Welcome to our Spring 2020 issue of Outlook

We are working as hard as ever during our 20th year and in this issue you will read about what our researchers and our fundraisers have been up to in the first few months of our anniversary.

We continue to feel as positive and excited about the future of cancer immunotherapy research as we did 20 years ago. As you know, our original focus on melanoma has extended over the years to include other cancers. We are particularly pleased to report on a new trial, due to start at the end of 2020, for patients with ovarian cancer. We are most grateful to those charitable trusts and private donors who are supporting this project. We are continuing to fundraise for some of the costs, so if you would like to help please do get in touch with Marie in our office.

We are also delighted to welcome a new trustee to our board, Saffron Guy. Saffron has a strong background in biochemistry which is a great asset to our charity.

Having friends who donate regularly is incredibly important as it helps us to plan our research projects carefully and efficiently, and I would really encourage you to do this. As always you can contact our charity’s office for any further information.
FUNDRAISERS

MARATHON RUNNERS – BOXING CLEVER!
ICVI were delighted to get a place in the London Marathon this year as we reported in our last issue. Sami Mason is training and fundraising hard.

We were also very pleased to hear that Charlotte O’Brien has chosen the ICVI to benefit from her marathon run. World champion boxer Barry McGuigan is helping Charlotte with her training. Charlotte is a family friend of the McGuigan family, who sadly lost their daughter and sister Nika to cancer last year. Blain McGuigan, Nika’s brother found out about the ICVI and asked Charlotte to run for us. Blain said, “I know that the ICVI are less known than many of the other larger cancer charities but the reason we chose them is because they’re a small team who we believe are working towards advanced treatment and one day prevention of certain cancers through immunotherapy and vaccines. Everything I’ve read about Professor Dalgleish suggests he’s a man who makes a difference (along with his excellent research team)!”

Charlotte said, “My Dad died from cancer when I was 6 so any charity that helps with the horrible disease is close to my heart and I completely share Blain’s views about you all.”

Not every marathon runner has a world champion boxer helping with their training! Fingers crossed that both of our runners will pack a punch with their fundraising too. If you would like to sponsor them please email marie@icvi.org.uk for details.

LUCY SANDS TRIBUTE FUND – SHOPPING AND SHOOTING FUNDRAISERS
Liz Sands and her husband attended a Charity Shoot day hosted by Mr John Phillips at The Wodehouse, Womborne, Wolverhampton. John had sadly lost his wife Carolyn to Melanoma.

Dr Richard Taylor of Westgate, Deans Street, Brewood Stafford organised the day and his wife Rosemary did the catering for lunch.

Nine guns attended and at the end of the day they were given a choice of charities suggested to give a donation for the days shooting.

Huge thanks to the seven guns who chose the ICVI, donating a total of £1,750 to the Lucy Sands Tribute Fund.

The Sands family and the ICVI are also very grateful to Mr Philip for hosting and Mr & Mrs Taylor for organising the wonderful event.

Lucy’s tribute fund also benefitted from the generous support of the South Staffs district of the Staffordshire Agricultural society, to the tune of £750, raised from raffles and events throughout the year.

Thanks to this tireless fundraising the Lucy Sands Tribute Fund now stands at over £120,000 - amazing!

OTHER FUNDRAISERS
A big thank you to Max Claren and his friends at Warwick University’s Handball Team who recently raised £84 for the ICVI.

FRIENDS OLD AND NEW
Since we started our charity 20 years ago we have acquired many friends, those who donate to us every month. As Mike Ellis, long time friend of the ICVI points out in the letter accompanying this issue, these donations are really important as they allow us to plan for our research. Friends have raised over £218,000 since 2000, funding many hours of our vital research. Huge thanks to all our current friends! Please become a friend! Email abi@icvi.org.uk if you would like more information.

Text CANCER10 to 70191 to donate £10  
Text CANCER20 to 70191 to donate £20
ICVI ARE FUNDING TWO STUDENTSHIPS BEGINNING IN 2020

The first PhD is funded by both the ICVI and Public Health England. This project will look at the effects of vaccination with BCG on our gamma-delta T cell population and from this work we hope to narrow down our idea of the appropriate cell we are trying to expand to target cancer (and also TB). This studentship is funded 30:70 with PHE contributing the larger share.

The advantage of this approach to funding is that all applications to PHE are subjected to rigorous external review. Of the 57 projects submitted, less than 10 were funded, and most were a 50:50 funding split.

The second PhD is solely funded by the ICVI and also builds upon research undertaken in recent years. In previous studies we have shown that gamma delta T cells can be activated by exposure to both live and dead Mycobacteria species. We have also shown that tumour cells resistant to gamma delta T cell directed killing can be weakened using a drug called Zoledronic Acid (ZA).

This project proposes to identify and purify mycobacterial component/s able to directly activate human gamma delta T cells. It will furthermore define the specific type/s of gamma delta T cells activated and quantify their ability to kill infected and/or cancer cells.

The study will complement the first PhD studentship described above.

Ultimately, we expect this work to contribute to the rationale for novel treatment regimens for both cancer and infectious disease.

If you would like further information on either of these projects, or would like to donate towards them, please email marie@icvi.org.uk

OVARIAN CANCER TRIAL

We are delighted to have raised enough funds to give the go ahead for a trial for patients with ovarian cancer.

This study, due to start later this year, aims to determine the cancer-specific immune status in patients with ovarian cancer by the assessment of standard anti-inflammatory and other markers indicative of changes in the intestinal microbiome, before and after standard of care treatment. Changes of the markers over time along with patients’ conditions will be recorded.

If you would like more information on the research behind this project, or to donate towards it, please email marie@icvi.org.uk

NEW RESEARCH TECHNICIAN

We are delighted to welcome Katarzyna Piadel (Kasia) to our research team. Kasia has a degree in Immunology and Infection from University College London. She then undertook a research project based at the Royal Free Hospital which focused on genetically modified CD4 T cells and its application in cancer immunotherapy.

Kasia’s main focus is to support Dr. Alberto Fusi and Dr. Peter Smith with clinical trials on melanoma. There are two ongoing studies: one with IMM-101 in combination with checkpoint inhibitors and one with targeted combination therapy in patients with BRAFV600 mutation. Soon we will be involved in two more related to checkpoint inhibitors in resected melanoma and in combination with adjuvant immunotherapy.

Kasia is interested in how we can stimulate the immune system to achieve better response in cancer treatment and mechanisms that underlie those responses. Her research project is focused on characterising the immunomodulatory effects of IMM-101 on dendritic cells and subsequently the activation of NK cells and CD8 T cells which play a major role in fighting cancer. By knowing the exact effect of IMM-101 on immune cells there is hope that ways could be found to improve it even further or use it in combination with other immunotherapies.

If you would like to donate towards Kasia’s project please contact marie@icvi.org.uk

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GLIOMA – A REFLECTION FROM PROFESSOR DALGLEISH

When the ICVI first started over twenty years ago (as the CVI) our focus was very much on addressing the abysmal prognosis of melanoma. Today outcome and five-year survival of metastatic melanoma has increased dramatically. It is said that if you know somebody with a condition in your personal life then it is likely to be common. The occurrence of primary malignant brain cancer, known as glioma, in five personal contacts, one being a colleague at work, two related to close friends and two being immediate family, has had a major impact on me in this regard. Yet all the figures suggest that glioma is a rare disease, albeit one whose incidence is slowly rising. It has an appalling prognosis and the standard treatment of surgery, radiotherapy and very limited chemotherapy, has not been improved on for over thirty years. I have therefore taken a particular interest in applying the work of the ICVI on melanoma to glioma, to try and improve the dismal outcome of this devastating disease, as well as to explore other possible treatments that appear to have been ignored.

Imagine my surprise to find that there are four randomised studies showing greatly improved outcome and survival in four different approaches, none of which have been accepted as a standard of care. Two of these approaches are well known to us. The first is the use of the dendritic cell vaccine approach, whereby the patient’s dendritic cells are cultured in the laboratory and then pulsed with the patient’s tumour before making a series of vaccines (an approach we have used to make vaccines for melanoma, renal cell cancer and several paediatric cancers). The second is the use of the cannabinoids, including Sativex, with standard treatments showing a very impressive improved outcome, compared to standard treatments plus a placebo. This latter study was extremely gratifying as we have previously published very strong data that the cannabinoids can sensitise radiotherapy (RT), enhancing its impact on a glioma model, where it induced a near complete response, compared with standard RT.

The third and most recent impact is the use of the melanoma antibodies in patients with glioma, where previous studies have been marginal or disappointing. The major impact in a recent report from California showed that when the treatments were given before standard surgery/radiotherapy, etc., the outcome was significantly better than when given afterwards. This difference, which was part of a randomisation study is so impactful that I can see no reason why it shouldn’t be standard of care here and, indeed, I have been involved in making sure appropriate patients can receive it.

The last of these studies involved the use of an anti-viral agent (Valcyte) which was used in a randomised study and showed a very significant outcome. However, it was used based on the fact that many gliomas are involved with herpes viruses. In spite of the very positive outcome, the logic of this and the reliability of the virus associated with tumour was heavily disputed. This has prevented a repeat of this study and progress to approval, in spite of the fact the raw figures show that this agent is clearly an anti-cancer drug, in spite of its anti-viral activity.

All of these approaches have very low toxicity, which can be combined with standard treatments, and all of them are relatively cheap compared to the current standard costs of approved oncology drugs. We now tend to focus on combining these treatments and looking for potential synergy, in the meantime I see no problem in patients being treated with these approaches to gather proof of efficacy and lack of toxicity to encourage their registration and approval to try to improve the outcome of this dreadful condition, where significant improvement has been lacking for decades.
In December last year ICVI staff, Drs Joe Fenn, Laura Ridgley, Jonathan Caron and Mark Bodman-Smith presented data generated from ICVI funded projects at the British Society for Immunology meeting in Liverpool. This is a flagship meeting for Immunology in the UK and is attended by over 1000 UK and international scientists. Our group presented data on the role of (myco) bacteria in activating an anti-tumour response in human immune cells (the gamma-delta T cell population). This area of research, and the greater field of immunotherapy had its own dedicated sessions at this prestigious meeting indicating that it is an expanding field within immunology.

ICVI funded work generated interest and goes further in advertising our ideas to the wider scientific community.

Please find below the two lay summaries for our data. If you would like more information please email marie@icvi.org.uk for the full papers.

INVESTIGATING ANTI-TUMOUR RESPONSES OF MYCOBACTERIA RESPONSIVE GAMMA DELTA T-CELLS

The gamma delta T cell population can be activated by (myco) bacteria. Mycobacteria are currently being used in the clinic by Dr Alberto Fusi and Prof Dalgleish in combination with checkpoint inhibitor drugs and this combination is showing encouraging results. Our laboratory-based work aims to understand how this interplay of treatments occurs and how to improve any responses seen. Checkpoint inhibitor drugs (CPI) release the brakes of the immune system allowing immune mediated anti-cancer responses to be enhanced. Thus far CPI are known to affect the main population of effectors but very little is known about their effect on the gamma delta cells we believe to be activated by Mycobacteria. Laura’s work has identified a unique pattern of checkpoint molecules on the gamma delta cells and this may imply that CPI therapy might need to be modified to maximise the anti-cancer effect of gamma delta cells. Laura is currently assessing the role of novel, and currently used, CPI on this anti-cancer cell population.

BACILLUS CALMETTE–GUÉRIN (BCG) POTENTIATES ANTI-TUMOUR RESPONSES IN VΔ2+ T-CELLS

Joe’s work has focussed on the comparison of two ways of eliciting the anti-cancer activity of gamma-delta T cells. The clinical use of Zometa (aka Zoledronic acid, used in cancer with bone involvement) has been associated with the activation of the gamma-delta T cell subset. We believe that mycobacteria can reproduce this anti-cancer activity and this is borne out by the clinical use of IMM101 by Professor Dalgleish. Bacillus Calmette-Guerin (BCG) is the mycobacteria-based vaccine for tuberculosis and is a model for IMM101 which we can use in the laboratory. Joe’s data show that BCG is better at activating the gamma delta T cells to kill tumour (in this case a tumour cell line called THP-1). Moreover, the release of the molecule granulysin (which we have recently shown to be a chemoattractant for key immune cells) by BCG activation suggests that the recognition of tumour will recruit other immune cells to the fight.

PHD SUCCESS

We reported last time that Emma Sparrow, a previous ICVI supported PhD student, and Mark Bodman Smith have had a review accepted in Immunology Letters entitled ‘Granulysin: The attractive side of a natural born killer’, based on Emma’s ICVI funded PhD. This paper has now been published. If you would like a copy of the paper please email marie@icvi.org.uk
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One hour of research undertaken by the whole of the research team costs £400 and £2,000 per patient per year for a trial (this is an average cost, including salaries, consumables and supervision)

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- Other

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