



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

MONTHLY NEWSLETTER #83

March 2023

Study update

To date, a total of 2520 cases have been submitted to the study team and 1349 (54%) of these have started a treatment within DRUP.

Selpercatinib

We are very pleased to finally be able to inform you that selpercatinib has become available for shipment to all participating sites. All patients who have an activating RET gene alteration (fusion or mutation) will be eligible for treatment with selpercatinib. Important to note is that only RNA-NGS is considered as an acceptable method to detect RET fusion. Most commonly observed RET-fusion partners are: *NCOA4*, *CCDC6*, *KIF5B*, *ETV6*, *TRIM24*, *ERC1*, *GOLGA5*, *GPHN*, *PRKAR1A*, *RASAL2*, *CGNL1*, *SPECC1L*, *TAF3*, *TFG* and *TRIM33*. Patient submissions can be done via the eCRF (Alea) or the DRUP email.



Study team update



Hello everyone!

My name is Soemeya Haj Mohammad and since February I am the newest addition to the DRUP study coordinating team, working from both the LUMC and the NKI-AVL.

I am 27 years old and graduated as a medical doctor in the beginning of 2022. For the past year I worked as a medical resident not in training at the Alrijne Hospital in Leiderdorp in the departments of internal medicine, gastroenterology and hepatology and pulmonary diseases.

My main interests lie in the oncology and hematology, so when I heard about the DRUP study I was immediately excited.

I feel honored to be part of such innovative research. Focusing on the PCM4EU project we can hopefully further implement DRUP-like protocols and get closer collaboration all across the European Union.

Scientific output

We are pleased to announce that the DRUP manuscript "Efficacy, safety and biomarker analysis of durvalumab in patients with mismatch-repair deficient or microsatellite instability-high solid tumors" by Birgit Geurts has been accepted for publication in *BMC Cancer*. The manuscript describes the treatment outcomes in one of the 2nd stage DRUP cohorts, in which patients with advanced solid tumors harboring mismatch repair deficiency or microsatellite instability have been treated with the PD-L1 inhibitor durvalumab. Durvalumab showed durable

responses, with 13 patients (13/24; 54%) experiencing clinical benefit, including 7 (7/24; 29%) patients with an objective response.

Furthermore, biomarker analysis revealed high structural variant burden, *JAK1* mutations and low IFN- γ expression as possible resistance mechanisms, providing a rationale for larger studies to validate these findings. The manuscript will soon be available.

Best regards,

Principal Investigators: Henk Verheul, Hans Gelderblom, Emile Voest

Study Coordinators: Laurien Zeverijn, Birgit Geurts, Ilse Spiekman, Karlijn Verkerk, Georgy Gomon, Soemeya Haj Mohammad

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>MSD</u> Pembrolizumab	<u>Roche</u> Erlotinib Trastuzumab+ Pertuzumab Vemurafenib+ Cobimetinib Vismodegib Atezolizumab+ bevacizumab Alectinib Entrectinib
<u>BMS</u> Nivolumab Ipilimumab	<u>AstraZeneca</u> Olaparib Durvalumab	<u>Lilly</u> Abemaciclib Selpercatinib	
<u>Novartis</u> Dabrafenib Nilotinib Trametinib Alpelisib	<u>Pfizer</u> Axitinib Crizotinib Sunitinib Talazoparib Dacomitinib Lorlatinib	<u>Janssen</u> Erdafitinib	

Committed

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

IDMC meeting 21st of March 2023

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

March 1st, 2023

