

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

Study Update

To date, a total of 1899 cases have been submitted to the study team and 957 (50.4%) of these have started a treatment within the DRUP study. For the 3rd stage Nivolumab cohort, a number of 139 patients have been included and this cohort has been put on hold, because the maximum number has been reached. New submissions will be placed on a waiting list until further notice. However, we do not expect to be able to provide treatment to more patients within this cohort unfortunately.

Recently the Crizotinib cohort for MET exon 14 skipping mutated NSCLC mutations was also put on hold. However one slot has become available, so if you have a potential case: do not hesitate to submit it to the study team.

Next to the above we are also pleased to share with you that the finishing touches are being put on the preparations to make compound erdafitinib available for the DRUP study soon. Patients who have FGFR1-4 amplified tumors will be eligible for treatment with this drug within DRUP, urothelial cell carcinoma patients excluded.

We are very happy to inform you that the Nordic countries (Denmark, Sweden, Norway, and Finland) are setting up national clinical trials, modeled on the DRUP trial in the Netherlands. To empower this collaboration, a *Memorandum of Understanding (MoU)* was signed by the leaders of the DRUP and the Nordic Precision Medicine Trial Network. This MoU intends to facilitate data sharing between the participating parties. Please find herewith the link to more information on this topic: [link](#)

Study Protocol Amendment

Last month, study protocol amendment number 15 was submitted to the Ethics Committee and the Competent Authority. In the meanwhile, both bodies have given their approval!

The main item of this substantial amendment was the addition of two new investigational products: selpercatinib and niraparib. We hope to be able to add both new treatment options to the study soon. We will keep you posted on the progress!

Information for Participating Sites

The updated documents related to protocol amendment #15 have been distributed to and will be also available on the DRUP study website: www.drupstudy.nl

In the previous newsletter you were asked to submit drug (re-)order forms timely, as there is a minimum of 5 working days delivery time. We are very happy to see, that at the moment nearly all sites are responding to our request. We would like to thank you for that!

Last month you were requested to address the drug reorder form only for drug-order purposes. This in contrast to the past, when the form was also used to inform us about patient status in the study/cycle when no drug delivery was needed. So far we have noticed that this new approach is well applied by all sites.

We are almost at the end of this year in which we have achieved a lot together and we can look back on a very successful year for the DRUP study. We are already looking forward to next year with great joy and hope for an equally pleasant cooperation with you as this year. Many thanks for the great efforts and we wish you happy holidays and a prosperous and healthy 2022!

Warm regards,

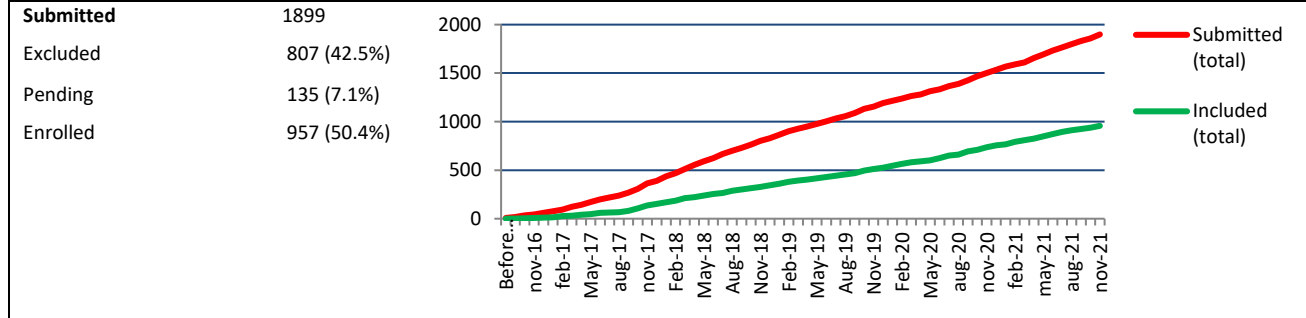
Henk Verheul, Hans Gelderblom and Emile Voest: Principle Investigators
Maxime van Berge Henegouwen, Laurien Zeverijn, Gijs de Wit and Birgit Geurts: Study Coordinators
Hassan Mkadmi: Clinical Projects Manager

List of pharmaceutical companies & study drugs			
Confidential, list might be subjected to change			
Currently available			
<u>Amgen</u>	<u>Eisai</u>	<u>Bayer</u>	<u>Roche</u>
Panitumumab	Lenvatinib	Regorafenib	Erlotinib
			Trastuzumab + Pertuzumab
<u>BMS</u>	<u>AstraZeneca</u>	<u>Clovis Oncology</u>	Vemurafenib + Cobimetinib
Nivolumab	Olaparib	Rucaparib	Vismodegib
Ipilimumab	Durvalumab		Atezolizumab + bevacizumab
		<u>MSD</u>	Alectinib
<u>Novartis</u>	<u>Pfizer</u>	Pembrolizumab	Entrectinib
Dabrafenib	Axitinib		
Nilotinib	Crizotinib	<u>Lilly</u>	
Trametinib	Sunitinib	Abemaciclib	
Ribociclib	Palbociclib		
Alpelisib	Talazoparib, dacomitinib	<u>BI</u>	<u>Janssen</u>
	Lorlatinib	Afatinib	Erdafitinib
Committed			
<u>Lilly</u>	<u>GSK</u>		
Selpercatinib	Niraparib		

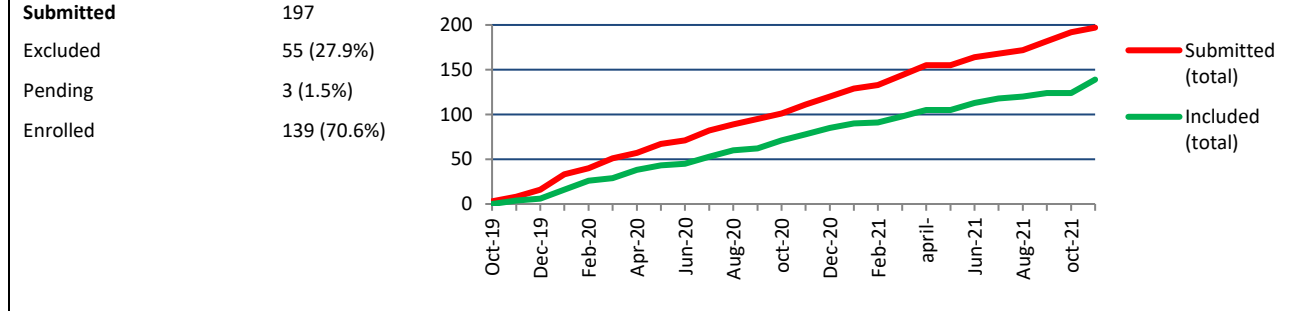
Calendar & publicity

November 16th
 Study protocol amendment #15 was approved by Ethics Committee and Competent Authority (CCMO).

Submission and accrual overview
December 3rd, 2021



Submissions and accrual 3rd stage cohort Nivolumab for MSI tumors
December 3rd, 2021



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 (n=2)**
- Maasstad
 - Bernhoven

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	MSI tumors	HML tumors	3 rd stage MSI tumors
Nivolumab + ipilimumab	HML tumors		
Olaparib	ATM _{mut} tumors	BRCA _{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
	RAF/RAS _{wt} GBM	RAF/RAS _{wt} vulvar ca	RAF/RAS _{wt} ACUP
	RAF/RAS _{wt} anal ca		
Pembrolizumab	HML CRC	HML eso/card/stomach	HML HNSCC
	HML prostate ca	HML breast ca	HML miscellaneous
	HML > 290 (all type)		
Regorafenib	RET+ NSCLC	RET+ neuroblastoma	KIT _{mut} melanoma
	KIT _{mut} Thymuscarcinoma	BRAF _{mut} ACC	FLT1 _{ampl} duodenal carcinoma
Dabraf + Tramet	BRAF _{mut} NSCLC	BRAF _{mut} GBM	BRAF _{mut} low grade glioma
	BRAF _{mut} NEC	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} (pilocytaire) astrocytuum	NRAS _{mut} yolk sac tumor
	GNA11 _{mut} melanocytair tumor	NRAS _{mut} cholangio cancer	BRAF _{exon 12 deletion} NSCLC
	BRAF _{mut} NSCLC	NRAS _{mut} salivary duct ca	MAP2K4 _{mut} pancreas cancer
	NF1 _{mut} low grade glioma	BRAF _{mut} pancreas cancer	MAP2K1 _{mut} pancreas cancer
	MAP2K1 _{mut} stomach cancer	BRAF _{mut} fusie Urothelcelca	
Trastuz. + Pertuz.	HER2 _{ampl} CRC	HER2 _{ampl} cholangio ca	HER2 _{mut} NSCLC
	HER2 _{mut} ovarian ca	HER2 _{ampl} salivary duct ca	HER2 _{ampl} NSCLC
	HER2 _{mut} CRC	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	
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		
Vismodegib	PTCH1 _{mut} sarcoma	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 _{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		
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	FTL3 _{ampl} CRC
	CSF1R _{mut} CRC	KIT _{ampl} NSCLC	FGFR2 _{ampl} ovarian cancer
	RET-CCDC6 fusion pancreatic cancer		
Crizotinib	ALK _{mut} IMT	MET _{ampl} CRC	ALK _{mut} CRC
	MET _{mut} NSCLC	MET _{ampl} esophageal ca	MET _{ampl} NSCLC
	ALK _{mut} thyroid	ALK _{mut} leiomyosarcoma	ALK _{mut} CUP
	MET _{mut} anaplastic tyroid cancer	MET _{ampl} HCC	MET _{mut} GEJ-tumor
	MET _{amp} ovarium cancer	MET _{mut} (papillair) kidney cell cancer	
Axitinib	FLT1 _{ampl} CRC		
Rucaparib	HRR _{alt} ovarian cancer	HRR _{alt} prostate cancer	HRR _{alt} pancreatic cancer
	HRR _{alt} miscellaneous	HRR _{alt} Breast cancer	
Alectinib	ALK fusion (all tumor types)		
Abemaciclib	CCND1 _{ampl} UCC	CCND1 _{ampl} NSCLC	CCND1 _{ampl} prostate cancer
	CCND1 _{ampl} melanoma	CCND3 _{ampl} small intestine	CDK4 _{ampl} (lipo)sarcomen
	CCND1 _{ampl} urachusca	CDK4 amp GBM	
Alpelisib	Miscellaneous tumors with PIK3CA _{mut}	PIK3CA _{mut} SCC gynecologic tumors	PIK3CA _{mut} gynecologic tumors
	PIK3CA _{mut} upper-GI tumors	PIK3CA _{mut} HNSCC	PTEN _{loss} prostate cancer
	Double hit cohort (histology-agnostic)	PIK3CA _{mut} prostaatacarcinoom	PTEN _{loss} RCC
Talazoparib	Tumors with HRD signature		
Legend	Cohort closed	Cohort on hold	Slots available

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} mucocpidermoid 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	