|  |  |
| --- | --- |
| ***Attendance list*** | |
| **Name** | **Function, Organisation** |
|  |  |
|  |  |
|  |  |

1. **STUDY OUTLINE**

| **Item** | **Yes** | **No** |
| --- | --- | --- |
| * 1. Below are the main eligibility criteria.   Will any of them be a limiting factor to enrolling subjects in this study?  Please also specify in the comment section any of the limiting factors that outweigh the others and if applicable any factors that are not specified below.  Inclusion criteria:   * First episode of steroid-sensitive idiopathic nephrotic syndrome.   + At first presentation:     - Hypalbuminaemia <25 g/L or 2.5 g/L     - Nephrotic range proteinuria: urinary protein-creatinine ratio (uPCR) >200 mg/mmol or > 2000 mg/g or >300 mg/dL.     - Oedema     - Complement C3 not below lower limit of normal.   + At 4 weeks after first presentation:     - Complete remission after 4 weeks of oral prednisolone therapy confirmed by negative dipstick and quantitative urinalysis (<50 mg/mmol or <50 mg/g). * Children aged 2 – 16 years. * Weight >10 kg. * Ability to swallow IMP (successful swallowing test of a 5 or 10 mg tablet for children   aged under 6 years).   * Absence of contraindication for levamisole: no neutropaenia <1.5 x 109 at inclusion   (confirmed by laboratory of participating site), no elevated liver enzymes (ALAT or ASAT >3x ULN).   * Negative pregnancy test (urine or serum) and use of appropriate contraception in girls who are of childbearing potential. * Written informed consent by legal representative(s) (parent(s) or guardian) and, depending on age and country legislation, by participant. Informed assent/consent by the child needs to be obtained for every child in a manner that is appropriate for their age and understanding. * Ability to comply to protocol.   Exclusion criteria:   * Steroid resistant INS: failure to achieve complete remission after 4 weeks of initial   treatment with oral prednisolone.   * History of malignancy, diabetes mellitus, convulsions, or active liver disease. * Pregnant (or desiring to be pregnant) or lactating girls. * Known hypersensitivity to levamisole or one of its substances (including lactose).   *If yes*, please specify the reason why in the comment section. |  |  |
| **Comment:** | | |
| * 1. Which prednisolone schedule are you currently using?   ISKDC (US): 4 weeks 60 mg/m2/day, followed by 4 weeks of 40 mg/m2 alternate days  APN (GE): 6 weeks 60 mg/m2/day, followed by 6 weeks of 40 mg/m2 alternate days  SNP (FR): 4 weeks 60 mg/m2/day, followed by 8 weeks of 60 mg/m2 alternate days, followed tapering with 15 mg/m2 every 2 weeks until 15 mg/m2 (total 18 weeks)  If you are currently not using the ISKDC schedule, are you willing to implement the ISKDC schedule for this trial?  *If no*, please specify why you are not willing to implement the ISKDC for this trial. |  |  |
| **Comment:** | | |
| * 1. Do you currently implement in your standard medical care administration of Vitamin D for children presenting with a first episode of INS?   *If no*, please specify in the comment section the reason. |  |  |
| **Comment:** | | |
| * 1. Do you think it’s feasible to avoid any live-attenuated vaccine administration until at least 1 month after stop of levamisole administration, if possible (final decision is at the discretion of the investigator)?   *If no*, please specify in the comment section the reason. |  |  |
| **Comment: We usually used live-attenuated vaccine administration until at least 3 weeks after prednisolone stop in current practice**. **We don't wait for the end of immunosuppressives drugs** | | |
| * 1. Are you willing to participate in the PK/PD sub-study?   *If no*, please specify in the comment section. |  |  |
| **Comment:** | | |
| * 1. A relapse is defined as the recurrence of nephrotic range proteinuria after complete remission had been achieved.   Nephrotic range proteinuria (uPCR>200 mg/mmol or 3+ on urine dipstick) should be present for 3 consecutive days or a minimum of 3 days between two measurements. The first day of relapse is defined as the third day or second day after an interval of at least 3 days between the first day of nephrotic range proteinuria OR when treatment for a relapse was started.  Are those definitions consistent with the definitions you use in your daily routine medical practice?  *If no*, please specify in the comment section. |  |  |
| **Comment:** | | |
| * 1. Once the patient has been randomized, the IMP will be shipped to the patient’s home or the hospital pharmacy, depending on the country requirements. Do you think it’s feasible that administration of levamisole can start within 7 days after randomization?   *If no*, please specify in the comment section. |  |  |
| **Comment:** | | |
| * 1. Page 19 of the current version of the protocol outlines the study flowchart.   Are the indicated timings of the visits feasible?  The standard of care practice for INS can vary among countries, hospitals and/or physicians. Currently, it is assumed that all activities as described in the study flowchart are part of the Standard of Care (SoC), except for the completion of the questionnaires and the samples for the PK/PD sub-study. Are you willing to use the study flowchart as your SoC?  *If no*, please specify in the comment section. |  |  |
| **Comment:** | | |

1. **Subject population**

| **Item** | **Yes** | **No** |
| --- | --- | --- |
| * 1. Start of the study is planned for January 2023. The recruitment period is planned for 30 months.   Do you foresee any problems to participate in this trial during this period?  *If yes*, please specify in the comment section. |  |  |
| **Comment:** | | |
| * 1. Do you have any competing trials ongoing/planned which target the same patient population during the recruitment period of the LEARNS-2 trial?   *If yes*, please specify in the comment section how the decision is made to which study the participants will be included. If possible, could you provide for each study the end date of the recruitment period? |  |  |
| **Comment:** | | |
| * 1. Do you foresee any recruitment problems with the proposed study design and/or study procedures?   *If yes*, please specify in the comment section. |  |  |
| **Comment:** | | |
| * 1. Do you anticipate any problems obtaining informed assent/consent from the child and informed consent from the legal representative(s), according to national legislation?   *If yes*, please specify in the comment section. |  |  |
| **Comment:** | | |
|  | | |
| * 1. Would other centers be willing to refer patients to your center if they know you participate to this trial?   *If yes*, please specify in the comment section how this can be organized.  *If no*, please specify in the comment section the reason(s). |  |  |
| **Comment:** | | |
| * 1. Please complete the table below to have a realistic idea about the recruitment potential.  |  |  |  |  | | --- | --- | --- | --- | |  | 2019 | 2020 | 2021 | | # new patients diagnosed with a first episode of INS aged 2-16 years at your center (including referrals from other centers) |  |  |  | | # new patients diagnosed with a first episode of INS aged 2-16 years at your center that would be eligible to participate in this trial (including referrals from other centers) |  |  |  |   According to your opinion, which % of eligible patients would be willing to participate in this clinical trial? 50 %  On average, how many patients would be eligible per year to participate? ….. patients  On average, how many patients would you be able to enroll per year? ……patients  How many patients would you be able to enroll in total, considering 30 months recruitment?  ……. patients  On average, which % of drop-out of patients do you anticipate during the 2-year FU period? 5 % | | |
| * 1. The ICF will be available in English, Dutch and French. Do you need any other language (e.g., Arabic)?   *If yes*, please specify in the comment section. |  |  |
| **Comment:** | | |
| * 1. How many qualified staff and time, besides the Principal Investigator, do you have available to perform clinical trials at your center?   Please specify the number per function (e.g., 2 co-investigators) and their %FTE availability for LEARNS-2.  Co-Investigator: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Study Nurse/Research Nurse: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Study Coordinator/Research Coordinator: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_  Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | | |

1. **Study team**

| **Item** | **Yes** | **No** |
| --- | --- | --- |
| 1. Do you have experience with the following systems?   Castor eCRF:  Castor randomization:  Only for BE centers: Clinical Trial Management System – EDGE (lead admin available for EDGE?):  Please specify in the comment section any relevant information. |  |  |
| **Comment:** | | |
| 1. This trial will be submitted according to the new “Clinical Trial Regulation” (CTR) procedures.   Are you familiar with this CTR procedure?  Does your center have any local procedures to follow before/after the official CTR procedure?  Please specify in the comment section any relevant information. |  |  |
| **Comment:** | | |

1. **Financial aspects**

This is an academic study but there will be a compensation for the sites to cover the costs for the personnel and any additional interventions that are not considered standard of care. The compensation will be based on academic rates, but final amounts still need to be agreed.

1. **Contact details**

Please provide us your up-to-date contact details:

|  |  |
| --- | --- |
| Site name: |  |
| Name PI: |  |
| Address: |  |
| Phone: |  |
| E-mail: |  |