

Monthly DRUP Study Newsletter #74, 01 May 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

Congratulations to UMC Utrecht with the inclusion of DRUP patient number 100!



Highlights:

- 1) To date 1177 patients have started a DRUP treatment
- 2) UMC Utrecht celebrated DRUP patient number 100, congratulations!
- 3) The inclusion of patients for erdafitinib can start
- 4) New DRUP paper accepted for publication

Study Update

To date, a total of 2237 cases have been submitted to the study team and 1035 of these have started a treatment within the DRUP stage 1 and 2 cohorts and 142 within the DRUP stage 3 cohort. The 3rd stage cohort is currently on hold because the maximum number of inclusions has been reached.

This month, one of our participating sites, UMC Utrecht, celebrated the inclusion of DRUP patient number 100 with cake for the whole study team. Congratulations with this great achievement and thank you for all the hard work!

In this issue of our monthly newsletter we are very pleased to finally be able to inform you that erdafitinib has become available for shipment to all participating sites. Patients who have FGFR1-4 amplified tumors will be eligible for treatment with erdafitinib, urothelial cell carcinoma patients excluded. Patient submissions can be done via Alea or the DRUP email.

Scientific output

We are pleased to announce that the “Efficacy and toxicity of vemurafenib and cobimetinib in relation to plasma concentrations, after administration via feeding tube in patients with BRAF mutated thyroid cancer – a case series” manuscript of Maxime van Berge Henegouwen has been accepted for publication in *Cancer Chemotherapy and Pharmacology*! The manuscript describes two cases of patients with thyroid cancer, treated with vemurafenib and cobimetinib via a feeding tube in DRUP. A partial response was observed in both patients, but they also experienced significant toxicity. As the study team believed that these cases had educational value for the oncology society, a case series was written. The manuscript will soon be available in *Cancer Chemotherapy and Pharmacology*.

Event & meetings

On 19th of April our semi-annual pharma meeting took place in the AVL. The DRUP team was happy to be able to give a study update and share recent data output. We appreciated everyone’s attendance and look back at a very successful meeting.

On the 9th of May, we will host a meeting with members of the Norwegian DRUP like trial IMPRESS. The IMPRESS trial has been open for inclusion 1 year now and 17 hospitals across Norway are participating. The purpose of this meeting is to exchange experiences and to discuss our further collaboration.

Study team update

In the AVL Lena Bilet is back from pregnancy leave and will continue her function as trial manager for DRUP. A big thanks to Hassan Mkadmi, who did a great job keeping it all running during her leave.

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

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

Committed

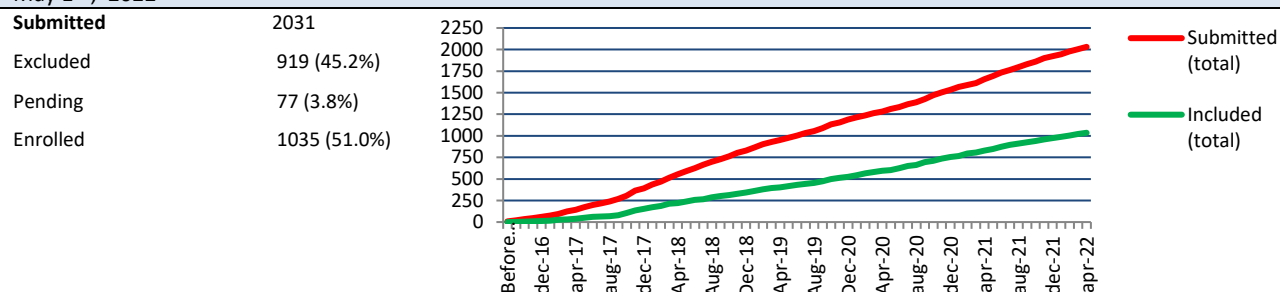
<u>Lilly</u> Selpercatinib	<u>GSK</u> Niraparib
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Calendar & publicity

May, 9th IMPRESS visit

Table 2: Submission and accrual overview

May 1st, 2022



Submissions and accrual 3rd stage cohort Nivolumab for MSI tumors

May 1st, 2022

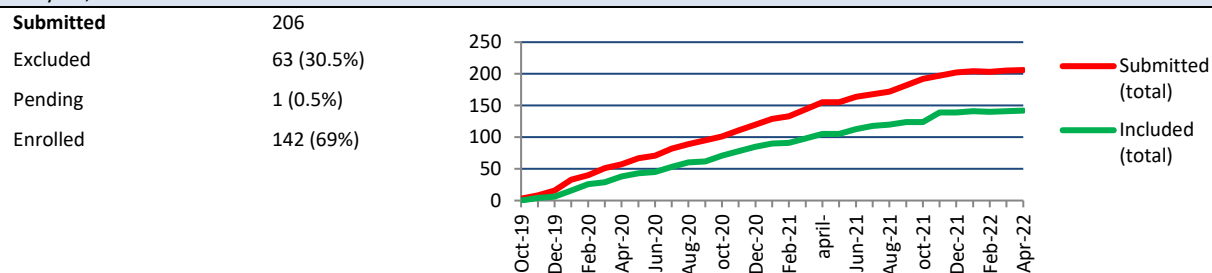


Table 3 : Participating sites

Currently open for inclusion (n = 35)

- | | | | |
|---|--|---|---|
| <ul style="list-style-type: none"> • AMC • AVL • Amphia • Bravis • Deventer Ziekenhuis • Erasmus MC • ETZ • Franciscus • Gelderse Vallei • Gelre Ziekenhuizen | <ul style="list-style-type: none"> • Haaglanden MC • Haga ziekenhuis • Isala • Martini • Maxima MC • MC Leeuwarden • Meander • Nij Smellinghe • Treant Zorggroep • NWZ | <ul style="list-style-type: none"> • Reinier de Graaf • Rijnstate • Spaarne Gasthuis • St. Antonius • UMC Groningen • UMC Leiden • Maastricht UMC • Radboud UMC • UMC Utrecht • VieCuri | <ul style="list-style-type: none"> • 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)		
Regorafenib	RET+ NSCLC	RET+ esthesioneuroblastoma	KIT _{mut} melanoma	
Dabraf + Tramet	KIT _{mut} Thymuscarcinoma	BRAF _{mut} ACC	FLT1 _{ampl} duodenal carcinoma	
	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 _{mut} (pilocytair) astrocytoom	NRAS _{mut} yolk sac tumor	
	GNA11 _{mut} melanocyttaire tumor	NRAS _{mut} cholangio cancer	BRAF _{del} exon 12 deletion NSCLC	
	BRAF _{mut} NSCLC	NRAS _{mut} salivary duct ca	MAP2K4 _{loss} pancreas cancer	
	NF1 _{mut} low grade glioma	BRAF _{mut} pancreas cancer	MAP2K1 _{mut} pancreas cancer	
	MAP2K1 _{mut} stomach cancer	BRAF _{mut} fusie Urothelcelca	MAP2K1 _{mut} CUP	
	KRASmut Erdheim Chester disease	BRAF fusie glioneurale tumor	NF1 _{mut} GBM	
	MAP2K4 _{mut} /loss CRC			
	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	HER2 _{ampl} melanoom	
Vemur. + Cobimet.	BRAF _{mut} salivary duct	BRAF _{mut} ACUP	BRAF _{mut} ovarian ca	
	BRAF _{mut} thyroid ca	BRAF non-V600 _{mut} NSCLC	BRAFV600E _{mut} Erdheim Chester Disease	
	BRAFV600 mut pap craniofaryngeoom			
Vismodegib	PTCH1 _{mut} 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 _{mut} ACUP	FGFR2 _{mut} 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 _{mut} GBM	FGFR2 _{mut} digital papillary cancer	FGFR2 _{mut} fusion pancreas cancer	
	FGFR2 _{amp} NSCLC	FGFR3 _{mut} 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	FGFR1 _{mut} glioma	
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} thyroid cancer	FLT3 _{ampl} CRC	
	CSF1R _{mut} CRC	KIT _{amp} NSCLC	FGFR2 _{ampl} ovarian cancer	
	RET fusion pancreatic cancer	FLT3 _{mut} CRC	FLT3 mut PMP	
Crizotinib	ALK _{mut} 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 thyroid 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)	ALK mutations/amplification (all tumor types)		
Abemaciclib	CCND1 _{ampl} UCC	CCND1 _{mut} NSCLC	CCND1 _{ampl} prostate cancer	
	CCND1 _{ampl} melanoma	CCND3 _{ampl} small intestine	CDK4 _{ampl} (lipo)sarcomen	
	CCND1 _{ampl} urachusca	CDK4 amp GBM	CDK4 amp duodenumcarcinoom	
	CCND1 _{ampl} plaveiselcelca blaas	CCND3 _{ampl} oesofagusca	CCND1 _{ampl} ovariumcarcinoom	
Alpelisib	Miscellaneous tumors with PIK3CA _{mut}	PIK3CA _{mut} SCC gynecologic tumors	PIK3CA _{mut} gynecologic tumors	
	PIK3CA _{mut} upper-GI tumors (esophagus, stomach)	PIK3CA _{mut} HNSCC	PTEN _{loss} prostate cancer	
	Double hit cohort (histology-agnostic)	PIK3CA _{mut} prostaatcarcinoom	PTEN _{loss} RCC	
	PTEN _{loss} gyn tumors (ovarian/endometrial)	PIK3R1 _{mut} gyn tumors (cervix/endometrial)	PTEN _{loss} salivary gland carcinoma	
Talazoparib	Tumors with HRD sign (with/without BRCA VUS)			
Irlotinib	ROS-1 fusion NSCLC			
Dacomitinib	HER2 _{amp} oesophaguscarcinoom	HER2 _{ampl} endometriumca	EGFR _{amp} peniscarcinoom	
	EGFR _{amp} CRC	EGFR _{amp} UCC		
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 _{amp} NSCLC	CDKN2A _{loss} RCC
	CDKN2A _{loss} HNSCC	CDKN2A _{del} esophageal ca	CCND1 _{amp} melanoma
	CDKN2A _{mut} uveal melanoma	CDK4 _{amp} Sarcoma	CCND1 _{amp} NET
	CDKN2A _{loss} pancreatic ca	CDKN2A _{loss} vulvar ca	CDK4 _{amp} astrocytoma
	CDKN2A _{del} NSCLC	CDK4 _{amp} prostate cancer	CDK4 _{amp} esophageal cancer
	CDKN2A _{loss} pNET	CDKN2A _{loss} ovarian cancer	CCND2 _{amp} CRC
CDK6 _{amp} prostate cancer	SMARCA4 _{mut} CRC		
Durvalumab	MSI tumors		
Cabozantinib	MET _{amp} melanoma	RET _{fusion} NSCLC	MET _{amp} teratoma
	NTRK2 _{mut} GIST	MET _{mut} oesofagus cancer	
Ribociclib	CDKN2A _{loss} prostate cancer	CDKN2A _{loss} ependymoma	CDK4 _{amp} 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 _{fusion} NSCLC	NRG1 _{fusion} breast ca	NRG1 _{fusion} GI tumors
	NRG1 _{fusion} 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		