PE1783/B
Abbie's Army submission of 1 April 2020

My name is Amanda Mifsud, I am Founder and Trustee of 'Abbie's Army' a children's DIPG brain cancer research charity in the UK. This is the same childhood cancer that affected the family Fiona Govan, the Petitioner in this case.

Foremostly I am a bereaved parent of a child who also sadly lost her life to this uniformly fatal and highly aggressive brain cancer at the age of six, this was only five months post diagnosis.

I am truly grateful to be able to provide this patient/family perspective of such a devastating condition and thank you for the opportunity to respond.

'Abbie's Army' as far as I'm aware is the only UK research charity totally designated for DIPG, formed to bridge the clear unmet need for pre-clinical and clinical research. We specifically support targeted research initiatives to help find a cure for DIPG and inform clinical trial treatments that can be more easily accessed by UK families.

As a 'research Trustee' I constantly see many more opportunities to help and support this group of patients than we can fund ourselves, there is no lack in my personal view of applications of quality, tackling new routes for treatment with available new technologies that were never previously possible. All of our funded projects are approved via our own small specialised Scientific Advisory panel made up of DIPG experts.

My daughter Abbie did not receive one drug in 2011 as a 'curative' protocol during her short illness, it was a compelling case for us and is still today for many other advocates. Much DIPG research is parent led worldwide, but we should really be asking ourselves whether this should be the burden of parents and families that have already paid the ultimate price?

Diffuse Intrinsic Pontine Gliomas (DIPGs) are the most aggressive of all childhood cancers, due to their location within the brainstem these tumours cannot be removed surgically, they do not respond to chemotherapy, and radiotherapy only slows their growth giving a temporary respite in symptoms (in approx 70% of cases) this has been 'front-line' and palliative therapy for DIPG for decades.

It was all that was available in our case in 2011 and it is the same today in the UK. This makes absolutely no sense to parents to hear that their child has this most fatal cancer, with the absolute least that can be done.

Working within the DIPG community for the past seven years for research advocacy, and in also providing some parental support, I am acutely aware of the wake of complete devastation around all affected DIPG families… and only that it will continue to devastate until we have some degree of therapeutic success.

The lack of proven effective treatments and scarce trial 'options' are an extremely prevalent constant cause of anger, and a huge frustration to parents, the suffering they have to witness is immense. I have lost count of the number of children I have watched succumb in a very short space of time, with little hope and no options.

We know if everyone could see this it would be stopped.

Currently there is no National trial available on the NHS for DIPG children diagnosed, although prior to COVID 19 arrangements for BIOMEDE 2.0, a second iteration of a previous trial (that our charity was connected to on the biology at ICR) was in progress.

It's my personal view that although biopsy is included, we would still be offering a sub-optimal therapy with this 'single-agent' trial when research already clearly points to a multi modal, multi-combination needed to combat the disease, and indeed combinations are what patients want, as well as require.

It is also randomised with one trial arm Everolimus being used as the most 'tolerable' (based on the previous trial) already knowing that it offers no life extension, until patients 'progress' they will not have the option to try any other promising targeted agents…this I personally find unacceptable. Waiting until progression with a disease like DIPG is also far too late.

There are many global collaborative efforts taking place and with a uniformly fatal cancer such as DIPG where there are research outputs of benefit to the worldwide community those need to be not only shared, but also utilised.

Our research contacts have grown over time with the community and the field is now thankfully highly active, families in the UK see these options available elsewhere and want greater access to those showing promise, it is making travel for treatment overseas become increasingly prevalent, taking hundreds of thousands of pounds out of the UK economy.

Provision of course is hugely complex with many stakeholders involved, but always requires substantial funding!

Efforts have been focused on molecular profiling, and we strongly believe in the necessary funding of targeted research initiatives to improve any understanding of how DIPG develops and progresses. It is the only way to lead development of effective treatment options for all emerging 'subsets' of children with DIPG identified.

We also understand that highly organised clinical trials are crucial, BUT this feasibility to include many patients across countries is a huge challenge within a small patient community. Numerous trials are open worldwide and take too long to accrue patients and data fully to move forward in a meaningful way. As we head further into the realms of personalised 'genomic' medicine this is likely to also only become more difficult, as tumour profiling increases but requires more flexible and nimble study design.

We have always engaged and tried to help on previous Petition applications on this topic, position statements from 'The Institute of Cancer Research' where we have invested £450,000 in the laboratories of Professor Chris Jones, the leading genomist in the world working on DIPG - are quite clear that an expansion in Early Phase Clinical Trials is needed.

"*The ICR would like to see an expansion of early-stage paediatric clinical trials – including for brain tumours such as DIPG – in order to accelerate development of safe, effective, innovative treatments for children. Paediatric cancer medicine needs to incorporate advances seen in adult cancer treatments such as molecularly targeted drugs and the use of biomarkers, and this can only occur through more trials.*

We would like to see additional measures to support the basic scientific research which feeds the delivery of novel drugs and treatments for children to the clinic as early research into paediatric drug targets is currently underfunded.

There is a shortage of early-stage clinical trials testing new cancer drugs in children, and this acts as a major barrier to efforts to improve survival rates from paediatric cancers. Few cancer drugs are developed specifically for children, and when drugs are developed for adults, they are often either not tested in children at all, or not for some years afterwards. The lack of paediatric cancer trials restricts or delays access for children to the latest drugs, some of which could be of significant benefit to them."

In May 2018 the Government announced £40 million over five years for brain tumour research as part of the TJBCM (Tessa Jowell Brain Cancer Mission). Whilst we welcome this hugely, considering the size of the task of course we would always like to see more and there are National charities campaigning actively on the shortfall in this figure. In order to keep some equality with NCRI funding to the more prevalent adult cancers the estimate required to provide a more sustainable research environment is more likely around £35 million needed each year.

Government also have 'welcomed the launch of the Tessa Jowell BRAIN MATRIX, a new trials platform that will give people with brain cancer, **including children**, access to trials of treatments that are best suited to their individual tumour profile'

Again this is not yet recruiting any patients, when it does it will initially be adults and will not be for DIPG/HGG patients….this really is such a specialised area…and dependant on processing surgical tissue or biopsy that is not routinely carried out for DIPG children.

Although trials such as BIOMEDE 2.0 still don't go far enough they are disease specific and therefore important that it is re-instated as soon as possible, if only to be under a Principle Investigator that is an advocate for these patients, and they receive the correct support.

I would be grateful if you would question precisely how the announced figures have directly impacted or even related to childhood brain cancer research and diffuse intrinsic pontine glioma.

It's inevitable that when trying to improve policy and care for all patients that the 'rare' and less significant disease areas within the subject are going to be overlooked. It's perhaps also inevitable that if there is a historical lack of funding going to these projects that are not considered to 'make a wider impact' that researchers simply won't apply, and they will look to other funders to get pre-clinical research moving.

It's therefore important to understand fully after the funding call for brain cancer research was also highlighted by NIHR how many research proposals for childhood brain cancer projects specifically were received and approved? and what those reasons were if they were declined? Is it truly the case that NIHR do not see applications of quality or quantity?

We ourselves know that the stringent 'peer review' process through NIHR may just not suit or be conducive to funding small cohorts of childhood cancer patients…a potential and very promising application for a clinical trial of CAR-T therapy , the first of its kind for DIPG in the UK was recently denied MRC funding because of one opinion of a statistician, it was for twelve patients! So how do we get around this point when the prevalence is low?

We cannot ignore these cases that are 100% fatal in every instance, surely, we should be commissioning the research we need to overturn that statistic or funding those proposals that 'scientifically' make sense, of course backed up by robust pre-clinical data. The CAR mentioned above for example is already in use in neuroblastoma trials and it is known that there is no 'off-target' activity, mitigating steps have been taken as far as is possible for use in the brain stem, anatomically a very precarious area for inflammation.

Apologies if this is longer than needs be, I just find it incredibly frustrating to discover that where there is any potential for changing the 'inevitable' outcome for all these young patients every effort is not made to accelerate implementation. We can only do what we can.

Thank you again for the opportunity to provide a few thoughts on the Petition from the perspective of a DIPG diagnosis.

There is information relating to DIPG on our website at www.abbiesarmy.co.uk please do not hesitate to contact myself again should you require any additional support.