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Cancer Institute

OPTIMALISATIE VAN ZORG RONDOM DOELGERICHTE THERAPIE

Prof Anne-Marie Dingemans

Longarts

Erasmus MC Cancer Institute

18 juni 2026

The Boston Globe

A drug that works — for some

Researchers try to solve mystery of lung cancer medicine

GLOBE STAFF PHOTO/SUZANNE KREITER

The drug Iressa has allowed Kate Robbins to resume activities and spend precious time with her family.

By Raja Mishra
GLOBE STAFF

CONCORD — Early last year, Kate Robbins started her death journal. It was meant to guide her two children after lung cancer killed her. Robbins poured out advice: on dating, on morality, on family. The things a mother explains to her teens.

She also memorialized quiet, poignant moments. One rainy day, watching 10-year-old Hillary board the school bus, Robbins began weeping. She wrote simply, "You looked really pretty today." The kids would read the journal years later, she hoped, and feel their mother's love.

Advanced lung cancer patients rarely live one year. Robbins had months left. Then, last autumn, she began taking an experimental drug called Iressa, as did hundreds of other patients in the United States. Most continued to worsen.

But a small group, including Robbins, thrived. Doctors were stunned because lung cancer, the speediest and most widespread killer among cancers, had resisted virtually every treatment.

Now researchers are racing to unravel why Iressa — the first significant new lung cancer drug in a generation — appears to help only select patients. They are studying the DNA of patients for clues, hoping to develop a genetic screening test that would enable them to get the drug to the right people quickly. If they succeed, a small portion of lung cancer victims would get extra years of life. Given that 157,000 Americans die annually from the disease, the impact could be considerable.

The effort is part of an emerging area of medicine seeking to genetically match patients to drugs. Such personally-tailored medicating promises to be a hallmark of 21st-century health care.

Robbins's doctor, Thomas Lynch of Massachusetts General Hospital, said he has other lung cancer patients who also are doing well as many as three years after starting on Iressa.

"I've been treating this cancer since 1989, 500 patients a year, and this is the most significant development I've seen," he said.

Last week, Robbins, 46, had her first checkup in five months: Out of 16 once-bulging tumors scattered throughout her organs, there appeared to be none.

"It's the most amazing thing," she said.

Robbins has big eyes and a round, girlish face. She talks with energy and enthusiasm, her Boston accent occasionally poking through. Robbins was raised in Chelmsford and moved to Concord from rural Connecticut four months ago to be near MGH. She worked as a nurse but stopped to raise her children, Tom, now 13, and Hillary, 11. Her husband, Mark, is a cancer doctor at Emerson Hospital.

Attentive to her health, Robbins was an unlikely candidate for lung cancer in her 40s. About 85 percent of the disease's victims are current or former smokers, but Robbins has never smoked. She rarely drinks, and, moved by the suffering of animals, became a vegetarian at age 10. But one day in January 2002, she developed an intense headache. "I thought it was post-holiday stress," she said.

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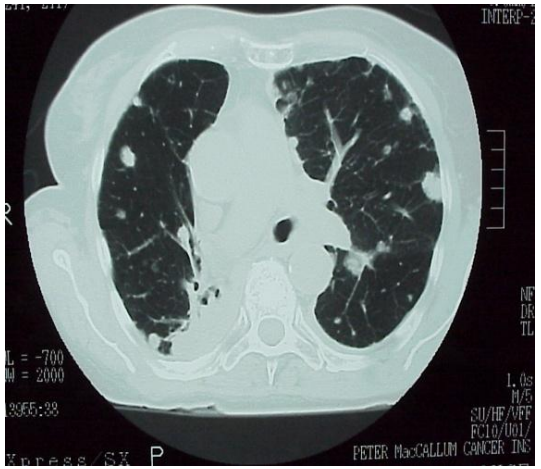

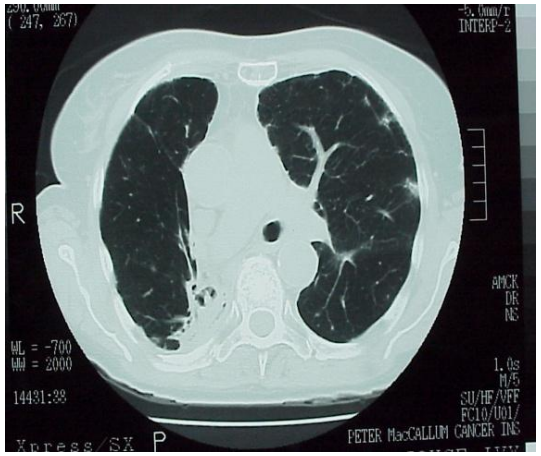

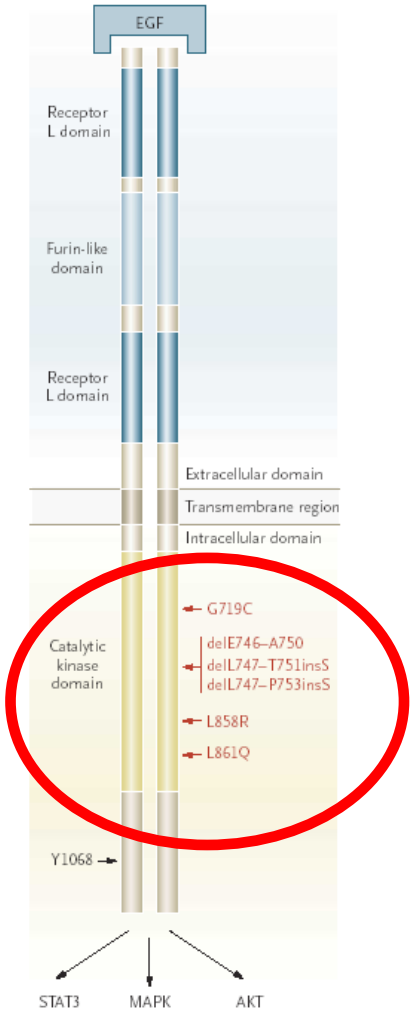

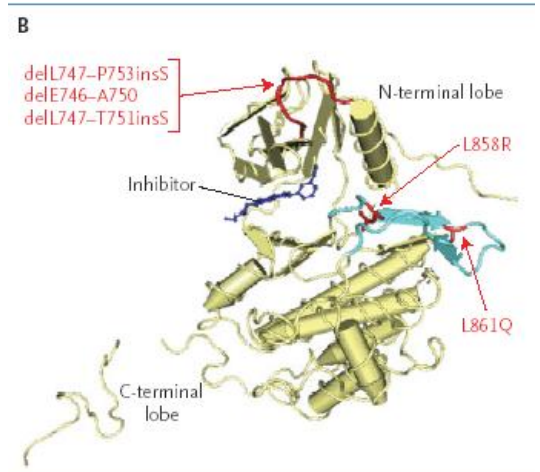

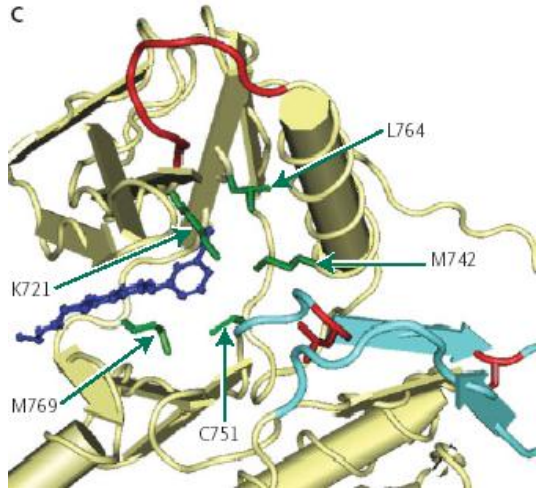

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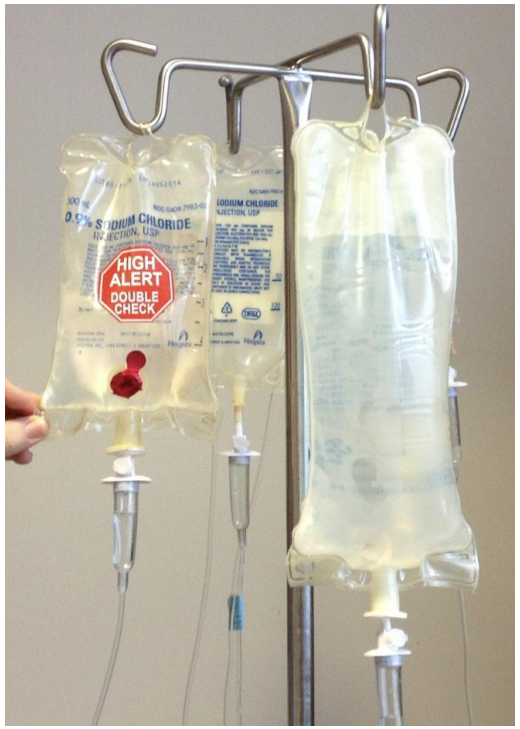
Lynch NEJM 2004

DE JUISTE DOSIS

CHEMOTHERAPIE



MAXIMALE DOSIS: TOXICITEIT

DOELGERICHTE BEHANDELING

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Common Terminology Criteria for Adverse Events (CTCAE)

v6.0 (MedDRA 28.0)

Published July 22, 2025

Paronychia

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Nail fold edema or erythema; disruption of the cuticle	Local intervention indicated; oral intervention indicated (e.g., antibiotic, antifungal, antiviral); nail fold edema or erythema with pain; associated with discharge or nail plate separation; limiting instrumental ADL or mild/moderate impact on age-appropriate normal daily activity (pediatric)	Operative intervention indicated; IV antibiotics indicated; limiting self-care ADL or severe impact on age-appropriate normal daily activity (pediatric)	-	-

Fatigue

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL or mild/moderate impact on age-appropriate normal daily activity (pediatric)	Fatigue not relieved by rest, limiting self-care ADL or severe impact on age-appropriate normal daily activity (pediatric)	-	-

Definition: A disorder characterized by a state of generalized weakness with a pronounced inability to summon sufficient energy to

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BIJWERKINGEN

Diarrhea

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Change in consistency or frequency	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL or mild/moderate impact on age-appropriate normal daily activity (pediatric); change in consistency or frequency AND limiting instrumental ADL or mild/moderate impact on age-appropriate normal daily activity (pediatric)	Increase of >=7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; requires IV intervention; limiting self-care ADL or severe impact on age-appropriate normal daily activity (pediatric)	Life-threatening consequences; urgent intervention indicated	Death

Weight gain

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
5 - <10% from baseline	10 - <20% from baseline	>=20% from baseline	-	-

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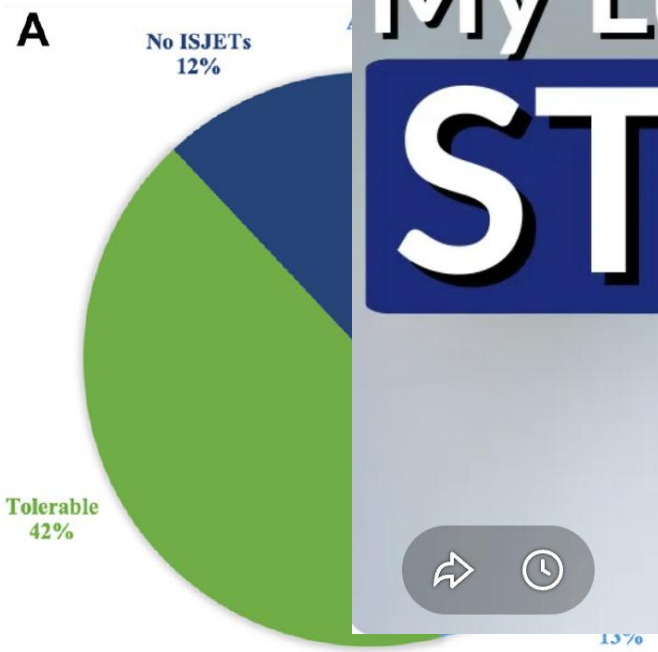
CTCAE v6

The Use of Investigator-Assigned Subjective or Judgmental Efficacy and Toxicity Reporting in Early Phase Clinical Trials of Lung Cancer Treatments



w safety signals," and "consistent to

ria for defining "treatment related"

of AEs by CTCAE or MedDRA organ

in each grouped term
e AEs separately by dose level and at

was held, or discontinued treatment

reduction, dose delay, or treatment

investigations, qualified by relevant

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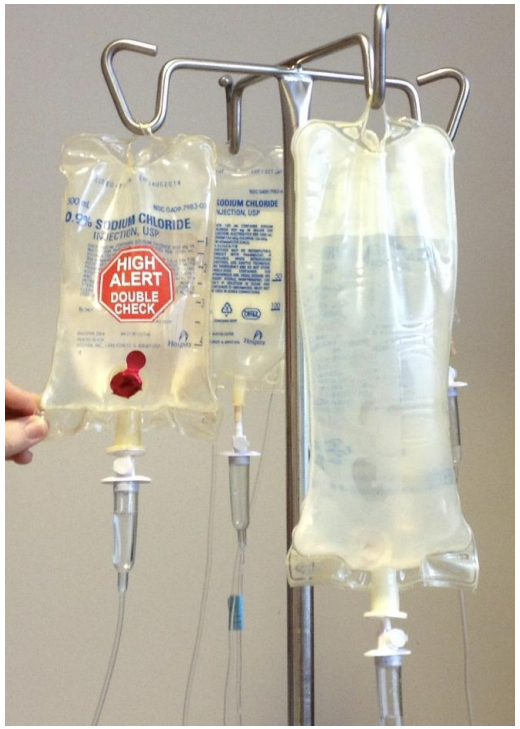
DE JUISTE DOSIS

CHEMOTHERAPIE



MAXIMALE DOSIS: TOXICITEIT

MAXIMALE DOSIS: WERKZAAMHEID

DOELGERICHTE BEHANDELING

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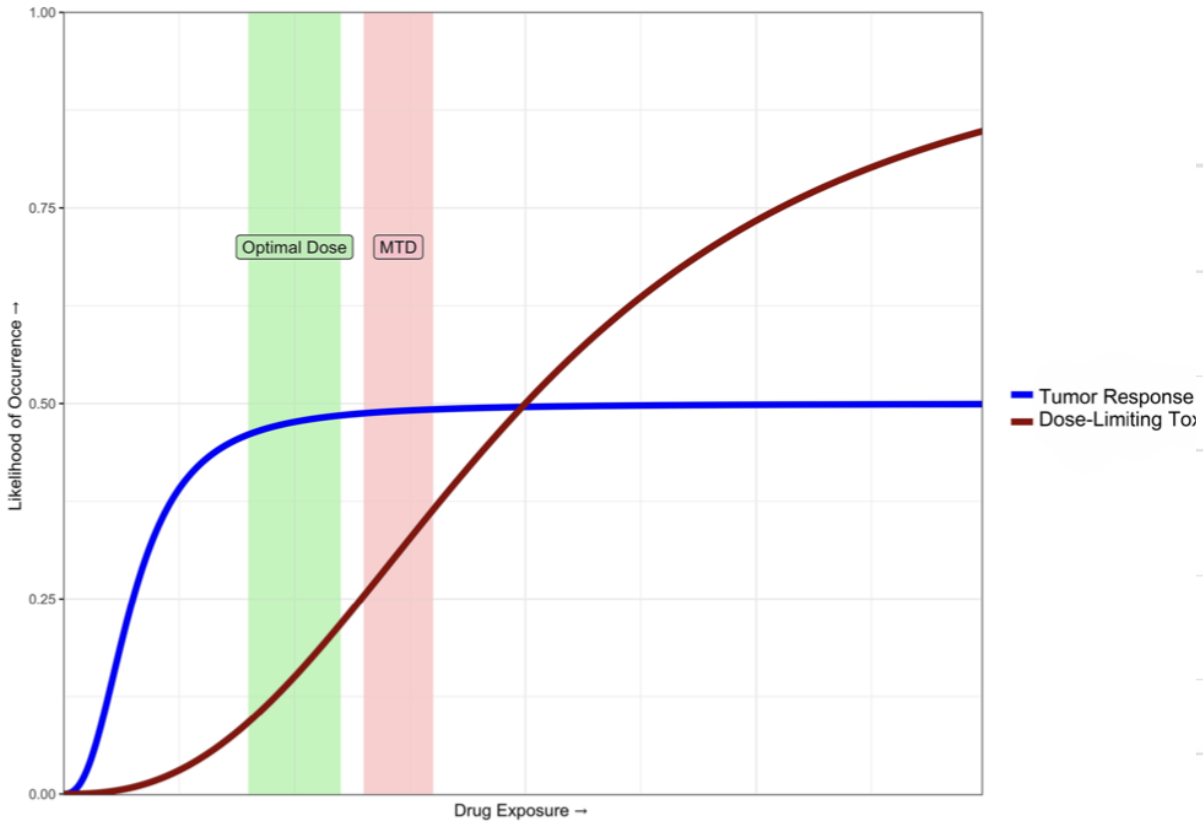
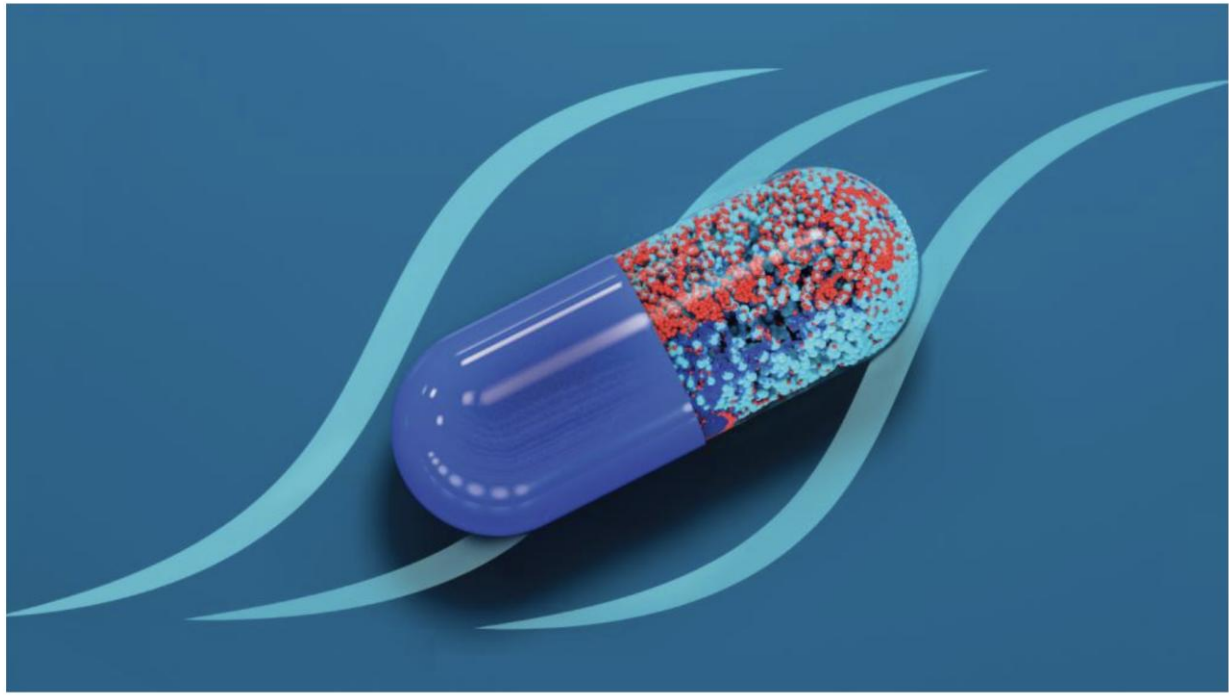
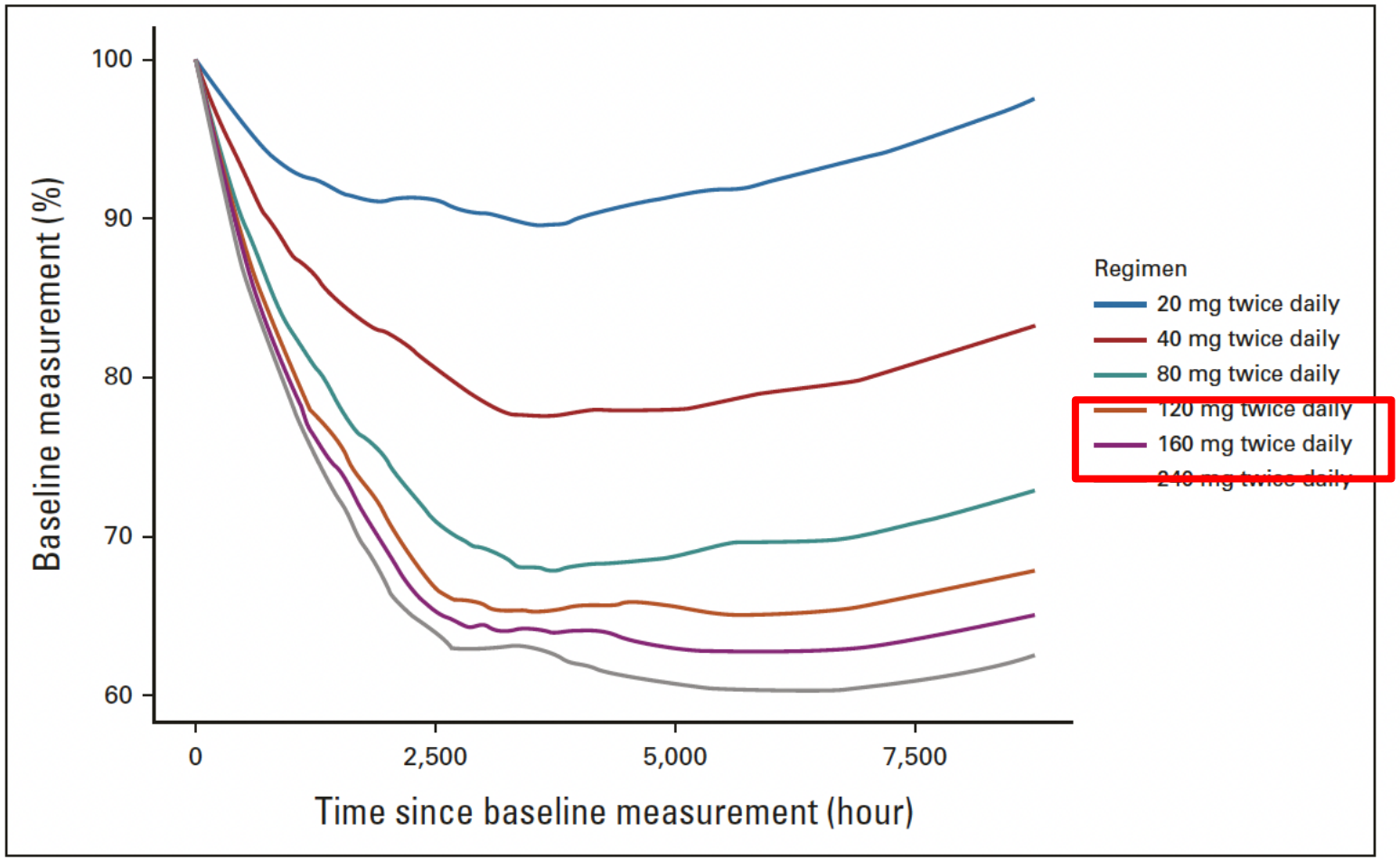


Project Optimus

Reforming the dose optimization and dose selection paradigm in oncology



RET+: SELPERCATINIB

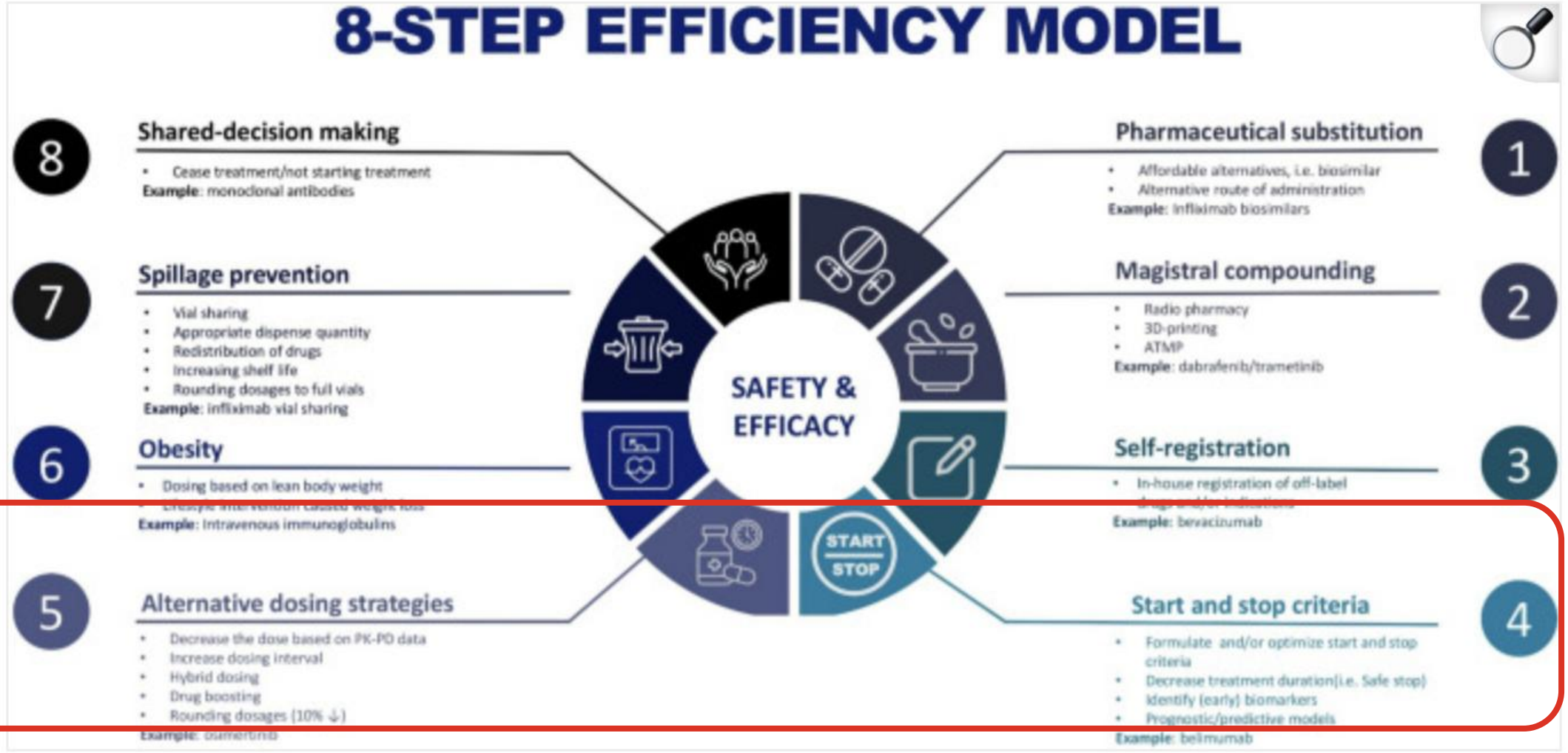


Geen relatie
dosis en bijwerkingen

Cancer Institute Ezafung

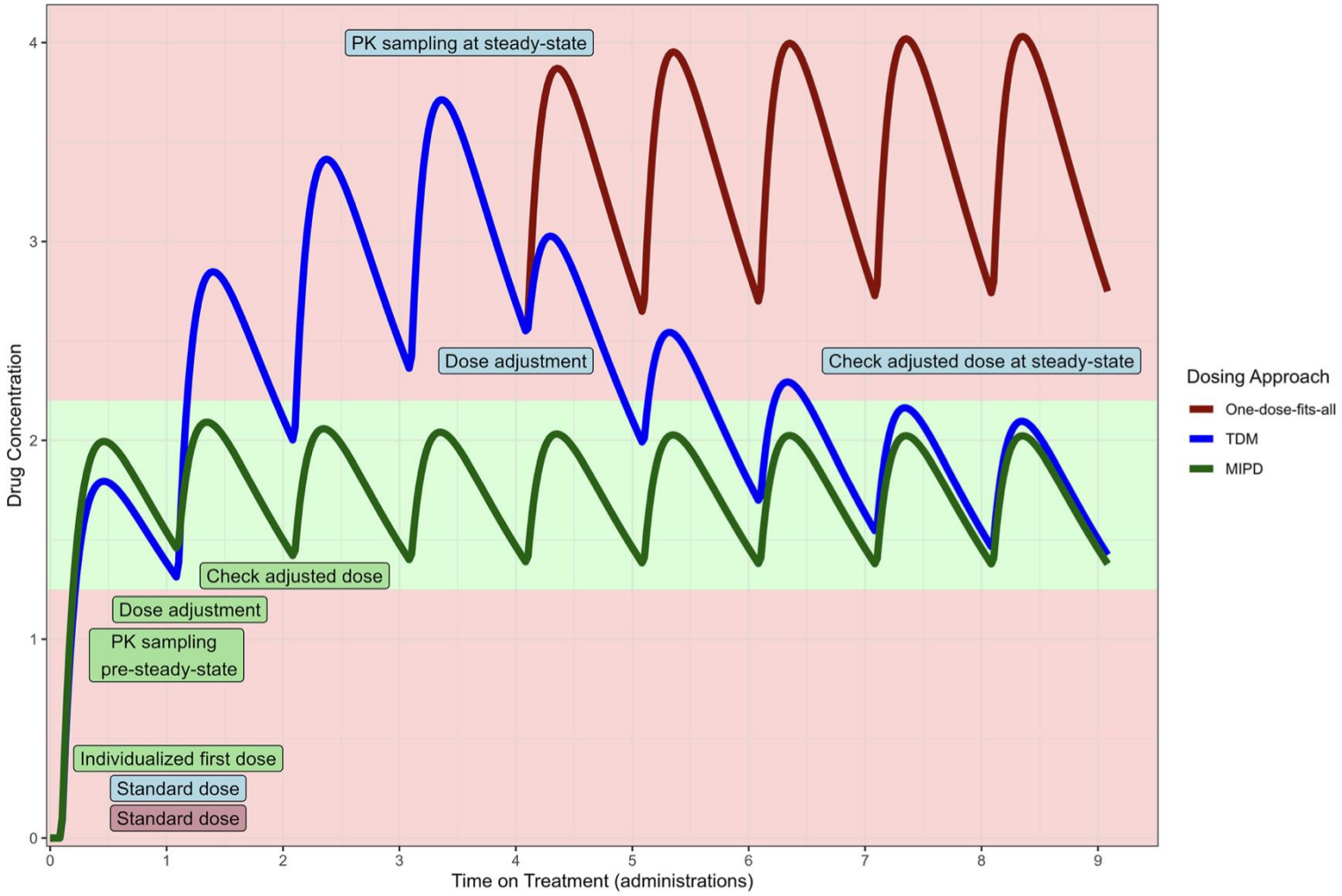
Zirkelbach JCO 2022

8-STEP EFFICIENCY MODEL

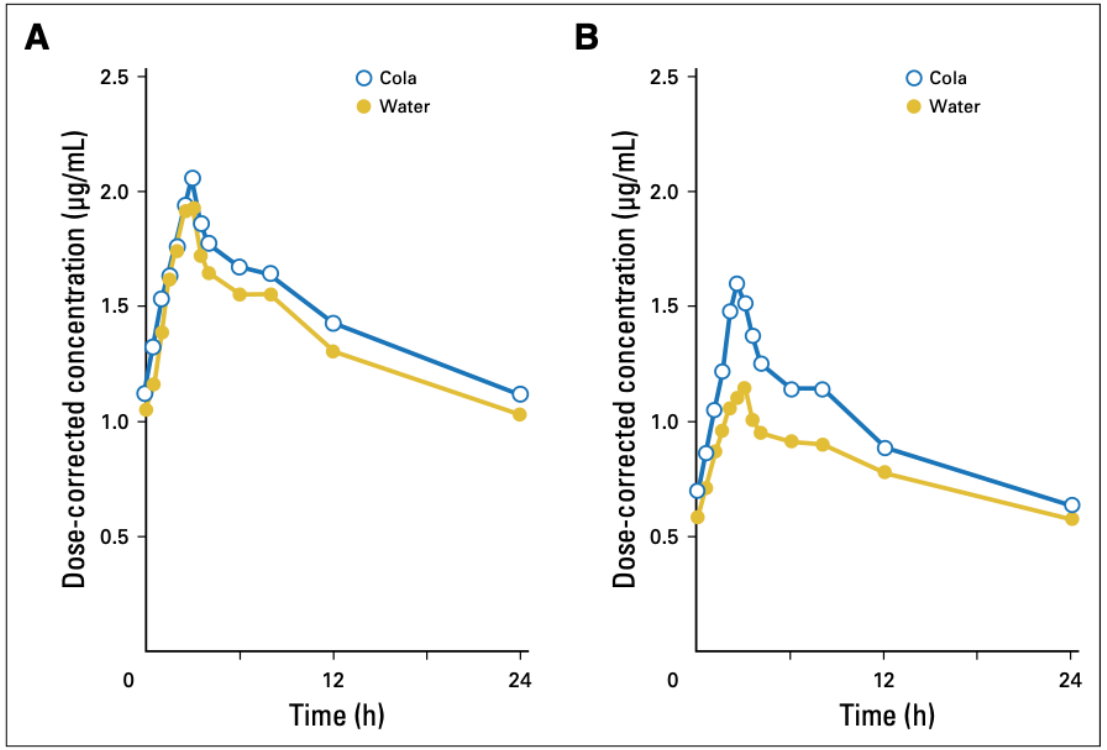


Zietse Appl Health Econ Health Policy 2024

TDM: THERAPEUTIC DRUG MONITORING



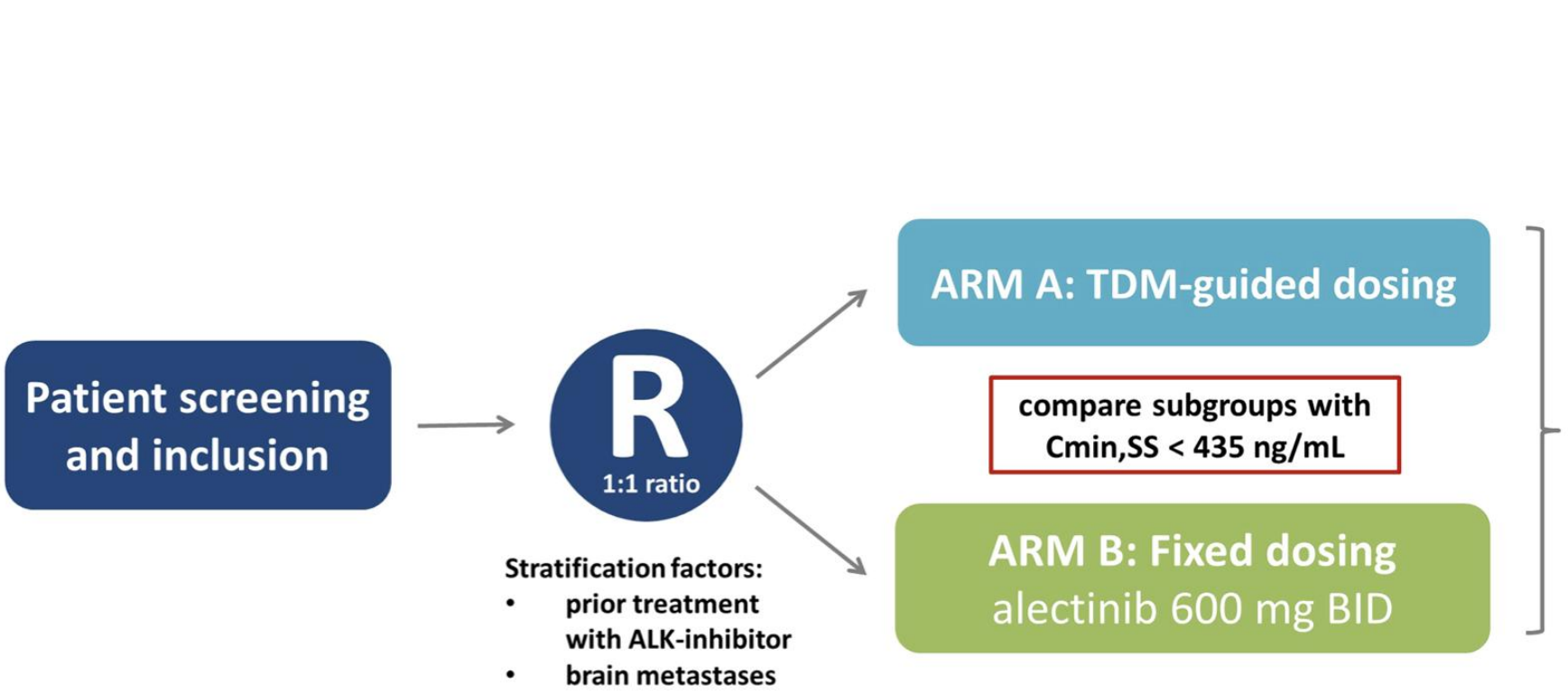
Influence of the Acidic Beverage Cola on the Absorption of Erlotinib in Patients With Non–Small-Cell Lung Cancer



MAAGZUUR REMMER
+
COLA

Van Leeuwen JCO 2016

ADAPT-ALEC



Primary endpoint:
- mPFS

Secondary endpoints:
- Feasibility and tolerability of TDM
- ORR
- mOS
- Intracranial PFS
- Patient and physician adherence
- Quality of life
- Cost-effectiveness
- Alectinib-M4

Exploratory endpoints:
- ctDNA
- Body composition

PK samples at week 4 and every 8 weeks (year 1), thereafter every 12 weeks of treatment:
- TDM-guided dosing (arm A): measured immediately and dose recommendations are provided within 2 weeks
- Fixed dosing (arm B): remains blinded until end of the study

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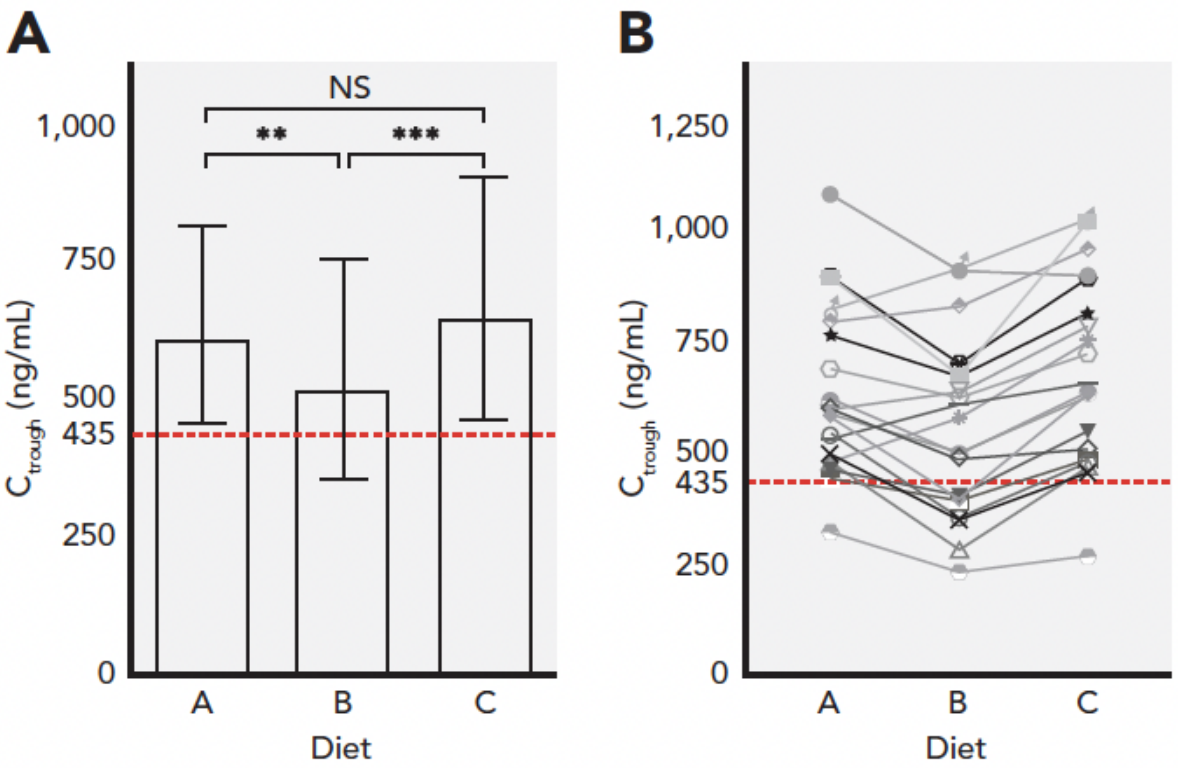
Meertens Frontiers in Oncology 2023

Influence of Food With Different Fat Concentrations on Alectinib Exposure: A Randomized Crossover Pharmacokinetic Trial



A: normaal ontbijt
B: low-fat yoghurt
C: lunch naar keuze

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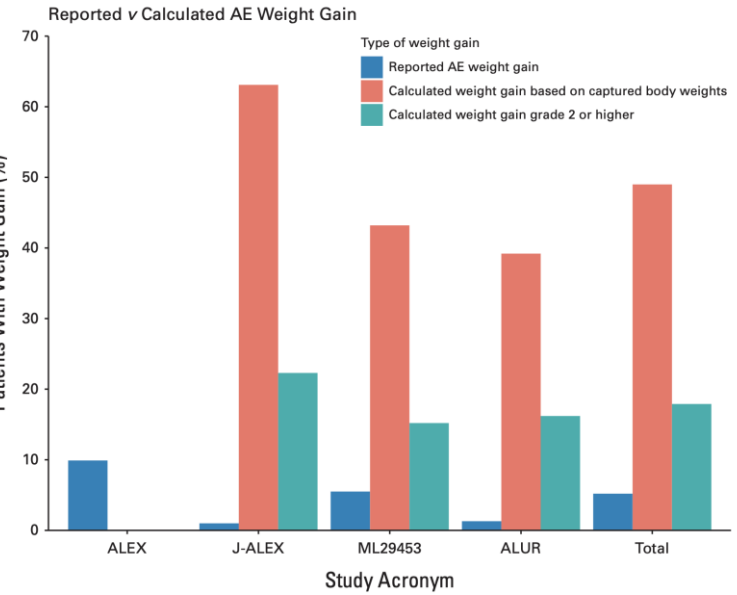
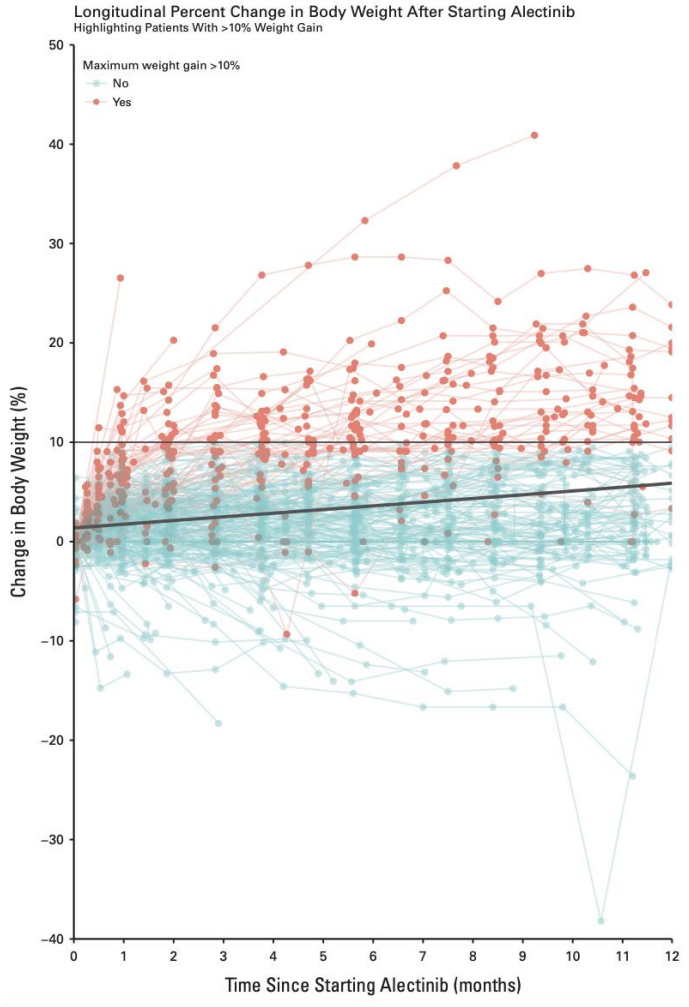
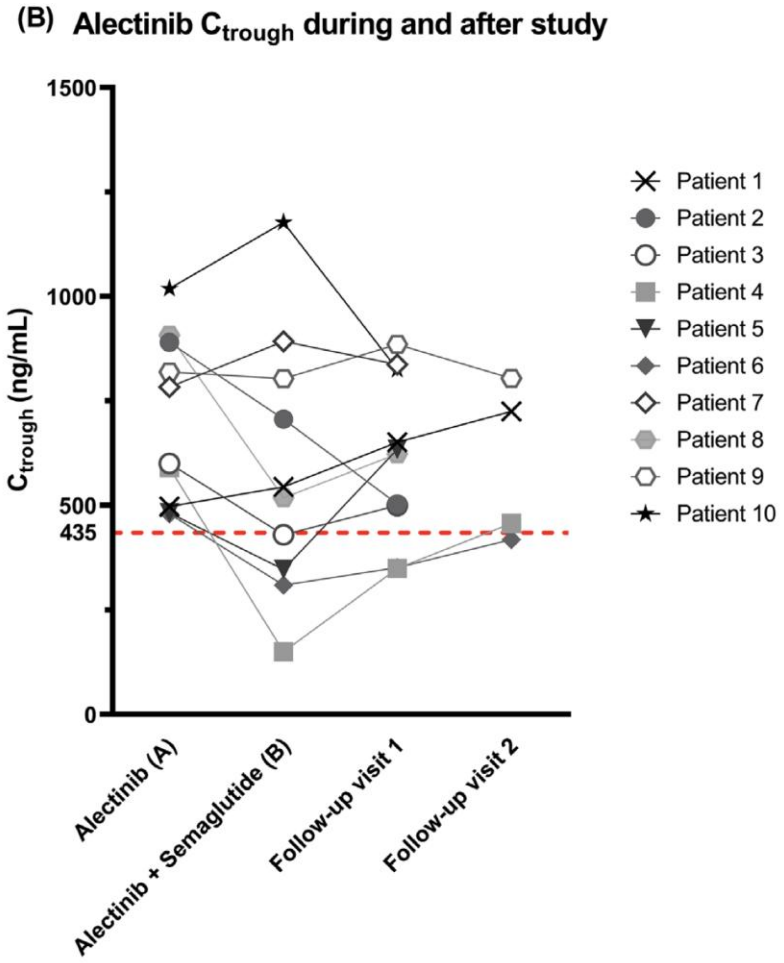
Lanser JNCCN 2023

ALECTINIB EN GEWICHTSTOENAME







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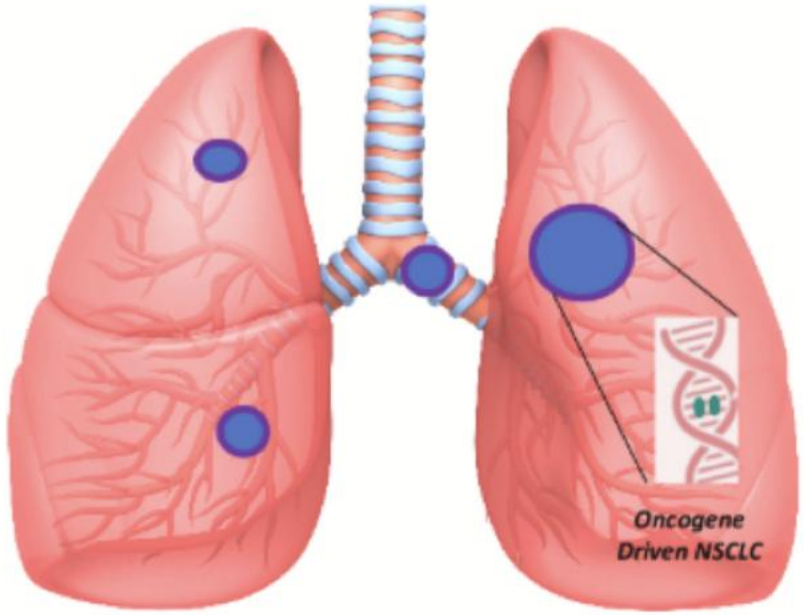
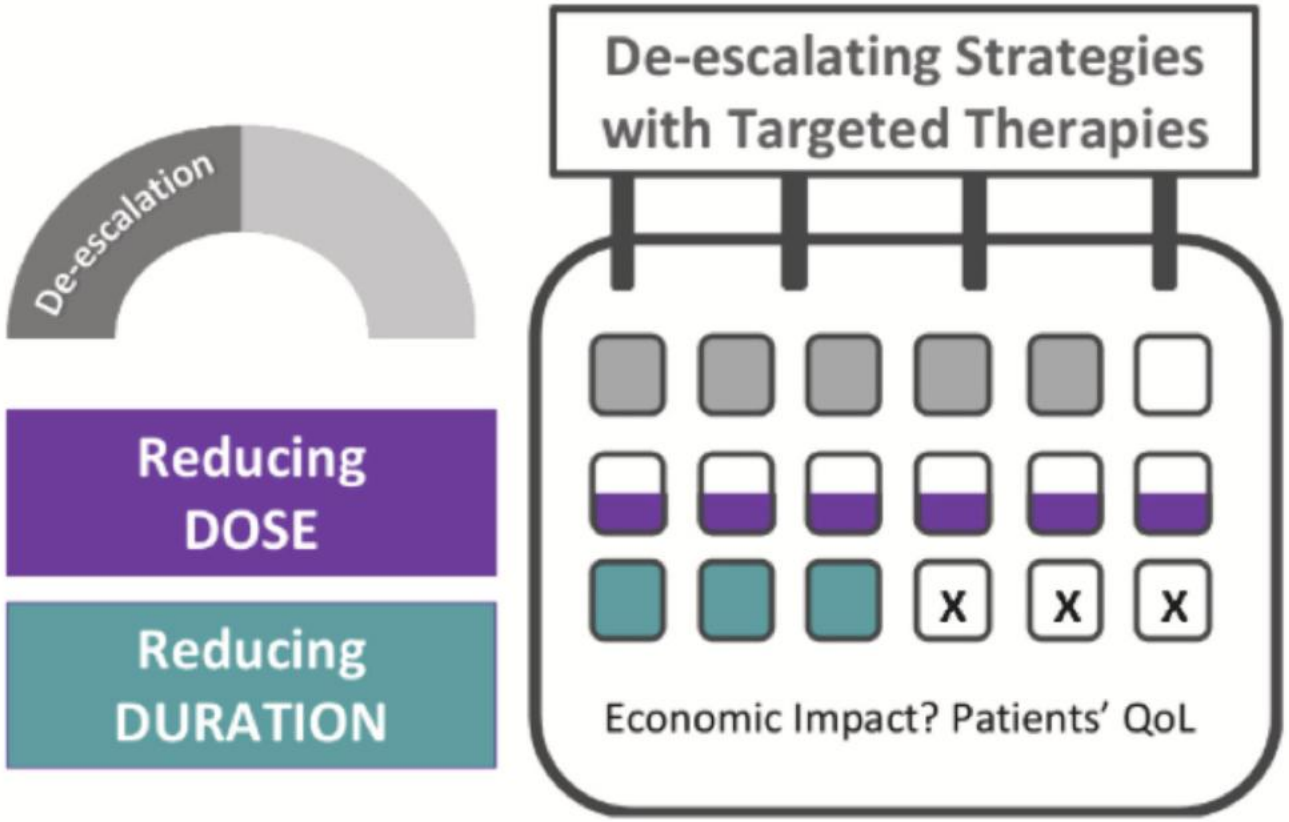
Sikkema JCO 2025
Heersche Cancer Comm 2024

OPTIMALISATIE VAN BEHANDELING





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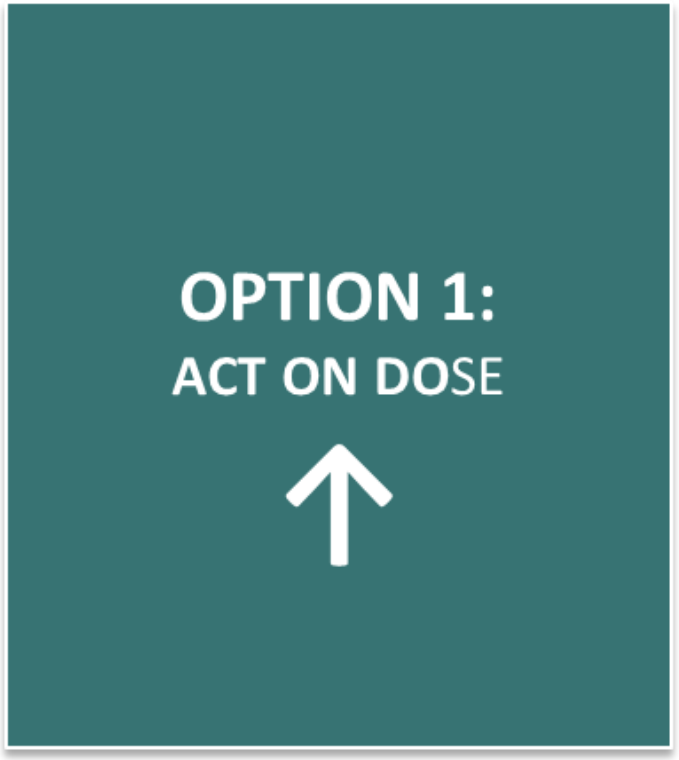
Bortolot Cancer Treatment Reviews 2025

Optimalisatie



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16
jan

NFU en Zorgverzekeraars Nederland sluiten transformatiedeal

De kosten van dure geneesmiddelen stijgen ontzettend snel. Zo snel dat de reguliere zorg onder druk komt te staan. Om gepast gebruik van dure geneesmiddelen te stimuleren hebben NFU en Zorgverzekeraars Nederland (ZN) de handen ineengeslagen in een unieke samenwerking: de Transformatiedeal Dure Geneesmiddelen. De deal werkt als een katalysator om het gebruik doelmatiger in te zetten, via initiatieven in alle umc's.

Externe link: https://jaarbeeld.2023-nfu.nl/dure-geneesmiddelen-en-dienstverlening/

GIDS-programma

Binnen het GIDS-programma (Geneesmiddel Initiatieven op Doelmatigheid & Spillagereductie) zetten de umc's en UMCNL in op gepast gebruik van dure geneesmiddelen. Dat gebeurt door optimaal te doseren, doelmatig voor te schrijven, verspilling tegen te gaan en onderzoek te doen naar nieuwe behandelstrategieën. Voorbeelden zijn dosisverlaging, intervalverlenging, eerder stoppen bij voldoende effect en heruitgifte van ongebruikte medicatie. Artsen en apothekers werken hierbij samen, met steun van Zorgverzekeraars Nederland en andere partners.

Het programma is inmiddels uitgegroeid tot een vliegwiel. De aanpak wordt steeds breder toegepast, in nauwe samenwerking met partners in de regio, zodat steeds meer patiënten hiervan profiteren. Het GIDS-programma laat zien dat samenwerking en onderzoek cruciaal zijn om dure geneesmiddelen duurzaam toegankelijk te houden voor alle patiënten in Nederland.

TRANSFORMATIE DEAL DURE GENEESMIDDELEN

- Erasmus MC apotheek: 25 geneesmiddelen met hoogste kosten
- Osimertinib, derde generatie EGFR-TKI
- Eerste lijn behandeling
- 1 dd 80 mg osimertinib

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1. Soria et al . N Engl J Med. 2018
2. Hendriks et al. Ann Oncol. 2025.
3. U.S. Food and Drug Administration, assessment report of osi

OSIMERTINIB

- No exposure (20-240 mg) – response relationship [1,]

	20 mg	40 mg	80 mg	160 mg	240 mg	Total
AURA-1 (second line, first/second generation EGFR-TKI resistant and T790M+) [3]						
ORR	50% (5/10) 95% CI, 19% to 81%	59% (19/32) 95% CI, 41% to 76%	70% (30/43) 95% CI, 54% to 83%	61% (17/28) 95% CI, 41 to 79%	50% (7/14) 95% CI, 23% to 77%	61% (78/127) 95% CI, 52% to 70%
Expansion cohort AURA-1 (treatment-naive) [16]						
ORR			67% (20/30) 95% CI, 47% to 83%	87% (26/30) 95% CI, 69% to 96%		77% (46/60) 95% CI, 64% to 87%
FLAURA-1 (treatment-naive, no CNS metastases) [1]						
ORR			81% (183/226) 95% CI, 75% to 86%			

1. Soria et al . N Engl J Med. 2018
2. Agema et al. Ther Adv. Med Oncol. 2018
3. Janne et al. N Engl. J Med. 2015
16. Ramalingam et al. J Clin Oncol. 2018.

- MEER BIJWERKINGEN BIJ HOGERE DOSIS[1]

Table 2. Adverse Events According to Daily Dose of AZD9291.*

Event	20 mg (N=21)	40 mg (N=58)	80 mg (N=90)	160 mg (N=63)	240 mg (N=21)	Total (N=253)
			number of patients (percent)			
Any adverse event	21 (100)	56 (97)	83 (92)	63 (100)	21 (100)	244 (96)
Any adverse event that was considered to be drug-related	14 (67)	38 (66)	71 (79)	59 (94)	21 (100)	203 (80)
Any adverse event of grade 3–5	6 (29)	21 (36)	26 (29)	24 (38)	5 (24)	82 (32)
Any adverse event of grade 3–5 that was considered to be drug-related	2 (10)	2 (3)	10 (11)	16 (25)	3 (14)	33 (13)

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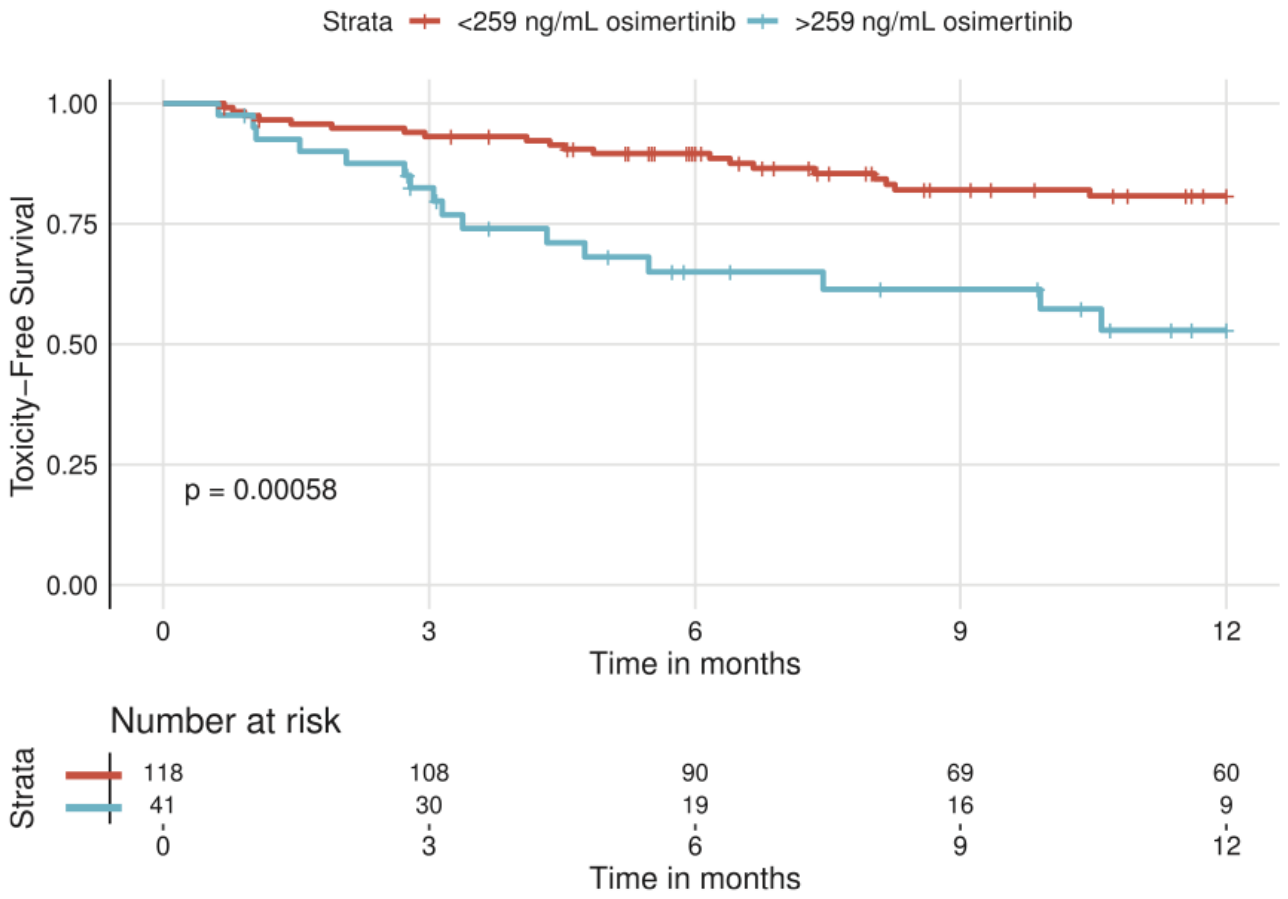
1. Soria et al . N Engl J Med. 2018
2. Agema et al. Ther Adv. Med Oncol. 2018
3. Janne et al. N Engl. J Med. 2015
16. Ramalingam et al. J Clin Oncol. 2018.

Improving the tolerability of osimertinib by identifying its toxic limit



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Agema Ther Adv Med Oncol 2022

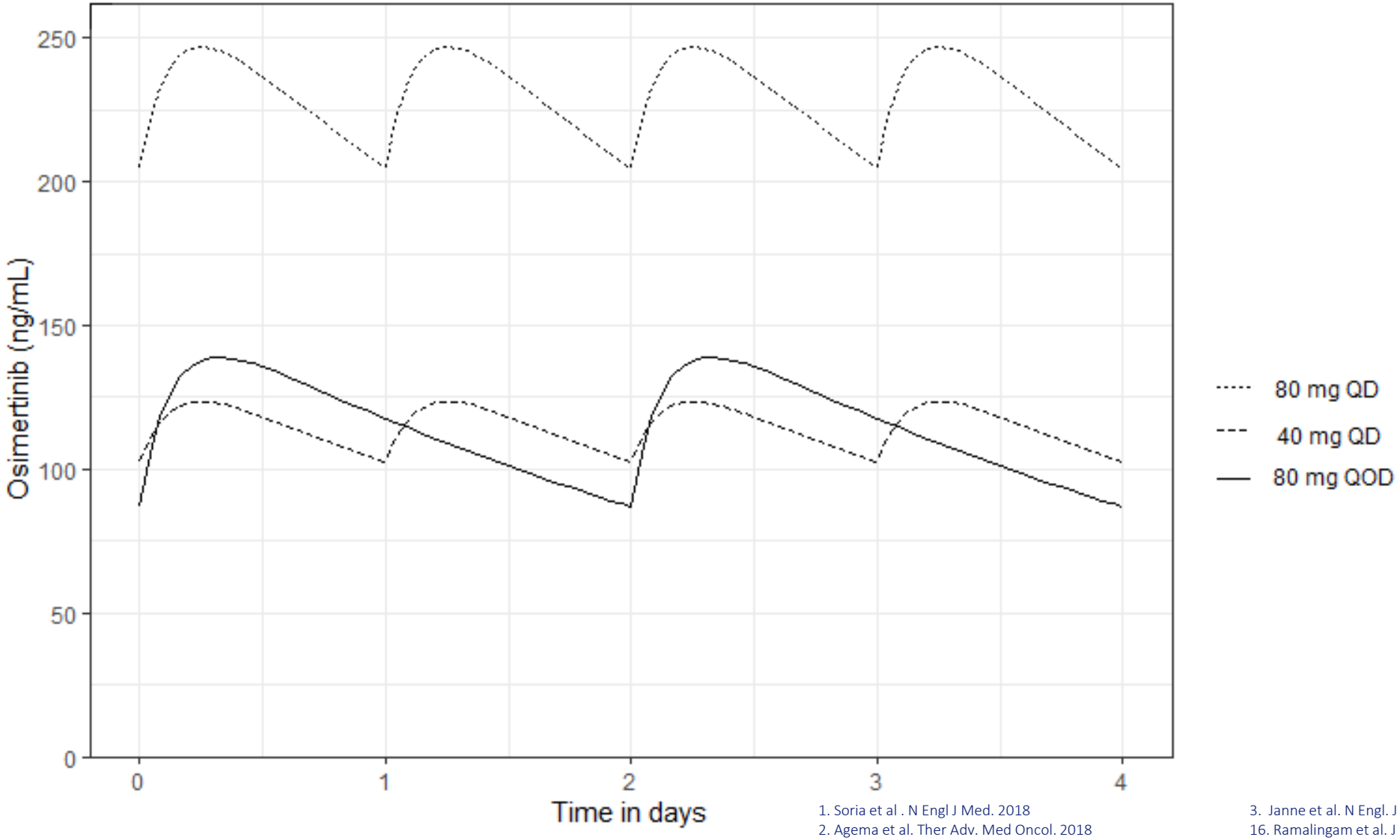
OSIMERTINIB APPROVED DOSE

- No exposure (20-240 mg) – response relationship [1, 3, 16]
- Distinct exposure-toxicity relationship [1,2, 3]
- Elimination half-life 44-48 hours -> AUC 40 mg QD = 80 QOD [1, 2]

- Costs
  - Osimertinib tablet 80 mg € 205,01 per tablet (~ € 6.250 pm, ~ € 75.033 py)
  - Osimertinib tablet 40 mg € 205,01 per tablet

1. Soria et al . N Engl J Med. 2018
2. Agema et al. Ther Adv. Med Oncol. 2018
3. Janne et al. N Engl. J Med. 2015
16. Ramalingam et al. J Clin Oncol. 2018.

ELIMINATION HALF-LIFE 44-48 HOURS -> AUC 40 MG QD = 80 QOD



1. Soria et al . N Engl J Med. 2018
2. Agema et al. Ther Adv. Med Oncol. 2018
3. Janne et al. N Engl. J Med. 2015
16. Ramalingam et al. J Clin Oncol. 2018.

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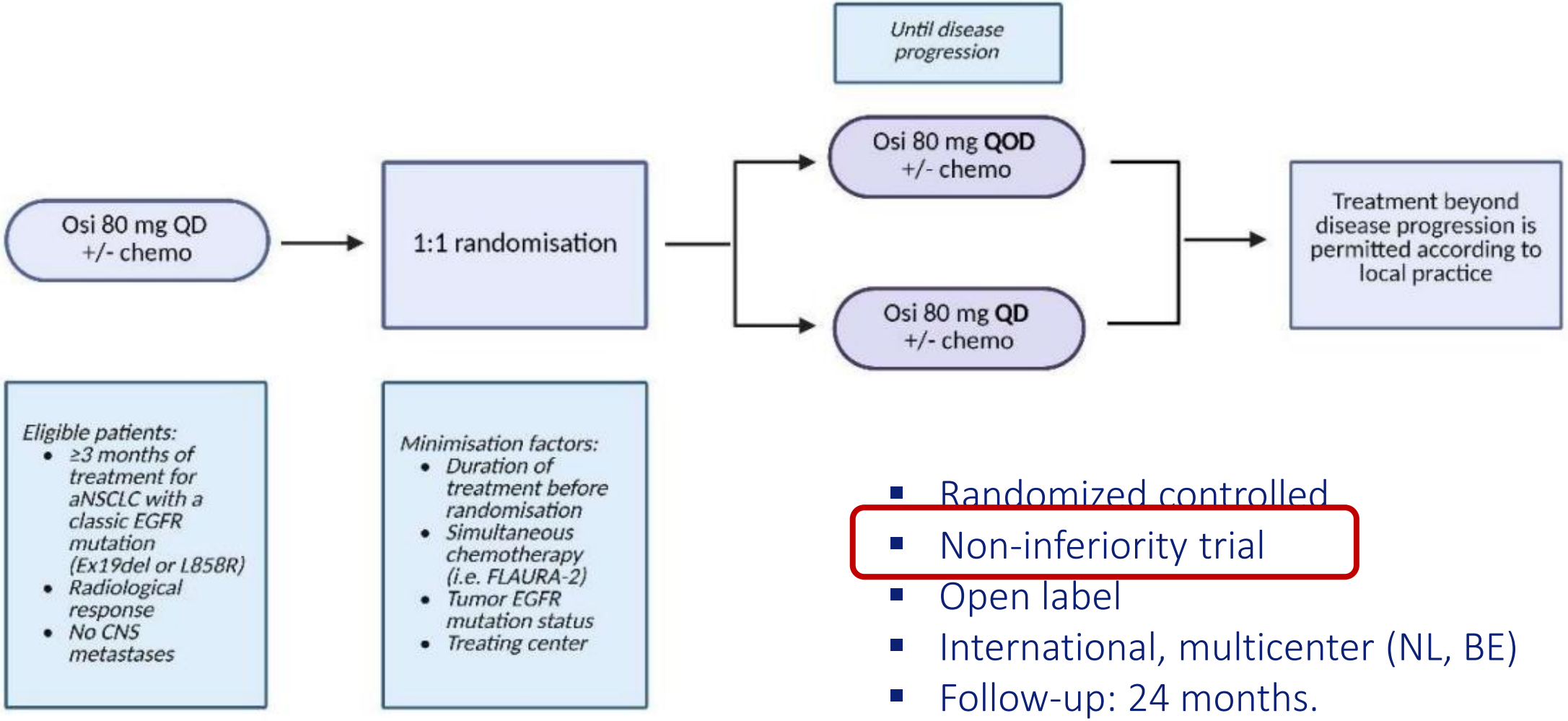
OSI-SAVE

OPTIMALISATIE



- Randomized controlled
- Non-inferiority trial
- Open label
- International, multicenter (NL, BE)
- Follow-up: 24 months.

STUDY PROCEDURES

Standard care

Every 3 months

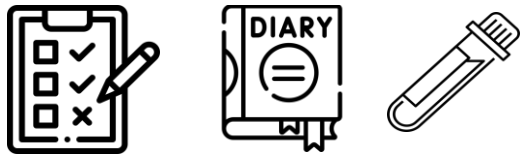
- Outpatient visit
- Regular blood draw
- CT thorax-upper abdomen
- MRI-cerebrum (once a year)

Study-related care

MANDATORY

Every 3 months

- Patient reported questionnaires
- Patient diary (or app)
- PK-levels (1st year)



Study-related care

OPTIONAL

Every 3 months

- ctDNA for ddPCR
- PG-analyses (one-time)
- PK-levels (2nd year)

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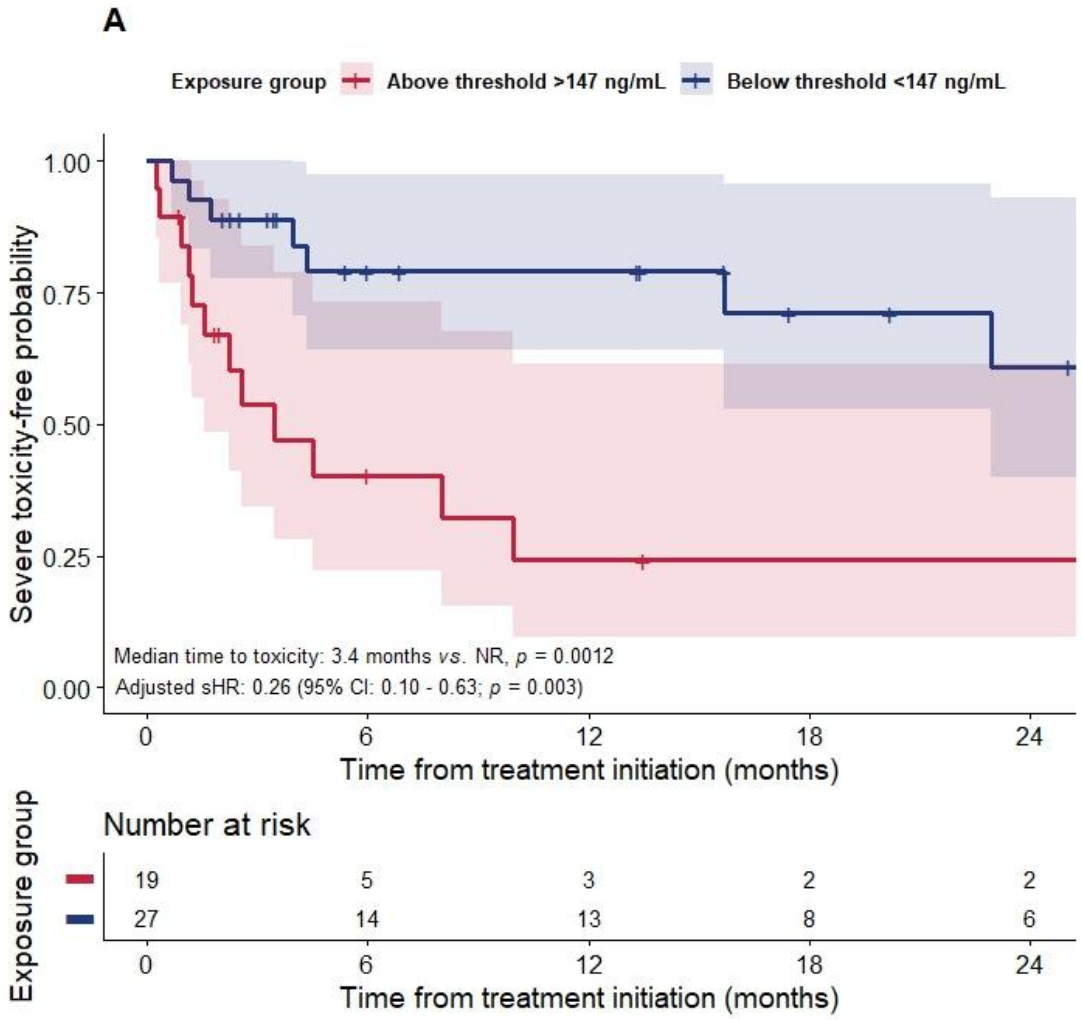
LORLATINIB EN BIJWERKINGEN



Hogere spiegel = meer bijwerkingen
Zelfde uitkomsten bij lagere dosis

Lanser JTO 2026 under revisiion

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OPTION 1:
ACT ON DOSE

OPTION 2:
ACT ON SCHEDULE

OPTION 3:
ACT ON DURATION

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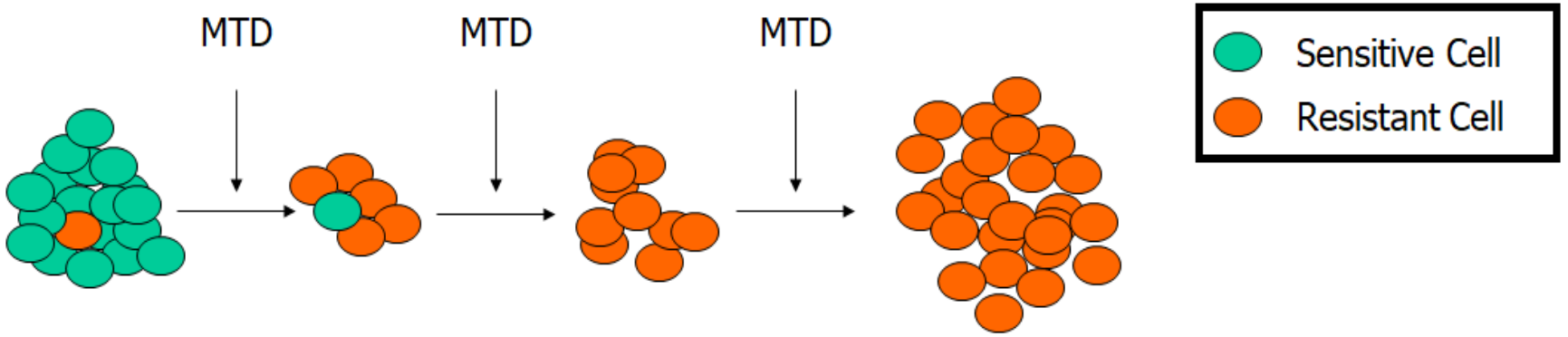
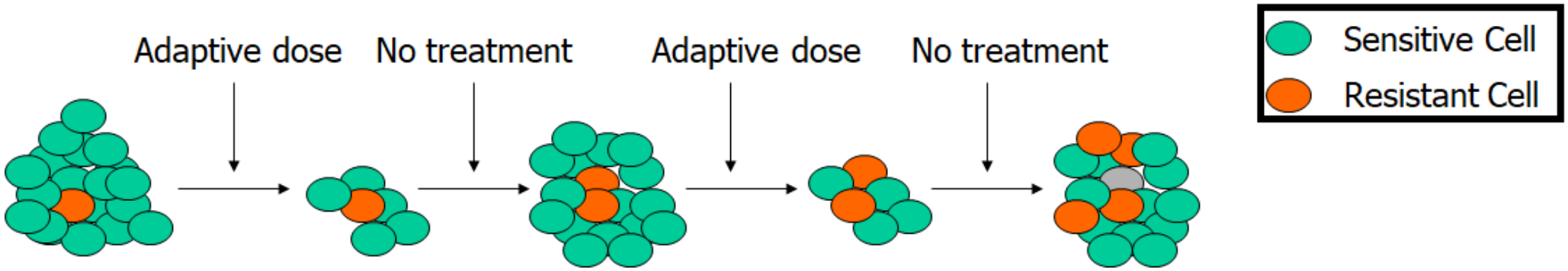
Evolutionary therapy

Standard of care in metastatic cancers: apply maximum tolerable dose (MTD)



Evolutionary therapy:

- based on game-theoretic models
- targets treatment-induced resistance
- outperforms Standard of Care in clinical trials



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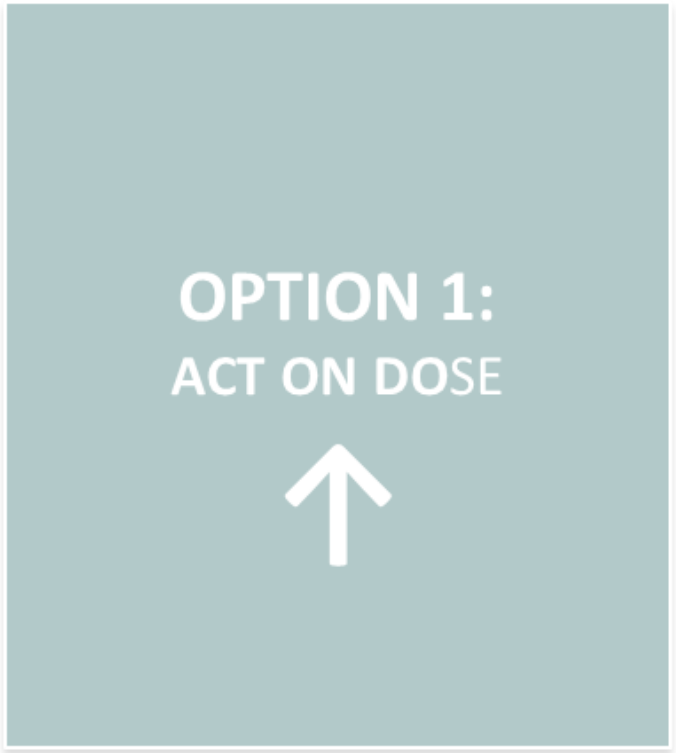
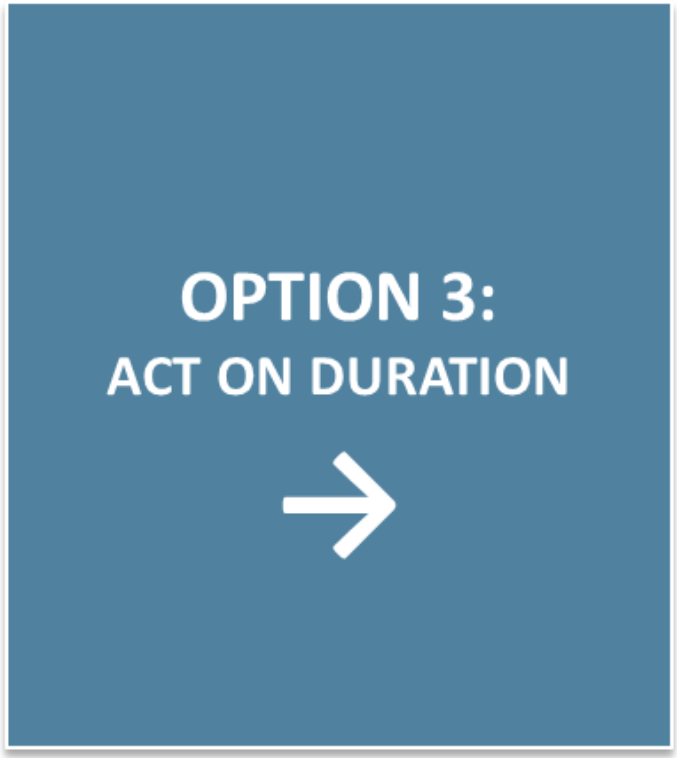
Staňková, *JAMA Oncology* 2019

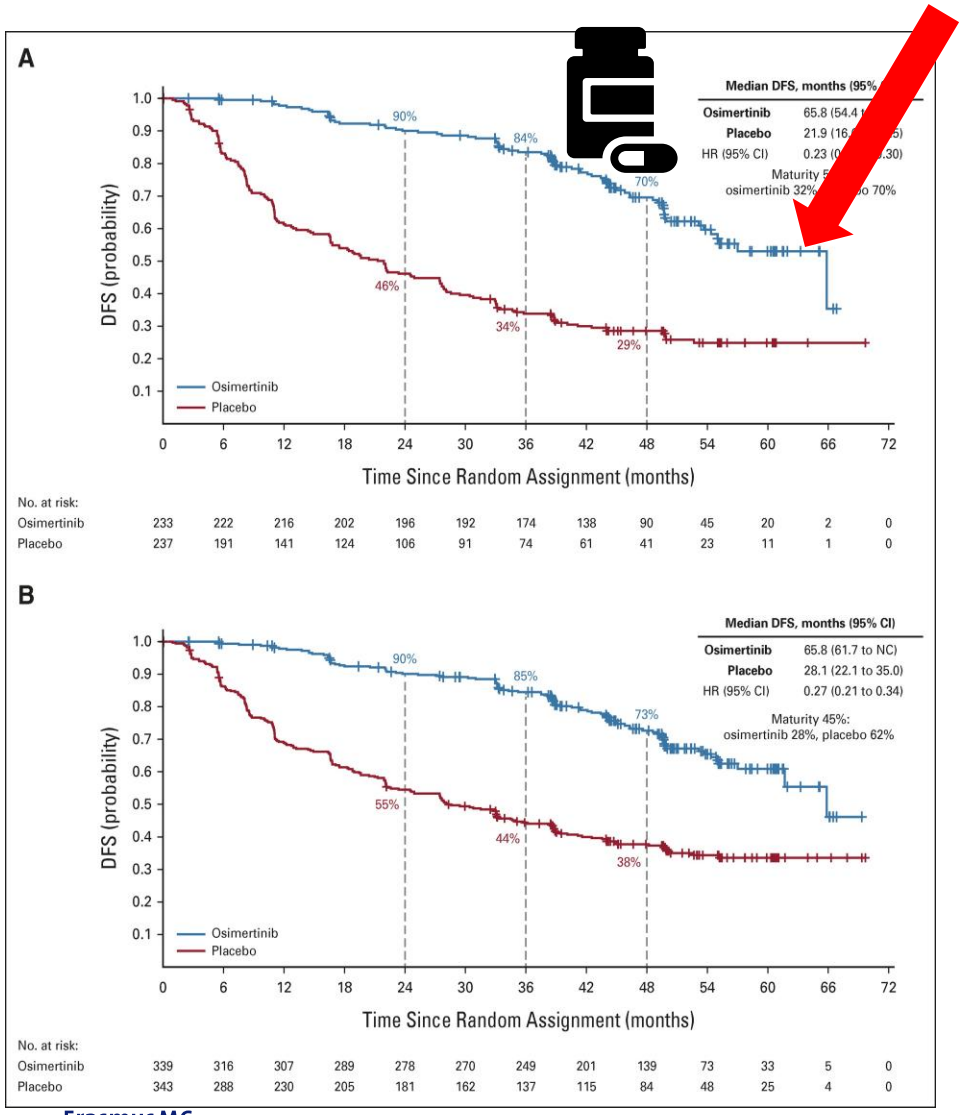
Staňková (2019) Resistance Games. *Nature Ecology and Evolution*

Optimizing treatment strategy





ADJUVANT OSIMERTINIB NA OPERATIE (ADAURA)



St II-IIIA

AEs[a]	Osimertinib (n = 337)	Placebo (n = 343)
Any AE	330 (98)	309 (90)
Any AE ≥ grade 3	79 (23)	48 (14)
Any SAE	68 (20)	47 (14)
Any AE with outcome of death[b]	1 (< 1)	2 (1)
Any AE leading to treatment discontinuation	43 (13)	9 (3)
Any AE leading to dose interruption	91 (27)	43 (13)
Any AE leading to dose reduction	42 (12)	3 (1)
Any AE causally related to study drug[c]	308 (91)	199 (58)
AE ≥ grade 3 causally related to study drug[c]	36 (11)	7 (2)
SAE causally related to study drug[c]	10 (3)	2 (1)
AE with outcome of death causally related to study drug[c]	0	0
AE leading to treatment discontinuation causally related to study drug[c]	35 (10)	5 (1)

St Ib-IIIA

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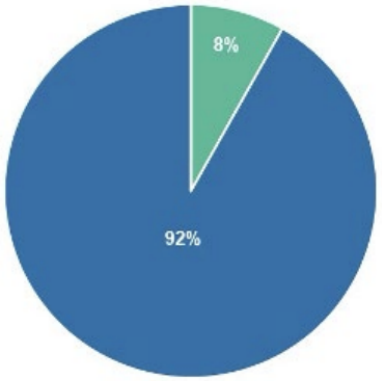
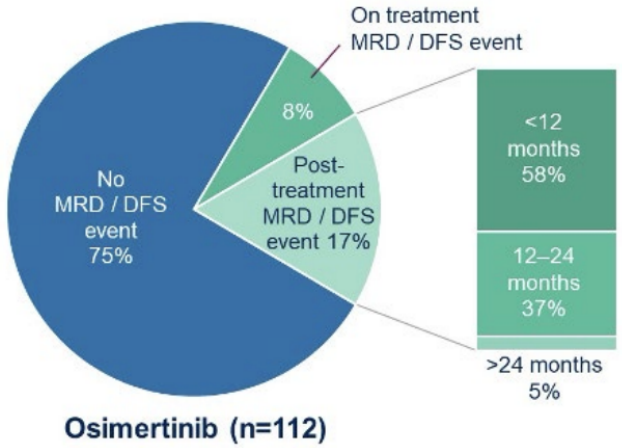
MRD: MINIMAL RESIDUAL DISEASE

MRD After Surgery



MRD During Treatment



Osimertinib (n=112)

MRD- ⟶ LOW RISK ⟶ DE-ESCALATION

MRD+ ⟶ HIGH RISK ⟶ ESCALATION

~90% relapse if untreated

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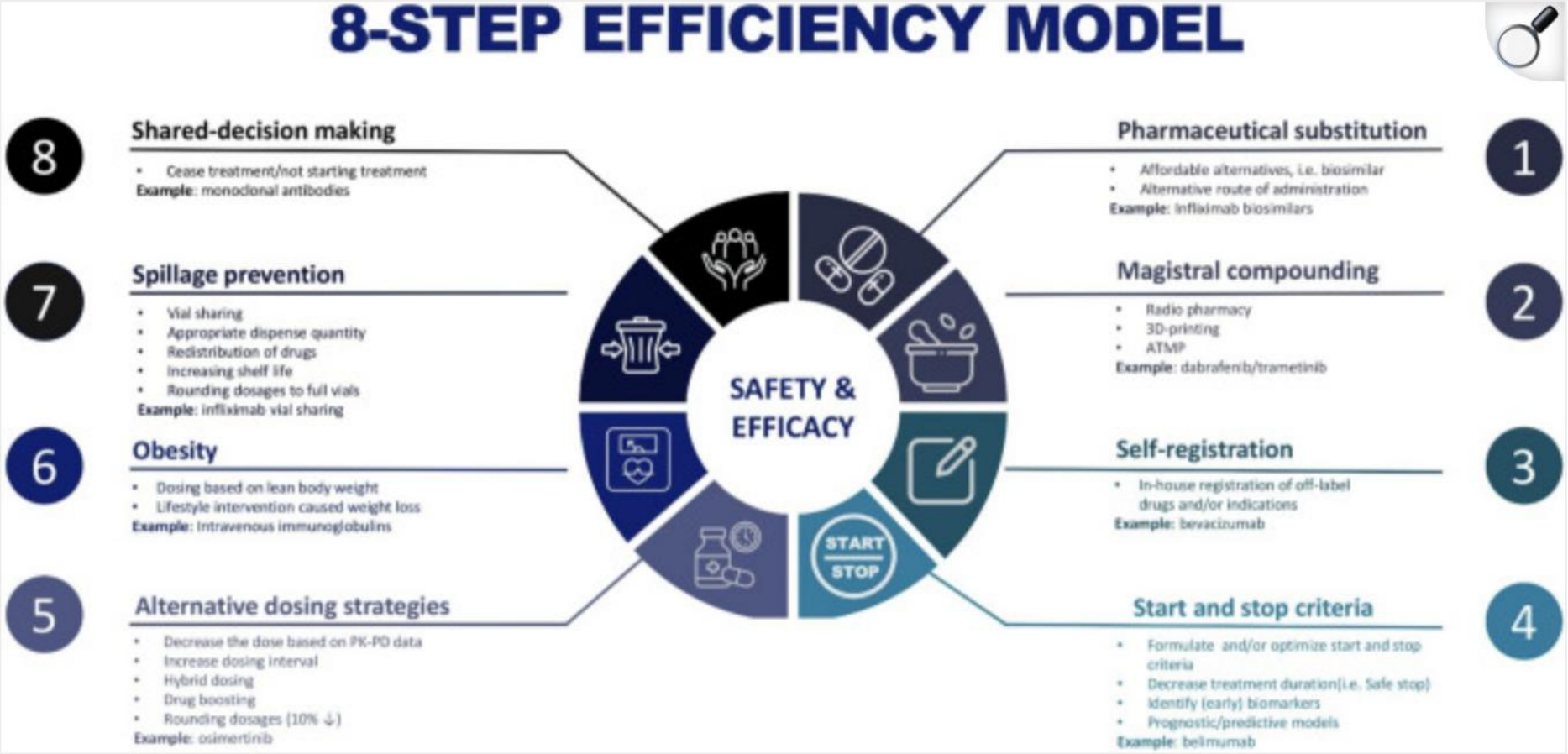
MAXIMALE DOSIS ≠ OPTIMALE DOSIS



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THANK YOU FOR LISTENING