







Foreword

We proudly present our highlights of 2024, a transformative year at CHDR. With a change in leadership on our Executive Board, we embraced a renewed vision for the future. We celebrated a record number of PhD and Clinical Pharmacology graduates, reflecting our commitment to advancing knowledge and nurturing talent. Our expansion to a new site in Twente further strengthened our capabilities in cutting-edge research. We were also honored with recognition for our contributions to the field, underscoring our impact on drug development and methodological innovation. This report offers a glimpse into our upcoming annual report, celebrating a year of change, collaboration, and growth at CHDR.



2024 in numl CHDR news Branding cam Dermatology Immunology Infectious Dise Internal Medie Neurology Oncology Pain Psychiatry Trial@Home Education PhD Graduate

CHDR Highlights 2024

GENEESMIDDELENONDERZOEK

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2024 in numbers



>16,000 volunteer applications 4,763 patients 11,345 healthy volunteers

8 clinical pharmacology graduates

>92% studies executed as planned

overall study participant satisfaction



increased lab capabilities: bioanalysis and tissue culture



articles published in peer-reviewed journals

8.6/10 overall client satisfaction

Biomarker	71%
PK/PD	59%
Single ascending dose (SAD)	29%
Proof of Concept	27%
First in Human (FIH)	20%
Method development	15%
Multiple ascending dose (MAD)	14%
Observational	7%
Food effect (FE)	3%
Drug combination trial	3%
Drug-drug interaction (DDI)	2%
Elderly	2%

STUDIES PER RESEARCH AREA

22%
14%
12%
12%
10%
8%
8%
5%

CHDR **NEWS**

This year we welcomed a new Executive Board, we got recognition for our work and opened a new research unit.

February

as the new CFO.

June



June

CHDR is expanding! We have signed a cooperation agreement with Medisch Spectrum Twente (MST) and TechMed Centre for our new location in Twente. Stay tuned for the opening of CHDR Twente in 2025.

Branding campaign

This year, we launched a new branding campaign to increase awareness for clinical research. The text on the poster translates to: "Your daily bike ride... make an impact with it. Participate in clinical research."





GENEESMIDDELENONDERZOEK



Dermatolog





- Epidermal wound and full-thickness wound healing.
- Keyhole Limpet Hemocyanin (KLH), Imiquimod (IMQ), Lipopolysaccharide (LPS) and Ultraviolet B (UV-B).
- Implemented a novel methodology: line-field confocal tomography.
- Monthly meetings with 7 patient advocacy groups for common dermatological conditions; Hidradenitis Suppurativa, Atopic Dermatitis, Cutaneous Lupus Erythematosus (CLE), Chronic Spontaneous Urticaria, Cutaneous T-Cell Lymphoma, and Psoriasis.
- First CLE patients enrolled in deepphenotyping study.
- Published 15 papers in high-ranking journals.



GigE Vision

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OFLIR .

Key publications

A suction blister model to characterize epidermal wound healing and evaluate the efficacy of the topical wound healing agent INM-755 in healthy volunteers. Ten Voorde, W., Wind, S., Abdisalaam, I., et al., 2025. European Journal of Pharmaceutical Sciences, 204, p.106867. DOI: 10.1016/j.ejps.2024.106867

Guselkumab induction therapy demonstrates long-lasting efficacy in patients with mild psoriasis, results from a randomized, placebocontrolled exploratory clinical trial. Rousel J, Bergmans ME, van der Meulen LWJ et al., 2024. Journal of the American Academy of Dermatology, 90(2), pp.395-397. DOI: 10.1016/j.jaad.2023.09.071

Lesional skin of seborrheic dermatitis patients is characterized by skin barrier dysfunction and correlating alterations in the stratum corneum ceramide composition. Rousel, J., Nădăban, A., Saghari, M., et al., 2024. Experimental dermatology, 33(1), p.e14952. DOI: 10.1111/exd.14952

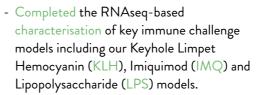
DERMATOLOGY



- Key lectures in Boston, Berlin, Cambridge, San Francisco, Utrecht and Colorado Springs.
- A total of 21 oral and poster abstracts presented at GUF, ESDR, EADV, AAD, Dermatology Drug Summit Europe & US, ASCPT and BPS Pharmacology.
- Advanced our collaboration with nearby laboratories to establish a multi-omics analysis pipeline including proteomics, metabolomics, lipidomics and microbiomics.
- Successful launch of the Dutch flagship project Next Generation ImmunoDermatology: we hired 20 FTE's nationwide.

Immunology





- Set-up full-service sample handling, bioanalysis, and bioinformatics-based analysis of tissue specimens. The tissue specimens include blood, bone marrow, and liquid and solid skin biopsies. To achieve this, we partnered strategically with specialised labs to complete -omics analysis.
- Started the development and validation of a unique human in vivo vascular leakage model.
- Executed several LPS- and KLH-based proofof-mechanism and first-in-human trials for pharma companies.



Key publications

Extending the IMQ Model: Deep Characterization of the Human TLR7 Response for Early Drug Development. Van den Noort, J.A., Assil, S., Ronner, M.N., et al., 2024. Inflammation, pp.1-12. DOI: 10.1007/s10753-024-02127-x

Immune responsiveness in stable kidney transplantation patients: Complete inhibition of T-cell proliferation but residual T-cell activity during maintenance immunosuppressive treatment. In't Veld, A.E., Eveleens Maarse, B.C., Juachon, M.J., et al., 2024. Clinical and Translational Science, 17(6), p.e13860. DOI: 10.1111/cts.13860

The oral IRAK4 inhibitors zabedosertib and BAY1830839 suppress local and systemic immune responses in a randomized trial in healthy male volunteers. Jodl, S.J., Ten Voorde, W., Klein, S., et al., 2024. Clinical and Translational Science, 17(3), p.e13771. DOI: 10.1111/cts.13771

Immunomodulating effects of the single bacterial strain therapy EDP1815 on innate and adaptive immune challenge responses—a randomized, placebo-controlled clinical trial. Maarse, B.C.E., Ronner, M.N., Jansen, M.A., et al., 2024. Immunologic Research, 72(4), p.776. DOI: 10.1007/s12026-024-09484-7

IMMUNOLOGY

- Conferences: ECI in Dublin; Figon in Leiden, NVVI in Noordwijkerhout, Complement Summit in Boston, EADV in Amsterdam.
- 4 strategic collaborations:
 - Collaborating with the Leiden Complement Network to advance research on the complement system in immunology.
 - Collaboration with the Dutch Competent Authority for Clinical Research (CCMO), the Dutch Medicines Evaluation Board (CBG-MEB) and Leiden University Medical Center (LUMC) on testing of Advanced Therapy Medicinal Products.
 - Collaborated with the Department of Experimental Vascular Research of the LUMC on translational work on endothelial responses.
 - Start of clinical study on leukocyte toxicodynamics with LACDR and the European Food Safety Agency.

Infectious Diseases

Highlights

- Completed the setup of a Rhinovirus Controlled Human Infection Model (CHIM) study in 4 months.
- Identified 64 subjects with the required background immunity of titer <1:4 of rhinovirus type 39 for the CHIM study in 4 months.
- Completed 1240 nasal lavages for pharmacokinetic, cytokine, and transcriptomic measurements in 3 months.
- A PhD graduate of the infectious diseases team won 2 prizes for his PhD thesis on vaccine development for respiratory virus infections: 1 for best thesis and 1 for best publication (see key publications).

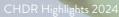


Key publication

Safety and immunogenicity of Ad26. COV2. S in adults: A randomised, double-blind, placebo-controlled Phase 2a dose-finding study. Cárdenas, V., Le Gars, M., Truyers, C., et al., 2024. Vaccine, 42(16), pp.3536-3546. DOI: 10.1016/j.vaccine.2024.04.059

Prize-winning PhD article: Causal chemoprophylactic activity of cabamiquine against Plasmodium falciparum in a controlled human malaria infection: a randomised, double-blind, placebo-controlled study in the Netherlands. Van der Plas, J.L., Kuiper, V.P., Bagchus, W.M et al., 2023. The Lancet Infectious Diseases, 23(10), pp.1164-1174. DOI: 10.1016/S1473-3099(23)00212-8

Prize-winning PhD thesis: Advances in clinical development for vaccines and therapeutic against respiratory virus infections. Van der Plas, J.L., 2023. CHDR PhD thesis Library. Link: CHDR.nl/library/van der Plas



INFECTIOUS DISEASES

- CHDR assisted in the establishment of **INFECT-NL**, a collaborative initiative involving the 4 largest university hospitals, Centre for Future Affordable Sustainable Therapy Development (FAST) and CHDR to increase pandemic preparedness in the Netherlands by creating a network and infrastructure to develop vaccines.
- We presented on optimising drug development for infectious diseases and presented a poster on the implementation of a Rhinovirus CHIM at the 2024 World Vaccine Conference in Barcelona.
- Visited Imperial College London, an expert centre for CHIM studies, to harmonise our clinical approach to these studies.
- Had a kick-off meeting with the CEPI MusiCC consortium, for which CHDR will conduct the Human Coronavirus OC43 CHIM studies.



- Specialised in systemic autoimmune diseases, the microbiome, and metabolic disorders.
- Initiated a clinical trial using the KLH challenge in patients with rheumatoid arthritis and inflammatory bowel disease.
- Actively involved in multiple studies evaluating T cell engagers for rheumatological conditions.
- Achieved the top recruiter position out of 6 sites, by enrolling 17 out of 38 patients with celiac disease. Patients underwent a controlled gluten challenge with 2 cookies containing 6 grams of gluten and extensive pharmacodynamic assessments.
- Developed a database of over 1,200 patients with knee osteoarthritis, including 45 patients who received intra-articular study drug injections, with outcomes assessed using advanced 7T MRI sodium coil imaging.



Key publications

Licogliflozin for nonalcoholic steatohepatitis: a randomized, double-blind, placebo-controlled, phase 2a study. Harrison, S.A., Manghi, F.P., Smith, W.B., et al., 2022. Nature medicine, 28(7), pp.1432-1438. DOI: 10.1038/s41591-022-01861-9

First-in-human study to assess the pharmacokinetics, tolerability, and safety of single-dose oxybutynin hydrochloride administered via a microprocessor-controlled intravaginal ring. De Laat, W., Pagan, L., Malcolm, R.K., et al., 2023. Drug Delivery, 30(1), p.2180113. DOI: 10.1038/s41591-022-01861-9

The oral IRAK4 inhibitors zabedosertib and BAY1830839 suppress local and systemic immune responses in a randomized trial in healthy male volunteers. Jodl, S.J., Ten Voorde, W., Klein, S., et al., 2024. Clinical and Translational Science, 17(3), p.e13771. DOI: 10.1111/cts.13771

INTERNAL MEDICINE

- ASL in Milano, EACPT in Rotterdam, BSL in Harrogate.
- 2 successfull collaborations with the department of rheumathology at the Leiden University Medical Center and the Haga Hospital, the Hague.

MCF-B65



- Started using the phosphorus magnetic resonance spectroscopy (31P-MRS) coil on the 7T MRI scanner for studies investigating mitochondrial function.
- Conducted the first study at CHDR integrating 2 excitability methods:
 - Transcranial Magnetic Stimulation (TMS) and Nerve Excitability Threshold Tracking (NETT).
- Completed the first TMS study in epilepsy patients, where we showed that we can measure antiepileptic properties of antiepileptic drugs with TMS.
- Submitted the first intravenous (IV) Lipopolysaccharide (LPS) challenge study to the ethics committee in the neurology group. LPS will be used to study neuroinflammation in CSF and blood.
- Received ethics committee approval for an IV Biperiden challenge study, which aims to demonstrate the reversal of cognitive deficits with oral donepezil in healthy volunteers.



Key publications

Target engagement and immunogenicity of an active immunotherapeutic targeting pathological alpha-synuclein: a phase 1 placebocontrolled trial. Eijsvogel, P., Misra, P., Concha-Marambio, L., et al., 2024. Nature Medicine, 1-10. DOI: 10.1038/s41591-024-03101-8

The CIC-1 chloride channel inhibitor NMD670 improves skeletal muscle function in rat models and patients with myasthenia gravis. Skov, M., Ruijs, T. Q., Grønnebæk T. S et al., 2024. Science translational medicine, 16(739), eadk9109. DOI: 10.1126/scitranslmed.adk9109

Cognitive Effects of Three Beta-Adrenoceptor Acting Drugs in Healthy Volunteers and Patients with Parkinson's Disease. Eijsvogel, P.P., Borghans, L.G., Prins, S., et al., 2024. Journal of Parkinson's Disease, 14(6), pp.1149-1161. DOI: 10.3233/JPD-240039

NEUROLOGY

Collaborations & conferences

- Organised 2 symposia, attended by over 50 Parkinson's disease (PD) patients, to introduce PD patients with CHDR, clinical research and the role of the GBA1 gene in PD. At the event 2 study participants shared their study experiences, leading to increased screenings and participant enrollments for our PD studies.



At the second symposium, CHDR made a donation on behalf of the first 500 patients from our GBA1 genetic screening study. We contributed €8,250 to ParkinsonNL and €8,250 to Stichting Parki to accelerate Parkinson's research.

- Started successful collaborations with 17 hospitals to identify GBA-PD patients.
- Attended 5 conferences: 1 poster at ADPD in Lisbon, 1 oral presentation at EACPT in Rotterdam, 1 poster at MDS in Philadelphia, 2 posters at ILAE in Europe, 1 poster at ACNP 2024.



- Conducted a proof-of-pharmacology trial evaluating the effects of c-kit inhibitor Imatinib in healthy subjects, based on bone marrow- and blood-based endpoints.
- Completed the 50th bone marrow analysis in healthy volunteers.
- Strategic oncology studies with Leiden University Medical Center:
 - Fit-for-purpose validation of multimodal imaging biomarkers for cutaneous T-cell lymphoma in 74 patients.
 - Successfully established deep immunophenotyping pipeline of vulvar malignancies and disorders.
 - Concluded multi-omics tumour microenvironment profiling study of mycosis fungoides (proteomics, metabolomics, transcriptomics, imaging mass cytometry).
 - Real-world study in patients with cutaneous T-cell lymphoma launched.
- Initiated an observational study in oncology patients at the Netherlands Cancer Institute (NKI), executed by CHDR staff, to investigate complement-driven hypersensitivity reactions following firsttime chemotherapy administration.



Key publications

Remote Patient Monitoring Using Mobile Health Technology in Cancer Care and Research: Patients' Views and Preferences. Stuijt, D.G., van Doeveren, E.E., Kos, M., et al., 2024. JCO Clinical Cancer Informatics, 8, p.e2400092. DOI: 10.1200/CCI.24.00092

The development of in vitro organotypic 3D vulvar models to study tumor-stroma interaction and drug efficacy. Wu, S., Huisman, B.W., Rietveld, M.H., et al., 2024. Cellular Oncology, 47(3), pp.883-896. DOI: 10.1007/s13402-023-00902-w

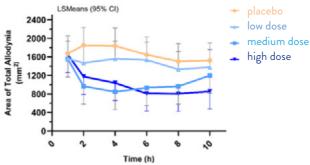
ONCOLOGY



- 1 oral presentation at ESMO 2024 in Barcelona, 1 oral and 2 poster presentations at EORTC-CLTG 2024 in Lausanne, 2 posters at BPS 2024 in Harrogate.
- Started a strategic collaboration with Netherlands Cancer Institute (NKI) and presented 1 poster at Cancer Research Day in Leiden.



- Appointed Dr Marieke Niesters, Anaesthesiologist and Pain specialist as Associate Research Director Pain.
- Completed 1434 PainCart measurements for 3 studies in 2024.
- Initiated a drug repurposing study funded by our R&D budget to evaluate Ambroxol, the active ingredient in many cough syrups and a selective sodium channel inhibitor, as a potential analgesic agent for treating neuropathic pain.
- Investigated 2 analgesic drugs with novel mechanism of action which showed promising results for future pain treatment.



Our capsaicin model applied: a study demonstrated a significant dose-dependant reduction in total allonynia following capsaicin application at a low, medium and high study drug dose, compared to placebo. After topical application of capsaicin, pain sensation was measured by Von Frey hair stimulation, a validated model for neuropathic pain.



Key publications

Cannabidiol Increases Psychotropic Effects and Plasma Concentrations of Δ9-Tetrahydrocannabinol Without Improving Its Analgesic Properties. Gorbenko, A.A., Heuberger, J.A., Klumpers, et al., 2024. Clinical Pharmacology & Therapeutics. DOI: 10.1002/cpt.3381

PAIN



- presentation at the Pain Summit in Boston and gave 2 presentations for QSPainRelief.
- Completed the 2nd study under the QSPainRelief grant, a collaboration aimed at identifying effective therapeutic interventions by novel combinations of existing drugs to treat chronic pain.
- Expanded our collaboration with the Leiden University Medical Center to identify patients with neuropathic pain for our deep phenotyping study, which aims to enroll 200 patients. To date, we have included 38 out of 200 patients.

Psychiatry

Highlights

- Completed a first-in-human (FIH) study with a novel, non-hallucinogenic neuroplastogen, a potential treatment for Major Depressive Disorder (MDD).
- Started a proof-of-concept study in MDD with a novel subtype-selective NMDAR antagonist.
- Received approval for a CHDR-funded R&D biomarker study to characterise the sustained pharmacodynamic effects of the 5-HT2A receptor agonist dimethyltryptamine (DMT).
- Started a FIH study with the psychedelic compound 5-MeO-MiPT, a member of the tryptamine family, and a potential treatment for mental health conditions.
- A research physician of the psychiatry team, Pauline Nettesheim, reached the final qualification round in the Olympic qualification for Breakdance at the 2024 Paris Olympic Games.



English Versi

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Key publications

Clinical Pharmacokinetics of Psilocin After Psilocybin Administration: A Systematic Review and Post-Hoc Analysis. Otto, M.E., van der Heijden, K.V., Schoones, J.W., et al., 2025. Clinical Pharmacokinetics, pp.1-14. DOI: 10.1007/s40262-024-01454-4

Clinical pharmacokinetics of N, N-dimethyltryptamine: a systematic review and post-hoc analysis to guide future clinical studies for neuropsychiatric indications. Van Der Heijden, K., Otto, M., Schoones, J.W. et al., 2024. Neuroscience Applied, 3, p.104854. DOI: 10.1016/j.nsa.2024.104854

Ketamine effects on resting state functional brain connectivity in major depressive disorder patients: a hypothesis-driven analysis based on a network model of depression. Recourt, K., Van Gerven, J., Drenth, N., et al., 2024. Frontiers in Neuroscience, 19, p.1531375. DOI: 10.3389/fnins.2025.1531375



No. S. Sussian, J. Janava, R. B.

W. J. million J. F. Marriel

PSYCHIATRY

- 1 poster at PAGE in Rome, 2 oral presentations at ICPR in Haarlem, 1 oral presentation at the Annual Neuropsychiatric Drug Development Summit in Boston, 1 poster at ECNP in Milan, 1 poster at Pharmacometrics Network Benelux meeting in Utrecht.
- Established Leiden Psychedelic Network, a collaboration with Leiden University Medical Center, National Psychotrauma Centrum (ARQ Centrum'45), and the Department of Social Sciences of Leiden University.







- Completed enrolment for the ProPark trial, where Trial@Home is used to monitor motor behaviour, social behaviour and vocal characteristics of participants.
- Reached the half way point in the eBladder trial in bladder cancer patients. Trial@Home is used to monitor mobility, sleep, and health status.
- The LAPSTAR trial for pancreatic cancer has started, employing Trial@Home to monitor mobility, sleep, and behaviour.



In these trials, Trial@home is used for exploratory endpoints as well as a convenient follow-up tool increasing the trial output and reducing the burden of clinical trials on participants.



Key publications

Older adults exercising ON TIME: protocol for a randomized controlled cross-over study to assess the effect of physical activity timing on insomnia severity. Albalak, G., Noordam, R., van der Elst, M, et al., 2024. Trials, 25(1), p.523. DOI: 10.1186/s13063-024-08310-7

Remote Patient Monitoring Using Mobile Health Technology in Cancer Care and Research: Patients' Views and Preferences. Stuijt, D.G., van Doeveren, E.E., Kos, M., et al., 2024. JCO Clinical Cancer Informatics, 8, p.e2400092. DOI: 10.1200/CCI.24.00092

TRIAL@HOME



- A fruitful collaboration with Leiden University Medical Center is further extended with the use of Trial@Home in 3 trials.
- The start of the LAPSTAR trial marks the beginning of an exciting collaboration with the University of Utrecht.
- The collaboration with Amsterdam Medical Center is strengthened through the eBladder trial.





8

28 Interns at CHDR

Introduced a PhD wall in our lecture hall to celebrate the exceptional work that lies at the heart of CHDR's mission: advancing drug development, pioneering new methods, and supporting the development of people.

Education News: Koos Burgraaf appointed as Dean of CHDR Academy

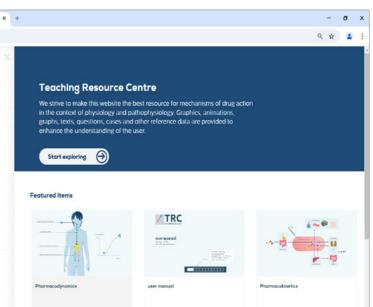
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Acute medicine
Cardiology
Endocrinology & metabolism
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EDUCATION



education



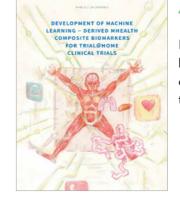


use platform TRC-P provides a wealth of educational content. In partnership with en working to enhance and expand the TRC-P knowledge platform. The upgraded version is set to launch in mid-2025 - stay tuned!

CHDR Highlights 2024

PhD theses

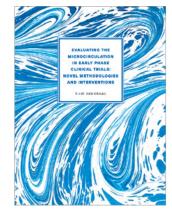
Nine PhD candidates successfully defended their thesis in 2024: Bas van Kraaij, Titia Ruijs, Gert-Jan Hassing, Eva Thijssen, Ahnjili ZhuParris, Jannik Rousel, Eveline in 't Veld , Mahdi Saghari, and Wouter ten Voorde.



MONITORING IMMUNE RESPONSIVENESS

Ahnjili ZhuParris

Development of machine learning: derived mhealth composite biomarkers for trial@home clinical trials



Bas van Kraaij

Evaluating the microcirculation in early phase clinical trials: novel methodologies and interventions



Titia Ruijs

Measurement of cortical, nerve, and muscle excitability in early phase clinical drug development

FEASIBILITY OF INTERPRETING BLINDED PHARMACODYNAMIC DATA - INVESTIGATING NORMAL VARIATIONS IN HEALTHY SUBJECTS

Gert-Jan Hassing

Feasibility of interpreting blinded pharmacodynamic data: investigating normal variations in healthy subjects



Eva Thijssen

studies investigating novel formulations of dopaminergic drugs

Clinical pharmacology



Eveline in 't Veld

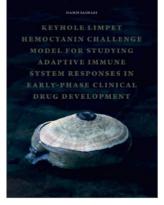
Monitoring immune responsiveness: Novel assays to explore immune system dynamics in health and disease

Wouter ten Voorde

Rubor, Calor, Tumor, Dolor: Objective assessments of inflammation

Jannik Rousel

Non-invasive biomarkers for inflammatory skin diseases: towards systems dermatology



Mahdi Saghari

Keyhole limpet hemocyanin challenge model for studying adaptive immune system responses in early-phase clinical drug development

Find their PhD thesis here: Library- CHDR

