

## Monthly DRUP newsletter 65, 01 aug 2021

### Study update

To date a total of 1763 cases have been submitted to the study team and the half of these patients have been offered a treatment within the DRUP study. Also, the 3<sup>rd</sup> stage nivolumab cohort expands on a constant basis with currently 118 patients enrolled.

The collection of the stool samples in the 3<sup>rd</sup> stage nivolumab cohort is also going well. Currently, we have collected 70 pre-treatment fecal samples. We would like to emphasize that this fecal sample is mandatory and has to be obtained prior to treatment start, after 8 weeks on treatment and again at progression of disease. Patients cannot start treatment before the baseline fecal sample has been collected.

### Important information for participating sites

The cohort **pembrolizumab for miscellaneous tumors with high mutational load 140-290** is currently on hold, as the final patients have been enrolled. When these patients reach the primary endpoint, the cohort will be formally closed for final analysis. New patients qualifying for this cohort could be placed on a waiting list for slots that may be released in the future (this is however not guaranteed). However, the ipilimumab and nivolumab cohort for tumors with high mutational load >199/ TMB 15-39 (TSO500)/ TMB 11-24 (Oncomime) is still open for inclusion.

### Scientific output

We are excited to inform you that the DRUP related **abstract “Results of trastuzumab/pertuzumab combination therapy in advanced pre-treated HER2 mutated non-small cell lung cancer”** for **ESMO Virtual Congress 2021** (which will be held 16-21 September 2021) has been accepted for E-Poster presentation!

Furthermore, the manuscript **“The importance of bi-allelic loss of function of BRCA1/2 in patients selection for olaparib – a Drug Rediscovery Protocol (DRUP) cohort”** has been provisionally accepted for Clinical Cancer Research! Briefly, in this paper we report the results of the completed cohort olaparib for BRCA 1/2 mutated tumors. The results indicate that olaparib is an effective treatment option for patients with tumors harboring bi-allelic BRCA inactivation, who exhausted all regular treatment options, regardless of tumor type. To confirm these results, we aim to open a 3<sup>rd</sup> stage cohort in the near future. Of course, we will inform you once this cohorts is formally opened.

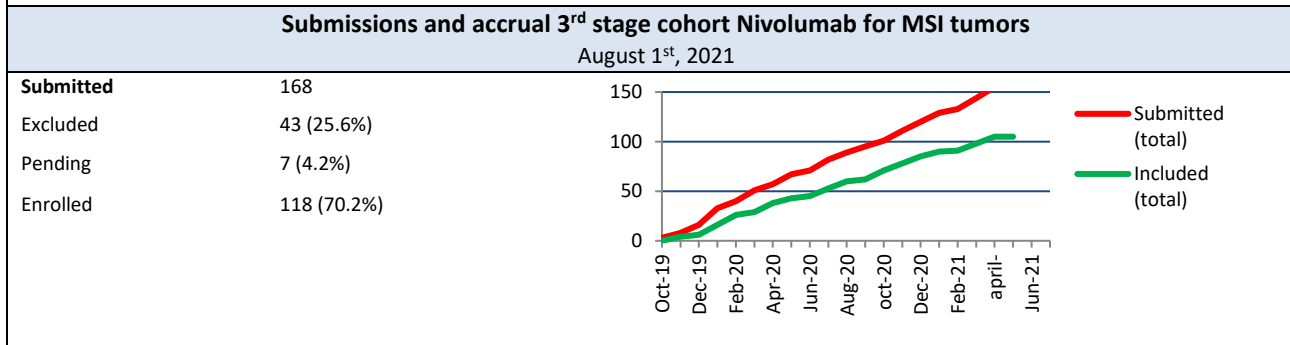
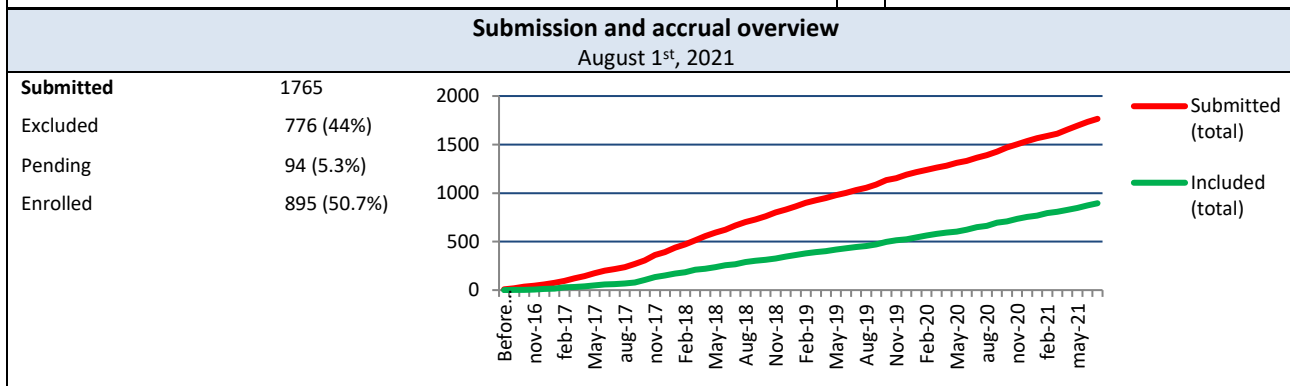
Last but not least, the DRUP team wishes all of you a lovely summer!

Best regards,

Henk Verheul, Hans Gelderblom and Emile Voest, Principle 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 – <a href="#">click here for profiles</a>			
<b>Currently available</b>			
<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		
<b>Committed</b>			
<u>Janssen</u>			
Erdafitinib			

Calendar & publicity
<b>AUGUST</b>
28 <sup>th</sup> of August Stelvio for life



Participating sites			
<b>Currently open for inclusion (n = 35)</b>			
• AMC	• Haaglanden MC	• Reinier de Graaf	• ZG Twente
• AVL	• Haga ziekenhuis	• Rijnstate	• Zuyderland
• Amphia	• Isala	• Spaarne Gasthuis	• Rivas Zorggroep
• Bravis	• Martini	• St. Antonius	• OLVG
• Deventer Ziekenhuis	• Maxima MC	• UMC Groningen	• VUMC
• Erasmus MC	• MC Leeuwarden	• UMC Leiden	<b>In preparation (n=2)</b>
• ETZ	• Meander	• Maastricht UMC	• Maasstad
• Franciscus	• Nij Smellinghe	• Radboud UMC	• Bernhoven
• Gelderse Vallei	• Treant Zorggroep	• UMC Utrecht	
• Gelre Ziekenhuizen	• NWZ	• VieCuri	

Opened cohorts			
Nilotinib	KIT <sub>mut</sub> GIST	PDGFRA <sub>mut</sub> GIST	PDGFRA <sub>mut</sub> mesothelioma
	PDGFRB <sub>amp</sub> CRC	KIT <sub>mut</sub> melanoma	
Nivolumab	MSI tumors	HML tumors	3 <sup>rd</sup> stage MSI tumors
Nivolumab + ipilimumab	HML tumors		
Olaparib	ATM <sub>mut</sub> tumors	BRCA <sub>mut</sub> tumors	HRR deficient tumors (2x)
Panitumumab	RAF/RAS <sub>wt</sub> sarcoma	RAF/RAS <sub>wt</sub> HNSCC	EGFR <sub>mut</sub> NSCLC
	RAF/RAS <sub>wt</sub> thyroid ca	RAF/RAS <sub>wt</sub> salivary duct ca	RAF/RAS <sub>wt</sub> cervical ca
	RAF/RAS <sub>wt</sub> endometrial ca	RAF/RAS <sub>wt</sub> meningioma	RAF/RAS <sub>wt</sub> eye melanoma
	RAF/RAS <sub>wt</sub> GBM	RAF/RAS <sub>wt</sub> vulvar ca	RAF/RAS <sub>wt</sub> ACUP
	RAF/RAS <sub>wt</sub> 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 <sub>mut</sub> melanoma
	KIT <sub>mut</sub> Thymuscarcinoma	BRAF <sub>mut</sub> ACC	FLT1 <sub>amp</sub> duodenal carcinoma
Dabraf + Tramet	BRAF <sub>mut</sub> NSCLC	BRAF <sub>mut</sub> GBM	BRAF <sub>mut</sub> low grade glioma
	BRAF <sub>mut</sub> NEC	BRAF <sub>mut</sub> cholangiocarcinoma	BRAFV600E <sub>mut</sub> breast cancer
	BRAFV600E <sub>mut</sub> grade 3 glioma		
Dabrafenib	BRAF <sub>mut</sub> GBM	BRAF <sub>mut</sub> UCC	
Trametinib	NRAS <sub>mut</sub> ovarian ca	MAP2K1 <sub>mut</sub> NSCLC	NRAS <sub>mut</sub> NSCLC
	MAP3K1 <sub>mut</sub> NEC	MAP3K1 <sub>mut</sub> cervical ca	MAP2K1 <sub>mut</sub> CRC
	MAP2K4 <sub>mut</sub> CRC	MAP3K1 <sub>mut</sub> ACUP	MAP2K4 <sub>mut</sub> cholangioca
	MAP2K4 <sub>mut</sub> ovarian ca	MAP3K1 <sub>mut</sub> breast ca	MAP2K4 <sub>mut</sub> breast ca
	NRAS <sub>mut</sub> thyroid cancer	MAP3K1 <sub>mut</sub> prostate	NRAS <sub>mut</sub> pleomorphic tumor
	NRAS <sub>mut</sub> prostate	BRAF <sub>fusion</sub> (pilocytair) astrocytoma	NRAS <sub>mut</sub> yolk sac tumor
	GNA1 <sub>mut</sub> melanocytair tumor	NRAS <sub>mut</sub> cholangio cancer	BRAF <sub>exon 12 deletion</sub> NSCLC
	BRAF <sub>fusion</sub> NSCLC	NRAS <sub>mut</sub> salivary duct ca	MAP2K4 <sub>loss</sub> pancreas cancer
	NF1 <sub>mut</sub> low grade glioma		
Trastuz. + Pertuz.	HER2 <sub>amp</sub> CRC	HER2 <sub>amp</sub> cholangio ca	HER2 <sub>mut</sub> NSCLC
	HER2 <sub>mut</sub> ovarian ca	HER2 <sub>amp</sub> salivary duct ca	HER2 <sub>amp</sub> NSCLC
	HER2 <sub>mut</sub> CRC	HER2 <sub>mut</sub> cervical ca	HER2 <sub>amp</sub> vulvar ca
	HER2 <sub>amp</sub> cervical ca	HER2 <sub>amp</sub> hidradenoca	HER2 <sub>amp</sub> UCC
	HER2 <sub>amp</sub> ovarian ca	HER2 <sub>amp</sub> NEC	HER2 <sub>mut</sub> UCC
	HER2 <sub>mut</sub> ACC		
Vemur. + Cobimet.	BRAF <sub>mut</sub> salivary duct	BRAF <sub>mut</sub> ACUP	BRAF <sub>mut</sub> ovarian ca
	BRAF <sub>mut</sub> thyroid ca	BRAF <sub>non-V600mut</sub> NSCLC	BRAF <sub>V600Emut</sub> Erdheim Chester Disease
Vismodegib	PTCH1 <sub>mut</sub> Sarcoma	PTCH1 <sub>mut</sub> medulloblastoma	
Erlotinib	EGFR <sub>mut</sub> GBM	CRC with EGFR mutations	
Lenvatinib	FGFR1 <sub>amp</sub> CRC	FGFR2 <sub>amp</sub> CRC	FGFR2 <sub>amp</sub> breast ca
	FGFR1 <sub>amp</sub> osteosarcoma	FGFR1 <sub>amp</sub> NSCLC	FGFR3 <sub>mut</sub> anal ca
	FGFR2 <sub>amp</sub> esophageal ca	FGFR2 <sub>mut</sub> endometrial ca	FGFR3 <sub>amp</sub> SGT
	FGFR2 <sub>fusion</sub> ACUP	FGFR2 <sub>fusion</sub> cholangioca	FGFR1 <sub>amp</sub> breast ca
	FGFR2 <sub>amp</sub> urachal ca	FGFR3 <sub>mut</sub> UCC	FGFR2 <sub>mut</sub> ACC
	FGFR3 <sub>amp</sub> NEC nasal cavity	FGFR1 <sub>mut</sub> glioneural tumor	FGFR3 <sub>mut</sub> HNSCC
	FGFR3 <sub>fusion</sub> GBM	FGFR2 <sub>mut</sub> digital papillary cancer	FGFR2 <sub>fusion</sub> pancreas cancer
	FGFR2 <sub>amp</sub> NSCLC		
Sunitinib	KIT <sub>mut</sub> thymus ca	PDGFRA <sub>mut</sub> prostate ca	FGFR1 <sub>amp</sub> UCC
	PDGFRB <sub>amp</sub> breast ca	PDGFRB <sub>mut</sub> osteosarcoma	PDGFRA <sub>amp</sub> ACC
	FGFR1 <sub>amp</sub> ovarian cancer	PDGFRA <sub>amp</sub> thyroid cancer	FTL3 <sub>amp</sub> CRC
	CSF1R <sub>mut</sub> CRC	KIT <sub>amp</sub> NSCLC	FGFR2 <sub>amp</sub> ovarian cancer
Crizotinib	ALK <sub>fusion</sub> IMT	MET <sub>amp</sub> CRC	ALK <sub>mut</sub> CRC
	MET <sub>mut</sub> NSCLC	MET <sub>amp</sub> esophageal ca	MET <sub>amp</sub> NSCLC
	ALK <sub>mut</sub> thyroid	ALK <sub>fusion</sub> leiomyosarcoma	ALK <sub>fusion</sub> CUP
	MET <sub>fusion</sub> anaplastic thyroid cancer	MET <sub>amp</sub> HCC	
Axitinib	FLT1 <sub>amp</sub> CRC		
Afinitinib	NRG1 <sub>fusion</sub> NSCLC	NRG1 <sub>fusion</sub> breast ca	NRG1 <sub>fusion</sub> GI tumors
	NRG1 <sub>fusion</sub> miscellaneous (all tumors)	HER4 <sub>mut</sub> NSCLC	
Palbociclib	CDKN2A <sub>loss</sub> GBM	CDKN2A <sub>loss</sub> CRC	CDKN2A <sub>loss</sub> PEComa
	SMARCA4 <sub>mut</sub> ovarian ca	CDKN2A <sub>mut</sub> cholangio ca	CDKN2A <sub>mut</sub> melanoma
	CDKN2A <sub>loss</sub> duodenal ca	CCND1 <sub>amp</sub> NSCLC	CDKN2A <sub>loss</sub> RCC
	CDKN2A <sub>loss</sub> HNSCC	CDKN2A <sub>del</sub> esophageal ca	CCND1 <sub>amp</sub> melanoma
	CDKN2A <sub>mut</sub> uveal melanoma	CDK4 <sub>amp</sub> Sarcoma	CCND1 <sub>amp</sub> NET
	CDKN2A <sub>loss</sub> pancreatic ca	CDKN2A <sub>loss</sub> vulvar ca	CDK4 <sub>amp</sub> astrocytoma
	CDKN2A <sub>del</sub> NSCLC	CDK4 <sub>amp</sub> prostate cancer	CDK4 <sub>amp</sub> esophageal cancer
	CDKN2A <sub>loss</sub> pNET	CDKN2A <sub>loss</sub> ovarian cancer	CCND2 <sub>amp</sub> CRC
	CDK6 <sub>amp</sub> prostate cancer	SMARCA4 <sub>mut</sub> CRC	
Durvalumab	MSI tumors		
Cabozantinib	MET <sub>amp</sub> melanoma	RET <sub>fusion</sub> NSCLC	MET <sub>amp</sub> teratoma
	NTRK2 <sub>mut</sub> GIST	MET <sub>mut</sub> oesofagus cancer	
Ribociclib	CDKN2A <sub>loss</sub> prostate cancer	CDKN2A <sub>loss</sub> ependymoma	CDK4 <sub>amp</sub> melanoma
	CDKN2A <sub>del</sub> anaplastic meningioma	CDKN2A <sub>loss</sub> thymus carcinoma	CDKN2A <sub>loss</sub> Ewing Sarcoma
	CDKN21 <sub>del/mut</sub> bladder cancer	CDK6 <sub>amp</sub> mucoepidermoid cancer	CDKN2A <sub>del</sub> mesothelioma
	CDKN2A <sub>loss</sub> ceruminous cancer	CDKN2A <sub>del</sub> salivary gland cancer	
Rucaparib	HRR <sub>alt</sub> ovarian cancer	HRR <sub>alt</sub> prostate cancer	HRR <sub>alt</sub> pancreatic cancer
	HRR <sub>alt</sub> miscellaneous	HRR <sub>alt</sub> Breast cancer	
Legend	Cohort closed	Cohort on hold	Slots available