Hoe werkt onderzoek en hoe kan ik eraan meedoen?

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	Boehringer
	Roche
	Lilly
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Betekenen de woorden onderzoek, trial en studie hetzelfde?

JA

Wanneer kan je aan een onderzoek meedoen?
Altijd of alleen als er geen bestaande behandeling meer voor je is?

- Alleen als er een studie is die bij uw situatie past.

Wat is het verschil tussen een fase 1, 2, 3 en 4 onderzoek?

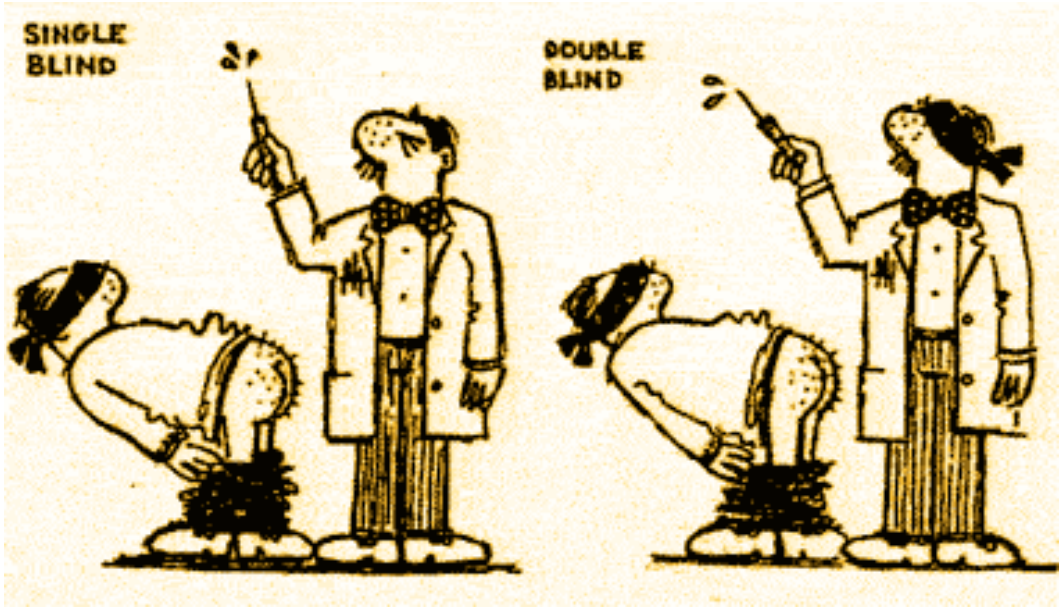
Vraagstelling

1. Veilige dosis? Bijwerkingen?
2. Hoe vaak krimpt de kanker?
3. Leef je langer?
4. ‘Post-marketing’

Aantal deelnemers

1. 3 tot 20
2. Tientallen
3. Honderden
4. Duizenden?

Wat betekent blind of dubbel blind onderzoek?



thejabberwock.org

Wat betekent blind of dubbel blind onderzoek?

fokkesukkearchief.nl

Wat kan meedoen aan een onderzoek mij opleveren?

- “U bent de eerste mens, die dit middel krijgt.”
- “De behandeling is prima, maar hiermee hopelijk nog beter.”

Wat kan voor mij een nadeel zijn om mee te doen aan een onderzoek?

Longkanker Nederland

- (altijd afweging maken o.a. wat kost meedoen aan tijd en wat levert het me mogelijk aan extra tijd op)

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Kan ik altijd meedoen aan onderzoek of zijn er speciale eisen?

- (o.a. graag uitleggen over de conditie van de patient ECOG score)

4.1 Inclusion Criteria

Subjects will be enrolled in this study only if they meet all of the following criteria:

1. Signed informed consent form (ICF) indicating an understanding of the purposes, risks, and procedures required for the study and willingness and ability to participate in the study.

   Subjects with a histologically confirmed diagnosis of pleural malignant mesothelioma, who are non-progressive (so CR, PR or SD) after 4 to 6 cycles with first line chemotherapy with antifolate/platinum (as determined by CT scanning). Subjects retreated with antifolate/platinum after a disease-free interval of 12 months after the first chemotherapeutic treatment are eligible. Concurrent bevacizumab during chemotherapy and during the first 6 weeks after completion of chemotherapy is allowed.
2. Subject must have signed informed consent within 8 weeks of their last chemo and the date of their informed consent must be such that all per protocol required procedures can be done in such a timeframe that the first treatment can be given within 9 and 13 weeks after their last chemotherapy.
3. Measurable disease has to be assessed by modified RECIST criteria on CT scanning by radiologic imaging. Even in the absence of measurable disease patients can be included in the study. In such case CT scanning will also be done to evaluate the disease.
4. Subjects must be at least 18 years old.
5. Subjects must have WHO-ECOG performance status of 0 or 1 (see Appendix 2).
6. Subjects must have adequate organ function and adequate bone marrow reserve at screening:
   - creatinine ≤ 1.5 × upper limit of normal [ULN] or glomerular filtration rate ≥ 50 mL/min
   - ALT, AST, bilirubin ≤ 1.5 × ULN
   - Absolute neutrophil count ≥1.5 x 10^9/L, platelet count ≥100 x 10^9/L, and Hb ≥9.0 g/dL.
7. Women of childbearing potential must have a negative serum pregnancy test at screening and a negative urine pregnancy test just prior to the first study drug administration on Day 1, and must be willing to use an effective contraceptive method (intrauterine devices, hormonal contraceptives, contraceptive pill, implants, transdermal patches, hormonal vaginal devices, infusions with prolonged release) or true abstinence (when this is in line with the preferred and usual lifestyle)* during the study and for at least 12 months after the last study drug administration.

*True abstinence is acceptable when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (such as calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.

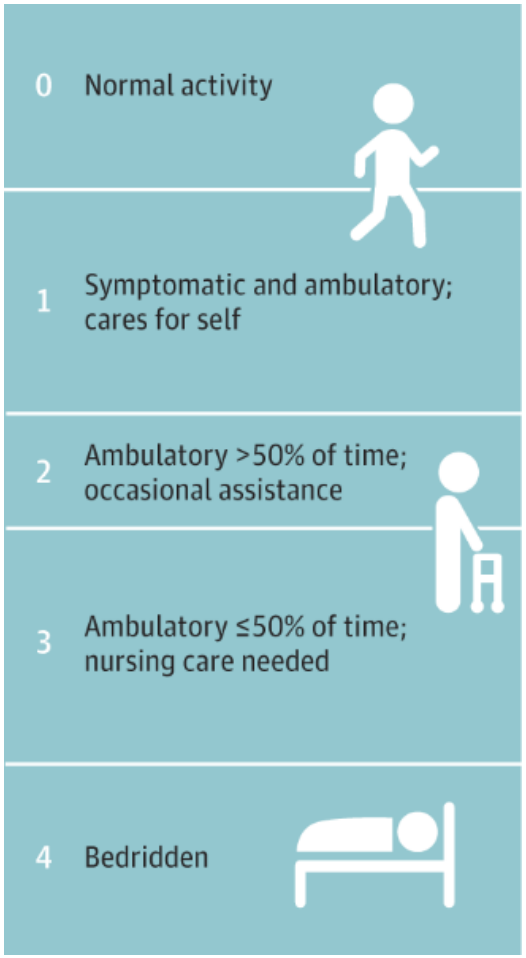
8. Men must be willing to use an effective contraceptive method (e.g. condom, vasectomy) during the study and for at least 12 months after the last study drug administration.
9. Subjects must be willing and able to follow the protocol requirements and must be willing and able to return to the study center for adequate follow-up visits.

4.2 Exclusion Criteria

Subjects will not be enrolled in this study if they meet any of the following criteria:

1. Subject with any concurrent medical, psychological or psychiatric disease or condition that is likely to interfere with study procedures or results, or that in the opinion of the investigator would constitute a hazard for participating in this study.
2. Subject with any serious intercurrent chronic or acute illness such as cardiac (New York Heart Association [NYHA] Class III or IV; see Appendix 3) or hepatic disease or other serious concomitant disease considered by the investigator to constitute an unwarranted high risk for investigational dendritic cell treatment.
3. Subject with any known active serious infection, including human immunodeficiency virus (HIV), hepatitis B or C virus, or syphilis infection.
4. Subject with a history of autoimmune disease, except for diabetes mellitus type I or other conditions, where patient can be eligible following discussion with medical monitor.
5. Subject who has received an organ allograft.
6. Subject with any previous malignancy except adequately treated basal cell or squamous cell skin cancer, superficial or *in-situ* cancer of the bladder or other cancer for which the subject has been disease-free for at least 3 years.
7. Subject with a known allergy to shell fish (may contain KLH).
8. Pregnant women, nursing mothers, lactating women, and women of child-bearing potential who are unwilling to use effective contraceptive methods (intrauterine devices, hormonal contraceptives, contraceptive pill, implants, transdermal patches, hormonal vaginal devices, infusions with prolonged release) during the study and for at least 12 months after the last study drug administration.
9. Subject with inadequate peripheral vein access to perform leukapheresis.
10. Use of >10 mg of steroids (or other immunosuppressive agents) during the past 6 weeks before the first study drug administration and throughout the study. Prophylactic usage of dexamethasone during chemotherapy is excluded from this 6-week interval. Inhaled or topical steroids, and adrenal replacement steroid ≤10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease.
11. Treatment with any investigational product within 4 weeks or 5 half-lives (whichever is longer) before the first study drug administration or concomitant participation in another clinical study.
12. Subject who is unwilling or unable to follow the protocol requirements, including availability for follow-up assessment.

De WHO-ECOG schaal



0. mankeert niets
1. hele dag in de weer
2. meeste tijd in de weer
3. meest in bed/op bank
4. bedlegerig

jamanetwork.com

Als er in het ziekenhuis waar ik behandeld word geen behandeling meer mogelijk is.
Hoe weet ik dan in welk ziekenhuis er mogelijk een onderzoek is waar ik aan mee kan doen?

- Vraag uw arts

- (Voor jou goed om te weten dat wij in de praktijk merken dat niet elk ziekenhuis/elke arts de moeite doet of tijd heeft om bij een collega ziekenhuis hiernaar te informeren, of maar bij 1 ziekenhuis informeert. Wanneer dat zo is, dan kunnen patiënten het ook aan ons vragen, dan nemen wij contact op met de academische ziekenhuizen of het AvL om te vragen of er een geschikte studie voor de patient is. Jammer dat dit nodig is overigens)

Zijn er in andere landen onderzoeken die niet in Nederland zijn? Hoe vind ik die?

clinicaltrials.gov

Bad Elster

Kurort Piestany

Wat is het risico als ik daaraan mee wil doen?

Als ik in een ander ziekenhuis mee doe aan een onderzoek. Lopen dan ook alle controles nu via dat nieuwe ziekenhuis of kan dat bij mijn eigen longarts?

- Alle studiehandelingen moeten in het ziekenhuis dat de studie doet.

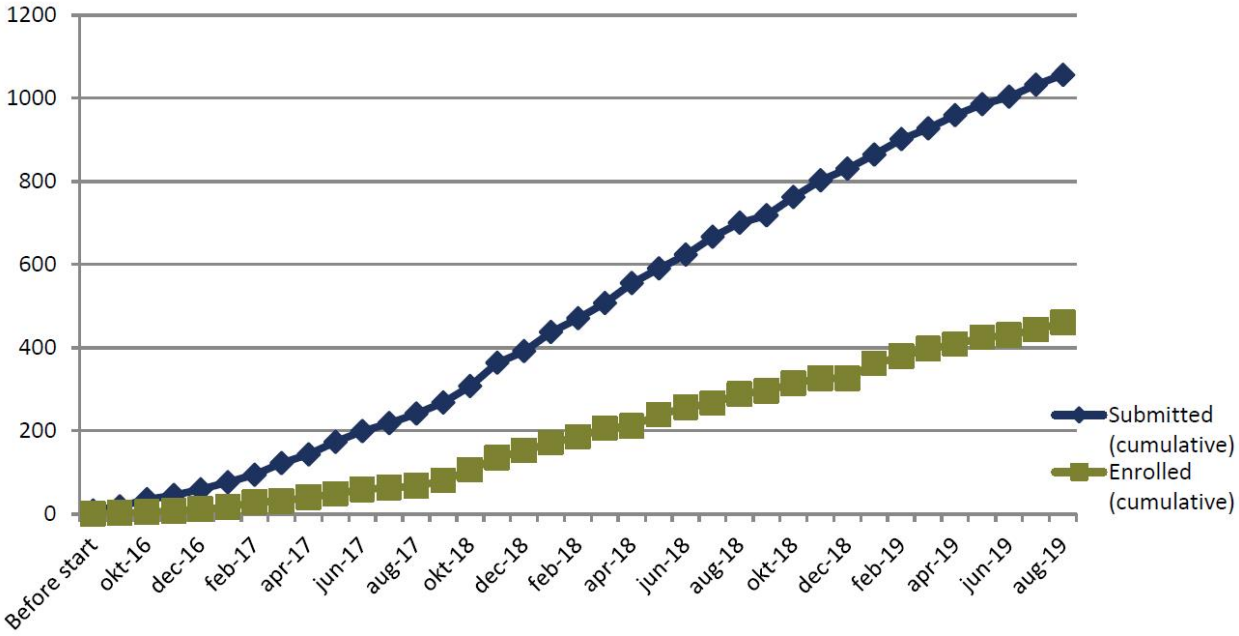
Moeten onderzoeken zoals scans en een biopt die bij mij al gedaan zijn opnieuw worden gedaan als ik aan een onderzoek mee doe?

Wat is de DRUP studie?

Wat zijn voor mij voordelen of nadelen om daaraan mee te doen?

DRUP: Nederlandse studie

CURRENT STUDY STATUS



1056 submitted cases
(as per September 1st 2019)

Enrolled: 460 (44%)
Pending: 29 (3%)
Not eligible: 571 (53%)

- 37 participating hospitals
- 129 opened cohorts
- 25 different drugs

BARCELONA 2019 ESMO congress

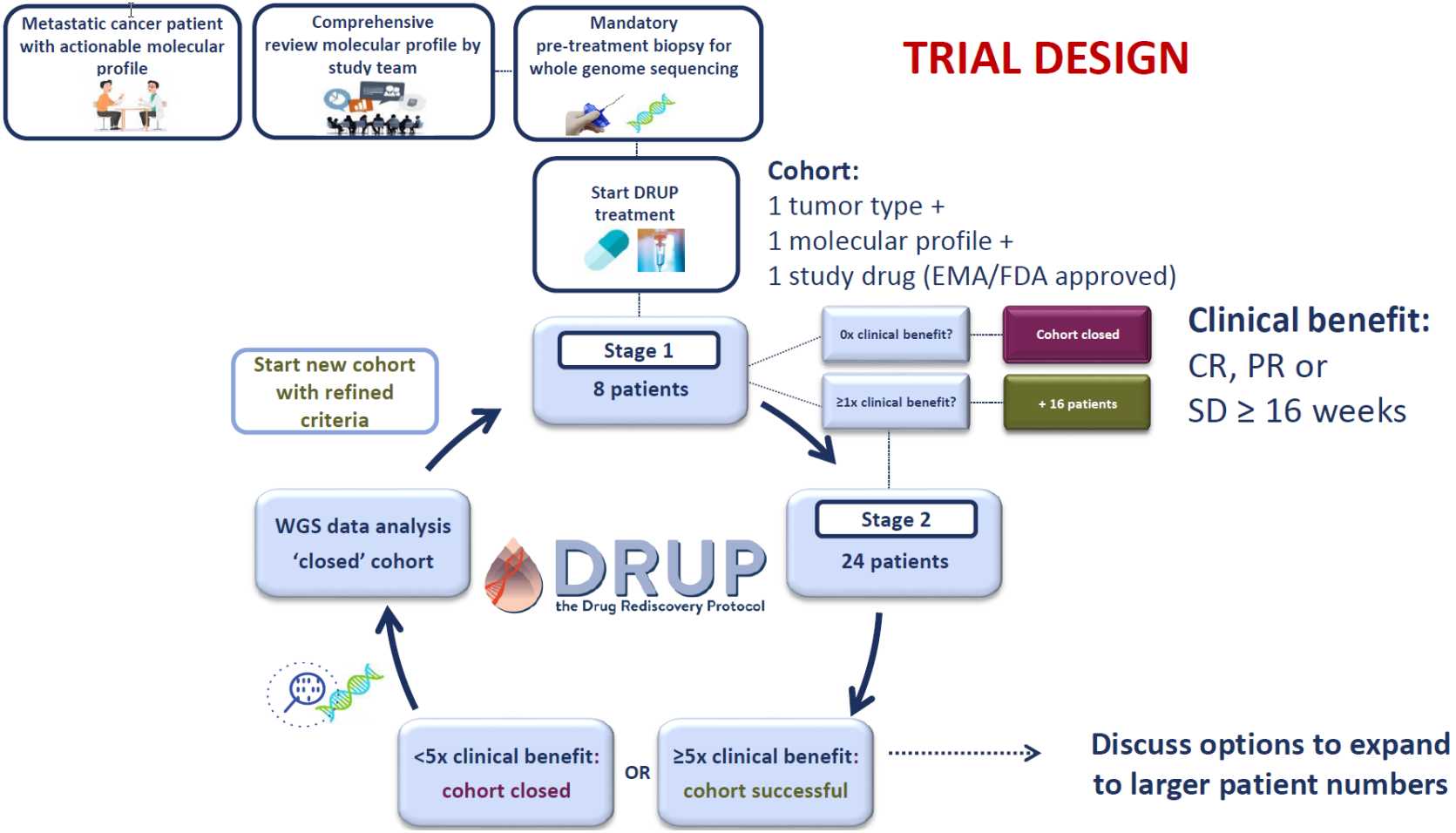
Voest, ESMO Barcelona 2019

DRUP: overwegingen bij de start

- Mutaties kunnen een kanker gevoelig maken voor een geneesmiddel.
- Het hangt af bij welk type kanker de mutatie aangetroffen wordt
- De DRUP kijkt naar het effect “doelgerichte middelen” bij andere tumortypen dan die waarbij al affect is aangetoond

Voest, ESMO Barcelona 2019

Studie-opzet



Gegevens van al 20 middelen bekend

DATA ARE PRESENTED FOR 20 DIFFERENT APPROVED DRUGS

- FDA and / or EMA approved drugs (or under revision)
- Targeted and / or immunotherapies
- Drug portfolio is constantly being expanded.

Supplier	Drug		Indications	Available
Amgen	Panitumumab	+	BRAF-KRAS-NRAS wild type tumors	September 2016
		-	Patients eligible for on-label panitumumab and BRAF-KRAS-NRAS mutated tumors	
AstraZeneca	Olaparib	+	ATM, BARD1, BRCA1/2, BRIP1, CDK12, CHEK1/2, FANCL, PALB2, PP2R2A, RAD51B/C/D, RAD54L inactivating mutations	September 2016
		-	Patients eligible for on-label olaparib or for the MEDIOLA, POLO, PROFOUND, REVIVAL or SUBITO trial.	
Bayer	Regorafenib	+	BRAF, CSF1(R), FLT1/4, KDR, KIT, PDGFRβ, RAF1, RET activating mutations, amplifications, fusion or overexpression	September 2016
		-	Patients eligible for on-label regorafenib	
Boehringer Ingelheim	Afatinib	+	ERBB4 activating mutations or NRG1 activating mutations or fusions in non-small cell lung cancer	September 2017
		-	All tumor types and profiles not fulfilling the subscription above	
Bristol-Myers Squibb	Nivolumab	+	High mutational load or micro-satellite instable tumors, with MLH1, MSH2/6 or PMS2 mutations or non-expression	September 2016
		-	Patients eligible for on-label nivolumab	
Eisai	Lenvatinib	+	FGFR1/2/3/4 activating mutations, amplifications or fusions	October 2017
		-	Patients eligible for on-label lenvatinib	
Merck Sharp & Dohme	Pembrolizumab	+	High mutational load tumors	September 2017
		-	Patients eligible for on-label pembrolizumab and multiple myeloma	
Novartis	Dabrafenib	+	BRAF V600D/E/K/R activating mutations	September 2016
		-	Patients eligible for on-label dabrafenib or for the ROAR trial, and tumors with MAP2K1/2 or NRAS mutations	
	Nilotinib	+	+ ABL1, KIT, PDGFRα, PDGFRβ activating mutations	September 2016
		-	Patients eligible for on-label nilotinib, or for the SUSTRENIM or NAUT trial	
	Trametinib	+	MAP2K1/2/4, MAP3K1 or NRAS activating mutations	November 2016
		-	Patients eligible for on-label trametinib or for the KRAS trial	
Pfizer	Axitinib	+	FLT1/4 or KDR activating mutations, amplifications or overexpression	October 2017
		-	Patients eligible for on-label axitinib	
	Crizotinib	+	ALK, MET, MST1R, ROS1 activating mutations, amplifications, fusions or overexpression	October 2017
		-	Patients eligible for on-label crizotinib, and tumors with known ALK-resistance mutations	
	Sunitinib	+	CSF1R, FGFR1/2/3, FLT1/3/4, KDR, KIT, PDGFRα/β, RET, activating mutations, amplifications, fusions or overexpression	October 2017
		-	Patients eligible for on-label sunitinib, and tumors with KIT D842V mutations	
	Palbociclib	+	CCND1, CDK4(R24)/6, FLT3, PIK3R4, GSK3b activating mutations, amplifications or overexpression. CDKN2A inactivating mutations.	August 2018
		-	Patients eligible for on-label palbociclib.	
Roche	Erlotinib	+	EGFR activating mutations or exon 19 deletions in the region E746_E759	September 2016
		-	Patients eligible for on-label erlotinib, and tumors with known EGFR-resistance mutations	
	Trastuzumab and pertuzumab	+	ERBB2 activating mutations, amplifications exon 20 insertions or overexpression	September 2016
		-	Patients eligible for on-label trastuzumab + pertuzumab or for the KAMELEON trial	
	Vemurafenib and cobimetinib	+	BRAF V600D/E/K/R activating mutations	September 2016
		-	Patients eligible for on-label vemurafenib + cobimetinib, and tumors with MAP2K1/2 or NRAS mutations	
	Vismodegib	+	PTCH1 activating mutations	September 2016
		-	Patients eligible for on-label vismodegib, and tumors with known SMO-resistance mutations or with GLI2 amplification	

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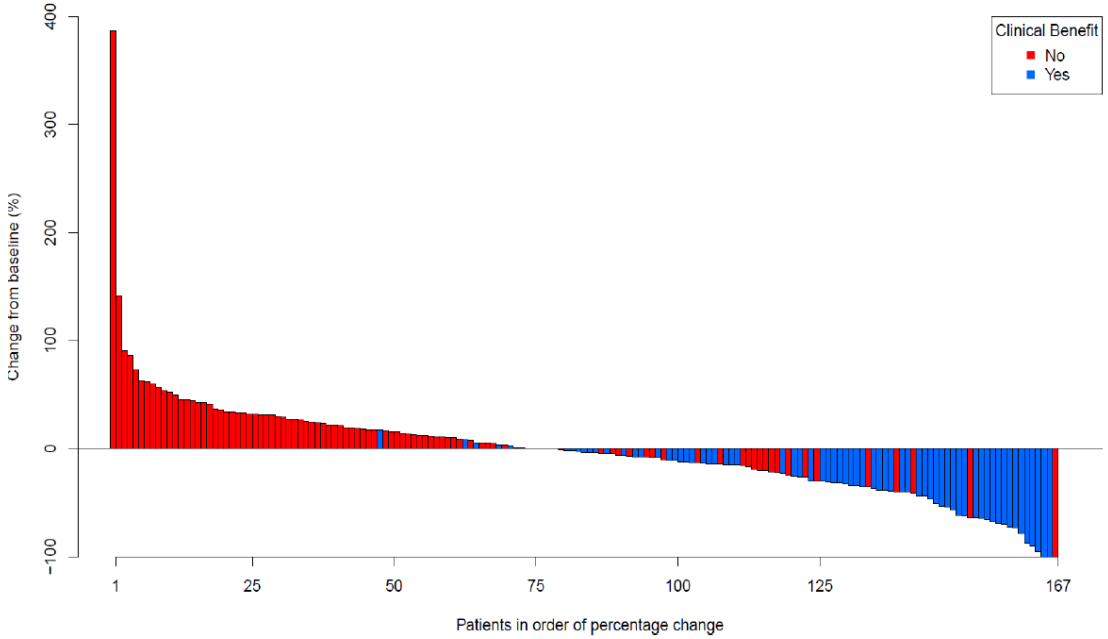
En werkt het?

CLINICAL BENEFIT WAS OBSERVED IN 34% OF THE 215 TREATED PATIENTS



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Clinical benefit was observed across all treatment types:

- immunotherapy (*n*=79; CB=38%)
- small molecule (including PARP) inhibitors (*n*=81; CB=36%)
-
- monoclonal antibodies (*n*=55; CB=27%)

Van der Velden, ... Voest; Nature 2019

Dank voor uw aandacht

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