

(April 2020)



Latest news from

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## General

Dear All,

Please take the time to find the latest news and updates of our R-LiNK project.

- Because of the coronavirus, the second annual R-Link meeting had to be postponed. The original date was scheduled for March 12-13th 2020 in Milano, Italy. Currently we postponed the meeting until November 2020.
- The R-LiNK sponsor and R-LiNK coordinator circulated guidelines for the R-Link clinical trial during COVID-19 pandemic.
- **Neuroimaging WPs.** Five centres still need approval: Copenhagen, Brescia, Oslo, Bergen, Goteborg, Brescia and Copenhagen will be ready soon.
- Overall, **all recruiting centres received the assessment package with SOPs. The eCRF testing phase is complete and there were only minor issues that were resolved through internal arrangements. All centres are approved and we are confident that recruitment can begin after national restrictions are eased due to the COVID 19 pandemic.**
- **We proudly announce the inclusion of the first patient into the European R-Link study on the January 10th 2020 in Dresden, Germany.**

Below, you will find a short overview from each work package.

All the best

WP leaders and PMT

**NOTABLE.** Remember if you need important documents such as SOPs, reports, ExCom Minutes, Protocol etc. you can find them here <https://rlink.eu.com/collaborative-research-project/>

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## WP1

The 2nd R-LiNK annual meeting, which was originally planned for March 12 and 13, 2020 in Milan, unfortunately had to be cancelled due to the COVID-19 pandemic. However, in consultation with all work package leaders, a new date was quickly found. The new date was set for November 10th to 11th. Because we were able to quickly find a new date, we hope that all participants have the opportunity to rebook their flights.

Everyone is looking forward to meeting in Milan in November to share the latest progress and insights of the project. In connection with the current events, WP1 emailed the European Commission and reported impacts that the COVID-19 pandemic has had on R-LiNK activities.

## WP2 / WP3

To date, five centres have been opened for recruitment. These include three locations in France, a centre in London, Great Britain and a centre in Dresden, Germany. In the last telephone conference (February 28th) work package 3 informed us that there was a potential patient in London ready for inclusion. They received all permits and then had to pause the entire recruitment process because of the COVID-19 pandemic. Before the COVID-19 pandemic emerged, two additional centres were about to open. An initiation visit was planned for March in Milan. Furthermore, Newcastle was also about to open. The initiation visits have been postponed until further notice. In the following, we would like to briefly outline the current recruitment status. Due to the ongoing COVID-19 pandemic, patients could only be recruited in Dresden, Germany. Four of the five open centres are currently unable to include patients. Due to the COVID-19 pandemic, these hospitals have decided to postpone not essential activities. Once the situation has eased the study will be up and running again. Finally, the sponsor of the clinical study and the coordinator have announced rules that apply to the initiation of new centres and the inclusion of new patients. (I) Due to the extensive restrictions in connection with COVID-19, the site initiation will be postponed until further notice. Centres that are not yet open need to postpone recruitment until further notice. (II) Centres that can still recruit need to take into account the current developments in the pandemic. Inclusion of new patients must be validated by the coordinator. All conditions necessary for optimal research must be ensured and complied. These guidelines have been distributed to all recruitment centres. At the present time, it is difficult to estimate how long the pandemic will affect the R-LiNK clinical trial.

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## WP4

With regard to the MRI scans, the protocol set up for Bergen and Oslo was put into operation in March. However, due to the COVID 19 pandemic, these centres are still waiting on validation. In Oslo, Norway the protocol was set-up and they performed a pilot scan on a healthy volunteer. However, the colleagues in Oslo did not have the opportunity to send the data to CEA for validation. In Bergen, Norway the protocol was set-up as well, but they did not have the opportunity to perform the pilot scan on a healthy volunteer. In both cases, the validation can be completed quickly as soon as the centres return to normal activities. Finally, the quality of the MRI data of the first R-LiNK patient in Dresden was good.

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## WP5

Work package 5 is responsible for validating the Li-MRI scanners for all R-Link centres. As planned in the original proposal, four lithium imaging centres are currently fully functional (Newcastle, Paris, Milan and Munich) and all centres have provided good data from humans. The guidelines are currently being finalized and will be published in the near future.

Two centres are still waiting for validation. Copenhagen has the same scanner system as Milan and Munich. The sequences need to be installed and tested (phantom and test subjects). The necessary equipment is available and the imaging sequences are installed. In this case, the validation should be uncomplicated. Dr. David Cousins, leader of WP5, believes that he can assist Copenhagen with the full set-up from Newcastle because he has good contacts with technicians at Siemens as well as the necessary technical and clinical staff.

There are minor problems in Dresden. Here the signal-to-noise ratio (SNR) is 20% lower than the SNR of the other centres. It is currently unclear why this is happening. In order to find out whether the coil works properly, the coil was sent to Munich. Unfortunately, due to the COVID-19 crisis and the restrictions imposed by the national authorities, an initial test cannot be carried out until the restrictions are eased again. Dr. David Cousins expects that the problem will either be solved with the support of the coil provider or that we will have to accept the lower signal quality and then prioritize data acquisition.

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## WP6

WP6 has completed the trial phase and all centres performed successfully. All of the blood kits were sent to the centres, thus all centres should be ready to begin the biological part of the study.

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## WP7

The French Alternative Energies and Atomic Energy Commission (CEA) is responsible for setting up a central database. Most recently, CEA worked on the guidelines (detailed SOP's) and is currently contacting all data providers to define the format to be followed which will allow the data to be transferred to the centralized database. In February it was still assumed that the database could be completed in the next 2 months and used for data collection. This goal was originally set to be achieved by April. Unfortunately, the completion of the centralized database is delayed by the COVID-19 pandemic until further notice. Due to the national restrictions, it is currently not possible for the responsible engineer to push ahead with the implementation of the centralized database. In addition, the delivery of the purchased data server is delayed due to the hygienic situation and the restart of the Asian economy.

With regard to the central database, no training of the recruitment centres is currently planned, since the data are transferred to the central database via the data providers (often WP leaders) and not directly from the recruitment centres

CEA had originally planned to meet every data provider in Milan. Now that the meeting has been postponed to November, they will contact you by email or phone.

## WP8 / WP9

Professor Bauer wrote an official letter to the work package leaders to encourage them to inform us with news and interesting updates. We are dependent on the support of the other work packages to write and distribute news feeds, newsletters and articles. In order to simplify this flow of information for everyone, we have developed a template "Request for updates and news about your WP", which we send out once a month to the WP manager and authorized colleagues who are known to us. With this request, we ask you to check whether there is any news and, if so, to write a few short sentences. So far it works quite well and we want to encourage you to continue supporting us with your feedback. By filling out our inquiry form and sending it back to us, you support us in our work for which we are grateful for. Recently we were able to publish a new page with national associations. You will find it on the R-Link website in the menu contact -> finding support. The page is still under construction and shows national associations that deal with bipolar disorders in a variety of ways. This overview is intended to give interested visitors to our R-Link website the opportunity to obtain information from different specialised associations and organisations in their own country. If you think important associations in your country are missing, but should definitely be listed, please contact us and let us know. We will contact the organizations and list them after approval. One of the main goals for this network is to pass on our knowledge and results that we obtained in R-Link to these associations and organisations. We hope that our results can have a sustainable effect in this way! In the near future we also would like to start to present the participating recruiting centres on the newsfeed using a short text and a link to the consortium page. We look forward to the future work with each and everyone of you.