# Syllabus

## Appendix

2026

## Contents


SIOP Ependymoma II ..... 5
SIOP HRMB ..... 9
ICC APL study 02 ..... 12
Da Vincy Trial ..... 14
LOGGIC Core ..... 16
5-ALA in children and adolescents ..... 18
ATRT01 ..... 20
FASTigial ..... 22
MAKEI-V ..... 24
PNOC022 DMG ..... 26
Randomet ..... 29
LuDO-N ..... 31
FaR-RMS ..... 33
Umbrella ..... 36
HR-NBL2 ..... 39
ML-DS 2018 ..... 41
LBL2018 ..... 43
CHIP-AML22 ..... 45
APAL2020D - Venetoclax AML ..... 47
ALCL-VBL ..... 49
Interfant-21 - KWF 15388 ..... 51
Pro-Teico ..... 53
IntReALL HR ..... 55
ALLTogether01 ..... 58
LCH-IV ..... 60
EWOG SAA 2010 ..... 63
EWOG MDS'06 ..... 65
Fanconi Anemie ..... 67
The Drug Access Protocol ..... 70
FOCUS ..... 72

7T MITCH ..... 74
LOGGIC Firefly-2 Europe ..... 76
Dabrafenib roll-over ..... 78
CIP ..... 80
Dulamp ..... 82
CO-IMPACT ..... 84
RELIVE ..... 86
SDM bottumoren ..... 88
PAVO studie - CCTL019A2205B ..... 90
LTF-304 ..... 92
Pinocchio ..... 94
Pilot ademonderzoek ..... 96
INTERACT - Kika 429 ..... 98
KinderOnconet ..... 100
LATER MetVasA - Kika 433 ..... 102
Educational priorities ..... 105
VANISH ..... 107
Symptom ap/Approach ..... 109
Hercules - sponsor ..... 112
Follow-on study ..... 114
ERNIE (iBrain) - sponsor ..... 116
SIMBA - Kika 450 ..... 118
QoL NEMO ..... 120
Testis biopsy/PRINCE ..... 122
FU poli botsarcomen ..... 124
FITco ..... 126
TRINGQS study - Kika 448 ..... 128
EndoWatch-II - KWF 14984 ..... 131
EthPOiB ..... 133
KiKa 416 Identify ..... 135
Belumosudil ROCKNROL1 EFC17757 ..... 137
PROMIS II KiKa 449 ..... 139

FU Sensory-2 - sponsor ..... 141
Astronaut study ..... 143
KOMPAS ..... 146

# Study information

## SIOP Ependymoma II

| | |
|---|---|
| Protocol: | An international Clinical Program for the diagnosis and treatment of children, adolcescents and young adults with ependymoma |
| Local Investigator: | Lugt, van der J. |
| National Coordinating Investigator: | Lugt, van der J. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | SIOP Ependymoma II |

### General

| | |
|---|---|
| Sponsor: | Centre Leon Berard |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | The Ependymoma Program is a comprehensive program to improve the accuracy of the primary diagnosis of ependymoma and explore different therapeutic strategies in children, adolescents and young adults, accordingly. This program is opened to all patients diagnosed with ependymoma below the age of 22 years. It will include a centralised review of pre and post-operative imaging to assess the completeness of the resection. It will also include a central review of pathology to confirm the histological diagnosis. The biological markers 1q gain, Tenascin C status, RELA-fusion, YAP fusion, H3.3K27me3 and molecular subgroup by methylation array will be prospectively assessed for prospective evaluation of disease subgroups. Further biological evaluations will be coordinated within the integrated BIOMECA study. After surgery and central review |

of imaging and pathology, patients will be offered the opportunity to undergo second look surgery, if possible. Patients will be enrolled in one of 3 different strata according to the outcome of the initial surgical resection (residual disease vs no residual disease), their age or eligibility / suitability to receive radiotherapy. These 3 different strata correspond to 3 therapeutic strategies according to the patient status.

- **Stratum 1:** is designed as a randomised phase III study for patients who have had a complete resection, with no measurable residual disease (as confirmed by centrally reviewed MRI) and are = 12 months and < 22 years at diagnosis. Those patients will be randomised to receive conformal radiotherapy followed by either 16 weeks of chemotherapy with VEC+CDDP, or observation
- **Stratum 2:** is designed as a randomized phase II study for patients who have inoperable measurable residual disease and who are = 12 months and < 22 years at diagnosis. Those patients will be randomized to two different treatment schedules of chemotherapy either with VEC or VEC+ high dose methotrexate (VEC +HD-MTX). After completion of the frontline chemotherapy, patients will be assessed for response (MRI) and will receive second look surgery when feasible. For those patients who remain unresectable with residual disease despite frontline chemotherapy and for whom second line surgery is not feasible, there will be a study of the safety of a radiotherapy boost of 8 Gy that will be administered to the residual tumour immediately after the completion of the conformal radiotherapy. Patients without evidence of residual disease after the chemotherapy and/or a second look surgery are not eligible for radiotherapy boost. All patients who have not shown progression under chemotherapy will receive, as maintenance therapy, a 16 week course of VEC+CDDP following completion of radiotherapy
- **Stratum 3:** is designed as a randomised phase II chemotherapy study in children <12 months of age or those not eligible to receive radiotherapy. These patients will be randomised to receive a dose dense chemotherapy alternating myelosuppressive and relatively non-myelosuppressive drugs at 2 weekly intervals, with or without, the addition of the histone deacetylase inhibitor, valproate
  Observational study: after staging phase, patients that do not fulfil the inclusion criteria of one of the interventional strata will be enrolled and followed up via an observational study which will be analysed descriptively

| | |
|---|---|
| Primary objective: | **Overall program**: to determine whether the assessment of residual disease can be improved by a centralized review of post-operative MRI and whether such review increases the rate of complete resection compared to historical controls. Does central neurosurgical and radiological review increase resection rates?<br>• **Stratum 1**: to test the hypothesis that there will be an improvement in progression-free survival in patients who receive 16 weeks chemotherapy (VEC+CDDP) following surgical resection and conformal radiotherapy when compared to those that undergo surgical resection and radiotherapy alone<br>• **Stratum 2**: to compare the activity of 2 post-operative chemotherapy schedules, VEC or VEC+HD-MTX in patients who have incompletely resected tumour<br>• **Stratum 3**: to evaluate the progression free survival in children unable to receive radiation therapy and who receive valproate, as a histone deacetylase inhibitor in addition to the primary chemotherapy strategy when compared to those that undergo chemotherapy without valproate |
| Study population: | **Stratum 1**: patients with no measurable residual disease and =12 months of age - phase III<br>**Stratum 2**: patients with inoperable measurable residual disease and =12 months of age - phase II<br>**Stratum 3**: randomized phase II chemotherapy study in children < 12 months of age or those not eligible to receive radiotherapy |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 30-06-2020 |
| Start national recruitment: | 06-07-2020 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 30 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 80 |
| Actual number of patients included: | 21 |

## SIOP HRMB

| | |
|---|---|
| Protocol: | An Internatinal prospective trial on high-risk medulloblastoma in patients older than 3 years |
| Local Investigator: | Plasschaert, S.L.A. |
| National Coordinating Investigator: | Plasschaert, S.L.A. & Franke, N.E. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | SIOP HRMB |

### General

| | |
|---|---|
| Sponsor: | University of Birmingham |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

Study design:

SIOP-HRMB is an international, prospective, phase III randomised trial in patients aged 3 years and older with 'high-risk' medulloblastoma with a high-risk biological profile. Prior to entry into the trial, patients will undergo a screening phase. This will include a clinical and molecular diagnostic assessment. Biological assessments will be carried out centrally in accordance with a national scheme, see section 18. Eligible and consenting patients will be entered into the SIOP-HRMB trial and randomised to R1 after a definitive diagnosis of high risk medulloblastoma, prior to starting induction chemotherapy.

**Randomisation 1 (R1)** will compare three different treatment arms. Patients will be randomised between:

- **Arm A**: Conventional radiotherapy (36 Gy CSI) (control arm)
- **Arm B:** HART radiotherapy (39.2 Gy CSI)
- **Arm C**: High-dose chemotherapy followed by conventional radiotherapy (36 Gy CSI)

All trial patients will be randomised at trial entry. For the majority of patients taking part in R1, randomisation will take place prior to the commencement of induction chemotherapy. However, in cases of clinical urgency to start induction patients may be treated with one cycle of induction chemotherapy prior to trial entry/randomisation at the discretion of the treating Investigator. Any patients who are found to be ineligible after trial entry e.g. due to SHH P53 germline mutation will be excluded from the analysis of R1 and will be withdrawn from the trial (see section 24). Enough time should be allowed after randomisation for stem cells to be harvested in patients randomised to the high-dose chemotherapy/conventional RT arm. Both experimental arms (Arms B and C) will be evaluated with an interim analysis with an aim to drop one of the experimental arms, so that the final analysis of R1 is a comparison of one experimental arm vs control. The interim analysis will take a 'pick-a-winner' selection design. One of the R1 treatment arms will be removed from R1 via substantial amendment. In the event that one of the experimental arms becomes unavailable for the trial, R1 will randomize between the remaining available treatment arms.

**Randomisation 2 (R2)** will compare two different maintenance regimens. Patients will be randomised between:

- **Arm D**: Maintenance therapy with vincristine (VCR)/CCNU/cisplatin alternating with VCR/cyclophosphamide (control arm)
- **Arm E**: Temozolomide maintenance therapy Participation in R2 is not mandatory. Randomisation will take place after completion of radiotherapy and within 7 days prior to the planned start of maintenance therapy. Patients who take part in R1 and are treated in accordance with Arm C (high-dose chemotherapy) will not be eligible to take part in R2, as it is felt that Arm D maintenance therapy will not be tolerated due to bone marrow suppression. This group of patients will be treated with Arm E temozolomide maintenance therapy; however will not contribute to the analysis of R2. Treatment and adverse event data will be collected for this group of patients. Patients who do not take part in R2 and have received either conventional radiotherapy alone or HART radiotherapy will be treated with standard maintenance therapy, as per arm D.

| | |
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| Primary objective: | **Overall program**:<br>• To evaluate whether the outcome in children, young people and adults with HR-MB is improved over standard therapy for those treated with: (i) conventional (once a day) radiotherapy (RT) (standard therapy), (ii) hyperfractionated-accelerated radiotherapy (HART), or (iii) high-dose therapy (HDT) with thiotepa followed by conventional RT.<br>• To evaluate whether the outcome in HR-MB is different for those treated with two different maintenance chemotherapy therapies. |
| Study population: | Children, teenagers and adults with newly diagnosed high-risk medulloblastoma. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 17-05-2022 |
| Start national recruitment: | 17-05-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 40 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 40 |
| Actual number of patients included: | 7 |

## ICC APL study 02

| | |
|---|---|
| Protocol: | Treatment study for children and adolescents with Acute Promyelocytic Leukemia |
| Local Investigator: | Kaspers, G.J.L. |
| National Coordinating Investigator: | Kaspers, G.J.L. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | ICC APL study 02 |

### General

| | |
|---|---|
| Sponsor: | Associazione Italiana Ematologia Oncologia Pediatrica |
| Coordinating Investigator: | - |
| Study status: | Closed for inclusion |
| Research phase: | Fase II |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | International, multi-center study, aimed at recruiting at least 46 SR patients |
| Primary objective: | To evaluate the efficacy in terms of event-free survival of a treatment combining arsenic trioxide (ATO) and all-trans retinoic acid (ATRA) in newly diagnosed APL standard-risk children and adolescents |
| Study population: | – Newly diagnosed APL confirmed by the presence of PML/RARa fusion gene<br>– Age <18 years<br>– Written informed consent by parents or legal guardians<br>– If applicable, female participants must have pregnancy test by beta-HCGdosing and be negative.<br>– Patients of child-bearing or child-fathering potential must be willing to practice and must contact their |

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|---|---|
| | physician. With their physician, they must agree on the most appropriate approach for birth control from the time of enrolment in this study and for 3 months after receiving the latest infusion. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 07-07-2023 |
| Start national recruitment: | 07-07-2023 |
| Expected date end of national recruitment: | 09-10-2025 |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 5 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 5 |
| Actual number of patients included: | 3 |

## Da Vincy Trial

| | |
|---|---|
| Protocol: | Da Vincy Trial: optimal Duration of Aprepitant therapy for nausea and Vomiting INduced by ChEmotherapY in children: a double-blind placebo-controlled crossover randomized phase III trial |
| Local Investigator: | Vos - Kerkhof, de E. |
| National Coordinating Investigator: | Zwaan, C.M. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Da Vincy Trial |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology, Clinical Unit: Neuro-oncology, Clinical Unit: Solid tumors, Quality of Life |

### Design

| | |
|---|---|
| Study design: | a double-blind placebo-controlled randomized cross-over phase III study |
| Primary objective: | To evaluate the effect of prolonged duration of (fos)aprepitant prophy-laxis on the prevention of delayed CINV (complete remission in the 24-72 hours after the final dose of chemotherapy) in children. The current 3-day regimen is compared to a regimen of (fos)aprepitant prophylaxis during the complete course of chemotherapy in the same patient in subsequent similar courses of chemotherapy, creating an intrapatient comparison of anti-emetic control. To ensure that treatment lasts equally long in both arms the 3-day regimen will be prolonged with placebo, and participants and medical staff (with the exception of phar-macy personnel) will be blinded. |

| | |
|---|---|
| Study population: | Patients (= 6 months to = 18 years) who have documented malignancy and who are scheduled to receive moderate and highly emetogenic chemotherapy. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 03-02-2022 |
| Start national recruitment: | 21-12-2021 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 76 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 76 |
| Actual number of patients included: | 78 |

## LOGGIC Core

| | |
|---|---|
| Protocol: | LOGGIC: Low Grade Glioma in Children |
| Local Investigator: | Schouten - van Meeteren, A.Y.N. & Kersbergen, K.J. |
| National Coordinating Investigator: | Plasschaert, S.L.A. & Schouten - van Meeteren, A.Y.N. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | LOGGIC Core |

### General

| | |
|---|---|
| Sponsor: | KiTZ |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | Non-interventional observational registry including biological and clinical data |
| Primary objective: | The overall aim of the LOGGIC Core BioClinical Data Bank is to set up a molecular and clinical data bank for pediatric low grade gliomas |
| Study population: | Children, adolescents and young adults 0 to 21 years old with all subtypes of LGG tumours at primary diagnosis or progression/relapse |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 12-05-2022 |
| Start national recruitment: | 12-05-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 5000 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 400 |
| Actual number of patients included: | 137 |

## 5-ALA in children and adolescents

| | |
|---|---|
| Protocol: | Clinical safety study on 5-Aminolevulinic acid (5-ALA) in children and adolescents with supratentorial brain tumors |
| Local Investigator: | Hoving, E.W. |
| National Coordinating Investigator: | Hoving, E.W. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | 5-ALA in children and adolescents |

### General

| | |
|---|---|
| Sponsor: | Universitätsklinikum Münster |
| Coordinating Investigator: | - |
| Study status: | Study finalisation |
| Research phase: | Fase II |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | The study protocol is a prospective, open, single-armed, multinational, multicenter, phase II study for application of 5-ALA in children and adolescents with supratentorial brain tumors. |
| Primary objective: | To determine the safety of 5-ALA for fluorescence-guided resections in children and adolescents with supratentorial, intra-axial brain tumors. |
| Study population: | Age 3 - <18 years<br>First radiological diagnosis of intra-axial, supratentorial contrast-enhancing tumor on MRI or recurrent supratentorial intra-axial brain tumor (malignant glioma, astrocytoma, malignant ependymoma, AT/RT, Oligodendroglioma, etc.) |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 01-02-2023 |
| Start national recruitment: | 01-02-2023 |
| Expected date end of national recruitment: | 28-11-2025 |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 10 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 10 |
| Actual number of patients included: | 10 |

## ATRT01

| | |
|---|---|
| Protocol: | An international prospective umbrella trial for children with<br>atypical teratoid/rhabdoid tumours (ATRT) including<br>A randomized phase III study evaluating the non-inferiority of<br>three courses of high-dose chemotherapy (HDCT) compared to<br>focal radiotherapy as consolidation therapy |
| Local Investigator: | Franke, N.E. |
| National Coordinating Investigator: | Franke, N.E. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | ATRT01 |

### General

| | |
|---|---|
| Sponsor: | German Paediatric Oncology Group |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | Prospective, open label multicentre, international, umbrella trial including a randomized phase III study evaluating the non-inferiority of 3 courses of high-dose chemotherapy compared to focal radiotherapy plus standard chemotherapy as a consolidation measure following conventional chemotherapy in children with ATRT ranging from 12 – 35 months at the time of consolidation (RT vs. HDCT). |

| | |
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| Primary objective: | **Part A**:<br>To test the non-inferiority, as evaluated by 2-year overall survival (OS), of three courses of HDCT compared to focal RT plus conventional chemotherapy as consolidation therapy following conventional chemotherapy in children with ATRT aged 12 – 35 months at consolidation therapy.<br>**Part B**:<br>To assess the efficacy, as evaluated by OS, of three courses of HDCT as a consolidation measure following conventional-type chemotherapy in children with ATRT aged <12 months or with contraindications to RT at the time of HDCT and not eligible for randomization within Part A of this protocol, compared to historical controls.<br>**Part C**:<br>To assess the efficacy, as evaluated by overall survival, of RT as a consolidation measure combined with conventional-type chemotherapy in children aged =36 months with ATRT or contraindications to HDCT and ineligibility for Part A, compared to historical controls. |
| Study population: | Patients with ATRT of any site and any stage. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

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|---|---|
| Start international recruitment: | 16-01-2023 |
| Start national recruitment: | 16-01-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 10 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 10 |
| Actual number of patients included: | 8 |

## FASTigial

| | |
|---|---|
| Protocol: | FASTigial: Finding Anatomical Substrates of neuropsychological outcome in children with posterior fossa tumors (add-on project to Nordic CMS study) |
| Local Investigator: | Partanen, M.H. |
| National Coordinating Investigator: | Partanen, M.H. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | FASTigial |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | Partanen, M.H. |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Neuro-oncology, Quality of Life |

### Design

| | |
|---|---|
| Study design: | This is a longitudinal, prospective observational cohort study, including 210 children who are scheduled for posterior fossa tumor surgery. Participating centers will enroll patients for ~30 months. Centers that have the capacity to conduct both advanced MRI and neuropsychological testing will be included for our primary objective; however, if a center can only collect MRI or neuropsychological tests, they will also be included for secondary objectives. |
| Primary objective: | The primary aim of this study is to investigate clinical and neuroradiological predictors of neuropsychological outcome in children with posterior fossa tumors. Secondary objectives are to identify group differences and changes over time in neuroradiological and neuropsychological measures for children who have higher versus lower CMS symptom severity. |

| | |
|---|---|
| Study population: | Inclusion criteria<br>• Eligible for Nordic CMS study (see separate study protocol)<br>• Patients 2-18 years old<br>Exclusion criteria<br>• No informed consent<br>• Patient received re-operation due to residual tumor within posterior fossa or relapse of tumor<br>• Inability to speak/understand local language (for neuropsychological testing)<br>Sample size<br>The primary aim is to determine predictors of neuropsychological outcome at 12 months after surgery. Required sample size was calculated in GPower330, which included the following parameters for multivariable linear regression (medium effect f2=0.15, alpha=0.05, power=0.95, estimated 10 predictors). Results suggested that 172 patients would be required to achieve desired power. There are approximately 300 patients who would meet inclusion and exclusion criteria within a 30-month period. It is expected that 80% of patients to consent to the study and 15% will be lost to follow-up31, leaving a final sample size of 204 participants. Therefore, a sufficient sample size should be achieved. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 18-07-2024 |
| Start national recruitment: | 18-07-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 210 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 210 |
| Actual number of patients included: | 34 |

## MAKEI-V

| | |
|---|---|
| Protocol: | Multicentre prospective trial for extracranial malignant germ cell tumours including a randomized comparion of Carboplatin and Cisplatin |
| Local Investigator: | Mavinkurve - Groothuis, A.M.C. |
| National Coordinating Investigator: | Mavinkurve - Groothuis, A.M.C. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | MAKEI-V |

### General

| | |
|---|---|
| Sponsor: | UK Bonn |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Solid tumors |

### Design

| | |
|---|---|
| Study design: | Prospective, multicentre phase III-trial in malignant extracranial germ cell tumours including a randomization between Carboplatin-and Cisplatin-combination standard chemotherapy based on a risk-stratification derived from the preceding MAKEI 96 trial andpublished data |
| Primary objective: | The primary objective of MAKEI V is to assess in a randomized comparison whether the efficacy of Carboplatin (600 mg/m² percycle) (AUC 7.9 mg/ml/min.) is not inferior to Cisplatin (100 mg/m² per cycle) in malignant GCT (MGCT) of intermediate, high andvery high risk with regard to Event-free survival (EFSr). |
| Study population: | All children and adolescents with MGCT up to 17 11/12 years of age, and patients with ovarian primaries up to 29 11/12 years of age. |

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| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

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|---|---|
| Start international recruitment: | 29-08-2023 |
| Start national recruitment: | 29-08-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 25 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 360 |
| Actual number of patients included: | 13 |

## PNOC022 DMG

| | |
|---|---|
| Protocol: | PNOC022: A Combination Therapy Trial using an Adaptive Platform Design for Children and Young Adults with Diffuse Midline Gliomas (DMGs) including Diffuse Intrinsic Pontine Gliomas (DIPGs) at Initial Diagnosis, Post-Radiation Therapy and at Time of Progression |
| Local Investigator: | Lugt, van der J. |
| National Coordinating Investigator: | Lugt, van der J. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | PNOC022 DMG |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | On hold |
| Research phase: | Fase II |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | This is a multi-arm, multi-cohort trial using a Bayesian drug combination platform design for children and young adults with DMGs. This trial will randomize participants at study entry who are at different stages of disease (newly diagnosed (Cohort 1), post-radiation therapy but with no evidence of progression (Cohort 2), and at time of progression (Cohort 3) to different combination therapies. Given the very favorable safety profile of ONC201 and anticipated known side effects of novel agents to be used in this trial, no specific phase 1 evaluations of the combination therapy will be conducted within the confines of this trial but, toxicity will be carefully monitored throughout the trial and stopping rules will be implemented. ONC201 will be used as a backbone and will |

| | |
|---|---|
| | be combined with novel agents that have been shown in preclinical studies to be additive or synergistic in combination. At this moment, study arms 2, 4 and 6 are open, which include paxalisib as novel agent. |
| Primary objective: | **Cohorts 1 and 2**<br>Maintenance Combinations:<br>– To assess efficacy of combination therapy with ONC201 and novel agent in participants with DMG based on median progression-free survival at 6 months (PFS6)<br>**Cohort 3**<br>– To assess efficacy of combination therapy with ONC201 and novel agent in participants with recurrent DMG based on overall survival at 7 months (OS7) |
| Study population: | This study will enroll children and young adults (2-39 years of age) with diffuse midline gliomas (DMGs; excluding Grade 2, H3K27M negative tumors) at different stages of their disease.<br>• **Cohort 1**: Will include participants with newly diagnosed DMGs.<br>• **Cohort 2**: Will include participants with DMGs who have completed focal radiation therapy and are within 4-14 weeks from completion of radiation therapy without evidence of progression.<br>• **Cohort 3**: Will include participants with DMGs who have evidence of progression but have not been treated for this progression and have not previously undergone re-irradiation therapy. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 22-11-2022 |
| Start national recruitment: | 21-11-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 30 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 30 |
| Actual number of patients included: | 14 |

## Randomet

| | |
|---|---|
| Protocol: | SIOP RANDOMET 2017<br>Randomized multi-centre open-label non-inferiority phase 3 clinical trial for patients with a stage IV childhood renal tumour comparing upfront Vincristine, Actinomycin-D and Doxorubicin (VAD, standard arm) with upfront Vincristine, Carboplatin and Etoposide (VCE, experimental arm) |
| Local Investigator: | Grotel, van M. |
| National Coordinating Investigator: | Heuvel - Eibrink, van den M.M. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | Randomet |

### General

| | |
|---|---|
| Sponsor: | German Paediatric Oncology Group |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Solid tumors |

### Design

| | |
|---|---|
| Study design: | Phase 3, open label, multi - centre, multi - national, randomized, noninferiority, two arms, open - label clinical tria |
| Primary objective: | To determine non-inferiority of preoperative 6 weeks of VCE to VAD in the overall metastatic rapid response rate (MetRR) in newly diagnosed stage 4 childhood renal tumours. The MetRR will include the pulmonary response rate (PRR) and the response rate on non-pulmonary metastasis (NPRR). |

| | |
|---|---|
| Study population: | Inclusion criteria:<br>– Age <18 years >3 months<br>– Patient suffering from metastatic renal tumour at initial diagnosis having at least one circumscript, non-calcified (pulmonary) nodule (or other lesion highly suspicious of metastasis according to criteria for metastatic disease) =3 mm as determined by chest CT-scan and abdominal CT-scan/MRI. Metastatic disease must be confirmed by central review.<br>– Understand and voluntarily provide permission (subjects and when applicable, parental/legal representative(s)) to the ICF prior to conducting any study related assessments/procedures<br>– Able to adhere to the study visit schedule and other protocol requirements<br>– No pre-existing and ongoing cardiac malfunction disease<br>– No pre-existing and ongoing liver function deficiency which is not controllable by substitution |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 05-04-2024 |
| Start national recruitment: | 09-04-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 25 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 406 |
| Actual number of patients included: | - |

**LuDO-N**

| | |
|---|---|
| Protocol: | A phase II trial of 177Lutetium-DOTATATE in children with primary refractory or relapsed high-risk neuroblastom LuDO-n |
| Local Investigator: | Noesel, van M.M. |
| National Coordinating Investigator: | Noesel, van M.M. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | LuDO-N |

**General**

| | |
|---|---|
| Sponsor: | Karolinska University Hospital |
| Coordinating Investigator: | - |
| Study status: | On hold |
| Research phase: | Fase II |
| Research areas: | Clinical Unit: Solid tumors |

**Design**

| | |
|---|---|
| Study design: | Phase II, open label, multi-centre, single arm two stage design clinical trial |
| Primary objective: | To correlate tumour dosimetry with response<br>To correlate somatostatin type 2 receptor (SSTR-2) expression with 68 Ga-DOTATOC PET/CT uptake<br>To correlate the uptake on 68 Ga-DOTATOC PET/CT with response to 177 Lu-DOTATATE therapy |
| Study population: | Children and young people > 18 months old with high-risk, relapsed or primary refractory neuroblastoma (INSS stage 4 or INRGSS stage M) |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 26-01-2023 |
| Start national recruitment: | 27-01-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 10 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 10 |
| Actual number of patients included: | 7 |

## FaR-RMS

| | |
|---|---|
| Protocol: | FaR-RMS - An overarching study of Children and adults with Frontline and Relapsed Rhabdomyosarcoma |
| Local Investigator: | Merks, J.H.M. |
| National Coordinating Investigator: | Merks, J.H.M. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | FaR-RMS |

### General

| | |
|---|---|
| Sponsor: | University of Birmingham |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Solid tumors |

### Design

Study design: FaR-RMS is an over-arching study for patients with newly diagnosed and relapsed RMS including multi-arm, multi-stage questions with three principal aims. These are to evaluate systemic therapy through the introduction of new agent regimens, the duration of maintenance therapy, and radiotherapy to improve local control.

Primary objective:

Phase I Dose Finding Studies

- To determine the recommended phase II dose (RP2D) of new systemic therapy regimens.
  o The first combination to be tested is irinotecan in combination with ifosfamide, vincristine and actinomycin D (IRIVA)

Frontline Chemotherapy Questions

- To compare systemic therapy regimens for patients with VHR disease at diagnosis (CT1A).
  o The first new combination regimens to be compared

are IVADo and IRIVA in a dose intense schedule

- To compare new systemic therapy regimens with standard chemotherapy for patients with HR disease at diagnosis. The standard chemotherapy is ifosfamide, vincristine, actinomycin D (IVA) (CT1B).
  o The first new combination regime to be compared is irinotecan combined with IVA (IRIVA) in a dose intense schedule

Radiotherapy Questions

- To determine whether pre-operative or standard post-operative radiotherapy is better for patients with resectable disease (RT1A).
- To determine whether dose escalation of radiotherapy improves the outcome in patients with a higher local failure risk (RT1B/C).
- To determine whether radiotherapy treatment of all sites of disease, including metastatic sites, when compared to radiotherapy treatment to the primary site and involved regional lymph nodes alone, improves the outcome for patients with unfavourable metastatic disease (RT2).

Maintenance Chemotherapy Questions

- To determine whether the addition of a further 12 cycles of vinorelbine and cyclophosphamide (VnC) to standard 12 cycles of maintenance chemotherapy (i.e. 24 cycles total) improves the outcome for patients with VHR disease at diagnosis (CT2A).
- To determine whether the addition of a further 6 cycles of to the standard 6 cycles (i.e. 12 cycles total) improves the outcome for patients with localised HR disease at diagnosis (CT2B).

Relapsed RMS Question

- To determine whether new systemic therapy regimens improve outcome in relapsed RMS (CT3). Initial new systemic therapy combination to be tested: The addition of temozolomide (T) to vincristine and irinotecan (VIR), (VIRT)

| | |
|---|---|
| Study population: | Patients with newly diagnosed or relapses rhabdomyosarcoma |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 26-10-2020 |
| Start national recruitment: | 26-10-2020 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 140 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 140 |
| Actual number of patients included: | 85 |

## Umbrella

| | |
|---|---|
| Protocol: | UMBRELLA PROTOCOL SIOP-RTSG 2016 Integrated research and guidelines for standardized diagnostics and therapy for paediatric renal tumours |
| Local Investigator: | Heuvel - Eibrink, van den M.M. |
| National Coordinating Investigator: | Heuvel - Eibrink, van den M.M. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | Umbrella |

### General

| | |
|---|---|
| Sponsor: | Universität des Saarlandes |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Solid tumors |

### Design

| | |
|---|---|
| Study design: | The study design of the UMBRELLA protocol includes data registration, biological sample collection and biological studies |
| Primary objective: | 1. To show the feasibility of storing serial blood, urine samples, tumour and germline material at diagnosis and at specific time points during treatment for international collaborative studies. These will be used to validate and quantify (using multivariate analysis), the relative adverse prognostic significance of specified somatic molecular biomarkers (listed in aim 2) in relation to blastemal volume (aim 3). They will also be used for exploratory analyses of potential novel biomarkers, including circulating nucleic acids detectable in blood and urine, for diagnosis and prognosis. |

2. To assess genomic 1q gain and other copy number variants as a prognostic biomarker in WT. Moreover, the feasibility of returning biomarker results to treatment centres within a clinically relevant time frame will be tested.
3. To optimize the definition of high risk WT, ‘blastemal type’ through accurate measurement of the residual blastemal cells volume including centralized ‘real time’ pathology and radiology review. The blastemal cell volume will be assessed in relation to other biomarkers and outcome measures including overall and event-free survival.
4. To optimize radiological diagnostics/review by (real time) central review to monitor and give appropriate feedback on diagnostic imaging quality, harmonies diagnostic procedures and standardize reporting of radiology findings. Additionally, diffusion-weighted imaging (DWI) results will be linked to pathological assessment of the tumour.
5. To optimize pathological diagnostics/review by (real time) central review to monitor and give appropriate feedback on local pathological diagnosis, stratify treatment based on central pathological review and store biological material according to standardized guidelines.

| | |
|---|---|
| Study population: | All children, adolescents or young adults with a primary or relapsed renal tumour diagnosed in a participating SIOP-RTSG center. The inclusion of patients is independent of the histology of the renal tumour, the age of the patiënt (except for RCC patients: <18 years old) or the country of residence. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 31-05-2019 |
| Start national recruitment: | 31-05-2019 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 1050 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 350 |
| Actual number of patients included: | 185 |

## HR-NBL2

| | |
|---|---|
| Protocol: | High-Risk Neuroblastoma Study 2 of SIOP-Europa-Neuroblastoma (SIOPEN) |
| Local Investigator: | Tytgat, G.A.M. |
| National Coordinating Investigator: | Kraal, K.C.J.M. & Tytgat, G.A.M. & Dierselhuis, M.P. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | HR-NBL2 |

### General

| | |
|---|---|
| Sponsor: | Department Direction de la Recherche Clinique. Gustave Roussy |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Solid tumors |

### Design

| | |
|---|---|
| Study design: | Randomized, international and multicentric phase 3 study that evaluates and compares 2 treatment strategies in 3 therapeutic phases (induction, high-dose chemotherapy and radiotherapy) for patients with high-risk neuroblastoma. |
| Primary objective: | R-I: Comparison of the EFS rate of 2 induction regimens, GPOH and RAPID COJEC, in patients with high-risk neuroblastoma.<br><br>R-HDC: Comparison of the EFS rate of single HDC with busulphan and melphalan (Bu-Mel) versus tandem HDC with Thiotepa followed by Bu-Mel in patients with high-risk neuroblastoma.<br><br>R-RTx: Comparison of the EFS rate of 21.6 Gy radiotherapy to the preoperative tumor bed versus 21.6 Gy radiotherapy |

| | |
|---|---|
| | and a sequential boost up to 36 Gy to the residual tumor in patients with macroscopic residual disease after HDC and surgery. |
| Study population: | Patients with High Risk Neuroblastoma |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 03-03-2021 |
| Start national recruitment: | 03-03-2021 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 70 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 70 |
| Actual number of patients included: | 42 |

## ML-DS 2018

| | |
|---|---|
| Protocol: | Phase II/III Clinical Trial for the Treatment of Myeloid Leukemia in Children with Down Syndrome 2018 |
| Local Investigator: | Goemans, B.F. |
| National Coordinating Investigator: | Goemans, B.F. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | ML-DS 2018 |

### Published articles

CPX-351inDownSyndrome-associatedMyeloidLeukemia:ResultsandPrognosticFactorsfromthePhaseIIIML-DS2018Trial: https://doi.org/10.1182/blood.2025030775

### General

| | |
|---|---|
| Sponsor: | German Paediatric Oncology Group |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | ML-DS 2018 is a prospective, non-randomized, open-label, historically-controlled, international and multicenter phase III trial for children with ML-DS. The single-arm non-inferiority trial will be compared against the historical control (ML-DS 2006 trial) with event free survival as the primary endpoint. |
| Primary objective: | Achieving an event-free survival, which is not inferior to the ML-DS 2006 trial. |

| | |
|---|---|
| Study population: | Children with myeloid leukemia associated with Down syndrome (ML-DS). |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 23-02-2022 |
| Start national recruitment: | 23-02-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 10 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 10 |
| Actual number of patients included: | 2 |

## LBL2018

| | |
|---|---|
| Protocol: | LBL 2018 - International cooperative treatment protocol for children and adolescents with lymphoblastic lymphoma |
| Local Investigator: | Loeffen, J.L.C.M. |
| National Coordinating Investigator: | Loeffen, J.L.C.M. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | LBL2018 |

### General

| | |
|---|---|
| Sponsor: | Universitätsklinikum Münster |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | International inter-group multi-centre open-label randomized prospective clinical trial |
| Primary objective: | • Randomization R1 Dexamethason vs Prednisolon in induction: Cumulative incidence of relapse with involvement of the CNS (CNS-relapse, pCICR). The time to relapse is the time from randomization to the first relapse or the date of last follow-up. Other events (non-response, progressive disease, relapse, second malignancy or death before and in CR) will be taken into account as competing events.<br>• Randomization R2 in High group (Notch1/FBXW7 wildtype) standard arm vs experimental arm with High risk blocks: Estimated probability of event-free survival (pEFS). The pEFS is the time from randomization to the first event (non-response, progressive disease, relapse, second malignancy or death from any cause) or date of last follow-up. |

| | |
|---|---|
| Study population: | Children and adolescents up to 18 years of age with untreated lymphoblastic lymphoma are potentially eligible for the study LBL 2018. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 21-06-2021 |
| Start national recruitment: | 21-06-2021 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 55 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 55 |
| Actual number of patients included: | 39 |

## CHIP-AML22

| | |
|---|---|
| Protocol: | CHildhood International Protocol – Acute Myeloid Leukemia (CHIP-AML) 2022: A phase III, open label trial in newly diagnosed pediatric de novo AML patients - A study by the NOPHO-DB-SHIP consortium. |
| Local Investigator: | Goemans, B.F. |
| National Coordinating Investigator: | Kaspers, G.J.L. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | CHIP-AML22 |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | This will be an multinational randomized phase III open-label study with two sequential randomisations and therefore two sequential parallel group comparisons , with safety run-ins for GO, flt3-inhibitor and venetoclax. Results will also be put into perspective of that of a large, historical and similarly defined cohort very recently treated according to protocol NOPHO-DBH AML-2012 with similar chemotherapy and allo-SCT, by the same consortium. That historical cohort is also well characterized regarding treatment response, as measured by flow cytometry-based MRD status at different time-points, and events such as refractory disease, relapse and death in remission. Several objectives of CHIP-AML21 can not be proven by adequately powered randomized studies, in view of the rarity of the subgroups, and require historical comparisons. |

| | |
|---|---|
| Primary objective: | The overall objective of this study is to improve event-free survival, and to reduce the burden of treatment toxicity through reduction of consolidation chemotherapy. |
| Study population: | Children and adolescents from birth up to and including 18 years of age, with newly diagnosed and de novo acute myeloid leukemia (AML). Enrollment into the study will be based on local diagnostics. For each randomization and arm, there will be specific inclusion and exclusion criteria. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 14-07-2023 |
| Start national recruitment: | 14-07-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 905 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 120 |
| Actual number of patients included: | 30 |

## APAL2020D - Venetoclax AML

| | |
|---|---|
| Protocol: | Randomized phase 3 trial of fludarabine/cytarabine/gemtuzumab ozogamicin with or without venetoclax in children with relapsed AML |
| Local Investigator: | Goemans, B.F. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | APAL2020D - Venetoclax AML |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | Zwaan, C.M. & Ishimaru, S.I. |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | This is an open-label phase 3 randomized multicenter international trial in children with relapsed acute myeloid leukemia (AML), to assess if venetoclax combined with FLA+GO (fludarabine, high-dose cytarabine, and gemtuzumab ozogamicin) will improve overall survival compared to FLA+GO. |
| Primary objective: | To compare the overall survival (OS) of venetoclax in combination with fludarabine and high dose cytarabine (FLA), and gemtuzumab ozogamicin (GO) (FLA+GO+VEN) compared with FLA+GO alone. |
| Study population: | The target population of this study is: children and adolescents under the age of 18, however a limited number of young adult patients between the age of 18 and 21 years of age may be included. A minimum of 80% patients under 18 years of age is required. |

This study includes children, adolescents, and young adults without FLT3/ITD mutation in:

- second relapse, who are sufficiently fit to undergo another round of intensive chemotherapy
- first relapse who per investigator discretion cannot tolerate additional anthracycline containing chemotherapy.

Refractory patients to the last line of therapy are not eligible as they will be treated in another subtrial.

| | |
|---|---|
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 01-04-2022 |
| Start national recruitment: | 17-08-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 80 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 5 |
| Actual number of patients included: | 6 |

## ALCL-VBL

| | |
|---|---|
| Protocol: | International cooperative prospective study for children and adolescents with standard risk ALK-positive anaplastic large cell lymphoma (ALCL) estimating the efficacy of vinblastine |
| Local Investigator: | Veening, M.A. |
| National Coordinating Investigator: | Veening, M.A. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | ALCL-VBL |

### General

| | |
|---|---|
| Sponsor: | German Paediatric Oncology Group |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | International prospective open-label study: a non-randomized study assessing the efficacy of a 24-months Vinblastine monotherapy in standard risk (SR) ALCL patients |
| Primary objective: | To show that it is possible to cure at least 75% of patients belonging to the SR group with Vinblastine-monotherapy for 24 months |
| Study population: | Children and adolescents with standard risk ALK-positive ALCL |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 31-10-2022 |
| Start national recruitment: | 04-11-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 10 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 10 |
| Actual number of patients included: | 7 |

## Interfant-21 - KWF 15388

| | |
|---|---|
| Protocol: | Interfant-21 - International collaborative treatment protocol for infants under one year with KMT2A-rearranged acute lymphoblastic leukemia or mixed phenotype acute leukemia |
| Local Investigator: | Sluis, van der I.M. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | Interfant-21 - KWF 15388 |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | Stutterheim, J. |
| Study status: | On hold |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | International multicenter open-label non-randomized phase 3 clinical trial conducted in the Interfant network. This protocol is a master protocol with sub-studies that may be performed in a limited number of countries or sites. The sub-studies are provided separately and described in section 19.2 of this protocol. During the course of this study new sub-studies may be added or sub-studies may end, which will be handled as amendments to the protocol. |
| Primary objective: | The primary objective is to improve the outcome (in terms of event-free survival (EFS) as the primary endpoint) of newly diagnosed KMT2A-rearranged (KMT2A-r) infant acute lymphoblastic leukemia (ALL) compared with the historical results of the Interfant06 protocol. |

| | |
|---|---|
| Study population: | The study will enroll 160 newly diagnosed infants (= 365 days of age at the time of diagnosis) with KMT2A-r ALL or B-cell mixed phenotype acute leukemia (MPAL). The planned enrollment period is 3 years. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 13-01-2023 |
| Start national recruitment: | 15-12-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 160 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 12 |
| Actual number of patients included: | 7 |

## Pro-Teico

| | |
|---|---|
| Protocol: | Teicoplanin as Infection Prophylaxis in Pediatric Acute Myeloid Leukemia (Pro-Teico study) |
| Local Investigator: | Goemans, B.F. & Heitink - Pollé, K.M.J. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Pro-Teico |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | Kaspers, G.J.L. |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology, Quality of Life |

### Design

| | |
|---|---|
| Study design: | Prospective, international, multicenter, open-label, randomized clinical trial, preceded by a safety run-in. The design for the safety run-in includes the Rolling 6 design based on dose-limiting toxicity (DLT). The sample size for the randomized phase of the study is 122 evaluable patients. |
| Primary objective: | To assess the safety of i.v. teicoplanin prophylaxis three times per week with a two to three days interval in children with newly-diagnosed AML. A patient will be considered evaluable for safety if they experience a DLT during a prophylactic cycle with teicoplanin or, in case no DLT occurs, if exposure to teicoplanin is either at least 2 consecutive weeks with at least 5 doses of teicoplanin or at least 3 weeks in total with at least 6 out of 9 doses of teicoplanin, or 8 out of 12 doses in case of 4 weeks, or 10 out of 15 doses in case of 5 weeks. |

| | |
|---|---|
| Study population: | Pediatric patients (aged 0-19 years) with newly-diagnosed AML registered and treated according to the international Nordic Society of Pediatric Hematology and Oncology-Dutch, Belgium, Hong Kong (NOPHO-DBH) AML 2012 study protocol, or a consecutive protocol. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 20-05-2021 |
| Start national recruitment: | 20-05-2021 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 130 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 55 |
| Actual number of patients included: | 44 |

## IntReALL HR

| | |
|---|---|
| Protocol: | International Study for Treatment of High Risk Childhood Relapsed ALL 2010 - A randomized Phase II Study Conducted by the Resistant Disease Committee of the International BFM Study Group |
| Local Investigator: | Stutterheim, J. |
| National Coordinating Investigator: | Stutterheim, J. & Stutterheim, J. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | IntReALL HR |

### General

| | |
|---|---|
| Sponsor: | Charité – Universitätsmedizin Berlin |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase II |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

Study design:

The IntReALL HR 2010 trial is an inter-group, international multi-centre, treatment optimization trial. It contains the following treatment arms:

- Induction: prospective, randomized, adaptive, open label phase II trial comparing arm A (modified ALL R3) versus arm B (modified ALL R3 + bortezomib).
- Post-induction single arm observational trial with intensive multidrug chemotherapy courses HC1 (modified AIEOP-BFM ALL 2009 HR1), HC2 (modified HR3).
- A third post-induction chemotherapy block HC3 (modified AIEOP-BFM ALL HR2) may optionally be given within the IntReALL HR 2010 trial or used as standard comparator for an investigational window trial.

- All patients in morphological CR2 will be subjected to allogeneic HSCT.
- Termination of the trial after completion of the 2nd or 3rd consolidation block before investigational window trial and/or allogeneic HSCT. Follow-up will be done until reaching secondary EFS / OS endpoints.
- Patients with insufficient treatment response (MRD = 10-3 after induction) may be allocated to individualized consolidation therapy based on individual biologic features of the leukemia, if such approaches are available.

| | |
|---|---|
| Primary objective: | Improvement of CR2 rates after induction with ALL R3 with bortezomib versus without bortezomib in HR relapsed ALL patients. |

Study population:

- Morphologically confirmed diagnosis of 1st relapsed precursor B-cell or T-cell ALL
- Children less than 18 years of age at date of inclusion into the study
- Meeting HR criteria (any T BM relapse, early/very early isolated BM relapse, very early isolated/combined extramedullary relapse)
- Patient enrolled in a participating centre
- Written informed consent
- Start of treatment falling into the study period
- No participation in other clinical trials 30 day prior to study enrolment that interfere with this protocol, except trials for primary ALL

| | |
|---|---|
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 18-06-2020 |
| Start national recruitment: | 18-06-2020 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 15 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 15 |
| Actual number of patients included: | 9 |

## ALLTogether01

| | |
|---|---|
| Protocol: | ALLTogether01: A Treatment study protocol of the ALLTogether Consortium for children and young adults (1-45 years of age) with newly diagnosed acute lymphoblastic leukaemia (ALL). |
| Local Investigator: | Sluis, van der I.M. |
| National Coordinating Investigator: | Sluis, van der I.M. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | ALLTogether01 |

### General

| | |
|---|---|
| Sponsor: | Karolinska University Hospital |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology, Stem Cell Transplantation |

### Design

| | |
|---|---|
| Study design: | The treatment protocol is an international multi-centre prospective, open label study arranged as a master protocol with additional non-randomised and randomized interventions. The randomised interventions are phase III and one of the non-randomised interventions is a phase II trial. |
| Primary objective: | he Primary Objective is to improve survival and quality of survival in children and young adults with acute lymphoblastic leukaemia (ALL) by testing a number of randomised and non-randomised interventions. Since failure of the current treatment of ALL in children and young adults are due to both under- and overtreatment, both under- and over-treatment related adverse outcomes are targeted. Thus, these interventions are designed to either:<br>– Decrease the risk of serious side-effects and therapy-failure by treatment-related death for patients at low risk of relapse. |

- Decrease the risk of relapse for patients at high risk of relapse and therapy-failure by death from disease.
- Decrease the risk of relapse and reduce toxic side-effects for patients with genetic lesions targetable by Tyrosine-kinase inhibition by the addition of Imatinib to standard chemotherapy.
- Decrease the risk of serious side-effects for patients with high-risk B-cell precursor ALL by making them available for experimental immunotherapy.

| | |
|---|---|
| Study population: | Patients with newly diagnosed T-lymphoblastic (T-cell) or B-lymphoblastic precursor (BCP) leukaemia (ALL), age 0- < 46 years, with the exception of infants with KMT2A-rearranged (KMT2A-r) BCP ALL. In the Netherlands patients with age 0 - = 25 years will be included. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 25-06-2020 |
| Start national recruitment: | 07-07-2020 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 825 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 550 |
| Actual number of patients included: | 518 |

## LCH-IV

| | |
|---|---|
| Protocol: | International Collaborative Treatment Protocol for Children and Adolescents with Langerhans Cell Histiocytosis |
| Local Investigator: | Naeije, L. |
| National Coordinating Investigator: | Bos, van den C. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | LCH-IV |

### General

| | |
|---|---|
| Sponsor: | St. Anna Children's Hospital, Vienna |
| Coordinating Investigator: | - |
| Study status: | Closed for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

Study design: The LCH-IV is an international, multicenter, prospective clinical study for pediatric LCH (age < 18 years).

Primary objective:

- To investigate whether mortality in MS-LCH can be further decreased by an early switch of patients with risk organ involvement who do not respond to front-line therapy to more intensive salvage treatment (Stratum III or Stratum IV).
- To investigate in a randomized fashion whether further prolongation (12 vs. 24 months) and intensification (± mercaptopurine) of continuation therapy will reduce the reactivation rate and permanent consequences in MS-LCH.
- To investigate in a randomized fashion whether prolongation of continuation therapy (6 vs. 12 months) will reduce the reactivation rate and permanent consequences in SS-LCH patients with isolated "CNS-Risk" lesion or multifocal bone lesions.

- To investigate whether second-line therapy with PRED/ARA-C/VCR for 24 weeks, followed by 24 months of continuation therapy (indometacin vs. 6-MP/MTX) can help achieve disease resolution, prevent further reactivations and permanent consequences in patients with non-risk LCH (MS-LCH without risk organ involvement, isolated “CNS-Risk” lesion, or multifocal bone lesions), who are non-responders to first-line therapy, or experience disease progression/ reactivation in non-risk organs on or off first-line therapy.
- To study the value of 2-CdA in patients with isolated tumorous CNS-LCH.
- To study whether systemic therapy with intravenous immunoglobulin (IVIG) or low dose cytarabine for patients with clinically manifest neurodegenerative CNS-LCH can achieve improvement of the neuro-psychological symptoms.
- To study the spectrum and incidence of permanent consequences in systemically treated patients, identify possible risk factors, and assess the role of systemic treatment in their prevention.
- To prospectively study the natural course of SS-LCH in patients who initially are not candidates for systemic therapy, with respect to disease progression, reactivations, need for medical interventions, as well as permanent consequences, at any time after diagnosis.

Study population:

Patients < 18 years with definitive diagnosis of Langerhans cell histiocytosis. Stratum I Group 1: Multisystem LCH: Two or more organs/systems involved, with or without involvement of “Risk Organs” (e.g. hematopoietic system, liver, or spleen)

**Stratum I Group 2**: Single-system LCH:

- Isolated “CNS-risk” lesion
- Multifocal bone lesions (MFB)

**Stratum II**: Second-line treatment for non-risk LCH:
Patients of Stratum I who have:

- Progressive disease (AD worse) in non-risk organs after 6 weeks.
- AD intermediate or worse in non-risk organs or AD better in risk organs after 12 weeks.
- Disease progression (AD worse) in non-risk organs at any time during continuation treatment, AD intermediate or worse in risk-organs, who do not meet organ dysfunction eligibility criteria at any time of Stratum I treatment.

- Active disease at the end of Stratum I treatment
- Disease reactivation in non-risk organs at any time after completion of Stratum I treatment.
- Disease reactivation in risk-organs, who do not meet organ dysfunction criteriaat any time or after completion of Stratum I treatment.

| | |
|---|---|
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 20-01-2014 |
| Start national recruitment: | 15-01-2014 |
| Expected date end of national recruitment: | 30-11-2025 |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 1400 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 85 |
| Actual number of patients included: | 129 |

## EWOG SAA 2010

| | |
|---|---|
| Protocol: | Acquired aplastic anemia: a best available treatment guideline for Dutch Childhood Oncology Group centers. |
| Local Investigator: | Bierings, M.B. |
| National Coordinating Investigator: | Bierings, M.B. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | EWOG SAA 2010 |

### General

| | |
|---|---|
| Sponsor: | University Medical Center Freiburg |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

Study design:

- To developed a nation-wide registry on pediatric aplastic anemia at the DCOG trial office including data on all patients diagnosed with AA in the Netherlands in children below 19 years of age, and to add these data to the EWOG-AA database.
- To improve the quality of the diagnosis of aplastic anemia by setting up a standardized central review process of blood and bone marrow smears and trephine biopsies.
- To build up a cell bank at the DCOG laboratory from left over material from peripheral blood and bone marrow for further research and add-on studie.

Primary objective: This protocol gives a guideline for diagnosis, treatment and follow up of children with Aplastic Anemia. It is especially important to clarify cases of patients presenting with pancytopenia as caused by inherited syndromes, pre-

| | |
|---|---|
| | leukemic myelodysplasia and auto-immune cytopenia. The protocol then gives guidelines for treatment and biological studies. |
| Study population: | Confirmed diagnosis of SAA<br>Age: 6 months to less than 18 year |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 31-10-2023 |
| Start national recruitment: | 03-09-2010 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 100 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 100 |
| Actual number of patients included: | 14 |

## EWOG MDS'06

| | |
|---|---|
| Protocol: | Prospective non–randomized multi-center study for epidemiology and characterization of Myelodysplastic Syndromes (MDS) and Juvenile Myelomonocytic Leukemia (JMML) in childhood. |
| Local Investigator: | Haas, de V. |
| National Coordinating Investigator: | Haas, de V. |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | EWOG MDS'06 |

### General

| | |
|---|---|
| Sponsor: | University Medical Center Freiburg |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | Prospective, non-randomized, multi-center study |
| Primary objective: | To assess the epidemiology and to characterize subtypes of MDS and JMML in childhood.<br>• To evaluate the frequency of the different subtypes of MDS in childhood and adolescence by a standardized diagnostic approach.<br>• To evaluate the frequency of cytogenetic and molecular abnormalities, using array-CGH to evaluate the frequency of subtle chromosomal imbalances, using mFISH to identify unknown chromosomal aberrations. |
| Study population: | Confirmed diagnosis of MDS or JMML (morphology, cytogenetics) Age less than 18 years. |

| | |
|---|---|
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 14-03-2007 |
| Start national recruitment: | 29-12-2006 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 100 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 100 |
| Actual number of patients included: | 43 |

## Fanconi Anemie

| | |
|---|---|
| Protocol: | Diagnostiek, behandeling en follow-up van patiënten met Fanconi anemie. |
| Local Investigator: | Bierings, M.B. |
| National Coordinating Investigator: | Bierings, M.B. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Fanconi Anemie |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | Doelstelling van deze richtlijn is te streven naar het verbeteren van levensduur en kwaliteit van FA patiënten. Dit kan worden gerealiseerd door een uniforme en geprotocolleerde patiëntenzorg in alle centra in Nederland die betrokken zijn bij diagnostiek, behandeling en follow-up van FA patiënten. Daarnaast worden de gegevens van de Nederlandse patiënten prospectief geregistreerd in een database die wordt beheerd door de Stichting Kinderoncologie Nederland (SKION, www.skion.nl). Dit is ook van belang voor Nederlandse participatie in internationale onderzoeken zoals bijvoorbeeld publicaties over het voorkomen van solide tumoren bij Fanconi anemie patiënten alsmede evaluatie van transplantatie-richtlijnen, m.b.t. effectiviteit en toxiciteit op korte en lange termijn. |

Primary objective:

1. Retrospectieve en prospectieve inventarisatie van de Fanconi anemie patiënten in Nederland, de medische problematiek van deze patiënten en hun behandelingstraject. Het gaathierbij om klinische en laboratoriumgegevens zoals leeftijd, geslacht, uitslag MMC-test en moleculaire diagnostiek, congenitale afwijkingen, hematologische parameters, androgeen gebruik, transfusies, transplantatiegegevens, solide tumoren, endocrinopathie en doodsoorzaken. Deze gegevens zullen worden verzameld en opgeslagen in een centrale database bij de SKION.
2. Geprotocolleerde diagnostiek voor Fanconi anemie patiënten, inclusief moleculaire subtypering.
3. Gestandaardiseerde centrale review van bloed- en beenmerg preparaten via de SKION. Het opzetten van een celbank voor opslag van beenmerg- en bloedmonsters van Fanconi anemie patiënten bij de SKION. Deze celbank is bedoeld voor toekomstige onderzoeksinitiatieven.
4. Het beschikbaar stellen van een “best available treatment “ behandelrichtlijn voor Fanconi anemie patiënten in Nederland.
5. Langdurige follow-up van Fanconi anemie patiënten volgens een gestructureerd follow-up schema, om het verdere beloop, complicaties en het voorkomen van secundaire tumoren te registreren.
6. De mogelijkheid bieden aan onderzoekers in en buiten Nederland verdere add-on studies te koppelen aan dit klinische protocol, dan wel te participeren in internationale studies naar FA.

Study population:

Fanconi anemie is zowel klinisch als genetisch zeer heterogeen. Inmiddels zijn 13 zogenaamde complementatie groepen gedocumenteerd, gebaseerd op cel-fusie experimenten (FA-A, B, C, D1, D2, E, F, G, I, J, L, M, N).6-11 Iedere complementatie groep representeert een ander gen en inmiddels zijn alle 13 genen geïdentificeerd.7;9;10
Van de meeste genen zijn vele verschillende mutaties beschreven, met verschillende functionele consequenties. De ziekte is doorgaans autosomaal recessief, met uitzondering van het FANCB gen, dat op het X-chromosoom gelegen is, en dus een geslachtsgebonden overervingpatroon heeft.12 In Nederland komt, in tegenstelling tot de rest van de wereld, met name de c.67delG mutatie van het FANCC gen, gelegen op chromosoom 9q22.3 relatief vaak voor. De indruk bestaat dat dit gepaard gaat met een relatief mild fenotype.

| | |
|---|---|
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 01-01-2008 |
| Start national recruitment: | 01-09-2007 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 1000 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 100 |
| Actual number of patients included: | 52 |

## The Drug Access Protocol

| | |
|---|---|
| Protocol: | A Dutch National Study Protocol to Facilitate Patient Access to Novel Anti-cancer Drugs Awaiting Regulatory Approval or Reimbursement; The DRUG Access Protocol |
| Local Investigator: | Dierselhuis, M.P. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | The Drug Access Protocol |

### General

| | |
|---|---|
| Sponsor: | Nederlands Kanker Instituut |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Solid tumors, Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | Prospective, open-label, non-randomized data collection trial. Patients will be enrolled in multiple parallel cohorts, each defined by the novel unauthorised drug and its requested label after authorisation or the authorised, not (yet) reimbursed drug with its registered indication. |
| Primary objective: | • To enable and assist oncologists to prescribe unauthorized anticancer drugs used for treatment of patients with solid tumors, awaiting FDA/EMA approval or authorized anticancer drugs, awaiting reimbursement in the Netherlands.<br>• To provide real-world safety and efficacy data by describing the anti-tumor activity and toxicity of unauthorized anti-cancer drugs awaiting FDA/EMA approval and of authorized anticancer drugs that are awaiting reimbursement in the Netherlands used for |

treatment of patients with solid tumors, that fulfill the required FDA/EMA selection criteria (including but not limited to genomic- or protein profiles known to be a drug target or to predict sensitivity to a drug).
- To provide controlled access to authorised anticancer drugs that are not being reimbursed for an on-label indication because of a gap in data, in order to provide the needed data for Zorginstituut to (re)assess the dossier for (full) reimbursement (e.g. voorwaardelijke toelating).
- To perform refined biomarker analyses, including (but not limited to) next generation sequencing, on a fresh tumor biopsy specimen.

| | |
|---|---|
| Study population: | Eligible adult and pediatric patients have solid tumors and acceptable performance status and organ function. For authorised indications or for drugs with a positive CHMP opinion, the eligibility will be based on the EMA label. If required, a molecular profile test must have been performed on a specimen of the tumor and the results must identify the target for the drugs included in this protocol. |
| Study participation: | Multicenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 14-09-2022 |
| Start national recruitment: | 14-09-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 4 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 4 |
| Actual number of patients included: | 1 |

## FOCUS

| | |
|---|---|
| Protocol: | Pharmacokinetics of fluconazole given orally or intravenously as prophylaxis or therapy to children and adolescents with invasive fungal infections (FOCUS) |
| Local Investigator: | Bont, L. J. |
| National Coordinating Investigator: | Bruggemann, R.M. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | FOCUS |

### General

| | |
|---|---|
| Sponsor: | Radboud Universitair Medisch Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase IV |
| Research areas: | Clinical Unit: Hemato-oncology, Clinical Unit: Solid tumors, Clinical Unit: Neuro-oncology, Stem Cell Transplantation, Quality of Life |

### Design

| | |
|---|---|
| Study design: | Prospective, open-label, multi-centre, observational pharmacokinetic study |
| Primary objective: | Primary objective:<br>• To establish an improved fluconazole dosing regimen for paediatric and adolescent patients aged 2-18 years.<br><br>Exploratory objectives:<br>• To explore the role of renal function on the clearance of fluconazole.<br>• To explore the bioavailability of oral fluconazole versus intravenous fluconazole in paediatric patients. |

| | |
|---|---|
| Study population: | Children and adolescents with invasive fungal infections |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 10-05-2023 |
| Start national recruitment: | 10-05-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 15 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 15 |
| Actual number of patients included: | 19 |

## 7T MITCH

| | |
|---|---|
| Protocol: | Non-invasive characterization of paediatric brain tumours using metabolic imaging at high magnetic field |
| Local Investigator: | Plasschaert, S.L.A. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | 7T MITCH |

### General

| | |
|---|---|
| Sponsor: | UMC Utrecht |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | This is an observational study. The study will be conducted at and coordinated from the University Medical Center Utrecht (UMCU) and includes children with a LGG or a DIPG. The majority of children will be included and centred in the Prinses Máxima Centrum (PMC) for Paediatric Oncology, Utrecht. Subjects will visit the research facility three times within 12 months (see section 5.3). The duration of the study depends on the inclusion of the required number of subjects, with an expected overall duration of 24 months. |
| Primary objective: | To determine whether metabolic imaging at 7 Tesla is feasible and suitable to detect changes in phospholipids and APT levels in paediatric brain tumours. |
| Study population: | Patients are recruited from the Prinses Máxima Centrum for Paediatric Oncology (PMC). Patients and their parents / legal |

| | |
|---|---|
| | guardian will be asked for participation in the study by their paediatric oncologist. On average, 30-50 children are diagnosed with a LGG in the Netherlands every year. We think it is feasible to include 20 patients with LGG in 2 years. Although pontine tumours are rare, we think it is possible to include 5 patients with a DIPG. |
| Study participation: | Multicenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 23-12-2020 |
| Start national recruitment: | 23-12-2020 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 25 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 25 |
| Actual number of patients included: | 22 |

## LOGGIC Firefly-2 Europe

| | |
|---|---|
| Protocol: | DAY101-002 A Phase 3, Randomized, International Multicenter Trial Of DAY101 Monotherapy Versus Standard Of Care Chemotherapy In Patients With Pediatric Low-Grade Glioma Harboring An Activating RAF Alteration Requiring First-Line Systemic Therapy |
| Local Investigator: | Lugt, van der J. |
| National Coordinating Investigator: | Plasschaert, S.L.A. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | LOGGIC Firefly-2 Europe |

### General

| | |
|---|---|
| Sponsor: | Day One Biopharmaceuticals, Inc. |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | This is a 2-arm, randomized, open-label, multicenter, global, Phase 3 trial to evaluate the efficacy, safety, and tolerability of DAY101 monotherapy versus SoC chemotherapy in patients with pediatric low-grade glioma harboring an activating RAF alteration requiring front-line systemic therapy. |
| Primary objective: | The primary objective is to compare the objective response rate (ORR) per Response Assessment in Neuro-Oncology for low-grade gliomas (RANO-LGG) criteria assessed by independent review committee (IRC) of DAY101 monotherapy versus standard of care (SoC) chemotherapy in patients with pediatric lowgrade glioma harboring an activating RAF alteration requiring front-line systemic therapy. |

| | |
|---|---|
| Study population: | Approximately 400 treatment naïve low-grade glioma patients will be randomized 1:1 to either DAY101 (Arm 1) or an Investigator's choice of SoC chemotherapy (Arm 2).<br>Patient is less than 25 years of age with a low-grade glioma harboring a documented known activating RAF alteration, as identified through molecular assays performed at CLIA or other similarly certified laboratories. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 13-09-2023 |
| Start national recruitment: | 13-09-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 10 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 10 |
| Actual number of patients included: | 11 |

## Dabrafenib roll-over

| | |
|---|---|
| Protocol: | An open label, multi-center, roll-over study to assess longterm effect in pediatric patients treated with Tafinlar (dabrafenib) and/or Mekenist (trametinib). CDRB436G2401 |
| Local Investigator: | Lugt, van der J. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Dabrafenib roll-over |

### General

| | |
|---|---|
| Sponsor: | Novartis Pharma B.V. |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase IV |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | This is a global single-arm, open-label, multi-center study to collect data on the long-term effects of dabrafenib, trametinib or the combination in pediatric subjects who have been treated on Novartis sponsored trials. No formal hypothesis will be tested. Additionally, this study will provide continued access to study medication(s) for subjects who have previously participated in dabrafenib and/or trametinib treatment studies (parent studies). |
| Primary objective: | To assess the long-term safety of treatment with dabrafenib, trametinib or the combination. |
| Study population: | Pediatric patients (or young adults at the time of consent to this study) who have participated in an eligible parent protocol will be eligible to enroll into the observational period of this study. In addition, those patients who are currently eligible to |

| | |
|---|---|
| | receive treatment with dabrafenib and/or trametinib in the parent protocol, and who in the opinion of the investigator, would benefit from continued treatment will be eligible to take part in the treatment period of this study. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 17-01-2023 |
| Start national recruitment: | 17-01-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 3 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 3 |
| Actual number of patients included: | 3 |

## CIP

Protocol:

| | |
|---|---|
| | Máxima is deelnemend centrum, EMC = NCC. NCC aangevinkt om dossier zichtbaar te krijgen |
| Local Investigator: | Heuvel - Eibrink, van den M.M. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | Yes |
| Link to protocol: | CIP |

### General

| | |
|---|---|
| Sponsor: | University Hospitals Leuven UZ Leuven |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

| | |
|---|---|
| Study design: | Registratie studie |
| Primary objective: | De studie bestaat uit twee delen. Het eerste deel betreft het verloop van de zwangerschap, bevalling en gezondheid van moeder. Het tweede deel betreft de lange termijn opvolging van de kinderen.<br><br>**DEEL 1**: Zwangerschap, bevalling en gezondheid van moeder<br><br>1.1A Registratiestudie moeder en pasgeborene. Het registreren van het verloop van kanker tijdens de zwangerschap en hoe de uitkomst is voor moeder en kind na kanker tijdens de zwangerschap. |

| | |
|---|---|
| | 1.1B Effecten van kanker(behandeling) op het pasgeboren kind: de placentastudie.<br><br>1.2 Psychologische vragenlijst – Hoe hebben patiënten (en partners) de diagnose kanker tijdens de zwangerschap ervaren en wat zijn de zorgen.<br><br>1.3 Biobank (enkel indien borstkanker werd vastgesteld). Het centraal opslaan van weefsel- en bloedstalen om verschillen vast te leggen tussen de biologie van borstkanker tijdens de zwangerschap, ten opzichte van borstkanker die niet met de zwangerschap samenvalt.<br><br>1.4 Farmacokinetiek – metingen van chemotherapie in bloed, ten tijde van 1 kuur chemotherapie.<br><br>**DEEL 2**: Opvolging van het kind – Invloed van kanker en behandeling daarvan op het kind – lange termijn effecten. |
| Study population: | Moeders en kinderen geboren na diagnose kanker tijdens de zwangerschap |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 06-06-2018 |
| Start national recruitment: | 06-06-2018 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 40 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 40 |
| Actual number of patients included: | 198 |

## Dulamp

| | |
|---|---|
| Protocol: | Divergent Low Level Laser Therapy as novel treatment for oral mucositis in pediatric cancer patients (DuLamp) |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Dulamp |

### General

| | |
|---|---|
| Sponsor: | Universitair Medisch Centrum Groningen - Division Laboratory and Pharmacy |
| Coordinating Investigator: | - |
| Study status: | Study finalisation |
| Research phase: | Fase III |
| Research areas: | Quality of Life |

### Design

| | |
|---|---|
| Study design: | Double-Blind Randomized Controlled Trial |
| Primary objective: | To assess the effect of divergent low level laser therapy on the number of days of mucositis > grade 1 in children with cancer. |
| Study population: | Children with cancer aged 4-18 years who develop mucositis moren than CTCAE grade 1. |
| Study participation: | Multicenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 12-07-2021 |
| Start national recruitment: | 12-07-2021 |
| Expected date end of national recruitment: | 27-11-2024 |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 41 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 41 |
| Actual number of patients included: | 20 |

## CO-IMPACT

| | |
|---|---|
| Protocol: | Experiences and process of the IMPACT ACP intervention for pediatric palliative care, a qualitative approach – Consortium 2 of the Co-IMPACT Advance Care Planning Program. |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | CO-IMPACT |

### General

| | |
|---|---|
| Sponsor: | UMC Utrecht |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

Study design:

As part of the Co-IMPACT project, 150 healthcare professionals will be trained in IMPACT-PZP, divided across four consortia (Consortium 1, Consortium 2, Consortium 3, and Consortium 4). A comprehensive questionnaire (demographics and implementation) will be administered to all participating healthcare professionals before the training (T0), after 4–8 weeks (T1), after 6 months (T2), and after 2 years (T3), to collect demographic information and gain insight into the implementation of IMPACT-PZP over time. To address all the objectives of Co-IMPACT Consortium 2, this study will be divided into three sub-studies. An exploratory interpretive qualitative study will be conducted using:

- A content study of the recorded PZP conversations with content analysis.
- An interview study on the conducted PZP conversations with thematic analysis.

- A follow-up study after the PZP conversations using a grounded theory approach (interview study and medical record review)

| | |
|---|---|
| Primary objective: | This study aims to explore experiences with the updated IMPACT approach in daily clinical practice. The new intervention is designed to enable advance care planning for all children – no matter their diagnosis, disease phase, or sociocultural background. |
| Study population: | Children (0-18 years) with life-limiting conditions and/or complex chronic care needs, their parents and healthcare providers who have attended the training 'Advance care planning with the IMPACT approach'. |
| Study participation: | Multicenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 23-10-2025 |
| Start national recruitment: | 23-10-2025 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 15 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 15 |
| Actual number of patients included: | - |

## RELIVE

| | |
|---|---|
| Protocol: | International registry for patients with a relapsed or refractory hepatoblastoma or hepatocellular carcinoma. |
| Local Investigator: | Kraal, K.C.J.M. & Zsiros, J. |
| National Coordinating Investigator: | Kraal, K.C.J.M. & Zsiros, J. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | RELIVE |

### General

| | |
|---|---|
| Sponsor: | University of Geneva |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Solid tumors |

### Design

| | |
|---|---|
| Study design: | The registry is designed as a REDCapTM database residing on a server hosted by Geneva University Hospital, with a web-based user interface allowing data entry, data cleaning, and data access for the purpose of data aggregation and evaluation according to the principles defined in section 10. |
| Primary objective: | 1. To achieve an overview of the past approaches and recent developments in the treatment of refractory or relapsed HB, HCC or HCN NOS in children, and<br>2. To investigate the short- and longterm outcomes in patients treated with these regimens in order to identify the most promising treatment approaches for this patient cohort. |

| | |
|---|---|
| Study population: | Patients with documented relapsed or refractory hepatoblastoma (HB), hepatocellular carcinoma (HCC) or hepatocellular neoplasm not otherwise specified (HCN NOS) |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 29-09-2021 |
| Start national recruitment: | 10-06-2021 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 100 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 100 |
| Actual number of patients included: | - |

## SDM bottumoren

| | |
|---|---|
| Protocol: | Evaluatie van “Shared Decision Making” (SDM) bij primaire maligne bottumoren chirurgie rond de knie bij kinderen en jongvolwassenen |
| Local Investigator: | Merks, J.H.M. |
| National Coordinating Investigator: | Merks, J.H.M. & Bramer, J.A.M. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | SDM bottumoren |

### General

| | |
|---|---|
| Sponsor: | Amsterdam UMC - Lokatie AMC |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Solid tumors, Quality of Life |

### Design

| | |
|---|---|
| Study design: | Het is een longitudinaal prospectieve multicenter cohort studie. |
| Primary objective: | Het doel van deze studie is het evalueren van “Shared Decision Making” bij de besluitvorming van de chirurgische interventie bij kinderen en jongvolwassenen met een primaire maligne bottumor rond de knie. De hypothese is dat door de patiënt goed te informeren en de keuze gezamenlijk te maken we een betere geïndividualiseerde keuze bij elke patiënt bewerkstelligen alsmede een beter verwachtingspatroon betreffende het uiteindelijke resultaat na operatie. De verwachting is dat daarmee op lange termijn de kwaliteit van leven zal verbeteren. |
| Study population: | Alle kinderen en jongvolwassen (0-25 jaar oud) die zich presenteren met een osteosarcoom of Ewing-sarcoom rond de knie in het AmsterdamUMC of het Prinses Máxima Centrum. |

| | |
|---|---|
| Study participation: | Multicenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 19-10-2021 |
| Start national recruitment: | 19-10-2021 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 35 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 35 |
| Actual number of patients included: | 24 |

## PAVO studie - CCTL019A2205B

| | |
|---|---|
| Protocol: | Long Term Follow-up of Patients Exposed to Lentiviral-Based CD19 directed CAR T-CELL Therapy |
| Local Investigator: | Zwaan, C.M. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | PAVO studie - CCTL019A2205B |

### General

| | |
|---|---|
| Sponsor: | Novartis Pharma B.V. |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Stem Cell Transplantation, Clinical Unit: Hemato-oncology |

### Design

| | |
|---|---|
| Study design: | This is a global, prospective, multi-center study that is designed as a basket protocol to follow all enrolled patients for safety and efficacy, who have received a Novartis or Penn CAR-T therapy. |
| Primary objective: | Describe selected, delayed AEs that are suspected to be related to previous CAR T-cell therapy as outlined in current Health Authority guidelines. |
| Study population: | All patients who have been treated with Novartis or Penn CAR-T for any indication. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 08-04-2020 |
| Start national recruitment: | 08-04-2020 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 25 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 25 |
| Actual number of patients included: | 2 |

## LTF-304

| | |
|---|---|
| Protocol: | Longterm Follow-up of Subjects With Cerebral Adrenoleukodystrophy Who Were Treated With Lenti-D Drug Product |
| Local Investigator: | Lindemans, C.A. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | LTF-304 |

### General

| | |
|---|---|
| Sponsor: | BlueBirdBio Inc |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | Fase III |
| Research areas: | Stem Cell Transplantation |

### Design

| | |
|---|---|
| Study design: | This is a multi-center, long-term safety and efficacy follow-up study for subjects with cerebral adrenoleukodystrophy (CALD) who have received eli-cel in parent clinical studies. |
| Primary objective: | • Monitor for long-term safety of the Lenti-D Drug Product (also known as elivaldogene autotemcel; hereafter referred to as eli-cel) administered in parent clinical studies.<br>• Monitor for long-term efficacy of eli-cel administered in parent clinical studies. |
| Study population: | Subjects who have received eli-cel in parent studies and who meet the eligibility criteria for LTF-304. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 07-02-2022 |
| Start national recruitment: | 07-02-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 2 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 2 |
| Actual number of patients included: | 2 |

## Pinocchio

| | |
|---|---|
| Protocol: | PINOCCHIO-study: Pharmacokinetics of cytostatic agents in children's oncology |
| Local Investigator: | Zwaan, C.M. |
| National Coordinating Investigator: | Zwaan, C.M. & Huitema, A.D.R. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Pinocchio |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life, Clinical Unit: Hemato-oncology, Clinical Unit: Neuro-oncology, Clinical Unit: Solid tumors |

### Design

| | |
|---|---|
| Study design: | This study has two strata. Stratum 1 will investigate the PK/PD of the most used chemotherapeutic agents in pediatric oncology. Stratum 2 will investigate the PK/PD of the most used target kinase inhibitors in paediatrics.<br>Prospectief observationeel |
| Primary objective: | To assess the pharmacokinetics of various cytotoxic agents (carboplatin, cisplatin, cytarabine, dactinomycin, daunorubicin, doxorubicin, etoposide, methotrexate and vincristine) TKIs (ALK inhibitors, MEK inhibitors, BCR-ABL inhibitors, EGF-R Inhibitors, FLT3 inhibitors, NTRK inhibitors, and Multikinase inhibitors) and their known metabolites (if applicable) in children to characterize the age-related changes in pharmacokinetics. |

| | |
|---|---|
| Study population: | **Stratum 1**: kinderen 0-17 jaar behandeld met chemotherapeutica<br>**Stratum 2**: kinderen 0-21 jaar behandeld met TKIs |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 26-06-2018 |
| Start national recruitment: | 26-06-2018 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 810 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 810 |
| Actual number of patients included: | 240 |

## Pilot ademonderzoek

| | |
|---|---|
| Protocol: | Detectie van schimmelinfecties in uitademingslucht: een pilot studie |
| Local Investigator: | Lindemans, C.A. |
| National Coordinating Investigator: | Lindemans, C.A. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Pilot ademonderzoek |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology, Stem Cell Transplantation, Quality of Life |

### Design

| | |
|---|---|
| Study design: | Het onderzoek is een prospectieve observationele pilot studie bij patienten die in het Prinses Máxima Centrum diagnostiek naar schimmelinfecties ondergaan. Ademmonsters worden afgenomen van de studie- en controlegroep. De ademmonsters worden geanalyseerd door middel van Gas chromatography – mass spectometry (GC-MS) om vast te stellen of er onderscheid gemaakt kan worden tussen een invasieve pulmonale schimmelinfectie versus de afwezigheid van een schimmelinfectie. |
| Primary objective: | Is het mogelijk om, door middel van het analyseren van uitgeademde lucht met behulp van GC-MS, immuun gecompromitteerde kinderen met en zonder een invasieve pulmonale schimmelinfectie accuraat van elkaar te onderscheiden? |

| | |
|---|---|
| Study population: | **Onderzoekspopulatie**: Kinderen van 1-18 jaar met een hemato-oncologische aandoening en een verdenking op een schimmelinfectie.<br>**Controlegroep**: Kinderen van 1-18 jaar zonder verdenking op een schimmelinfectie die gescreend worden voordat zij een stamceltransplantatie zullen ondergaan. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 17-02-2022 |
| Start national recruitment: | 17-02-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 42 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 42 |
| Actual number of patients included: | 52 |

## INTERACT - Kika 429

| | |
|---|---|
| Protocol: | INTERcultural heAlth CommunicaTion in pediatric oncology: achieving quality of care for all (The INTERACT study) |
| Local Investigator: | Grootenhuis, M.A. |
| National Coordinating Investigator: | Grootenhuis, M.A. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | INTERACT - Kika 429 |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

| | |
|---|---|
| Study design: | The INTERACT study is a prospective study and uses a multi-method observational approach. |
| Primary objective: | The overall objective of the INTERACT study is to identify intercultural health communication issues for pediatric oncology ethnic minority families, as well as to find indicators for interventions to provide adequate health communication for these families. |
| Study population: | In WP1, interviews will be conducted with N=15-20 ethnic minority parents (sample 1) and focus groups with N= 15-20 HCPs (sample 2). In WP2, N=10 families and HCPs (sample 3) will be asked for permission to make a video recording of one of their outpatient consultations. Participation in WP2 will be evaluated with all participants. In WP2 parents and HCPs will be invited for a video-reflexive session, using their own video-recorded consultation (see figure 1 for a flowchart of assessment and inclusion procedure). |

| | |
|---|---|
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 06-01-2025 |
| Start national recruitment: | 06-01-2025 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 20 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 20 |
| Actual number of patients included: | - |

## KinderOnconet

| | |
|---|---|
| Protocol: | Development and Evaluation of a National Network of Allied Health Professionals working with Children with Cancer to improve Participation and Quality of Life (KinderOncoNet) |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | Tissing, W.J.E. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | KinderOnconet |

### Published articles

Theviewsofparentsofchildrenwithcancerandpediatricphysicaltherapistsonanetworkforcontinuityandoptimalqualityofcareforchildrenwithcancer:KinderOncoNet: https://pubmed.ncbi.nlm.nih.gov/38055083/

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

| | |
|---|---|
| Study design: | The project will be a development and research design. The research part will be a mixed methods approach, with quantitative (survey) and qualitative focus groups to collect data on the needs of multiple stakeholders. Through co-creation sessions we will develop knowledge products in partnership with parents/children, define responsibilities and care processes. Subsequently, we evaluate the functioning of this network. |

| | |
|---|---|
| Primary objective: | The development and realization of a National Network of Allied Health Professionals working with children with cancer and their families, KinderOncoNet, informed by the results of identified needs of children, families and healthcare professionals. |
| Study population: | Healthcare professionals from the following selection of allied health professionals' disciplines: pediatric physiotherapy, dietetics, occupational therapy, and speech and language therapy, and with relevant stakeholders, including children and parents as well as service organizations. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 15-05-2023 |
| Start national recruitment: | 15-05-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 45 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 45 |
| Actual number of patients included: | 8 |

## LATER MetVasA - Kika 433

| | |
|---|---|
| Protocol: | Metabolic syndrome and vascular damage in relation to accelerated aging in survivors of hematopoietic stem cell transplantation for hematological malignancy: towards preventive lifestyle interventions. |
| Local Investigator: | Pluijm, S.M.F. & Bresters, D. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | LATER MetVasA - Kika 433 |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology, Quality of Life, Clinical Unit: LATER |

### Design

| | |
|---|---|
| Study design: | This is a retrospective (for data on childhood cancer and treatment) and cross-sectional (for sociodemographic factors, lifestyle behavior and end points) observational study in two cohorts of long term survivors of HSCT for a hematological malignancy. Data in the first cohort have already been collected in the Dutch Childhood Cancer Survivorship Study (DCCSS)-LATER2 study (cancer diagnosis between January 1963 and January 2002) and will be analyzed for this study. A second cohort of HSCT survivors with a cancer diagnosis between January 2002 and January 2021 will be invited for this study in the late effects clinic. |

| | |
|---|---|
| Primary objective: | The primary aims of this study include investigation of:<br>1. The prevalence and possible risk factors, including treatment and lifestyle behavior, of the metabolic syndrome (MetS) and its components (e.g. obesity and high blood pressure).<br>2. The prevalence and possible risk factors, including treatment and lifestyle behavior, of endothelial dysfunction (ED).<br>3. The prevalence and risk factors, including treatment and lifestyle behavior, of clinical phenotypes of accelerated aging, and its indicators, including: inflammation, “multimorbidity”, low muscle and high fat mass, muscle strength, poor physical performance and physical function. |
| Study population: | The first cohort (cohort I) consists of 102 adults (at least 18 years and older) HSCT survivors transplanted for a hematological malignancy, who participated in the Dutch Childhood Cancer Survivorship Study (DCCSS)-LATER2 study. The second cohort (cohort II) will consist of about 120 HSCT survivors, including children and adults, treated with HSCT between 01-01-2002 and 01-01-2021 for a hematological malignancy, who are 4 years of age or older at inclusion and at least 2 years after HSCT, and who will visit the LATER clinic of the Máxima between 2023 and 2026 for care. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 25-01-2024 |
| Start national recruitment: | 25-01-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 120 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 120 |
| Actual number of patients included: | 96 |

## Educational priorities

| | |
|---|---|
| Protocol: | Educational priorities in a paediatric oncology curriculum for general practice paediatricians: a national modified Delphi study |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | Tissing, W.J.E. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Educational priorities |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology, Clinical Unit: Neuro-oncology, Clinical Unit: Solid tumors, Quality of Life |

### Design

| | |
|---|---|
| Study design: | First, five focus groups will be performed with general pediatricians, pediatric oncologists, parents and patients. Hereafter, a three-round modified Delphi consensus technique will be performed among general paediatricians (n=100) working in different general hospitals in the Netherlands. |
| Primary objective: | This study will list general paediatricians' educational needs and priorities for a curriculum about paediatric oncology for general paediatricians in the CPD domain. This learner and task analysis is the starting point for this curriculum about this rare disease. |

| | |
|---|---|
| Study population: | **Study population in Part 1 (focusgroups)**: 8-10 paediatric oncologists, 8 -10 general paediatricians working in general hospitals, 8 -10 general paediatricians working in a shared care hospital and 8-10 parents/children >16 years.<br><br>**Study population in part 2**: Part 2 is a modified 3 round Delphi consensus among 100 general paediatricians in the Netherlands. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 10-03-2023 |
| Start national recruitment: | 10-03-2023 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 16 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 16 |
| Actual number of patients included: | - |

## VANISH

| | |
|---|---|
| Protocol: | The evolution of pulmonary lesions on high resolution computed tomography scans in immunocompromised children with an suspected invasive fungal disease |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | VANISH |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology, Stem Cell Transplantation, Quality of Life |

### Design

| | |
|---|---|
| Study design: | Prospective observational |
| Primary objective: | The primary objective of our study is to examine the evolution of pulmonary lesions on serial High Resolution Computed Tomography (HRCT) scans in pediatric patients with possible or probable/ proven IA by evaluating the volume of lesions of serial HRCT scans. |
| Study population: | Children with hemato-oncological malignancies or undergoing an allogenic hematopoietic stem cell transplantation (HSCT) diagnosed with possible or probable/proven invasive fungal infection. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 02-04-2024 |
| Start national recruitment: | 02-04-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 32 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 32 |
| Actual number of patients included: | 20 |

## Symptom ap/Approach

| | |
|---|---|
| Protocol: | KWF 14874 - Symptom management in children with advanced cancer: the development of a symptom app |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | Tissing, W.J.E. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Symptom ap/Approach |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

| | |
|---|---|
| Study design: | This is a prospective study using qualitative research methods, and codesign. Interviews will be conducted with patients with advanced cancer and parents/caregivers to explore their experiences with symptoms and their needs. In a focus group with parents of a deceased child, their experiences with symptoms and symptom management will be discussed. In a focus group with HCPs, their ideas about patient symptom assessment and symptom management and the integration of the app in the dayto-day workflow will be collected. After having obtained this information on needs and wishes, a co-design process with all involved stakeholders (HCPs, patients, and parents), consisting of three phases, will be conducted to develop the symptom app. |

| | |
|---|---|
| Primary objective: | We propose to develop an app for systematic symptom assessment using patient-reported outcomes (PROs) that supports children and their families in the palliative phase of cancer and helps to diminish the impact of distressing symptoms. The app should support parents in the care for their child, be helpful in communication with the healthcare professionals (HCPs), and support HCPs to deliver patient-centered and evidence based care. To ensure that the app meets the needs of patients and HCPs, we propose for the development of the app the co-design method with optimal user involvement in combination with traditional research methods. |
| Study population: | – Children aged 0-18 years with (advanced) cancer and/or their parents/caregivers.<br>– Parents of a child with cancer who passed away in the last five years.<br>– Healthcare professionals with at least twelve months experience in caring for children with advanced cancer (pediatric oncologists, pediatricians, nurse practitioners, (pediatric oncology)nurses and general practitioners)<br><br>**Work package 1** (select list of symptoms + PROM):<br>o 6-12 children with advanced cancer and 6-12 parents.<br>o 4-6 parents of a deceased child.<br><br>**Work package 2** (developing the app):<br>o 6-10 healthcare professionals (for focus group)<br>o Phase 1: 6-10 children with cancer (or their parents)<br>o Phase 2: 5-10 children with cancer (or their parents)<br>o Phase 3: 9-12 children with cancer (or their parents)<br>o In each phase, 4-6 HCPs can participate.<br><br>Children, parents, and HCPs can participate more than once in the co-design phases. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 08-02-2024 |
| Start national recruitment: | 08-02-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 73 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 73 |
| Actual number of patients included: | 28 |

## Hercules - sponsor

| | |
|---|---|
| Protocol: | Hypothalamic damage in pediatric brain tumor survivors: Effects of Radiotherapy and associations with Cognitive functioning; The HERCules Project |
| Local Investigator: | Santen, van H.M. |
| National Coordinating Investigator: | Santen, van H.M. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Hercules - sponsor |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Neuro-oncology, Quality of Life, Clinical Unit: LATER |

### Design

| | |
|---|---|
| Study design: | A prospective cohort study |
| Primary objective: | Development of a normal tissue complication probability (NTCP) model for hypothalamic dysfunction (for severe hypothalamic dysfunction, named hypothalamic syndrome) in childhood brain tumor survivors, incorporating cranial radiation dose in addition to other relevant predictors (such as surgery, age, location of the tumor, time since diagnosis). |
| Study population: | All patients with the age at diagnosis below 18 years and treated for a suprasellar tumor (craniopharyngioma, low-grade glioma, intracranial germ cell tumor) or a posterior fossa tumor (medulloblastoma, ependymoma, pilocytic astrocytoma) in the Netherlands between 01/01/2005 and 01/07/2022 will be contacted for participation through their treating physician. The participants (children and adults) must be diagnosed at least five years before participation. |

| | |
|---|---|
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 19-02-2025 |
| Start national recruitment: | 19-02-2025 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 252 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 252 |
| Actual number of patients included: | 61 |

## Follow-on study

| | |
|---|---|
| Protocol: | Very long-term FOLLOW-up of symptomatic OsteoNecrosis after treatment for childhood acute lymphoblastic leukemia |
| Local Investigator: | Heuvel - Eibrink, van den M.M. |
| National Coordinating Investigator: | Heuvel - Eibrink, van den M.M. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Follow-on study |

## General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology, Quality of Life |

## Design

| | |
|---|---|
| Study design: | The design of this study is a single-center observational cross-sectional descriptive study in a well-documented Dutch cohort of long-term childhood ALL survivors who have experienced symptomatic osteonecrosis during or shortly after discontinuation of treatment (DCOG ALL-9, 10, 11 and the EsPhALL protocol). |
| Primary objective: | To assess the long-term physical sequelae and prevalence of long-term physical morbidity in childhood ALL survivors who have experienced symptomatic osteonecrosis during or shortly after discontinuation of treatment (according to DCOG ALL-9, 10, 11 and the EsPhALL protocols). |

| | |
|---|---|
| Study population: | The very long-term follow-up of childhood ALL survivors who have experienced symptomatic osteonecrosis will be studied in a well-documented cohort of 70 Dutch patients who have been treated for ALL from 1997-2015, according to DCOG ALL-9 (1997-2004), ALL-10 (2004-2012), ALL-11 (2012-2015), Dutch EsPhALL 2004 (2005-2009), and Dutch EsPhALL 2010 (2010-2014) treatment protocols, and who have developed symptomatic osteonecrosis during or shortly after discontinuation of treatment. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 06-12-2022 |
| Start national recruitment: | 06-12-2022 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 72 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 72 |
| Actual number of patients included: | 40 |

## ERNIE (iBrain) - sponsor

| | |
|---|---|
| Protocol: | Evaluating response to individualized neuropsychological intervention for children with brain tumors |
| Local Investigator: | Partanen, M.H. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | ERNIE (iBrain) - sponsor |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Neuro-oncology, Clinical Unit: LATER, Quality of Life |

### Design

| | |
|---|---|
| Study design: | Single center, prospective, randomized controlled trial |
| Primary objective: | The primary research question is whether an individualized neuropsychological intervention leads to greater changes in goal attainment, goal satisfaction, and broader neuropsychological functioning, immediately after the intervention, when compared to a standardized intervention. |
| Study population: | patients with a primary brain tumor who are being followed at the Princess Máxima Center for Pediatric Oncology. Patients who are 8-17 years old and completed treatment for a primary brain tumor will be considered potential participants for this study, unless exclusion criteria apply. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 17-10-2024 |
| Start national recruitment: | 17-10-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 144 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 144 |
| Actual number of patients included: | 43 |

## SIMBA - Kika 450

| | |
|---|---|
| Protocol: | Seven Tesla Imaging Biomarkers of Cognitive Outcomes after Treatment for Pediatric Brain Tumor. |
| Local Investigator: | Partanen, M.H. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | SIMBA - Kika 450 |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Study finalisation |
| Research phase: | - |
| Research areas: | Clinical Unit: Neuro-oncology |

### Design

| | |
|---|---|
| Study design: | Single center observational study |
| Primary objective: | Age-standardized performance on a sustained attention task (K-CPT-2/CPT-3 measure) is the endpoint of the main analysis. The 7T MRI metrics measuring vasculature, metabolism, and white matter diffusion in the brain will be used to predict performance on this task. |
| Study population: | Participants (n=77) will include children aged 6-23 years old, who are at least 6 months and up to 5 years after diagnosis and who have completed treatment for a posterior fossa brain tumor. There will be 3 groups (with a minimum of 10 patients) who received:<br>– Surgery/chemotherapy only (no RT)<br>– Focal proton RT<br>– Cranial-spinal proton RT |

| | |
|---|---|
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 25-05-2022 |
| Start national recruitment: | 25-05-2022 |
| Expected date end of national recruitment: | 29-09-2025 |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 30 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 30 |
| Actual number of patients included: | 32 |

## QoL NEMO

| | |
|---|---|
| Protocol: | Longitudinal Monitoring of Neuropsychological Outcomes in Pediatric Oncology |
| Local Investigator: | Partanen, M.H. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | QoL NEMO |

### Published articles

NeuropsychologicalPerformanceandItsPredictorsintheEarlyTreatmentPhaseofNon-CNSPediatricCancer: https://doi.org/10.1002/pbc.31659

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Study finalisation |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

| | |
|---|---|
| Study design: | Single-center, prospective observational cohort study |
| Primary objective: | To examine whether changes in brief monitoring measures of cognition and behavior are associated with functional outcomes in pediatric cancer survivors. Additional objectives are to examine trajectories, risk factors, and frequencies of neuropsychological impairment in early phases of treatment and survivorship as well as to determine the feasibility and acceptability of a neuropsychology monitoring program. |
| Study population: | Patients (aged 6-18 years) newly diagnosed with a brain tumor, other solid tumor, or hemato-oncological condition, followed at the Princess Máxima Center. |

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|---|---|
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 11-06-2021 |
| Start national recruitment: | 11-06-2021 |
| Expected date end of national recruitment: | 19-05-2023 |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 168 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 168 |
| Actual number of patients included: | 173 |

## Testis biopsy/PRINCE

| | |
|---|---|
| Protocol: | Testicular Biopsies in Young Boys Diagnosed with Cancer To Cryopreserve Future Fertility; Towards a Safe and Feasible Future Autologous Cell Therapy |
| Local Investigator: | Wetering, van de M.D. |
| National Coordinating Investigator: | Wetering, van de M.D. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Testis biopsy/PRINCE |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

Study design: Intervention (prospective cohort) and retrospective follow-up

Primary objective:

1. To preserve testicular tissue of young boys with cancer with high risk of infertility and to develop the optimal tools to identify and propagate SSC (spermatogonial stem cells) in and from this tissue to allow possible autologous transplantation in the future if infertility has become apparent.
2. To gain insight in the molecular profile of isolated testicular cell fractions, including SSCs and supportive (niche) cells, before and after propagation in vitro to develop the most optimal and safe standard operation protocol for SSC isolation and in vitro propagation, to prepare for optimal circumstances of SSCs to thrive to mature spermatozoa.
3. To follow up the unique cohort of testicular biopsied prepubertal boys diagnosed with cancer with regards to testicular damage. We will focus on local damage (ultrasound), function of the Leydig cells (androgen

| | |
|---|---|
| | production) and function of the Sertoli cells (semen production and/or inhibin B) This cohort will be followed yearly x 5 years during their usual visit to the outpatient clinic. We will perform this for the prospective cohort and the retrospective cohort from the previous study NL27690.000.09. |
| Study population: | All young boys who are diagnosed with cancer and who are scheduled to undergo treatment at high risk of infertility and who are unable to produce semen by masturbation.<br>In addition a retrospective follow up of the previous cohort Amsterdam UMC, location AMC (102 patients). |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 17-09-2021 |
| Start national recruitment: | 17-09-2021 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 80 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 80 |
| Actual number of patients included: | 78 |

## FU poli botsarcomen

| | |
|---|---|
| Protocol: | Functional outcome, quality of life and adverse events after local therapy for bone sarcoma in children; a multidisciplinary and standardized approach feeding into optimal follow-up care for the future’ |
| Local Investigator: | Merks, J.H.M. |
| National Coordinating Investigator: | Merks, J.H.M. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | FU poli botsarcomen |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Solid tumors, Quality of Life |

### Design

| | |
|---|---|
| Study design: | Prospective cross-sectional nationwide cohort study |
| Primary objective: | To determine functional outcome after local therapy in pediatric bone sarcoma survivors |
| Study population: | patients and survivors of pediatric Ewing sarcoma or osteosarcoma |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 01-11-2021 |
| Start national recruitment: | 01-11-2021 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 125 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 125 |
| Actual number of patients included: | 146 |

**FITco**

| | |
|---|---|
| Protocol: | Changes in body composition, dietary intake, and physical activity in children with cancer - a master protocol |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | FITco |

**General**

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life, Clinical Unit: Hemato-oncology, Clinical Unit: Neuro-oncology, Clinical Unit: Solid tumors |

**Design**

| | |
|---|---|
| Study design: | This is a master protocol for a longitudinal cohort study focusing on all relevant aspects of malnutrition, including body composition, dietary intake, and physical activity in children with cancer. |
| Primary objective: | To study the risk factors (personal, clinical, and lifestyle factors) for-, and consequences of-, changes of nutritional status (both over- and undernutrition) in children with cancer. Based on the results of this first phase, we will develop and evaluate interventions aiming to improve the nutritional status, to finally improve clinical outcomes (i.e., survival, and quality of life) for children with cancer. |

| | |
|---|---|
| Study population: | All newly diagnosed patients between 0 and 18 years old with a haematological, solid, brain malignancy, or a craniopharyngioma. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 09-12-2024 |
| Start national recruitment: | 09-12-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 500 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 500 |
| Actual number of patients included: | 77 |

## TRINGQS study - Kika 448

| | |
|---|---|
| Protocol: | Tinnitus and its Relation wIth heariNg loss, biomarkers, Genetics and Quality of life in childhood cancer Survivors |
| Local Investigator: | Heuvel - Eibrink, van den M.M. |
| National Coordinating Investigator: | Heuvel - Eibrink, van den M.M. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | TRINGQS study - Kika 448 |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life, Clinical Unit: LATER |

### Design

Study design: The current study has a cross-sectional design.
A subset of Dutch CCS who previously participated in the DCCS LATER study will be approached. Previously (2014-2020), they completed a general health questionnaire including at least one tinnitus query. This CCS cohort that participated in the LATER 2 study (questionnaire and recruitment study) will be identified, and called before their clinical surveillance appointment in the Máxima late effects clinic for study participation between January 2024-2028 (Figure 1). At that time, they will be asked if they (still) suffer from tinnitus (aim 1). If so, a full audiological evaluation will be offered to these CCS, in order to identify possible hearing loss, as a standard of care procedure, at time of their visit at the Máxima late effects clinic. In the general population an audiological evaluation is standard of care in patients with tinnitus, as described in the Guideline for audiological evaluation in Tinnitus of the Federation of Medical Specialists81.

(richtlijnendatabase.nl/richtlijn/tinnitus/audiologisch_onderzoek_bij_tinnitus.html)

The generated data will be used, after informed consent, to determine in the full included cohort, the association between tinnitus and hearing loss presence (aim 1), and to identify clinical and treatment related risk factors (aim 6). In addition, the CCS with tinnitus will be asked to complete the TFI, a specific tinnitus-related questionnaire, to evaluate the association between tinnitus and daily functioning and QoL (aim 3). This will be used to identify those CCS that may benefit from additional psychological support and/or intervention. For prestin (biomarker) assessment, we will analyse historical serum (50mcl available serum as per patient, sufficient for triplo-analyses) drawn, with informed consent, from CCS that suffered from tinnitus at the time of the LATER 2 study, and we will compare the prestin levels of the estimated n=200 cases with tinnitus complaints at that time point with prestin levels in 400 age and gender matched CCS without tinnitus (aim 4). The correlation of these prestin levels with hearing loss will also be evaluated. From the already by us generated GWAS data from the DCCS LATER 2 study, we aim to identify specific genetic variants associated with treatment related ototoxicity. This includes replication of already known variants by candidate SNP analyses, as well as an identification for new genetic SNPs (aim 5).

Primary objective: To gain insight into the determinants of tinnitus and its impact in CCS of the DCCS LATER study.

Study population: Eerder deelgenomen aan DCCS LATER studie (behandeld tussen 1964 en 2002) >18 jaar

Study participation: Monocenter

Scope: National

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 12-09-2024 |
| Start national recruitment: | 12-09-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 90 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 90 |
| Actual number of patients included: | - |

## EndoWatch-II - KWF 14984

| | |
|---|---|
| Protocol: | ENDO-Watch (eerder hypo-watch) genoemd; the device that may serve as “external hypothalamus “to improve quality of life in children and young adolescents with hypothalamic dysfunction after surviving a supra-sellar brain tumor. |
| Local Investigator: | Santen, van H.M. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | EndoWatch-II - KWF 14984 |

### General

| | |
|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Neuro-oncology, Quality of Life, Clinical Unit: LATER |

### Design

| | |
|---|---|
| Study design: | This is a prospective longitudinal observational study. |
| Primary objective: | The primary objective of this study is to explore if patients or caregivers find the EndoWatch supportive in the management of hypothalamic dysfunction. |
| Study population: | In total 50 subjects will be included, with n=10 subjects per age category (6-10y, 10-12y, 12-16y-, 16-18y, 18+ y). Subjects will be patients between 6-40 years old (n=40 <18 years, n=10 =18-40 years), with hypothalamic dysfunction after childhood diagnosis of a (suprasellar) brain tumour. |
| Study participation: | Multicenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 20-05-2025 |
| Start national recruitment: | 20-05-2025 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 50 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 50 |
| Actual number of patients included: | 28 |

## EthPOiB

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|---|---|
| Protocol: | Ethics of a Pediatric Organoid Biobank |
| Local Investigator: | Merks, J.H.M. |
| National Coordinating Investigator: | Merks, J.H.M. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | EthPOiB |

### General

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| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Solid tumors, Clinical Unit: Neuro-oncology, Quality of Life, Clinical Unit: Hemato-oncology |

### Design

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|---|---|
| Study design: | Qualitative interviews |
| Primary objective: | To explore the perspectives of pediatric patients (aged 10-18), their parents and health care professionals on the ethics of pediatric tumor organoid biobanking. |
| Study population: | Pediatric oncology patients (n=20), parents (n=20), health care providers/researchers (n=15). |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

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|---|---|
| Start international recruitment: | 03-09-2025 |
| Start national recruitment: | 03-09-2025 |
| Expected date end of national recruitment: | - |

***International recruitment:***

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|---|---|
| Recruitment target protocol: | 50 |

***National recruitment:***

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|---|---|
| Recruitment target national: | 50 |
| Actual number of patients included: | - |

## KiKa 416 Identify

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|---|---|
| Protocol: | Towards improvement of The KLIK-PROM portal at the Princess Máxima Center: inclusive implementation of oncology-specific reference curves |
| Local Investigator: | Litsenburg, van R.R.L. |
| National Coordinating Investigator: | Litsenburg, van R.R.L. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | KiKa 416 Identify |

### General

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|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

Study design:

This study will have a qualitative design, comprising interviews and focus groups. Two sub studies will be conducted:

- Study 1: exploration preferences
- Study 2: implementation pilot

Primary objective:

1. Explore preferences for dashboard feedback of the implementation of pediatric oncology reference curves in children, caregivers and professionals.
2. Evaluate the implementation in clinical practice.

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| Study population: | In both studies the research population consists of caregivers of children (aged 0-21 years), children/survivors (aged 12 -21 years) not yet transitioned to adult survivorship care, and health care professionals (HCP) who provide care (during treatment/follow up/survivorship care) at the Princes Máxima Center, and who are active users of the KLIK PROM portal. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

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|---|---|
| Start international recruitment: | 06-03-2024 |
| Start national recruitment: | 06-03-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

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|---|---|
| Recruitment target protocol: | 80 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 80 |
| Actual number of patients included: | - |

## Belumosudil ROCKNROL1 EFC17757

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|---|---|
| Protocol: | A randomized, double-blind multicentre phase 3 study to evaluate efficacy and safety of belumosudil in combination with corticosteroids versus placebo in participants at least 12 years of age with newly diagnosed chronic graft versus host disease (cGVHD) |
| Local Investigator: | Lindemans, C.A. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Belumosudil ROCKNROL1 EFC17757 |

### General

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|---|---|
| Sponsor: | Sanofi-Aventis Recherche & Developpement |
| Coordinating Investigator: | - |
| Study status: | Study finalisation |
| Research phase: | Fase III |
| Research areas: | Clinical Unit: Hemato-oncology |

### Design

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|---|---|
| Study design: | A randomized, double-blind, Phase 3, two-arm, multicenter study to evaluate efficacy and safety of belumosudil in combination with corticosteroids versus placebo in combination with corticosteroids in participants at least 12 years of age with newly diagnosed cGVHD. |
| Primary objective: | Demonstrate the superiority of belumosudil in combination with prednisone vs placebo in combination with prednisone in Event-Free Survival (EFS). |

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| Study population: | This is a parallel, Phase 3, two-arm study for the treatment of newly diagnosed moderate or severe chronic GVHD. Approximately 240 participants will be randomized in a 1:1 ratio to receive either belumosudil in combination with prednisone or placebo in combination with prednisone. |
| Study participation: | Multicenter |
| Scope: | International |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 08-04-2025 |
| Start national recruitment: | 15-05-2025 |
| Expected date end of national recruitment: | 07-07-2025 |

***International recruitment:***

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|---|---|
| Recruitment target protocol: | 260 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 260 |
| Actual number of patients included: | - |

## PROMIS II KiKa 449

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|---|---|
| Protocol: | Improving measurement of health-related quality of life using PROMIS: Validation of PROMIS instruments in the oncology population. |
| Local Investigator: | Grootenhuis, M.A. |
| National Coordinating Investigator: | Grootenhuis, M.A. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | PROMIS II KiKa 449 |

### General

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|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology, Clinical Unit: Neuro-oncology, Clinical Unit: Solid tumors, Quality of Life |

### Design

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|---|---|
| Study design: | Test-retest/validation study: the PedsQL and PROMIS questionnaires will be administered to (parents of) children who were diagnosed with cancer via the KLIK (Kwaliteit van Leven In Kaart) portal at the Princess Máxima Center at two time points: T1 and T2, which will be two weeks apart, and will be analysed quantitatively. |
| Primary objective: | To assess the psychometric properties for the PROMIS item banks in the pediatric oncological population in the age groups 1-4, 5-7, 8-17 and 18+ years. |
| Study population: | 400 (parents of) children diagnosed with pediatric cancer (100 per age group). |

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| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

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|---|---|
| Start international recruitment: | 15-10-2024 |
| Start national recruitment: | 15-10-2024 |
| Expected date end of national recruitment: | - |

***International recruitment:***

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|---|---|
| Recruitment target protocol: | 400 |

***National recruitment:***

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|---|---|
| Recruitment target national: | 400 |
| Actual number of patients included: | 210 |

## FU Sensory-2 - sponsor

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|---|---|
| Protocol: | Taste and Smell Changes in Childhood Cancer Patients – a Follow-up |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | FU Sensory-2 - sponsor |

### General

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|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Study finalisation |
| Research phase: | - |
| Research areas: | Quality of Life, Clinical Unit: Hemato-oncology, Clinical Unit: Neuro-oncology, Clinical Unit: Solid tumors |

### Design

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| Study design: | This study is a follow-up of a previous longitudinal study called SENSORY-2 (METC 19/809). All patients who participated in the first part of the SENSORY-2 study and gave consent to be contacted again, are eligible for participation in this follow-up study. All children (aged 6 – 18 years) newly diagnosed with cancer and treated with chemotherapy were asked to participate in SENSORY-2 between November 2020 and January 2022 at the Princess Máxima Center in Utrecht. The follow-up period ended in March 2023. During the SENSORY-2 study, at four time points (6 weeks (T0), 3 months (T1), 6 months (T2) after starting chemotherapy and 3 months (T3) after the stop of chemotherapy) a measurement of taste and smell function was be performed. For children with ALL, T3 took take place during maintenance phase (approximately 12 months after starting chemotherapy). |

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| Primary objective: | To study smell and taste function in childhood cancer survivors 2 – 5 years after stopping chemotherapy. |
| Study population: | All patients who participated in the SENSORY-2 study (n=96) and gave consent to be contacted again, are for eligible for participation in this follow-up study. During the study period, 8 children left the study because they died (n=6) or dropped out (n=2). From the remaining 88 participants, 3 children did not gave consent to be contacted again. In sum, 85 children (88.5%) will be eligible for participation in this follow-up study. |
| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

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|---|---|
| Start international recruitment: | 07-11-2024 |
| Start national recruitment: | 07-11-2024 |
| Expected date end of national recruitment: | 08-10-2025 |

***International recruitment:***

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|---|---|
| Recruitment target protocol: | 85 |

***National recruitment:***

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|---|---|
| Recruitment target national: | 85 |
| Actual number of patients included: | 66 |

## Astronaut study

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| Protocol: | ASsessment of the paTient Reported Outcome 'NAUsea' using a Tool |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | Tissing, W.J.E. |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | Astronaut study |

### General

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|---|---|
| Sponsor: | Prinses Máxima Centrum |
| Coordinating Investigator: | - |
| Study status: | Study finalisation |
| Research phase: | - |
| Research areas: | Clinical Unit: Hemato-oncology, Clinical Unit: Neuro-oncology, Clinical Unit: Solid tumors, Quality of Life |

### Design

Study design:

This is an exploratory qualitative study using semi-structured interviews with parent(s) of children with cancer aged 2-7 years and children with cancer aged =7 years old and/or their parent(s).

The updated Consolidated Framework for Implementation Research (CFIR) will be used as the study's theoretical and conceptual foundation (Damschroder et al., 2022). The CFIR is a theoretical framework that guides systematic assessment of potential barriers and facilitators, which helps to tailor an implementation strategy to the specific and local context, in order to increase the likelihood of successful and effective implementation (Damschroder et al., 2022). The CFIR constructs will serve as a topic list for the interview guide, providing the opportunity to explore in-depth personal perspectives of children experiencing CINV and their

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| | parent(s) on barriers and facilitators regarding the implementation of the BARF. |
| Primary objective: | The aim of this study is to explore the perspectives of children experiencing CINV and their parent(s) on possible barriers and facilitators regarding the implementation of the BARF in the clinical nursing departments of the Princess Máxima Center for pediatric oncology. |
| Study population: | Purposive sampling will be used to define the study population, which will consist of: (1) children and young adults with cancer aged 2 years or older on their active treatment schedule consisting of moderate and/or high emetogenic chemotherapy and therefore expected to experience CINV and/or (2) their parent(s).<br>When children are feeling too ill to use the BARF or are too young for self-report, a parent proxy-report will be needed. For some PROMs, such as the PedsQL 4.0, parent proxy-reports for children from 2 years old are included (Varni et al., 2001). Therefore, in this study the minimum age of the child for parent proxy-report is set at 2 years old.<br>Since the BARF is validated for children =7 years, the minimum age for self-report and thus for participating in an interview is set at 7 years. During the interview, the parent(s) may be present at any time if the child so wishes. However, the interview will be focused on having the conversation with the child itself. When the child is feeling too ill to participate in the interview, or is not willing to participate, the parent(s) can be interviewed instead.<br><br>To ensure we obtain rich and in depth data, we propose to recruit a heterogeneous sample in terms of gender, diagnosis (hematological, solid or brain malignancies) and developmental differences due to age (Linder & Wawrzynski, 2018). Therefore, a distinction will be made between the perspectives on barriers and facilitators regarding the implementation of the BARF for parent(s) of younger children and older children and/or their parent(s). The two groups are defined as follows:<br>Group I: Parent(s) of younger children (2 – 7 years)<br>– Group II: Older children (=7 years) and/or their parent(s)<br>The classification system of the Canadian Pediatric Oncology Group of Ontario (POGO) will be used to determine the emetogenicity level of chemotherapy (Dupuis et al., 2011; Patel et al., 2023). |

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| Study participation: | Monocenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

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|---|---|
| Start international recruitment: | 27-02-2025 |
| Start national recruitment: | 27-02-2025 |
| Expected date end of national recruitment: | 19-08-2025 |

***International recruitment:***

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|---|---|
| Recruitment target protocol: | 24 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 24 |
| Actual number of patients included: | 15 |

## KOMPAS

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|---|---|
| Protocol: | Short title KOMPAS-study: Proactive interdisciplinary collaboration in paediatric palliative care – action intervention phase |
| Local Investigator: | Tissing, W.J.E. |
| National Coordinating Investigator: | - |
| Is Princess Máxima Center the national coordinating center?: | No |
| Link to protocol: | KOMPAS |

### General

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|---|---|
| Sponsor: | UMC Utrecht |
| Coordinating Investigator: | - |
| Study status: | Open for inclusion |
| Research phase: | - |
| Research areas: | Quality of Life |

### Design

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| Study design: | The overall design of the KOMPAS-project is participatory action research. This method, involving researchers and stakeholders working together, aims to sustainably work on a research-based solution for an undesirable situation and is therefore highly suitable for this project. In addition to changing the current situation, participatory action research generates knowledge on the process of change itself (14).<br><br>The identification of the problem that stakeholders want to solve and the development of improvement interventions, including a strategy for evaluation, are part of the participatory action research process. Therefore, we outline the overall research plan for the action intervention phase in this protocol, however, not all details can be provided in advance. |

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| Primary objective: | The objectives of the action intervention phase are:<br>1. To identify goals for improvement for interdisciplinary collaboration within situational care networks in pediatric palliative care in response to identified obstacles.<br>2. To identify and describe an improvement intervention, and an accompanying implementation and evaluation plan per action research group that aligns with the identified improvement goals.<br>3. To evaluate the extent to which the improvement interventions contribute to the perceived quality of interdisciplinary collaboration within situational care networks in pediatric palliative care, according to healthcare professionals and parents.<br>4. To understand which factors influence the implementation of the improvement interventions. |
| Study population: | – Primary and tertiary care healthcare professionals (e.g. pediatricians, general practitioners, home care nurses, pediatric palliative care team nurses and/or physicians, physiotherapists).<br>– Expert parents, i.e. parents of a (deceased) child with a life-limiting or life-shortening condition.<br>– Researchers of the project team. |
| Study participation: | Multicenter |
| Scope: | National |

**Planning and Recruitment**

***Planning:***

| | |
|---|---|
| Start international recruitment: | 09-10-2025 |
| Start national recruitment: | 09-10-2025 |
| Expected date end of national recruitment: | - |

***International recruitment:***

| | |
|---|---|
| Recruitment target protocol: | 30 |

***National recruitment:***

| | |
|---|---|
| Recruitment target national: | 30 |
| Actual number of patients included: | - |