Biannual newsletter
March 2024

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Leadership insight: reflections and projections

As the initiators of DARE-NL, it is our privilege to share a few words about the DARE-NL mission. Halfway into the second year of the project, we like to look back on achievements and ahead on challenges we face to make DARE-NL a success. Our collective efforts have already yielded remarkable results, with the establishment of a knowledge exchange platform and stakeholder sandbox; inventories of current technologies and QC assays; harmonization of the first procedure across centers; and a successful annual consortium meeting. These results reflect what can be accomplished when working together toward a common goal. Our strength lies in the team effort between all Dutch academic ATMP developers. As medical needs are evolving and new challenges arise, it is crucial that we pool our strengths and find creative solutions for the hurdles we all face.

The ambition of DARE-NL is to become a durable and sustainable infrastructure for the Dutch ATMP field beyond the lifespan of the project. To lay the groundworks for this ambition, the management team together with Ian Bell and Harma Feitsma from Oncode Institute have been discussing

the mission, assets and potential revenue models for DARE-NL, supported by impact officer Erik van Tilborg. This is an ongoing exercise and we will get back to and consult on these sustainability plans with the DARE-NL community in the (near) future. We think this will be crucial for the DARE-NL mission to drive clinical translation of oncology-specific ATMPs.

Together we strive to enable the realization of innovative therapies with the potential to profoundly improve the lives of patients. DARE-NL is built on all collective contributions, which are invaluable to realizing our shared mission. We also actively seek connections with international networks to achieve greater impact together. Looking back, we sincerely thank each of you for the dedication and commitment you have shown to DARE-NL and, looking forward, hope to jointly realize our ambitious goals in the years ahead. Let us continue to learn from each other and collaborate to achieve excellence.

Trudy, Harry, Inge & Edwin

DARE-NL consortium meeting 2024

Register now to attend the annual consortium meeting at the UMC Utrecht on 20 September.

We are honored to host DARE-NL members presenting their latest insights and international experts sharing their work and perspectives. Additionally, distinguished ATMP experts will chair the sessions and facilitate panel discussions with a lineup of incredible professionals.

So do not miss out on this unique opportunity to meet a diverse array of ATMP experts, network and discuss current developments in ATMP training, QC and new technologies. We hope to welcome you in Utrecht that day!

DARE-NL progress highlights

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

Lead: Emma de Pater, Erasmus Medical Center

The layout and organization of the website have been modified to improve effective communication: find information in Dutch, an up-to-date calendar of ATMP-related events and more. All DARE-NL partners now also have access to the DARE-NL Zenya platform, so each WP is exploring possibilities to share data. The Belgian members of the ATMP Working Party have also been provided access to the relevant resources in Zenya.

The overview of available courses and gaps has been completed. Emma de Pater and Soura Mardpour are exploring options to merge the overview with the European overview of ATMP education prepared by the ISCT. The result will be published on the DARE-NL website. Based on the needs expressed in the interviews, a conversation has been initiated with Avans to setup an ATMP bachelor program. The inventory on internship exchanges has been completed and a workshop will be organized for operators to discuss how to implement this.
Harry Dolstra and Friso Calkoen have completed the Market Approval course, Trudy Straetemans is following it now and they started continuation of the Regulatory Affairs program together with Mara Tihaya and Inge Jedema.

Harma Feitsma takes over the responsibilities of Ian Bell at the Oncode Institute partner for DARE-NL. Harma is appointed as business developer both

at the Oncode Institute and KWF, matching very well with DARE-NL. Harma, Ian, impact officer Erik van Tilborg and the DARE-NL management team are running a couple of workshops to work out the DARE-NL business model, supported by the steering committee and IP management committee.

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

Lead: Trudy Straetemans, University Medical Center Utrecht

The overviews of suppliers and materials approved to be used in ATMP manufacturing are available as so-called 'card files' in Zenya. The supplier qualification documentation is also available in Zenya. New general guidelines on the risk assessment of raw materials will be available for review soon.

A procedure to harmonize general GMP standard operating procedures (SOPs) has been established. The first harmonized SOP 'assessment on excursions of environmental monitoring' is being finalized and will be sent for feedback in the near future and published in Zenya. A survey on the organization and technologies of GMP facilities is prepared together with GoCART, T2Evolve, EBMT and NXTGEN-HIGHTECH and will be distributed throughout Europe. A Zenya card file to share inspection results have been based on an internal survey and discussion at the WP2/3 meeting at the Radboudumc in November. The results will be shared with the WP2.3 team members when testing is completed.

Trudy Straetemans, Anna de Goede, Cynthia Nijenhuis, Inge Jedema, Laureen ten Berg-Lammers and Simone Punt visited Christianne Reijnders and Gwylim Janssens (IGJ) in October and described the harmonization efforts in DARE-NL. IGJ applauded the initiative to harmonize and share best practices between DARE-NL members. Although IGJ can not provide advice on the harmonized documents based on their role as assessor, there was a constructive conversation on the possibilities to learn from each other.

WP2.4 was launched in September, where a working group on data digitization and the sharing of (manufacturing procedure) data is assembled – let us know if you are interested to join!

WP3: QC harmonization and assay development

Lead: Inge Jedema, NKI/AVL

The results from the QC assay survey were discussed at the WP2/3 meeting at the Radboudumc in November and a follow-up Teams meeting in December. The overview will be shared in Zenya soon. Potential options for harmonization of assay performance between partners, centralized execution of certain assays and options for interlaboratory performance assessments for different QC assays for ATMPs were also discussed. A first draft overview of a selection of assays to be developed by specific DARE-NL partners was made and development started for some assays.

WP4: Setup of a Dutch academic GMP vector manufacturing platform

Lead: Edwin Bremer, University Medical Center Groningen

Work is ongoing to generate the Master Cell Bank (MCB) and Working Cell Bank (WCB) for use in GMP-grade lentiviral manufacturing. In addition, adaptation of HEK293 producer cells to high density bioreactor culture is ongoing. The pre-GMP scale-up and manufacturing process for LV production has been validated, with the focus moving to GMP engineering runs after WCB set-up and the validation of the downstream manufacturing process. In addition, the QC requirements for LV batch release have been defined, with the majority of QC tests for the lentiviral vector having been validated.

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

Lead: Harry Dolstra, Radboud University Medical Center

Harry Dolstra and Iris Hagemans visited the UMC Utrecht to discuss plans and requirements for non-viral novel ATMP technologies. The team is now looking into establishing a roadmap for GMP-grade CRISPR reagents. Iris inquired with several companies about their offers concerning quality as well as pricing, which forms a major bottleneck for academic clinical translation of CRISPR.

Several meet-the-expert sessions were organized and more are planned for the coming year, find the agenda on Teams (for DARE-NL members). A meeting was held to discuss joint outsourcing as well as in-house production. The results on a questionnaire on GMP-grade CRISPR quantity and quality requirements will be discussed at an upcoming meeting.

WP6: Regulation, health economics, health technology assessment and patient access

Lead: Pauline Meij, Leiden University Medical Center

Ordered by ZonMw, in close collaboration with FAST, a report on the ATMP field with a bottleneck analysis, activity map and recommendations for actions was published – see the research highlights.

The framework for a regulatory roadmap is expected to be finalized and shared with members soon. The first list of topics for discussion in the sandbox is currently deduced from the interviews held with all partners and the RSNN-SIG ATMP meeting.

The setup of registries for ATMPs for cancer patients under hospital exemption or in clinical trials is constructively discussed with the CCMO and IKNL. The patient engagement plan for DARE-NL has been approved by both the patient representatives and WP leaders and is now active (link for members).

WP7: Project management

Lead: Trudy Straetemans, University Medical Center Utrecht

The milestones to define harmonization and impact were approved by KWF, as were the annual reports discussed in the progress meeting in October. The next interim KWF progress meeting is scheduled on 5 April.

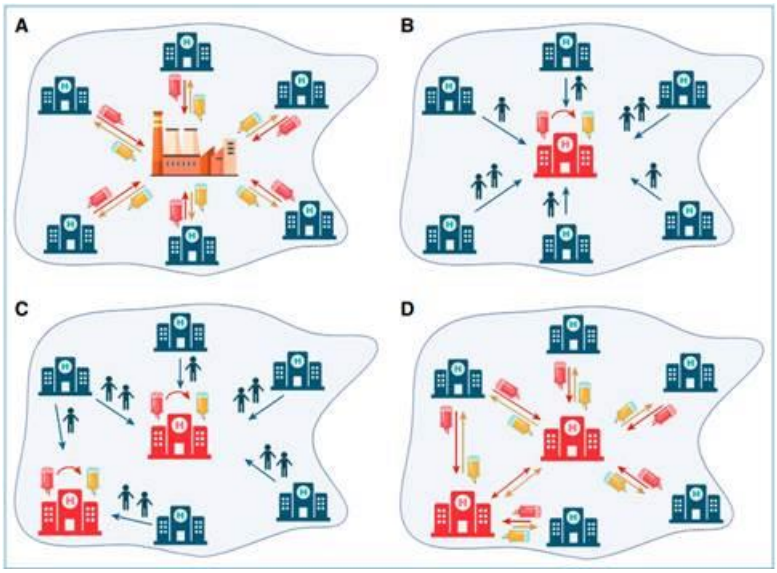
The following annual consortium meeting is scheduled on 20 September and preparations are in full swing – let us know if you have any thoughts! The patient advisory board, scientific advisory board, steering committee and KWF progress meeting are scheduled the day before on 19 September.

Research highlights: what is new in the field of ATMPs

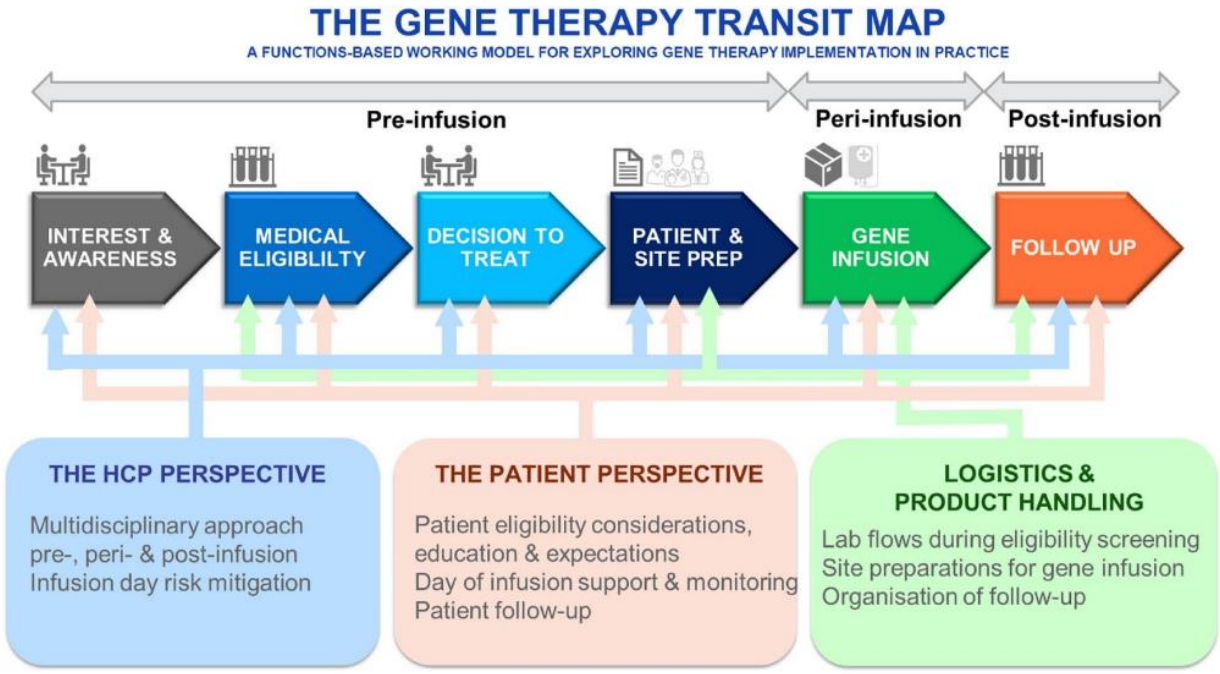
Report on the ATMP field with a bottleneck analysis, activity map and recommendations for actions ordered by ZonMw, in close collaboration with FAST (in Dutch, UU repository, December 2023).

Analysis of current government policy, highlighting a number of important challenges for embedding gene therapy in the Dutch healthcare system (in Dutch, Rathenau Instituut, December 2023).

Review of regulatory, pricing and reimbursement decisions for all ATMPs with centralized European marketing authorization in March 2022 (Frontiers in Pharmacology, November 2023).



Publication on identifying the best way forward in academic CAR development and implementation in the best interest of the patients (Journal of Clinical Oncology, November 2023).



A gene therapy transit map with key stakeholders was developed to describe critical milestones associated with gene therapy handling, administration, and follow-up to facilitate and implement an effective infrastructure for gene therapy introduction in hemophilia care in the Nordic context (Therapeutic Advances in Hematology, Oct 2023).

Quarterly highlights and approved ATMPs by the Committee for Advanced Therapies

ATMP landscape: what happens in the network

The Oncode Accelerator project officially started with their kick-off on 8 September 2023. The Cell and Gene therapy workstream is led by the NKI and managed by Inge Jedema. With multiple DARE-NL members active in Oncode Accelerator, we have tight connections between DARE-NL and Oncode Accelerator and hope this will lead to synergies on multiple aspects.

Soura Mardpour and Simone Punt attended ATMP Sweden 2023 to learn about the setup of Sweden's activities aimed at accelerating patient access to safe and effective ATMPs based on national coordination and communication (members can find notes on Teams).

Harry Dolstra and Trudy Straetemans participated in a workshop on "starting and raw material quality challenges for CAR T cells manufacturing" at the EBMT-EHA 6th European CAR T-cell Meeting. Harry gave a presentation about the qualification of starting and raw materials suppliers in DARE-NL. The initiative was very well received and we continue to tackle collaboration in sharing and harmonizing generic GMP processes together with European consortia such as T2Evolve and Join4ATMP in follow-up meetings. DARE-NL actively seeks connections with other infrastructures like this to achieve greater impact together.

Calendar:

see Teams (members) & website

DARE-NL will be present(ed) at these events:

- EBMT annual meeting (14-17 April) – *Harry presents DARE-NL*
- Innovation mission Switzerland (20-25 April) – *Trudy represents DARE-NL*
- DARE-NL annual consortium meeting (20 September)

Mailing list and newsletter

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