Monthly DRUP Study Newsletter #75, 01 June 2022

The Drug Rediscovery Protocol (DRUP Trial):

A Dutch National Study on Behalf of the CPCT 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 Profile

The Norwegian IMPRESS delegation visiting NKI

Highlights:

1) To date 1195 patients have started a DRUP treatment

2) Addition of tepotinib as new study drug

3) New DRUP paper accepted for publication in *the European Journal of Cancer*

Study Update

To date, a total of 2259 cases have been submitted to the study team and 1053 of these have started a treatment within the 199 DRUP stage 1 and 2 cohorts and 142 within the DRUP stage 3 cohort. The 3rd stage cohort is still on hold because the maximum number of inclusions has been reached.

This month we will submit the 16th DRUP protocol amendment including amongst other things the addition of tepotinib, from the pharmaceutical company Merck, as new study drug. We will keep you posted on the progress.

Scientific output

We are pleased to announce that the DRUP manuscript "Trastuzumab and pertuzumab combination therapy for advanced pre-treated HER2 exon 20 mutated Non-Small Cell Lung Cancer" by Maxime van Berge Henegouwen has been accepted for publication in *The European Journal of Cancer*. The manuscript describes the treatment outcomes in one of the 2nd stage DRUP cohorts, in which patients with metastatic and/or advanced NSCLC harboring a HER2 exon 20 mutation have been treated with the combination of trastuzumab and pertuzumab. Clinical benefit was observed in 9 patients (38%); 2 patients with partial response and 7 patients with stable disease for at least 16 weeks. The manuscript will soon be available.

Event & meetings

On the 9th of May, we had the Norwegian IMPRESS delegation over for a visit. We look back at a very successful meeting and diner, during which experiences and ideas were shared and further collaboration was discussed.

On the 3rd of September 2022, the 10th edition of **Stelvio for Life** will take place. Register now on https://www.stelvioforlife.nl/ and join the until now 582 participants climbing the 1533 altimeters of Passo dello Stelvio to support **the Barcode for Life Foundation** in their research into personalized cancer treatment, tailored to the individual patient and their specific tumor characteristics. 100% of the collected sponsorship money goes to charity!

Furthermore, on 17th of June we are arranging a sponsor meeting in the NKI. During this meeting the study team will be present to give an overview over the DRUP trial and why the support from the Barcode for Life is of crucial importance for the continuity of the study.

Warm regards,

Principal Investigators: Henk Verheul, Hans Gelderblom, Emile Voest
Study Coordinators: Laurien Zeverijn, Gijs de Wit, Birgit Geurts, Ilse Spiekman
Clinical Project Manager: Lena Bilet

Table 1: List of pharmaceutical companies & study drugs

Confidential, list might be subjected to change

Currently available

Amgen	Eisai	Bayer	Roche
Panitumumab	Lenvatinib	Regorafenib	Erlotinib
			Trastuzumab+
BMS	AstraZeneca	Clovis Oncology	Pertuzumab
Nivolumab	Olaparib	Rucaparib	Vemurafenib+
Ipilimumab	Durvalumab		Cobimetinib
		MSD	Vismodegib
Novartis	Pfizer	Pembrolizumab	Atezolizumab+
Dabrafenib	Axitinib		bevacizumab
Nilotinib	Crizotinib	Lilly	Alectinib
Trametinib	Sunitinib	Abemaciclib	Entrectinib
Ribociclib	Palbociclib		
Alpelisib	Talazoparib,	BI	Janssen
	dacomitinib	Afatinib	Erdafitinib
	Lorlatinib		

Committed

Lilly	GSK	Merck
Selpercatinib	Niraparib	Tepotinib

Calendar & publicity

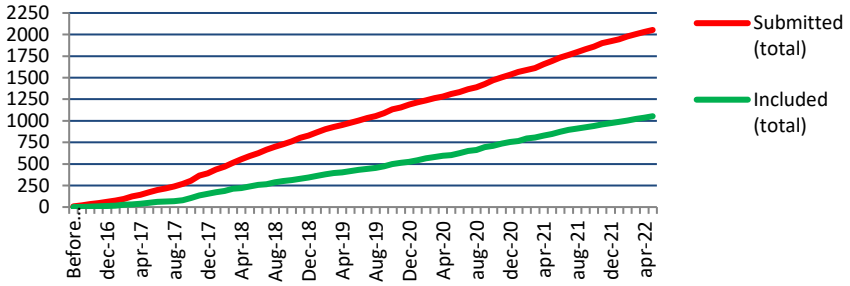
June, 17th Sponsor meeting Stelvio for life NKI

September, 3rd Stelvio for Life

Table 2: Submission and accrual overview

June 1st , 2022

Submitted	2053
Excluded	928 (45.2%)
Pending	72 (3.5%)
Enrolled	1053 (51.3%)



Submissions and accrual 3rd stage cohort Nivolumab for MSI tumors

June 1st, 2022

Submitted	206
Excluded	63 (30.5%)
Pending	1 (0.5%)
Enrolled	142 (69%)

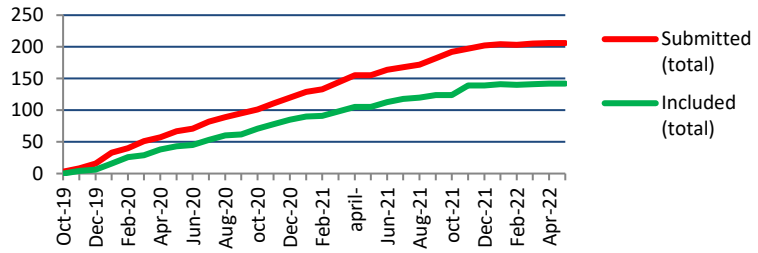


Table 3 : Participating sites

Currently open for inclusion (*n* = 35)

- AMC
- AVL
- Amphia
- Bravis
- Deventer Ziekenhuis
- Erasmus MC
- ETZ
- Franciscus
- Gelderse Vallei
- Gelre Ziekenhuizen
- Haaglanden MC
- Haga ziekenhuis
- Isala
- Martini
- Maxima MC
- MC Leeuwarden
- Meander
- Nij Smellinghe
- Treant Zorggroep
- NWZ
- Reinier de Graaf
- Rijnstate
- Spaarne Gasthuis
- St. Antonius
- UMC Groningen
- UMC Leiden
- Maastricht UMC
- Radboud UMC
- UMC Utrecht
- VieCuri
- ZG Twente
- Zuyderland
- Rivas Zorggroep
- OLVG
- VUMC

In preparation

- Maasstad

Table 4: DRUGS OPEN FOR INCLUSION			
Nilotinib	KIT_{mut} GIST	$PDGFRA_{mut}$ GIST	$PDGFRA_{mut}$ mesothelioma
	$PDGFRB_{ampl}$ CRC	KIT_{mut} melanoma	KIT_{mut} kiemcel tumor
Nivolumab + ipilimumab	HML tumors		
Olaparib	ATM_{mut} tumors	HRR deficient tumors (2x)	All other tumors with HRR alterations
Panitumumab	RAF/RAS_{wt} sarcoma	RAF/RAS_{wt} HNSCC	$EGFR_{mut}$ NSCLC
	RAF/RAS_{wt} thyroid ca	RAF/RAS_{wt} salivary duct ca	RAF/RAS_{wt} cervical ca
	RAF/RAS_{wt} endometrial ca	RAF/RAS_{wt} meningioma	RAF/RAS_{wt} eye melanoma
	BRAF-KRAS-NRASwt GBM	RAF/RAS_{wt} vulvar ca	RAF/RAS_{wt} ACUP
	RAF/RAS_{wt} anal ca		
Pembrolizumab	HML HNSCC	HML prostate ca	HML breast ca
	HML miscellaneous	HML > 290 (all type)	HML 140-290 CRC
	HML 140-290 oesophagus/stomack/cardiac		
Regorafenib	RET+ NSCLC	RET+ esthesioneuroblastoma	KIT_{mut} melanoma
	KIT_{mut} Thymuscarcinoma	$BRAF_{mut}$ ACC	$FLT1_{ampl}$ duodenal carcinoma
Dabraf + Tramet	$BRAF_{mut}$ GBM	$BRAF_{mut}$ low grade glioma	$BRAF_{mut}$ NEC colon
	$BRAF_{mut}$ cholangiocarcinoom	$BRAFV600E_{mut}$ breast cancer	$BRAFV600E_{mut}$ grade 3 glioma
	$BRAFV60_{mut}$ NSCLC		
Dabrafenib	$BRAF_{mut}$ GBM	$BRAF_{mut}$ UCC	
Trametinib	$NRAS_{mut}$ ovarian ca	$MAP2K1_{mut}$ NSCLC	$NRAS_{mut}$ NSCLC
	$MAP3K1_{mut}$ NEC	$MAP3K1_{mut}$ cervical ca	$MAP2K1_{mut}$ CRC
	$MAP2K4_{mut}$ CRC	$MAP3K1_{mut}$ ACUP	$MAP2K4_{mut}$ cholangioca
	$MAP2K4_{mut}$ ovarian ca	$MAP3K1_{mut}$ breast ca	$MAP2K4_{mut}$breast ca
	$NRAS_{mut}$ thyroid cancer	$MAP3K1_{mut}$ prostate	$NRAS_{mut}$ pleomorphic tumor
	$NRAS_{mut}$ prostate	$BRAF_{fusie}$ (pilocytair) astrocytoom	$NRAS_{mut}$ yolk sac tumor
	$GNA11_{mut}$ melanocytaire tumor	$NRAS_{mut}$ cholangio cancer	$BRAF_{exon\ 12\ deletion}$ NSCLC
	$BRAF_{fusie}$ NSCLC	$NRAS_{mut}$ salivary duct ca	$MAP2K4_{loss}$ pancreas cancer
	$NF1_{mut}$ low grade glioma	$BRAF_{fusie}$ pancreas cancer	$MAP2K1_{mut}$ pancreas cancer
	$MAP2K1_{mut}$ stomach cancer	BRAF-fusie Urotheelcelca	MAP2K4mut/loss CRC
	KRASmut Erdheim Chester disease	BRAF fusie glioneurale tumor	NF1mut GBM
Trastuz. + Pertuz.	$HER2_{ampl}$ CRC	$HER2_{ampl}$ cholangio ca	$HER2(exon20)_{mut}$ NSCLC
	$HER2_{mut}$ ovarian ca	$HER2_{ampl}$ salivary duct ca	$HER2_{ampl}$ NSCLC
	$HER2_{mut}$ CRC glio	$HER2_{mut}$ cervical ca	$HER2_{ampl}$ vulvar ca
	$HER2_{ampl}$ cervical ca	$HER2_{ampl}$ hidradenoca	$HER2_{ampl}$ UCC
	$HER2_{ampl}$ ovarian ca	$HER2_{ampl}$ NEC	$HER2_{mut}$ UCC
	$HER2_{mut}$ ACC	$HER2_{ampl}$ duodenal cancer	HER2ampl melanoom
Vemur. + Cobimet.	$BRAF_{mut}$ salivary duct	$BRAF_{mut}$ ACUP	$BRAF_{mut}$ ovarian ca
	$BRAF_{mut}$ thyroid ca	$BRAF_{non\text{-}V600mut}$ NSCLC	$BRAF_{V600Emut}$ Erdheim Chester Disease
	BRAFV600 mut pap craniofaryngeoom		
Vismodegib	PTCH1mut sarcoma (Ewing)	$PTCH1_{mut}$ medulloblastoma	
Erlotinib	$EGFR_{mut}$ GBM	CRC with EGFR mutations	EGFR fusions GBM
Lenvatinib	$FGFR1_{ampl}$ CRC	$FGFR2_{ampl}$ CRC	$FGFR2_{ampl}$ breast ca
	$FGFR1_{ampl}$ osteosarcoma	$FGFR1_{ampl}$ NSCLC	$FGFR3_{mut}$ anal ca
	$FGFR2_{ampl}$ esophageal ca	$FGFR2_{mut}$ endometrial ca	$FGFR3_{ampl}$ SGT
	$FGFR2_{fusie}$ ACUP	$FGFR2_{fusie}$ cholangioca	$FGFR1_{ampl}$ breast ca
	$FGFR2_{ampl}$ urachal ca	$FGFR3_{mut}$ UCC	$FGFR2_{mut}$ ACC
	$FGFR3_{amp}$ NEC nasal cavity	$FGFR1_{mut}$ glioneural tumor	$FGFR3_{mut}$ HNSCC
	$FGFR3_{fusie}$ GBM	$FGFR2_{mut}$ digital papillary cancer	$FGFR2_{fusion}$ pancreas cancer
	$FGFR2_{amp}$ NSCLC	$FGFR3_{fusie}$ cholangioca	$FGFR2_{mut}$ cholangioca/biliary tract
	$FGFR1_{amp}$ pancreas cancer	$FGFR2_{mut}$ salivary duct cancer	FGFR3 mut cholangiocarcinoma
	FGFR3 mut anaplastisch schildklierca	FGFR3 fusie NSCLC	FGFR1mut glioma
	$FGFR3_{ampl}$ endometrial ca		
Sunitinib	KIT_{mut} thymus ca	$PDGFRA_{mut}$ prostate ca	$FGFR1_{ampl}$ UCC
	$PDGFRB_{ampl}$ breast ca	$PDGFRB_{mut}$ osteosarcoma	$PDGFRA_{ampl}$ ACC
	$FGFR1_{ampl}$ ovarian cancer	$PDGFRA_{ampl}$ tyroid cancer	$FLT3_{ampl}$ CRC
	$CSF1R_{mut}$ CRC	KIT_{ampl} NSCLC	$FGFR2_{ampl}$ ovarian cancer
	RET fusion pancreatic cancer		
Crizotinib	ALK_{fus} IMT	MET_{ampl} CRC	ALK_{mut} CRC
	MET_{mut} NSCLC	MET_{ampl} esophageal ca	MET_{ampl} NSCLC
	ALK_{mut} thyroid	ALK+ sarcoom	ALK_{fusion} CUP
	MET_{fusion} anaplastic tyroid cancer	MET_{ampl} HCC	MET_{ampl} GEJ-tumor
	MET_{amp} ovarium cancer	MET_{mut} (papillair) kidney cell cancer	ALK+ Anaplastisch grootcellig T-cellymfoom
Axitinib	$FLT1_{ampl}$ CRC		
Rucaparib	HRR_{alt} ovarian cancer	HRR_{alt} prostate cancer	HRR_{alt} pancreatic cancer
	HRR_{alt} Breast cancer	All other tumor types	
Alectinib	ALK fusion (all tumor types)		
Abemaciclib	$CCND1_{ampl}$ UCC	$CCND1_{ampl}$ NSCLC	$CCND1_{ampl}$ prostate cancer
	$CCND1_{ampl}$ melanoma	$CCND3_{ampl}$ small intestine	CDK4ampl sarcoma
	CCND1ampl urachal cancer	CDK4 amp GBM	CCND3ampl esofagusca
	CCND1ampl ovariumcarcinoom		
Alpelisib	Miscellaneous tumors with $PIK3CA_{mut}$	$PIK3CA_{mut}$SCC gynecologic tumors	PIK3CAmut gynecologic tumors
	PIK3CAmut upper-GI tumors (esophagus, stomach)	PIK3CAmut HNSCC	$PTEN_{loss}$ prostate cancer
	Double hit cohort (histology-agnostic)	PIK3CAmut prostaatcarcinoom	PTENloss RCC
	PTENloss gyn tumors (ovarian/endometrial)	PIK3R1mut gyn tumors (cervix/endometrial)	PTENloss salivary gland carcinoma
Talazoparib	Tumors with HRD sign (with/without BRCA VUS)	ATM/ATRmut tumors	
lorlatinib	ROS-1 fusion NSCLC		
Dacomitinib	HER2amp oesophaguscarcinoom	HER2ampl endometriumca	EGFRamp peniscarcinoom
	EGFRampl CRC	$EGFR_{amp}$ UCC	
Atezo + bevaci	TMB ≥16 mut/Mb		
Legend	Cohort closed	Cohort on hold	Slots available

Table 5: DRUGS CLOSED FOR INCLUSION			
Palbociclib	$CDKN2A_{loss}$ GBM	$CDKN2A_{loss}$ CRC	$CDKN2A_{loss}$ PEComa
	$SMARCA4_{mut}$ ovarian ca	$CDKN2A_{mut}$ cholangio ca	$CDKN2A_{mut}$ melanoma
	$CDKN2A_{loss}$ duodenal ca	$CCND1_{ampl}$ NSCLC	$CDKN2A_{loss}$ RCC
	$CDKN2A_{loss}$ HNSCC	$CDKN2A_{del}$ esophageal ca	$CCND1_{ampl}$ melanoma
	$CDKN2A_{mut}$ uveal melanoma	$CDK4_{ampl}$ Sarcoma	$CCND1_{ampl}$ NET
	$CDKN2A_{loss}$ pancreatic ca	$CDKN2A_{loss}$ vulvar ca	$CDK4_{ampl}$ astrocytoma
	$CDKN2A_{del}$ NSCLC	$CDK4_{ampl}$ prostate cancer	$CDK4_{ampl}$ esophageal cancer
	$CDKN2A_{loss}$ pNET	$CDKN2A_{loss}$ ovarian cancer	$CCND2_{ampl}$ CRC
	$CDK6_{ampl}$ prostate cancer	$SMARCA4_{mut}$ CRC	
Durvalumab	MSI tumors		
Cabozantinib	MET_{ampl} melanoma	RET_{fusion} NSCLC	MET_{ampl} teratoma
	$NTRK2_{mut}$ GIST	MET_{mut} oesofagus cancer	
Ribociclib	$CDKN2A_{loss}$ prostate cancer	$CDKN2A_{loss}$ ependymoma	$CDK4_{ampl}$ melanoma
	$CDKN2A_{del}$ anaplastic meningioma	$CDKN2A_{loss}$ thymus carcinoma	$CDKN2A_{loss}$ Ewing Sarcoma
	$CDKN21_{del/mut}$ bladder cancer	$CDK6_{amp}$ mucoepidermoid cancer	$CDKN2A_{del}$ mesothelioma
	$CDKN2A_{loss}$ ceruminous cancer	$CDKN2A_{del}$ salivary gland cancer	
Afatinib	$NRG1_{fusie}$ NSCLC	$NRG1_{fusie}$ breast ca	$NRG1_{fusie}$ GI tumors
	$NRG1_{fusie}$ miscellaneous (all tumors)	$HER4_{mut}$ NSCLC	
Nivolumab	MSI tumors	HML tumors	
Olaparib	$BRCA_{mut}$ tumors		
Pembrolizumab	HML CRC	HML eso/card/stomach	
Dabraf + Tramet	$BRAF_{mut}$ NSCLC		
Trastuz. + Pertuz.	HER2 (exon 20) mut NSCLC		
Nivolumab	3^{rd} stage MSI tumors		