CTC Technologies Meeting: Minutes on Discussion Points

1. Parsortix Clinical System - FDA Clearance (*Michael O'Brien, ANGLE*)

Michael O'Brien (*ANGLE*):

- ANGLE recently received clearance from the FDA for the Parsortix® clinical system. This is based on the same core technology as the research system, which is extensively used especially across Europe and North America.
- The goal of attempting FDA clearance was to move the CTC field from research into the clinic.
- The "Intended use" is the critical aspect of regulatory approval and what the system is cleared for by the FDA but also via CE-IVD is "the capture and harvest of CTCs from mBCa patient blood (EDTA tubes) for subsequent analysis" → meaning it is a locked down system for the enrichment with flexibility in the enumeration and down-stream analysis
- Currently there are no down-stream assays by ANGLE that have been FDA cleared
- In one of the next meetings we would be happy to share more of the analytical and clinical data that went into gaining clearance

Nikolas Stoecklein:

- Thank you Michael and yes, it would be great if you could extend on this and the underlying data in one of the upcoming CTC technology meetings.

Evi Lianidou:

- Congratulations on this achievement Michael, this is a great accomplishment for the entire field and will hopefully open the door for additional CTC assays to receive regulatory clearance. It is also good to hear that we will be able to combine assays of our choice downstream of the system.

2. CTC Ringstudies/ EQA Schemes (*General Discussion*):

Evi Lianidou:

- We would like to continue with the idea of setting up ring-studies for users that have the same CTC technology within ELBS. We would like to organize smaller group meetings for users of e.g. CellSearch, Parsortix and other technologies to bring the critical mass of ELBS members together and start to organize ring-studies that will support in standardization of assays and labs. This data can be used by the labs to apply for CLIA certification or (in Europe) ISO1589 certification. We would therefore contact the respective ELBS members separately and actively involve the companies in parallel.

Klaus Pantel:

- I believe it would be highly beneficial to extend this beyond ring-experiments for the established platforms (such as CellSearch) and work on proficiency testing as form of external quality assessment. This could mean having standard samples sent to the users of different platforms on an annual basis and subsequently assessing the results. Participating centers of such "EQA

schemes" could then receive an ELBS certificate. This could give the centers additional confidence in their results.

Yong-Jie Lu (*Queen Mary University of London*):

- The logistics of this might be complicated, especially regarding the stability of the spiked cells in blood.

Klaus Pantel:

- You are right. This is easier for some platforms (e.g. CellSearch) and more difficult for others as we cannot send EDTA samples around. Stability of samples for 3-4 days would be a requisite.

Michael O'Brien (*ANGLE*):

- We have a control test – would this be a solution?

Klaus Pantel:

- Sure as long as the test is stable. We should not aim for over-night shipment.
- Also, I want to emphasize that we are open to all interested vendors that would like to participate in such a scheme.

Evi Lianidou:

- Absolutely. We are thinking of starting with a "pilot" using CellSearch and Parsortix as most ELBS members use one or both of these systems, meaning we have a critical mass. We also need to keep in mind that we would need to do the same down-stream assay to allow for direct comparison of results. We could think of using an FDA-cleared test also for subsequent analysis.
- One additional aspect to think about: for such an EQA scheme to be valid it has to be initiated by an organization/provider that has an ISO for doing intra-laboratory quality controls. Does IBBL have such an ISO?

Wim Ammerlaan (*IBBL*):

- We are 100% compliant to the regulations of this ISO, but we do not have full ISO certification so far. Therefore, if you aim at clinical validation of this type of proficiency testing, it most likely will be questioned. This could be a point of critique.

Evi Lianidou:

- Yes, the difference in this case is that nobody has such an ISO certification in the field of CTCs so far. Personally, I can say that ISO certification was given to my lab for CellSearch enumeration based on a small ring study with 3 labs. This was because, at this point in time, there were no certified external quality controls available.

Wim Ammerlaan (*IBBL*):

- We would potentially be open to organizing this. However, we need to come to an agreement with everybody to see how far we can push this.

Nikolas Stoecklein:

- We did perform proficiency tests with the Parsortix in the past during CANCER-ID. However, this was of course with the research device and not with the clinical system. So this might be something to look at.

Michael O'Brien (*ANGLE*):

- Yes, this is something that we need to discuss internally.

Klaus Pantel:

- Great, Michael. I guess if we initiate this effort we should focus on the most standardized system to ensure we do not go into repeated cycles of similar experiments.
- Also I completely agree with Wim, we need to be careful with our claims. After all, we are still operating at a research level.

Nikolas Stoecklein:

- Yes, definitely. However, our main goal here in ELBS is to work towards clinical implementation and that is truly the strength of this network. Therefore, we need to take steps in this direction.

Klaus Pantel:

- Absolutely and harmonization and standardization of assays/methods are vital in this regard.

3. <u>COST Action proposal (*Nikolas Stoeklein*)</u>

Nikolas Stoecklein:

- Due to the pandemic, the ELBS meetings have taken place primarily digitally. While we should keep most meetings this way, I believe it would be a nice addition to be able to meet in person from time to time. The idea that I would like to propose is to initiate a COST Action for "Liquid Biopsy". At the beginning of this year we participated in an excellent liquid biopsy training school for young researchers that was partly funded by a running COST Action grant. We would like to keep doing this and in this context, I would like to make you aware of what COST is and see if this is something the network would be interested in investing time into.
- COST Action proposals can be submitted at any time. However, there are collection dates that need to be kept in mind. The idea is mainly to bring people together and facilitate networking between experienced and junior researchers thus allowing for exchange and collaboration to solve a specific open question. Meetings, Training Schools, Short term Scientific Missions, Networking Tools are funded.
- We need to have a common idea and apply with at least 7 participating institutions (can be much more). However, we require the participation of so-called "Inclusive Target Countries". The proposals are anonymous; the proposer should not be discernible. The financing runs for 4 years. We would have some support from a prior COST Action organizer.
- Would this be of interest for the group? – I am seeing lots of positive responses in the chat.

Yong-Jie Lu (*Queen Mary University of London*):

- I think this is a great idea. However, I did not see the UK on the list of COST Action countries. Would it be possible for us to participate?

Nikolas Stoecklein:

- I will find this out and we will take this further in the upcoming months.