Invitation Letter

Treatment of children with Vanishing White Matter (VWM)

Dear Sir/Madam,

We would like to ask you whether you agree to receive information about a clinical trial for a disease that is officially called “Vanishing White Matter”, in brief “VWM”. We pose this question because you have a child or are legal representative of a child with VWM.

VWM is a serious brain disease that mainly affects children, especially young children. In most cases, the disease starts before the age of 4 years. Affected children become increasingly handicapped, wheelchair-dependent and die after several years. No treatment is available. We can only follow the patients and offer symptomatic treatment for their complaints.

We are searching for better treatment options. Guanabenz is an old and well-known medicine for the treatment of high blood pressure. It has been approved by the FDA, the American medicines agency. Given the mechanism of action of Guanabenz, we estimated it likely to be beneficial in VWM. We have laboratory mice with VWM and have treated them with Guanabenz. The results indicate that long-term high-dose Guanabenz treatment ameliorates VWM in these mice and leads to both important improvement of motor function and amelioration of brain pathology. Because we have shown previously that the disease mechanism of VWM and the mode of action of Guanabenz are the same in mice and patients, our expectation is that long-term treatment with high doses of Guanabenz could also be beneficial in patients with VWM. However, mice are different from humans and the effect of Guanabenz in humans with VWM still has to be investigated.

As Guanabenz has been used for years by adults for treatment of high blood pressure and has proven to be safe in this patient population, and research also supports the safe use of Guanabenz in teenagers with high blood pressure, we want to treat children with VWM with Guanabenz.

The trial is specifically aimed at young children, in whom the disease is most frequent. Young children with VWM have a faster disease course compared to older children and adults; therefore, research in young children will clarify more quickly whether Guanabenz helps or not. The duration of the clinical trial will be at least 1 year but may be extended to 4 years, depending on how fast the planned number of 30 patients can be enrolled in the study. We treat patients in early disease stages, before the brain is extensively irreversibly damaged. As this will be the first study of Guanabenz use in young children, the safety of Guanabenz will be carefully monitored throughout the trial. Because it is still unclear whether young children will tolerate higher doses of Guanabenz, dose titration will take place under intensive supervision. Because there are no biomarkers in body fluids known in VWM that allow monitoring of the disease, we will also use the study to search for suitable biomarkers.

To be eligible for participation, the disease onset should be before the age of 6 years and the patient’s current maximum disease duration should be 8 years. The patient should still be able to stand up and walk without or with some support. The diagnosis of VWM should be proven by a

DNA test and MRI scan. The patient should not have another significant disease, he/she should not participate in another medical-scientific study, and he/she should be able to undergo MRI examination (ie, the patient should not have metal-containing implants, such as cochlea implant, neurostimulator or pacemaker).

If you would agree to receive more information about the study, please let us know and we will send more details. You can best reach us via e-mail: TreatVWM@amsterdamumc.nl.

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