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Dear Lori

Tocilizumab for SJIA – Single Technology Appraisal

Thank you for the opportunity to make a submission in regard to the STA in respect of Toclizumab for the treatment of juvenile idiopathic arthritis.

The scale of the problem

JIA is an inflammatory condition of unknown cause which causes chronic arthritis in children and young people. In the United Kingdom, approximately 12,000 children (1 in 1,000), under the age of 16 have Juvenile Idiopathic Arthritis. JIA is one of the commonest causes of physical disability beginning during childhood. Systemic JIA is a subset of JIA that describes systemically ill children comprising between 10 and 20 per cent of all JIA cases and mortality rate is higher than in other JIA sub-types.

The Need for Tocilizumab

My Paediatric Consultant friends tell me that TNF blockade has been disappointing in its effects in methotrexate resistant children and adolescents, therefore given the severity of disease in Systemic JIA and a higher mortality rate, having access to a biologic with a different mode of action, i.e. Tocilizumab, is vital. Clinical Trials in Japan have demonstrated that many of the symptoms of SJIA can be controlled with periodic infusions of Tocilizumab and we await the publication of current UK trials for this agent in SJIA (TENDER) and in polyarticular JIA (CHERISH).

Potential Economic Benefits of using Tocilizumab vs standard (failing) treatment

The cost to individuals and their families of SJIA is high and can impact an individual their life long. Therefore giving them the possibility of trying a drug which could bring huge improvement in quality of life, the ability to remain in school, enjoy further educational opportunities, function normally in regard to socializing, and take part in leisure and sporting activities, etc. cannot be underestimated. The societal costs and savings if SJIA enters remission before causing damage allowing children to become adults better able to enter the workplace are considerable. There is the probability of being able to reduce other medication, importantly steroids, which are extremely damaging taken long term.

The costs of caring for children with JIA can also be considerable, especially when parents have to leave work or reduce their working hours to look after the child and the financial cost of reduced income simply adds to the overall burden of stress on the whole family.

Multi-Disciplinary Team Care

All types of JIA should be treated in a holistic manner by an appropriately qualified and specialist, expert multi-disciplinary team. Such tertiary teams are not available in all areas of the UK and children and their families often have to travel considerable distances to obtain treatment adding significantly to the overall burden of disease.

The Impact to Children and their Families

I attach to this submission **Appendix 1**, The Family's Perspective – [redacted] Story and Appendix **2**, The Individual's Perspective – [redacted] Story. These two moving accounts of the impact and burden of SJIA on the child and the family will, I hope, help the Appraisal Committee to understand the true impact of this disease much more eloquently than I could do.

Both [redacted] and [redacted] mother, Sarah Sugden, will accompany me to the Appraisal meeting as NICE have given permission for our team to extend to 3 instead of the usual two Patient Experts as the view of the family is so crucial.

You can clearly see the enormous potential to return an extremely sick child requiring significant on-going and expensive NHS services, to 'normal' health in [redacted] story, and the huge and positive impact of this to the individual, their siblings and the whole family involved. Steroid burden and toxicity can be huge in SJIA, and there is considerable evidence now available that disease control with tocilizimab will allow steroid reduction potentially to zero as in [redacted] case. I hope that the Committee will also take this into account when considering the health economics of passing Tocilizumab for use in the NHS.

Yours sincerely

[redacted]

Appendix 2 to NRAS submission on Tocilizumab

An Individual's Perspective

Living with Systemic Juvenile Idiopathic Arthritis – [redacted] Story

As a child being diagnosed with JIA just before my 3rd birthday, there was a big impact, not only on my life but friends and families.

Trying to ensure joints were held in a reasonable position, I would wear night splints. These consisted of full length leg splints and hand paddle splints. Initially they were put on using velcro straps but being a child and them not giving you the most comfortable of sleeps, I would take them off. In the end the splints would be bandaged on.

Due to the splints this meant that in the night if I needed a drink or wanted to go to the bathroom, I would have to call out for my parents who would then carry me or hold a drink for me to sip. Even during the day, although I was old enough and capable of going to the toilet, I needed help wiping my bottom as I didn't always have the strength.

Morning stiffness and pain was a big factor. I would have a warm bath each morning, partly to help refresh me after being clammy during the night but mainly to help ease my joints and help with stiffness. I would need to be lifted into the bath and because by this point my dad had gone to work, my younger brothers had to stay in their bedroom until Mum could help with them. I would need help with getting dressed, particularly with buttons, socks and shoes. While I had breakfast my Mum would see to my brothers.

Going to school had its own challenges. Only being able to walk very short distances, I would often share a pushchair with my youngest brother while the other brother walked. This would cause friction.

I would be very self aware of my legs, my knees were swollen and I had to wear callipers. The school agreed that I could wear trousers but looking back now, this set me apart from the other girls probably the same as what the callipers would have done.

At school, I would have difficulty writing for long periods and although I had work splints, I found these too warm and restrictive. During assembly, I would sit on a chair as getting onto the floor was too difficult. At lunchtimes I would eat my food and then go to the medical room where I would rest. Luckily I was able to take a friend so I didn't feel excluded.

I had problems climbing stairs so for lessons that were upstairs I would miss out on them, often doing extra English. Due to limited mobility, I would also leave lessons 5 minutes early to make it to my next lesson. Even though I enjoyed it, I couldn't always take part in PE. I definitely didn't take part in things such as hockey.

With the fatigue side, I really struggled. It was catch 22 because being in constant pain meant I couldn't always settle. I would then cry in distress which kept my brothers awake . If

I didn't sleep due to the pain and discomfort I would then fall asleep at school, or if I had medication to induce sleep I'd then be drowsy for the next day. This affected my mood and concentration levels as well as having an impact on family life. During secondary school, the amount of books rose considerably and I struggled trying to carry them. Mum thought she was helping when she got me a trolley bag (old fashioned one) but it ended up isolating me even more.

Hospital visits were 3 times a week; 1 physio, 1 hydro and 1 gold injection. Most of the time these appointments were early morning. When it was before both my brothers were at school, they would have to come along unless Mum could get someone to look after them. Facilities at the children's centre weren't really equipped for families so Mum would have to take them to a nearby café while I had treatment. This would be frustrating for my brothers, especially when all they wanted to do was play. At the time my parents didn't have a car and Mum found it very difficult trying to get 3 children and a double buggy onto public transport. Lots of forward planning was always needed.

Holidays meant we were more like a splinter group with my Mum looking after me as I walked along slowly, resting every now and then while my Dad would take the boys off to play football and feel like they were having a holiday. I would get tired easily and so we'd head back to the hotel for me to rest.

Playtime was a pretty isolated affair. I wasn't able to walk far, let alone run so didn't often play outside with friends. If I was invited to birthday parties I couldn't take part in some of the usual games such as musical chairs or statues. I couldn't really dance much, even though I loved dancing because of the pain in my feet. I would sit out on most of the activities, unless it was something like pass the parcel but even then I sometimes struggled with unwrapping the paper.

My brothers also felt isolated. While I had attachment with my Mum, my brothers didn't so much. This was down to the splinter group effect. If I had hospital appointments that lasted most of the day, Mum couldn't pick my brothers up from school. Once a month my youngest brother had a book club where he could choose a book to take home and read. All the other Mums would arrive slightly earlier and help choose a book. My Mum wasn't always able to do this and so my Nan would help. While Mum tried to spread herself equally between us all, sometimes my needs took priority over my brothers and this did have an effect.

Additional day to day things that I needed help with included cutting up food, opening doors especially if they had door knobs rather than door handles, making drinks, opening bottles and turning taps on/off. Stair bannisters had to be reinforced because I would put all my strength into them to get up stairs. I had beautiful long blonde hair but I struggled with brushing it so it would often get knotted up. It would then hurt for Mum to brush it so in the end I had it cut shorter to make it more manageable. Short hair combined with wearing trousers to hide my callipers, I felt more like a boy than a girl.

Illness was another big thing, particularly with having a compromised immune system and being on steroids.This meant I was more prone to infections such as impetigo. Chicken pox left me severely ill and it took me a long time to get over it. I also ended up being admitted into hospital aged 7, when I caught hepatitis A at school.

Teenage years was a whole other ball game... Trying to fit in with my peers, comprehensive

school became a competitive playground. Wearing orthopaedic shoes and callipers was like having a spotlight shone on you. To be considered a “loser” was one of my biggest fears and insecurity was a regular feeling. The journey to being a teenager can be a difficult one but when you are also trying to accept you have a disability, it can be filled with dread. Your body is changing, hormones are racing but you still feel like a child with the things that you still can't do..

Appendix 1 to NRAS submission on Tocilizumab

A Family's Perspective

Living with Systemic Juvenile Idiopathic Arthritis – [redacted] Story

Up until he was 2 years old [redacted] had been a happy, healthy young boy. He went to bed on the day of his second birthday, March 2003, after an afternoon spent with family. Through the night [redacted] was awake running a high temperature, and saying he hurt. The following morning when we got up [redacted] was still feeling slightly unwell and was slightly lame. This same pattern continued for about three months. We visited his G.P on many occasions and he was given courses of antibiotics as it was felt there was some underlying infection that was causing the fevers. Every time the medicine, including pain killers, was stopped the symptoms would recur. After several hospital visits/stays we were referred to the Paediatric Rheumatologist at the Leeds General Infirmary. This is where we were given the diagnosis of SJIA. Our reaction was one of shock. We thought arthritis was a disease old people suffered from. The information leaflets we were given were as if they had been written about [redacted].

[redacted] was started on a small doses of steroids and for a time this seemed to keep things under control. The first joints to be affected were his knees shortly followed by his wrists.
A couple of months after starting the steroids, Methotrexate was introduced. Things seemed under control once again. At this time [redacted] was managing to carry on as a child of his age apart from some early morning stiffness. This took about an hour before we could carry on with the day.

As time progressed, more and more of [redacted] joints became swollen and painful. [redacted] was struggling to get out of bed in the morning and was unable to walk down stairs, having to be carried. When [redacted] was at his worst he had to be dressed and needed help feeding.

[redacted] has a brother seven years older than him, [redacted]. It was so difficult trying to carry on with life without it affecting him also. He was trying not to get upset seeing his brother in pain, unable to play, and in the extreme, unable to feed himself. One of the worst memories for us all was Christmas day 2007, [redacted] was in so much pain he was unable to open any of his presents. I was once asked by a lady in our local shop why my little boy always looked so miserable, I was too upset to speak.

[redacted] has had several different drugs since developing SJIA, all of them seemed promising at the start, but after two to three months the arthritis took hold again. The most harrowing one for all of us was a daily injection. [redacted] soon became afraid of having this and once again the whole family was under stress, as the day could not carry on until this injection was done. [redacted] got very upset each morning knowing what he had to go through.

On numerous occasions [redacted] has been admitted into hospital for joint injections. The most injections he had was 46 in the summer of 2008.
Around this time we were asked to consider taking [redacted] to Newcastle for a bone marrow

transplant. This was not compulsory, the final decision had to be our choice. There was no guarantee with this, the arthritis could go into remission, remain the same or even become worse. To go down this road would have meant putting our lives on hold for a year, we would have been in Newcastle for six months, then would have had to stay at home for a further six months, missing work for us, and most of all [redacted] missing out on important school work and play.

From around 2006 the disease became very severe, there were no joints in [redacted] body that were not affected by this crippling disease. We were having to use a major buggy at this point, imagine how [redacted] felt when we saw his friends and they would ask him why he's in a pram ! [redacted] was being carried into school every morning and this was heart breaking. I cannot even begin to think how [redacted] felt being carried into school when you are seven years old. On some occasions he was carried into the dinner hall by his teacher.

The steroid dose was increased to help, he was on the maximum dose for quite some time. As a result of this [redacted] had a spinal crush fracture, and steroids slowed his growth. [redacted] also looked very bloated due to the steroids. Luckily [redacted] has some very good friends at school who have grown up with him being unwell, all his class friends have looked after and helped him as much as they can. There are no words to describe the feeling you have seeing one of your children living this kind of life and being in so much pain. We felt [redacted] was missing out on a lot, he was unable to take part in sports. One of his favourite sports is golf but he was unable to grip the club and therefore had to stop his lessons.

In the summer of 2008 we were given the chance to start Tocilizumab, at this time the drug was at the end stage of its trial. This option was far better than the bone marrow transplant. This was started with an infusion every two weeks. Within a short space of time we began to see an improvement. This is what we had been dreaming of. After about eight months the infusions then went to four weeks, and for the past eighteen months they have been six weekly.

The difference is unbelievable. Since starting Tocilizumab, the steroids have been stopped for the first time in six years, and [redacted] is now able to have a growth hormone that is working well, he is now catching up to his friends, and is enjoying life to the full.

If we had not had the opportunity to have Tocilizumab, as a family we cannot even begin to imagine where we would be with [redacted] today. This medication has changed [redacted] and the rest of our family's lives. To see [redacted] enjoying himself as he does, is what we thought on many occasions we would never see. We now have a happy, healthy nine year old.
When we look back at old photographs the difference in [redacted] appearance is amazing, he has lost the bloating of his face and tummy. Also [redacted] is back to playing golf and is also doing very well with the local cricket team, to the point of playing for a team two years older than himself. [redacted] has also become more confident in himself now that he is feeling better and is able to get on with everything he enjoys. To see the smiles on his face is so heart warming. We feel that since starting the drug our family life has finally become as it should be.

No child should have to suffer the way [redacted] did if there are drugs available to help this most horrific disease.