



Actionable Alterations in Cholangiocarcinoma

Elisya Muhamad Faizul

Process

The aim of this project is to determine the effectiveness of existing treatments for patients who have cholangiocarcinoma with actionable alterations. (cholangiocarcinoma = bile duct cancer, actionable alterations = mutations that play a biological role in cancer and have a known response to a drug). The information for this study is primarily gathered from the next generation sequencing (NGS) profiles of patients (a form of genetic analysis) and from Epic which is a hospital database used by some NHS trusts to store patient information.

My supervisor is Professor John Bridgewater, and I worked closely with my co-supervisor, Dr Sarah Howlett. Sarah began to work on this project before I joined the team and she had begun to gather information from the NGS profiles of patients.

My role is to collect information from Epic. It has extensive information on patients, detailing their diagnoses, treatments, test results, imaging reports and current patient status. NGS profile reports are not on Epic but in the form of separate reports that have to be read alongside information on Epic. Patients are divided up into three categories during data collection as three different companies were used to carry out NGS profiling. This division made it easier to fill in the spreadsheet when looking at reports.

There are three main pieces of information to be found for each patient: the patient's response to treatment, time to progression (when the treatment began to fail) and overall survival of the patient.

As well as this information, I also gather basic details such as date of birth, gender, ethnic background (if mentioned), precise cancer diagnosis as well as their NHS/MRN numbers which would make it easier to find them on the database again should I need to review any information. The patient's best outcome from CT scan reports is recorded as well (whether the report concluded that the tumour was fully removed, partially removed, has a stable appearance or if there was regression).

This information can be found on letters exchanged between doctors (within the same hospital or between hospitals) where the patient history would be outlined in detail along with the latest imaging/testing results.

It was also useful to note down the success of NGS testing. Not all tests will succeed on the first attempt and many of the failed tests are due to insufficient blood/tissue samples or biopsies. These tests are expensive, well-advertised and take a relatively long time to process so it is important to look at the percentage that worked for the first time as a way to gain an idea of the efficacy of these tests and if they are really worth doing.

The data is input into an excel spreadsheet that was already formatted. The initial spreadsheet was rough and only information from the NGS profiles was completed. As I began to fill in the information from Epic, I added in a few columns for more information that might be useful for the study and cleaned up the spreadsheet to make it more organised and easier to read.

My role is to mainly focus on collecting patient information from Epic as Sarah focuses on classifying the mutations. However, I was given the NGS profiles of 35 patients so filled in the information for their respective patients. I understood the common actionable alterations and their associated treatments as well as the classification of mutations but allowed Sarah to complete the organisation part for the actionable alterations.

Not every patient with a successfully processed NGS profile had actionable alterations. This means that they are not included in the study as the focus is only on patients with actionable alterations. For

those patients without identifiable and known actionable alterations, only universally standard treatment is provided (cisplatin with gemcitabine) which is not as effective as precision medicine treatment. However, it was still useful to note down the outcomes of these patients, whether they are deceased or alive, to look at their survivability compared to those patients who had actionable alterations and were treated with precision medicine.

This research is part of a study led by Professor Bridgewater and there are hopes for it to be published in a medical journal next year. There are around 190 patients involved in this study and the full data collection for all of the patients is yet to be completed. Once all of the data is collected and organised accordingly, then the analyses and write-ups can begin to form the final paper.

Therefore, this study is ongoing and we have yet to arrive at a conclusion. The final conclusion that we are working towards is to determine a number for the survival of the group of patients with actionable alterations that were treated with precision medicine vs the survival of the group of patients with actionable alterations but no treatment. It is hoped that the findings of this study will help to improve the outcome of precision medicine treatments for patients with cholangiocarcinoma which can be applied to other types of cancer as well.

Reflections

This project mainly involved data collection and I learnt a lot throughout the process. I gained insight into the in-depth procedure of a scientific study from gathering patient lists, to collecting and organising data, to the eventual analysis of this data to arrive at a final conclusion. Through the use of Epic, I was able to observe how a hospital trust wide database operates and also learn a bit about how doctors communicate with each other.

I came across a lot of jargon too, in terms of both research and patient care aspects so I spent some time looking up and trying to understand these terms and their contexts. Due to the large number of specialised vocabularies, it was difficult to remember what everything meant but repetition of these terms allowed me to recall them easily over time (for example PD was mentioned on many imaging reports and it stands for progressive disease; PS was on majority of the letters exchanged between doctors, meaning performance status as a measure of patient health).

The project has gone smoothly so far. Once I familiarised myself with how to navigate Epic and was clear with the specific information that needed to be collected for each patient, the data collection was quite straight forward. I worked well with my supervisors by having weekly meetings with Sarah. My meetings with Professor Bridgewater were less common, once in two weeks or so; we would meet with him when major tasks had been completed so he could check on the work we had done, provide feedback and explain the next steps. Overall, communication within the team was effective.

There were however some hiccups during the project. The first and most significant downside was the very late start. As I needed to gain access to a database full of sensitive patient information, I had to obtain an honorary contract with UCLH which required an extensive approval process. Professor Bridgewater had already mentioned that the process would take weeks so I was sure to apply as early as possible, in May.

Unfortunately, the period of application was during the summer, a time when many people working in the hospital admin departments took their leave and as such, the process was often disrupted. Even after the approval of my initial application, there were more checkpoints to pass such as a virtual verification of identification documents and a criminal record check.

Once receiving my honorary contract, I was required to complete online Epic training and had to wait an additional 2 weeks before being given my log in details. In the end, the whole process took over 3 months leaving me with just enough time to complete the required 6 weeks for the Laidlaw project. The big delay was quite frustrating as I was eager to begin the project early but ended up waiting for weeks as I wasn't able to complete any research without access to Epic. During the waiting period, I carried out some background reading and further research on the topic which gave me more insight and understanding which proved to be useful.

Looking back on the project, I would have made sure that I was working more efficiently. What I would do differently would be to have taken a look at Epic before asking about the exact information that I would need to gather. Whilst I familiarised myself with the software and how it operates, I didn't look into detail at the patient information present on Epic and so wasn't aware of what information was displayed and the depth of that information.

As a result, when I carried out the data collection for the first time, I wasn't prepared for the overwhelming amount of information for each patient and wasn't sure of what to filter out to include for the study. I was advised to always include more detail rather than less so that I would only have to cut down information that was already on the spreadsheet. Despite this, after weekly meetings, I often

spent some time backtracking through patients I had already completed, editing their information to ensure that I was applying the feedback given to me by my supervisor.

The amount of information for each patient greatly varied, depending on whether they were at UCLH for the entire duration of their treatment or if they were transferred there from another hospital (as Epic only had information from UCLH). This meant that the time spent on going through the information for each patient was very different; some patients took around 15 minutes, others could take up to an hour each. So, it wasn't efficient to have to go back to some patients to edit the information that I had already scoured through. However, I always wanted to make sure that the data collected was only what was absolutely necessary and that it was clear and accurate for when data analysis would take place.

After looking through so many patients on Epic, I made some observations that were not related to the study but that I believe are important to note as well. As mentioned before, not all NGS tests succeeded on the first attempt which meant that patients had to give another biopsy and wait an additional 2-3 weeks before they received their results. This led to further delay to the start of their treatment.

Unfortunately, many patients passed away before having a repeat NGS test, before receiving the results of a successful NGS or even before receiving treatment based off the results of an NGS profile. This was quite sad to see as treatment could have helped many of these patients and I can't help but wonder if the outcome would have been different with earlier action. Similarly, in some patients, NGS profiles were delayed by weeks due to issues of funding for studies, which was only detrimental to patient care.

One thought that I had before beginning the project is that in scientific studies like this, researchers become detached from patients and simply see them as numbers on a list. Patient letters are often very detailed so they tell the story of the patient. These are normal people with families and jobs, with lives that are disrupted due to illness. These patients have to spend months on treatment, many of them with side effects that greatly diminish their quality of life, others become hospitalised due to secondary conditions from treatment and can stay in hospital for weeks at a time.

Doctors would sometimes put in extra details such as patients feeling well enough to return to work or to go out and play some golf or to even go on holiday with family which was pleasant to read. Through small details like these, I was able to see the side of the patient that doesn't just involve diagnosis and treatment and their time at the hospital. It helped to constantly remind me of the reason behind this hard work.

Reading the stories of these patients made me remember why I chose this project. I lost a loved one to cancer, specifically cholangiocarcinoma so this project is very important to me. Though my task may be small compared to the efforts of other researchers, I know that I am still part of the cause towards finding more effective treatments for cancer patients and I sincerely hope that this study can make a significant contribution.