

Monthly DRUP Study Newsletter #79, 01 November 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

The DRUP study is winning this year's **Patient impact award 2022** of the Netherlands Cancer Institute- Antoni van Leeuwenhoek hospital



The Patient Impact Award is the annual award of the Netherlands Cancer Institute for a clinical innovation that has improved diagnostics, treatment and/or quality of life of patients with cancer or is expected to do so in the future. The board of directors established this award in 2018 to highlight the importance of all groundbreaking clinical innovations that are being developed within the Netherlands Cancer Institute or Antoni van Leeuwenhoek hospital.

Medical director and jury member Jacqueline Stouthard about the DRUP study: *"This is truly wonderful, innovative research. The trial has a direct positive impact on the lives of a large group of patients with metastatic cancer, regardless of the location of their primary tumor. This is an innovative trial in various ways, from its study design to the innovative way the treatments are financed by having a pharmaceutical company and health insurance providers sharing the costs".*

The DRUP team feels very honored to win this award! We would like to thank all collaborators for their effort as well, without your support this would not have been possible!

Medical director Jacqueline Stouthard will present the award to our team on November 16th during a special edition of Science on Wednesday in the Piet Borst Auditorium in the Netherlands Cancer Institute in which Emile Voest will present the latest developments of the trial. You are all more than welcome to attend this award ceremony at 12 pm.

Study update

To date, a total of 2407 cases have been submitted to the study team and 1297 of these have started a treatment within DRUP. With no less than 12 collaborating pharmaceutical companies we are currently able to offer 29 different treatments. However, we are always looking to expand and have more new drugs in the pipeline. Amongst these we have niraparib and selpercatinib, which we hope add to the study in the very near future. We will keep you posted on the progress.

Scientific output

We're excited to share with you that the paper titled "γδ T cells are effectors of immunotherapy in cancers with HLA class I defects" has been accepted in Nature! The paper describes the findings of how B2M (b2-microglobulin) mutant MMR-d/MSI-H cancers in the DRUP study showed significantly enhanced responsiveness to immune checkpoint inhibition (ICI) and also consistently showed increased infiltration by γδ T cells. With further in vitro experiments and by comparing tumour samples obtained before and after ICI, it was found that ICB profoundly increased the intratumoral frequency of γδ T cells in HLA class I-negative cancers, indicating that γδ T cells are effectors of ICI therapy in patients with HLA class I-negative, MMR-d colon cancers.

This research would not have been possible without the efforts and cooperation of all people involved in the DRUP trial and we thank everyone who contributed.

A reminder for participating sites about resupply of laboratory kits

As you all know, from all patients who have been registered on-study, a fresh pre-treatment tumor biopsy and a blood sample should be obtained and transferred to the Hartwig Medical Foundation. We would like to use this opportunity to remind you that new laboratory kits can be ordered through <https://www.labkithartwigmedicalfoundation.nl/Hartwig>. The laboratory kits will be delivered within three business days. For any questions concerning the resupply of the laboratory kits, please contact the central laboratory by email: x-lab@hartwigmedicalfoundation.nl. In case resupply of biopsy sampling kits is necessary, please contact the central laboratory by email: x-lab@hartwigmedicalfoundation.nl. Orders made via the DRUP mail can unfortunately not be processed. The above information can also be found in the DRUP study manual.

Warm regards,

Principal Investigators: Henk Verheul, Hans Gelderblom, Emile Voest

Study Coordinators: Laurien Zeverijn, Gijs de Wit, Birgit Geurts, Ilse Spiekman, Karlijn Verkerk

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

Committed

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

November 16th Patient impact award ceremony, NKI

November 30th IDMC meeting

December 20th Pharma meeting

Table 2: Submission and accrual overview stage 1,2 & 3 cohorts

Nov 1st, 2022

