



# UMBRELLA Newsletter

For parents and survivors



Issue 2 – 11<sup>th</sup> January 2021

## Update on the UMBRELLA study & associated Projects

- From 2019, the UMBRELLA study has been implemented as an amendment to the IMPORT study across the UK. The national sponsor continues to be GOSH and the international coordination is under the auspices?? of the SIOP Renal Tumours Study Group (SIOP-RTSG).
- Despite temporary halts to recruitment due to COVID19, the international study has registered over 581 patients from 17 countries, with some of these countries joining the study for the first time. The UK has recruited 80 patients. The first report has been shared with the RTSG Steering Committee.
- On the 27<sup>th</sup> Feb 2020 we launched our newly funded project 'The Little Princess Wilms Tumour Knowledge Bank'. It is a collaboration between UCL/GOSH and the Sanger Centre in Cambridge, PI: Dr Sam Behjati.
- To date, Whole Genome Sequencing (WGS) has been performed on 250 Wilms tumours collected in the UK and Germany with a focus on metastatic cases and infants diagnosed under the age of 12 months. A further 80 WT will have WGS, with results expected in Spring 2021.
- Despite the delays caused by lockdown, we also managed to continue two projects to assess circulating molecular biomarkers:
  1. a liquid biopsy study (whole exome sequencing on circulating tumour DNA from plasma of WT patients) in conjunction with Dr Gudrun Schleiermacher, Paris
  2. Analysis of microRNAs in diagnostic serum, with Dr Matt Murray, Cambridge.



## Updated CCLG clinical guidelines

The clinical guidelines that accompany the amendment of IMPORT into the UMBRELLA study explain the changes that have updated our previous standard of care. These are based on the SIOP WT 2001 randomised trial and aim to incorporate new evidence from international partners on significance of tumour volume after pre-op chemo, as well as definitions of metastatic disease. There is also an agreed international standard approach to treatment of relapsed Wilms tumour that incorporates our national experience from UKWR. The updated guidelines are published on the CCLG website 'members' area'.

## The Little Princess Wilms Tumour Knowledge Bank

On the 27<sup>th</sup> Feb 2020, we launched our newly funded project 'The Little Princess Wilms Tumour Knowledge Bank' which has been named after the charity that kindly donated the funds. Dr Sam Behjati hosted the project launch meeting at the Sanger Centre, Cambridge where the LPT charity founders, CEO, the study Chief Investigator Prof Kathy Pritchard-Jones and a group of clinicians and scientists from UCL Great Ormond Street Institute of Child Health attended and discussed the plans to start this collaboration.



From left to right: Dr Karin Straathof, Mr Phil Brace, Mrs Wendy Tarplee-Morris, Prof Kathy Pritchard-Jones, Mrs Reem Al-Saadi, Dr Kristina Dzuma, Mr Simon Tarplee, Dr Sam Behjati

## UK PPIE meeting, 6<sup>th</sup> Feb 2020

Prof Kathy Pritchard-Jones, Mr Max Pachi (paediatric surgeon) and Mrs Reem Al-Saadi (study manager) met with the UK patient and parent group, led by Mrs Angela Polanco (PPIE lead) in Birmingham to plan new projects. We discussed the importance of collecting long term outcome data and have taken into account their views and priorities. We talked about linking clinical trial data to national cancer registries and other routine health care data to aid long term outcomes research. This was seen to both add value to the original trials as well as being an important research priority in itself.





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## RTSG General Assembly & Brazilian PPIE Meeting

The annual SIOP RTSG GA took place in Rio de Janeiro on 11-13<sup>th</sup> March 2020, hosted by Dr Beatriz De Camargo & Dr Joaquim Caetano Aguirre Neto for the Brazilian WT group. Five UK delegates attended the meeting which also included a Brazilian parents and survivors group meeting.



During the PPIE meeting we linked with Mrs Angela Polanco (Founder of Bethany's Wish) via teleconference for her input of her experience and the UK perspective, which was warmly welcomed. It was great to meet the group in person; which included 2 survivors in their 30s now, one of who attended with her baby. The Brazilian group met afterwards virtually and is planning to hold monthly follow meetings virtually in 2021. They aim to attract more parents, develop new initiatives and support research.



## Survivor and now Researcher donates hair to LPT

Suzi Tugnait, a medical student and research assistant in the Wilms team, was five-years-old when she underwent chemotherapy which led her to lose her hair. At the time she struggled to find a wig, therefore Suzi said she was delighted to be able to help The Little Princess Trust by donating her long locks. The charity will use these to make a wig for a young person who has lost their own hair. Friends and family also sponsored her big cut – which has so far raised more than £3,000 for LPT.

## Recent Abstracts

- **SIOP 2020 presented abstracts:**
  - Variation in adherence to protocol recommendations for pre- and post-operative treatment of children with Wilms tumour in two consecutive studies in the UK and Ireland (oral, S Tugnait).
  - Wilms tumours with intravascular extension in the UK and Ireland IMPORT study: reasons for stage III (poster, K Dzhusa).
- An update on the UMBRELLA study was presented during the CCLG Winter meeting on the 27-28 January 2020, and a trials update was presented during the NCRI trials meeting on the 29<sup>th</sup> January 2020
- Poster at CCLG conference Jan 2020: S Tugnait et al, Review of chemotherapy delivery for Wilms tumours in the UK and Ireland in the SIOP WT 2001 and IMPORT studies



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## Relevant meetings in 2021

UK Renal SIG	Virtual meeting 29 <sup>th</sup> January 2021
CCLG Winter Meeting	Virtual 22-24 <sup>th</sup> Feb 2021
SIOPE Annual meeting	Virtual meeting- Valencia 28-30 <sup>th</sup> April 2021
SIOPE RTSG GA	Utrecht 24-25 <sup>th</sup> June 2021 (TBC)
SIOPE RTSG Biology Meeting	Marseille 22-24 <sup>th</sup> Sept 2021 (TBC)
CCLG Renal SIG	London 10 <sup>th</sup> Sept 2021 (TBC)
53 <sup>rd</sup> SIOPE congress 2021	Honolulu 21-24 <sup>th</sup> October 2021 (hybrid meeting TBC)

Thank you to all our supporters, and especially to the charities Bethany's Wish and The Little Princess Trust.

Stay safe!

## BEST WISHES FROM THE UK UMBRELLA TEAM



From left to right:

Dr Kristina Dzhuma (clinical surgical fellow), Mrs Reem Al-Saadi (study manager), Dr Guillaume Morcrette (pathologist), Dr Angela Lopez (data manager), Dr Tanzina Chowdhury (oncologist), Prof Kathy Pritchard-Jones (chief investigator), Dr Susan Sheldermine (radiologist), Ms Suzanne Tugnait (research fellow)



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## Recent Publications

CCLG Parent's Guide Factsheet: Wilms Tumour (updated 03/06/2020)

## Scientific Papers published in 2020

- 1: Hol JA, Jongmans MCJ, Sudour-Bonnange H, Ramírez-Villar GL, Chowdhury T, Rechnitzer C, Pal N, Schleiermacher G, Karow A, Kuiper RP, de Camargo B, Avcin S, Redzic D, Wachtel A, Segers H, Vujanic GM, van Tinteren H, Bergeron C, Pritchard-Jones K, Graf N, van den Heuvel-Eibrink MM; International Society of Pediatric Oncology Renal Tumor Study Group (SIOP-RTSG). Clinical characteristics and outcomes of children with WAGR syndrome and Wilms tumor and/or nephroblastomatosis: The 30-year SIOP-RTSG experience. *Cancer*. 2020 Nov 4. doi: 10.1002/cncr.33304. Epub ahead of print. PMID: 33146894.
- 2: Nakata K, Colombet M, Stiller CA, Pritchard-Jones K, Steliarova-Foucher E; IICC-3 Contributors. Incidence of childhood renal tumours: An international population-based study. *Int J Cancer*. 2020 Jun 16. doi: 10.1002/ijc.33147. Epub ahead of print. PMID: 32902866.
- 3: Ray S, Jones R, Pritchard-Jones K, Dzhuma K, van den Heuvel-Eibrink M, Tytgat G, van der Beek J, Oades G, Murphy D. Pediatric and young adult renal cell carcinoma. *Pediatr Blood Cancer*. 2020 Sep 1:e28675. doi: 10.1002/pbc.28675. Epub ahead of print. PMID: 32869954.
- 4: van der Beek JN, Geller JI, de Krijger RR, Graf N, Pritchard-Jones K, Drost J, Verschuur AC, Murphy D, Ray S, Spreafico F, Dzhuma K, Littooj AS, Selle B, Tytgat GAM, van den Heuvel-Eibrink MM. Characteristics and Outcome of Children with Renal Cell Carcinoma: A Narrative Review. *Cancers (Basel)*. 2020 Jul 3;12(7):1776. doi: 10.3390/cancers12071776. PMID: 32635225; PMCID: PMC7407101.
- 5: Atun R, Bhakta N, Denburg A, Frazier AL, Friedrich P, Gupta S, Lam CG, Ward ZJ, Yeh JM, Allemanni C, Coleman MP, Di Carlo V, Loucaides E, Fitchett E, Girardi F, Horton SE, Bray F, Steliarova-Foucher E, Sullivan R, Aitken JF, Banavali S, Binagwaho A, Alcasabas P, Antillon F, Arora RS, Barr RD, Bouffet E, Challinor J, Fuentes-Alabi S, Gross T, Hagander L, Hoffman RI, Herrera C, Kutluk T, Marcus KJ, Moreira C, Pritchard-Jones K, Ramirez O, Renner L, Robison LL, Shalkow J, Sung L, Yeoh A, Rodriguez-Galindo C. Sustainable care for children with cancer: a Lancet Oncology Commission. *Lancet Oncol*. 2020 Apr;21(4):e185-e224. doi: 10.1016/S1470-2045(20)30022-X. PMID: 32240612.
- 6: Calandrini C, Schutgens F, Oka R, Margaritis T, Candelli T, Mathijssen L, Ammerlaan C, van Ineveld RL, Derakhshan S, de Haan S, Dolman E, Lijnzaad P, Custers L, Begthel H, Kerstens HHD, Visser LL, Rookmaaker M, Verhaar M, Tytgat GAM, Kemmeren P, de Krijger RR, Al-Saadi R, Pritchard-Jones K, Kool M, Rios AC, van den Heuvel-Eibrink MM, Molenaar JJ, van Boxtel R, Holstege FCP, Clevers H, Drost J. An organoid biobank for childhood kidney cancers that captures disease and tissue heterogeneity. *Nat Commun*. 2020 Mar 11;11(1):1310. doi: 10.1038/s41467-020-15155-6. PMID: 32161258; PMCID: PMC7066173.
- 7: Pasqualini C, Furtwängler R, van Tinteren H, Teixeira RAP, Acha T, Howell L, Vujanic G, Godzinski J, Melchior P, Smets AM, Coulomb-L'Hermine A, Brisse H, Pritchard-Jones K, Bergeron C, de Camargo B, van den Heuvel-Eibrink MM, Graf N, Verschuur AC. Outcome of patients with stage IV high-risk Wilms tumour treated according to the SIOP2001 protocol: A report of the SIOP Renal Tumour Study Group. *Eur J Cancer*. 2020 Mar;128:38-46. doi: 10.1016/j.ejca.2020.01.001. Epub 2020 Mar 5. PMID: 32109849.
- 8: Watson T, Oostveen M, Rogers H, Pritchard-Jones K, Olsen Ø. The role of imaging in the initial investigation of paediatric renal tumours. *Lancet Child Adolesc Health*. 2020 Mar;4(3):232-241. doi: 10.1016/S2352-4642(19)30340-2. Epub 2020 Jan 31. PMID: 32007136



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## LAY SUMMARIES OF PUBLICATIONS

### 1. WILMS TUMORS AND THEIR PRECURSORS: RADIOLOGICAL DIAGNOSIS VERSUS HISTOLOGY

K. Dzhuma, H. Ducou Le Pointe, A. Coulomb, MD. Tabone, C. Bergeron, G. Audry, S. Irtan

**Background:** This research addresses a difficult issue in clinical practice regarding the diagnosis of patients with multiple renal nodules. The aim of this study was to compare the imaging features of renal nodules with their final histology and identify radiological factors that would better differentiate Wilms tumors (WT) from nephrogenic rests (NR) - benign lesions from which Wilms tumors may arise.

**Methods:** Images of the patients with bilateral and unilateral multiple renal tumors were reviewed by a senior radiologist blinded to histology findings. All nodules were classified as Wilms tumors or nephrogenic rests according to the radiological criteria.

**Results:** 175 nodules were resected after a median of five courses of chemotherapy for the first side and 13 courses for the second side. The radiology/pathology correlation showed 118 (74.6%) nodules adequately classified, 20 (11.3%) false positive for WT (9 patients) and 20 (11.3%) false negative (9 patients). WTs were significantly bigger at diagnosis and preoperative assessment and their size decreased quicker than NR ( $p < 0.0001$ ) under chemotherapy. WT and NR had a similar homogeneity rate. Only 5% of nodules thought NR that were finally WT were heterogeneous while 17% of nodules initially diagnosed as WT that were finally NR were homogeneous.

**Conclusion:** Radiological misdiagnosis occurred in 25% of kidney nodules. The size of nodules at diagnosis and their decrease under neoadjuvant chemotherapy may be a helpful criterion recognizing WT from NR before surgery. Other criteria like homogeneity did not seem key features and lost value in small lesions.

**For more lay summaries please email us at:**

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