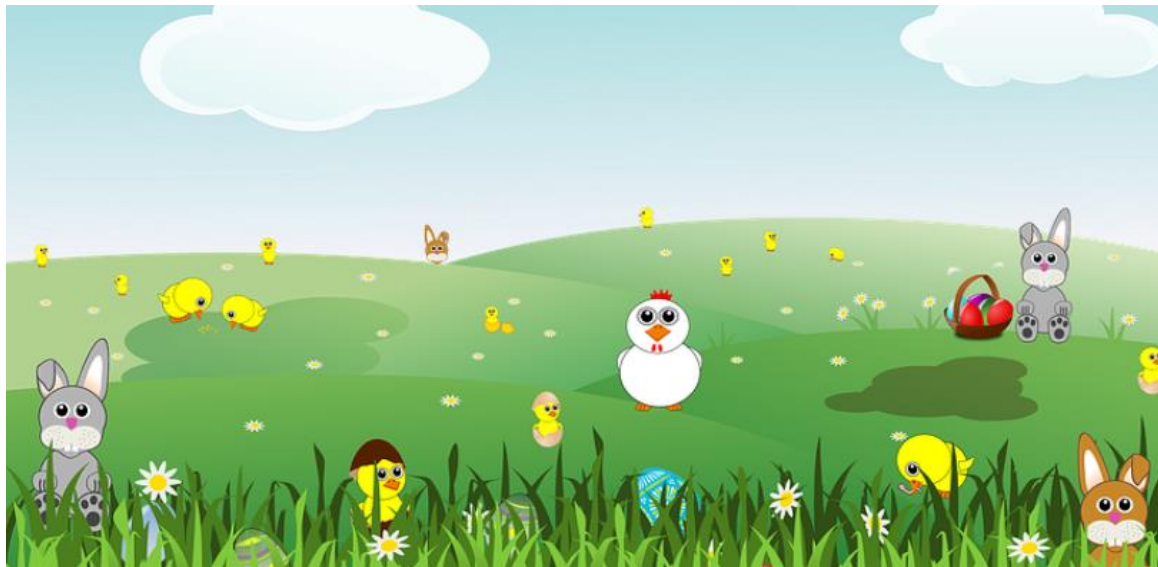


Monthly DRUP Study Newsletter #73, 01 April 2022

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

Thank you very much for the great job you are doing for this study. Please keep up the good spirit!



Highlights:

- 1) To date, a total of 1163 patients have been enrolled, of which 141 in stage 3
- 2) 3rd stage Nivolumab cohort data analysis is in full swing
- 3) Erdafitinib is in the final release phase, and will be available very soon!
- 4) The number of submissions is growing fast!

Study Update

To date, a total of 2211 cases have been submitted to the study team and 1163 (52.6%) of these have started a treatment within the DRUP study. For the 3rd stage Nivolumab cohort, a number of 141 patients have been included and this cohort has been put on hold, because the maximum number of inclusions has been reached. New submissions will be placed on a waiting list until further notice.

Erdafitinib is in the final release phase, and will be available for shipment to clinical sites very soon. Patients who have FGFR1-4 amplified tumors will be eligible for treatment with this drug, urothelial cell carcinoma patients excluded.

For selpercatinib, all necessary steps have been completed and this drug will be available as soon as a delivery from our pharmaceutical partner is received, which is expected to take place in June/July this year. Patients with RET mutations and RET fusions will be eligible for treatment with this compound.

The availability of niraparib is still being finalized, the required administrative works are in full progress. Niraparib is a PARP inhibitor, for which patients with an alteration in one of the HRD genes might be eligible.

Information for Participating Sites

The availability of erdafitinib will be communicated with you in due course. It will be shipped to your site from our pharmacy.

Please be informed that a re-order of the combination vemurafenib + cobimetinib includes 2 cycles, and should be ordered as such. Sporadically we see a re-order placed for 3 cycles instead of 2. Furthermore, we noticed that many sites have an economic policy when it comes to ordering medication, our compliments for that!

We like to share with you some common findings that were identified by our monitor during last site monitoring visits:

- Some delay concerning eCRF data entry, and some of the pages were not fully completed
- A few of the mandatory assessments were occasionally not (fully) performed (e.g. WHO performance status, blood collection, vital signs, etc.)
- Submission of a few SAEs follow-up forms was delayed
- Delegation log was in some cases not completely up to date
- Some missing forms in Investigator Site File (e.g lab certificate, normal ranges, etc)

Please pay attention to the above mentioned monitor observations within your site and ensure good/adequate follow-up if applicable. This to help ensure that the study meets the quality and compliance requirements at all times.

Warm regards,

Principal Investigators: Henk Verheul, Hans Gelderblom, Emile Voest

Study Coordinators: Maxime van Berge Henegouwen, Laurien Zeverijn, Gijs de Wit, Birgit Geurts, Ilse Spiekman

Clinical Project Manager: Hassan Mkadmi

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> Afatinib	
			<u>Janssen</u> Erdafitinib

Committed

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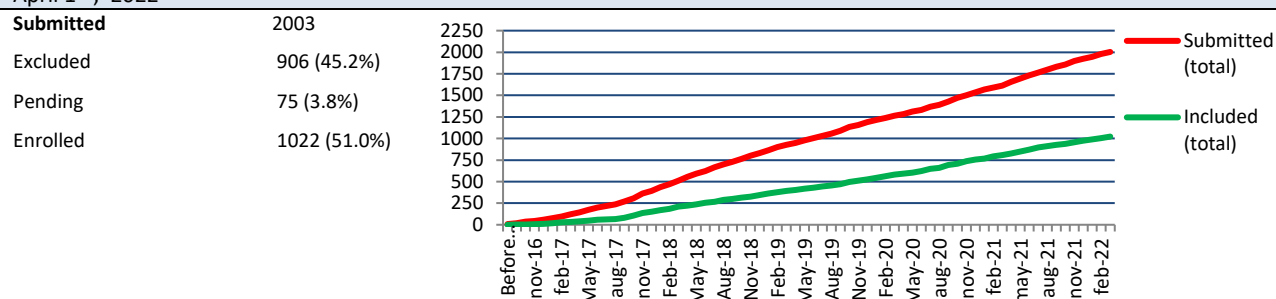
Calendar & publicity

April, 11th IDMC meeting

April, 19th Pharma meeting

Table 2: Submission and accrual overview

April 1st, 2022



Submissions and accrual 3rd stage cohort Nivolumab for MSI tumors

April 1st, 2022

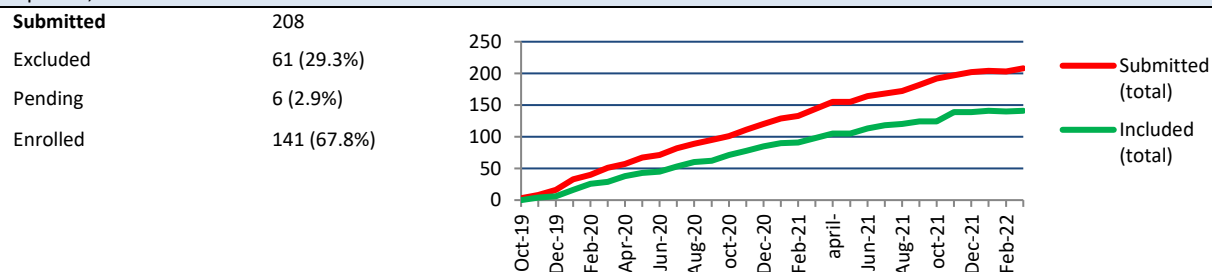


Table 3 : Participating sites

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 <p>In preparation</p> <ul style="list-style-type: none"> • 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
	KIT _{mut} Thymuscarcinoma	BRAF _{mut} ACC	FLT1 _{ampl} duodenal carcinoma
	RAF1mut NSCLC		
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
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 _{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} Urothelcelca	MAP2K1 _{mut} CUP
	KRASmut Erdheim Chester disease	BRAF _{mut} fusie glioneurale tumor	NF1mut GBM
	MAP2K4mut/loss CRC		
	Trastuz. + Pertuz.	HER2 _{ampl} CRC	HER2 _{ampl} cholangio ca
HER2 _{mut} ovarian ca		HER2 _{ampl} salivary duct ca	HER2 _{ampl} NSCLC
HER2 _{mut} CRCglio		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 _{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-V600mut} NSCLC	BRAF _{V600Emut} Erdheim Chester Disease
	BRAFV600 mut pap craniofaryngeoom	BRAFV600E mut NSCLC	
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 _{mut} 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} 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 _{mut} fusie NSCLC	FGFR1mut 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 _{ampl} NSCLC	FGFR2 _{ampl} ovarian cancer
	RET fusion pancreatic cancer	FLT3mut 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 _{mut} CUP
	MET _{mut} 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 _{ampl} NSCLC	CCND1 _{ampl} prostate cancer
	CCND1 _{ampl} melanoma	CCND3 _{ampl} small intestine	CDK4ampl (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	PIK3CAmut gynecologic tumors
	PIK3CAmut upper-GI tumors (esophagus, stomach)	PIK3CAmut HNSCC	PTEN _{loss} prostate cancer
	Double hit cohort (histology-agnostic)	PIK3CAmut prostaatacarcinoom	PTEN _{loss} RCC
	PTEN _{loss} gyn tumors (ovarian/endometrial)	PIK3R1mut gyn tumors (cervix/endometrial)	PTEN _{loss} salivary gland carcinoma
Talazoparib	ATM/ATRmut tumors	FANCA/FANCC/FANCD2/FANCF/FANCMmut tumors	RAD51/RAD51B/RAD54L/NBN/MRE11mut tumors
	mutations in other HRR genes (BARD1/BRIP1/CHEK1/2/PALB2/PRA1)	Tumors with HRD signature (with or without BRCA VUS)	Tumors with double-hit in HRR pathway
Iorlatinib	ROS-1 fusion NSCLC		
Dacomitinib	HER2amp oesophaguscarcinoom	HER2ampl endometriumca	EGFRamp peniscarcinoom
	EGFRamp CRC		
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
	CDKN2A _{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	BRCAMut 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		