Pancreatic Cancer APPG Inquiry

Research community – 9th June 2014

Eric Ollerenshaw: Good afternoon, ladies and gentlemen. Sorry for rushing; there are things going on in this place. There usually are things going on, but more than normal on a Monday and early, so I'm really grateful people got here. Let me introduce myself; I'm Eric Ollerenshaw, Member of Parliament for Lancaster and Fleetwood and chairing this All-Party Group.

For the benefit of witnesses, this inquiry is trying, in a sense like a select committee, to take evidence for a final report, but we are not a select committee and we're not trying to catch you out; we're trying to find out whatever information we can in terms of this specific investigation into where research is and funding is in terms of pancreatic cancer.

We hope to produce a report before the end of this year, which we will give, like the previous report, to the Secretary of State for Health and hoping that way we can get some movement in terms of outcomes in this particular dreadful disease.

I'll just ask members here if we can start. Baroness Morgan, do you want to introduce yourself?

Baroness Morgan: I'm Baroness Morgan of Drefelin and I am Vice-Chair of the All-Party Group on Pancreatic Cancer. I'm also involved in the All-Party Group on Cancer and Breast Cancer as well.

Lord Walton: Yes, I'm John Walton, a neurologist, a former Dean of medical school. I have to confess that I know very little about pancreatic cancer, though in 1950, when I was a medical registrar, I and a colleague wrote a paper on cancer of the body and tail of pancreas, which was published in the Annals of Internal Medicine.

I think our only conclusion at that time was that the disease was very difficult to recognise until it was too late. The question really that I'd like to ask in due course is: how much improvement has occurred in diagnosis since that time?

Eric Ollerenshaw: I think we'll get to that, my Lord, at some point.

Lord Aberdare: Alastair Aberdare, a crossbench member of the House of Lords and a member of the All-Party Group, with no specialist knowledge whatsoever, but I have a concern about the disease.

Eric Ollerenshaw: I think what I'm going to ask is for the Novartis team to introduce themselves. We've had a written submission, which we're extremely grateful for. If you want to say anything beyond that or one or two other points and then we'll come to questions from members and see where that leads us. Over to you, Barbara McLaughlan and Ali Rees, I think.

Barbara McLaughlan: Thank you. My name is Barbara McLaughlan. I'm Head of External Affairs at Novartis Oncology and my colleague is:

Ali Rees Rees: I'm Ali Rees. I'm a Clinical Development Advisor in Novartis Oncology, so I work in solid tumours but I specialise in neuroendocrine tumours.

Barbara McLaughlan: Really, as you said, we've sent you some briefing, but I thought it would perhaps be helpful to just summarise very briefly what we outlined in those briefings.

To frame the discussion, we thought really there were two aspects that we'd like to touch on; one is how Novartis Oncology takes trial placement decisions, and the other one is what our approach is to research in cancer.

In terms of trial placement decisions, Novartis of course is a global business and we invest around £7bn in research every year. Not all of that is cancer research, so this is pharmaceutical research across the board.

When it comes to trial placement decisions, it's very much a competition between the 131 countries where we operate to say, "We want that investment," because each country will say, "We would like investment in trials, so that patients benefit but also so that clinicians get experience with the drugs that we are developing early on."

The criteria we use to decide where we place our trials are very much partly about the research environment. This is: how quickly can trials be set up? How quickly can patients be recruited into the trials? What is the cost and what is the quality of the research?

In relation to quality, the UK obviously is a country with very high-quality research. Unfortunately, that's not necessarily a distinguishing factor anymore, because there are so many other countries these days where research is of very high quality.

In terms of the other elements, so speed of trial set-up and patient recruitment and cost, there are certainly still things that need to be done to improve on those, even though in the last few years there have been improvements and we have certainly found that we've been able to place a lot more trials in the UK than previously.

When it comes to our approach to research, I think it's important to understand that we are moving, like so many other companies, into the area of targeted research; that's been a big change in the last 15 years. As you may know, the approach to that is that by and large, to put it very simply, you identify a molecular pathway that determines tumour growth and then you find a medicine to inhibit that pathway.

The advantage of that is that response rates are usually a lot higher, that you only treat patients whose cancers have that particular characteristic, and also that the treatment you develop often works in other indications as well.

When we look at the treatment we have for pancreatic neuroendocrine tumours, for instance, that was initially developed as a treatment for advanced renal cell carcinoma and then we found that the same molecular pathway worked for pancreatic neuroendocrine tumours.

In summary, what we really need to understand: that these days whether or not a company invests in research in the particular tumour type is very different to previous times, when you went for really the big populations, because now even a common cancer like breast cancer is subdivided into so many smaller populations. The type of research we do depends, to some extent, on the molecular work that we do.

For pancreatic cancer itself, we would say, "We are doing work, we are continuing to do work in pancreatic cancer, but one of the biggest challenges is that patients are not diagnosed early enough." Where you are in a situation where you have a small patient population already and then the patients get diagnosed very late, you can often not enrol them in any trials anymore.

That's a major challenge, apart from other issues around molecular diagnostics, where also the UK is behind some of the European countries. For that as introductory remarks, I hope that's helpful and we look forward to your questions.

Eric Ollerenshaw: Very helpful. Do you want to add anything to it at all?

Ali Rees: No, I'm okay.

Eric Ollerenshaw: Who wants to kick off then? Sorry, did you want to?

Dr Diana Tait: Me to go next?

Eric Ollerenshaw: Yes, go on.

Dr Diana Tait: I'm Diana Tait and I'm Vice-President for Oncology at the Royal College of Radiologists, the RCR. Maybe I should just explain that the RCR, although it's got radiology in its title, is two faculties. It's got a faculty of radiology, the diagnostic people, who would be the people to help with early diagnosis approaches, and it's also got a faculty of oncology – clinical oncologists who give both chemotherapy and radiotherapy.

We're very relevant to all of this area; particularly the oncology side, we're using both chemotherapy and radiotherapy. This disease is obviously something that requires all sorts of approaches, because it not only has problems with local failure but also with widespread disease.

I think just thinking about it as a rare cancer, obviously immediately that brings up difficulties that you've alluded to in terms of numbers of patients. Also, it's a sticky one because it doesn't have a standard response to treatment. If you think about other rare cancers, say like the childhood cancers, they have the advantage that they tend to respond very well, so there have been amazing advances made there. Maybe this is to be more

likened to things like sarcoma, where it's difficult and there's probably the same heterogeneity or mixed content of the tumours.

I think what we feel at the RCR is that of course the systemic approaches are very important but that we mustn't forget local treatment, so surgery and radiotherapy. There are some very exciting developments at the moment in advanced radiotherapy techniques being able to focus. Of course, if you want to use those techniques, you've got to diagnose the cancers early to be able to make that the main focus of approach.

I think undoubtedly when you use radiotherapy for pancreatic cancer, you see very different responses. It's not like many cancers, where you can fairly well predict; you'll see some cancers that just progress on treatment and others that respond very well, to such an extent if they go on to have surgery there's no cancer there, you've got a complete path response.

We need to be able to hone down on this mixed population and be able to pick out patients that are likely to respond to radiotherapy, I think, to be able to see the benefit of radiotherapy. Of course, that's the whole area of personalised oncology, where you are going to be able to do a profile on a patient's cancer and understand that cancer better in terms of its biological markers and what it's likely to respond to. I think that's a big area of work that it would be very, very relevant to this, a rare cancer.

We've got a lot of data in a lot of patients, treated both in trials and outside trials that we can go back, if we have appropriate tissue banks and going forward have tissue banks, to look at that profile and tie it up with the outcomes – did they do well with radiotherapy? Did they do well with chemotherapy? – To try and make sure we know in the future. I think tissue samples/tissue banks are important.

I'm representing the clinical coalface of this disease, and I suppose one of the big issues is how clinicians have appropriate time and resources to do these trials that we talk about. Most trials are carried out by, in terms of putting patients in, NHS consultants in NHS posts. They find it very hard to get any support from trusts for research time in their job planning, so they tend to end up doing it on the hoof on the back of everything else. I think there is a problem there with the sort of recognition that all oncologists should have in their job plans time to devote to research and clinical trials.

Then when you go to the people who take on an academic type of career and have training in oncology, they then have a lot of difficulties finding funding. It's not a particularly attractive career structure, compared with staying in the NHS; it's got much less security and there are other difficulties with it.

I think if we look, that's one of the big problems for academics in oncology, is the career structure and the lack of an oversight or an overall organisation of the research workforce. We're trying to have good workforce planning for the service delivery, but we don't have anything as similar for research activities, so I think that's something that would very much help.

I'm pleased to see that CRUK, the Cancer Research UK organisation's latest cancer strategy aims to focus on lung, brain, and pancreas. I think for all of us that is going to give us a focus for our activities.

Eric Ollerenshaw: Thank you; thank you very much. Baroness Morgan, do you want to kick off now?

Baroness Morgan: Yes, I was obviously coming back to the points about clinical trials and I suppose in simple terms for me – more clinical trials, more patients having access to clinical trials, that's got to be a good thing. Obviously we want really high-quality well-planned, well-supported clinical trials, but I'm hearing that one of the problems with patients with pancreatic cancer getting access to clinical trials is late diagnosis.

One of the problems with late diagnosis must be that the research hasn't been done in order to find new and better ways, or more effective ways, of diagnosing pancreatic cancer. It just seems to me here we are in this terrible cycle of despair, really, for the patients who really need to have access to better treatments and more options.

How do we break that cycle? Obviously we are in a climate where resources are very limited. My own view is that we've seen all the architecture that supports cancer service improvement undermined or dismantled and rearranged. It would be great if we could put it all back together again, but what do you see as the really important steps that we need to do to start to tackle that cycle, which is having the result that patients don't get access to these trials?

Dr Diana Tait: There was a major strategy just launched last week about early diagnosis, again through CRUK. Of course, it's a big area of disgrace really, isn't it that 25% of all cancer patients present at accident and emergency? We've got to, either partly through public awareness, through primary care awareness, and then having the right techniques and perhaps screening methods to get to this.

I think probably other members of the panel will know more about this than I do about the familial pancreatic cancer, which is obviously very rare. I treat pancreatic cancer; I don't think I've ever seen anybody with that sort of segment of the disease, but there is work going on there to look at what are the right diagnostic tests to pick up cancers very early. Perhaps learning from that, we could apply it to a larger group of patients, such as patients who present with late-onset diabetes who are smokers; you could define a profile of patients that are at higher risk and maybe investigate that, not in a widespread way but starting with a pilot.

Again, it is resource-intensive and the approaches being used at the moment are MRI and endoscopic ultrasound. They're both rare, scarce, and difficult to come by, so that wouldn't be without considerable funding.

Eric Ollerenshaw: Ali Rees?

Ali Rees: Yes, if I can add a point, I think it starts with the patients as well. There's a global quality of life study going on at the moment, where they're looking at the quality of life and the symptoms in patients who may be suffering from pancreatic, lung, or colorectal cancers. I think we need to have patients understanding the symptoms they have and verbalising those symptoms very early, so we can understand how many patients we do have in the UK. From a pharmaceutical company perspective, that helps us to get the trials into the UK. If we have a very broad understanding of how many patients there are and if we have early access and early referrals of those patients, it will help us when we're asking for all those trials in the UK.

When we have trials placed with us, we have to demonstrate that we have patient populations in order to fulfil the trial criteria. If we have a commitment to a trial of, for example, 20 patients, we need to demonstrate in advance that we have a referral pathway for all those patients. It's really important that we have that link in from the patients, via their GPs into us and the clinicians we engage with, so we understand where the patients are.

Barbara McLaughlan: Can I just quickly add to that? There's also Sean Duffy, the new Director for Cancer. He's talking a lot about a culture change in the NHS in relation to early detection of cancer, especially rarer cancers. That's in recognition of the fact that you cannot raise awareness of all the rare cancers that exist, because there are just too many and to expect every GP to know what to do in particular cancers is not realistic.

What he is talking about – and I think it was the Teenage Cancer Trust who had started with that idea – was that patients who return over and over again to their GPs, after three times or whatever the cut-off point is, you would say, "Some further investigation needs to be instigated."

I'm not sure, perhaps you could find this out; that's one possibility of finding out from Sean Duffy where he is with his plans for doing that and starting that culture change, which obviously will take time.

Eric Ollerenshaw: Baroness Morgan, do you want to pick that up?

Baroness Morgan: I just had one other point. You're talking there in some ways about strengthening the patient voice, so what do you think, for the pharmaceutical companies particularly, what can you do? Given the benefit that a strong patient voice can bring in the policy arena, what can you do to help that voice, without compromising independence and so on for the patients?

Barbara McLaughlan: I think in terms of the early detection and making sure that people are aware of symptoms, it's difficult to say that that could be the role of one particular charity necessarily, although perhaps Cancer Research UK again could take that lead role. I don't think it's necessarily the role of the pharmaceutical companies to help with that.

Having said that, what we do try to do is to involve more patients in the setup of trials and finding out more what endpoints are in trials that are

significant for the patients. We capture quality of life issues, for instance, that we possibly wouldn't have captured previously.

Ali Rees: I think also one of the initiatives that have taken place in the UK over the last few years is linking in with the National Cancer Research Network, who we work with very closely with our trials. That helps to publicise the trials that we have and helps to reach patient groups, as I say, across all the indications that we work in.

I think it's helping to publicise the fact that patients should be very self-aware, irrespective of the cancer, and also supporting the patient groups, as Barbara McLaughlan is saying, no matter what cancer we're working in, supporting the patient group so that we can be there to try and help educate the not only the patient, but also educating the nurses and hospital staff as well.

Barbara McLaughlan: That's almost secondary care more though than primary care; in primary care I don't think pharmaceutical companies by and large do that much, apart from generic awareness-raising, sometimes in collaboration with charities.

Eric Ollerenshaw: Lord Walton?

Lord Walton: Yes, can I clarify one or two points first? I begin with an apology, because one of the problems of ageing is that my hearing is not as good as it used to be and I've got two hearing aids. I got most of what you said, but I may have missed one or two points.

First of all, can I ask you, in relation to the incidence of pancreatic cancer, if you leave out the very rare tumours of the islets of Langerhans, the so-called 'insulinomas', how many different varieties of cell type have you identified in different forms of pancreatic cancer? Does the response to radiotherapy and to drugs vary according to the cell type – that's point number one – of the cancer that you've identified?

Secondly, the biological markers you referred to briefly, are there any circulating biological markers which can be identified in the circulation of which give a clue to the presence of pancreatic cancer?

Eric Ollerenshaw: Is that better for you, so the gentleman in the audience over there?

Charles Akle: I can perhaps help you.

Eric Ollerenshaw: Go on.

Charles Akle: I'm sure our colleague here is most eminent. Shall I give a lay version as I understand it as a surgeon? It's interesting in breast carcinoma and various other tumours, it's all very well looking at the histology, as one used to; the problem is if you do two biopsies 1mm apart, you will get different cell types. Therefore, trying to define a tumour on a single biopsy – and often in pancreatic cancer you've only got a needle biopsy.

Lord Walton: Roughly how many cell types?

Charles Akle: As many as you can think of really; that's the problem. The daughters are different; the metastases are different and each metastasis behaves differently to the other metastases, so you're dealing with a very polymorphic thing. Basically, it's pleomorphic; there are probably four or five different phenotypes of cancer of that type, certainly in surgery, and the chances are there are a lot more in pathology. The problem is identifying them.

Lord Walton: What roughly is the survival, on average, of people with the most malignant form, as compared with those with the least malignant form of pancreatic cancer?

Ali Rees: The recent figures that I was looking at show that for a Stage 1A cancer the survival rate is around about 14%, and for Stage 4 it's around about 1%, so there's a big jump between the two.

Lord Walton: Thank you.

Eric Ollerenshaw: Lord Aberdare? I'll bring you in afterwards.

Lord Aberdare: I'm even more baffled than usual. I think my problem is my brain is in Monday mode; I can't blame anything else. It is slightly depressing that everything always comes back to this early diagnosis thing, but the one thing I've picked up in the Novartis brief is this issue about molecular testing. Is that something about which something can be done, is being done, and should be being done, and something that we should maybe focus on?

Barbara McLaughlan: It's definitely something that needs to be addressed, but NHS England is starting to do work, so we're waiting for a service specification on molecular testing. There are big issues around the quality of testing; the standardised testing isn't provided necessarily or isn't available necessarily. The costs, in some instances it's the manufacturers who are supposed to pay for the costs.

I think Simon Stevens, the new Chief Executive of the NHS, has said on Friday that he wanted the UK to be the "Global leader in molecular diagnostics and targeted medicines." I think, to be honest, we're quite far away from that; a lot more needs to be done.

Lord Aberdare: The implication of what you say here is that we are actually some way behind other countries.

Ali Rees: Yes, I would think to a degree. A specific example I have at the moment is feasibility, which is our process for assessing whether we can take part in a trial in the UK. For a trial in thyroid cancer, it requires a specific type of testing which we don't fund in the UK. We have the options where we say, "We can't do the trial because we don't fund the testing," or we pay for that test ourselves, so there's a cost implication.

It's not always feasible, but it can mean it's a yes or no for that trial in the UK – and, therefore, those patients – and there's an unmet need for these patients. There's definitely work that we can be doing to expand and become more advanced in the testing that we offer. That way, you then have access to more trials for your patients.

Eric Ollerenshaw: Sorry, did you want to add to that?

Barbara McLaughlan: No.

Eric Ollerenshaw: He's desperate to get in; go on, go for it.

Prof Andrew Biankin: I'm just listening to this conversation and this is what I do every day, so I thought I might contribute. Just by way of background, I'm Andrew Biankin; I'm the Regius Chair of Surgery at the University of Glasgow. I did live in Australia until about 18 months ago.

Eric Ollerenshaw: I think we can detect that.

Prof Andrew Biankin: Yes, you probably noticed that. I also sit on international expert panels, review boards, etc., advisory committees for the Australian Government, although I'm probably giving that up at this point in time. I also sit on the International Cancer Genome Consortium and head up the pancreatic cancer effort for that.

The reason we moved to the UK is to really enhance molecular phenotyping and genetic testing for pancreatic cancer. Something we do in a global community is really trying to understand and fix this gap between what pharmaceutical needs, which is patients, but patients that are diagnostically tested for their subgroups versus the delivery of those patients, because that's expensive.

For one pharmaceutical to do one drug, because of what we're understanding about the diversity of cancer, particularly pancreatic cancer – and I'll get to that later – is that you need to do 1,000 tests to get 100 patients. The cheapest test you can get is from Foundation Medicine, which is this, $6000, and it's not a great test, so all of a sudden you don't have a very viable business model.

Where we're moving towards a research community, a clinical community in cancer, particularly pancreatic cancer, is the ability to provide pharma with patients who have their tumour already subtyped, developing networks and infrastructure for us to be able to do that. I'll speak about that at length a little bit later.

Eric Ollerenshaw: That's really interesting. Can I ask, and it's following up Lord Aberdare's question to Novartis, because you made some comment earlier that we're behind on research here for some reason, or is that connected to what you were just saying? I think you, Barbara McLaughlan, said in answer to the question, "Why should your company do it here and not somewhere else?" and that the research field here you say is behind.

Ali Rees: I think we are doing a lot more research here than we used to a few years ago. From a Novartis perspective, we have high quality in the UK and the things that we continue to need to focus on is the time taken to open our trials and the cost of those trials, because there are 131 other countries that are also looking to be involved in our trials.

We're not behind; we have a lot of translational meta, which is the very early phase trials going on in the UK, but it's becoming more competitive because other countries can open their trials faster. They may be cheaper; the quality is of the same level as it is in the UK, so the competition gets higher.

Eric Ollerenshaw: Sorry, why can they open their trials faster than we can, is it simply regulation?

Ali Rees: There are a number of elements; some countries have different setups, in that their trials are all run in one specialist trial facility and not through an NHS structure. They're not running the trial in hospital; it's a specific trial centre where all they do is run trials.

The other point is around the regulation involved. Of course, we have the MHRA approval system we have to gain for our trials and the ethics approval we have to get. They're there for patient safety, so they're of course approvals we have to have, but they're added in and some countries have a slightly less complicated system around opening trials than we do in the UK.

Barbara McLaughlan: I think where we are behind is in relation to molecular testing. In other countries, you have a better system of making sure that the diagnostic tests that are required to do the trials and to identify the patients whose tumours have particular molecular characteristics are done and funded by the health system, which isn't the case here, where only at the moment if you have a NICE-approved drug then the testing will be funded.

In other countries, they are much further advanced and they see it as a key priority. It's good to hear that now the NHS is taking that on board that it also needs to happen in the UK, but it is partly funding. Equally, when we look at trial placement, one of the issues we do look at is whether patients are likely to get access to the drugs that we develop once we've done all the trials. The reimbursement side of things is always there in the background.

Eric Ollerenshaw: Has the Cancer Drugs Fund helped, hindered, or where would you put it?

Barbara McLaughlan: The Cancer Drugs Fund has helped in terms of making sure that the standard of treatment that we have in the UK is equal to the standard of treatment in European countries. If you compare it, for instance, with Scotland, for the last few years we haven't been able to place some of our trials in Scotland because the standard of care is now different, because they don't have access to the same drugs that are being provided on the CDF, so yes, the Cancer Drugs Fund has helped in that respect.

Eric Ollerenshaw: Is that an advert for the United Kingdom staying together, or is that a different question?

Barbara McLaughlan: Scotland is doing other things now to improve access that don't involve the Cancer Drugs Fund. They are changing the SMC system and some other ways of providing better access, but there is recognition that there's inequity in access at the moment.

Eric Ollerenshaw: There's someone who tells me that NICE and the Cancer Drugs Fund every year is underspent.

Barbara McLaughlan: At the moment, I don't think it is. It's on the verge or it is already; the Cancer Drugs Fund is being overspent. I think the whole reimbursement question there's recognition among all parties, I think, that parties, not only political parties but all stakeholders, that the Cancer Drugs Fund is a sticking plaster and that we need to find a long-term solution.

Eric Ollerenshaw: Yes, I think everybody sees this. Of course, this precise time the political parties are going to go to a general election next year and will want to put something in their manifesto, so people like yourselves need to be lobbying quite hard if you can suggest some way that that issue can be dealt with.
In terms of the company, because from the Chancellor's perspective he's done very well in terms of corporation tax and should be encouraging companies like yourselves to invest more and develop more here, does that have an impact, "cuts in corporation tax"?

Barbara McLaughlan: I don't think it's affected us as much, because we're based in Switzerland so it's different. For global companies, if you talk to GSK or AstraZeneca then it's a different picture. The same goes for some other initiatives like the Patent Box; again, it applies to local companies rather than international ones.

Eric Ollerenshaw: Thank you. Can I ask the radiologist then? I've just received, funnily enough, today 'The future of innovative radiotherapy in our schools' – apparently high-tech radiotherapy machines lying idle and unable to be used on NHS patients, because since 1st April 2013 the commissioning for their use is not being approved. Do you have any evidence?

Dr Diana Tait: Yes, there is a whole issue around these very advanced techniques, such as something called SABR; you may have heard of CyberKnife.

Eric Ollerenshaw: I've heard of it, yes.

Dr Diana Tait: CyberKnife is a form of SABR and then the stereotactic radiosurgery techniques mainly for brain lesions, both benign and malignant. They're not funded; the techniques and their use in cancer are not funded, except for non-small cell lung cancer, early lung cancer, where it is approved.

These machines are sitting there; we've got one at the Marsden and we can't get NHS patients funded to have the treatments because there isn't the evidence. If you're trying to allocate money and you've got a treatment

that there's no evidence for, and that's all you've got to go on as a provider of the monies, that's the very simplistic approach.

What we've been trying to push for is to have commissioning through evaluation and have an evaluation process, because we'll never get big trials set up for the use of these technologies.

As I understand at the moment, that is still being looked at with James Palmer in Specialised Commissioning, but again this may be going a little bit down that slippery slope of no money. That's why there is capacity that is not being used for these very exciting approaches, yes.

Eric Ollerenshaw: There is a problem; interesting. You said earlier on, when somebody was asking about the use of these in diagnosis, and you were talking about taking samples of people you regard at risk. Did I understand it correctly?

Dr Diana Tait: Yes, I think there are two things; there are people who have got a very identifiable high risk and it's a very rare subgroup of a very rare cancer, so these families that have got a lot of pancreatic cancer in them and you can identify genetic abnormalities in the cancers.

With those people you can start to do a monitoring and a looksee to try and get the cancers very early. It's then taking that out beyond this very glorified little group of people; most people who are going to get pancreatic cancer do not fall into that group and it's much more difficult to detect.

We talked about early diagnosis and patients' symptoms; one of the big problems with pancreatic cancer – most patients have very little in the way of symptoms until they come along with either their jaundice, because the cancer has blocked the bowel drainage, it's that big, or they've developed secondaries and they've got pain.

It's probably 20% that have grumbling other issues, but I agree this idea that if you've been going to your GP repeatedly and nothing is found, it's a good group to start putting in some sort of screening.

Eric Ollerenshaw: Go on.

Lord Walton: Talking about those very rare cancers, are any of them single gene disorders and have the genes been identified and localised and so on? Because looking back to what was raised a moment ago about the Cancer Drugs Fund, NHS England of course has now established a rare disease consultative group and so on to examine the whole problem of rare diseases in general.

In my team of neurology there's a very large number of progressive neurological diseases which are due to single genes, where the actual abnormal gene has been identified, the missing gene product or the abnormal gene product has been located. As a result of this, drugs are beginning to merge, which are called either 'orphan' drugs or 'ultra-orphan' drugs, depending upon the number of individuals involved.

The question is: in the cancer field or in pancreatic cancer, do any of these cancers at all fall into that category? Because you're talking about the next election; there is a rumour that the Cancer Drugs Fund may not survive and that, hence, some of these cancers may come under the rare disease examinations.

Prof Andrew Biankin: You've hit the nail of the problem right on the head; there are many drugs out there that can potentially work in subgroups of pancreatic cancer. What we need to do is develop the systems where we can measure and identify those patients and link them with the drugs; that's what we need to do.

Lord Walton: We are in a position to talk, in certain forms of pancreatic cancer, about targeted therapy which is actually directed specifically at the individual cancer cell?

Prof Andrew Biankin: Yes, so the challenge we face is that the system at the moment, both from the patient care perspective and from the research perspective, is not set up to advance this stratified, personalised therapy or therapeutic approach. That perhaps is why we're failing in pancreatic cancers, because maybe that is the approach that is necessary, but we don't have the systems in place to do that. We need to re-engineer those systems, all the way through to regulation, how we look at regulation; how do we identify these small subgroups and get the right drug to the right patient?

Eric Ollerenshaw: Which is perfect for me to move on, but somebody was desperate to coming on this point, I think; go on.

Celia Goodman: I just wanted to say a comment as a layperson, as the parent of a child who died of pancreatic cancer, particularly picking up about this patient awareness. She tried, we tried and was fobbed off by GPs, so as far as I'm concerned there's a GP education need because when you're a fit 29-year-old presenting with nebulous symptoms it's not expected to be cancer.

Also, her pancreatic cancer was not diagnosed through an MRI scan or an ultrasound scan; it was diagnosed when they operated to remove the tumour. That was all far too late.

Eric Ollerenshaw: Point taken. Quickly, then I want to move on to the professors.

Mr Giuseppe Fusai: Just on the comment from the lady, I think we've discussed this, where the incidence of the disease is such that for every single GP in this country seeing one patient per year with pancreatic cancer is almost rare, so inevitably it's not their fault. In some respects, one of the problems with early diagnosis compared to other European countries, the primary care in this country is very strong and that a patient who reports to their GP might not be in a position, as you say, to identify these kinds of symptoms, which are already quite sparse.

One of the solution might be to then install some guidelines for the GP, national guidelines, to give them very clear guidelines on, for instance, as you said, any unexplained abdominal pain, practice, anything, any unexplained weight loss, so very clear.

Eric Ollerenshaw: Thank you for that. Sorry, Professors, I know you're desperate. Shall we start with Andrew or do you want to start with Professor Duncan?

Prof Andrew Biankin: Yes, I've spoken enough already; I might let my colleague.

Eric Ollerenshaw: Professor Duncan, come on; you've been really polite.

Prof Duncan Jodrell: I'm Duncan Jodrell. I'm the Professor of Cancer Therapeutics in Cambridge. I'm also a medical oncologist and I practice in a pancreatic cancer clinic every week. One of the advantages of going a bit later on in the session is you can pick up on one or two things that people have said previously and comment on those.

I'm going to be fairly brief about just two or three issues; one is the clinical trials issue. Baroness Morgan has already raised that issue about "How do we get more patients into trials?" and our colleagues from Novartis have commented on the delays in getting trials set up in the UK.

I think it's not doubted that the European Union Trials Directive has slowed down academic research. Whether it has adequately improved quality to offset that delay I'm not convinced. I think the big thing is it's not actually the MHRA and the ethics system that causes the major delays, it's getting the R&D approvals in multiple sites.

A trial may open in one site on 1st January and it may be a year later before the other sites are open. I would, therefore, support the Health Research Authority's initiative to centralise R&D approval for clinical trials, because I think that will accelerate trials opening and will make trials more accessible for our patients.

Access to trials should be through the multidisciplinary teams, and I think it's essential that each of the multidisciplinary teams has a research representative present at those meetings to identify the trials that are suitable for patients.

Andrew may come back to it, but I think that we've talked about biomarker-led studies and facilitating personalised medicine. I think we have a real opportunity at the moment in the UK to develop a network of excellence, because of the major centres and the major input that Cancer Research UK is putting into this setting and the other cancer charities, and bringing together those major centres to form, if you like, what might be akin to the Dream Teams that we have seen developing in the USA.

I'm actually lucky enough to be part of one of those Dream Teams. We've managed to access research funding from both Lustgarten and Stand Up 2 Cancer in America, and we're proud to be part of a dream team that is working on immunotherapy, which is another very rapidly growing area. Sadly, at the moment pancreatic cancer appears to be resistant to this form of treatment and we need to work on that.
I think as part of a network of excellence, we would institute training programmes that would be shared amongst the various centres. Therefore,

we would ensure that we train the next generation of scientists and clinicians and also, I think, clinical nurse specialists and people who work in similar roles, who are fundamentally important to the care of our patients and are often overlooked. I think that network of excellence will also give the opportunity of coordinating industrial collaboration, so that trial participation is more efficient and we produce both rapid and high-quality trials.

One of the things that I guess I would like to see – and obviously I am biased, as I now work in this area – is some focusing of funding on pancreatic cancer research. As soon as you suggest that, you hear chimes from the other tumour types – and the Baroness may want to comment on this – that "Why should we disadvantage other tumours in order to support pancreas cancer?" and that "Everyone is as deserving of our research money."

I think there are lessons that we can learn from pancreatic cancer that would extend into other tumour types. His Lordship mentioned the molecular markers of disease; KRAS is part of a signalling pathway and as a protein which is mutated in 95% of tumours in pancreas cancer. If we could find a drug to target that target, we would make a major difference to the majority of patients with adenocarcinoma, but also to lung cancer and to colon cancer, if we were able to unlock that target.

The other area where I have some research interest is in the impact of the stroma. There are many cells surrounding the tumour cells in this disease which protect the tumour cells from immunotherapy, radiation therapy and from chemotherapy. Again, if we can unlock that key as to the role of the stroma in resistance to therapies, I think again we will make a major difference in this disease, but also that will impact on other cancers. I think investing in pancreatic cancer is a very sensible way to go forward.

Eric Ollerenshaw: That's really interesting, thank you; I'll come back to you. Sorry, Andrew?

Prof Andrew Biankin: First of all, I'd like to echo exactly pretty much what Duncan Jodrell has said. I'd like to though approach it from a slightly different perspective and that is: what can we do with our current systems? What can we do with the capacity we now have to really look at pancreatic cancer and why we've failed so terribly for the last 50 years or more, 60 years, to make any advances?

We are starting to understand that even though cancers look the same under the microscope, they can be profoundly different. We are seeing associations between particular molecular profiles and a particular therapeutic. If you can imagine in a cancer that has a dominant subtype – the oestrogen receptor in breast cancer – that is the ultimate targeted therapy; it's been around for 30 years and perhaps the most successful target therapy are anti-oestrogen therapies. That's when we have one target that's present in about 60 or 70% of a particular cancer type.
We're making inroads into those where the subgroups get smaller and smaller, like in lung cancer, but what happens with those cancers where you have a lower incidence and you have small subgroups? What we're

seeing in pancreatic cancer from a genetic perspective is that we see a diversity of diseases, but we see dramatic responses in individual patients, where just through luck the specialist has managed to pick off the shelf some particular drug.

It doesn't happen in the UK that often, but where there are booming private practices it often does. You see these patients, patients that are often part of my practice, that will just suddenly get the right drug and they will respond dramatically. We call these 'exceptional responders'.

To a certain degree, our system is not set up, not just from this perspective but also due to the rapid progress of pancreatic cancer. Countries like Canada, the US are setting up systems, usually in hospital environments, to accelerate the assessment of a cancer, to interact directly with the research world, so that you're bringing your service delivery closer together to your research practice, so that you've got an integrated system so that you don't have six weeks waiting around to see whether a patient is eligible for a clinical trial. You action that almost immediately, because what we're doing now just doesn't work, unless just through luck we just happen to get it right.

We need to re-engineer the way we approach pancreatic cancer, from a clinical care perspective and from a treatment perspective, to be specific to that disease. What it needs is rapid assessment, direct integration with research, and overcoming those barriers between clinical care and research that tend to be growing further apart but coming closer together.

Eric Ollerenshaw: Fascinating. Lord Aberdare, do you want to kick off? Go on.

Lord Aberdare: I'm not sure I have anything to ask on that.

Eric Ollerenshaw: Baroness Morgan, you were challenged.

Baroness Morgan: I hope I wasn't challenged; I was invited just to comment. The barriers between academia and clinical practice, you're saying you want to see those broken down or that there's been a trend for greater barriers to be established, so I'm just wondering, in really direct, blunt terms, what does that really mean? Is that code for something, because it would be really good to know?

Prof Andrew Biankin: No, it's not code at all. Basically, the clinical service delivery is focused on clinical service delivery, the research is focused on the research component, and then we're trying to fill in this translational gap from the edges. What we need to do is how do we integrate the systems? What are the particulars?

In some ways we can do it; as researchers, we often purchase NHS clinician time to bring them into the system. As clinician scientists, we work in the clinic, but what we need is the research to be an integral component of the system, which I think pancreatic cancer needs.

When a patient presents with a query of suspected pancreatic cancer, they don't just go through the standard routine; it's important for us to do this quickly and it's important for us to offer research options to that patient, in the setting of a clinical trial, rapidly, as compared to where we have the luxury of waiting in other particular disease types.

Baroness Morgan: What would promote that change in the practical, real world?

Prof Andrew Biankin: What they're doing in Ontario as well is something they've created called the McCain Centre, colleagues do it at MD Anderson, they do it in various focus centres in the United States. That is when a patient presents with pancreatic cancer or is referred to the MDT, they go straight down a pathway of rapid assessment, assessment for their clinical care.

Part of the assessment of their clinical care is their research care as well, so they get their scans done within a week, they get assessed within a week. This is not through repeated visits to the MDT; all the data are presented at the first interaction with the patient. This is the decision for treatment and these are also your research options for clinical trials, because the care we give at the moment isn't really working.

Baroness Morgan: That doesn't happen now because there isn't the leadership or there aren't the resources?

Prof Andrew Biankin: I think it's a complex of all of those; it's because pancreatic cancer needs to be treated differently for these particular circumstances. We're set up for a broad approach, but doing this rapidly, simply re-engineering some of these processes within the confines of the current budget or current expenses, would it accelerate how many patients get onto clinical trials, if we have a patient right at the first interaction being assessed for their feasibility or their opportunity for clinical trials?

Ali Rees: Yes, it would. If you had an aspiration, it would be that when a patient presents you might have 10 options of clinical trials. All the trials are open, the patient is screened and, depending on the outcome of the screening, the patient goes into that trial, irrespective are where they are geographically in the country. That's done quickly and we talked of cutting down time in terms of regulations, cutting down times in terms of individual R&D.

Baroness Morgan: What I'm trying to get to is, as parliamentarians, we're wanting to understand. You're saying, "That's the way to go." What I'm really trying to understand is what is stopping us from doing that and what are those steps? If we were to make recommendations, if the key policymakers were listening now, what would we say? What has to change to make that possible for you in your working environment?

Charles Akle: Can I just add to that the extent to which this is specific to pancreatic cancer, which seems to me to be quite a hard sell, or whether there are other conditions which would require a similar approach, in which case we're setting up a special channel for those conditions and diseases which require this kind of very close link from the patient to the research?

Prof Andrew Biankin: What I'm saying is that that probably is the case for many diseases and many cancers but most profoundly in pancreas. Perhaps why we're failing, why 50% of patients don't actually receive any treatment, is because by the time they get the opportunity to get treatment it's six weeks or two months and the average survival of untreated pancreatic cancer is six weeks to two months.

Eric Ollerenshaw: Yes. Sorry, Duncan, you want to get in; go on.

Prof Duncan Jodrell: Really it was just to pick up on a point that Dr Diana Tait mentioned earlier. Probably to expand on that a little, we talked about the fact that the way job plans are set up these days and the pressure has come on to take on more and more service sessions. Actually, I'm surprised at the number of colleagues of mine for whom the multidisciplinary team meeting is not actually factored into their job plans.

Obviously multidisciplinary team meetings are the first time a patient is presented, in theory, to the multidisciplinary team so that everybody is there. For me, that should be the route into research, but if these multidisciplinary teams are not appropriately resourced in terms of sessional commitments and time to discuss patients appropriately, then that will be lost.

You've already heard about putting sessions for research into job plans as well, and I think those are things that over the last few years we have seen be squeezed incredibly by the service load that we're taking on. Therefore, these things are being missed. It probably is relevant to other cancers too.

Eric Ollerenshaw: Sorry, Lord Walton.

Lord Walton: Yes, a couple of practical points. Has the actual planning and conduct of clinical trials become any easier following the establishment of the Health Research Authority? Of course, this was based upon a report by Sir Michael Rawlins, chaired by Michael Rawlins, for the Academy of Medical Sciences. That really is point number one.

Point number two: if you look at the whole prospect of funding for the field of oncology, including particularly pancreatic cancer, the major players presumably are still Cancer Research Campaign, Medical Research Council, BBSRC. To what extent does the support that comes from those different bodies, how does it compare and is there any support coming, for instance, from the National Institute for Health Research? Looking forward to the Crick Centre in London, do you think that this is going to help to further the programme of the research into pancreatic cancer?

Prof Duncan Jodrell: I think taking the first question, the Health Research Authority; I would say over the years that the passage of a protocol through the ethics system and through the MHRA has become more efficient.

The point I alluded to earlier is that then still, if it's a multicentre study, which for a rare cancer you need to do because no single centre will have the volume, you need to have multiple, separate R&D contracts.

I think the coordination of that and a single sign-off for that would be the next big step in making clinical trials more effective, and I would just ask that everyone supports that initiative and that is pushed through.

Lord Walton: And funding?

Prof Duncan Jodrell: Andrew may want to answer on the funding side, in relation to the MRC. In Cambridge, we have an NIHR Biomedical Research Centre and clearly that supports our activity in pancreatic cancer. Whether organisations are coordinating their funding and whether they could be encouraged to do that to support a network of excellence may be something to consider.

Prof Andrew Biankin: Most funding bodies don't have specific calls for pancreatic cancer; they will have general calls and one may choose to focus on pancreatic cancer as one of those calls. There are some funding bodies that do focus on pancreatic cancer.

Lord Walton: Do you have any problem with the overheads, the so-called 'well-funded' laboratory, which used to be the basic requirement in universities and so on, so that the host institution covered the actual availability of the infrastructure, whereas the research organisations paid the actual direct cost? I know that's been eroded, but is it eroded badly?

Prof Andrew Biankin: It's one of the challenges we constantly face and that is the bit that nobody wants to pay for. These are the bits that make things happen. One of the elements of integrating with the NHS and having team s network side, is who runs the network? Who makes that particular effort even happen?

The universities want to avoid paying these overheads, because often getting funding that doesn't attract specific overheads is challenging for them to deal with. I think this discussion happens everywhere in the world – it happens in Australia, it happens in the United States – is that who pays for the bits that nobody wants to pay for?

Eric Ollerenshaw: Barbara McLaughlan, you want to come back on something, I know; go on.

Barbara McLaughlan: Yes, just taking up on the point you made about MDTs, of course there is now a service specification on pancreatic cancer that the new NHS England system has introduced. I'm not sure to what extent it would be possible to make those links with research in those service specifications. Since Simon Stevens has just started a big review of specialised services, I'm wondering whether that's something you could follow up on to see whether those service specifications actually help the research side of things, or whether they reinforce the silo working that you also referred to.

Prof Andrew Biankin: Yes, a key element is that we have made no progress in this disease for 50 years. Perhaps the ones that we have cured we got the diagnosis wrong. What we're doing now just isn't working and so there needs to be some

degree of freedom that research becomes an integral component of it, somehow alleviating the fear of clinicians that "If I don't do what everybody says I should do, I'll get sued or I'll get the finger pointed at me."
We just keep doing the same stuff; it doesn't work. A way to get past that is research and there are some people around the world that say, "Research medicine is the best medicine." To a certain degree, we have to start to move back to that.

Eric Ollerenshaw: Duncan, then Dr Diana Tait, go on.

Prof Duncan Jodrell: I think the other stark figure that we have to be aware of is that although pancreatic cancer is the tenth most common cancer, it's the fifth most common cancer killer. The projections from the American Association of Cancer Research are that in five to ten years' time it will be number one or number two because of the lack of progress we're making in this disease.

Eric Ollerenshaw: It's important figures, thank you. Sorry, Dr Diana Tait, go on.

Dr Diana Tait: I think we ought to somehow get the NHS to buy into research, so that trusts in some way are judged more on the research that they do and the number of patients that go into trials, because there are all these various assessments they go on and reviews, but in terms of if you're putting only 2% of your patients across the board into trials or other places are putting in 30/50%, the patients are getting, as you say, a better quality of care and something that everybody can benefit from and learn from. I think for some way for the NHS to be rewarded more for taking part in trials.

Eric Ollerenshaw: Or at least make it part of the inspection regime.

Dr Diana Tait: Yes, or make it part of the inspection routine

Eric Ollerenshaw: I don't know if it is or it isn't; I've no idea what the criteria are.

Dr Diana Tait: Make it part of the stick rather than the carrot, but the carrot is always more appealing.

Eric Ollerenshaw: It's useful, yes. Sorry, Baroness Morgan?

Baroness Morgan: I was going back a bit to the R&D centralisation of approval; what has to happen for that to become a reality, does there have to be legislation? What are the practical steps that will get us to that? Is it going to happen anyway? You all mentioned it as being important.

Lord Walton: The health researchers already can give approval, can't it, before they conduct clinical trials? That's one of the major developments of the last 12 months.

Baroness Morgan: It's not happening yet.

Ali Rees: Yes, so we essentially have three approvals you have to gain. You have to have the MHRA approval; you have to have an ethics approval. Both of these are centralised UK processes, but the R&D say, "It's local to each

individual trust," and it's still varied. There are steps being made towards having a centralised R&D, but we're not yet there and I think the discussion around a centralised R&D has been going on for some time.

I'm not sure where we are exactly with that process, but we need to push that through, because if you have one centralised R&D then you have all your trial sites open round the UK at the same time. The patients have access to the trials potentially 12 months earlier in some areas of the country.

Baroness Morgan: At the moment, we don't know what's stopping that from happening. We're expecting it to happen.

Ali Rees: Yes, there's nothing specific that I know that's stopping that from happening, but it hasn't yet happened. Whether there's a legislation change that's ongoing, but it's something that would make a huge difference in allowing patients access to the trials a lot quicker.

Hollie Chandler: Can I just make a point? The Department of Health has approved for the centralised approval system for the R&D.

Charles Akle: I'm not sure that's relevant to the trials that we do at the moment, is it? Is it the specific subset of trials with the pilot?

Hollie Chandler: They're looking to harmonise all the R&D approvals across the trust guidance and that's part of the pilot.

Lord Walton: The Government's recent decision, surely, to allow the use of unlicensed drugs in specific circumstances has actually been a welcome development, has it not? That's one. Have you any views about the Saatchi Bill, which is at present being reintroduced into the House of Lords?

Eric Ollerenshaw: What is it, the Saatchi Bill?

Lord Walton: Lord Saatchi has tabled a private members' bill, which has been reintroduced into the House to make it possible for a doctor to introduce an unlicensed form of medicine as a matter of urgency, in the belief that it might be effective in patients with, for instance, advanced terminal cancer.
It's very controversial, but it's getting a great deal of support in the public view. It's not getting so much support in the medical and scientific circles, except there are certain people who have given it considerable support, because the general belief is that the so-called 'Bolam Principle' – do you know about the Bolam principle? – the Bolam Principle, based upon a legal judgement, Bolam versus Friern Hospital Management Committee years ago, which decreed that it was not negligent if a doctor were to give unlicensed drugs or treatment which was based upon a considered view of a number of people in the medical fraternity. It did not have to be the majority view.

That Bolam Principle is in law still sufficient to protect people who do start unlicensed treatment. There's still, nevertheless, a lot of support for the

Saatchi Bill and I think it's important to recognise that it probably will be debated, I think, in the next year in the House of Lords.

Prof Andrew Biankin: That's a very important issue, because the systems we have in place are not dealing with where we are and where we're moving to in cancer treatment and cancer research, in that it's very drug based. Can you imagine if we start to understand that cancer is not grouped by organ; it's thousands of different subtypes. Every different subtype is an orphan cancer. How do we deal with that in regulation?

Eric Ollerenshaw: Yes. Sorry, gentleman.

Charles Akle: I've actually spoken to Maurice Saatchi and his intentions are wonderful, but what he doesn't realise is that he's trying to protect doctors from lawyers – actually, he needs to protect doctors from other doctors.

I think part of the issue that was alluded to colleagues is that it's the ethos of the national multidisciplinary committee and doctors not to rock the boat. If there's something that is slightly out of the ordinary, they tend to go against it. Five years ago, most doctors believed immunotherapy was magic; after last week in Chicago, every oncologist has suddenly become an immuno-oncologist, so people can be persuaded.

The Saatchi Bill is not broken; the law allows a doctor to use anything he wants. The problem is that the European Clinical Trials Directive has made that kind of experiment difficult.

Then the other point about the polymorphism of cancer and the fact that it's very difficult in a rare condition when you need a combination of treatment – one treatment doesn't work in cancer, particularly in the pancreas; single agents do not work or they don't work. Coalition may not be popular in government but they work very well in cancer.

How on earth, if you've got four or five variables, particularly when you've suddenly discovered four or five pathways, which our brilliant colleagues have done, and you think, "We'll mix-and-match these four"? You can't do it without four variables into it; it's a nightmare, especially in a rare condition.

What you need and to answer your question about facility, because otherwise every other cancer type will say, "Hang on, what's so special about you? My son have; I've got so and so," you need to achieve the achievable. The last Government did actually produce 15 or 16 centres of medical excellence that were supposed to be able to, let's say, push the envelope; they were allowed, in theory, within that envelope to do slightly crazy things, given that the patients would permit it.

The danger with Maurice's bill on a regulatory aspect is the danger that poses to charlatans and protecting the poor patient; we must protect the patient. These things are done within the centres of medical excellence with full patency and publication both of positive and negative results. We shouldn't be afraid of having negative publications. There's always been a problem, we always have to publish something that is positive; why can't

we publish things that don't work? Sometimes you have to be allowed to that.

Sorry, I've gone off quite a bit but the principle is there. The centres of medical excellence are already there, the Government doesn't have to pay any more money; just let the doctors within those centres, like in Cambridge, like in Glasgow, like in Liverpool, leave them within their area to get on with it and protect them from things like the R&D issue; set the European Working Times Directive. That's what the Government needs to do and it won't cost it any more money.

Eric Ollerenshaw: You'd be very good in the civil service, actually; ministers will like you a lot. In fact, I'm picking up myself on that this European Trials Directive has actually been raised before. I thought there'd been some, dare I say, watering down of it or something, or is it still the big issue? You raised it to begin with, Professor Jodrell, but I think you were going to respond.

Barbara McLaughlan: The European Trials Directive is being replaced by new regulations.

Eric Ollerenshaw: Right, that must be where I picked up on it.

Barbara McLaughlan: Which will apply within all the countries, without any need to translate it into the legislation of the individual countries. Therefore, there should be consistency in the way that trials are set up in the way that results are reported. This includes rules about reporting clinical trial study reports within a year of a trial having completed.

I don't know all the details, but there are also some rules about the way a trial will be approved across the European Union. Anyway, I think basically there have been a lot of concerns about the European Trials Directive and a lot of them are now being addressed; that's anyway what I hear from my colleagues in Europe, but I'm not sure whether you have more insights.

Eric Ollerenshaw: Sorry, Professor Jodrell?

Prof Duncan Jodrell: I don't have any additional insight to that, but I do know that it *(the European Trial Directive)* is something that needs to be relaxed, but maybe not to the extent of being able to administer drugs in an unregulated way, which is effectively undertaking a clinical trial but in a completely unregulated fashion.

Eric Ollerenshaw: We need to find out about that, I think, where we're up to with it. You also talk about KRAS and stroma and leading to other cancers, and I thought that's a very good political angle with a small 'P'. If you're saying, "It will help in other cancers," what's the argument against "Why not start with the other cancers and then come back to pancreatic?"

Prof Duncan Jodrell: I think I suppose what I feel is that KRAS is at the start of a pathway; Professor Biankin has already alluded to the fact that within that grouping, if you like, there are multiple subgroups, which may well benefit from other therapeutics.

I think people need to come together collectively as these Dream Team concepts of approaching these things, rather than necessarily waiting and relying on someone else to come up with it.

The RAS project in the US, now the NIH is putting $10 million a year into trying to tease that project or to tease a solution to that problem. Hopefully something will happen there, but again you're right – you can sometimes focus on the targets in the disease. I think we would benefit by having a network of people interested in pancreatic cancer per se.

Eric Ollerenshaw: Could we use the argument which you raised, those horrifying statistics that everybody's looking at, if we don't get something moving in terms this cancer that that's the reason to start with this one?

Prof Andrew Biankin: We're not really starting with this one; we have developed advances in a personalised and a stratified approach in other cancer types. Because of the diversity of pancreatic cancer, there are drugs out there that will work in pancreatic cancer or a particular subtype, but we have no method or system to detect the right patient at the right time.

It's called 'rescuing and repurposing therapeutics'. The fastest road to market is to have a drug that you already have present and use it in new disease, but there are all sorts of regulatory challenges, economic challenges about doing that.

Eric Ollerenshaw: What I'm trying to get to is an argument to ministers and civil servants that this deserves extra research funds. That's what I'm trying to see in my mind, how we get to that point to convince them.
One is obviously the horrifying figures if we don't do anything and we remain like the last 50 years, but two: that in doing it, like you suggested, then it will help in terms of other cancers. I'm trying to be a politician at the moment.

Prof Duncan Jodrell: I do think it's a compelling argument. As I say, immunotherapy – we heard at the American meetings just two weeks ago about all the advances that are being made in melanoma and renal cancer with the antibodies to PD-1, PD-L1, just to use the jargon. They have very little activity in pancreatic cancer and we don't understand that. Again, if you could unlock that, using the model systems that we have, then again you may provide insights into resistance in other tumours.

Eric Ollerenshaw: The Dream Team you keep talking about, can you just elucidate how that works in American circumstances and how it would work here?

Prof Duncan Jodrell: Funding is allocated for a specific project within a disease, so rather than just accepting bids from everybody and choosing the best, a strategic decision is made to provide funding for a particular issue within a particular disease.

Eric Ollerenshaw: By whom, the Government?

Prof Duncan Jodrell: By Stand Up 2 Cancer and the American Association of Cancer Research. There is the act in the US about rare cancers, where people are encouraged to focus on these cancers. Again, that has been contentious in the USA because of this concept – should you focus on one particular cancer, potentially at the expense of others? Certainly I think that has provided some of the impetus for doing that.

The NIH are involved, but it's the American Association of Cancer Research that are leading that. What they say is they will take a project, they want it to be collaborative, and then sometimes they will say, "We think this is a good project, but actually why don't you bring so-and-so in, because we think they would handle it very well too?" They actually then amalgamate people to form what they call the 'Dream Team'.
One of the problems that we have in the UK is that amongst academics we're still set up to try and compete with each other. I think as we go forward we have to find a way of crediting senior academics for team science and, rather than having the single-author paper in Nature which makes your career, that you actually get credit for being on a 25-author paper which actually makes an impact on a disease.

Prof Andrew Biankin: The physicists have managed to do it in biology, and in clinical science we haven't been able to do it. This is from someone who publishes papers with 125 authors.

Eric Ollerenshaw: For the layperson we have this view, don't we? We've got this incredible NHS, which I do think is incredible what it does and so on, and therefore there is a well-structured, centralised system. You did say I think at some point that we have, in a sense, a unique opportunity in the UK, perhaps because we have got that structure, but then you're telling me in a sense that doesn't work. Is it because the academic system is outside of it?

Prof Duncan Jodrell: I personally think that because of the development of a number of major centres now, a lot of the funding that has come from Cancer Research UK is being pushed towards us collaborating with each other. I think that environment has been developed.

I think pancreatic cancer is seen as an emerging disease and people are not particularly siloed. Because it's a rare disease or a relatively rare cancer, people realise they have to collaborate to make a difference.

Also, it's a difficult problem and I think we realise, therefore, again that we need to work together to solve it, but I think the opportunity is there right at the moment. Andrew Biankin has moved from Australia, Glasgow; we have set up a potential network with support.

Eric Ollerenshaw: Why did you do that, given all these problems in the British system?

Prof Andrew Biankin: Not just me, our whole team, our whole Interventional Cancer Genomics Consortium team have moved. We looked at all around the world where we can achieve what we wanted to achieve next, and it's to take things from the laboratory or looking at tumours in isolation for the genomic issues to

the next step, which is improving patients' outcomes. The NHS is a system that, if unlocked, can allow us to do that.
Certainly Genomics England Ltd has attempted to do that from the other perspective, taking the NHS data, NHS patients, enriching it with genomics and then there's the potential there.

Similarly, in pancreatic cancer and in other cancers we see by closely integrating and linking with the NHS the patient care processes, introducing research at an earlier point in the patient journey is where we can really unlock things that we couldn't do anywhere else – we couldn't do in Australia, we can't do in the US.

Eric Ollerenshaw: Why not, sorry, is that because of the size of private sector or what is it?

Prof Andrew Biankin: It's a massive sized private sector, very large, and then the data just disappears. Even then, there are certain barriers to accessing the data, even in the public sector, that the NHS in the UK has seemed to have overcome, particularly in Scotland with the ability to link things through a client number to access those data, be it through a safe haven, etc.

You can't do that in Australia, you can't do that in the US; you might be able to do it within a hospital or within something like US Oncology or Sarah Cannon, but certainly as a country the UK is immensely powerful to advance this next phase of personalised medicine because of the way patients are looked after. They're all there and we get a full picture.

Eric Ollerenshaw: Really interesting. I always give opportunities to other people who might want to comment; has anybody else got something burning at the moment on this positive point? I'm trying to get that we have a positive point for once. Yes, go on.

Charles Akle One other focal point that came up the other day, because we were trying to run a trial on pancreatic cancer. One of the issues that comes up and why it's easier here – and you're absolutely right, the NHS is a fantastic resource, is the investigative-led trials as well, which again raises the cost.

An investigative-led trial allows someone like Professor to supervise the studies. The Americans now will not do it because of the litigation that's involved. Dan wouldn't do it, wouldn't touch it with a barge pole, because it needs one patient to go wrong in the American system and litigation absolutely devastates the funding.

It's something that can still be done I think in this country, so again we have an advantage. We've lost the advantage of the resurge in clinical trials; everybody's gone off to India, and Russia, and Timbuktu and goodness knows where, whereas we led the way, in my view. I'm sorry to see that it is lost, but I think there is a chance to regroup. The NHS is a wonderful thing.

Eric Ollerenshaw: Yes.

Baroness Masham: If it's so wonderful, why are we so bad at diagnosing?

Prof Andrew Biankin: Because we're in the interim the way we're thinking about how healthcare and research integrate. As we're understanding the diversity of disease, the real ultimate endpoint is where we're working rather than in discrete clinical trials but in large knowledge banks, so we have enough clinical data and enough biological data about the individuals that we treat that every treatment episode is part of a clinical trial. All those data points are recorded and they're in a large knowledge bank that you can access because of the diversity of disease not allowing us to do discrete clinical trials anymore.

If you come to me as a patient and you say, "I've got pancreatic cancer," I can measure what you have in your particular tumour. Then I can look in this knowledge bank and say, "Within the UK we've only had 20 patients like you in the last five years with your particular tumour type, and guess what? Five of them got this treatment and they responded and the rest didn't respond, so this is the right treatment for you."

That's where we're looking at with regard to diversity of disease, personalised medicine in the future. How we get there is the challenge, and the NHS in the UK has the greatest opportunity to do that.

Eric Ollerenshaw: I've got one last, because you mentioned this; is it the Recalcitrant Drugs Research Act, is that what you mentioned? Someone mentioned the act, Duncan.

Prof Duncan Jodrell: Yes.

Eric Ollerenshaw: Is that seen as a good thing or a bad thing in the States?

Prof Duncan Jodrell: I don't really have enough evidence to make a learned judgment on it, but I am aware that when it was put forward there was some resistance from people working in other areas of research. I don't know whether someone else wants to comment on this as to whether since it was put in place it has been a good thing or a bad thing.

Prof Andrew Biankin: This is the NCI, Julie Fleshman, is that what you're talking about?

Dr Diana Tait: Yes, it's the NCI.

Prof Andrew Biankin: Yes, there was a bit of pushback very early on; I remember Carol Weil was having a stand-up fight with one of the congressman.

Prof Duncan Jodrell: I think it's this issue about strategically funding research, as opposed to allowing research to bubble up. I think there are times when actually strategically commissioning research, if you like, or pushing people into certain areas and ring-fencing those areas would be helpful.

I think if we had designated research fellowships within established training centres and an established training network, we would encourage more young people into this disease.

The nihilism that has gone with the clinical aspects is probably a reason why in the past people have not wanted to invest in this or to come into this area. We should encourage them, by trying to attract them.

Eric Ollerenshaw: It was raised in the previous evidence session, wasn't it, about the lack of attractiveness for researchers for some reason. Yes, sorry, Dr Diana Tait?

Dr Diana Tait: I'm just wondering, I think the Academy of Medical Sciences have just published 'Nurturing the Next Generation of Medical Researchers'. That may be something that's worth exploring, looking up what the avenues that they're recommending in that.

Dr Diana Tait: It's the Academy of Medical Sciences.

Eric Ollerenshaw: Useful. Sorry, Baroness Morgan?

Baroness Morgan: Just one point about data – I think it's more from an England perspective – have you experienced issues around data release from Public Health England now that the NCIN has gone into Public Health England? Do you have any views about Public Health England, should they have a cancer strategy now in Public Health England now they have responsibility for that really vital data service?

Dr Diana Tait: It seems to be very clunky. There are some fantastic datasets. Just thinking of the chemotherapy dataset and the radiotherapy dataset – unique; no-one else in the world has them. It's then how do we, say, in the commissioning groups get the data that might tell you what are the patterns of care and where we should be going?

Again, I presume it's funding or it's an organisational problem; it's just very hard to make those links and that needs to be hugely easier. Everybody can't have access to all the data and there are protections that have got to be in place, but I think when the commissioning groups, the CRGs for radiotherapy and chemotherapy, can't get the data they need to plan, there's something wrong.

Lord Walton: To follow that point up though, would you regard the treatment to which you're referring as a kind of routine treatment or is it a highly specialised treatment? Because if it's a highly specialised treatment, it doesn't come under commissioning groups; it comes under the highly specialised groups.

Dr Diana Tait: It does, yes.

Lord Walton: Which are all of them dealing with this in a very specific way.

Dr Diana Tait: These are the specialist commissioning groups I'm referring to, so for radiotherapy and chemotherapy, although I understand there's a possibility that that's not going to be the way forward and that they're not specialist enough, that maybe there will be a different model. That's another story.

Barbara McLaughlan: As you wanted to know what parliamentarians can do from a political point of view, I wanted to raise the fact that the Department of Health is currently

looking at the refresh of Innovation, Health and Wealth, which I think was the policy the Government adopted in 2011 and picks up on a lot of the points around what the NHS needs to do in research to improve that aspect of what the NHS can achieve. So I think looking at the refresher, it would be quite interesting to see whether they are going to pick that up and whether there has been some attempt to look at what has actually happened in those four years and whether they have any other improvements or what further policy options there might be to focus on the NHS doing more in researching and being incentivised in a better way to deliver the opportunities.

Eric Ollerenshaw: Thank you. That's useful. I am wary of the time. In this place, there may be 600 people struggling to get in in three minutes. Or there may be three. I have no idea.

Can I just say that we are extremely grateful, it has been extremely useful. We'll obviously write this up – it would be a draft and you will see a draft. If you want to alter it, you can alter it and what I'll also say is when you leave here and get on the tube or on the train, and you suddenly wish you should have said something which you didn't say, then please let us know. We are trying to get the best, if you like, targeted piece so that we can get the Secretary of State and the Department of Health to wake up on these issues. In that sense, do not feel this is the end of the matter, so if you wish to comment further or put something in, we will be more than grateful for your time. Thank you very much indeed. Thank you.