DRUP
The Drug Rediscovery Protocol

A national study on behalf of the Centre for Personalized Cancer Treatment

to facilitate patient access to commercially available, targeted anti-cancer drugs

to determine the potential efficacy in treatment of advanced cancers

with a known molecular tumor profile

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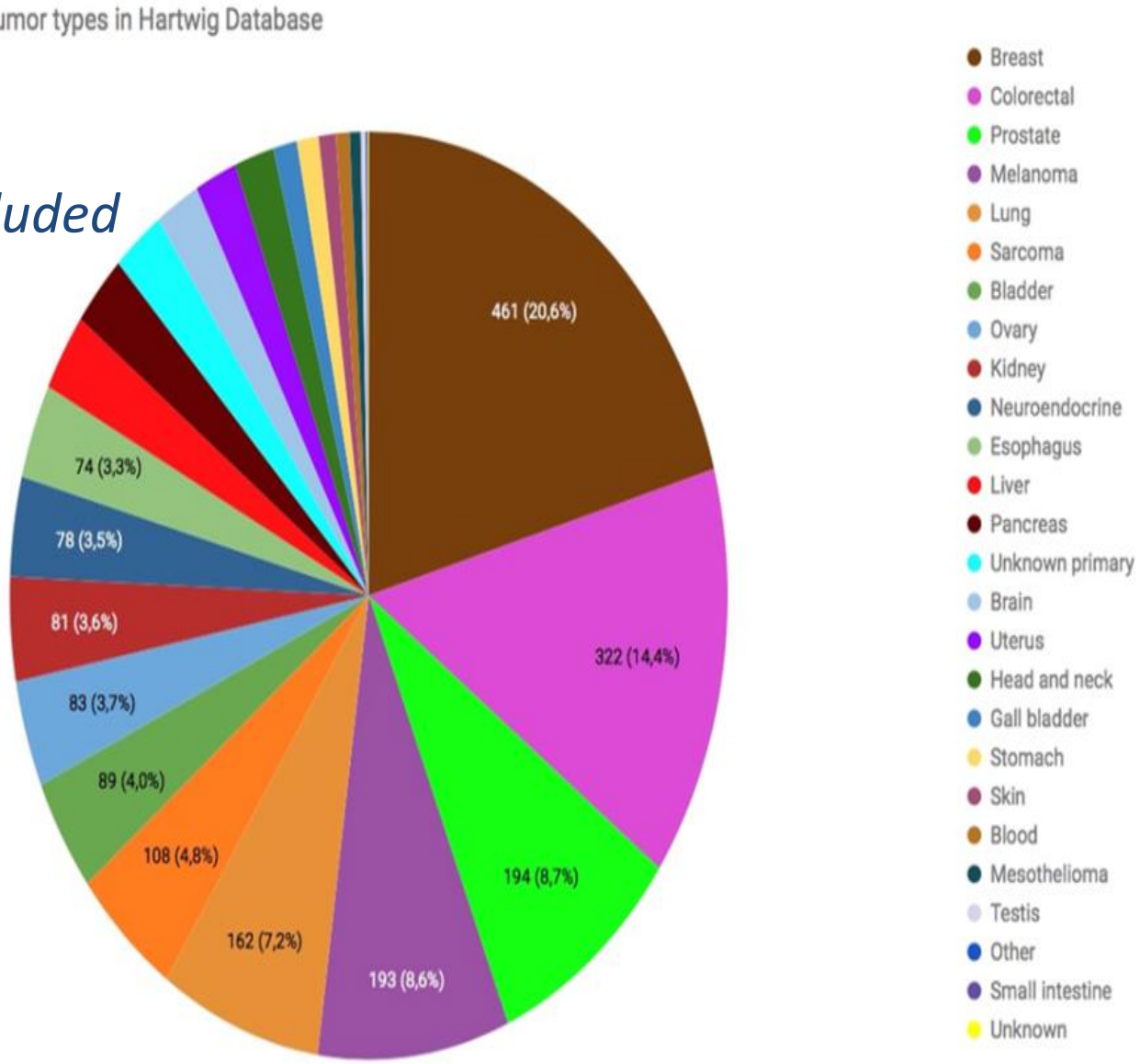
CPCT / HMF sequencing

> 3500 patients included



Background

More extensive genomic sequencing = more ‘uncommon’ findings:

- $BRAF_{mut}$ in melanoma vs. $BRAF_{mut}$ in NSCLC?
- $HER2_{ampl}$ in breast cancer vs. $HER2_{ampl}$ in CRC?
- $BRCA_{mut}$ in ovarian cancer vs. $BRCA_{mut}$ in prostate cancer?

Treating patients based on such findings can be challenging:

- Significance of ‘uncommon’ mutations often unknown
- Limited drug-access outside of the registered indication
- No learning curve for off-label treatment in daily practice

Initiation of DRUP

- Treatment based on tumor and mutational profile
- With approved targeted (or immuno) therapies

→ Access to potentially effective therapy for patients

→ Evaluation of efficacy and toxicity

How does it work?

Patient with advanced cancer

Who has exhausted standard treatment options

And whose molecular tumor profile has been analyzed:

Submit to DRUP study team:

- Actionable target present?
- Matching drug available?
- Literature / rationale?

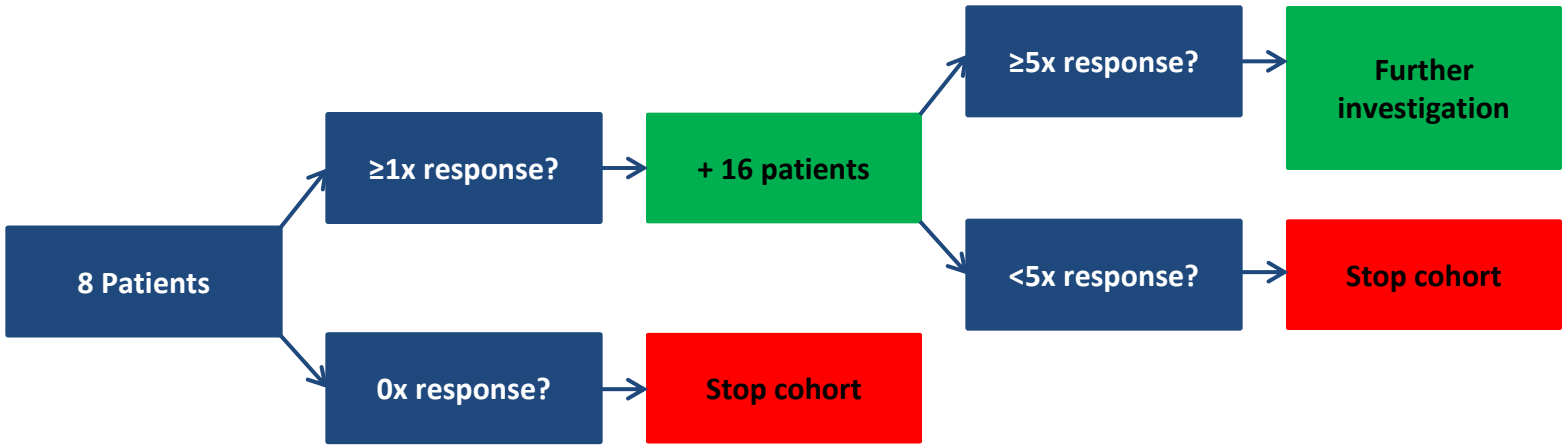
If yes:

- Inform and screen patient
- Register patient on-study
- Pre-treatment tumor biopsy

Start treatment

When do we consider a drug effective?

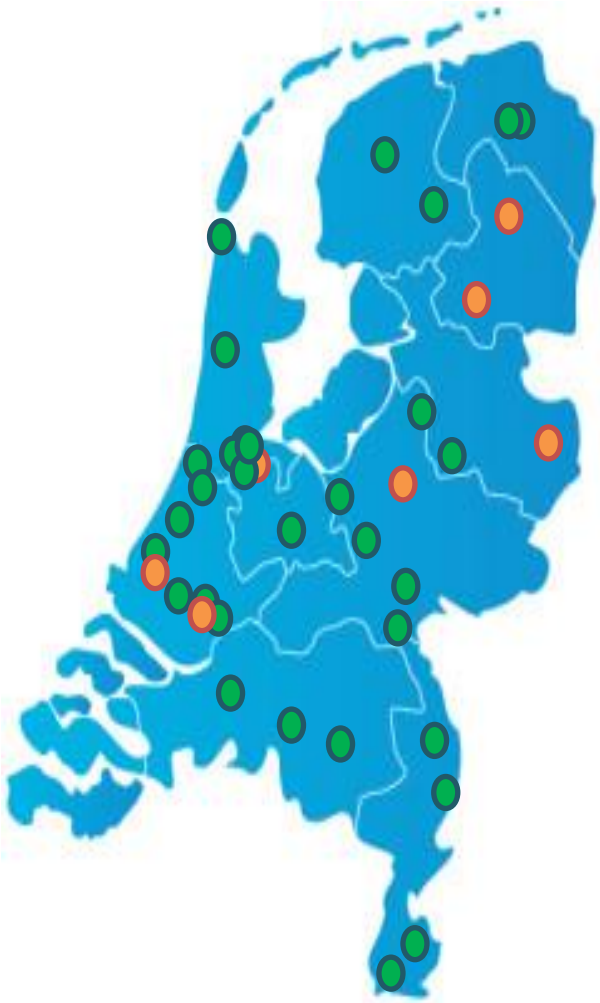
- Patients are enrolled in multiple parallel cohorts
- Cohorts are defined by study drug, histologic tumor type and molecular tumor profile
- Efficacy (defined as CR, PR or SD ≥16 weeks) is analyzed per cohort, with a 2-stage-design:



Current study status & preliminary results

- Study was launched in September 2016
- 34 participating hospitals, of which 27 are open for inclusion

Participating sites			
Currently open for inclusion (*n* = 27)			
• AVL	• Haaglanden MC	• NWZ	• UMC Maastricht
• Amphia	• Isala	• OLVG	• UMC Radboud
• Deventer ZH	• Martini	• Reinier de Graaf	• UMC Utrecht
• Erasmus	• Maxima MC	• Rijnstate	• VieCuri
• ETZ	• MC Leeuwarden	• Spaarne Gasthuis	• VUMC
• Franciscus	• Meander	• UMC Groningen	• Zuyderland
• Gelderse Vallei	• Nij Smellinghe	• UMC Leiden	
In preparation (*n* = 7)			
• AMC	• Haga ziekenhuis	• Treant Zorggroep	• ZG Twente
• Gelre Ziekenhuizen	• Maasstad Zkh	• Wilhelmina zkh	



20 different drugs

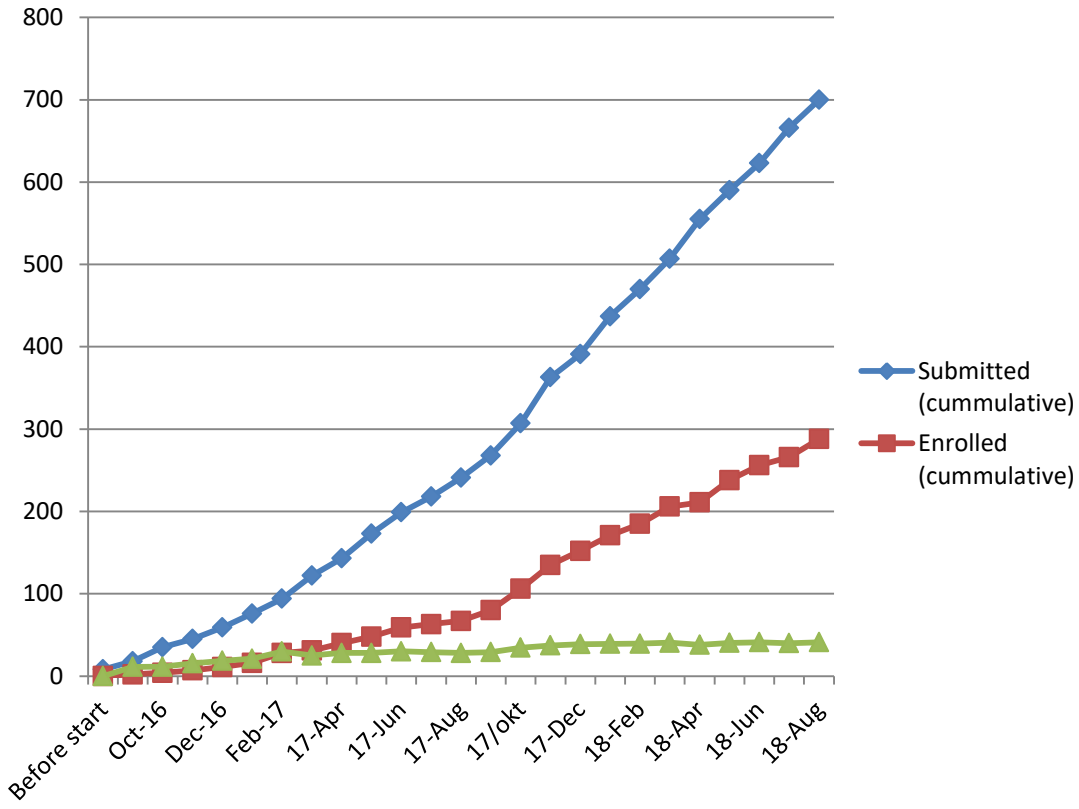
Available

Amgen	Panitumumab	KRAS-BRAF-NRAS$_{WT}$
AZ	Olaparib	BRCA 1/2, ATM
Bayer	Regorafenib	RET, VEGFR1,2,3, KIT, PDGFRB, RAF-1, BRAF
BMS	Nivolumab	MSI or high mutational load
Roche	Erlotinib	EGFR
	Trastuzumab + Pertuzumab	HER2
	Vemurafenib + Cobimetinib	BRAF V600
	Vismodegib	PTCH1
	Dabrafenib	BRAF V600
	Nilotinib	KIT, ABL1, PDGFRA, PDGFRB
	Trametinib	BRAF V600, NRAS
BI	Afatinib	ERBB4, NRG1
Eisai	Lenvatinib	FGFR1, 2, 3, 4
MSD	Pembrolizumab	High mutational load
Pfizer	Axitinib	VEGFR1, 2, 3
	Crizotinib	ALK, MET, MST1R, ROS1
	Sunitinib	CSF1R, FGFR1,2,3, VEGFR1, 2, 3, KIT, PDGFRA, PDGFRB, RET, VHL
	Palbociclib	CDK4/6, CDKN2A

Committed:

Clovis	Rucaparib	BRCA1/2, ATM
Ipsen	Cabozantinib	MET, AXL, RET, KIT
AZ	Durvalumab	MSI

700 patients submitted for review



Included: 288 (41%)

Pending: 28 (4%)

Excluded: 384 (55%)

1st successful cohort

- Nivolumab for MSI tumors
  - Clinical benefit at 6 months: 61% (at 16 weeks: 71%)
  - Median PFS: not reached, 50% still on study (mPFS to date: 32.2 weeks)
  - Discussion with ZIN how to proceed

Oncode Institute

Scientific Excellence | **Collaboration** | **Valorization**

- **€120 million**
- **560 researchers**
- **43 principal investigators**
- **9 research institutes**
- **6 research themes**

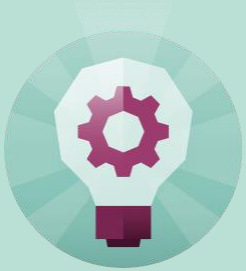
Common Strategy → *Outsmarting cancer*
Impacting lives

Scientific themes

Understanding
tumor growth & resistance

Identifying
critical drug combinations
& biomarkers

Developing
novel technologies



Mobilizing
immune defence

Researching
causes & consequences
of genetic instability

Analysing
network perturbations in tumors
& tumor-host interactions

Oncode Research Management Committee

Geert Kops
(Chair)

Hubrecht Institute

Madelon Maurice

UMC Utrecht

Jan Paul Medema

amc

Karin de Visser

Antoni van Leeuwenhoek
Nederlands Kanker Instituut

Thijn Brummelkamp

Antoni van Leeuwenhoek
Nederlands Kanker Instituut

Ruud Delwel

Erasmus MC
University Medical Center Rotterdam

Henk Verheul

VUmc

Building a link to the clinic

Why?

Bridging the gap between fundamental and clinical research

How?

Connecting clinicians to fundamental research and basic scientists to clinical research

What?

Training for Oncode researchers about (pre-)clinical research and clinical challenges

Clinical proof of concept programme

Programme manager:

Ester Frische

Goal:

- Facilitate translation of fundamental research to the clinic

Status:

- 5 proposals approved in first call

Next steps:

- Finalize terms & conditions and set up second call
- Design workshops to address e.g. study design, target product profile

Affordable health care programme

Programme manager:

Irene Kanter-Schlifke

Goals:

- Make future cancer treatments more (cost-) effective

Status:

- First open call together with ZonMw

Next steps:

- Finalize strategy with programme committee
- Set up training on HTA, patient engagement etc.