

UMBRELLA Newsletter



UMBRELLA is the international childhood kidney cancer research study open in the UK & Ireland

- The UMBRELLA study opened in the UK in 2019 and builds on the previous national Improving Population Outcomes for Renal Tumours of childhood (IMPORT) study. The national sponsor is Great Ormond Street Hospital (GOSH) and international coordination is through the International Society of Paediatric Oncology Renal Tumours Study Group (SIOP-RTSG).
- Dr Tanzina Chowdhury, consultant oncologist at GOSH, replaced Prof Kathy Pritchard-Jones as chief investigator in Sept 2022. The study is funded by a CCLG/Little Princess Trust grant until 31st January 2024.
- Patients are registered in the study through their childhood cancer Principal Treatment Centre, who are all open for research again after the COVID pandemic. Being registered in UMBRELLA means that your/your child's clinical data, imaging scans and tissue samples undergo central review and are available for use in several research projects that are described here.
- The UMBRELLA study has registered over 2030 patients from 26 countries, with some countries joining the study for the first time. The UK has recruited 268 patients (plus 724 in IMPORT).

Active projects

- The UMBRELLA study will show which changes in the tumour genetic material (DNA and RNA) are most useful to predict risk of relapse and explain why some children develop Wilms tumour and other kidney cancers at a young age. This is the main aim of the Little Princess Trust Wilms Tumour Knowledge Bank project.
- Sequence analysis of tiny amounts of circulating tumour DNA and microRNAs found in the bloodstream is in progress. This is called 'liquid biopsy' research and is expected to reveal if a simple blood test can improve diagnosis and treatment planning. We collaborate with the Institut Curie, Paris and with the University of Cambridge in these studies.
- Tumour Organoids collaboration with Princess Maxima Center (Netherlands). If a tumour grows back (relapse), we send samples to a team of scientists who can test several drugs to suggest new treatments.
- A new project with pathologists at the University of Liverpool looks at proteins expressed on hundreds of renal tumours collected through the study. This could improve diagnosis and predicting prognosis.
- Analysis of data from children diagnosed 2002– 2018 shows that survival chances are the same in small and large centres. This is very reassuring for the quality of care delivered across the treatment centres in the UK and Ireland.

The Little Princess Trust Wilms Tumour Knowledge Bank

Launched in February 2020, this project is led jointly by Dr Sam Behjati, Wellcome Sanger Institute and Prof Kathy Pritchard-Jones, University College London. The research team (pictured right) has made great progress, despite pandemic delays. Dr Taryn Treger, clinical PhD student (Sanger Institute) is analysing DNA and RNA sequencing data from hundreds of Wilms tumours from patients from the UK, Germany, and the Netherlands. We expect to complete the experimental work in 2023 and publish full results by 2024.

Dr Guillaume Morcrette, a visiting French pathologist, joined the team for 1 year, focusing his research on local stage I and II Wilms tumours. He continues to collaborate with us following his return to France.



From left to right: Aleksandra Letunovska, Guillaume Morcrette, Taryn Treger, Sam Behjati, Reem Al-Saadi



From left to right: Reem Al-Saadi, Louise Ocaka



From left to right: Louise Ocaka, Aleksandra Letunovska, Emilia Robertson

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11th International Paediatric Renal Tumours Biology meeting, 7-9th Sept 2022

The meeting was very well attended, with colleagues from N America, Singapore, Europe and three representatives of parent organisations. Talks from our teams were:

Dr Taryn Treger - a comprehensive overview of the Little Princess Trust Wilms Tumour Knowledge Bank project with a focus on Wilms tumour predisposition genes.

Dr Harriet Rogers - predicting the % of stromal tissue in Wilms Tumours using Advanced Diffusion Image analysis of MRI scans collected through IMPORT/UMBRELLA

Dr Daniyal Jaffrey - investigating lymphatic vasculature in Wilms tumours – a new area never looked at before that may have implications for how tumours spread.

Prof Kathy Pritchard-Jones - Bridging biology and epidemiology to a global strategy for paediatric renal tumours



From left to right (upper): Reem Al-Saadi, Daniyal Jafree, Kathy Pritchard-Jones, Guillaume Morcrette, Catriona Duncan, Aleksandra Letunovska. (lower) Tanzina Chowdhury, Taryn Treger, Ronald Kuiper, Sam Behjati



Group photo at the international paediatric renal tumours biology meeting, Marseille, September 2022.



From left to right: Arnauld Verschuur, (local host), Reem Al-Saadi

International Society of Paediatric Oncology (SIOP) 2022 Congress

The annual SIOP congress was held in person this year in Barcelona, Spain, after two virtual congresses in 2020 & 2021. Prof Kathy Pritchard-Jones completed her 3 year term as SIOP president. Our group had 4 abstracts presented, as follows:

1. **SINGLE CELL DERIVED ORGANOID FROM INFANT WILMS TUMOUR REVEAL NOVEL INSIGHTS INTO THE REST TUMOUR SUPPRESSOR GENE** (presented by Dr Taryn Treger)
2. **STAGE II WILMS TUMORS: DO THEY ALL NEED THE SAME TREATMENT?** (presented by Dr Guillaume Morcrette)
3. **OUTCOME OF PATIENTS WITH RELAPSED LOW/INTERMEDIATE-RISK WILMS TUMOR AFTER UPFRONT TREATMENT WITH VINCISTINE AND ACTINOMYCIN-D ONLY, BASED ON THE SIOP-93-01 AND 2001 PROTOCOLS** (presented by Dr Alissa Groenendijk)
4. **ADHERENCE TO PROTOCOL RECOMMENDATIONS FOR CHILDREN WITH WILMS TUMOUR IN TWO CONSECUTIVE STUDIES IN THE UK AND IRELAND – DOES VARIATION MATTER?** (presented by Suzanne Tugnait)



From left to right: Suzanne Tugnait, Reem Al-Saadi, Kathy Pritchard-Jones, Aisha Al Mahdy, Angela Lopez



From left to right: Angela Lopez, Suzanne Tugnait, Kathy Pritchard-Jones, Reem Al-Saadi at the Little Princess Trust stand in SIOP 2022, Barcelona



Professor Kathy Pritchard-Jones, SIOP president 2019-2022

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Our study in the news



Outcomes of the IMPORT study was presented at the annual NCRI conference held virtually in November 2021. It was titled: "Efforts to achieve earlier diagnosis of renal tumours in childhood are required to improve survival rates in the UK and Ireland", presented by Reem Al-Saadi. It was covered by several media stories.



From left to right: Reem Al-Saadi, Kathy Pritchard-Jones

In October 2022 Prof Kathy Pritchard-Jones and Ms Reem Al-Saadi were invited to take part in a Global Health meeting held at the 57357 Children's Cancer Hospital Egypt, Cairo. The network of children's cancer hospitals in Egypt is joining the UMBRELLA study and this visit allowed a broader discussion of their clinical and research environment and opportunities for further collaboration on biomarker research in Wilms tumour.



Group photo at the 57357 Children's Cancer Hospital Egypt, Cairo, October 2022

Congratulations to Professor Kathy Pritchard-Jones!

In April 2022, Professor Kathy Pritchard-Jones received a Life -Time Achievement Award from the CCLG. The award highlights Professor Pritchard-Jones's significant role within the paediatric oncology community for over 30 years, outstanding performance, excellence, and dedication to children's cancer. As the President of SIOP, Professor Pritchard-Jones was the Keynote speaker at the CCLG meeting.



Professor Kathy Pritchard-Jones



CCLG Lifetime Achievement Award



Left to right: Ashley Ball-Gamble (CCLG CEO), Prof Richard Grundy (CCLG Chair), Prof Kathy Pritchard-Jones

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Visits to the Little Princess Trust Headquarters

Our team has an annual visit to the Little Princess Trust headquarters. New team members learnt about how LPT operates and the amazing and complex process of making real hair wigs. The meeting focused on discussing current projects and achievements as well as future directions and funding.



Meeting at the LPT headquarters, November 2021



Meeting at the LPT headquarters, November 2022

Support from GOSH Histopathology

Our research could not be the same without the help of the Pathology department at Great Ormond Street Hospital. Consultant pathologist Dr Ciaran Hutchinson dedicates his time towards histological analysis of renal tissue to aid the UMBRELLA research. We are very grateful for all the help we receive!



Ciaran Hutchinson and Aleksandra Letunovska

Relevant meetings held in 2022

CCLG Renal Special Interest Group	Virtual meeting 21 January 2022
CCLG Winter Meeting	Nottingham April 2022
SIOP Europe Annual meeting	Valencia 21-25 March 2022 (virtual)
SIOP RTSG Annual meeting	Seville 27-29 June 2022
International WT Biology Meeting	Marseille 7-9 Sept 2022
54th SIOP congress 2022	Barcelona 28 September -1 Oct 2022 (hybrid meeting)
CCLG Renal SIG	London 7 October 2022
Meeting with funders (LPT)	Hereford 21 November 2022

Upcoming Meetings in 2023

CCLG Annual Conference	Nottingham 20-21 March 2023
SIOPe 4th Annual Meeting	Valencia 8-12 May 2023
SIOP RTSG Annual meeting	Wroclaw, 22-23 June 2023
CCLG Renal SIG	TBC
SIOP 55th Congress	Ottawa 11-14 October 2023

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Thank you to all our supporters and especially to The Little Princess Trust, Bethany's Wish and the Children's Cancer and Leukaemia Group.

Best Wishes from the UK UMBRELLA team!



From left to right: Dr Kristina Dzuma (clinical surgical fellow), Mrs Reem Al-Saadi (study manager), Dr Guillaume Morcrette (pathologist), Dr Angela Lopez (data manager), Miss Aleksandra Letunovska (biomedical scientist), Dr Tanzina Chowdhury (oncologist & UMBRELLA study Chief Investigator), Prof Kathy Pritchard-Jones (previous chief investigator), Dr Richard Williams (bioinformatician), Dr Susan Shelmerdine (radiologist), Ms Suzanne Tugnait (research fellow), Prof Gordan Vujanic (pathologist)



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We have published 21 papers in the last 2 years, 3 Wilms Tumour booklets and presented 10 studies at international conferences. All these studies were possible thanks to your help by allowing us to use the patients' anonymous samples and clinical information. It's helping us find better and possibly shorter treatments in the future.

Published Booklets for Patients, Parents and Carers:

- ✓ [A Parent's Guide to Kidney Tumours](#)
- ✓ [Wilms Tumour in Children](#)
- ✓ [Treatment Options for Relapsed Wilms Tumour in Children](#)



All are available for free for families affected by renal tumours

Scientific Papers published in 2021 & 2022

1. Vujanic GM, Graf N, D'Hooghe E, Chowdhury T, Vokuhl C, Al-Saadi R, Pritchard- Jones K, Melchior P, Furtwängler R. Outcomes of patients with Wilms' tumour stage III due to positive resection margins only: An analysis of patients treated on the SIOP-WT-2001 protocol in the UK-CCLG and GPOH studies. *Int J Cancer*. 2022 Nov 28. doi: 10.1002/ijc.34371. Epub ahead of print. PMID: 36444500.
2. Brok JS, Shelmerdine S, Damsgaard F, Smets A, Irtan S, Swinson S, Hedayat V, Jacob J, Nair A, Oostveen M, Pritchard-Jones K, Olsen Ø. The clinical impact of observer variability in lung nodule classification in children with Wilms tumour. *Pediatr Blood Cancer*. 2022 Oct;69(10):e29759. doi: 10.1002/pbc.29759. Epub 2022 Jun 2. PMID: 35652617.
3. Jackson TJ, Brisse HJ, Pritchard-Jones K, Nakata K, Morosi C, Oue T, Irtan S, Vujanic G, van den Heuvel-Eibrink MM, Graf N, Chowdhury T; SIOP RTSG Biopsy Working Group. How we approach paediatric renal tumour core needle biopsy in the setting of preoperative chemotherapy: A Review from the SIOP Renal Tumour Study Group. *Pediatr Blood Cancer*. 2022 Sep;69(9):e29702. doi: 10.1002/pbc.29702. Epub 2022 May 19. PMID: 35587187.
4. De Aguirre-Neto JC, de Camargo B, van Tinteren H, Bergeron C, Brok J, Ramírez-Villar G, Verschuur A, Furtwängler R, Howell L, Saunders D, Olsen O, Coulomb A, Vokuhl C, Godzinski J, Smets AM, Vujanic GM, van den Heuvel-Eibrink MM, Graf N, Pritchard-Jones K. International Comparisons of Clinical Demographics and Outcomes in the International Society of Pediatric Oncology Wilms Tumor 2001 Trial and Study. *JCO Glob Oncol*. 2022 May;8:e2100425. doi: 10.1200/GO.21.00425. PMID: 35537105; PMCID: PMC9126524.
5. Mifsud W, Furtwängler R, Vokuhl C, D'Hooghe E, Pritchard-Jones K, Graf N, Vujanic GM. Treatment of patients with stage I focal anaplastic and diffuse anaplastic Wilms tumour: A report from the SIOP-WT-2001 GPOH and UK-CCLG studies. *Eur J Cancer*. 2022 May;166:1-7. doi: 10.1016/j.ejca.2022.01.036. Epub 2022 Mar 4. PMID: 35255331.
6. Vujanic GM, Mifsud W, Chowdhury T, Al-Saadi R, Pritchard-Jones K; Renal Tumour Special Interest Group of the Children's Cancer and Leukaemia Group. Characteristics and outcomes of preoperatively treated patients with anaplastic Wilms Tumors registered in the UK SIOP-WT-2001 and IMPORT study cohorts (2002-2020). *Cancer*. 2022 Apr 15;128(8):1666-1675. doi: 10.1002/cncr.34107. Epub 2022 Feb 4. PMID: 35119702.
7. Groenendijk A, van Tinteren H, Jiang Y, de Krijger RR, Vujanic GM, Godzinski J, Rube C, Schenk JP, Morosi C, Pritchard-Jones K, Al-Saadi R, Vaidya SJ, Verschuur AC, Ramírez-Villar GL, Graf N, de Camargo B, Drost J, Perotti D, van den Heuvel-Eibrink MM, Brok J, Spreafico F, Mavinkurve-Groothuis AMC. Outcome of SIOP patients with low- or intermediate-risk Wilms tumour relapsing after initial vincristine and actinomycin-D therapy only - the SIOP 93-01 and 2001 protocols. *Eur J Cancer*. 2022 Mar;163:88-97. doi: 10.1016/j.ejca.2021.12.014. Epub 2022 Jan 15. PMID: 35042071.
8. Spreafico F, Fernandez CV, Brok J, Nakata K, Vujanic G, Geller JI, Gessler M, Maschietto M, Behjati S, Polanco A, Paintsil V, Luna-Fineman S, Pritchard-Jones K. Wilms tumour. *Nat Rev Dis Primers*. 2021 Oct 14;7(1):75. doi: 10.1038/s41572-021-00308-8. PMID: 34650095.
9. Falcone MP, Pritchard-Jones K, Brok J, Mifsud W, Williams RD, Nakata K, Tugnait S, Al-Saadi R, Side L, Anderson J, Duncan C, Marks SD, Bockenbauer D, Chowdhury T. Long-term kidney function in children with Wilms tumour and constitutional WT1 pathogenic variant. *Pediatr Nephrol*. 2022 Apr;37(4):821-832. doi: 10.1007/s00467-021-05125-5. Epub 2021 Oct 4. PMID: 34608521; PMCID: PMC8960606.

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11. Legge D, Li L, Moriarty W, Lee D, Szemes M, Zahed A, Panousopoulos L, Chung WY, Aghabi Y, Barratt J, Williams R, Pritchard-Jones K, Malik KTA, Oltean S, Brown KW. The epithelial splicing regulator ESRP2 is epigenetically repressed by DNA hypermethylation in Wilms tumour and acts as a tumour suppressor. *Mol Oncol.* 2022 Feb;16(3):630-647. doi: 10.1002/1878-0261.13101. Epub 2021 Sep 28. PMID: 34520622; PMCID: PMC8807366.
12. Graf N, Bergeron C, Brok J, de Camargo B, Chowdhury T, Furtwängler R, Gessler M, Godzinski J, Pritchard-Jones K, Ramirez-Villar GL, Rube C, Sandstedt B, Schenk JP, Spreafico F, Sudour-Bonnange H, van Tinteren H, Verschuur A, Vujanic G, van den Heuvel-Eibrink MM. Fifty years of clinical and research studies for childhood renal tumors within the International Society of Pediatric Oncology (SIOP). *Ann Oncol.* 2021 Nov;32(11):1327-1331. doi: 10.1016/j.annonc.2021.08.1749. Epub 2021 Aug 17. PMID: 34416363.
13. Polanco A, Al-Saadi R, Tugnait S, Scobie N, Pritchard-Jones K. Setting international standards for patient and parent involvement and engagement in childhood, adolescent and young adult cancer research: A report from a European Collaborative Workshop. *Cancer Rep (Hoboken).* 2022 Jun;5(6):e1523. doi: 10.1002/cnr2.1523. Epub 2021 Aug 12. PMID: 34383382; PMCID: PMC9199507.
14. Hol JA, Jewell R, Chowdhury T, Duncan C, Nakata K, Oue T, Gauthier-Villars M, Littooi AS, Kaneko Y, Graf N, Bourdeaut F, van den Heuvel-Eibrink MM, Pritchard-Jones K, Maher ER, Kratz CP, Jongmans MCJ. Wilms tumour surveillance in at-risk children: Literature review and recommendations from the SIOP-Europe Host Genome Working Group and SIOP Renal Tumour Study Group. *Eur J Cancer.* 2021 Aug;153:51-63. doi: 10.1016/j.ejca.2021.05.014. Epub 2021 Jun 13. PMID: 34134020.
15. Gatta G, Botta L, Capocaccia R, Cañete A, Pritchard-Jones K; JARC Pilot Study Toronto Guidelines Working Group. Staging childhood cancers in Europe: Application of the Toronto stage principles for neuroblastoma and Wilms tumour. The JARC pilot study. *Pediatr Blood Cancer.* 2021 Sep;68(9):e29020. doi: 10.1002/pbc.29020. Epub 2021 Jun 11. PMID: 34114308.
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