

Study update

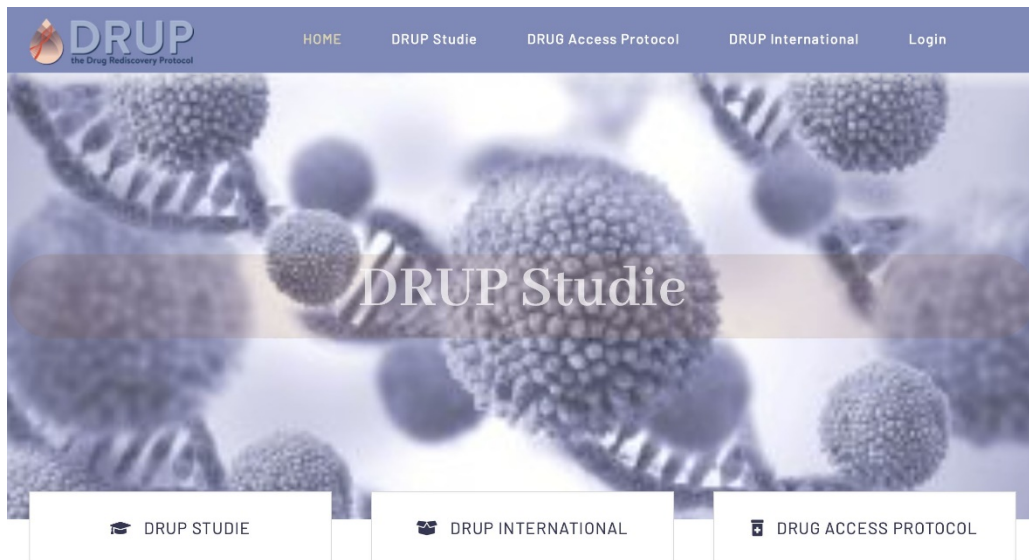
To date, a total of 1733 cases have been submitted to the DRUP study team 872 patients have started on one of the study treatments. Also for the 3rd stage nivolumab cohort inclusion is going well, with 113 patients currently enrolled. There are still a few slots available for this cohort, so we will be happy to receive submissions of potential candidates.

In the meantime we are working closely with the payers and ZINL to see how we can continue providing access to nivolumab after the cohort is completed. This is key to make sure patients will benefit from all the work done in the past years.

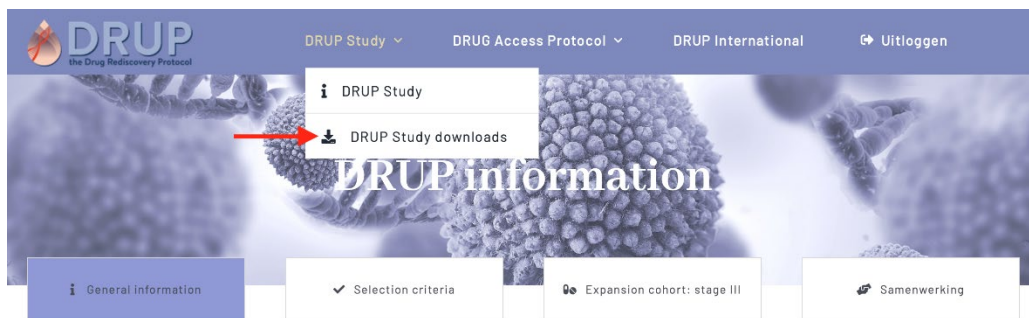
New DRUP website

This month we are very excited to share with you that our new website has been launched! The website can be visited via www.drupstudy.nl

Next to information about the DRUP study, the new website also includes information about our international collaborators and their DRUP-like trials and a recently started sister study of DRUP, DRUG ACCESS.



Under the heading 'DRUP study' you will find general information about the study. However, by logging into our password protected area, you will be able to find more specific material, including all study related documents. Use the drop down menu as shown below to access the study downloads.



We would kindly ask everyone to take this new website in use from now on. The CPCT website will no longer be updated for DRUP. The login information will be sent to all sites in a separate email.

If you have any suggestions to optimize the quality of our website, please let us know.

Scientific output

We are pleased to announce that the “Paired biopsies” manuscript of Joris van de Haar and Louisa Hoes has been accepted for publication in *Nature Medicine*! The study, with WGS data derived from the CPCT, DRUP and WIDE study, focusses on the added value of obtaining and analyzing multiple tumor biopsies during the course of disease. The study demonstrates that over time, only minor changes are seen in the genomic landscape of a tumor, therefore justifying only one biopsy analysis per cancer patient. The manuscript will soon be available in *Nature Medicine*.

Furthermore, the manuscript “Rare cancers + first 500 patients treated in DRUP” has been drafted and is reviewed by the participating sites and pharma. We hope that manuscript is finalized soon so we can submit it for publication. Briefly, in this paper we report on the first 500 patients treated in the DRUP and compare the outcomes in rare cancer patients with non-rare cancer patients. The take home message is that patients with rare cancers are equally benefitting from drugs in the DRUP as more common cancers.

Study team update

This month we unfortunately have to say goodbye to one of our DRUP study coordinators, Hanneke van der Wijngaart. After 4 years as a PhD student in the VUMC, she has returned to the clinic to continue her training to become a medical oncologist. We would like to thank her for a great collaboration and all her hard work for the study and wish her all the best in her future challenges. We are definitely going to miss her in the team!

Best regards,

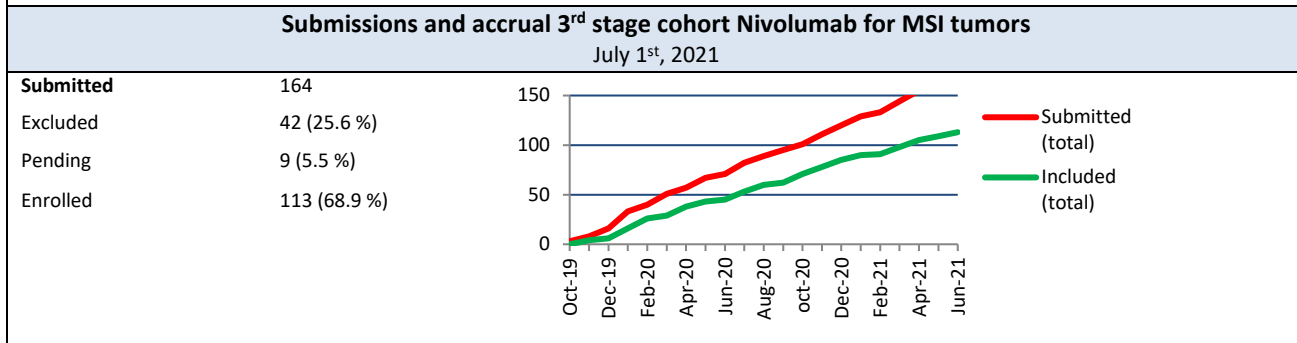
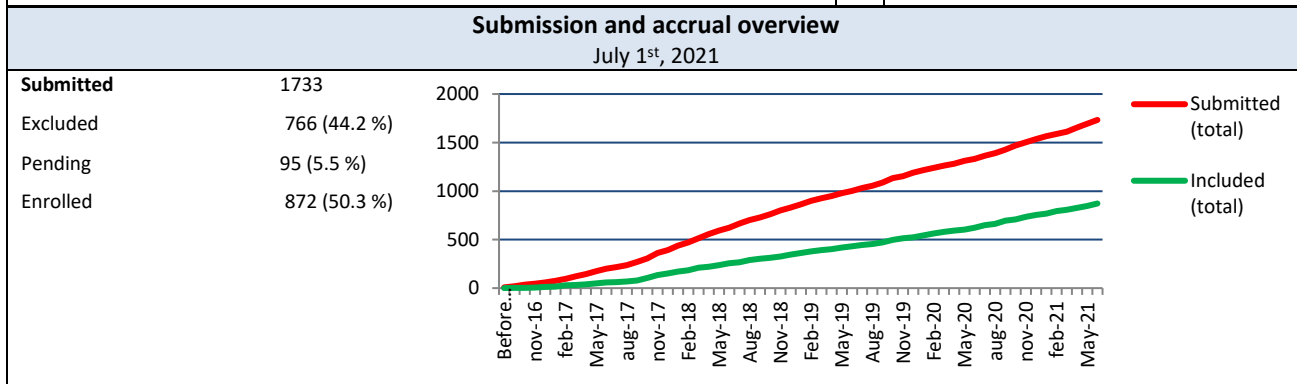
Henk Verheul, Hans Gelderblom and Emile Voest, Principal Investigators

Maxime van Berge Henegouwen, Laurien Zeverijn, Gijs de Wit and Birgit Geurts, study coordinators

Lena Bilet, trial 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 +
<u>BMS</u>	<u>AstraZeneca</u>	<u>Clovis Oncology</u>	Pertuzumab
Nivolumab	Olaparib	Rucaparib	Vemurafenib +
Ipilimumab	Durvalumab		Cobimetinib
		<u>MSD</u>	Vismodegib
<u>Novartis</u>	<u>Pfizer</u>	Pembrolizumab	Atezolizumab +
Dabrafenib	Axitinib		bevacizumab
Nilotinib	Crizotinib	<u>Lilly</u>	Alectinib
Trametinib	Sunitinib	Abemaciclib	Entrectinib
Ribociclib	Palbociclib		
Alpelisib	Talazoparib,	<u>BI</u>	
	Dacomitinib	Afatinib	
	Lorlatinib		
Committed			
<u>Janssen</u>			
Erdafitinib			

Calendar & publicity
JULY: 5 th of July IDMC meeting
AUGUST: 28 th of August Stelvio for life



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 (n=2)			
<ul style="list-style-type: none"> Maasstad Bernhoven 			

DRUGS OPEN FOR INCLUSION			
Nilotinib	KIT _{mut} GIST	PDGFRA _{mut} GIST	PDGFRA _{mut} mesothelioma
	PDGFRB _{amp} CRC	KIT _{mut} melanoma	
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)
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 _{amp} duodenal carcinoma
Dabraf + Tramet	BRAF _{mut} NSCLC	BRAF _{mut} GBM	BRAF _{mut} low grade glioma
	BRAF _{mut} NEC	BRAF _{mut} cholangiocarcinoma	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 _{fusion} (pilocytair) astrocytoma	NRAS _{mut} yolk sac tumor
	GNA1 _{mut} melanocytair tumor	NRAS _{mut} cholangio cancer	BRAF _{exon 12} deletion NSCLC
	BRAF _{fusion} NSCLC	NRAS _{mut} salivary duct ca	MAP2K4 _{loss} pancreas cancer
	NF1 _{mut} low grade glioma		
Trastuz. + Pertuz.	HER2 _{amp} CRC	HER2 _{amp} cholangio ca	HER2 _{mut} NSCLC
	HER2 _{mut} ovarian ca	HER2 _{amp} salivary duct ca	HER2 _{amp} NSCLC
	HER2 _{mut} CRC	HER2 _{mut} cervical ca	HER2 _{amp} vulvar ca
	HER2 _{amp} cervical ca	HER2 _{amp} hidradenoca	HER2 _{amp} UCC
	HER2 _{amp} ovarian ca	HER2 _{amp} NEC	HER2 _{mut} UCC
	HER2 _{mut} ACC		
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
Vismodegib	PTCH1 _{mut} sarcoma	PTCH1 _{mut} medulloblastoma	
Erlotinib	EGFR _{mut} GBM	CRC with EGFR mutations	
Lenvatinib	FGFR1 _{amp} CRC	FGFR2 _{amp} CRC	FGFR2 _{amp} breast ca
	FGFR1 _{amp} osteosarcoma	FGFR1 _{amp} NSCLC	FGFR3 _{mut} anal ca
	FGFR2 _{amp} esophageal ca	FGFR2 _{mut} endometrial ca	FGFR3 _{amp} SGT
	FGFR2 _{fusion} ACUP	FGFR2 _{fusion} cholangioca	FGFR1 _{amp} breast ca
	FGFR2 _{amp} lurchal ca	FGFR3 _{mut} UCC	FGFR2 _{mut} ACC
	FGFR3 _{amp} NEC nasal cavity	FGFR1 _{mut} glioneural tumor	FGFR3 _{mut} HNSCC
	FGFR3 _{fusion} GBM	FGFR2 _{mut} digital papillary cancer	FGFR2 _{fusion} pancreas cancer
	FGFR2 _{amp} NSCLC		
Sunitinib	KIT _{mut} thymus ca	PDGFRA _{mut} prostate ca	FGFR1 _{amp} UCC
	PDGFRB _{amp} breast ca	PDGFRB _{mut} osteosarcoma	PDGFRA _{amp} ACC
	FGFR1 _{amp} Ovarian cancer	PDGFRA _{amp} thyroid cancer	FTL3 _{amp} CRC
	CSF1R _{mut} CRC	KIT _{amp} NSCLC	FGFR2 _{amp} Ovarian cancer
Crizotinib	ALK _{rus} IMT	MET _{amp} CRC	ALK _{mut} CRC
	MET _{mut} NSCLC	MET _{amp} esophageal ca	MET _{amp} NSCLC
	ALK _{mut} thyroid	ALK _{rus} leiomyosarcoma	ALK _{fusion} CUP
	MET _{fusion} anaplastic thyroid cancer	MET _{amp} HCC	MET _{amp} GEJ-tumor
Axitinib	FLT1 _{amp} CRC		
Afatinib	NRG1 _{fusion} NSCLC	NRG1 _{fusion} breast ca	NRG1 _{fusion} GI tumors
	NRG1 _{fusion} miscellaneous (all tumors)	HER4 _{mut} NSCLC	
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 _{amp} UCC	CCND1 _{amp} NSCLC	CCND1 _{amp} prostate cancer
	CCND1 _{amp} melanoma	CCND3 _{amp} small intestine	
Alpelisib	Miscellaneous tumors with PIK3CA _{mut}	PIK3CA _{mut} SCC gynecologic tumors	
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} mucoepidermoid cancer	CDKN2A _{del} mesothelioma
	CDKN2A _{loss} ceruminous cancer	CDKN2A _{del} salivary gland cancer	
Legend	Cohort closed	Cohort on hold	Slots available