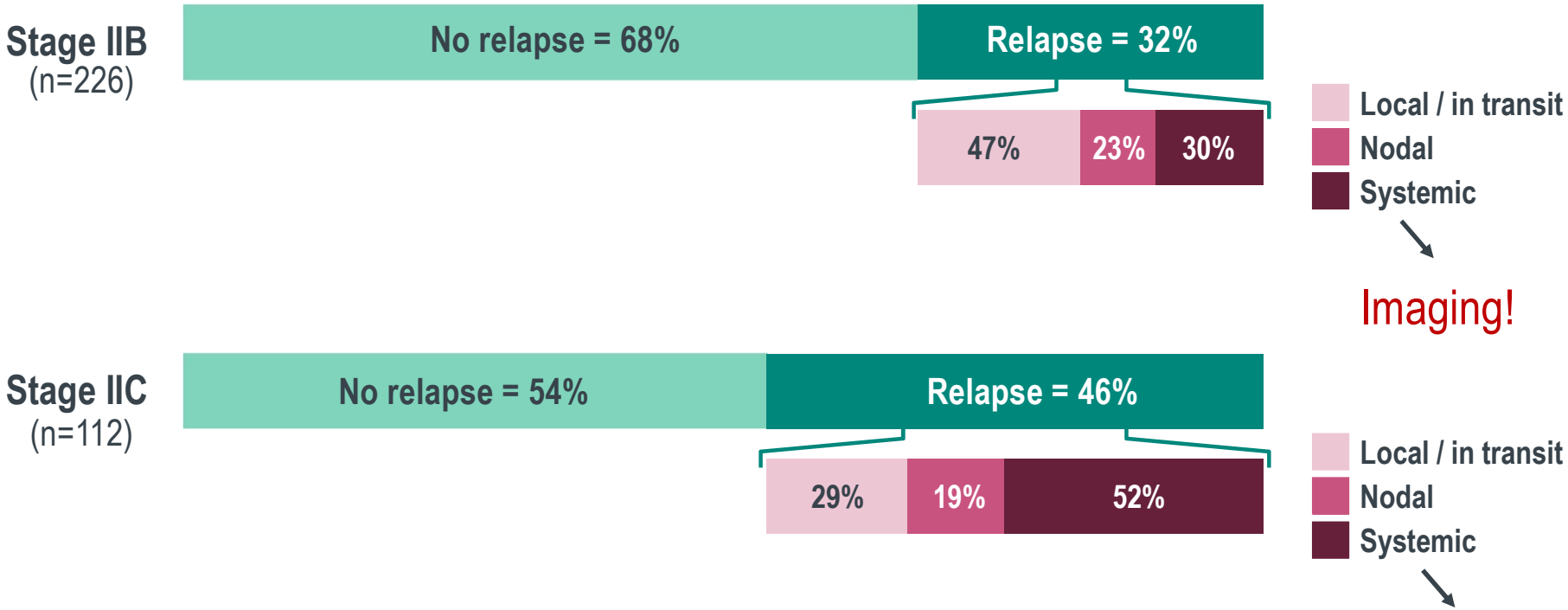
[a]Retrospective review of 738 adult patients with stage II resected melanoma from 1993 to 2013; 338 patients had melanoma stage IIB or IIC. Median follow-up time was 4.3 years. Patients in this study were treated at Memorial Sloan Kettering Cancer Center. Staging based on AJCC 7th edition.

[b]Retrospective chart review of 251 patients from 2011 to 2016 with stage III resected melanoma followed by watch-and-wait. Median follow-up time was 3.1 years. Patients included in this study were from North America, South America, and Europe. Staging based on AJCC 7th edition.

1. Lee AY, et al. *Ann Surg Oncol.* 2017;24:939-946. **2.** Mohr P, et al. *Melanoma Manag.* 2019;6:MMT33.

Pattern of Relapse in Stage IIB and Stage IIC Melanoma

Risico op herval – lokaal / klieren / op afstand



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Lee AY, et al. *Ann Surg Oncol*. 2017;24:939-946.

Benefits of pembrolizumab adjuvant

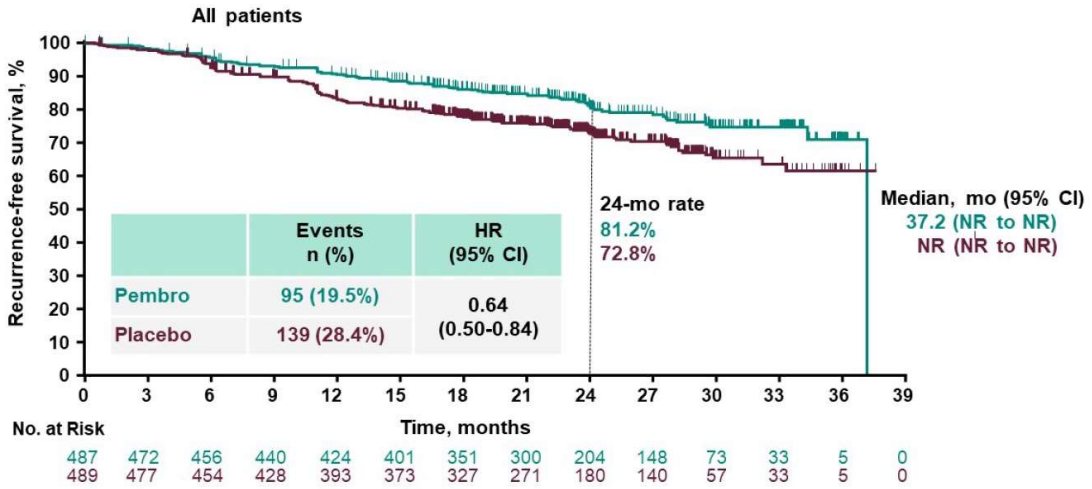
Stadium IIb/IIc

Recidief-vrije overleving - winst van 8,4% na 2 jaar

Public

ADJUVANT THERAPY | KEYNOTE-716

IA3: RFS (Primary End Point)



Median follow-up of 27.4 months (range 14.0-39.4 months). Data cutoff: January 4, 2022.
Long GV, et al. Presented at ASCO 2022.

MSD

MSD

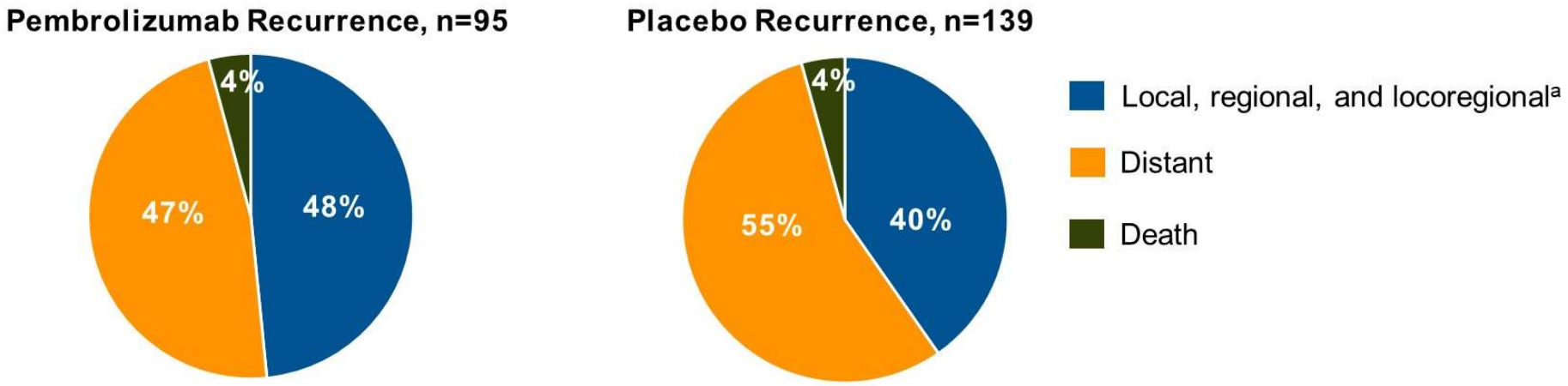
Pub

Adjuvant pembrolizumab verlaagt het risico op meta's op afstand

Pattern of First Recurrence

Stadium IIb/IIc

	Pembrolizumab	Placebo
Recurrence-free survival status	**N = 487**	**N = 489**
All events, n (%)	95 (20)	139 (28)
Local, regional, and locoregional[a]	46 (9)	56 (11)
Distant	45 (9)	77 (16)
Death	4 (1)	6 (1)



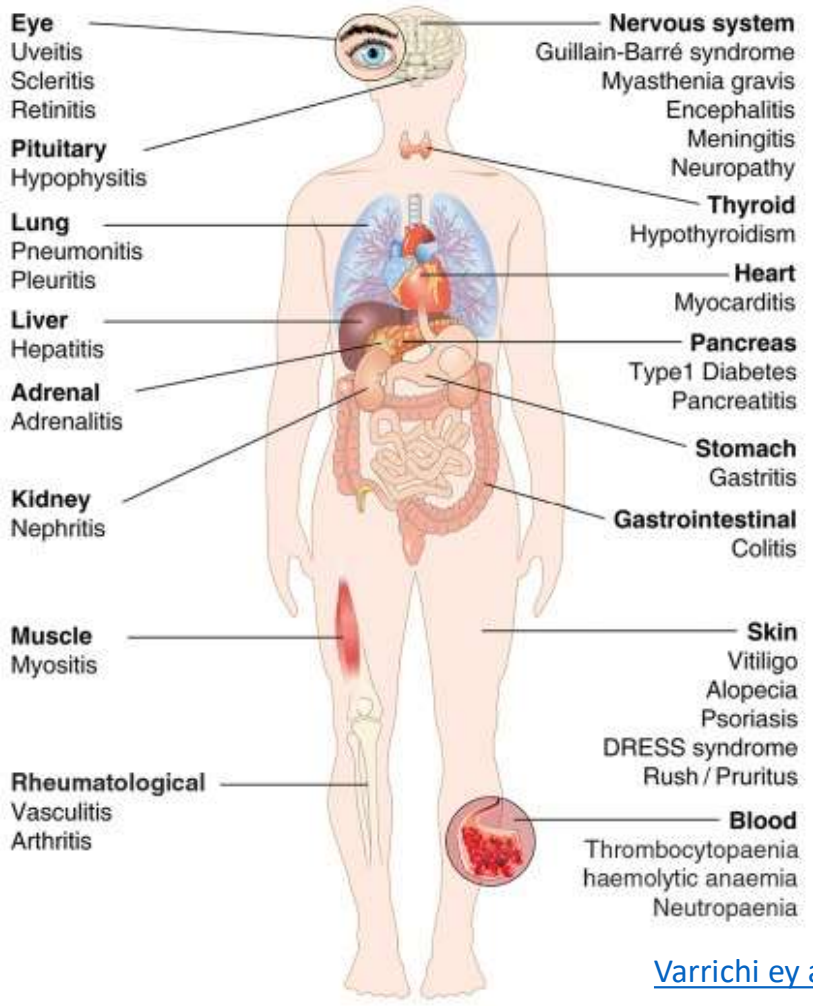
[a]Includes recurrence in the immediate vicinity of the primary tumor (local), regional lymph node basin involvement (regional), or in transit metastases (regional) or any combination of the aforementioned patterns of recurrence; Data cut-off January 4, 2022.

PRESENTED BY:
Georgina V. Long, MD, PhD

MSD

Bijwerkingen

Immune related adverse events (irAE's)



Varrichi ey al. ESMO Open 2017

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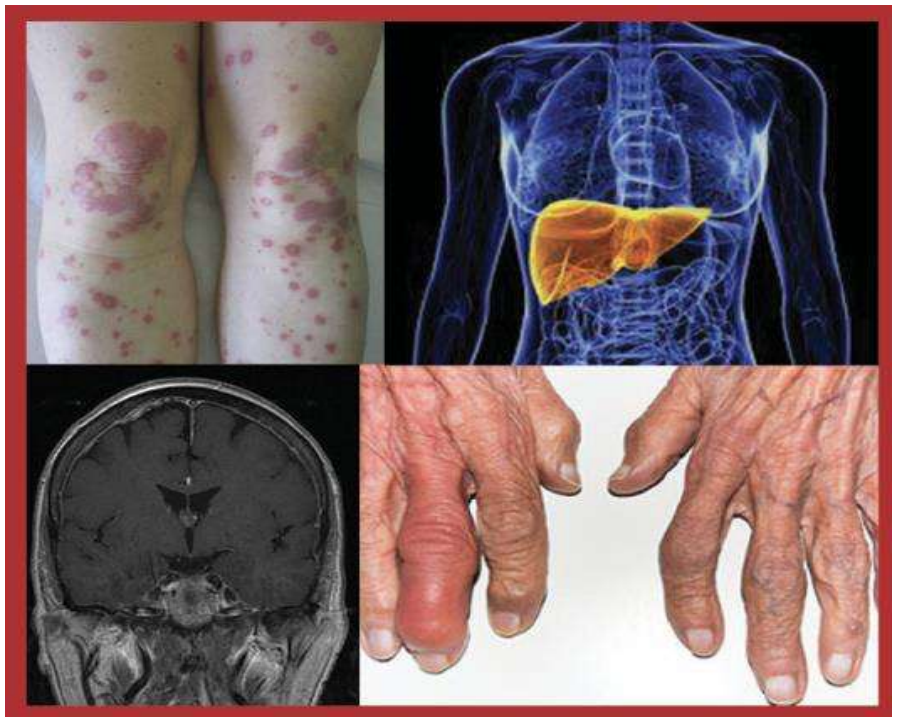
Bijwerkingen

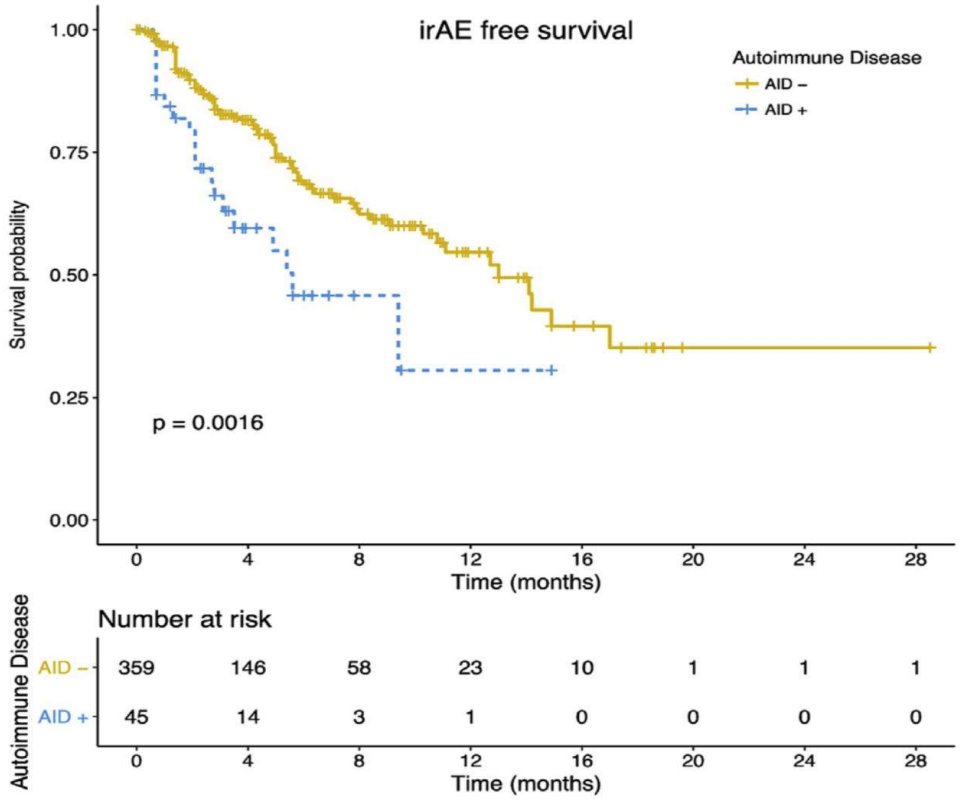
IA3: Adverse Events in the Treated Population[a]

	Pembrolizumab (n=483)		Placebo (n=486)	
	Any, n (%)	Grade ≥3, n (%)	Any, n (%)	Grade ≥3, n (%)
Any cause adverse event	462 (96)	–	445 (92)	–
Any treatment-related event	400 (83)	83 (17)	309 (64)	24 (5)
Discontinued	77 (16)	–	12 (2)	–
Died	0	–	0	–
Immune-mediated events and infusion reactions	182 (38)	–	45 (9)	–
Treatment-related events occurring in ≥15% of patients in each group				
Fatigue	103 (21)	1 (<1)	92 (19)	1 (<1)
Hypothyroidism	77 (16)	0	13 (3)	0
Arthralgia	81 (17)	2 (<1)	39 (8)	0
Pruritus	119 (25)	3 (1)	52 (11)	0
Rash	78 (16)	7 (1)	34 (7)	1 (<1)
Diarrhea	90 (19)	5 (1)	56 (12)	1 (<1)

Median follow-up of 27.4 months (range 14.0-39.4 months). Data cutoff: January 4, 2022.
Long GV, et al. Presented at ASCO 2022.

Patients with preexisting autoimmune disease





Danlos et al. Eur. J. Cancer 2018;91:21–29

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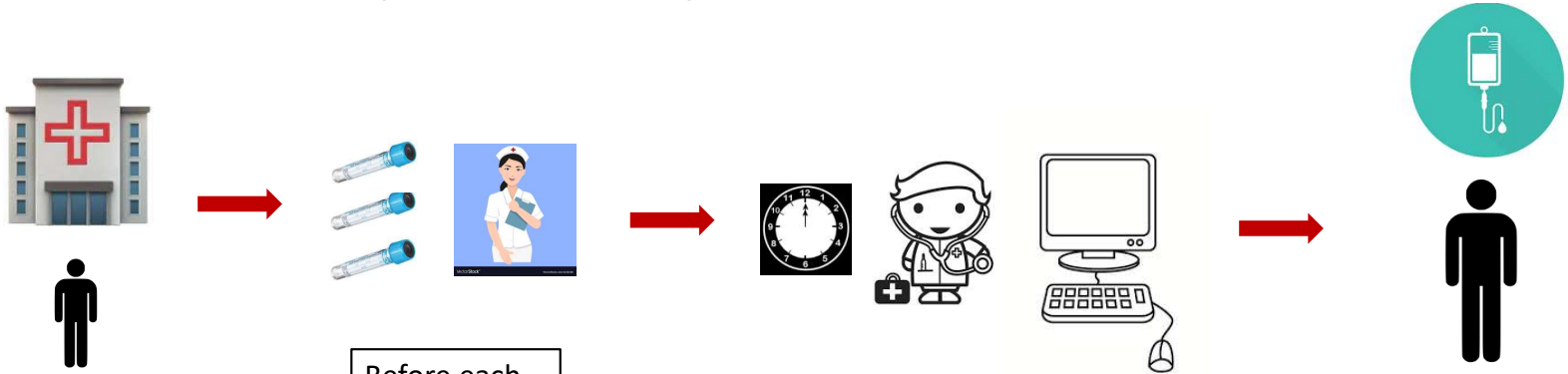
Courtesy of Prof. dr. S. Aspeslagh

Behandeling op het dagziekenhuis

Treatment schedule – pembrolizumab q3 or 6 w



Before each cycle an extensive blood test is done (d -1 or d0)

Before each cycle a consultation with a physician takes place

The administration of pembrolizumab +/- 30 min

Therapieduur : 1 jaar

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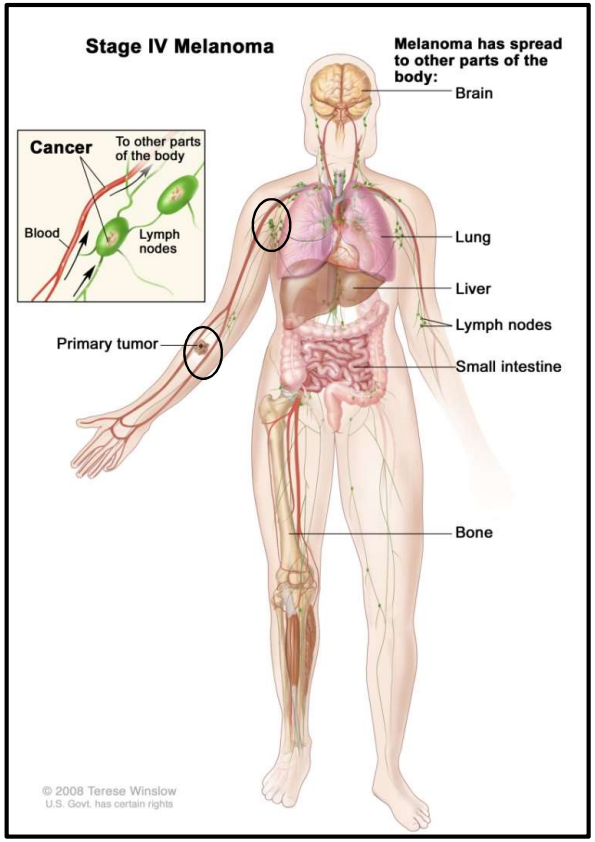
Beschikbare geneesmiddelen

BRAF inhibitor + MEK inhibitor
(targeted therapy)

Anti-PD1-antibody
(checkpoint-inhibitor)



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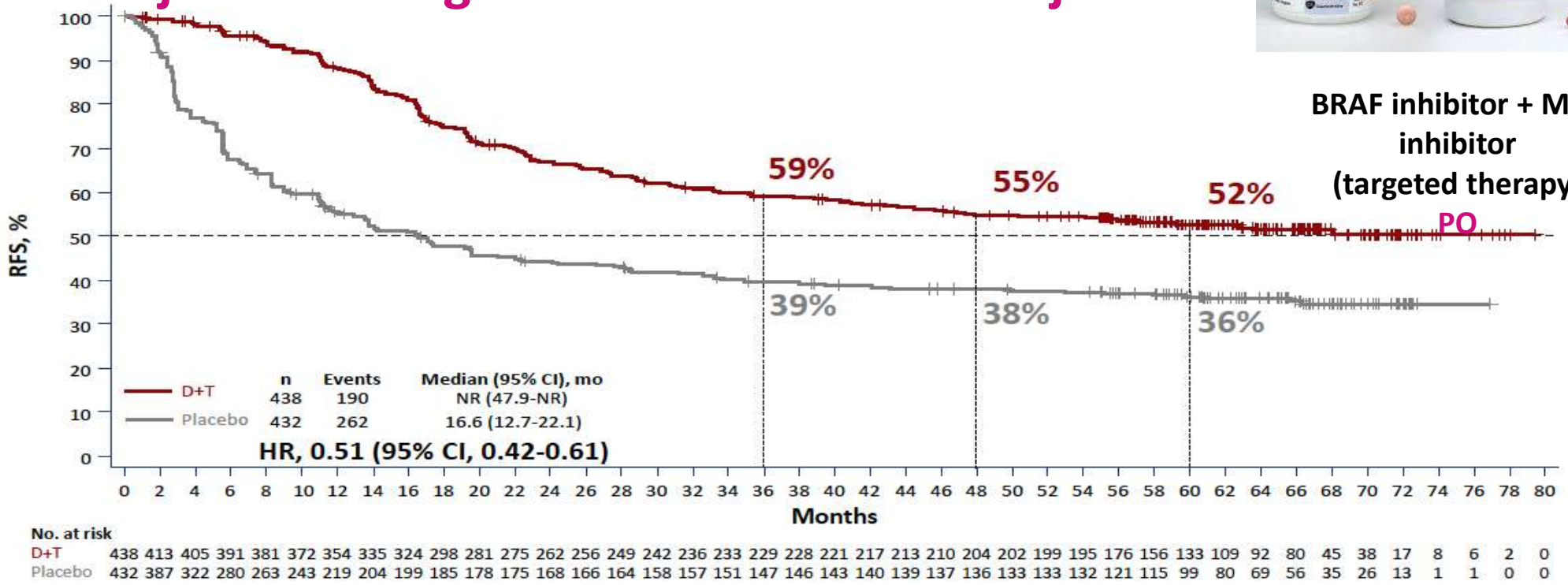
COMBI-AD: 5-Year RFS With D+T

Recidief-vrije overleving - winst van 16% na 3 jaar

BRAF inhibitor + MEK inhibitor (targeted therapy) PO



NR, not reached.

Hauschild A, et al. ASCO 2020 [abstract 10001].

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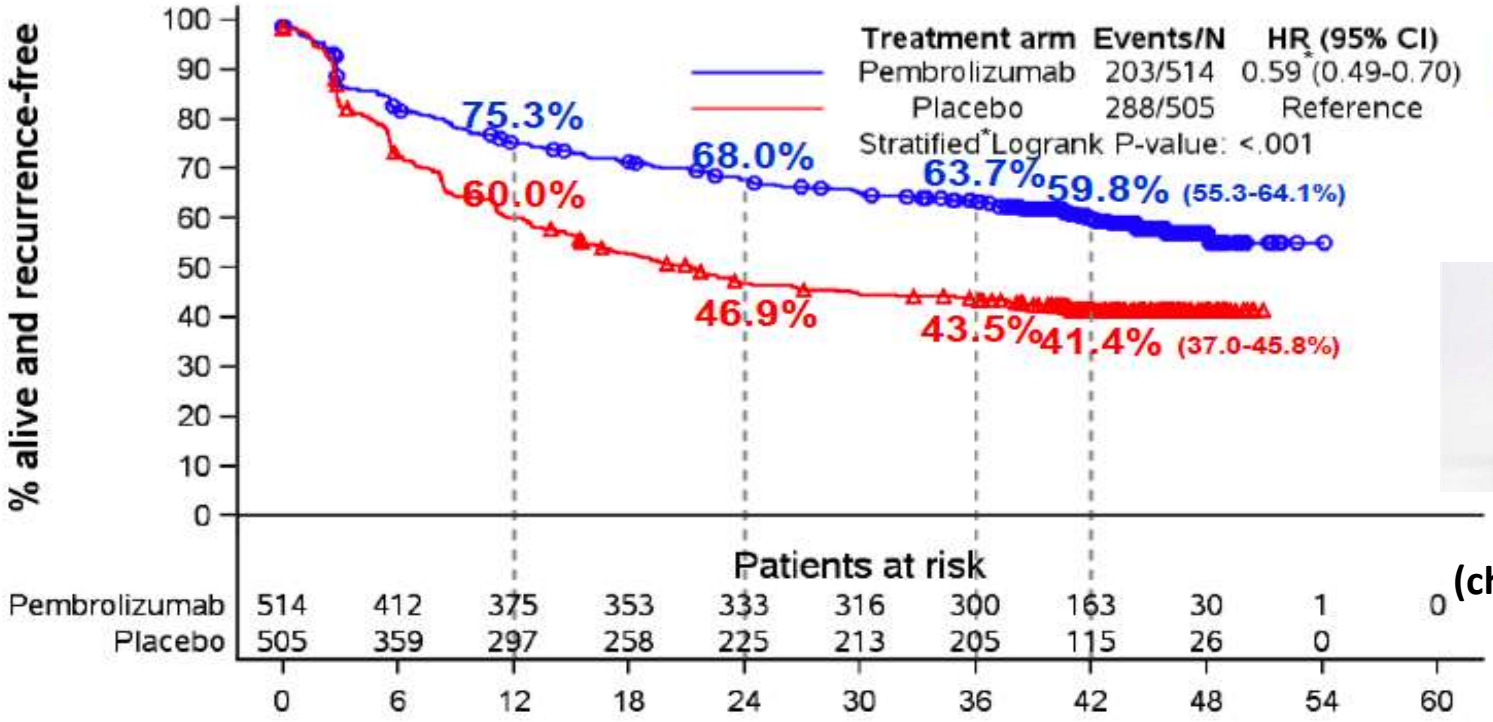
Updated RFS analysis (ESMO 2020)

- **Cut-off date** (3-Apr-2020); median duration of follow-up: **3.5** years; **491** RFS events



HR 0.59

Anti-PD1
(checkpoint inhibitie)
IV

*Stratified by stage given at randomization

Eggermont et al. ESMO 2020.

Recidief-vrije overleving - winst van 18,4% na 3,5 jaar

Samenvatting

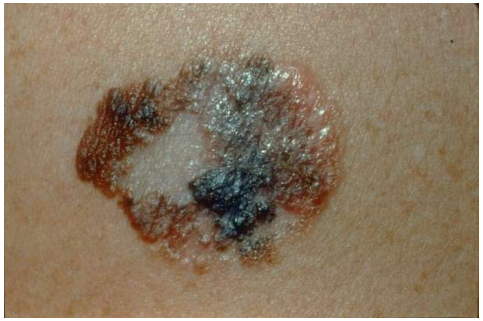
Adjuvante therapie bij melanoom

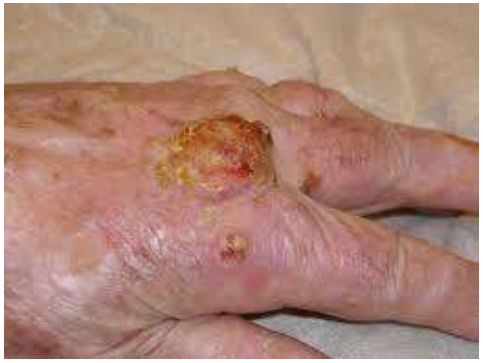
- Mogelijk bij stadium IIb en IIc (vanaf 2,1mm m/ulceratie of > 4mm +/- ulceratie)
  - pembrolizumab (immunotherapie)
  - winst +/- 8% op 2 jaar (RFS)
  - duur therapie: 1 jaar
  - (klein) risico op bijwerkingen!

- Mogelijk bij stadium III :
  - Tafinlar/Mekinist (Targeted therapy - PO – enkel bij BRAFmut / 40%) of (nivolumab of pembrolizumab – IV - immunotherapie)
  - Winst 16-18 % op 3jaar
  - Duur therapie: 1 jaar
  - Bijwerkingen afhankelijk van geneesmiddelen (targeted therapie >< immuno)

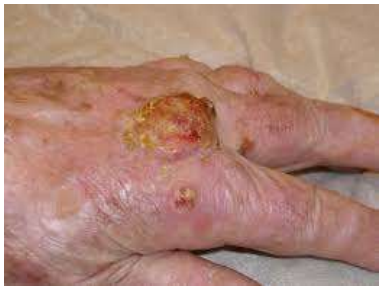
Huidkanker

- melanoom
- non-melanoma huidkanker (NMSC)
  - **spinocellulair carcinoom**
  - basocellulair carcinoom
  - ...





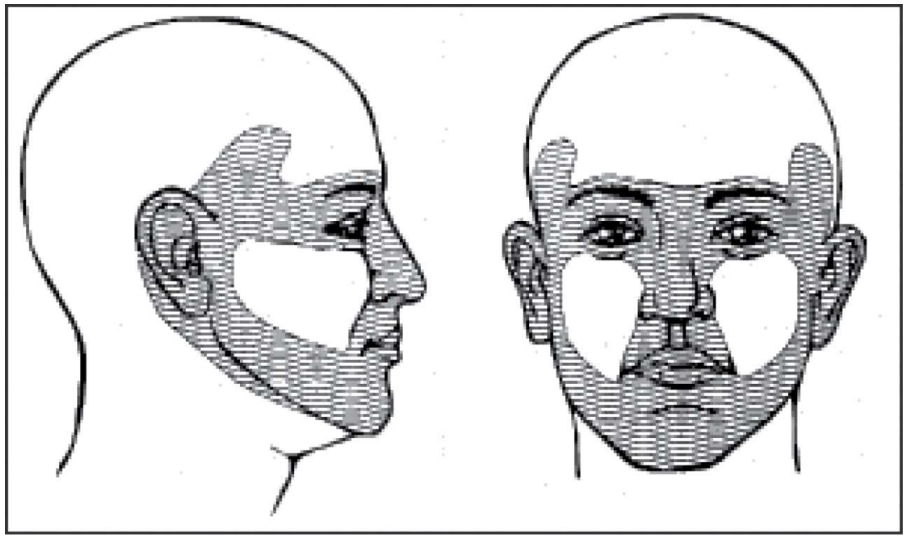
Epidemiologie - spinocellulair carcinoom



- Na BCC 2e **meest frequente** huidkanker
- 20% van alle gerapporteerde huidkankers; toenemend
- Overwegend **hoofd-hals** regio (80-90%)
- **Bleke huid**, >mannen, **zon**blootstelling
- Littekens, brandwonden, ulcera, sclerodermie, radiodermitis
- Immunosuppressie (medicatie, HIV, CLL, transplantpatiënten,...)
- Roken

Risicofactoren recidief of metastase

- **Ligging**: Temporaal, lip, oor
- **Immunosuppressie** (HIV, transplant, CLL)
- **Diameter** >20mm
- **Tumordikte** >6mm of invasie voorbij subcutane vet
- Slechte **differentiatie**graad
- Microscopische, symptomatische of radiologische perineurale invasie
- Boterosie

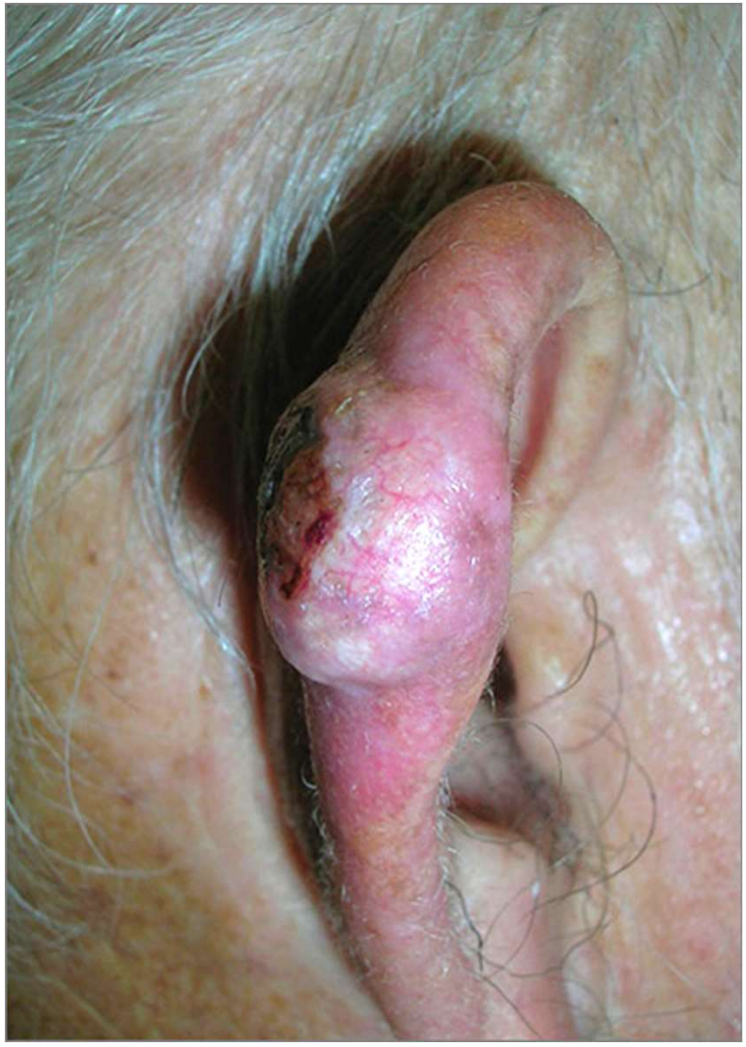


Arch Dermatol 1983;119:761–773.

Prognose

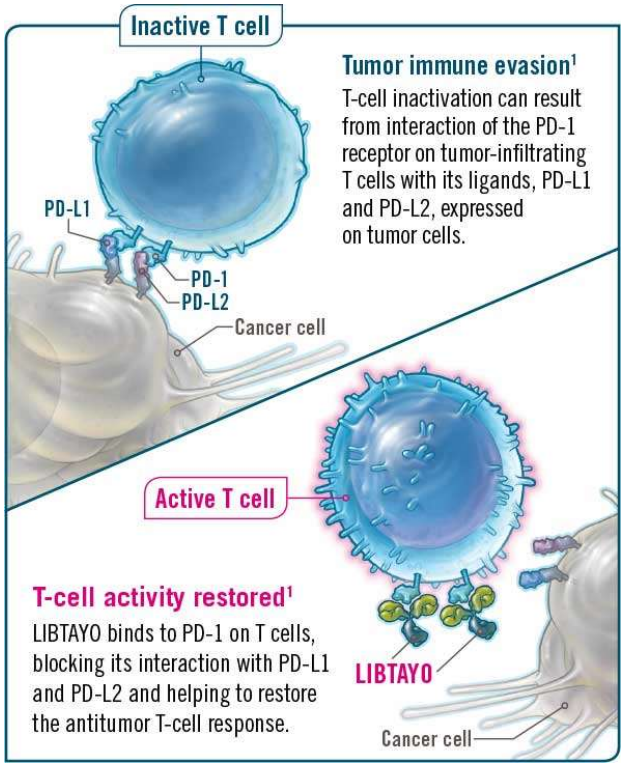
- **Risico op metastase laag**; indien vroeg en correct behandeld
- 5-jaars genezingskans van ≥90%

- ± 3% lokaal recidief
- 1-4% metastasen (meestal binnen de twee jaar)
- 2% mortaliteit



Cemiplimab (anti-PD1) BIJ SCC

Lokaal gevorderd of gemetastaseerd spino van de huid (la/mSCC)



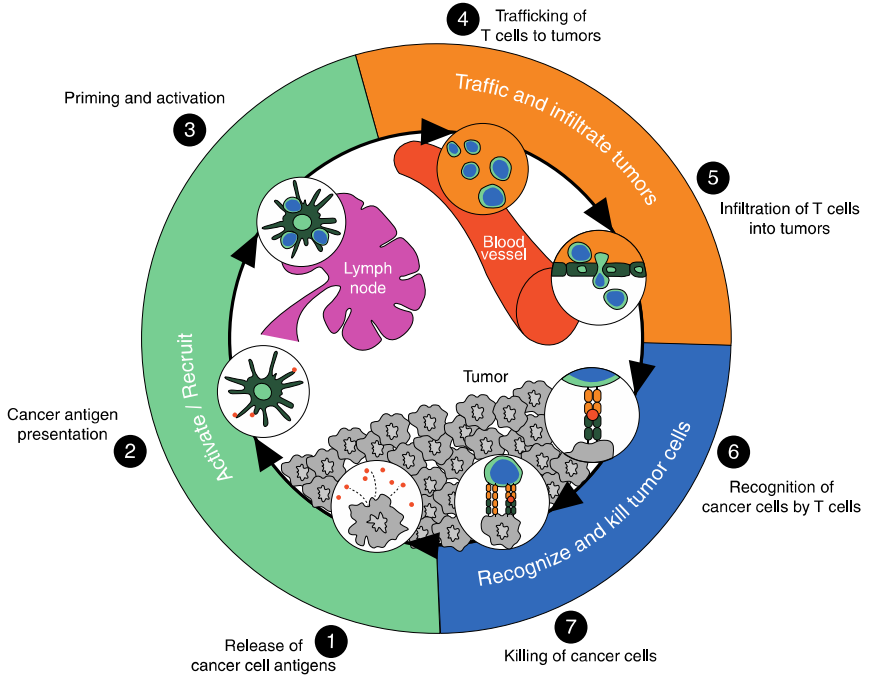
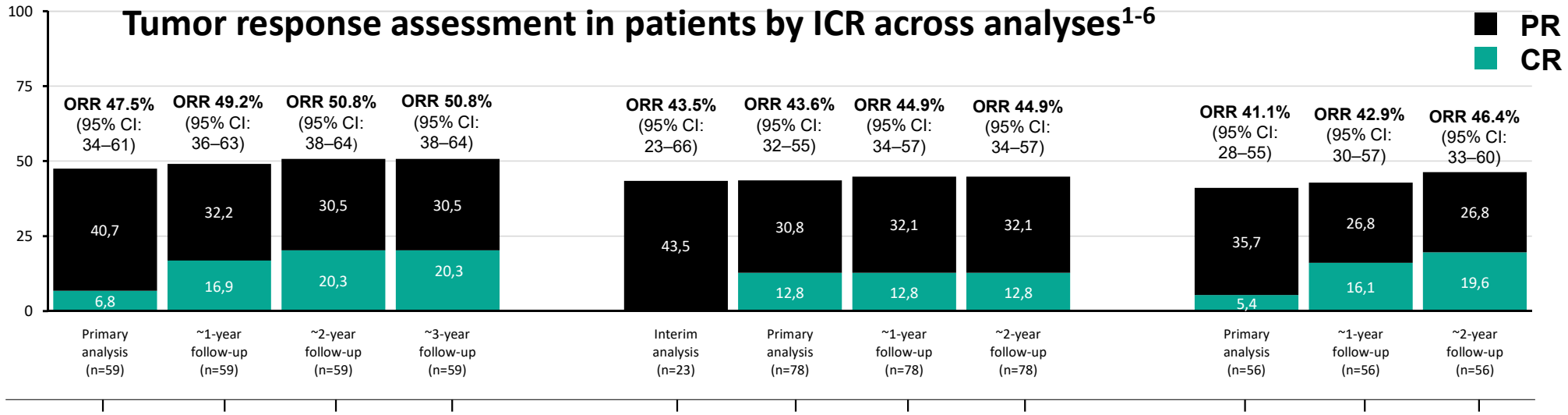


Figure 1. The cancer-immunity cycle. Figure modified from Chen and Mellman [1], with permission from Elsevier.

The tumor microenviroment is characterized by changes in the immune cell populations, immune checkpoint expression and immuosupression ➔ tumor escape from immune surveillance

Response Rates Over Time per ICR (Groups 1–3)

In het algemeen werkt immuuntherapie eerder traag !



CI=confidence interval; CR=complete response; CSCC=cutaneous squamous cell carcinoma; ICR=independent central review; ORR=overall response rate; PR=partial response; Q2W=every 2 weeks; Q3W=every 3 weeks.

1. Rischin D, et al. *J Immunother Cancer* 2021;9:e002757. doi:10.1136/jitc-2021-002757. 2. Migden MR, et al. *N Engl J Med.* 2018;379(4):341–351. 3. Rischin D, et al. *J Immunother Cancer* 2020;8(1):e000775. doi: 10.1136/jitc-2020-000775. 4. Migden MR, et al. Poster presented at the 27th European Academy of Dermatology and Venereology Congress; 5. Migden MR, et al. Lancet Oncol. 2020;21(2):294–305.
6. Rischin D, et al. Presented at the 10th World Congress of Melanoma in conjunction with 17th European Association of Dermato Oncology Congress 2021, April 15–17, Virtual Scientific Meeting.

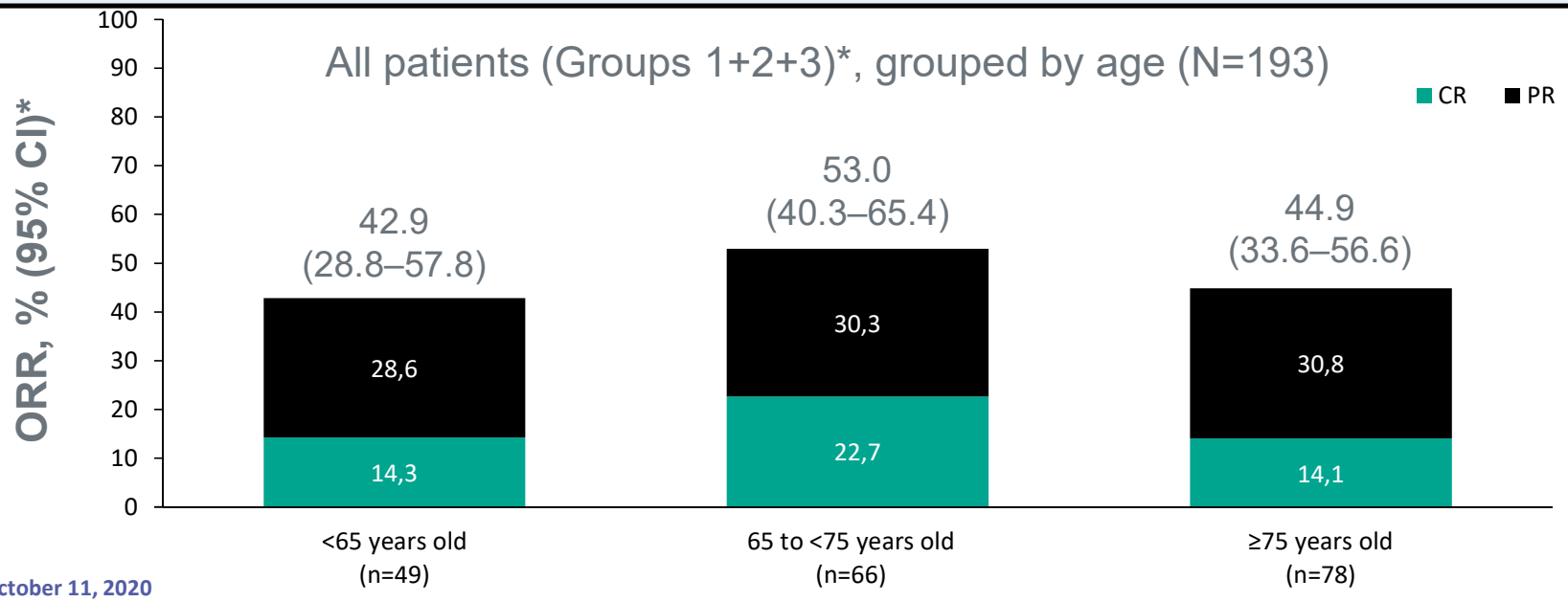
VITAZ

REGENERON

ORR – Cemiplimab per leeftijdscategorie in ptn met gevorderd CSCC (groep 1-3)

Leeftijd is geen contra-indicatie!

Clinical activity with cemiplimab by independent central review was observed regardless of patient age



Data cut-off date: October 11, 2020

*Group 1: mCSCC 3 mg/kg Q2W (N=59); Group 2: laCSCC 3 mg/kg Q2W (N=78); Group 3: mCSCC 350 mg Q3W (N=56).

CI=confidence interval; CR=complete response; CSCC=cutaneous squamous cell carcinoma; laCSCC=locally advanced CSCC; mCSCC= metastatic CSCC; N=total number of patients; ORR=objective response rate; PR=partial response Q2W=every 2 weeks; Q3W=every 3 weeks.

Rischin D, et al. Poster presented at: European Association of Dermato Oncology (EADO) Congress Virtual Meeting; April 15–17, 2021:Poster.

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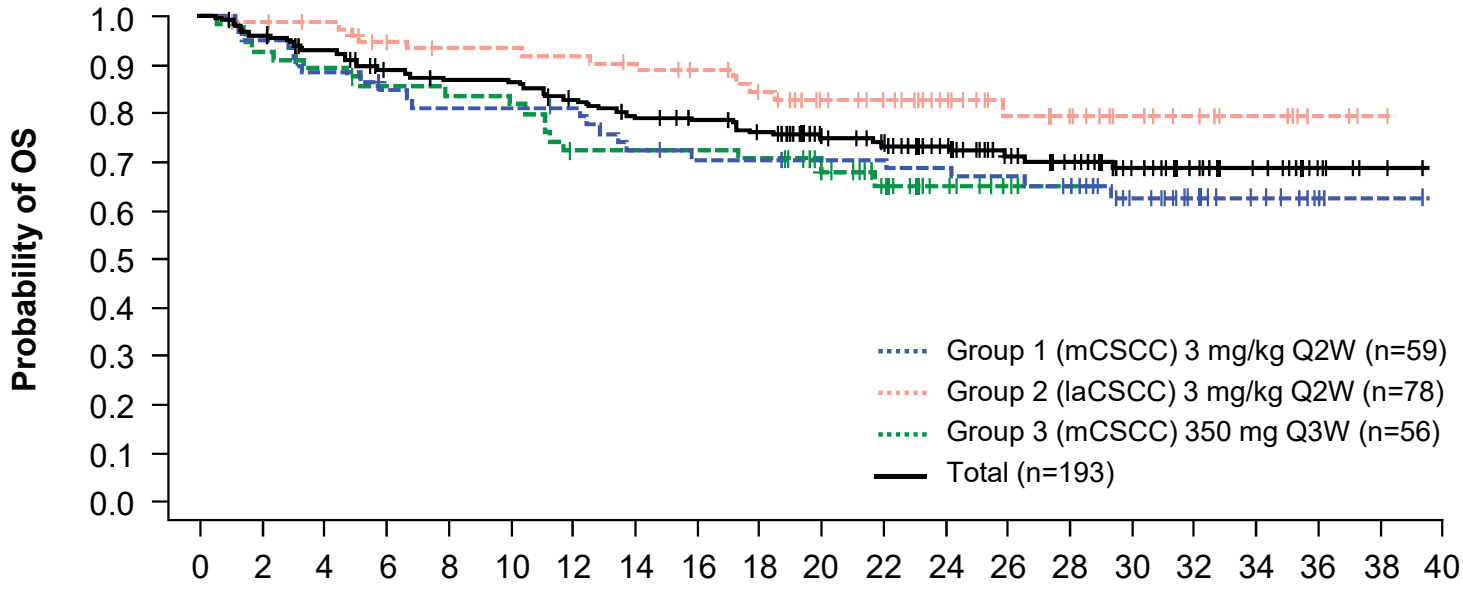
Kaplan–Meier curves for OS (laCSCC eb mCSCC)



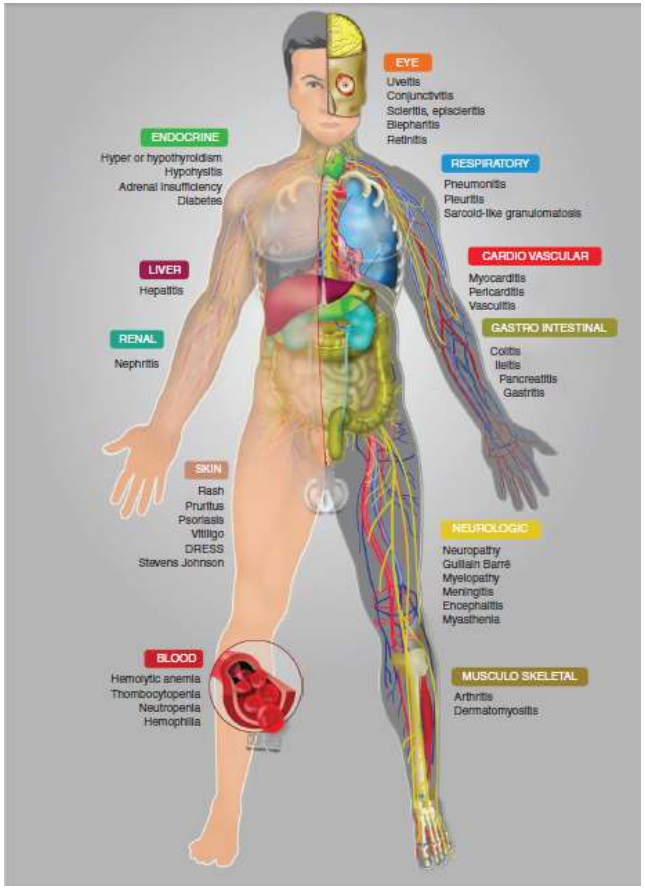
- **Median OS has not been reached**. The Kaplan–Meier estimated probability of OS at 24 months was 73.3% (95% CI: 66.1–79.2)

Number of patients at risk																					
Group 1 (n=59)	59	56	52	49	47	47	46	41	39	39	38	38	37	35	33	24	16	11	4	1	0
Group 2 (n=78)	78	76	73	67	65	65	64	62	59	54	44	41	33	25	22	15	12	8	3	1	0
Group 3 (n=56)	56	52	49	46	45	44	38	38	38	37	29	20	9	2	0	0	0	0	0	0	0
Total (n=193)	193	184	174	162	157	156	148	141	136	130	111	99	79	62	55	39	28	19	7	2	0

CSCC, cutaneous squamous cell carcinoma; CI, confidence interval; laCSCC, locally advanced CSCC; mCSCC, metastatic CSCC; OS, overall survival; Q2W, every 2 weeks; Q3W, every 3 weeks.

Data cut-off date: October 11, 2019. Median duration of follow-up among all patients: 15.7 months (range: 0.6–36.1).

Spectrum van immuungerelateerde bijwerkingen



Champiat *et al*. *Annals of Oncology*, 2016;27:559-74.

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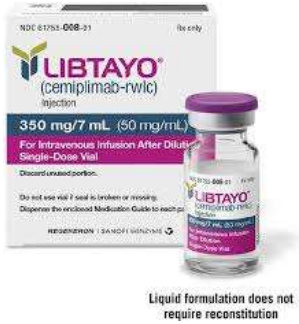
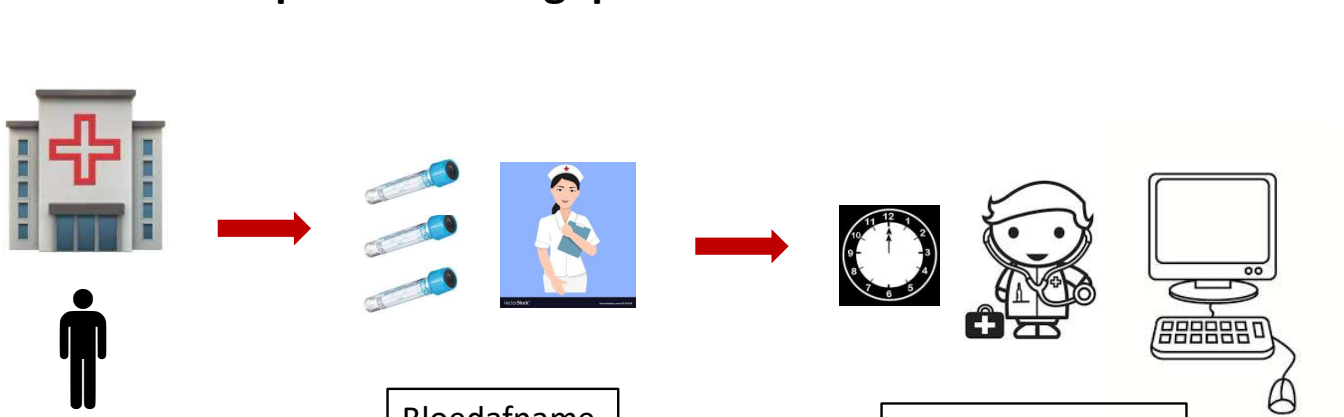
Behandeling op het dagziekenhuis



Schema – cemiplimab 350 mg q3w



Bloedafname vóór elke cyclus (d -1 or d0)

Consultatie met de behandelend oncoloog vóór elke cyclus

Toediening van cemiplimab +/- 30 min

Therapieduur: ?

Herevaluatie: CT of PET/CT om de 3-4 maanden

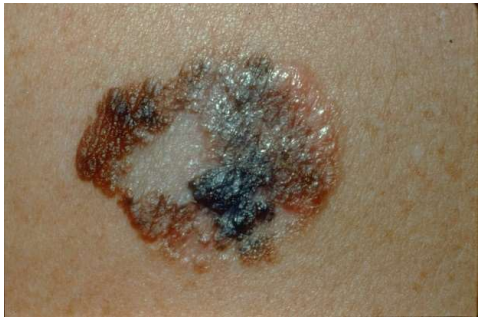
Samenvatting

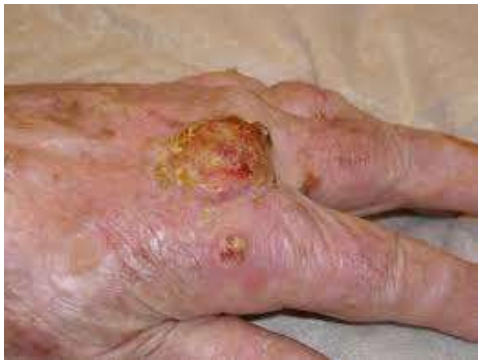
Systeemtherapie bij spinocellulair carcinoom van de huid (SCC)

- Kans op respons (PR of CR) +/- 45% (= afname metastasen > 30%)
- Cemiplimab werkt eerder traag
- Leeftijd is geen contraindicatie

Huidkanker

- melanoom
- non-melanoma huidkanker (NMSC)
  - spinocellulair carcinoom
  - basocellulair carcinoom
  - ...

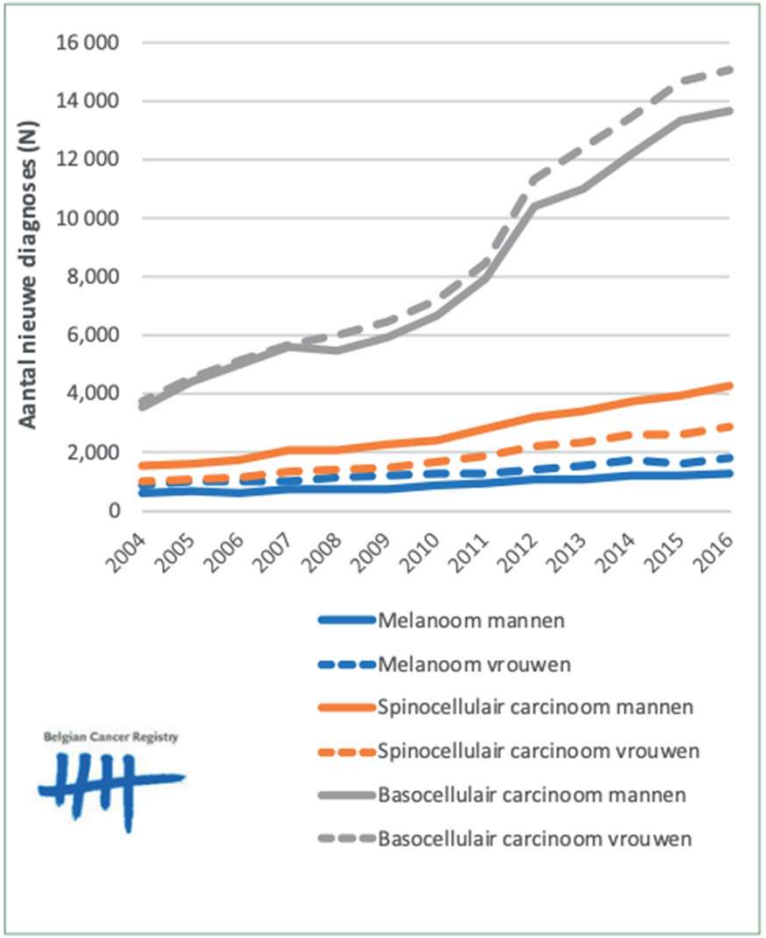




Epidemiologie

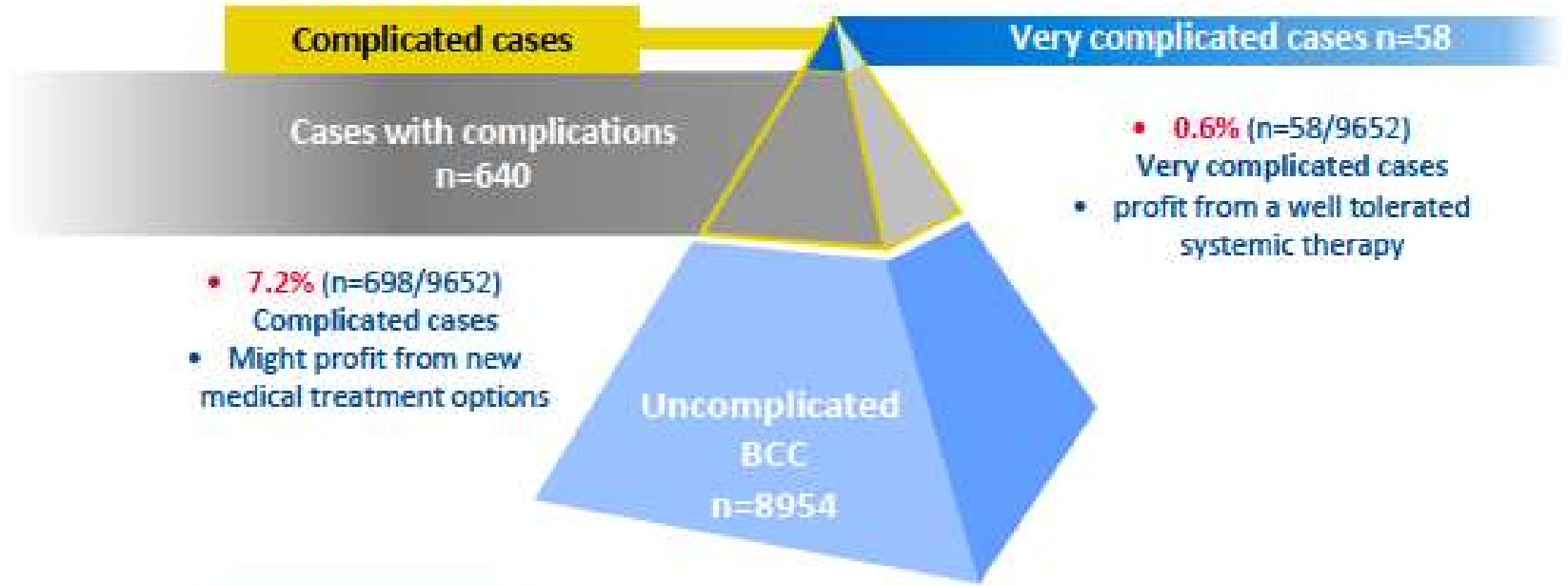
- Meest voorkomende vorm van kanker (i.h. algemeen!)
- USA: 1/5 krijgt BCC
- Zonschade!
- Man > vrouw
- Bij voorgeschiedenis van BCC 10x hoger risico op volgend BCC
- Risico op metastasen zeer klein!

Figuur 1: Evolutie van de incidentie van kwaadaardige huidtumoren, België, 2004-2016.



What is the frequency of difficult-to-treat BCC?

Total collective dermatopathology database:
BCC patients 1 January 2007 – 31 December 2011 (n=9652)



- 7.2% (n=698/9652) Complicated cases
- Might profit from new medical treatment options

- 0.6% (n=58/9652) Very complicated cases
- profit from a well tolerated systemic therapy

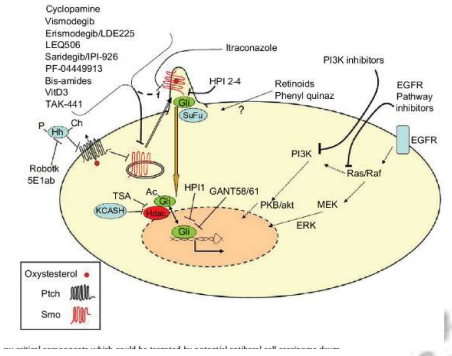
BARCELONA 2019 ESMO congress

DERMATOLOGICAL SURGERY AND LASERS

Basal cell carcinomas in a tertiary referral centre: a systematic analysis*

British Journal of Dermatology (2014) 171, pp1064–1072

presented by Prof. R. Dummer



ORIGINAL ARTICLE

Efficacy and Safety of Vismodegib in Advanced Basal-Cell Carcinoma

Aleksandar Sekulic, M.D., Ph.D., Michael R. Migden, M.D., Anthony E. Oro, M.D., Ph.D., Luc Dirix, M.D., Ph.D., Karl D. Lewis, M.D., John D. Hainsworth, M.D., James A. Solomon, M.D., Ph.D., Simon Yoo, M.D., Sarah T. Arron, M.D., Ph.D., Philip A. Friedlander, M.D., Ph.D., Ellen Marmur, M.D., Charles M. Rudin, M.D., Ph.D., Anne Lynn S. Chang, M.D., Jennifer A. Low, M.D., Ph.D., Howard M. Mackey, Ph.D., Robert L. Yauch, Ph.D., Richard A. Graham, Ph.D., Josina C. Reddy, M.D., Ph.D., and Axel Hauschild, M.D.

Outcome	Metastatic Basal-Cell Carcinoma (N=33)		Locally Advanced Basal-Cell Carcinoma (N=63)	
	Independent Review	Site Investigators	Independent Review	Site Investigators
Objective response — no. (%)	10 (30)	15 (45)	27 (43)	38 (60)

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Long-Term Efficacy of Vismodegib in Advanced BCC: Results From the ERIVANCE BCC Trial

Efficacy outcome	Primary analysis (9 months after accrual) INV[1,2]		Final analysis (39 months after accrual) INV[2]	
	mBCC (n=33)	laBCC (n=63*)	mBCC (n=33)	laBCC (n=63*)
ORR, n (%)	15 (45%)	38 (60%)	16 (48%)	38 (60%)
Complete response	0	20 (32%)	0	20 (32%)
Partial response	15 (45%)	18 (29%)	16 (48%)	18 (29%)
Stable disease	15 (45%)	15 (24%)	14 (42%)	15 (24%)
Progressive disease	2 (6%)	6 (10%)	2 (6%)	6 (10%)
Non-evaluable/missing	1 (3%)	4 (6%)	1 (3%)	4 (6%)
Median duration of response, months (95% CI)	12.9 (5.6–12.9)	7.6 (7.4–NE)	14.8 (5.6–17.0)	26.2 (9.0–37.6)
Median PFS, months (95% CI)	9.2 (7.4–NE)	11.3 (9.5–16.8)	9.3 (7.4–16.6)	12.9 (10.2–28.0)
Median OS, months (95% CI)	NE (13.9–NE)	NE (17.6–NE)	33.4 (18.1–NE)	NE (NE)
1-year survival rate, % (95% CI)	75.5 (57.3–93.6)	91.6 (83.5–99.7)	78.7 (64.7–92.7)	93.2 (86.8–99.6)

Note: Only investigator assessments are included in the efficacy-evaluable population.
*Eight patients were excluded from the efficacy analysis because the independent pathologist did not identify BCC in baseline or post-baseline biopsy specimens.

BCC=basal cell carcinoma; CI=confidence interval; INV=investigator assessment; laBCC=locally advanced basal cell carcinoma; mBCC=metastatic basal cell carcinoma; NE=not estimable; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; US=United States.

1. Sekulic A, et al. *N Engl J Med.* 2012;366:2171–9. 2. Sekulic, A, et al. *BMC Cancer.* 2017;17:332.

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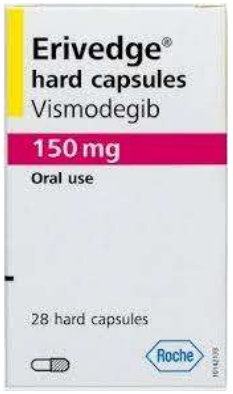
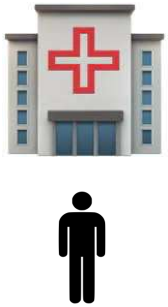
Behandeling op het dagziekenhuis



Schema – vismodigib (een cyclus = 4w)



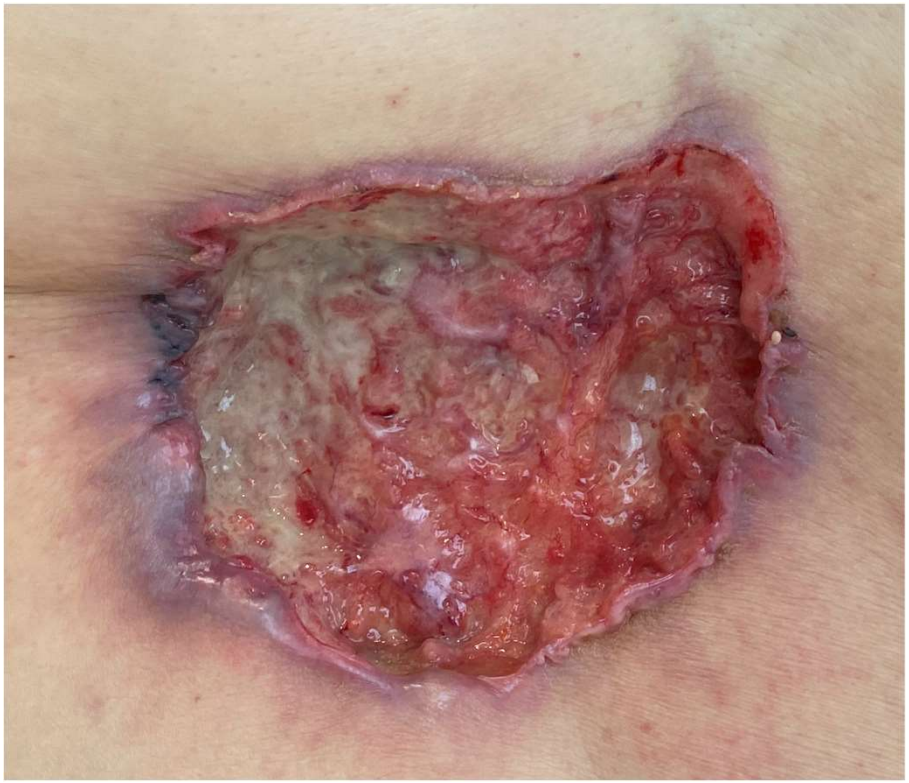
Bloedafname vóór elke cyclus (d -1 or d0)

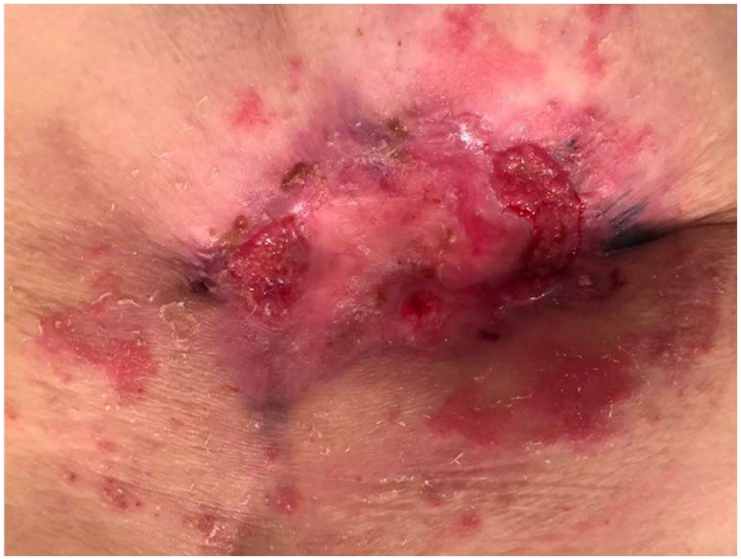
Consultatie met de behandelend oncoloog vóór elke cyclus (om de 2 à 4w)

Medicatie wordt meegegeven via het dagziekenhuis

Therapieduur: ?
Herevaluatie: Klinisch

Inoperabel BCC thv de onderug bij start en na 3m





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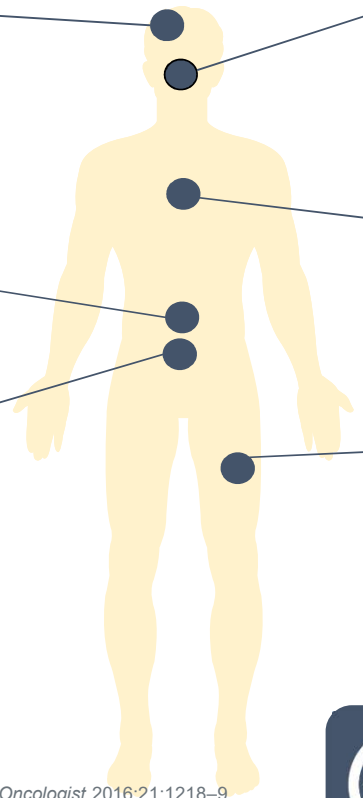
Management of Common Adverse Events with HHIs[1,2]

Alopecia
- Minoxidil 5% to scalp, oral DHT inhibitors
- Cosmetic solutions

Weight loss (decreased appetite)
- Nutritional approaches
- Dietary supplement, THC, steroids

Gastrointestinal disturbance (nausea, diarrhea)
- Serotonin inhibitors, breakthrough agents
- Gastrointestinal motility medications



Taste disturbance (dysgeusia, ageusia)
- Nutritional approaches
- THC, zinc supplement

Asthenia
- Physical activity, psychology consult
- Test/treat for anemia, psychostimulants

Muscle spasms
- Hydration and gentle activity
- Pharmacologic treatments include calcium channel blockers, nerve stabilizers, magnesium, lidocaine, vitamin B

These adverse events can also be managed by dose interruption or intermittent dosing

DHT=dihydrotestosterone; HHI=hedgehog pathway inhibitor; THC=delta-9-tetrahydrocannabinol.

1. NCCN Guidelines, Basal Cell Skin Cancer, version 2.2021–Feb 15, 2021. 2. Lacouture M, et al. *Oncologist* 2016;21:1218–9.

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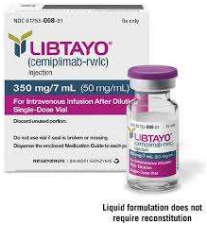
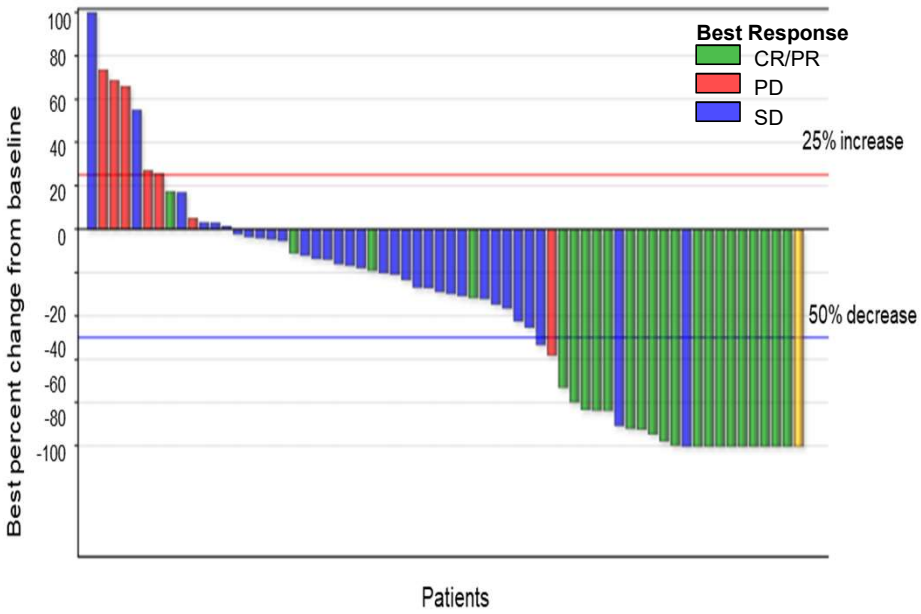
Wat bij progressie op vismodigib?

EMPOWER-BCC 1: Evaluation of Response in laBCC (ICR)



Primary analysis (ICR)	laBCC N=84
Median follow-up, months (Range)	**16** (0.5–28.1)
Overall response rate, % (95% CI)	**32.1%** (22.4%–43.2%)
Complete response, n (%)	**6 (7.1%)**
Partial response, n (%)	**21** (25.0%)
Stable disease, n (%)	**40** (47.6%)
Progressive disease, n (%)	9 (10.7%)
Not evaluable, n (%)*	8 (9.5%)
Number of responders	**N=27 responders**
Disease control rate, % (95% CI)†	**79.8%** (69.6%–87.7%)
Durable disease control rate, % (95% CI)‡	**59.5%** (48.3%–70.1%)

Waterfall Plot per WHO criteria by ICR



Waterfall plot displays the best percentage change in the sum of target lesion diameters during study period from baseline. Lesion measurements after progression are excluded. Increase in sum of target lesion diameters greater than 100% is reported as 100%

Data cut-off as of June 30th, 2020

*Of the 8 patients who were not evaluable, 4 did not have any post-baseline tumour assessments, 3 patients were not considered to have evaluable lesions by either photographic or radiologic assessment methods and one patient had a second target lesion not imaged after baseline; †Defined as the proportion of patients with CR, PR, SD or non-PR/non-PD at the first evaluable tumor assessment, scheduled to occur at Week 9 (defined as 56 days to account for visit windows in the protocol); ‡Defined as the proportion of patients with CR, PR, SD or non-PR/non-PD for at least 27 weeks without PD (defined as 182 days to account for visit windows in the protocol).

CI, confidence interval; CR, complete response; ICR, independent central review; laBCC, locally advanced basal cell carcinoma; PD, progressive disease; PR, partial response; SD, stable disease; WHO, World Health Organization.

LIBTAYO® SmPC, Jun 2021. Available at: https://www.ema.europa.eu/en/documents/product-information/libtayo-epar-product-information_en.pdf; TFL-DCO-30 Jun 20 - Table 14.2.1.1f, 14.1.1.7f; Figure 14.2.1.9.2.

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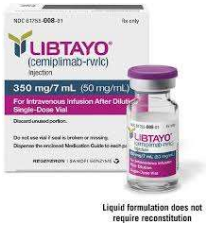
EMPOWER-BCC 1: Evaluation of response in mBCC
Interim Analysis: Investigator Assessment[1–2]



Interim Analysis	mBCC (N=35) Investigator Assessment
Overall response rate, % (95% CI)	**28.6%** (14.6%–46.3%)
Complete response, n (%)	1 (2.9%)
Partial response, n (%)	9 (25.7%)
Stable disease, n (%)	14 (40.0%)
Non-CR/non-PD, n (%)	0
Progressive disease, n (%)	9 (25.7%)
Not evaluable, n (%)	2 (5.7%)
Disease control rate, % (95% CI)	**68.6%** (50.7%–83.1%)
Durable disease control rate, % (95% CI)	**42.9%** (26.3–60.6%)

Data cut-off as of June 30th, 2020

CI, confidence interval; mBCC, metastatic basal cell carcinoma.

1. LIBTAYO® SmPC, Jun 2021. Available at: https://www.ema.europa.eu/en/documents/product-information/libtayo-epar-product-information_en.pdf; 2. TFL-DCO-30 Jun 20 - Table14.2.1.2f.

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Samenvatting

Systeemtherapie bij basocellulaire carcinoom van de huid (SCC)

Vismodigib (PO)

- Kans op respons (PR of CR) 30-60%
- Redelijk snel effect!
- CAVE! Toxiciteit

Cemiplimab (IV)

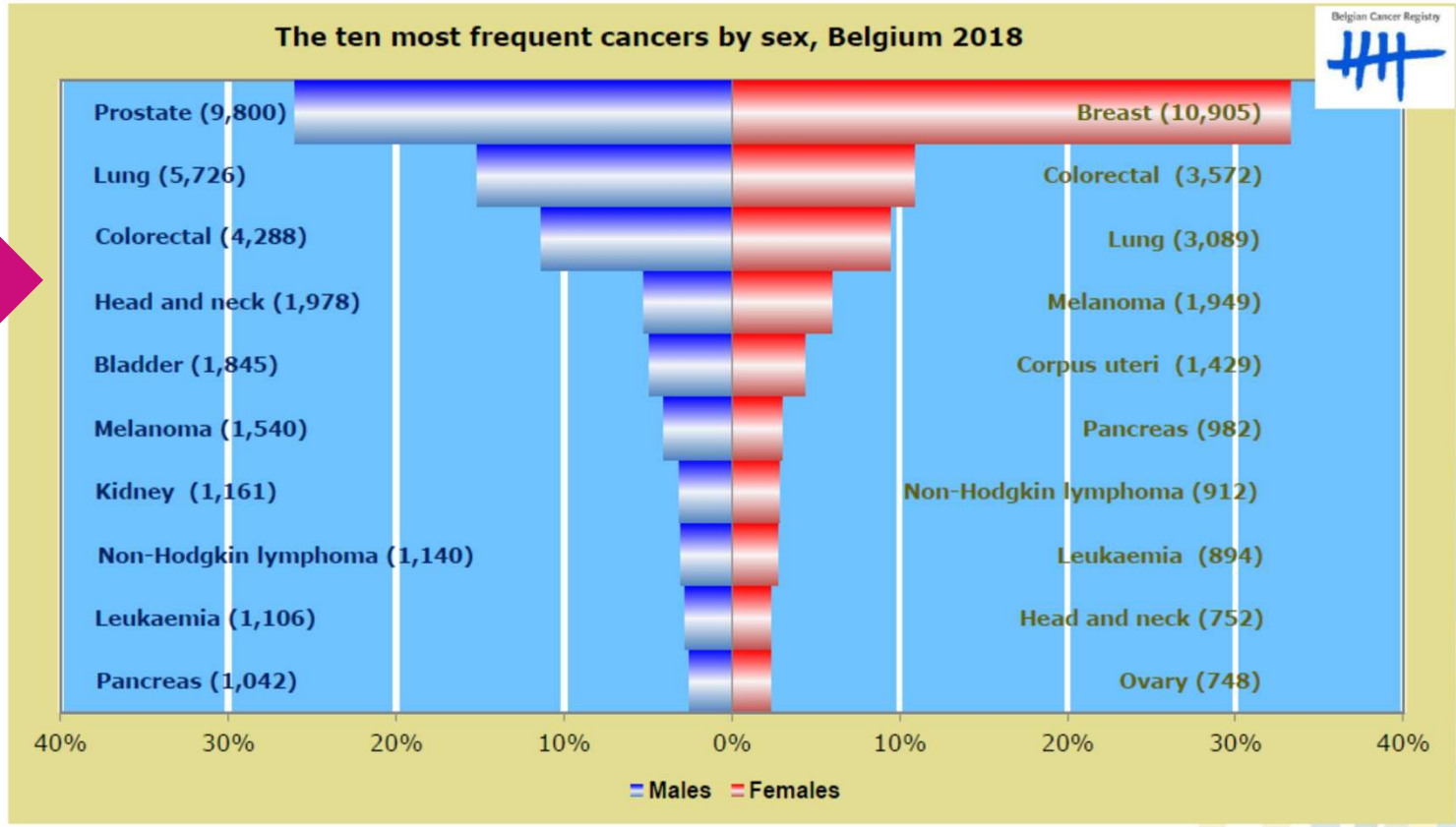
- Na vismodigib
- Kans op respons (PR of CR) +/-30%
- Immuunregelateerde bijwerkingen

Bedankt voor jullie aandacht!

BEHANDELING GEMETASTASEERD COLONCARCINOOM - 2022

DR. HANS DEDECKER
DIGESTIEVE ONCOLOGIE - VITAZ

Incidence of cancer in Belgium – locations



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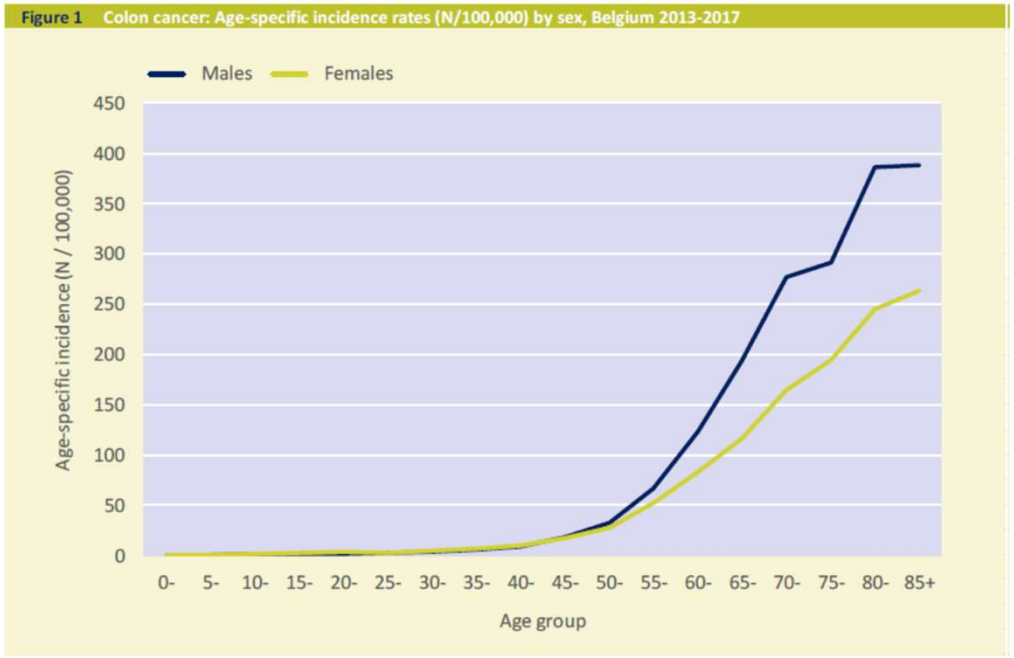
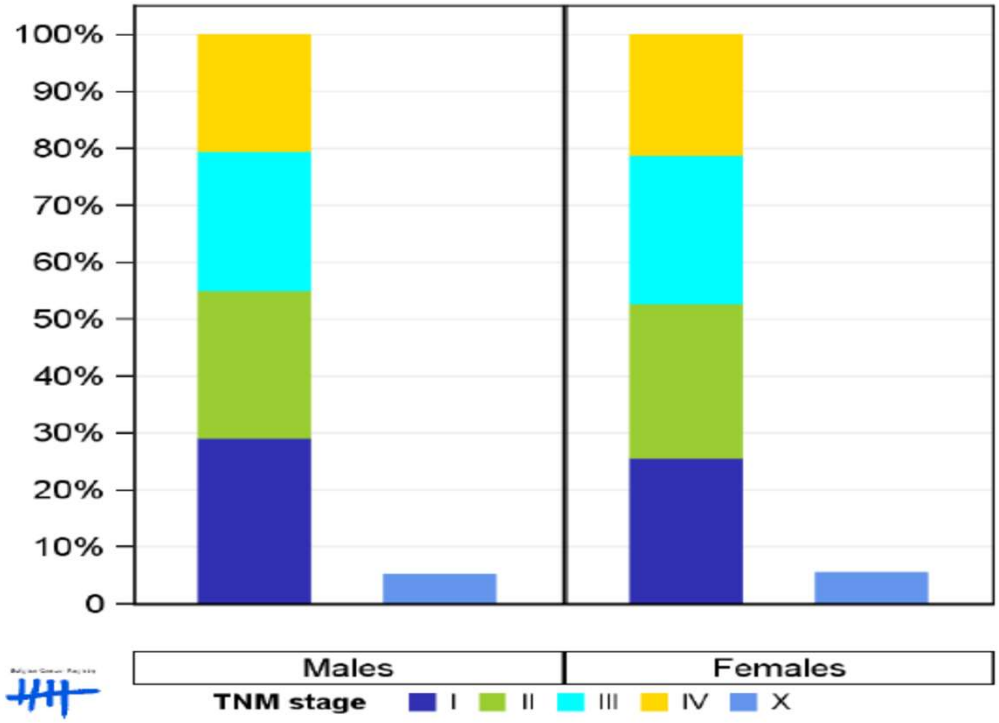
Colon cancer – Facts in Belgium, age and stage

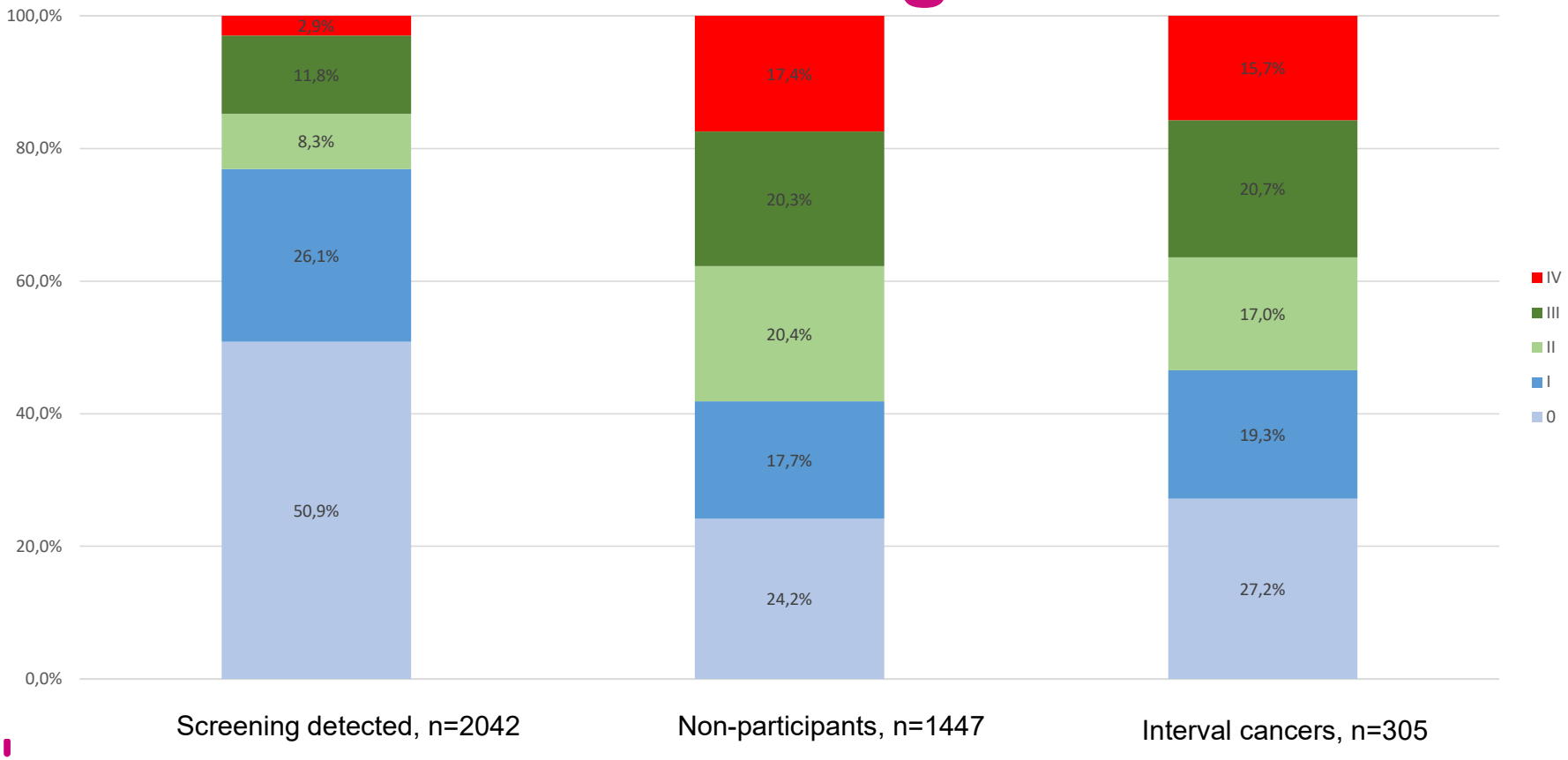


Cancer Burden in Belgium 2004-2017; Belgian Cancer Registry, 2020



Belgian Cancer Registry, 2018

Colon cancer – Flemish Colon cancer screening



Flemish Colon cancer screening, 2020

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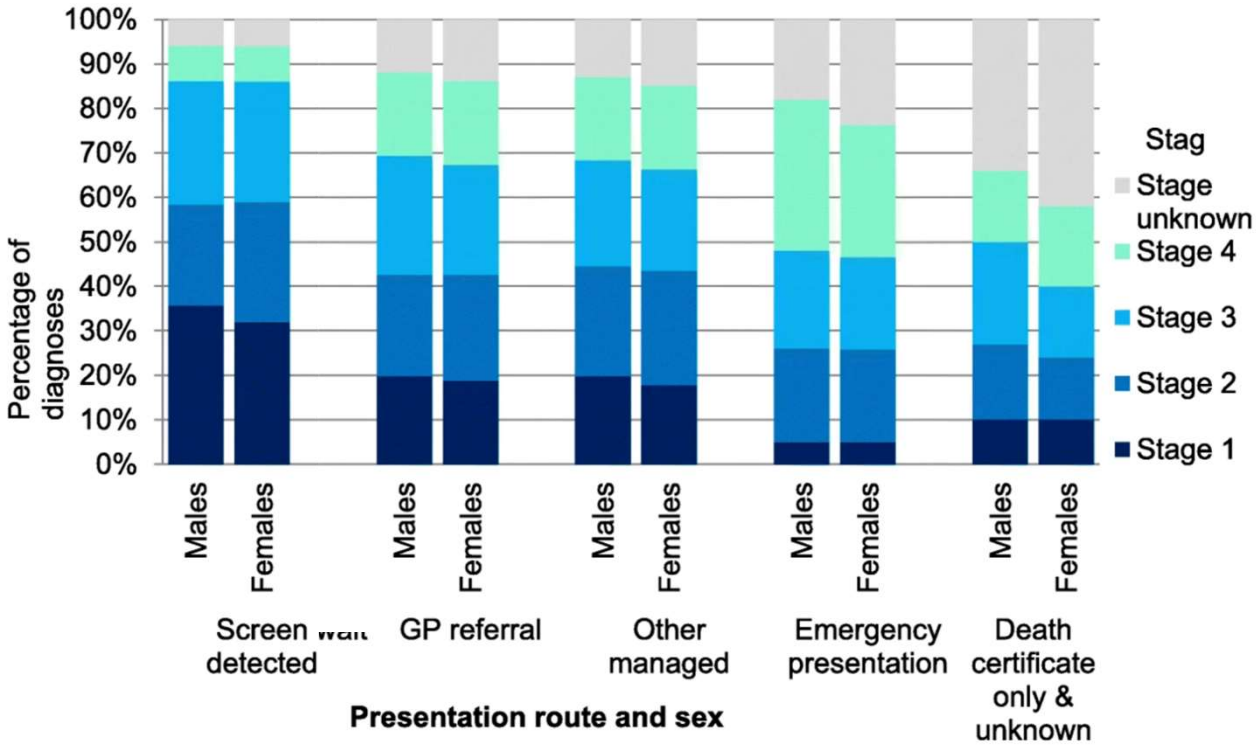
Colon cancer – stage at diagnosis



White A et al. BMC Cancer 2018;18:906

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Casus

- 53-jarige patiënte
- Geen majeure voorgeschiedenis / co-morbiditeiten
- Tweedegraads familielid met CRC op 50-jarige leeftijd

Anamnese

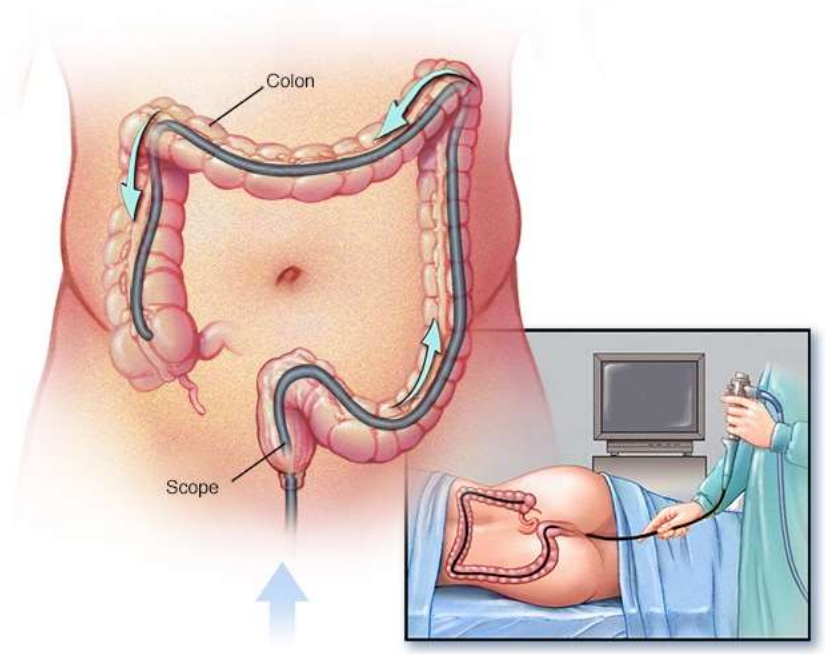
- Atypische abdominale pijn (”stress”)
- Vermoeidheid
- RBPA
- Constipatie, koorts, gewichtsverlies (-5kg/2 maanden)

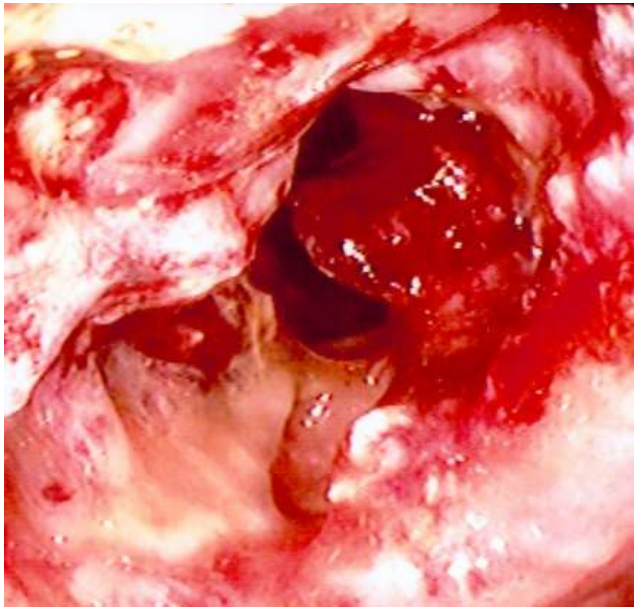
9 maanden

Bloedafname

Hemoglobine (g/dl)	Alk. Phosph. (U/l)	AST (U/l)	ALT (U/l)	LDH (U/l)	CEA (µg/l)
9.4 (12.0-15.0)	173 (53-141)	34 (< 31)	43 (< 34)	1367 (84-246)	14507 (< 3.0)

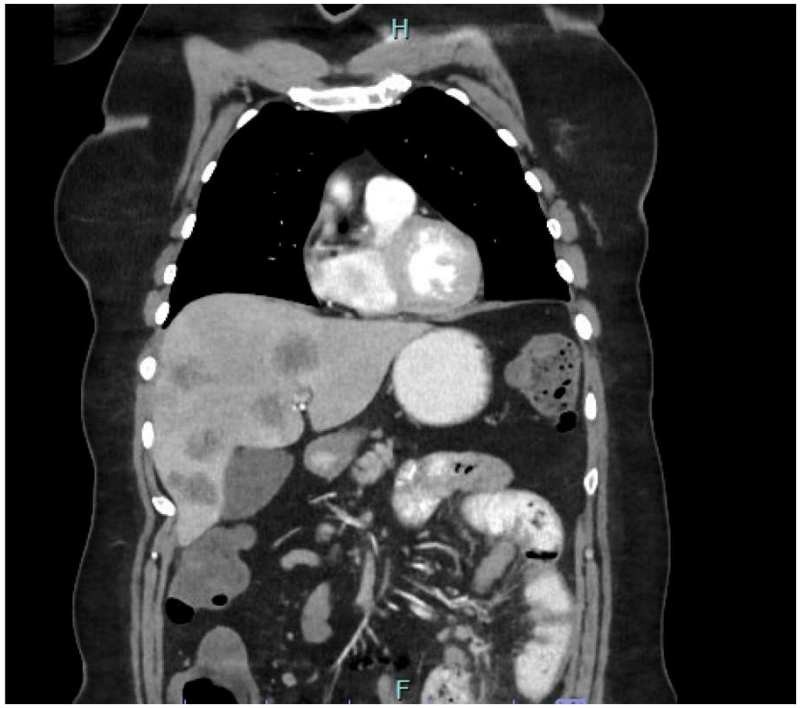
Coloscopie

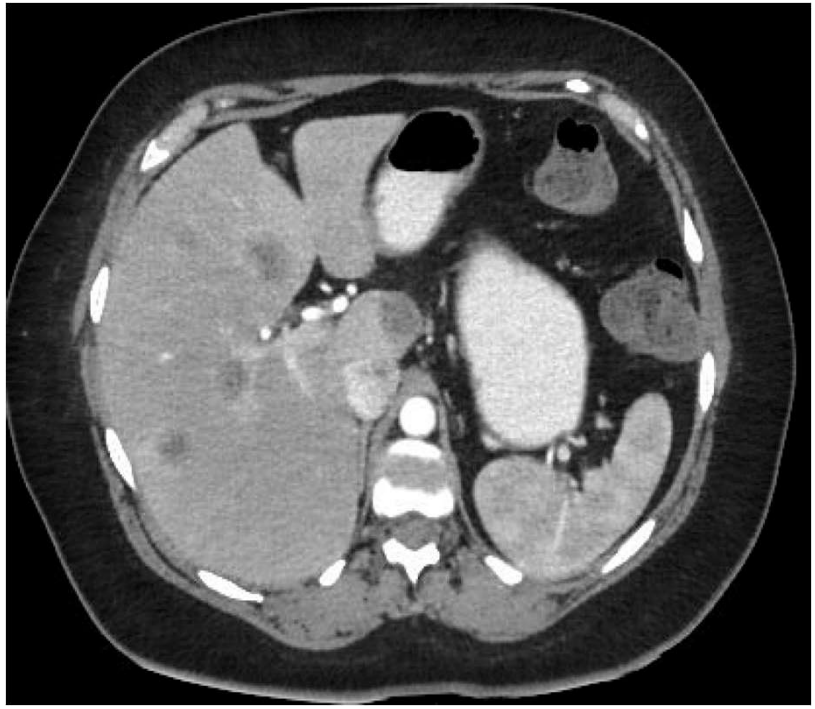




Sigmoid - matig gedifferentieerd adenocarcinoom

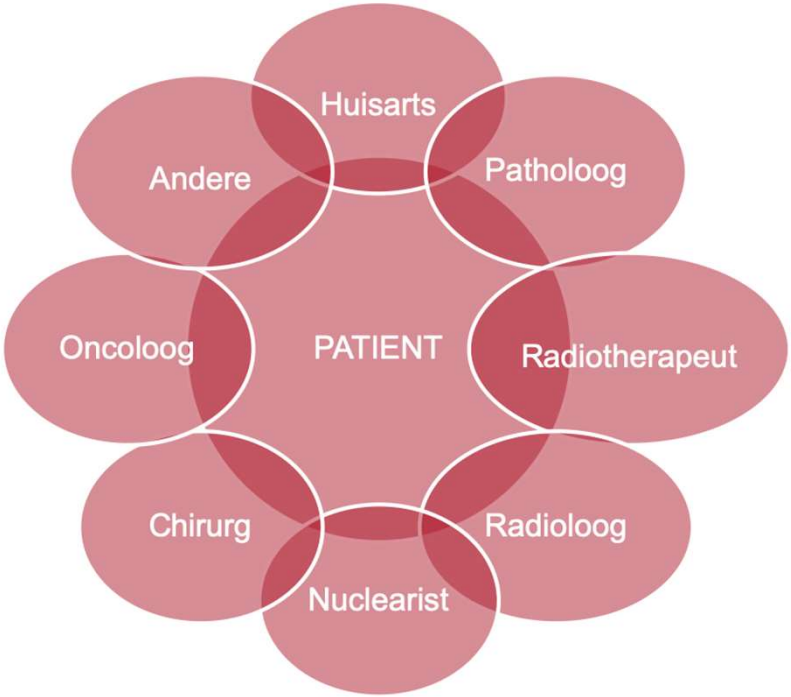
Staging





Klier- en levergemetastaseerde ziekte

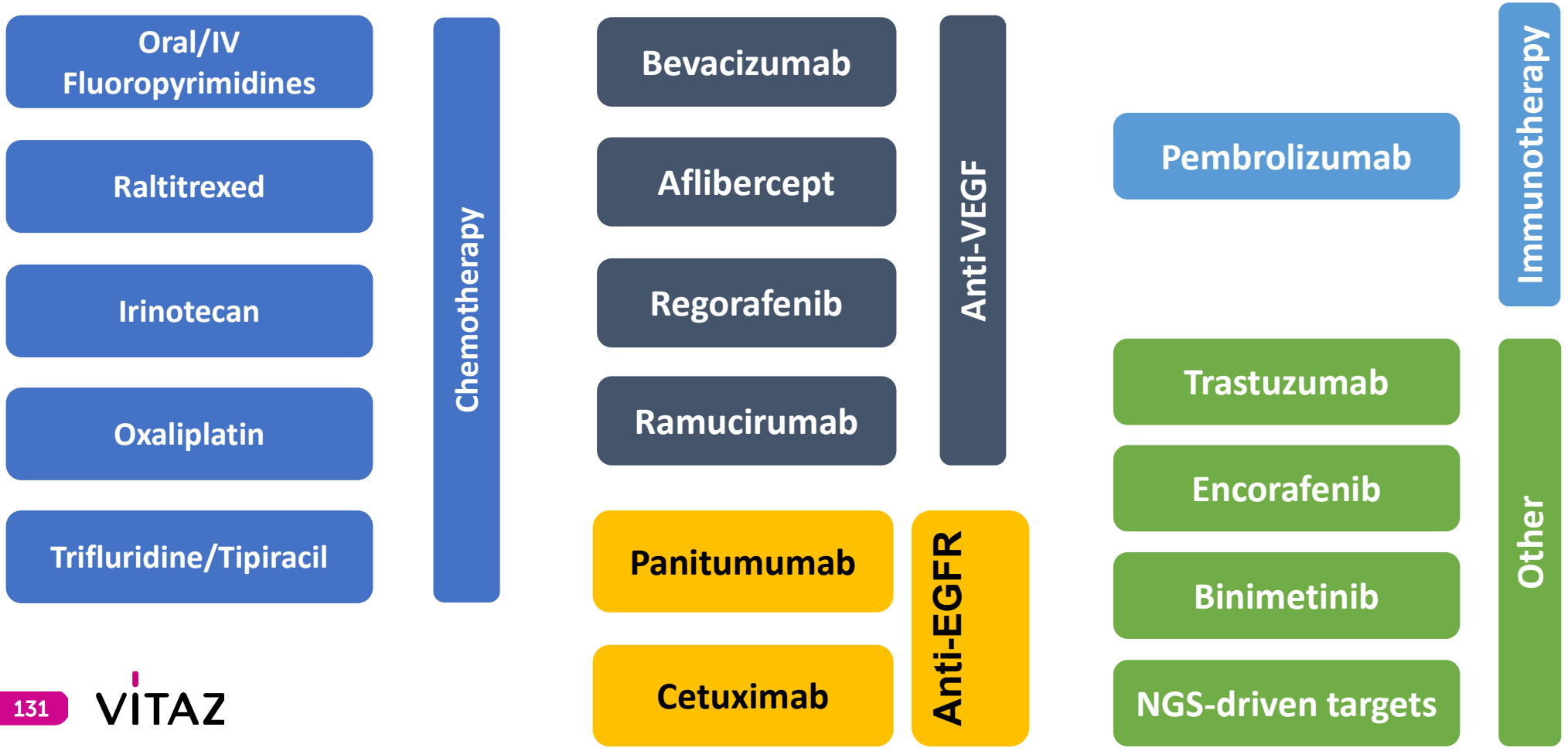
MOC bespreking



mColorectal Cancer (mCRC) – continuum of care, multi-optional

Heelkunde	Orgaan-gericht	Systemisch
Primaire tumor	Radiofrequente ablatie (RFA)	Chemotherapie
Metastase	Chemoembolisatie (TACE)	‘Target’ therapie
	Radio-embolisatie	Immunotherapie
	Radiotherapie	

Systemische therapie



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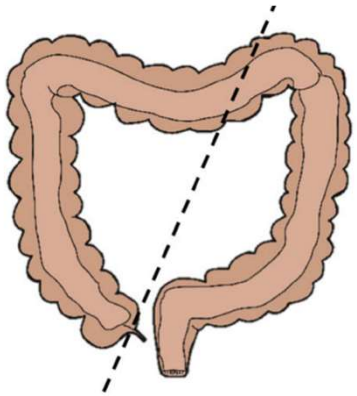
mCRC – heterogene populatie

- Locatie (links vs. rechts)
- Oligometastase – multimetastase
- Locatie van metastase
- Moleculair profiel
- Performance status, co-morbiditeiten

Locatie primaire tumor

Rechtszijdig:
- Meer bij vrouwen
- Oudere leeftijd
- Micro-sateliet instabiel
- Geen voordeel van anti-EGFR



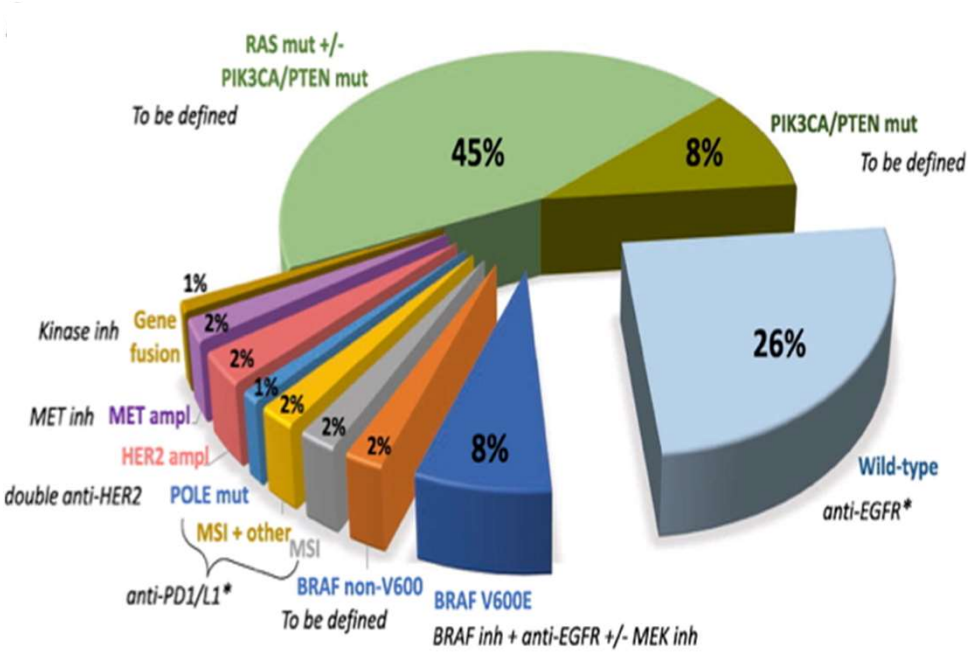
Linkszijdig:
- Meer bij mannen
- Jongere leeftijd
- Chromosomaal instabiel
- Voordeel van anti-EGFR
- Betere prognose

Moleculair profiel

Bij diagnose van mCRC wordt genetische analyse op het tumorweefsel uitgevoerd.

Next Generation Sequencing (NGS) + MSS/MSI

- RAS / BRAF mutatie
- NTRK fusie
- HER2 amplificatie
- Andere actionable targets
- MSS/MSI



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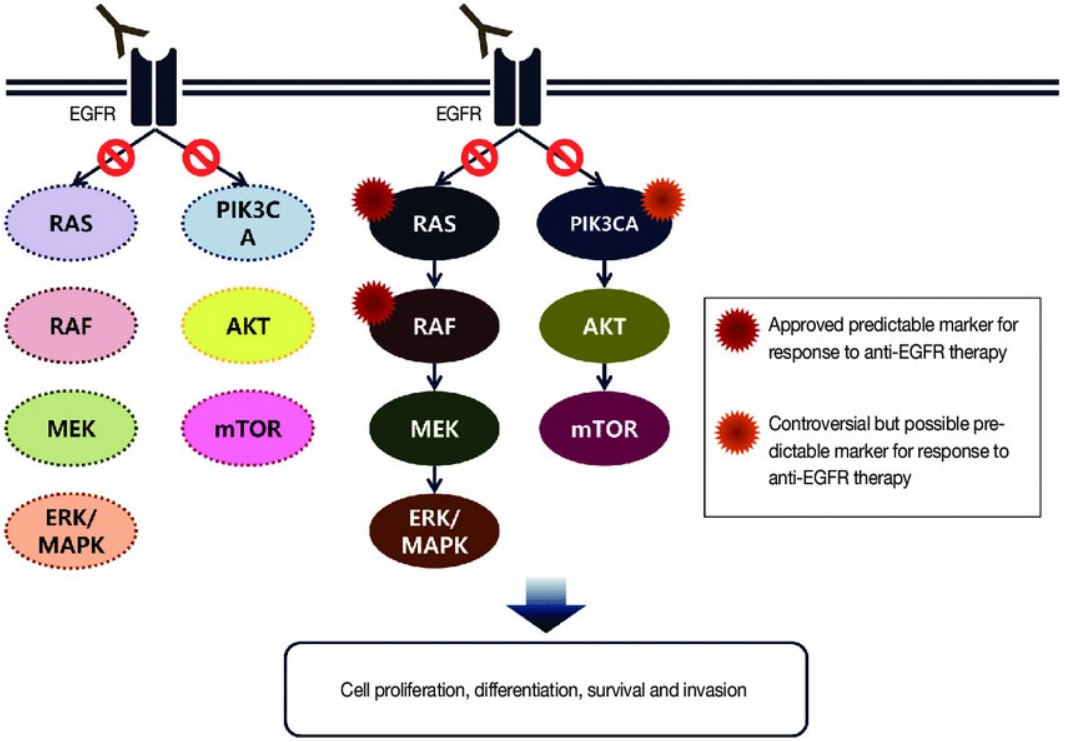
RAS-mutant



Non-responder anti-EGFR

Lee et al. Molecular Testing for Gastrointestinal Cancer. *J Pathol Transl Med*. 2017;51(2):103-121.

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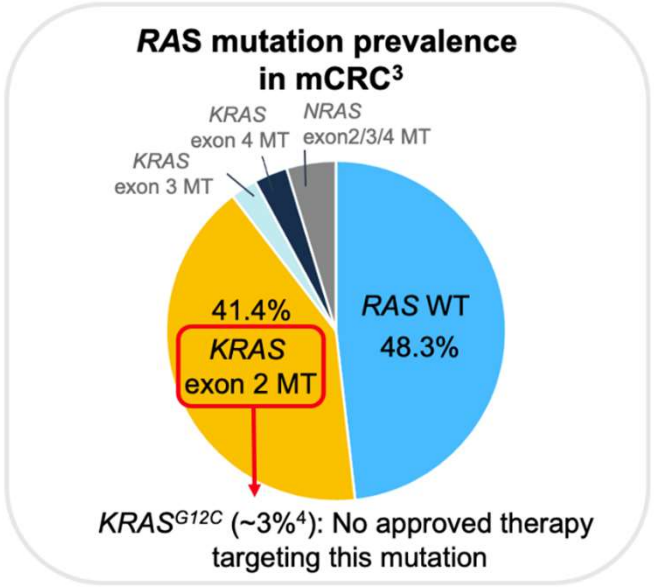
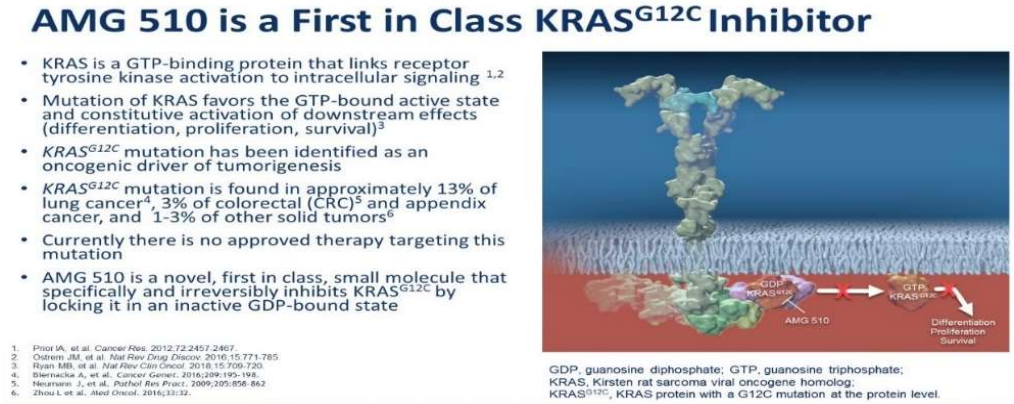
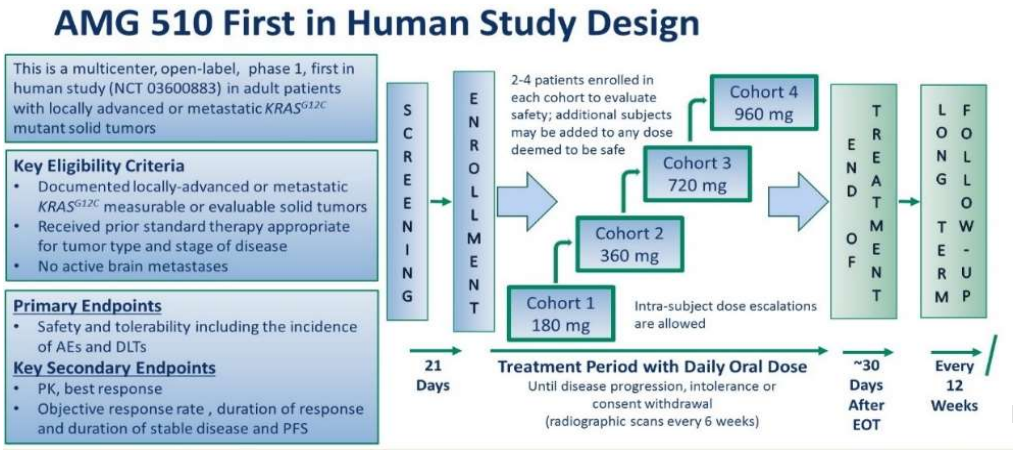
KRAS G12C mutatie



Zarour LR, et al. Cell Mol Gastroenterol Hepatol 2017;3:163–73





Fakih MG et al. A3003

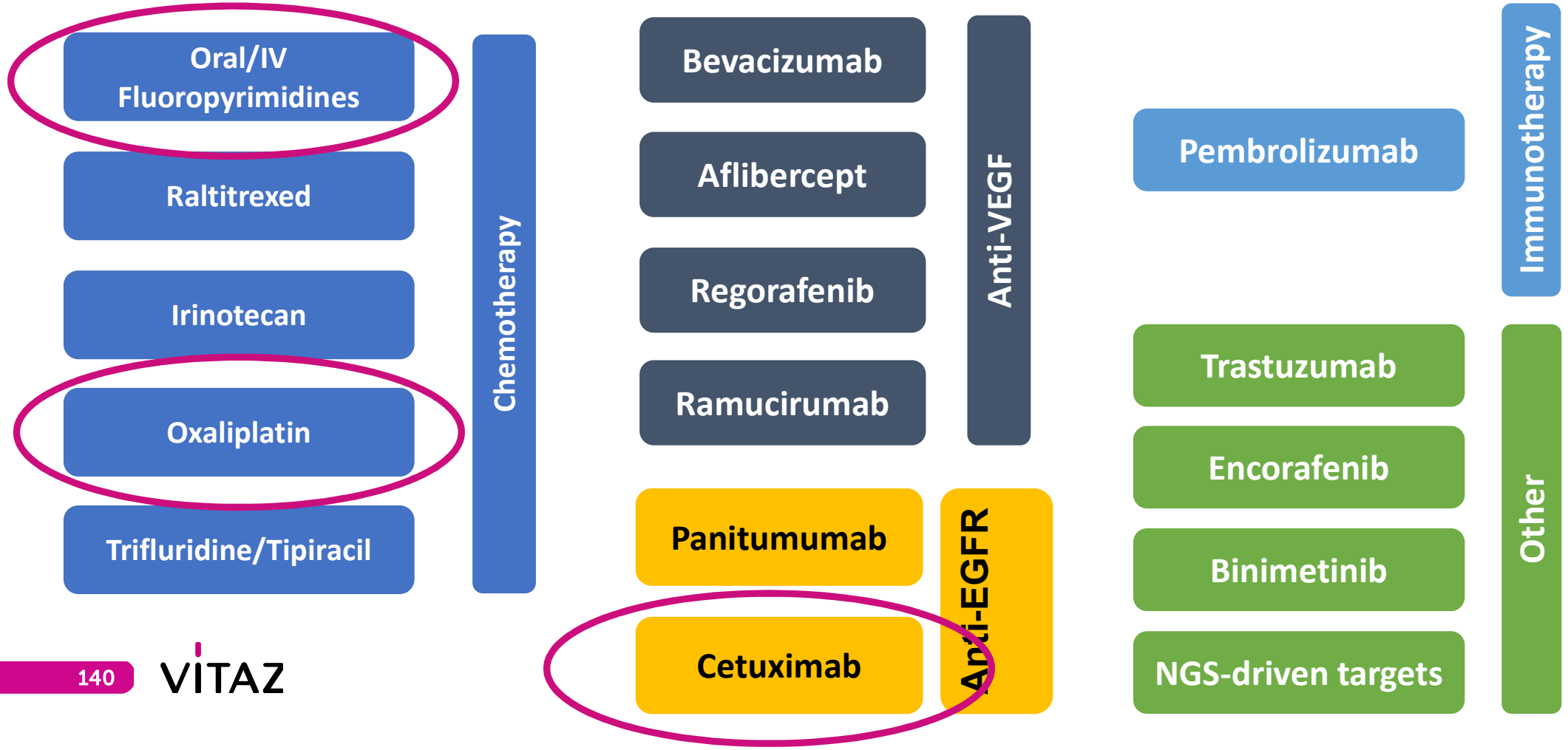
Performance status

ECOG	Description
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.
4	Completely disabled. Cannot carry on selfcare. Totally confined to bed or chair

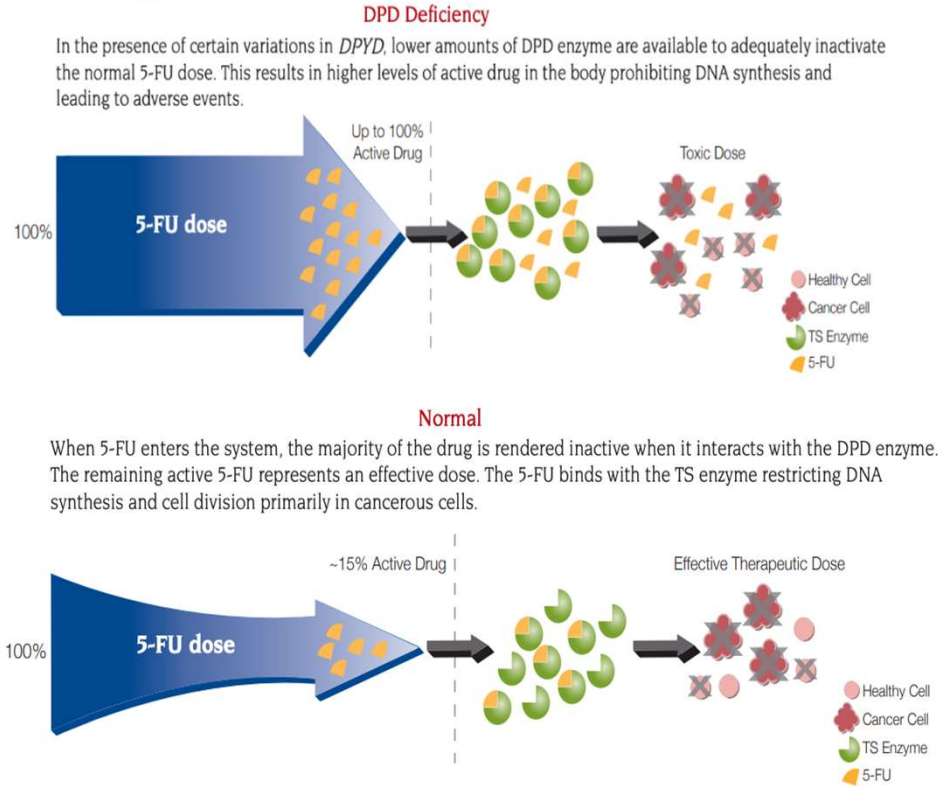
Terug naar de casus

- Diagnose lever- en kliergemetastaseerd coloncarcinoom – linkszijdig
- Moleculair profiel – NGS:
- Matig gedifferentieerd adenocarcinoom – RAS wild-type - geen actionable targets - MSS
- Uitstekende performance status – afwezigheid van orgaanfalen

Terug naar de casus
Eerstelijns therapie:



Dihydropyrimidine dehydrogenase (DPD)

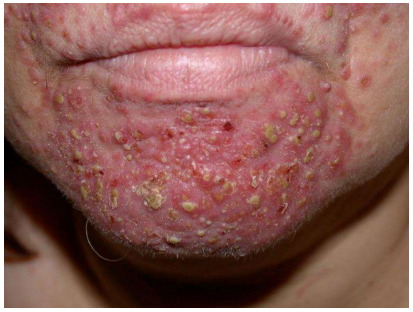


Myriad Genetic Laboratories, Inc.

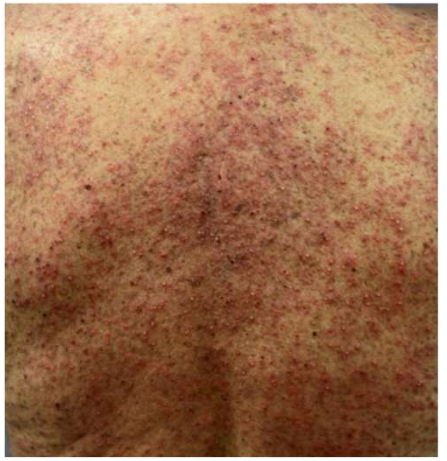
- Enzyme verantwoordelijk voor fluoropyrimidine metabolisme
- 3%-5% van de patiënten hebben deficiëntie
- Verhoogde fluoropyrimidine toxiciteit:
  - Hematologisch toxiciteit
  - Diarree
  - Hand- en voetsyndroom
  - Mucositis

Lee et al. Clinical advances in hematology & oncology. 2004; 2(8):527-32

Nevenwerkingen – anti-EGFR



- Papulopustulaire acneïforme eruptie
- Paronychia
- HypoMg
- Preventie:
  - Minocycline 100mg eenmaal daags
  - Metronidazole crème tweemaal daags
  - Hand- en nagelhygiëne



Lacouture et al. J Clin Oncol. 2010;28:1351-1357.

Predictor of response

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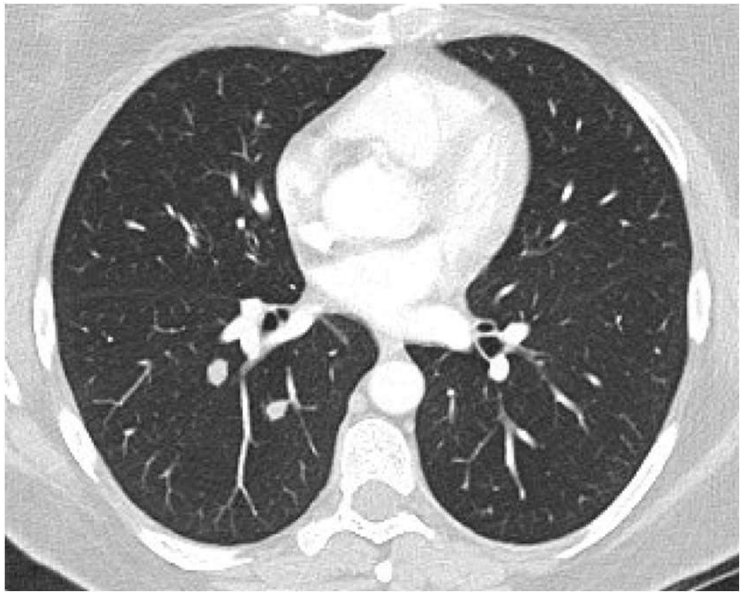
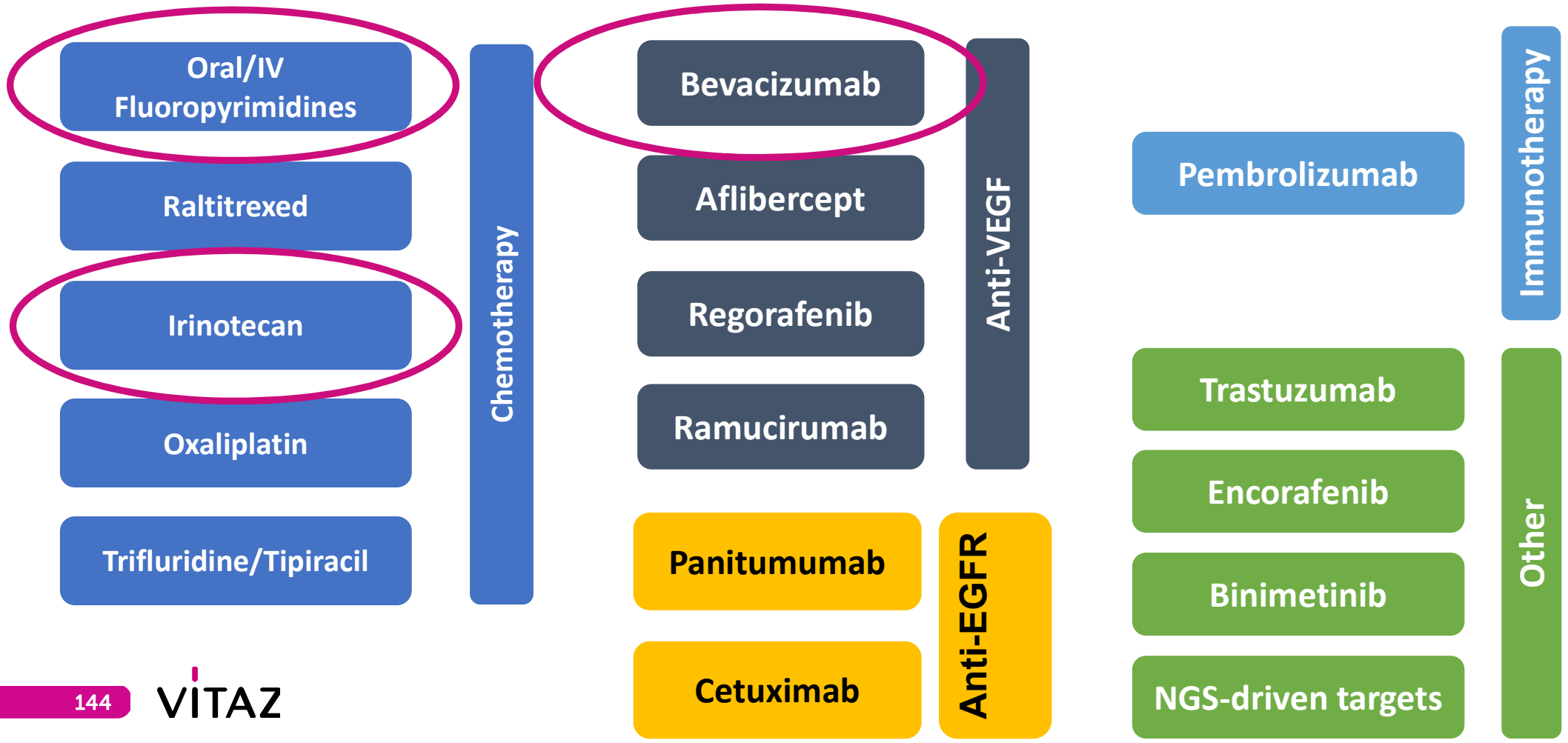
Herevaluatie na 24 cycli middels CT-scan



- Ontstaan van meerdere longnodulen verdacht voor longmetastasen + toename leverletsels
- Blijvend uitstekende performance status

Tweedelijns therapie



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Nevenwerkingen – anti-VEGFR

Important adverse events associated with bevacizumab.

Adverse event	Incidence all grades[‡]
Bleeding/Hemorrhage	39.1% (2524/6449) *Up to 44.2% (354/801) in NSCLC*
Pulmonary hemorrhage	2.1% (134/6449) *Up to 8.9% (71/801) in NSCLC*
Proteinuria	10.5% (729/6950) *Up to 20.2% (68/337) in RC*
Arterial thromboembolic events (ATE)	2.5% (173/6950) *Up to 3.8% (24/624) in GBM*
Hypertension	27.1% (1881/6950) *Up to 36.4% (227/624) in GBM*
Congestive heart failure (CHF)	1.2% (78/6449) *Up to 3.3% (46/1399) in BC*
Wound healing complications	3.2% (204/6449) *Up to 5.4% (34/624) in GBM*
GI perforations	1.9% (121/6449) Up to 9.2% (20/218) in CC
Posterior Reversible Encephalopathy Syndrome (PRES)	0.2% (11/6449)
Neutropenia	43.1% (2777/6449) *Up to 71.1% (1584/2208) in OC*
Venous thromboembolic events (VTE)	6.7%% (469/6950). *Up to 11.7% (159/1363) in CRC*
Fistulae (Non-GI)	1.0% (64/6449) *Up to 3.7% (8/218) in CC*
Thrombotic microangiopathy	< 0.1% (2/6449)
Pulmonary hypertension	0.1% (5/6449)
Ovarian failure	None in clinical trials Sporadic cases reported
Hypersensitivity and infusion reactions	27.6% (1720/6449) *Up to 35.5% (784/2208) in OC*
Gallbladder perforation	< 0.1% (1/6449) in OC
Peripheral sensory neuropathy	25.4% (1638/6449) *Up to 61.5% (134/218) in CC*
Non-CHF/ATE cardiac disorders	2.7% (174/6449) *Up to 3.8% (85/2208) in OC*
Osteonecrosis of the jaw (ONJ)	0.1% (4/6449). *Up to 0.2% (3/1399) in BC*
Necrotizing fasciitis	0% in clinical trials 87 reported in ARISg and MedDRA safety databases
Off-label intravitreal use	17,332 cases reported in safety databases up to 31 December 2014: • *SAEs*: 23.3% (5595/17332) • *Drug-related systemic AEs*: 27.8% (4812/17332) • *Anterior eye AEs*: 8.9% (1537/17332) • *Posterior eye AEs*: 39.0% (6759/17332)
Infection (use with temozolomide and radiotherapy in GBM)	44.9% (2896/6449) *Up to 52.7% (329/624) in GBM*
Thrombocytopenia	26.8% (1726/6449) *Up to 50.1% (1106/2208) in OC*

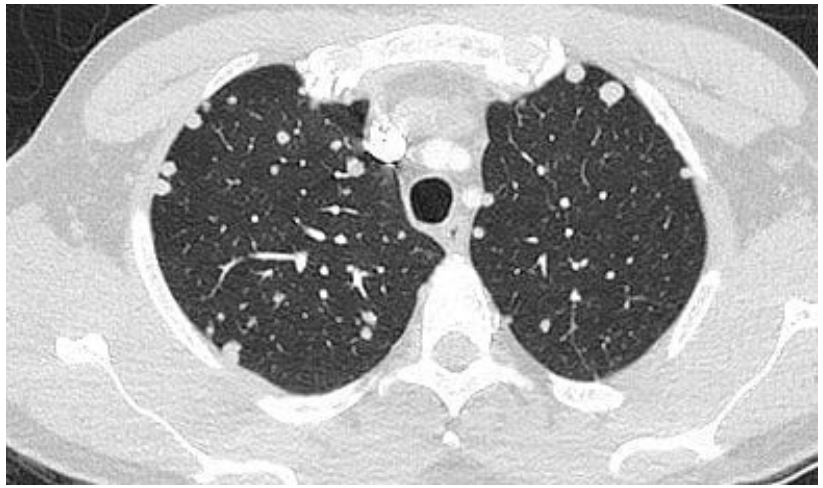
Abbreviations: AE: Adverse event; ATE: arterial thromboembolic event; BC: Breast cancer; CC: Cervical cancer; CHF: Congestive heart failure; CRC: Colorectal cancer; GBM: Glioblastoma; GI: Gastrointestinal; NA: Not applicable; NSCLC: Non-small cell lung cancer; OC: Ovarian cancer; RC: Renal cancer; SAEs: Serious adverse event.

Footnotes:

[‡] All incidence values based upon calculated incidence from Bevacizumab / Avastin® PSUR/PBRER [19].

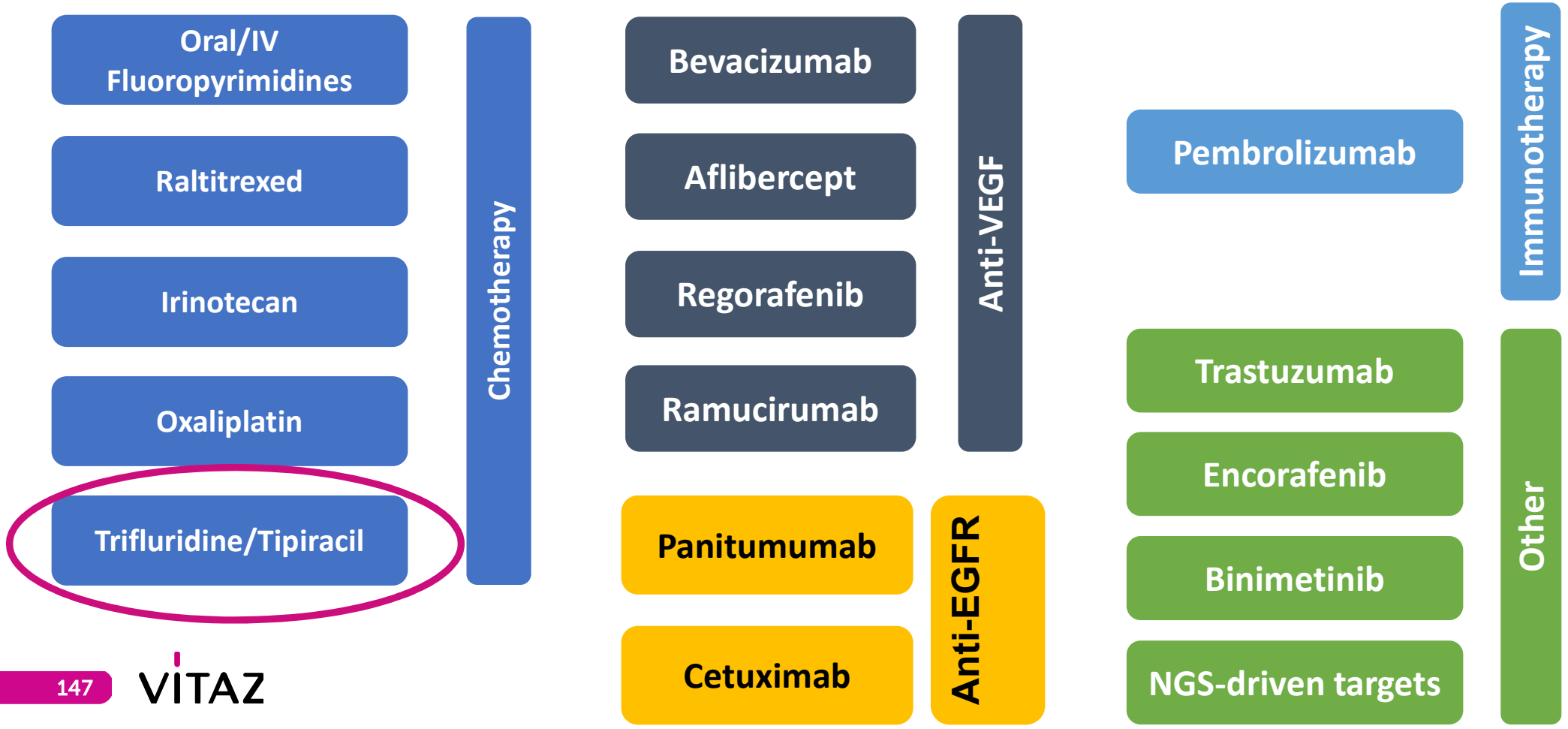
Garcia et al. Cancer Treat Rev . 2020 Jun;86:102017.

Herevaluatie na 12 cycli FOLFIRI-Bevacizumab



- Patiënt voelt zich prima
- Fietst +/- 35km per dag
- Het gewicht blijft stabiel
- Helaas opnieuw toename van meerdere longnodulen

Derdelijns therapie



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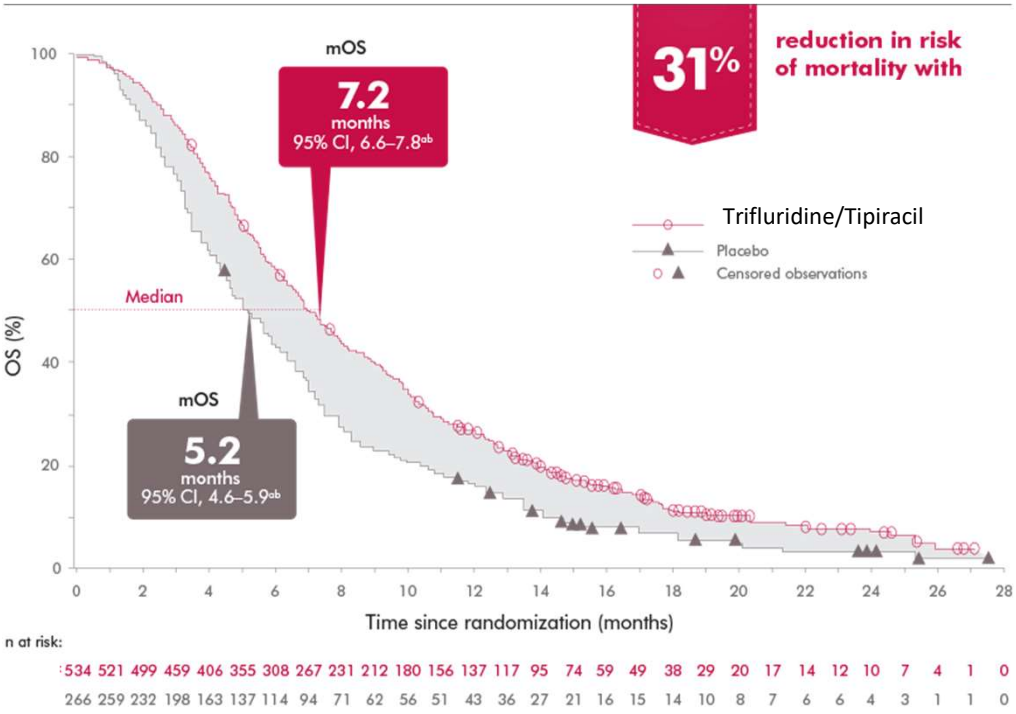
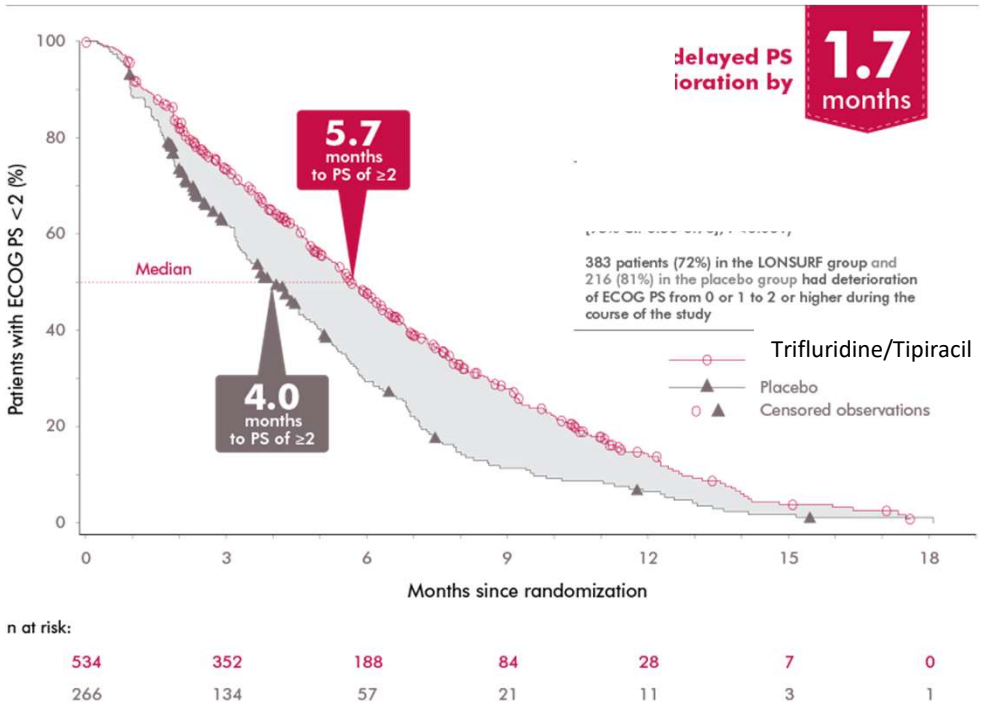
Derdelijns therapie

- Trifluridine/Tipiracil (pyrimidine antagonist)
  - Oraal chemotherapeuticum – 35mg/m2 tweemaal daags

Week 1	Twice daily for 5 days with food	2 days rest
Week 2	Twice daily for 5 days with food	2 days rest
Week 3	Rest	
Week 4	Rest	

Derdelijns therapie





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Nevenwerkingen Trifluridine/Tipiracil

	Trifluridine/Tipiracil + BSC (n=533), %		Placebo + BSC (n=265), %	
	All Gr[a]	Gr 3-4	All Gr[a]	Gr 3-4
Anemia[b]	77	18	33	3
Neutropenia	67	38	1	0
Thrombocytopenia	42	5	8	<1
Febrile neutropenia	4	4	0	0

	Trifluridine/Tipiracil + BSC (n=533), %		Placebo + BSC (n=265), %	
	All Gr	Gr 3-4[a]	All Gr	Gr 3-4[a]
General				
Asthenia/fatigue	52	7	35	9
Pyrexia	19	1	14	<1
Gastrointestinal				
Nausea	48	2	24	1
Diarrhea	32	3	12	<1
Vomiting	28	2	14	<1
Abdominal pain	21	2	18	4
Stomatitis	8	<1	6	0
Metabolism and nutrition				
Decreased appetite	39	4	29	5
Infections[b]	27	6	16	5
Nervous system				
Dysgeusia	7	0	2	0
Skin and subcutaneous tissue				
Alopecia	7	0	1	0

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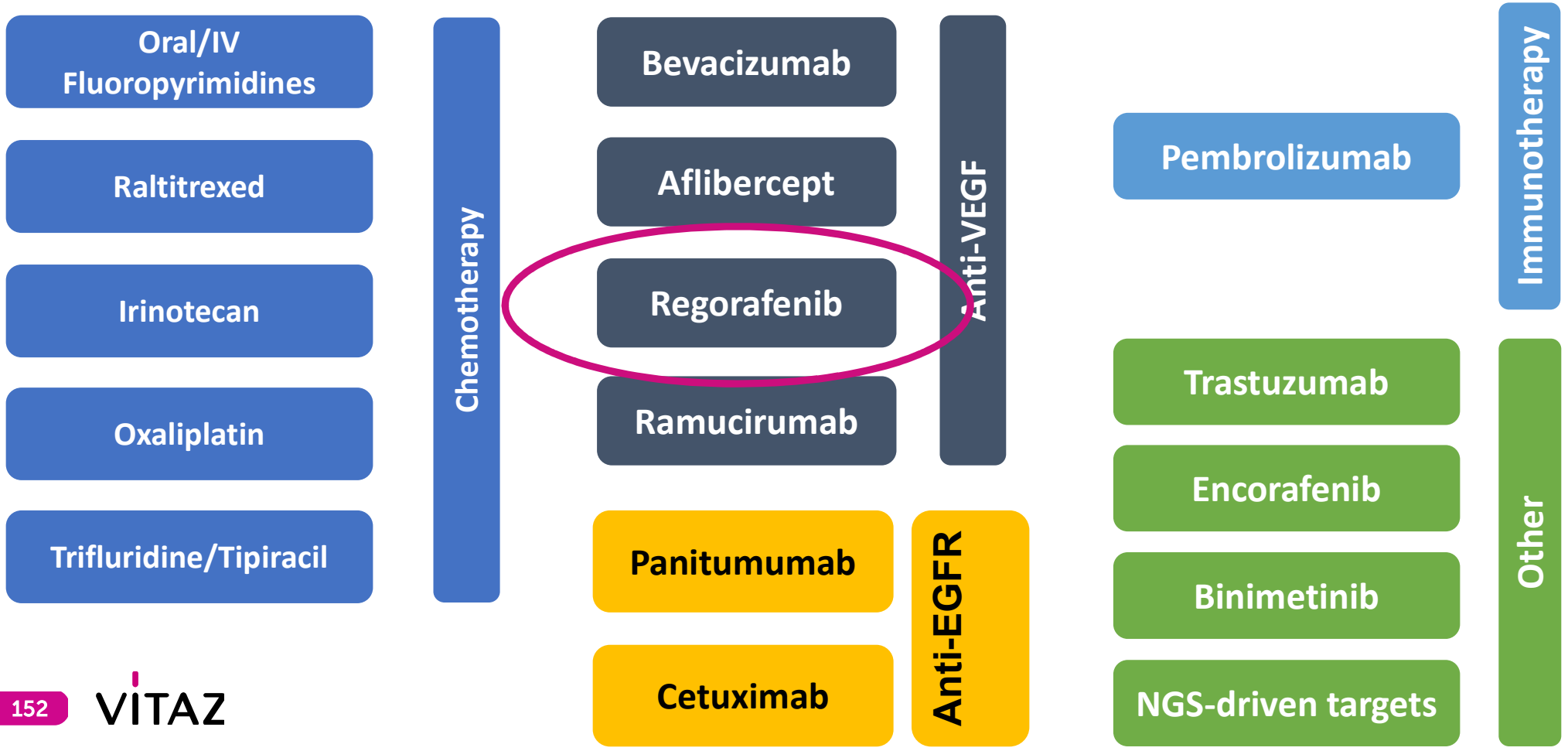
Herevaluatie na 3 cycli trifluridine/Tipiracil

- Manifeste ziekte-progressie op CT
- Houdt nog dagelijkse wandelingen van +/- 5km
- Gewichtsverlies van 4 kg/3 maanden
- Blijvende uitgesproken therapiewens van patiënte

Vierdelijns therapie



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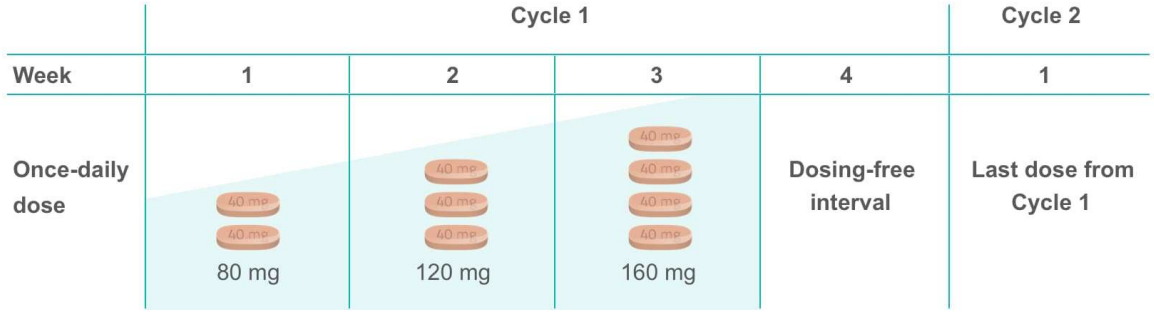
Vierdelijns therapie

- Regorafenib
  - Multikinase inhibitor (80-120-160mg) eenmaal daags



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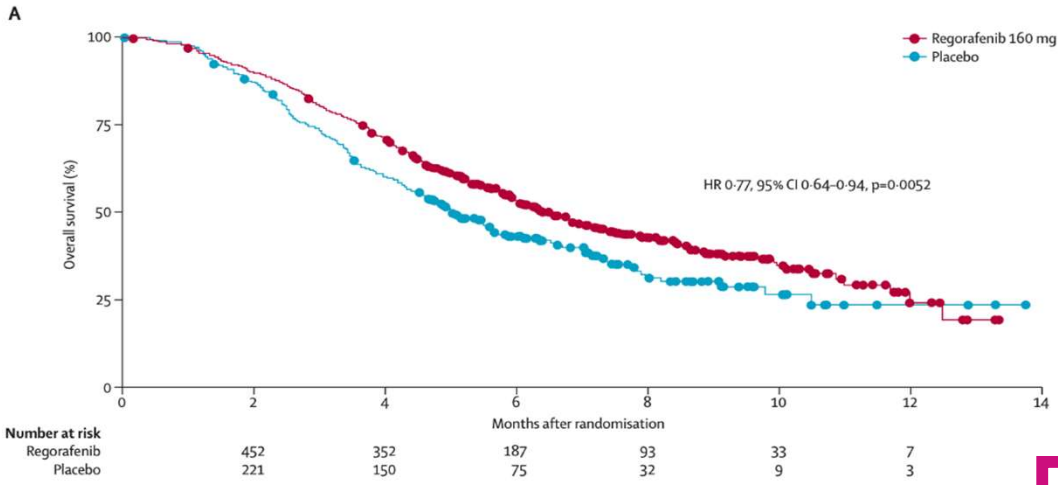
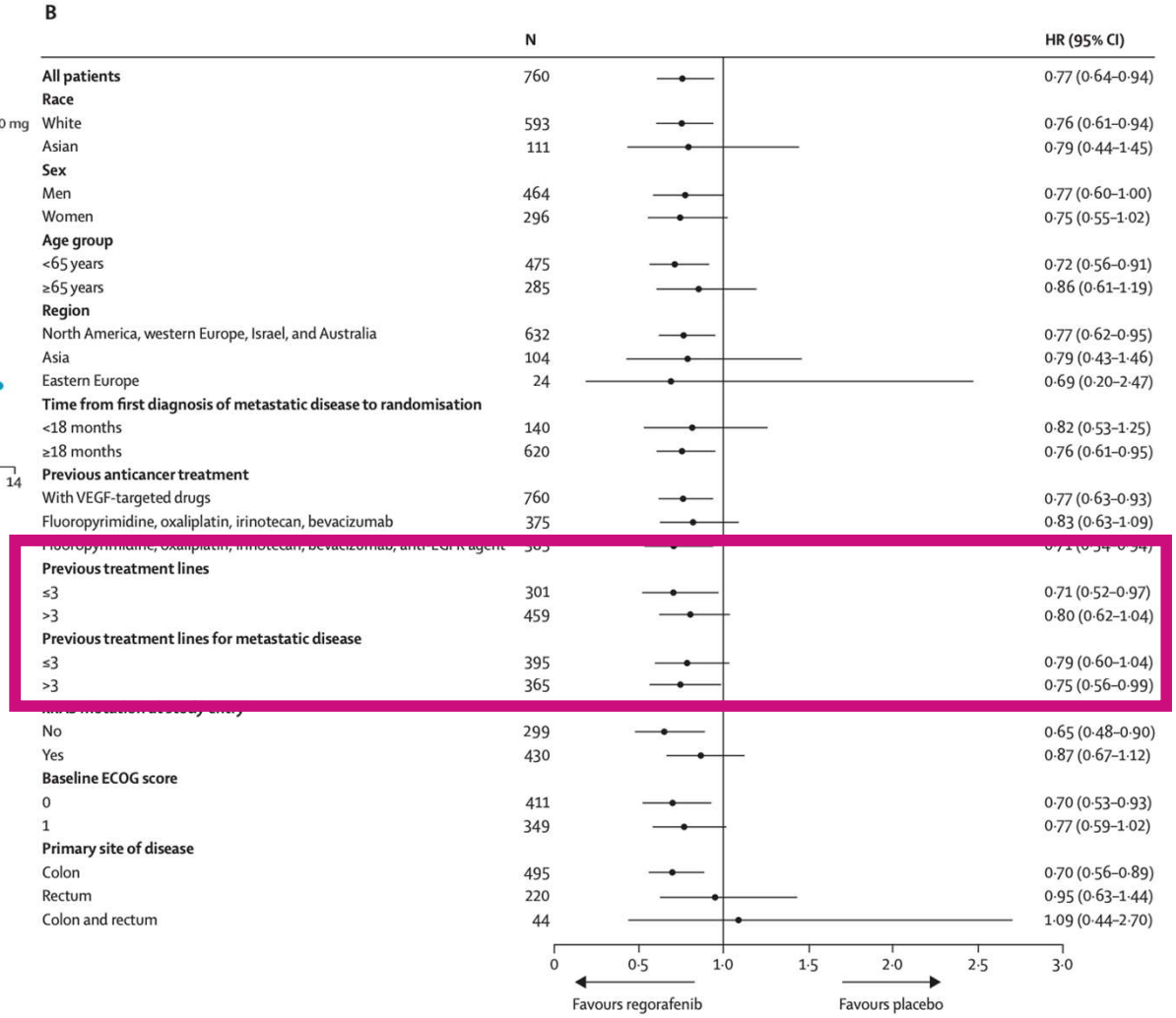
Regorafenib





Grothey et al. The Lancet 2013;381:303-312.

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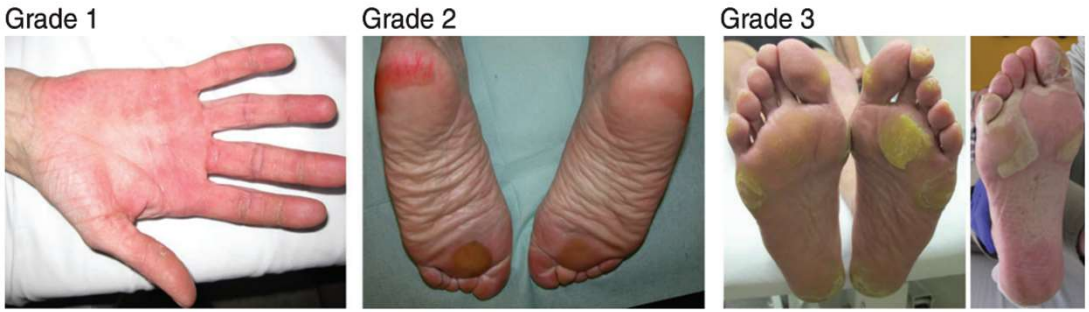
Nevenwerkingen Regorafenib

- Hematologische toxiciteit
- Vermoeidheid
- Gastro-intestinale intolerantie (diarree – anorexie – nausea)
- Arteriële hypertensie
- Hand- voet syndroom



McLellan et al. Annals of Oncology 26: 2017–2026, 2015

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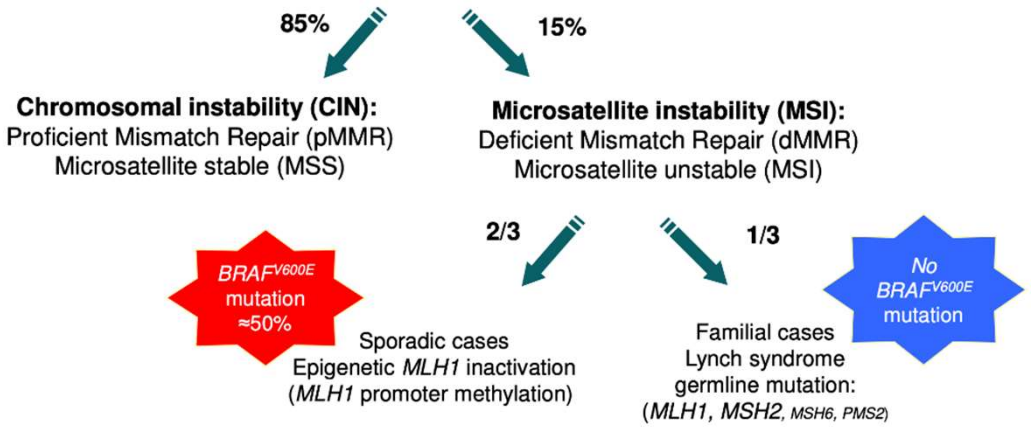
Vervolg van casus

- Na 3 cycli Regorafenib – helaas beeld van progressieve ziekte
- Evolutie naar best-supportive care
- Netwerk palliatieve zorg

Immunotherapie in mCRC?

- Mismatch Repair Deficient Colorectal Cancer
  - Genetisch defect in DNA mismatch repair

  => microsatelliet instabiliteit (MSI-H)



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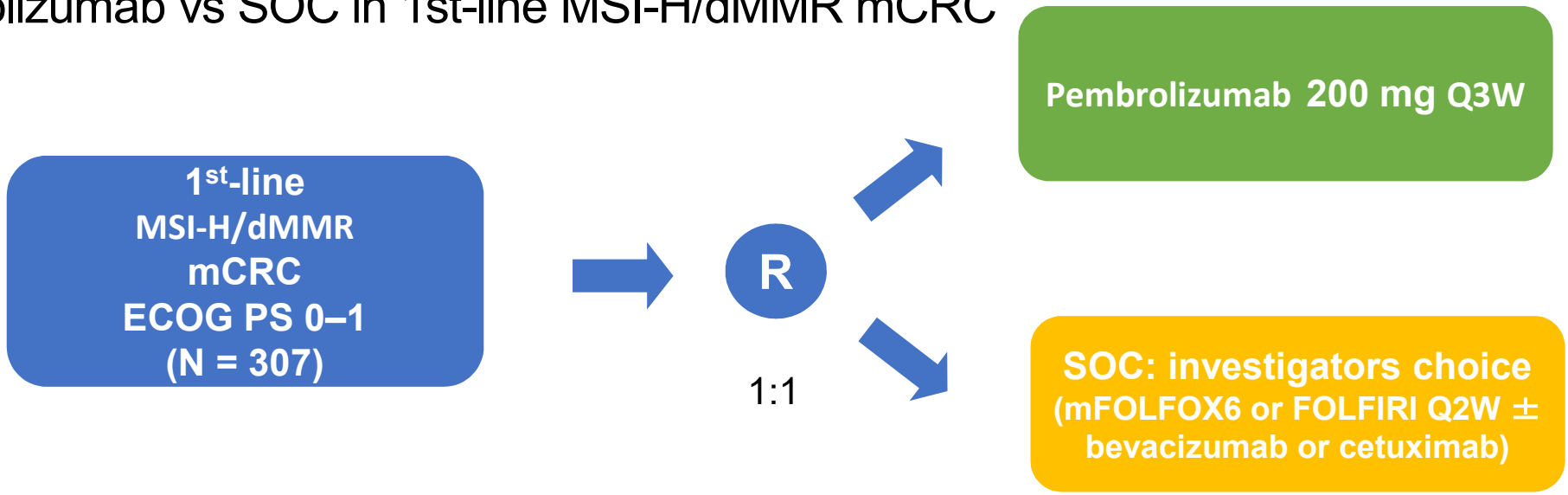
Immunotherapie in mCRC?

Phase 3 KEYNOTE-177 study

Pembrolizumab vs SOC in 1st-line MSI-H/dMMR mCRC



André T et al. NEJM 2020;383:2207-18

Primary endpoint: PFS and OS

Key secondary endpoints: ORR and safety

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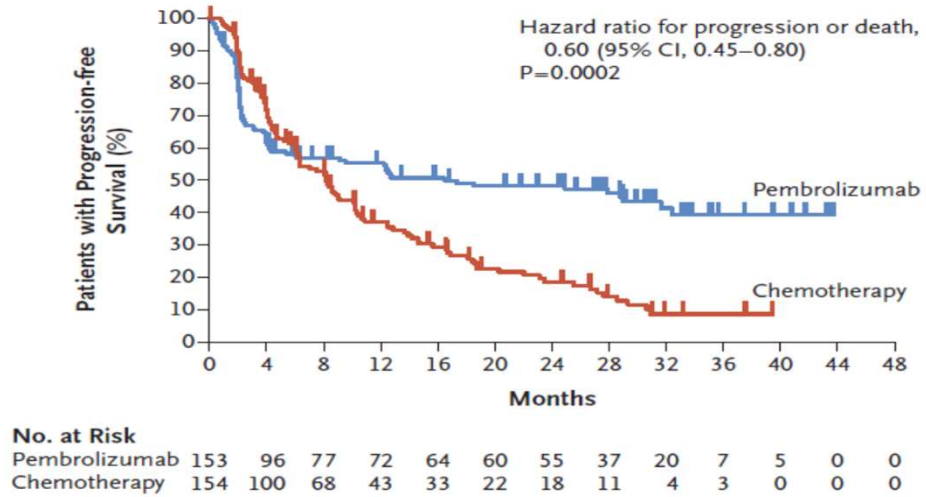
Immunotherapie in mCRC?



André T et al. NEJM 2020;383:2207-18

MSI-H/dMMR	Pembrolizumab (n = 153)	SOC (n = 154)
Median PFS, months	16.5	8.2
12-month PFS rate, %	55.3	37.3
24-month PFS rate, %	48.3	18.6
ORR, %	43.8	33.1
Median DoR (range), months	NR (2.3–41.4)	10.6 (2.8–37.5)

Nevenwerkingen - immunotherapie

Table 3. (Continued.)

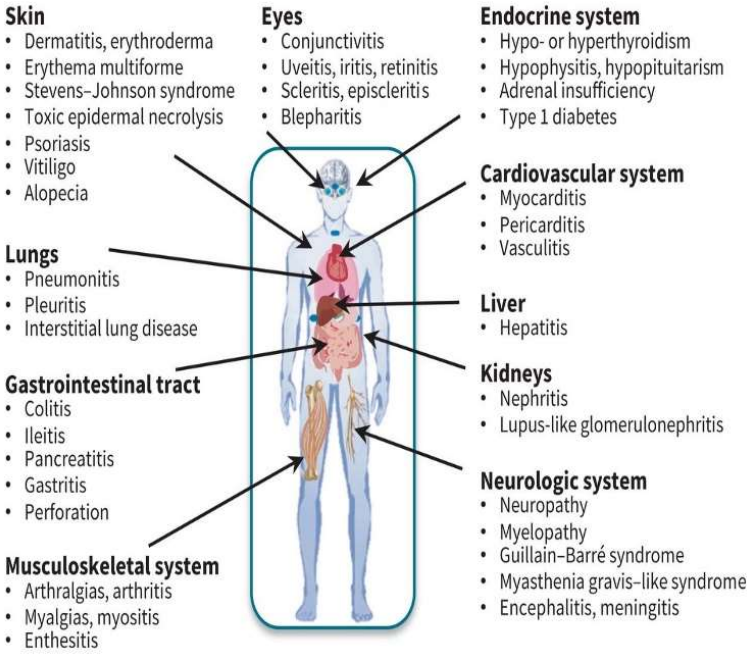
Event	Pembrolizumab (N=153)		Chemotherapy (N=143)	
	Any	Grade ≥3	Any	Grade ≥3
	number of patients (percent)			
Peripheral sensory neuropathy	3 (2)	0	31 (22)	3 (2)
Neutrophil count decrease	2 (1)	0	33 (23)	24 (17)
Neutropenia‡	3 (2)	0	30 (21)	22 (15)
Epistaxis	2 (1)	0	23 (16)	0
Peripheral neuropathy	1 (1)	0	27 (19)	1 (1)
PPE syndrome	1 (1)	0	25 (17)	1 (1)
White-cell count decrease	1 (1)	0	17 (12)	6 (4)
Adverse events of interest§	47 (31)	14 (9)	18 (13)	3 (2)
Hypothyroidism	19 (12)	0	3 (2)	0
Colitis	10 (7)	5 (3)	0	0
Hyperthyroidism	6 (4)	0	0	0
Pneumonitis	6 (4)	0	1 (1)	0
Adrenal insufficiency	4 (3)	2 (1)	0	0
Hepatitis	4 (3)	4 (3)	0	0
Infusion reactions	3 (2)	0	11 (8)	1 (1)
Severe skin reactions	2 (1)	2 (1)	2 (1)	2 (1)
Thyroiditis	2 (1)	0	0	0
Hypophysitis	2 (1)	0	0	0
Myocarditis	0	0	1 (1)	0
Nephritis	1 (1)	0	0	0
Pancreatitis	1 (1)	1 (1)	0	0
Type 1 diabetes mellitus	1 (1)	1 (1)	0	0
Myositis	1 (1)	0	0	0

irAEs

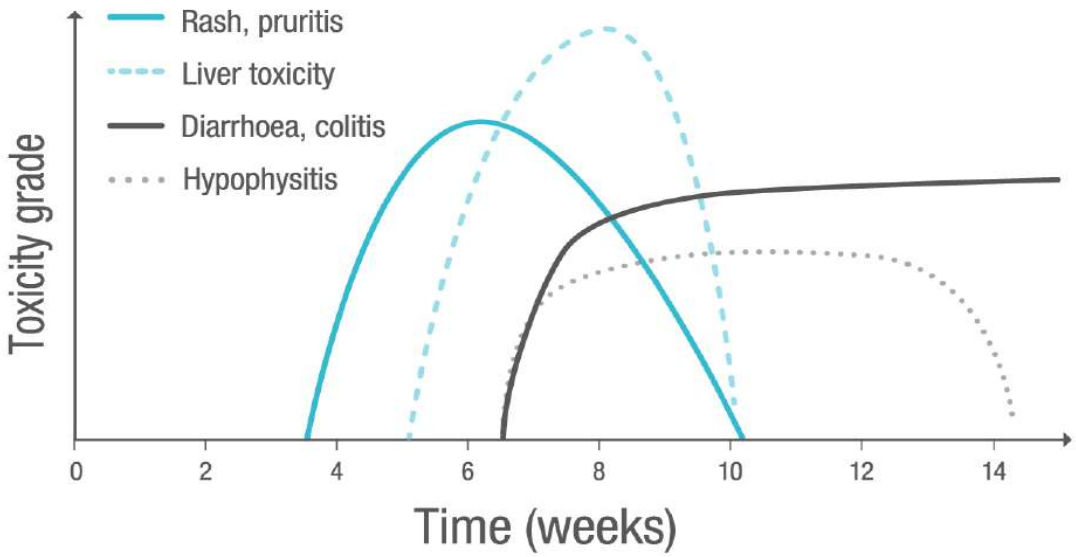
- Hypothyroidie (12%, 0%)
- Colitis (7%, 3%)
- Hyperthyroidie (4%, 0%)
- Pneumonitis (4%, 0%)

André T et al. NEJM 2020;383:2207-18

Organs affected by and manifestations of immune-related adverse events



Esfahani Kh. et al. CMAJ 2019;191:E40-E46



ESMO: European Society of medical Oncology

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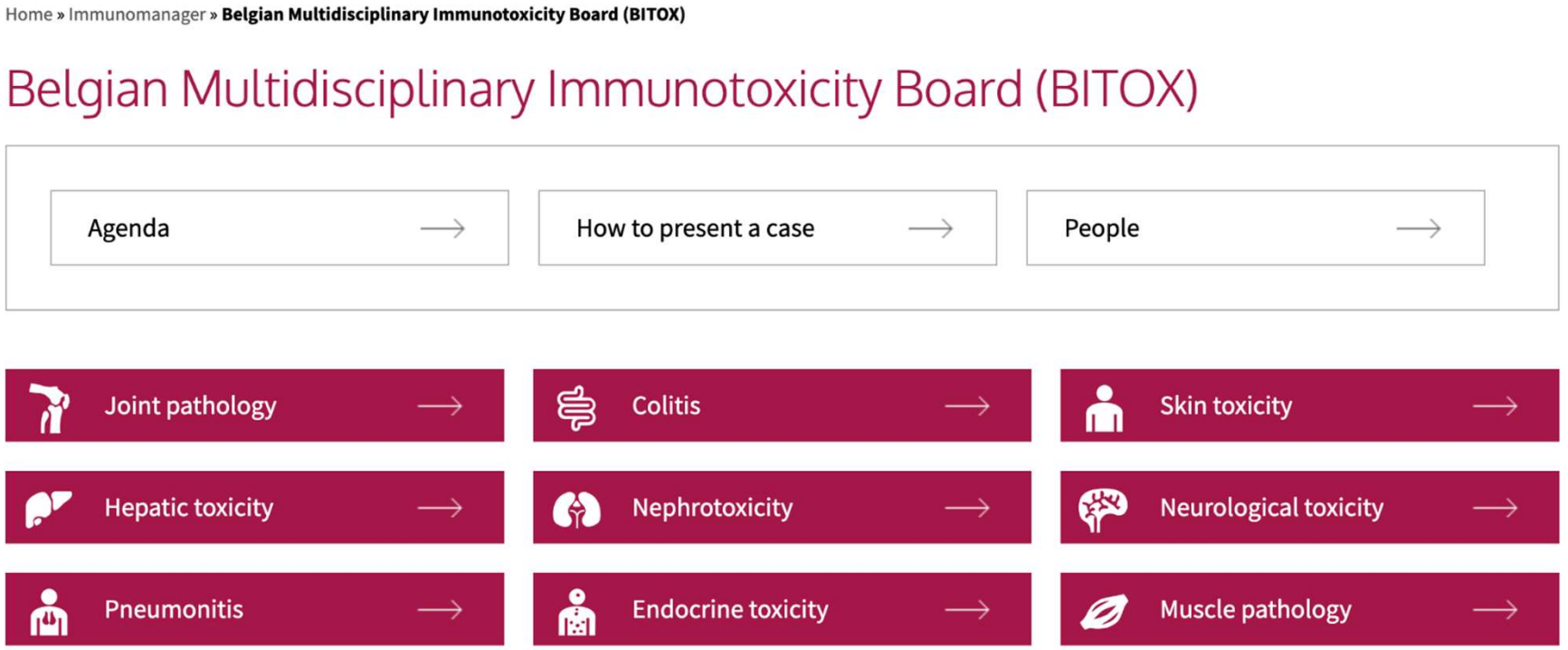
Belgian Society of Medical Oncology



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Conclusie - mCRC

- Multidisciplinaire aanpak van gemetastaseerde ziekte is essentieel
- No “one size fits all” ➔ gepersonaliseerde aanpak
- Na 5-FU gebaseerde doublet is er evidentie voor derde- en zelfs vierdelijns therapie
- Belang van performance status
- En slechts een minderheid van mCRC komt in aanmerking voor immunotherapie

BEDANKT VOOR UW AANDACHT

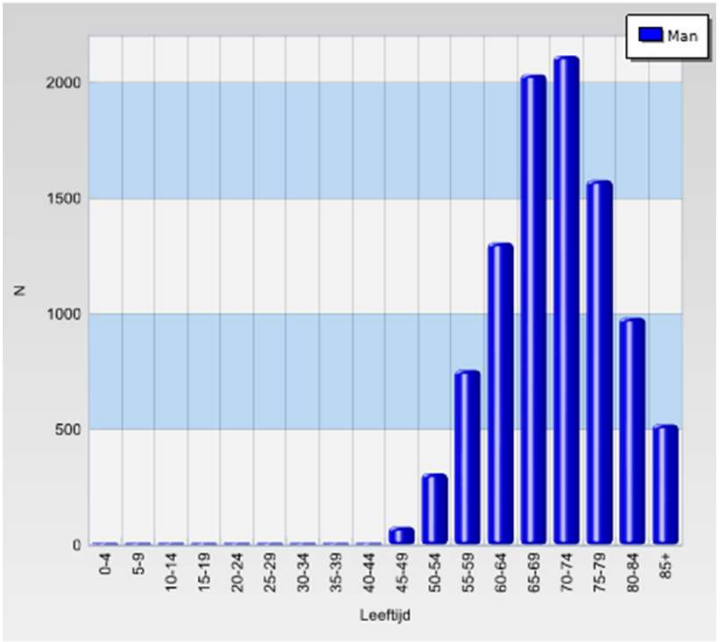
?

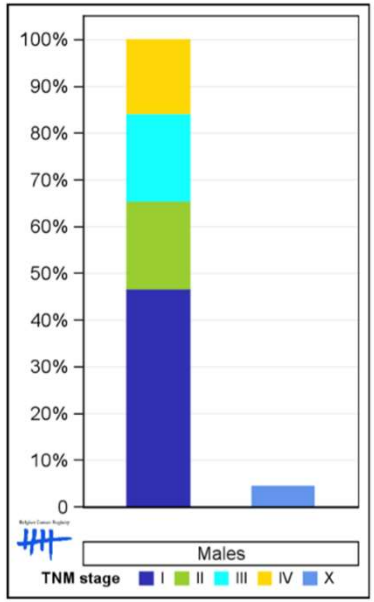
PROSTAATKANKER:

DOOR DE BOMEN HET BOS NOG ZIEN MET ALLE NIEUWE THERAPIEËN IN UITGEZAAIDE PROSTAATKANKER: HOE MEER HOE BETER VOOR DE PATIËNT?

DR. YANINA DOCKX
DR. ELS EVERAERT

Prevalentie





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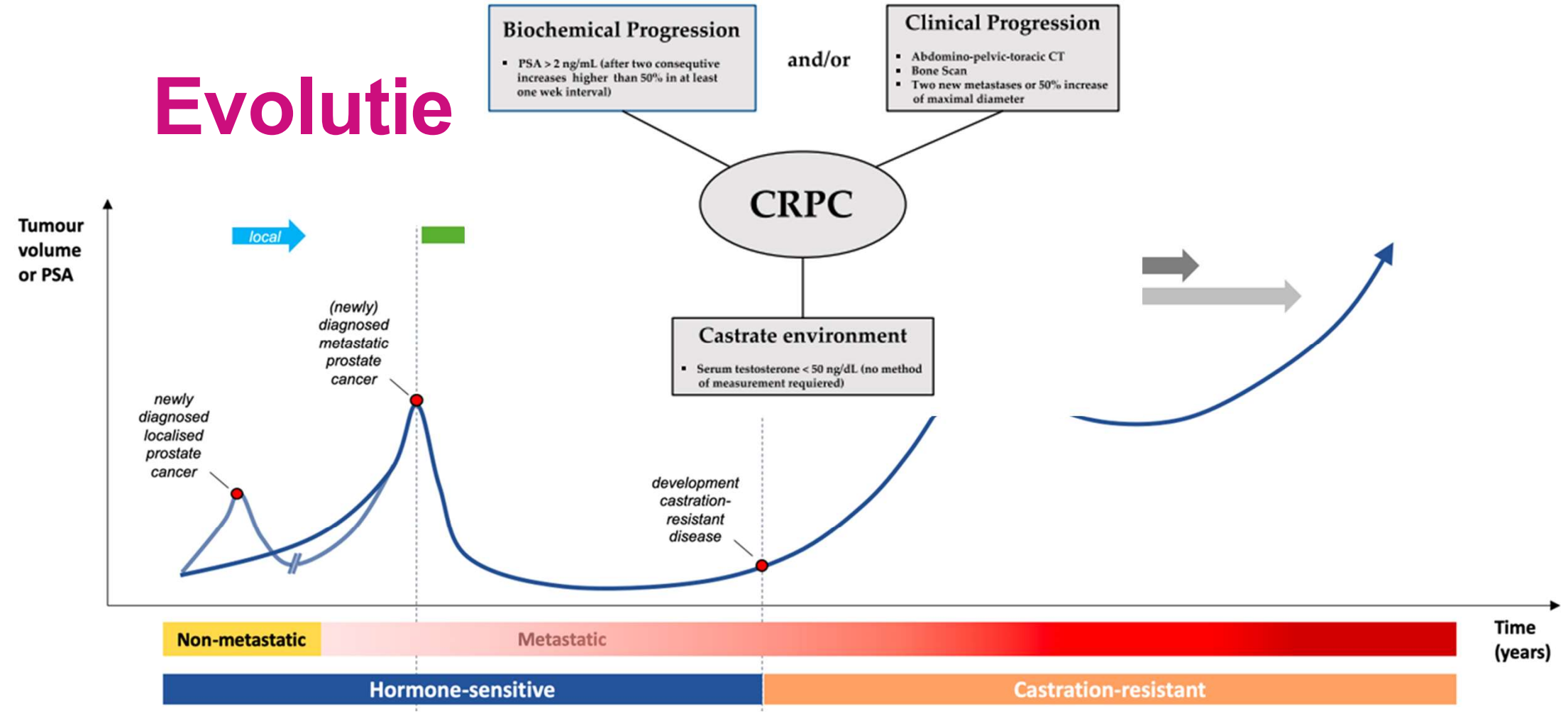
1. https://kankerregister.org/default.aspx?PageId=344

Evolutie



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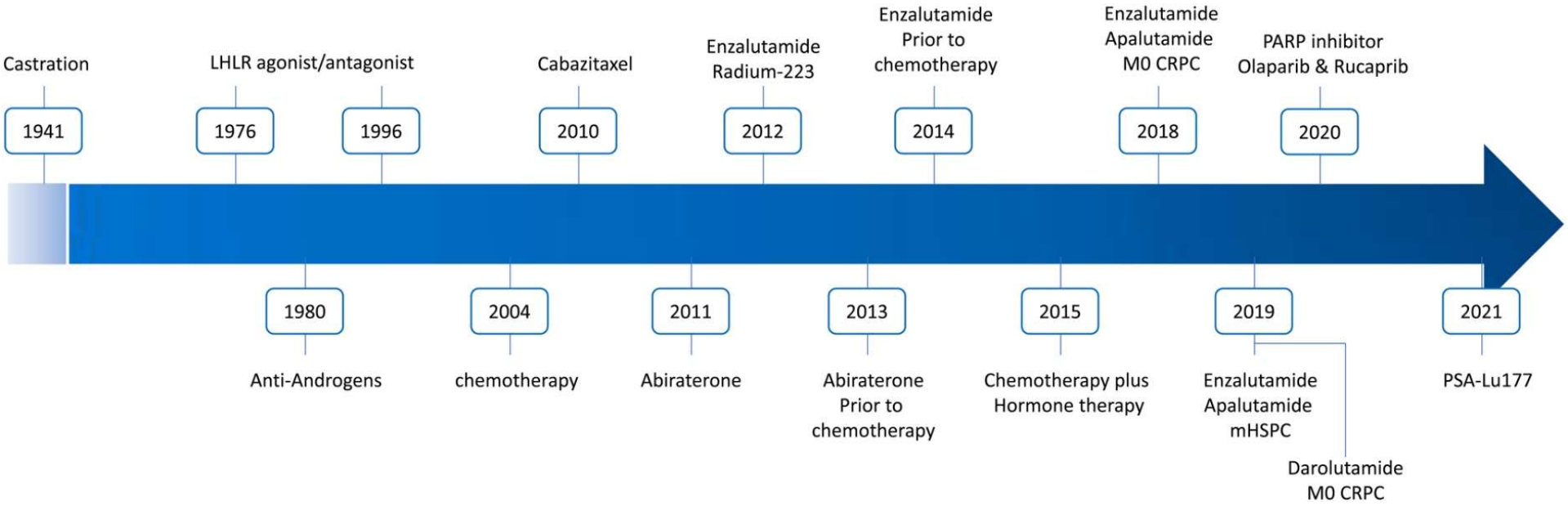
LPC = local prostate cancer, BCR = biochemical recurrence, mHSPC = metastatic Hormone Senstive Prostate Cancer, nmCPRC = non metastatic Castration Resistant Prostate Cancer, mCRPC = mestastatic Castration Resistant Prostate Cancer

Welke therapieën zijn beschikbaar?



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Zoubeidi et al. 2021 Endocrine-Related Cancer

Welke therapie kiezen we?

- Effectiviteit
- Neveneffecten
- Profiel van patiënt
- Terugbetalingscriteria

Overzicht anti-androgenen

	Abiraterone	Enzalutamide	Apalutamide	Darolutamide
				
Indicatie	mHSPC* mCRPC	nmCRPC mHSPC mCRPC	nmCRPC mHSPC	nmCRPC mHSPC**
Toediening	Oraal lege maag	Oraal	Oraal	Oraal bij maaltijd

Bijwerkingen anti-androgenen

	Abiraterone	Enzalutamide	Apalutamide	Darolutamide
Moe	✓	✓	✓	✓
GI	✓			
aHT	✓	✓	✓	
Leverstoornissen	✓			✓
Epilepsie		✓ (alcohol)	✓	
Hartproblemen			✓	✓
Huiduitslag			✓	✓
Vallen			✓	✓

Interacties

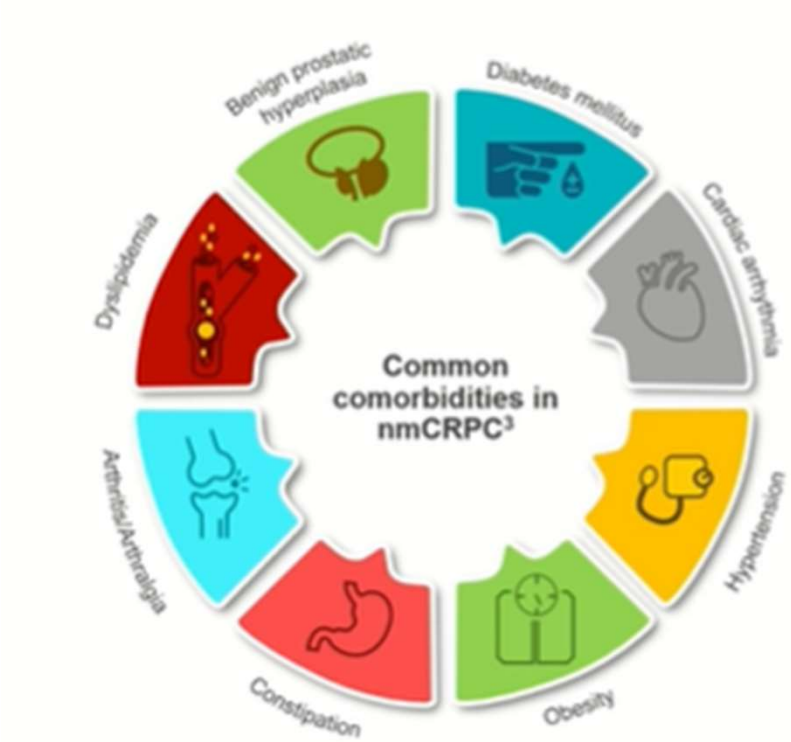


Table 6 Examples of potential drug–drug interactions between enzalutamide, apalutamide, or darolutamide and concomitant medications

A. Effects of enzalutamide, apalutamide, or darolutamide on the exposure of CYP enzyme or transporter substrates

Enzyme/transporter	Apalutamide [13, 14]	Enzalutamide [11, 12]	Darolutamide [23]	Examples of drugs [4, 29, 30, 32, 33]
	Effect on substrate exposure			
CYP3A4	↓	↓	–	**Analgesics:** fentanyl, oxycodone **Anticoagulants:** rivaroxaban **Antihypertensives / CV agents:** amlodipine, amiodarone, dronedarone, felodipine, nisoldipine, ranolazine **Antiplatelet agents:** ticagrelor **CNS drugs:** alprazolam, buspirone, donepezil, midazolam, quetiapine, triazolam **Lipid-modifying agents:** lovastatin, simvastatin **Urological agents:** avanafil, darifenacin, dutasteride, oxybutynin, solifenacin, tamsulosin, tolterodine, vardenafil
CYP2C9	↓	↓	–	**Anticoagulants**: warfarin **Antidiabetics:** glimepiride **Antihypertensives:** losartan **Anti-inflammatories:** celecoxib **Lipid-modifying agents:** fluvastatin
CYP2C19	↓	↓	–	**Beta-blockers:** propanolol **CNS drugs:** diazepam **PPIs**: lansoprazole, omeprazole, rabeprazole
UGT	↓	↓†	–	**Analgesics:** buprenorphine **Antiretrovirals:** zidovudine **CNS drugs:** morphine **Anti-epileptics:** valproic acid
P-gp	↓	↑↓	–	**Analgesics:** fentanyl, oxycodone **Anticoagulants:** dabigatran etexilate **CV agents:** digoxin, ranolazine
BCRP	↓	↑↓	↑‡	**CV agents:** furosemide **Lipid-modifying agents:** atorvastatin, rosuvastatin, fluvastatin **DMARDs:** sulfasalazine
OATP1B1	↓	–	↑	**Hypertension/CV agents:** atenolol **Lipid-modifying agents:** atorvastatin, pitavastatin, rosuvastatin, pravastatin **Antidiabetics:** glyburide, nateglinide, repaglinide

Shore N. et al. 2019 Target Oncol

Chemotherapie

		Docetaxel	Cabazitaxel
		Taxotere	Jevtana
Toediening		IV 1x/3 weken of 1x/week	IV 1x/3 weken
Bijwerkingen			
	Hemato-toxiciteit	✓	✓
	Alopecie	✓	
	Neuropathie	✓	
	GI toxiciteit		✓

Radium-223-dichloride (Xofigo)

= radioactieve behandeling

- Toediening: IV 1x/4 weken tot max 6 toedieningen
- Bijwerkingen
  - Hemato-toxiciteit
  - Misselijkheid
  - Diarree

Lutetium-177-PSMA

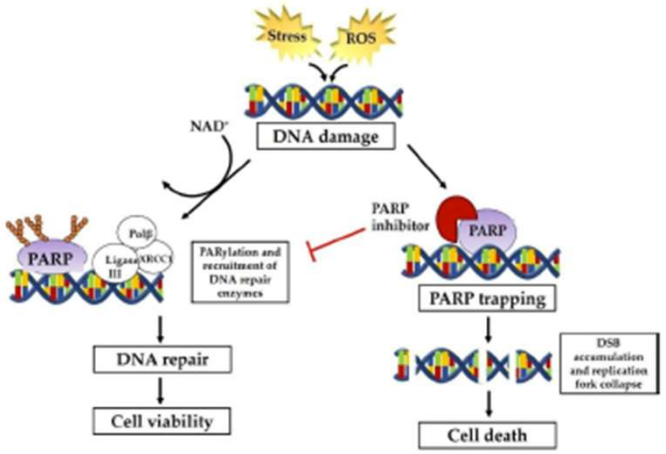
= radioactieve behandeling

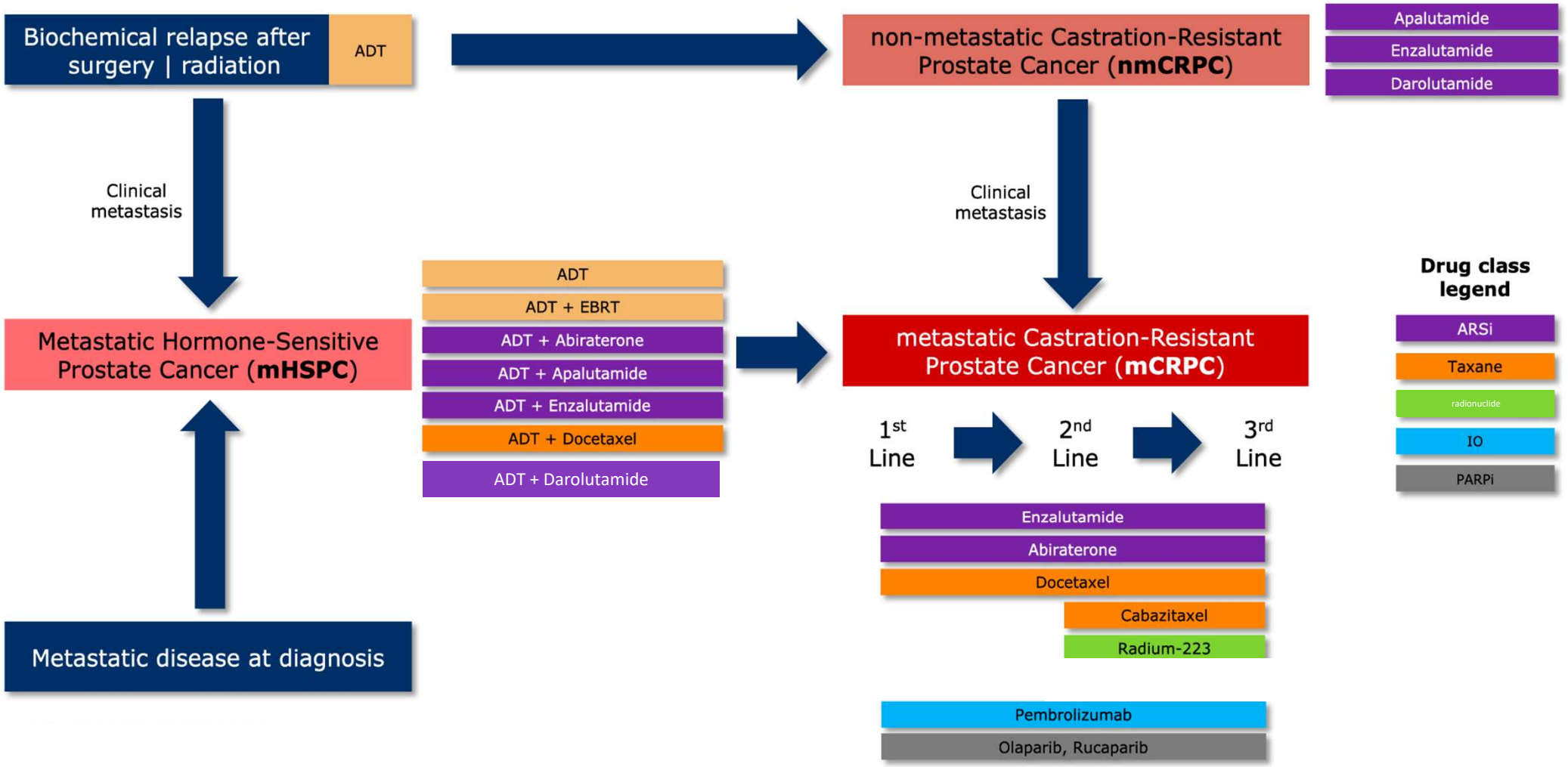
- Toediening: IV 1x/6weken tot max 4 behandelingen. Opname 24u
- Bijwerkingen
  - Hemato-toxiciteit
  - Verminderde nierfunctie
  - Droge mond en ogen
  - Misselijkheid

Olaparib (Lynparza)

= PARP-inhibitor enkel bij BRCA1/2 mutatie mCRPC

- Toediening: 2x150mg, 2x/dag met of zonder eten.
- Bijwerkingen
  - Hemato-toxiciteit
  - Spierpijn
  - GI: diarree, misselijkheid en braken





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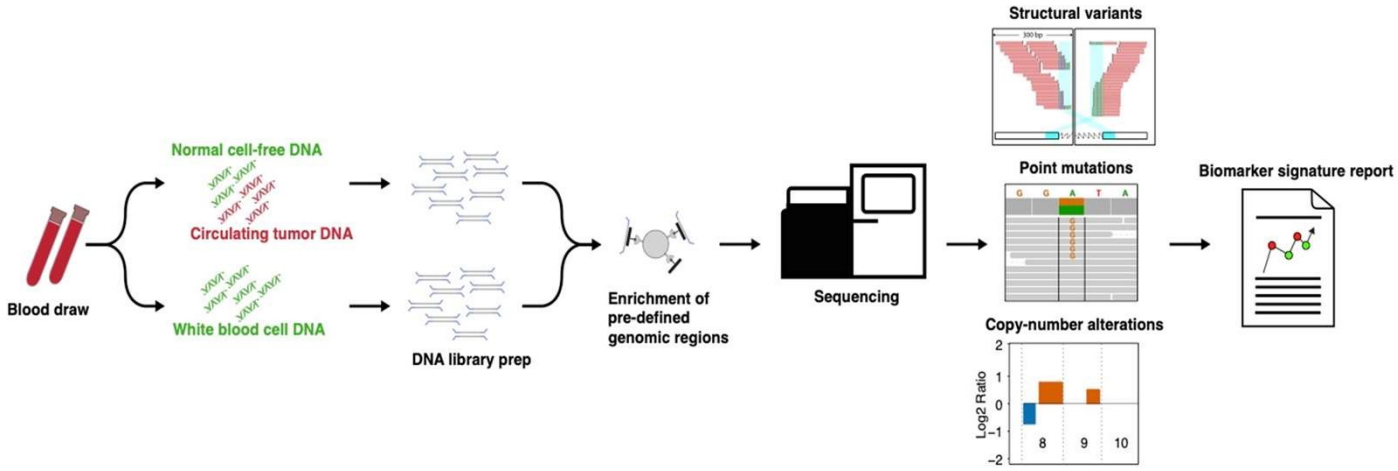
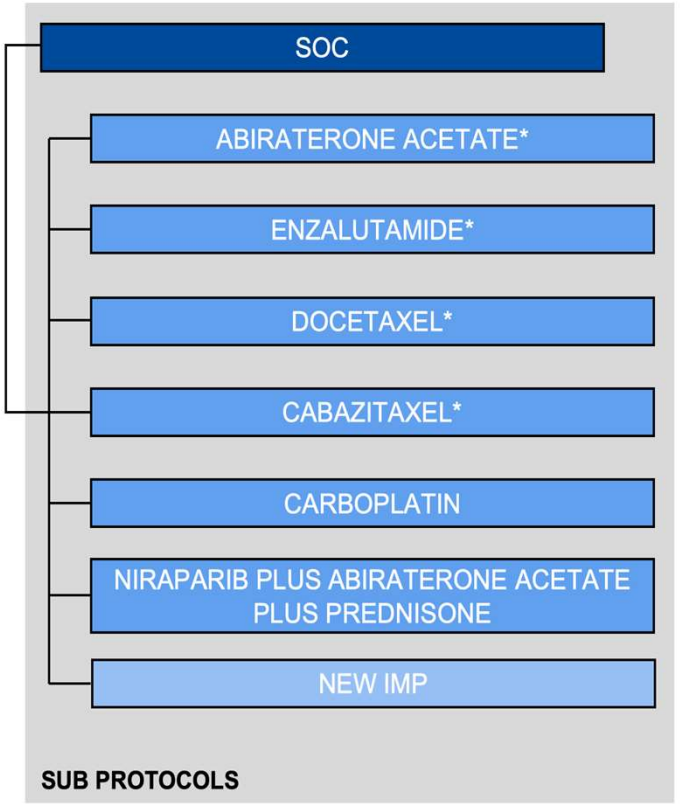
Mateo. et al. 2020 Nat Can

proBIO studie





Uro-oncokliniek

- MOC urologie: 1x/week op woensdag, start 7u30

- Uro-oncokliniek: 1x/week op woensdagnamiddag
  uroloog
  oncoloog
  radiotherapeut
  uro-oncoverpleegkundige

Conclusie

- Therapiemogelijkheden
  - Anti-androgenen
  - Chemotherapie
  - Radio-actieve behandeling
  - PARP-inhibitoren
- Monitoring
  - Neveneffecten
  - Interacties

Waar ligt de rol van de oncocoach naar de patiënt en de huisarts toe?

Symposium Onco-Hematologie
Woensdag 26 oktober 2022

Dhr. Renzo Van Meulebroeck

Mevr. Kim Hemelaer

az Sint Blasius

Informeren / opvolgen van onze patiënten
Samenwerking met/doorverwijzing naar andere zorgverstrekkers
Ondersteunen van de kwaliteitszorg
Organiseren/meewerken nevenactiviteiten

Multidisciplinaire samenwerking

Na vaststellen diagnose => patiëntbespreking op MOC !

- Aanvragende arts
  - Verantwoordelijk voor de behandeling of doorverwijzing
  - Communicatie naar huisarts en andere disciplines
- Coördinator
- Deelnemers

medisch oncologen, orgaanspecialisten, hematologen, radiotherapeut, anatoompatholoog, klinisch bioloog, oncocoach/borstverpleegkundige, huisarts, radioloog, psycholoog,...

1. Informatieverstrekking aan patiënt en familie

- Indien aan patiënt een behandeling wordt voorgesteld, is het belangrijk dat de patiënt over zijn/haar behandeling wordt geïnformeerd. Ter aanvulling kan de arts een beroep doen op de borstverpleegkundigen of oncocoachen die specifiek opgeleid werden om de patiënten bijkomend te informeren.
- Er is een vaste oncocoach gekoppeld per discipline !
- Eerste kennismakingsgesprek bij voorkeur aansluitend na de raadpleging bij de arts.
- Of op verpleegkundig spreekuur (afspraak) of bij implantatie PAC of bij opstart therapie en nadien ZN of op vraag patiënt.

Wat wordt er besproken ?

- Verloop van de behandeling: duur-aantal cycli-toedieningswijze
- Mogelijke nevenwerkingen
- Interacties met andere geneesmiddelen en voedingsstoffen,...
- Correct gebruik van de anti-emetica, pré- en randmedicatie
- Gebruik van groeifactoren
- Gebruik van de ijskap en ijshandschoenen, nagelverharders
- Het veilig omgaan met lichaamsvloeistoffen, verzorgings-en afvalmateriaal

- Gebruik poortkatheter (of andere katheters):
  - Wat is een pac?
  - Waar wordt deze geïmplanteerd?
  - Pré- en postoperatieve nazorg/aandachtspunten
- Indicaties om naar spoed te komen
- Gebruik van de infusorpomp
- Organisatie OST-dagziekenhuis en verblijfsafdeling
- Risico op haarverlies-recht op premie
- Infectiepreventie
- …

Bij het kennismakingsgesprek krijgt de patiënt ook:

- Korte rondleiding op de afdeling of het oncologisch dagziekenhuis
- Map met specifieke informatie + contactgegevens (zie foto volgende dia)
- En wordt nagevraagd of er bijkomende ondersteuning noodzakelijk is (psychologisch-sociaal-levensbeschouwelijk,...)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ONCOLOGISCH DAG
INFOBROCHURE
TIPS VOOR DE ONCOLOGIS
PATIËNT
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Oncologisch supportteam
Mensen met kanker nabij
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Hoe verlopen onze gesprekken en de verdere opvolging?

- **Eerste kennismaking:** duur circa 1 uur
  - of bij start therapie op verblijfsafdeling of dagziekenhuis
  - of op afspraak tijdens verpleegkundig spreekuur

- **Tweede gesprek= opvolggesprek** bij start 2e kuur
  Doelstelling: problemen detecteren

- **Op vraag van patiënt** : meerdere gesprekken (bij voorkeur ambulant !)

- **Tijdens gesprekken**:
  - opvang/ondersteuning patiënt-partner en zorgverstrekkers
  - ZN doorverwijzing naar andere ondersteunende disciplines (sociale dienst, levensbeschouwelijk team, oncopsychologen, diëtisten,...huisarts)

Bereikbaarheid Oncocoachen?

- Tijdens de weekdagen steeds van 8u tot 16u30 !
  - Via email: oncocoachen@vitaz.be
  - Telefonisch => Pt krijgt steeds contactgegevens mee van oncocoach
  - Ambulant (enkel op afspraak)

- Andere opties zijn:
  - Via algemeen nummer oncosecretariaat: 03/ 760 29 85
  - Algemeen nummer ziekenhuis: 03/ 760 60 60

- Bij afwezigheid oncocoachen:
  - Spoedopname: 03/ 760 60 00

2. Doorverwijzing naar andere zorgverstrekkers

Wie ondersteunt de patiënt?

- 1ste lijn
  - Huisarts
  - Familie/mantelzorgers
  - Verpleegkundigen in de huisartspraktijk
  - Thuisverpleegkundigen, verpleegkundigen uit WZC

- 2de lijn
  - Oncoloog/hematoloog
  - Verpleegkundig specialist/consulent – oncocoach -borstverpleegkundigen
  - Psychologen

Vanuit ons oncologisch supportteam wordt bijkomende ondersteuning aangeboden door:

- Sociale dienst
- Oncodiëtiste(n)
- Oncopsychologen
- Levensbeschouwelijk team
- Tabakoloog
- Revalidatie,....

3. Ondersteunen van de kwaliteitszorg

Werken binnen de zorg is niet altijd evident.... !
Iedereen heeft te kampen met :

- De hoge werkdruk, tekort aan personeel
- De stijgende zorgvraag (door de vergrijzing van de bevolking)
- Het moeten anticiperen op “onverwachte gebeurtenissen” (waaronder bijvoorbeeld de coronapandemie)
- Besparingen
- Het moeten omgaan met veranderingen binnen de werkstructuur,...

Middelen en personeel dienen meer dan ooit efficiënt te worden ingezet !!

Maar niet ten koste van de zorgkwaliteit !

Oncocoachen hebben de taak om de kwaliteit van de zorg mee te helpen ondersteunen !!!!

Hoe? => door deel te nemen aan verschillende projecten

Welke projecten ?

- Opmaken/aanpassen van infofolders voor patiënten
- Aanpassen van bestaande procedures

vb. gebruik ijshandschoenen bij toediening van Oxaliplatine ter preventie van PNP

- Organiseren van opleidingen (intern en extern)
  - Jaarlijkse dagopleiding Onco-Hematologie (verplichte dagopleiding voor alle verpleegkundigen werkzaam op oncologie)
  - Opleiding 'algemene nevenwerkingen bij antitumorale therapieën (WZC)'
  - Opleiding 'aanprikken poortkatheters en afkoppelen van de infusorpomp' en aan verpleegkundigen uit de thuiszorg e.a.

- Waken over de kwaliteit van de zorg:
  - Nagaan of procedures correct worden opgevolgd Vb. het correct aanprikken van poortkatheters, gebruik ijshandschoenen

- Bijwonen van overlegmomenten
  - MOC
  - Dienstvergaderingen
  - Patiëntenbesprekingen,…

- Meehelpen aan interne audits binnen het ziekenhuis
- Opleiden/begeleiden van studenten
- Eigen beroepsbekwaamheid verbeteren:
  - Zelf opleidingen/vormingen volgen (VVRO-congres, BHS, post ESMO,…)

4. Organiseren/meewerken aan nevenactiviteiten voor kankerpatiënten

Jaarlijkse organisatie DTK (Dag Tegen Kanker) in samenwerking met Kom Op Tegen Kanker

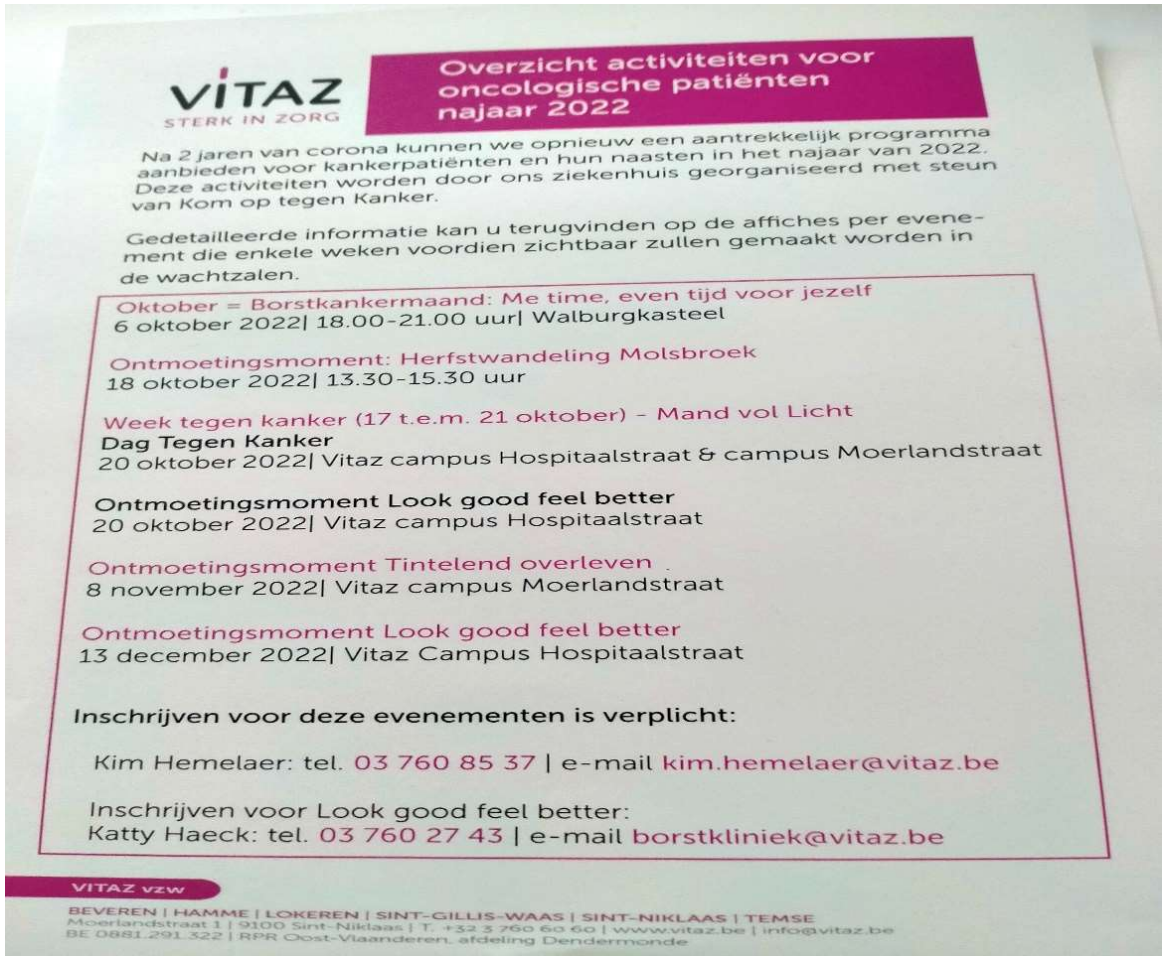
=> Steeds op de 3e donderdag van oktober

=> Verschillende activiteiten (pannenkoekenbak, uitnodigen van een BV, opstellen van standjes, dragen en verdelen van de gekende gele lintjes, 'Look Good, Feel Better', bloemschikken,...)

az Sint Blasius

Organiseren van lotgenotencontacten

(de zogenaamde praatcafés, nu ontmoetingsmomenten genoemd)



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Overzicht activiteiten voor oncologische patiënten najaar 2022

Na 2 jaren van corona kunnen we opnieuw een aantrekkelijk programma aanbieden voor kankerpatiënten en hun naasten in het najaar van 2022. Deze activiteiten worden door ons ziekenhuis georganiseerd met steun van Kom op tegen Kanker.

Gedetailleerde informatie kan u terugvinden op de affiches per evenement die enkele weken voordien zichtbaar zullen gemaakt worden in de wachtzalen.

Oktober = Borstkankermaand: Me time, even tijd voor jezelf
6 oktober 2022| 18.00-21.00 uur| Walburgkasteel

Ontmoetingsmoment: Herfstwandeling Molsbroek
18 oktober 2022| 13.30-15.30 uur

Week tegen kanker (17 t.e.m. 21 oktober) - Mand vol Licht
Dag Tegen Kanker
20 oktober 2022| Vitaz campus Hospitaalstraat & campus Moerlandstraat

Ontmoetingsmoment Look good feel better
20 oktober 2022| Vitaz campus Hospitaalstraat

Ontmoetingsmoment Tintelend overleven
8 november 2022| Vitaz campus Moerlandstraat

Ontmoetingsmoment Look good feel better
13 december 2022| Vitaz Campus Hospitaalstraat

Inschrijven voor deze evenementen is verplicht:

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Inschrijven voor Look good feel better:
Katty Haeck: tel. 03 760 27 43 | e-mail borstkliniek@vitaz.be

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az Sint Blasius

Patiënten sensibiliseren rond geplande activiteiten georganiseerd door andere organisaties:

- Activiteiten georganiseerd door Melanoompunt, Stichting Tegen Kanker, Kom op Tegen Kanker,...
- Lotgenotencontacten (lymfoomvereniging Vlaanderen,...)
- Cabrio-event (georganiseerd door ex-patiënt)
- Jongerenvakanties,....

Einde…..

Bedankt voor jullie aandacht !

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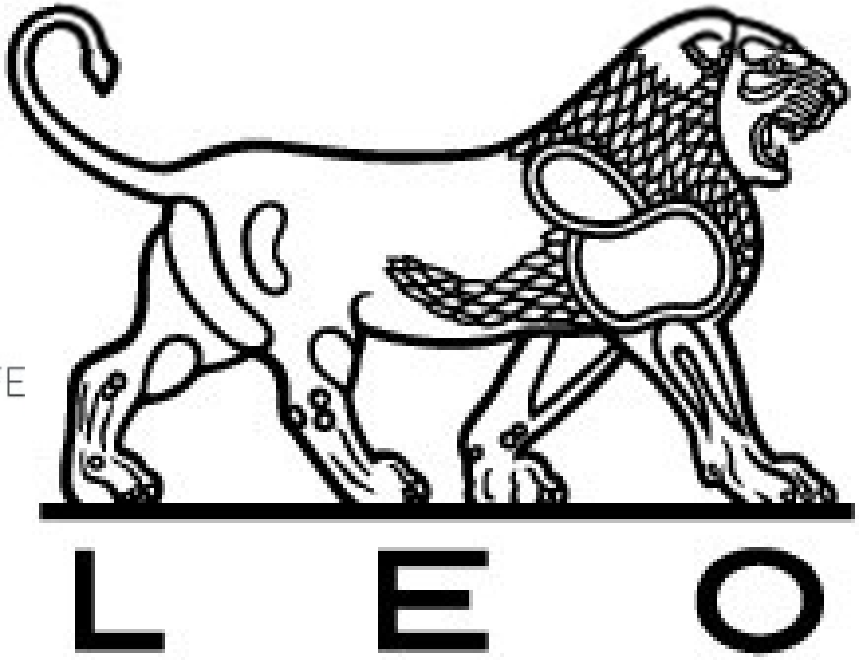
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