PROSPECTIEF
LANDELIJK
CRC COHORT

Learning from each patient with colon cancer

Geraldine Vink
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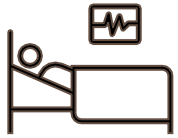
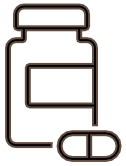
IKNL / UMC Utrecht

How do you learn from every patient?



biomarkers

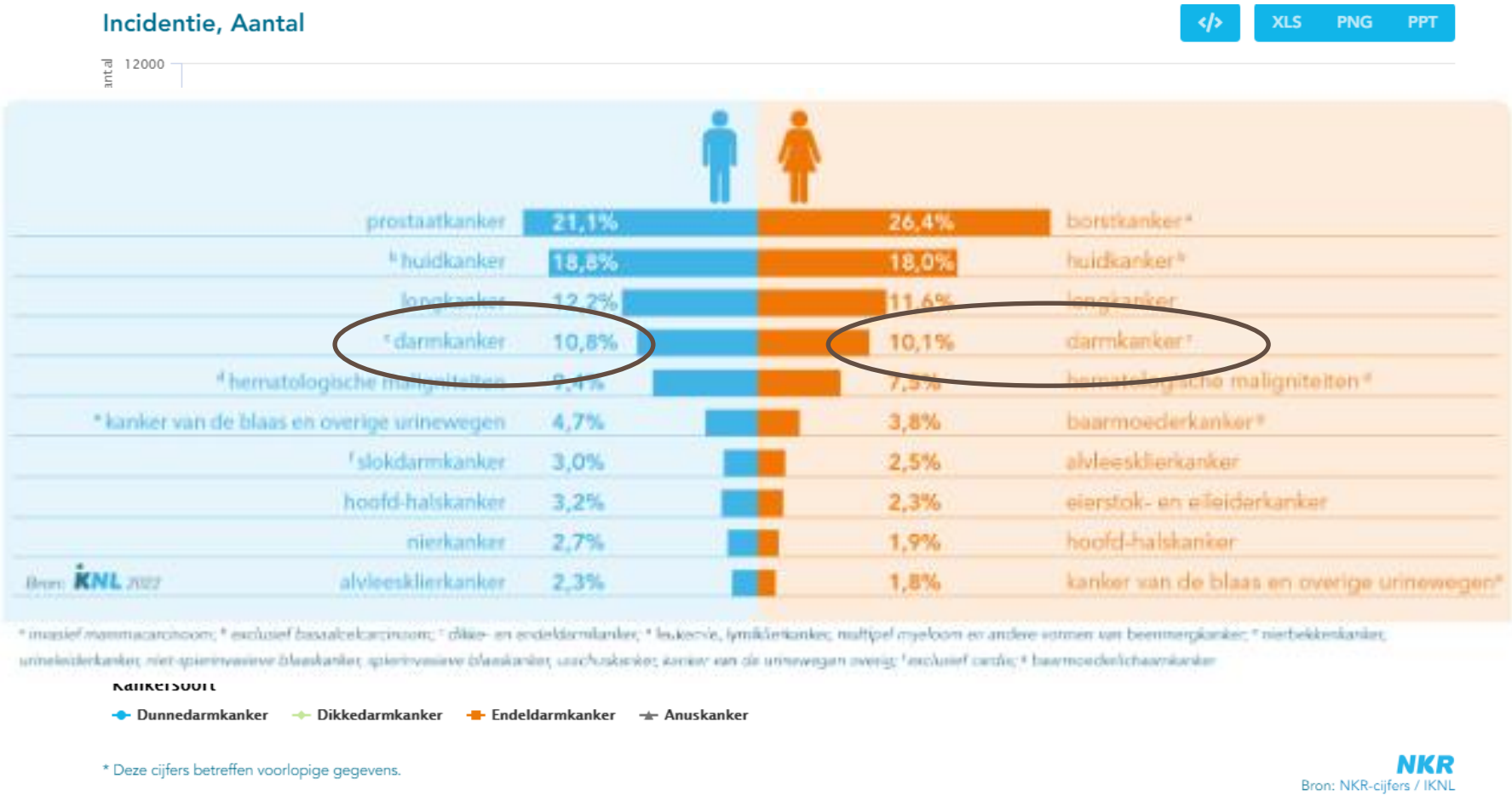


Medication

What do you want to know?

Some background

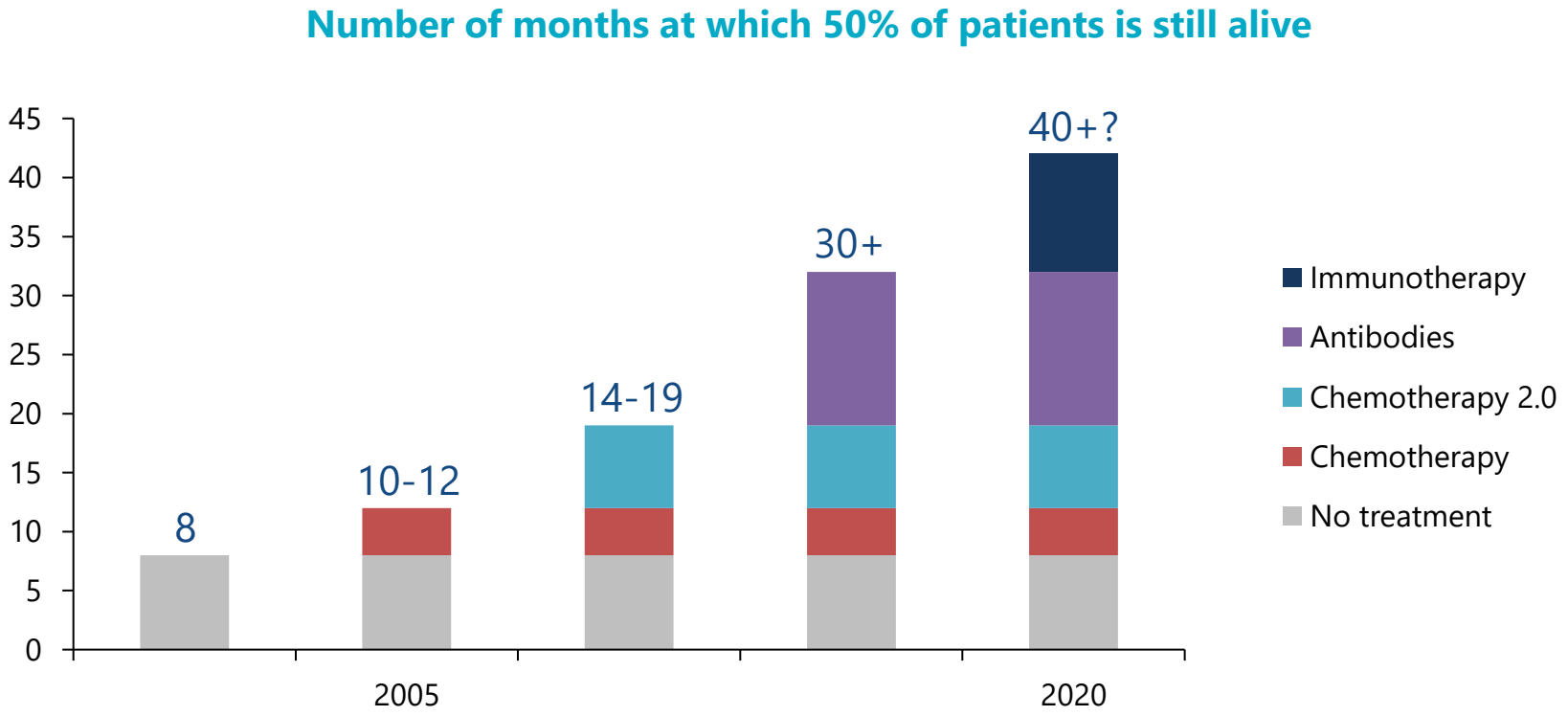
Incidence of colorectal cancer



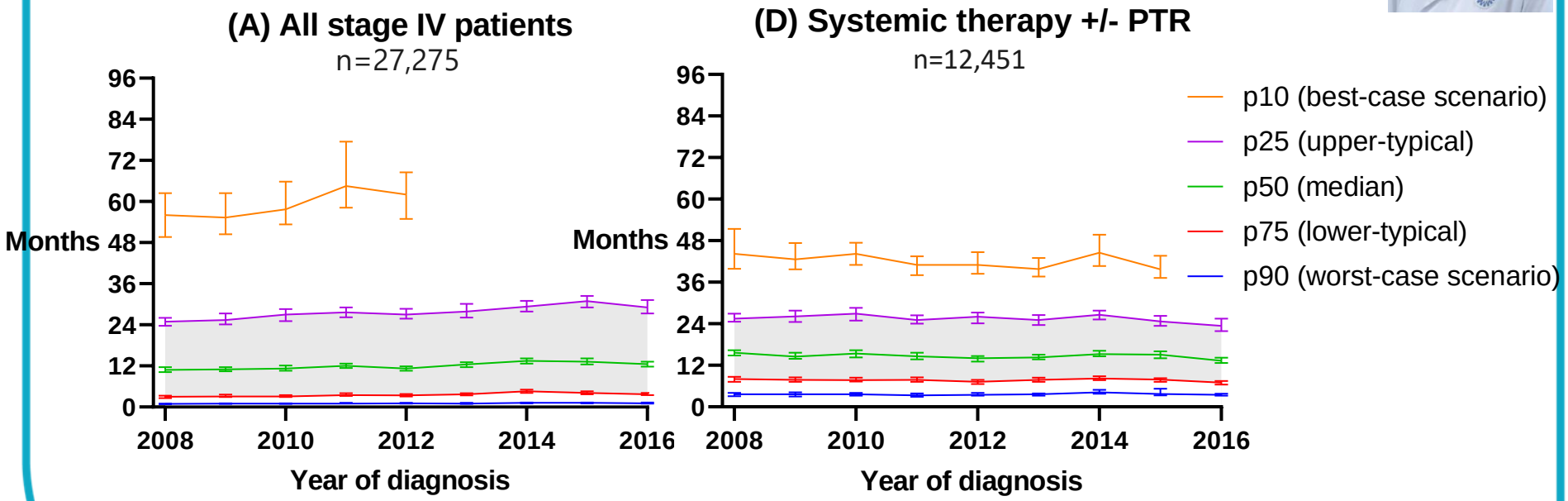
* Deze cijfers betreffen voorlopige gegevens.

NKR
Bron: NKR-cijfers / IKNL

mCRC: Increasing treatment options leading to improved survival



Real world data mCRC – Netherlands -
Overall survival in months for different percentiles of patients over time



*For some patients, survival time exceeded follow-up duration. mCRC=metastatic colorectal cancer; PTR = primary tumor resection

Hamers et al. Int J Cancer 2020


PROSPECTIEF
LANDELIJK
CRC COHORT

Prospective Dutch CRC cohort

Goal

To further personalize colorectal cancer treatment to achieve better outcomes with regard to prognosis and quality of life in (future) CRC patients

"In this way we can easily contribute to improving care that will benefit future patients"

(nurse in a participating hospital)

Unique design

Prospective Dutch Colorectal Cancer Cohort study (PLCRC)
all patients diagnosed with colorectal cancer (Stage I-IV)

Observational studies:


Clinical data


Tissue


Blood


PROMs

Interventional studies:

Trials within cohorts (TwiCs)

nationwide infrastructure
for research

1. Burbach M et al. *Acta Oncologica* 2016; 2. Coebergh van den Braak R et al. *Acta Oncologica*. 2018; 3. Derksen J. et al. *Nature Rev Clin Oncol* 2019;9:589.

Prospective Dutch CRC cohort

Who

Population: all patients with

CRC (stage I t/m IV)
small bowel cancer
anal cancer

who are seen in a participating center

Inclusion criteria:

- colorectal cancer (incl. appendix), small bowel cancer, or anal cancer, and
- ≥ 18 year
- mentally competent

Informed consent

- Ik geef toestemming voor het opvragen en het door de betreffende instelling beschikbaar stellen van mijn **relevante medische gegevens** ten behoeve van dit onderzoek.

- Ik geef toestemming voor het ontvangen van **vragenlijsten**.

O Ja O Nee

Zo ja, dan ontvang ik deze het liefst:

O Online → E-mailadres: _____

O Op papier

- Ik geef toestemming om mij te vragen voor **nieuw onderzoek** naar bijvoorbeeld een nieuwe experimentele behandeling, ondersteunende therapie of aanvullend onderzoek.

O Ja O Nee

- Ik geef toestemming voor het verzamelen en gebruiken van mijn **weefsel of ander lichaamsmateriaal** op de manier en voor de doelen die in de informatiebrief staan.

O Ja O Nee

- Ik geef toestemming voor het verzamelen en gebruiken van mijn **bloed** op de manier en voor de doelen die in de informatiebrief staan.

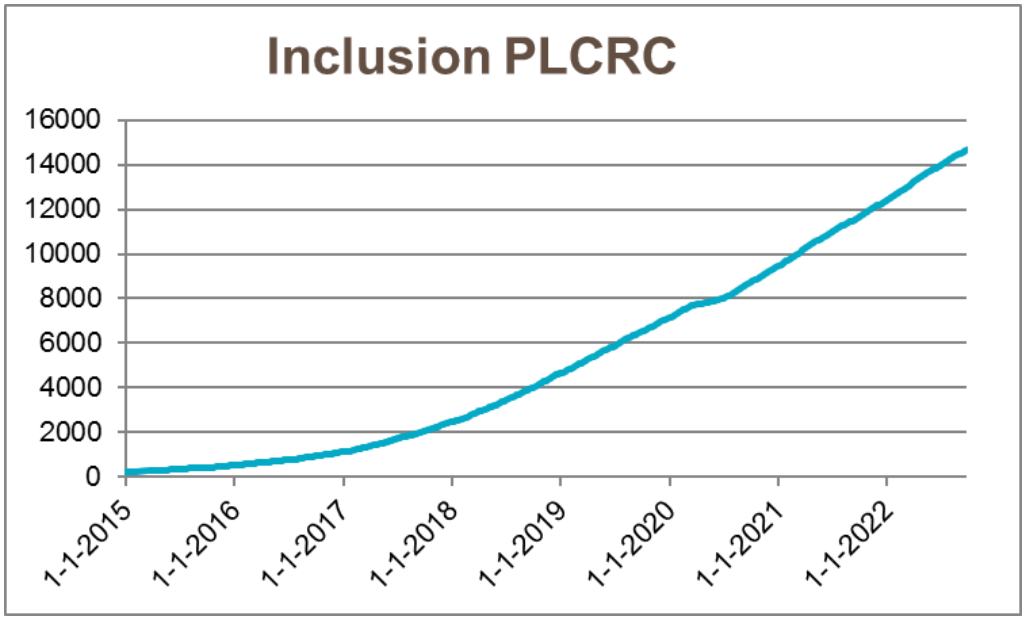
O Ja O Nee

- Ik geef toestemming om, via mijn behandelend arts, geïnformeerd te worden over eventuele **toevalsbevindingen** die in mijn bloed, tumorweefsel of ander lichaamsmateriaal zijn gevonden. Indien bevindingen directe gevolgen kunnen hebben voor mijn behandeling, wordt mijn arts altijd geïnformeerd.

O Ja O Nee

Prospective Dutch CRC cohort

- Number of included patients: 14.600
- Centers open for inclusion: 63



Prospective Dutch Colorectal Cancer Cohort study (PLCRC)

informed consent

> *"I want to help future patients, for example my own children. That is why I want to participate."*
> - Participant PLCRC

Challenge:

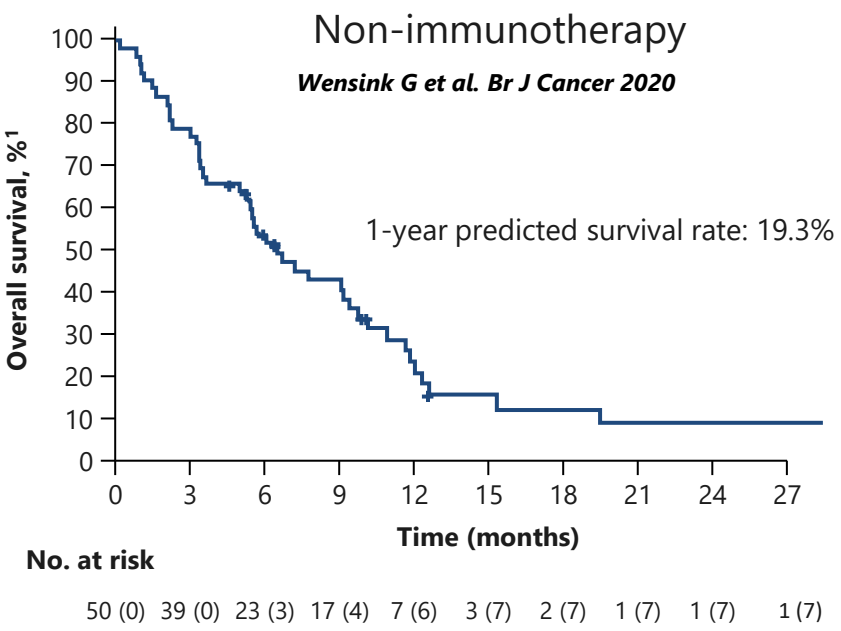
The patient is happy to give consent, but must be asked
-> integration in care process
-> extra time/manpower necessary for integration of care and research

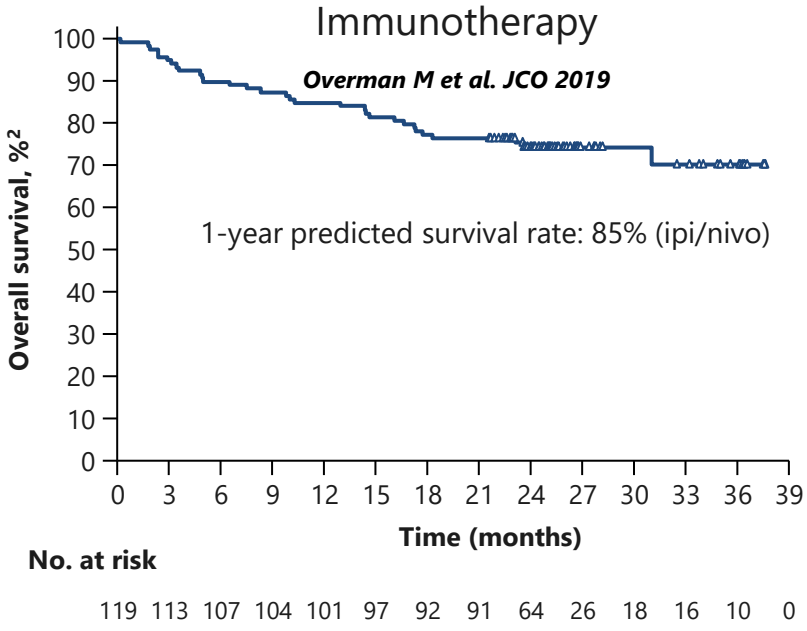
84%)

- Participation to 'PROMs' questionnaires (~ 81%)

- Consent to be approached for substudies (~ 78%)

Pretreated metastatic dMMR patients +/- immunotherapy

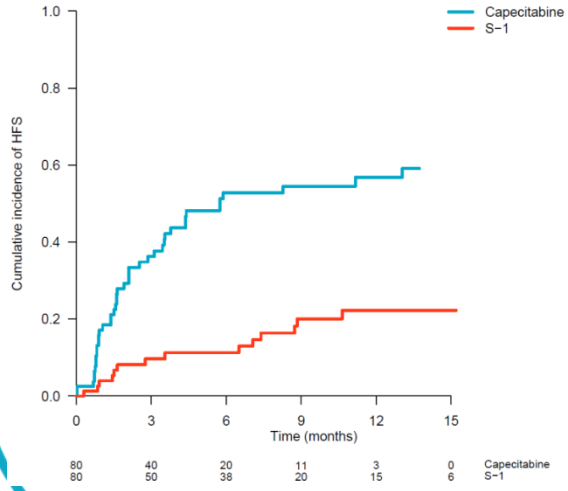




ipi=ipilimumab; nivo=nivolumab; no=number; OS=overall survival.

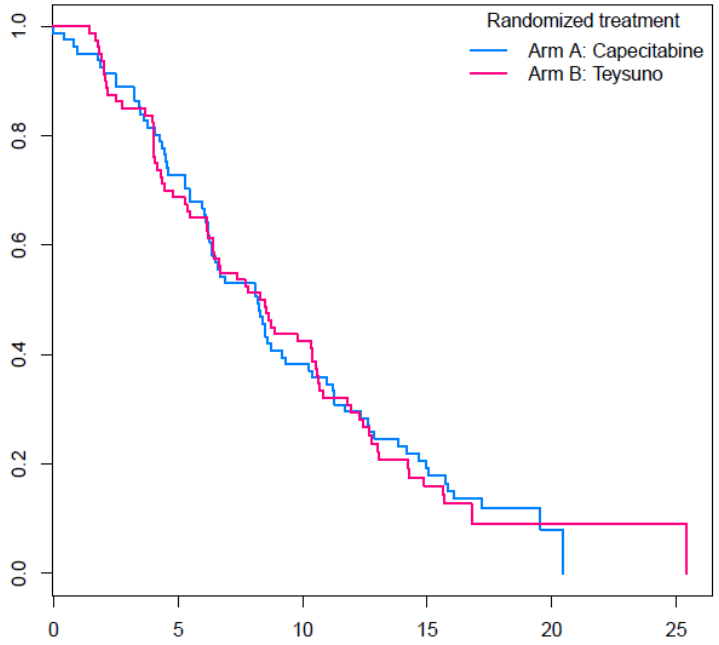
Comparison of S-1 with capecitabine as 1st-line treatment in metastatic CRC – randomized phase 3 study

	Capecitabine	S-1	p-value
Investigator-assessed HFS			
All grade	58 (73%)	36 (45%)	0·0005
Grade 3	17 (21%)	3 (4%)	0·003
Patient-assessed HFS			
All grade	43 (84%)	33 (58%)	0·004
Grade 3	9 (18%)	3 (5%)	0·05



Cumulative incidence curve of grade 2-3 HFS

	median PFS
S-1	**8.39 m**
Capecitabine	**8.18 m**



Kwakman et al. Ann Oncol 2017

Long-Term Safety Data on S-1 Administered After Previous Intolerance to Capecitabine-Containing Systemic Treatment for Metastatic Colorectal Cancer

Cornelis J.A. Punt,[1] Johannes J.M. Kwakman,[2] Linda Mol[3], on behalf of the PLCRC working group[#]

Table 4 Adverse Events

	CTC Grade	During Capecitabinen (%)	During S-1n (%)
Any Adverse Event	None	0	8 (17)
	1	1 (2)	15 (32)
	2	26 (55)	20 (43)
	3	20 (43)	4 (9)
Coronary Spasms	None	37 (79)	47 (100)
	1	1 (2)	0
	2	4 (9)	0
	3	5 (11)	0
Constipation	None	41 (87)	47 (100)
	1	5 (11)	0
	2	1 (2)	0
Diarrhea	None	35 (74)	34 (70)
	1	6 (13)	9 (19)
	2	3 (6)	5 (11)
	3	3 (6)	0
Mucositis	None	38 (81)	37 (79)
	1	7 (15)	6 (13)
	2	2 (4)	4 (9)
Terminal Ileitis	None	47 (100)	45 (96)
	1	0	1 (2)
	2	0	1 (2)
Anorexia	None	39 (83)	42 (89)
	1	6 (32)	5 (11)
	2	2 (4)	0
Fatigue	None	21 (45)	28 (60)
	1	20 (43)	14 (30)
	2	5 (11)	5 (11)
	3	1 (2)	0
Handfoot Syndrome	None	9 (19)	31 (66)
	1	2 (4)	15 (32)
	2	26 (55)	1 (2)
	3	10 (21)	0

Clinical Practice Points:

- All patients with CAP-induced HF syndrome experienced a lower grade or complete resulotion of symptoms after switch to S-1
- All pts with CAP-induced coronary artery vasospasm did not experience recurrent chest pain after switch to S-1
- S-1 is well tolerated in pts with CAP-induced toxicities
- A switch from CAP to S-1 does not appear to compromise efficacy of treatment

Punt et al. Clinical Colorectal Cancer 2022

Review

Systematic review and non-inferiority meta-analysis of randomised phase II/III trials on S-1-based therapy versus 5-fluorouracil- or capecitabine-based therapy in the treatment of patients with metastatic colorectal cancer

European Journal of Cancer

Jeroen W.G. Derksen*, Karel C. Smit, Anne M. May, Cornelis J.A. Punt

ESMO > Oncology News

EMA RECOMMENDS EXTENSION OF INDICATIONS FOR TEGAFUR

New indication concerns the treatment of patients with metastatic colorectal cancer for whom due to toxicity is not possible to continue treatment with another fluoropyrimidine

Date: 24 Dec 2021

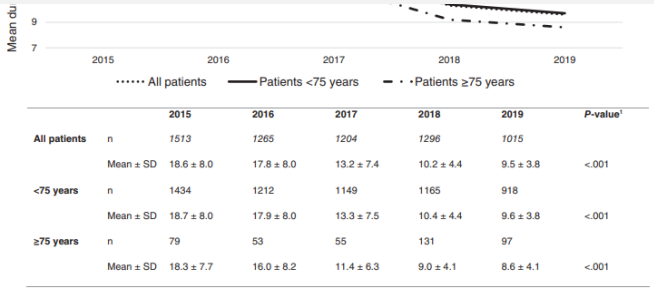

CANCER EPIDEMIOLOGY

Translation of IDEA trial results into clinical practice: Analysis of the implementation of a new guideline for colon cancer

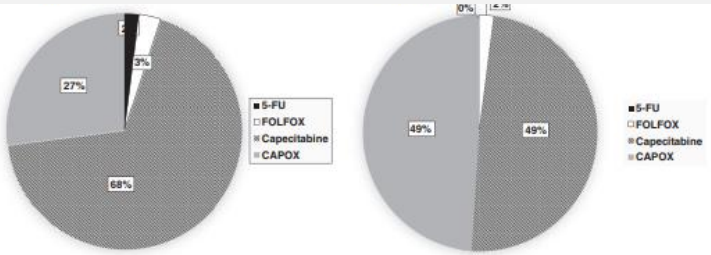
Karliin L. van Rooijen[1,2] | Jeroen W. G. Derksen[3] | Helena M. Verkooijen[3] |

- CONCLUSIONS:
- Rapid implementation of new guideline in practice, even decrease in ACT duration visible before guideline was published
- With shortening ACT: significantly more CAPOX in the elderly
- Significantly fewer st II patients received ACT: equal number of pT4N0, hardly any pT3N0

- -> disease-free survival and overall survival?



		2015	2016	2017	2018	2019	P-value[1]
All patients	n	*1513*	*1265*	*1204*	*1296*	*1015*	
	Mean ± SD	18.6 ± 8.0	17.8 ± 8.0	13.2 ± 7.4	10.2 ± 4.4	9.5 ± 3.8	<.001
<75 years	n	1434	1212	1149	1165	918	
	Mean ± SD	18.7 ± 8.0	17.9 ± 8.0	13.3 ± 7.5	10.4 ± 4.4	9.6 ± 3.8	<.001
≥75 years	n	79	53	55	131	97	
	Mean ± SD	18.3 ± 7.7	16.0 ± 8.2	11.4 ± 6.3	9.0 ± 4.1	8.6 ± 4.1	<.001



> 75 jaar oud

Unique design

Prospective Dutch Colorectal Cancer Cohort study (PLCRC)
all patients diagnosed with colorectal cancer (Stage I-IV)

Observational studies:

- Clinical data
- Tissue
- Blood
- PROMs

Interventional studies:

Trials within cohorts (TwiCs)

1. Burbach M et al. *Acta Oncologica* 2016; 2. Coebergh van den Braak R et al. *Acta Oncologica*. 2018; 3. Derksen J. et al. *Nature Rev Clin Oncol* 2019;9:589.

PROMs

Questionnaires:

sent centrally via PROFILES

time points:

- Local disease: baseline, 3, 6, 12, 18, 24 months, then yearly
- Metastatic disease: every 3 months

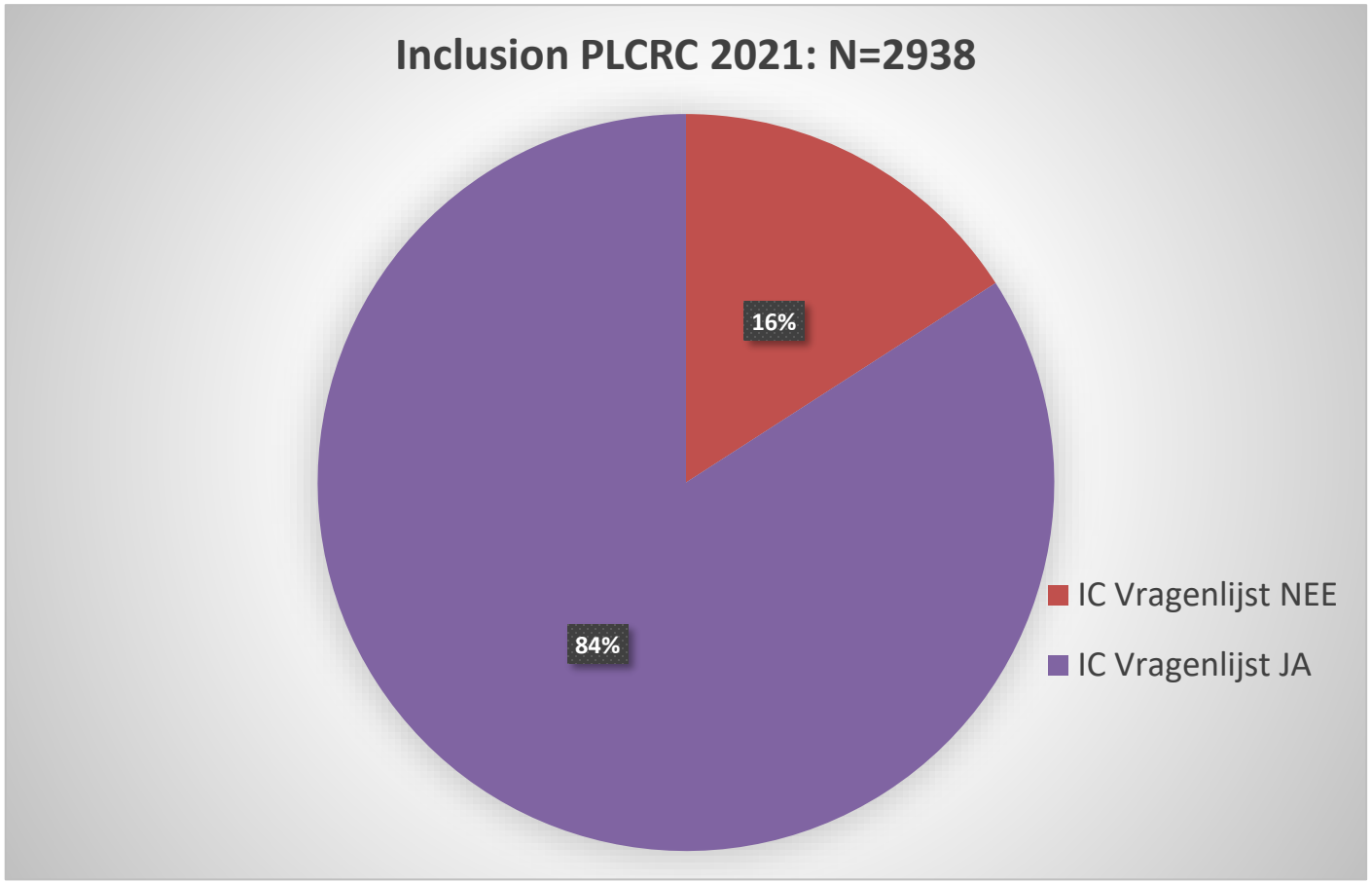
to be completed digitally or on paper

if completed digitally: patient receives feedback on QoL scores

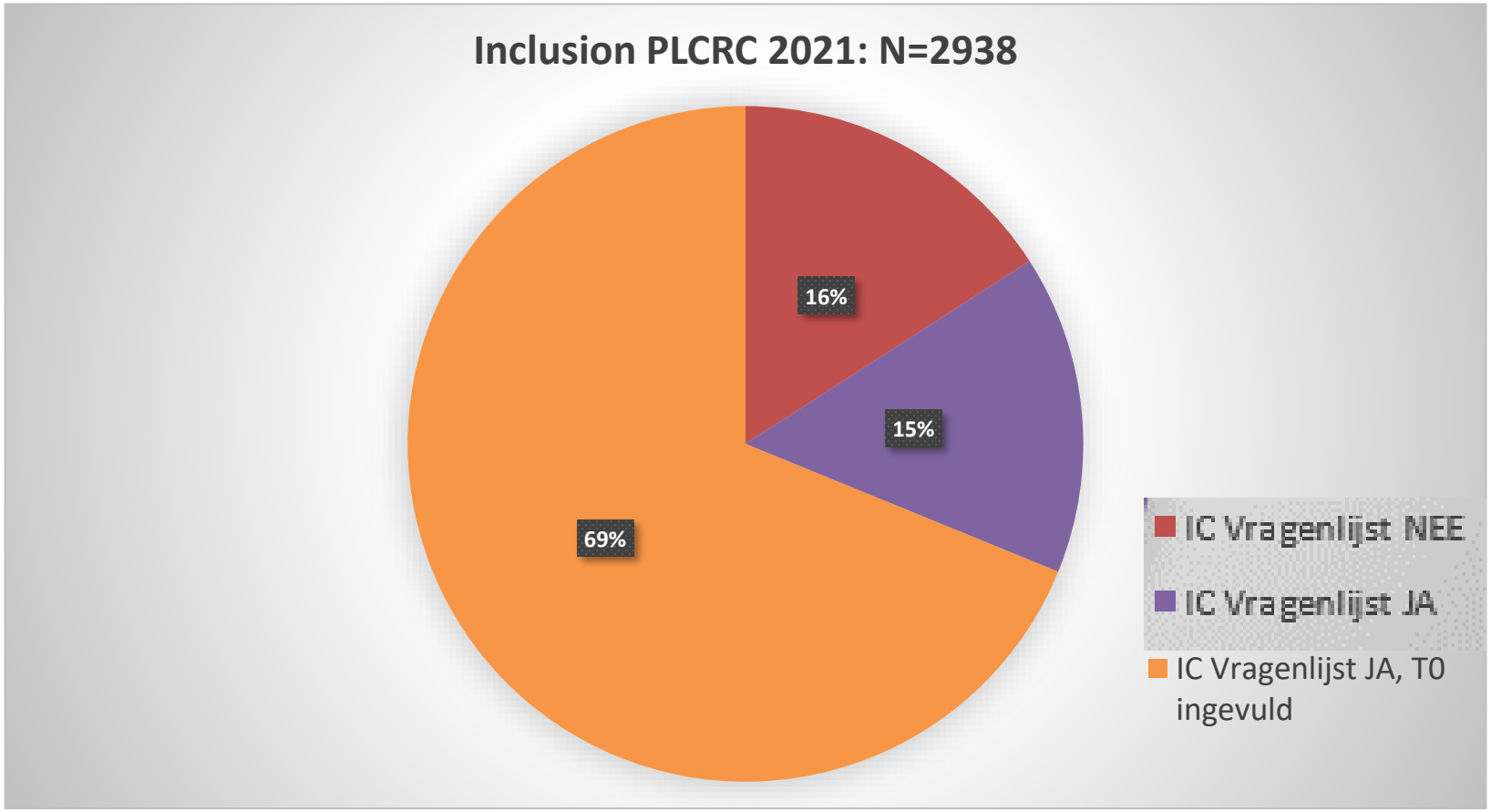
"Patiënten hebben er direct wat aan m.b.t. bewustwording van bijv. kwaliteit van leven, voeding en leefstijl (Protect-studie)."

oncologie verpleegkundige

Consent for questionnaires



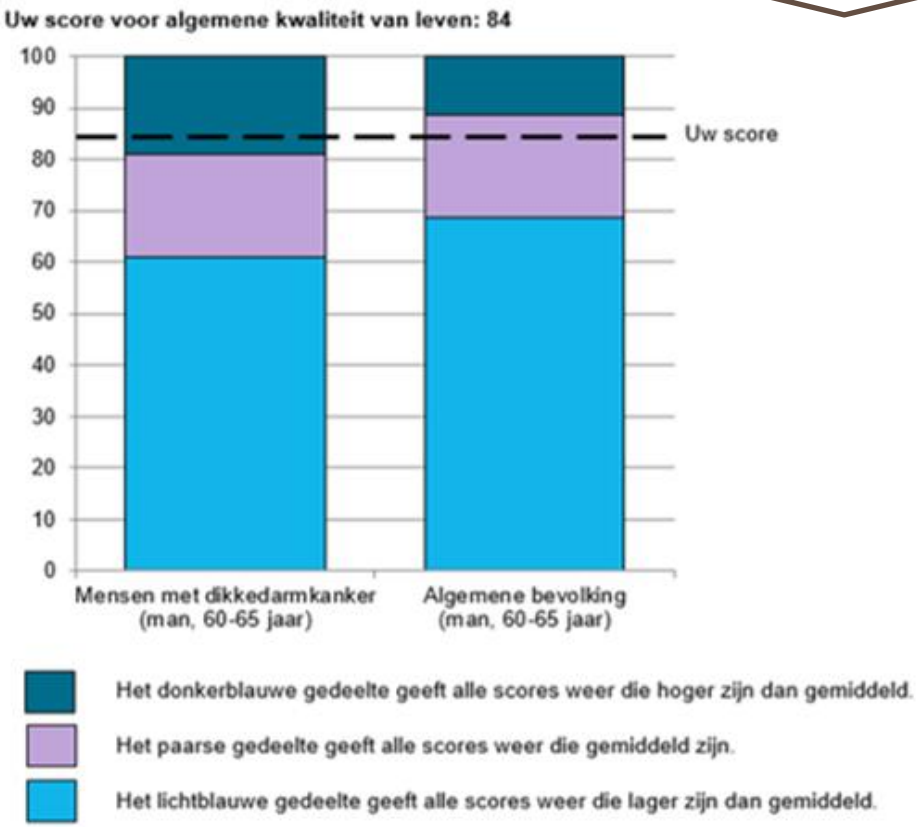
Response baseline questionnaires



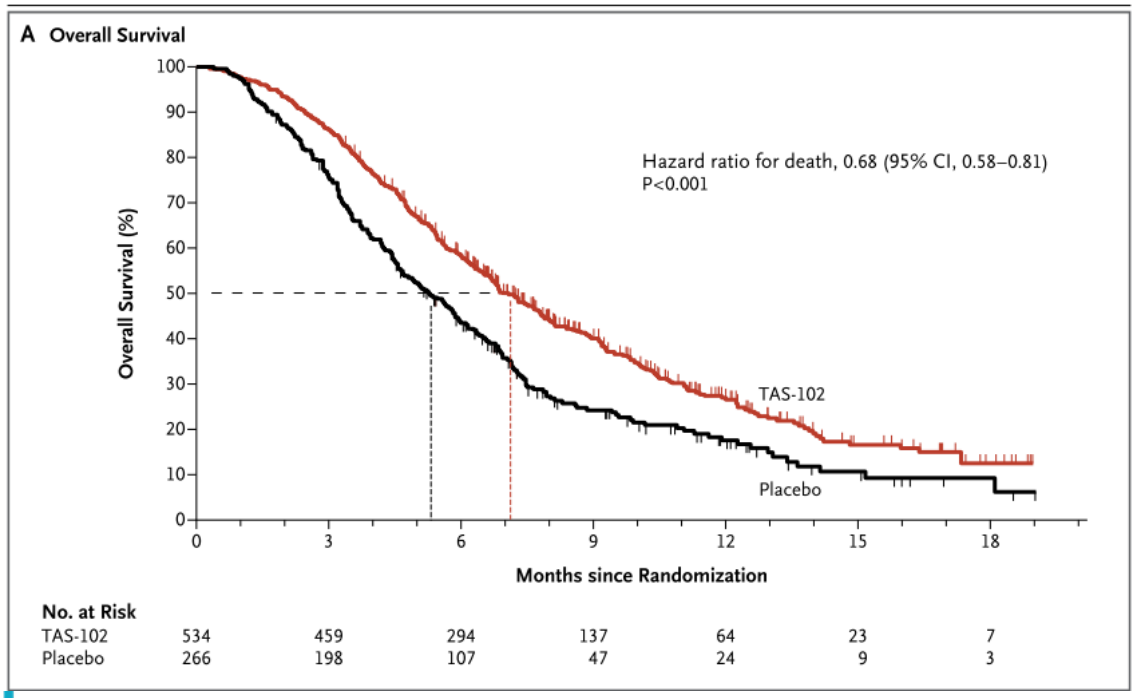
Feedback PROMs

"De resultaten uit de PROMs ondersteunen het gesprek in de kliniek"

oncologie verpleegkundige



RECOURSE trial



QUALITAS project in 150 mCRC pts

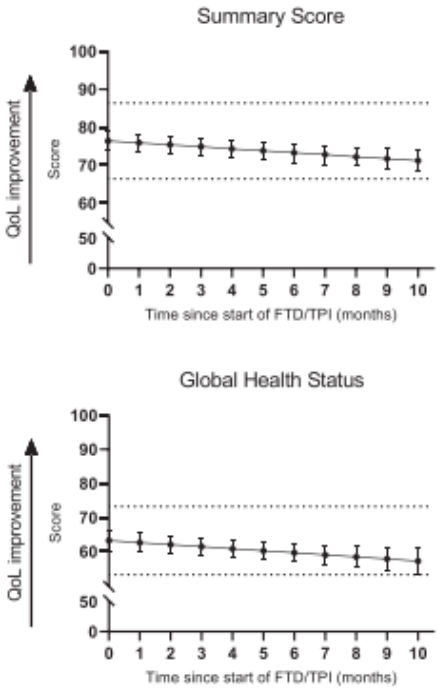
- **Aim QUALITAS**: evaluate QoL and survival of patients treated with TAS-102 in daily practice, analyze impact of baseline QoL on prognosis
- PROMS: monthly questionnaires QLQ-C30, QLQ-CR29, EQ-5D-5L
- Primary endpoint: quality of life (QoL)

Mayer et al. N Engl J Med 2015; Hamers et al. Clin Canc Res 2022

EORTC QLQ-C30 Summary Score

Functional scales
Physical functioning
Role functioning
Emotional functioning
Cognitive functioning
Social functioning

Symptom scales
Fatigue
Nausea and vomiting
Pain
Dyspnoea
Insomnia
Appetite loss
Constipation
Diarrhoea



Error bars represent 95% CI
Grid lines represent a clinically relevant 10-point change from baseline score.

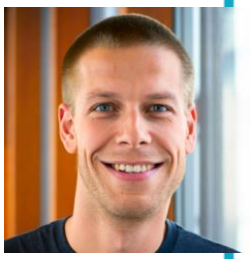
Qualitas Conclusions:

- Overall: no deterioration in QoL during TAS-102
- **Baseline QoL is strongly and independently associated with OS/PFS/TTF**

Giesinger et al. J Clin Epid 2016; Hussont et al. The Oncologist, 2019; Hamers et al Clin Canc Res 2022

Ib – Questionnaires

Effects of COVID-19 pandemic on patient welfare



Urgent need for data on effects COVID-19 pandemic on cancer patients

- April 2020: questionnaires send to 5000 patients in PLCRC
- Baseline pre-COVID data from these patients available
- 3247 patients (65%) responded within 2 months!

-> Most striking result: the pandemic has less effects on social loneliness of cancer patients compared to the general population

van de Poll-Franse L et al. JAMA oncol 2020; Derksen J et al. JNCI Cancer Spectrum 2021

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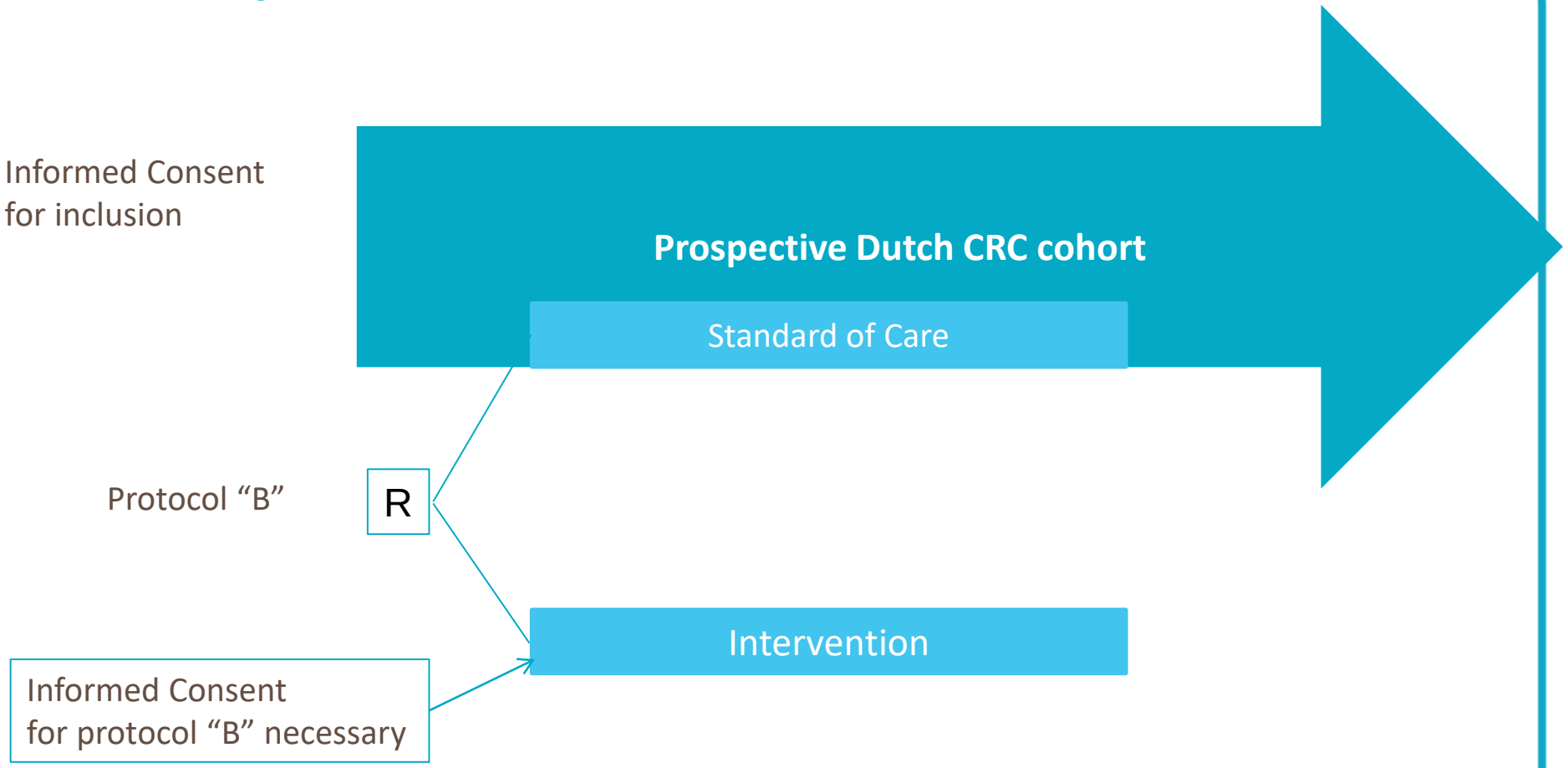
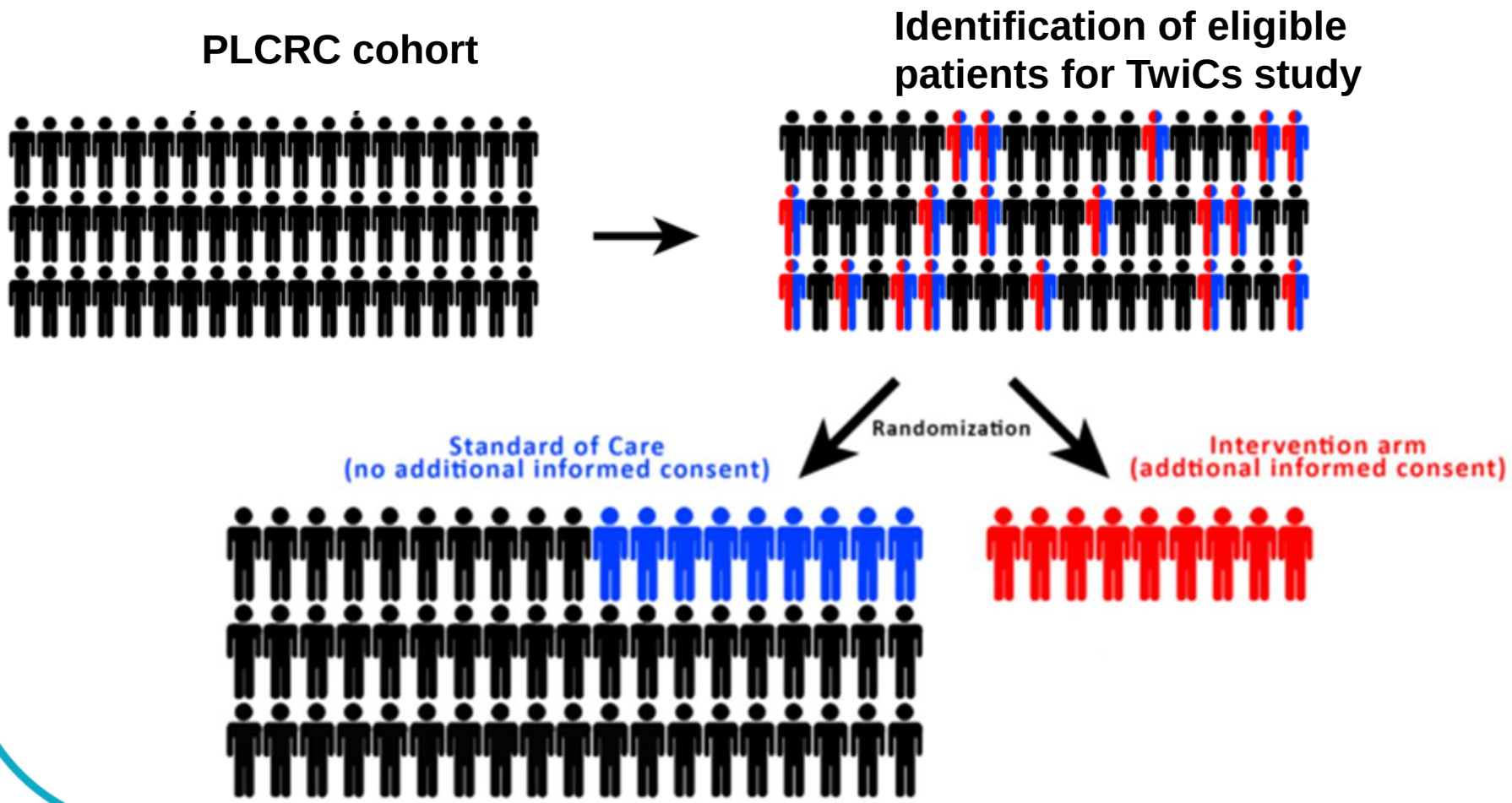
Trials Within Cohort Studies

TWICS design



Verkooijen et al. NTVG 2013

TwiCs


PLCRC cohort
Identification of eligible patients for TwiCs study
Randomization
Standard of Care
(no additional informed consent)
Intervention arm
(addtional informed consent)

Ambition:

PLCRC has a prominent role in learning health care cycle

-> real-life data contribute to individualized treatment