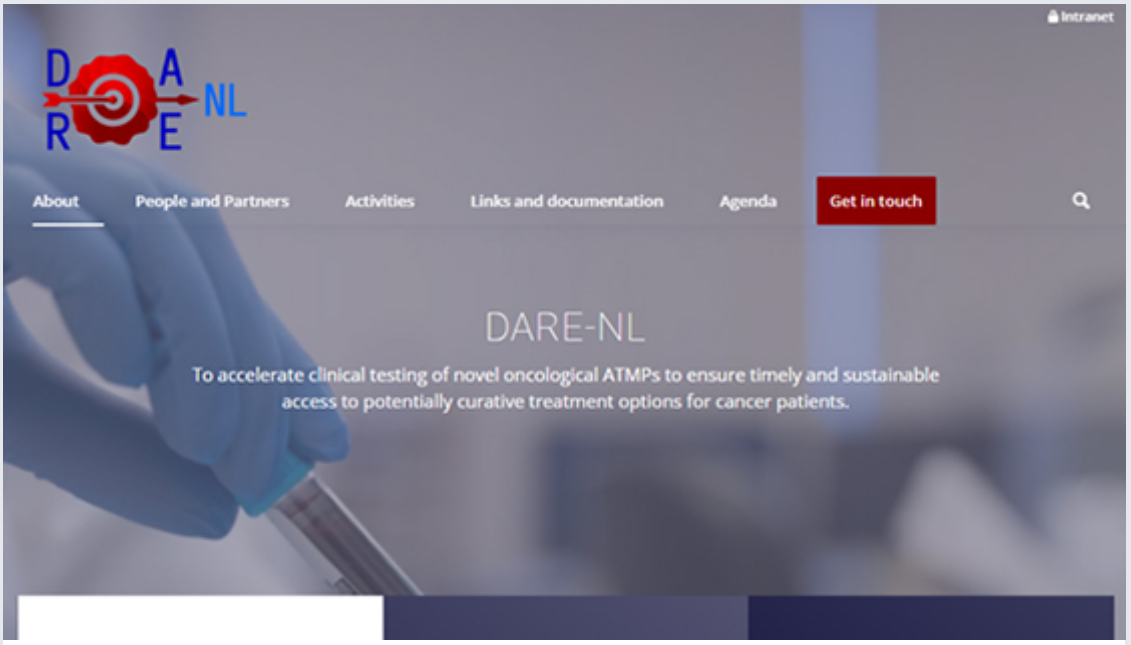
UMC Utrecht

14 maart 2023

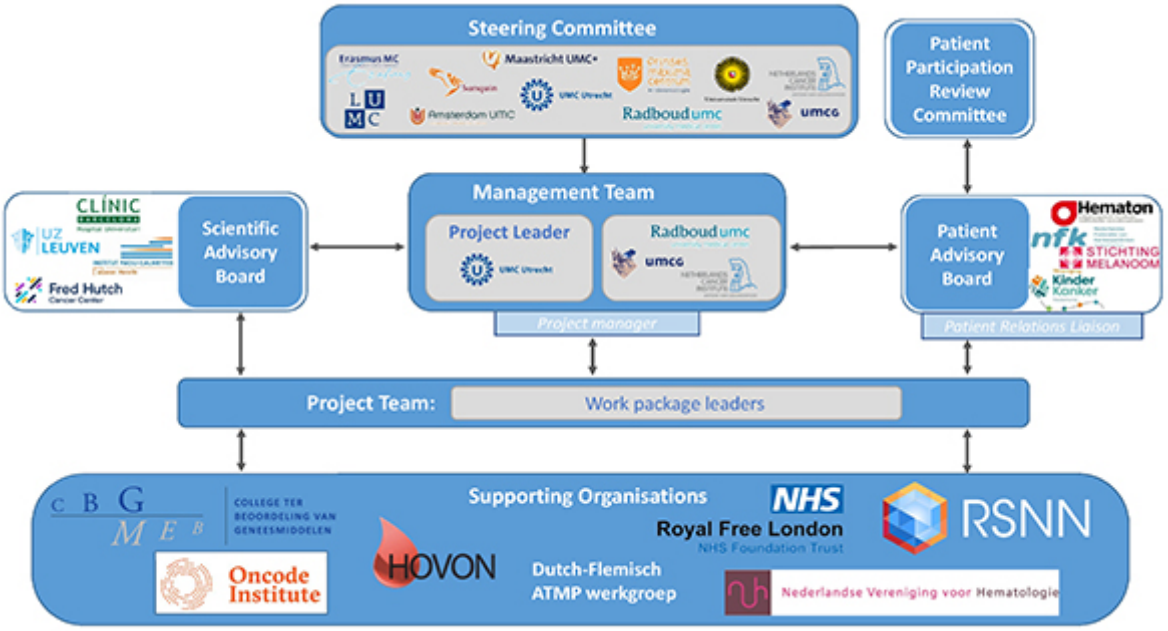
DARE-NL contact and logo

Six months from launching the **D**utch platform for cancer-specific **A**TMP **RE**search (DARE-NL), we present the first newsletter to inform you on the progress. You receive this newsletter because you are a DARE-NL team member or stakeholder in ATMP research in the Netherlands. Attached to this newsletter is the official DARE-NL logo, which may be used on official DARE-NL documentation. If you would like to contribute information for the next newsletter, send it to info@dare-nl.nl.



DARE-NL aim

DARE-NL will connect all academic developers of ATMPs for the treatment of cancer in the Netherlands. All academic ATMP centres in the Netherlands joined forces on 1 September 2022 to accelerate the integration of novel oncological ATMPs in patient health care. To reach this goal, DARE-NL will establish a national infrastructure to centralise knowledge, harmonize protocols, provide raw materials, develop biologics and technologies, and facilitate implementation and patient outreach. Find more information on ATMP research, development andproduction on www.dare-nl.nl.



DARE-NL partners

The idea for DARE-NL was shared for the first time at the HOVON Immune Effector Cell working group. Four ATMP researchers (currently the MT members) took the lead in writing the project plan. All 11 Dutch ATMP research institutes are represented in the DARE-NL steering committee. An international scientific advisory board and a patient advisory board comprising representatives from Hematon, the Nederlandse Federatie van Kankerpatienten, Vereniging Kinderkanker Nederland and Stichting Melanoom have been involved in the setup and organisation of DARE-NL. DARE-NL is proud that the CBG, Hospital Clínic de Barcelona and UCL Royal Free London have committed to contribute to the platform. Many other organizations are also involved and consulted through the different members.

DARE-NL progress highlights

WP1: Setup of DARE-NL data, training and valorisation platform

Lead: Emma de Pater, Erasmus Medical Center
The website (www.dare-nl.nl) has been setup and its content is in progress. The Zenya application for data sharing is nearing implementation. All partners will be contacted in April/May for their input on how to further setup the environment. A survey on ATMP education has been filled by all partners. There is a need for ATMP education on basic principles, procedures, GMP training, quality and validation, preclinical development, clinical trial design, regulatory affairs and exchanges. More detailed inventories are planned by talking to all DARE-NL partners to provide insight in which trainings could be made available more broadly and which trainings should be developed by DARE-NL. Once this overview is ready, Emma will consult with the PIs of the other WPs to see where information could bidirectionally be provided. Four DARE-NL members have been selected to start a tailor-made regulatory affairs education program this year. Ian Bell (Oncode Institute) is working on a valorization framework with a working group from the IP management committee.

WP2: Harmonising GMP processes for the manufacturing of cancer-specific ATMPs

Lead: Trudy Straetemans, University Medical Center Utrecht
A procedure for supplier audits and non-disclosure agreement are currently edited by WP2.1/2.2 team members. The WP2.3 team inventoried the current use of English documentation and language in the quality systems and facilities of all partners. This was used to perform a SWOT analysis on the use of English versus Dutch documentation in the quality system. A first enquiry for preferred generic procedures to harmonize has been discussed and will be extended soon.

WP3: QC harmonization and assay development

Lead: Inge Jedema, NKI/AVL
A first survey has been sent out to WP3 members to investigate the currently used QC and characterization assays and wishes for future applications. We will also request information on whether the assays are performed in-house or outsourced to other (commercial; CRO) parties and what the level of validation of the used assays is. Based on the survey results, we will propose a first set of assays to be developed by one of the partners. This will also be aligned with WP2 activities. The NKI/AVL started the set-up of a dedicated QC laboratory focused on ATMPs.

WP4: Setup of a Dutch academic GMP vector manufacturing platform

Lead: Edwin Bremer, University Medical Center Groningen
The set-up of an academic lentiviral manufacturing platform has initiated with the pre-GMP upscaling of the production process to bioreactor scale and a start in producing the master and working cell banks. In addition, an FTO search to determine the lentiviral transfer vector to be used as backbone in the manufacturing platform has been performed. The list of requisite process and release quality control tests for lentivirus have been defined and in-house development or outsourcing is being determined.

WP5: Identification and implementation of new technologies for the developmentand GMP-compliant manufacturing of ATMPs

Lead: Harry Dolstra, Radboud University Medical Center
A survey on technologies filled by all partners indicated that most ATMP research is at the preclinical stage, with clinical CRISPR/Cas9 experience at the NKI. Technologies most commonly used by DARE-NL partners are RNP complexes, mostly to modify receptors or inhibitory molecules on immune effector cells. Top ingredients considered for the GMP-compliant toolkit are thus Cas9, gRNA and electroporation buffers. A successful symposium with

WP5 team members to define which technologies DARE-NL partners are working on and their plans for the coming years was held on 9 January 2023.

WP6: Regulation, health economics, health technology assessment and patientaccess

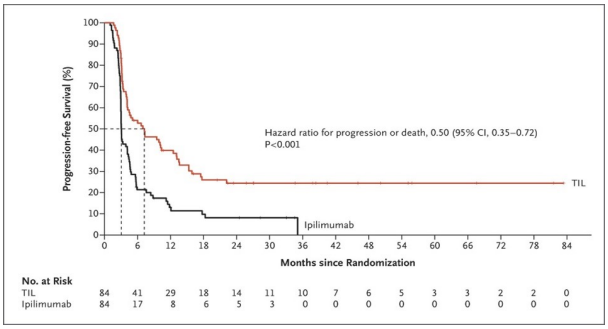
Lead: Pauline Meij, Leiden University Medical Center
Overviews of ATMP trials and a regulatory network roadmap are in progress. A database of ATMPs with a marketing authorization has been created and will be updated from now. A start has been made with setting up a database of ATMPs in clinical trials or with a hospital exemption and a start has been made with creating regulatory and HTA overviews as well. The stakeholder sandbox has been established: RSNN Special Interest Group Advanced Therapies | Regulatory Science NetworkNederland . Design and piloting of the costing tool is initiated in partnering institutes. Individual discussions with all partners to inventory what everybody can contribute to and requires from this work package are ongoing.

WP7: Project management

Lead: Trudy Straetemans, University Medical Center Utrecht

A consortium agreement has been signed by all partners. A Patient Advisory Board, Patient Participation Review Committee and Intellectual Property Management Committee have been established. Project teams in each working package have been formed and are meeting regularly. Project updates are sent to the steering committee and work package leaders at the beginning of every month. The first steering committee is scheduled on 14 March and the first annual consortium meeting on 8 September.

Research highlights: what is new in the field of ATMPs



In patients with advanced melanoma, progressionfreesurvival was significantly longer among those whoreceived TIL therapy than among those who receive dipilimumab.
Read the full publication

Overview of ATMP development by academia: a review of logistical, financial, and regulatory issues that might contribute to the changing role of Academia in ATMP development, with anoutlook into possible developments in the future and proposals for ways to reshape the academic environment under the auspices of what might truly have been meant by the hospital exemptionclause.

Advanced Therapy Medicinal Products and the Changing Role of Academia

Christoph Priesner[a] Martin Hildebrandt[b]

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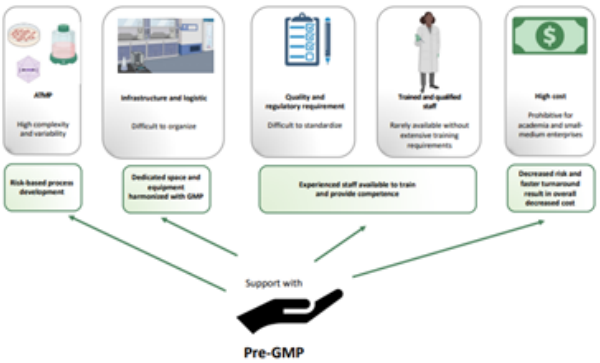
Read the full publication



ATMP development in academia: on the relevance of pre-GMP, underlining the advantages andthe possible disadvantages of this additional framework that may be key in accelerating the pace of ATMP toward clinic.

Read the full publication

What will (and should) be improved in CAR immunotherapy? A summary of the main aspects that can (and probably should) be improved for the expansion of immunotherapy with CAR proposals beyond onco-hematology.

Read the full publication

Quarterly highlights and approved ATMPs by the Committee for Advanced Therapies (CAT)

Read the full publication

ATMP landscape: what happens in the network

Many ATMP working groups, agencies, consortia, platforms and networks are represented or consulted by DARE-NL partners. The combined expertise in academic development and production of ATMPs is crucial for DARE-NL to be successful. We invite you to reach out if you would like to be (more) involved in the DARE-NL infrastructure.

Other initiatives are taking complementary approaches to optimize ATMP development in the Netherlands. The 'Nationaal Groeifonds' funded projects RegMed XB and Oncode-PACT build on the DARE-NL infrastructure. The RegMed XB consortium is building the Innovation Center for Advanced Therapies (ICAT) at the Utrecht Science Park and NecstGen at the Leiden Bio Science Park. Oncode-PACT is building a preclinical development infrastructure to de-risk and accelerate the oncological drug development process. Both initiatives offer the potential to synergize with DARE-NL in sharing knowledge, expertise and (pre)clinical facilities for the manufacturing of ATMPs. The Future Affordable Sustainable Therapies (FAST) initiative monitors the balance between entrepreneurship and accessible novel therapies. In the CBG ATMP committee, the CBG consults with chain partners about ATMP developments. The reNEW consortium , consisting of the LUMC, the Danstem Institute from the University of Copenhagen and the Murdoch Children's Research Institute in Melbourne, aims to bring new stem-cell based therapies from the lab to the patient. The European Alliance for TransformativeTherapies (TRANSFORM) is a multi-stakeholder alliance that connects Members of the European Parliament and policy-makers with patient groups, medical experts and associations, scientists, researchers, industry, networks and other relevant stakeholders. TRANSFORM aims to foster effective dialogue and provide evidence-based policy recommendations to enable safe and timely patient access to cell and gene therapies, whilst ensuring the sustainability of healthcare systems. InnoCAR-T is a Doctoral Network designed to provide training and carry out breakthrough research on the rapidly expanding and high-impact field of CAR T cell immunotherapy in a carefully integrated academic and

inter-sectoral program. These projects complement each other in providing different pieces of the puzzle to bring ATMPs quicker to the patient in a more sustainable and affordable way. DARE-NL provides the national harmonization of procedures, roadmaps and a central communication to regulators. The interaction between these platforms will enable the transformation of a patchwork of ATMP developers into a uniquely organized ATMP landscape in the Netherlands.

DARE-NL MT members presented DARE-NL at these events

- NVGCT annual symposium (15-16 June) - Inge presented DARE-NL
- ATMP event Berlin (17 November) - Inge presented DARE-NL
- 15th Dutch Hematology Congress (HOVON/NVVH, 25-27 January) - Zsolt and Harry presented DARE-NL
- EBMT-EHA 5th European CAR T-cell Meeting (9-11 February) - Harry presented DARE-NL

Calendar (ATMP events) 2023

MAR 13 — **CBG ATMP committee meeting - Inge presents DARE-NL**

MAR 14 — **DARE-NL steering committee meeting**

MAR 19-21 — **Netherlands Enterprise Agency (RVO) event to connect the Dutch-SwissLife Sciences Ecosystems - Trudy and Edwin represent DARE-NL**

APR

23-26 Annual EBMT meeting

JUN 26 CBG ATMP committee meeting

SEP 08 Annual DARE-NL consortium meeting

OCT 23 CBG ATMP committee meeting

Spread the word

Do you know anyone interested to receive DARE-NL information? Send a message to info@dare-nl.nl copying them. We will send two newsletters a year, plus very incidental time-sensitive items. Also feel free to reach out for anything related to oncological ATMPs. If you would like to opt out from receiving the newsletter, please send an e-mail to info@dare-nl.nl with UNSUBSCRIBE and we will remove your contact details from the distribution list.