

HELP

The HELP project has created two new cutting-edge products that will lead to a major breakthrough in the treatment of Parkinson's disease: a sensor that detects Parkinson's symptoms and an intraoral device that provides a non-invasive way of administering PD medication. Furthermore, the project has created other important products such as a Clinical Protocols Tool to assess doctors on their decisionmaking, which implements new treatment methodology including embedded guidelines for the healthcare providers. In addition, a platform which allows management of chronic conditions has been implemented. The sensor and intraoral devices are connected to the platform by means of a gateway application running on a mobile phone. All developed products were integrated in a system so that doctors were able to monitor and control Parkinson's disease patients. The condition of Parkinson's patients degenerates into a rigid akinetic state after 5 years without any treatment. There are many symptoms related to this disease such as tremors, freezing of gait (i.e. patient becomes blocked and cannot carry on walking for some seconds), bradykinesia (i.e. patient walks very slowly), falls, dyskinesia (i.e. excess of movement in the torso or limbs which is involuntary and not controlled by the patient). The first four symptoms are associated with the so-called OFF state while dyskinesia usually happens when a patient feels good (i.e. ON state) and is related to a relative overdose of medication. Current treatments improve symptoms but lead patients to develop a tolerance to the drug. Additionally, as the disease progresses it becomes more and more difficult to pinpoint the exact drug dosage which is sufficient to prevent the OFF state, but which is not excessive and could result in dyskinesia. To improve this situation, a new approach has been developed using a subcutaneous pump, which injects a gradual and constant flow of apomorphine (i.e. liquid drug for treating Parkinson's) throughout the day. This technique improves the control of symptoms. This, however, is still not sufficient as the pump administers a constant dose during the course of a day, whereas the patient's symptoms fluctuate throughout the day, and the "best dose" is not always the same.

The HELP project has designed a system that is able to anticipate when a patient will develop an OFF state or dyskinesia by means of a "Parkinson's" sensor which sends relevant information to the platform and which automatically establishes a new level of drug delivery for the pump to overcome that state. This aims to keep the patient in the ON state most of the time, thus avoiding the debilitating Parkinson's symptoms. In short, HELP is likely to provide the first Parkinson's pacemaker in history. Thanks to this sensor, symptoms can be captured and then medication adjustments can be carried out to mitigate them. The HELP project also developed a new methodology that enables neurologists to know in real time the status of their patients and a system for standardization of the treatment using clinical protocols for remote treatment of PD patients. This is an innovative approach that does not exist in other systems.

As well as doing all this work, the HELP project has worked on a cutting-edge drug delivery system that greatly improves the quality of life of patients wearing subcutaneous and duodenal pumps, but also patients following a very strict scheduled oral treatment. This invention is the intraoral device, which provides a constant level of medication and consists of a false tooth embedded in the patient's mouth (i.e. feasible approach for elderly people). This aims to achieve continuous dopaminergic stimulation, leading to better symptomatic benefits and minimizing concerns about complications resulting from intermittent medication dosage, as occurs in standard care at present. This is the first ever oral device for PD disease. This device will enable PD patients to forget about their treatment. They will only need to replace the tooth cartridge in the morning and forget about Parkinson's. The standard oral treatment for Parkinson's involves taking more than seven pills per day. The use of pumps, either duodenal or sub-cutaneous, is



clearly a very invasive solution for the patient. Both products (i.e. the sensor and the intraoral device) target PD's patients, usually people over 60.

However, the first one is intended for those PD patients presenting stronger symptoms. In the project, the intraoral device was tested on 12 patients and the sensor + subcutaneous pump system on 7 patients (i.e. the pump treatment is fairly new and only 800 people use it in Spain and less than 10 in Israel). The inclusion criterion prioritized people that are used to new technologies. In the case of the sensor + pump pilot, having a pump was a requirement to join the project. Both products will be distributed as part of the current PD treatment packages provided by pharmaceutical companies. In the case of the sensor, these companies are very interested in including this device in the product portfolio:

- ABBOTT distributes Duodopa (i.e. PD drug, Levodopa + Carbidopa gel, administered by a duodenal pump)
- Britannia/TEVA distributes Apogo (i.e. PD drug, Apomorphine that can be administered by a sub-cutaneous pump). Both companies are interested in securing an exclusive contract to include the sensor as a part of their treatment. The main idea is that the sensor would electronically control their pump, improving drug delivery. As for the intraoral device, two pharmaceutical companies are also interested in securing an exclusivity contract to use this device as a part of their treatment package to increase their product portfolio (i.e. different formulations: oral, pens, syringe, pump, intraoral device).
- ABBOTT using levodopa in the tooth
- Orion using COM-T inhibitors in the tooth

In the case of the sensor, the device is already in the market and distributed by the recently created spin-off, Sense4care. This company has been created by some partners in HELP and is participated in by the UPC. It is expected that during this year a potential agreement can be achieved with one of the two contenders. Regarding the intraoral device, this technology was patented in August of last year, and an exploitation partnership between HSG-IMIT and Peh-Med has been signed. The next step for this product is to enroll it in a large pilot, funded by the pharmaceutical company that gets exclusivity, to demonstrate final efficacy evidence. At least two more years will be necessary for this product to be launched as part of a treatment package in the market. Last but not least, the Clinical Protocol Tool implemented by NEVET will be sold to healthcare organisations around the world. In Israel there are four healthcare providers and Maccabi (NEVET) is the second largest. NEVET and Telefónica might establish a partnership to combine both Telefónica's platform and NEVET's Clinical Protocol Tool to provide a more comprehensive solution for dealing with an ample spectrum of chronic diseases including Parkinson.