UK UMBRELLA Newsletter

UMBRELLA

To Date:

- 364 UMBRELLA patients recruited from 19 PTCs since October 2019
- 730 from 20 PTCs registered on IMPORT
- Clinical data and biological samples collected and used in several ongoing and completed studies, some are highlighted here, and others published

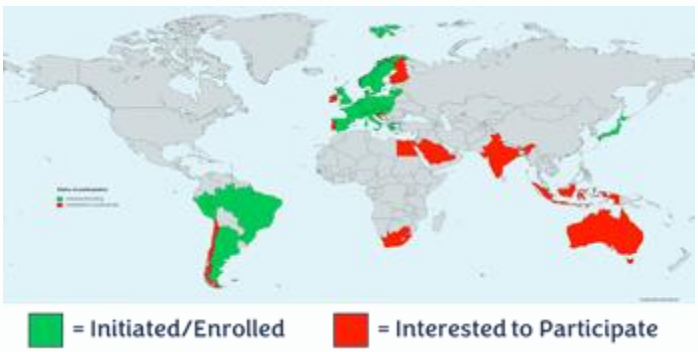
UMBRELLA to continue until 2025

Anticipated Changes To The Study From February 2024:

- Study to be extended to 31/01/2025
- Thank you to the CCLG/Little Princess Trust for their continued support
- CRR & CPR to be referred to NRAP until further notice, but please continue to send radiology images and study samples to the UMBRELLA Team @ GOSH/ICH

New Countries Joining The UMBRELLA Study

A total of 30 countries are participating in the international SIOP-RTSG (Renal Tumours Study Group) UMBRELLA study with a further 12 preparing to join. In the last year, Japan, Latvia, Lithuania, Slovakia and Hong Kong have opened the UMBRELLA Study, bringing the total of registered international patients to more than 2830. The UK has recruited 364 patients on UMBRELLA and 730 on IMPORT and all these patients' data and samples are being used in active projects by national and international projects where approval has been granted by the RTSG research committee.



The annual SIOP-RTSG conference took place in Wroclaw this year where the UK presented a total of 9 abstracts to the live and virtual audience in June 2023

- The continued initiation of new countries into the UMBRELLA study is of great importance in expanding inclusion of middle-income countries. This will allow international comparisons and should improve patient care and treatment.
- The RTSG has combined the data of 10,000 renal tumours patients into one database. This supports research on accepted studies to look at specific clinical questions in WT, especially rarer sub-groups, to improve patient outcomes and reduce risk of relapse and long term side effects.
- This database also contains data on non-WTs, allowing international collaboration to study these rare subtypes, such as Renal Cell Carcinomas, Clear Cell Sarcomas and Malignant Rhabdoid Tumours of the Kidney, and others. This should ultimately lead to improved patient care overall.
- In previous RTSG studies we have shown that the route to diagnosis differs between some countries, and the UK shows a slightly higher prevalence of metastatic patients at time of diagnosis, with larger tumours than in Germany for example as a comparator.
- The UK is participating in a study of testing new chemical compounds on organoids grown from relapse tissues of patients to test for cell-type specific sensitivities. Some preliminary results were shared in the SIOP-RTSG annual meeting, and the work is continuing in 2024. Please contact the UK UMBRELLA team if you would like your patients to participate or would like more information.

1000th Genome In The Little Princess Trust Knowledge Bank

Samples from 1,000 children with renal tumours have now been sequenced as part of the Little Princess Trust Wilms Tumour Knowledge Bank project.

Multiple samples from 1,000 patients registered in the IMPORT/UMBRELLA (CCLG centres) or SIOP WT 2001 (Germany & UK) studies have now undergone either whole genome or whole exome sequencing at The Sanger Institute, under the direction of Prof Sam Behjati, as part of this joint project with University College London/GOSH. This is an important milestone in this international collaboration to create the "Little Princess Trust Wilms Tumour Knowledge Bank". This comprehensive resource includes the genomic landscape of the entire spectrum of clinical behaviours in Wilms tumour (infants, intermediate risk histology, relapsed and metastatic disease). The Knowledge Bank approach will allow current patients to be compared with similar patients already treated to better predict their outcome. It will also be available to researchers in the field to generate and test new ideas. Full article here.

IMPORT Comparison To National Cancer Registry Data

The UMBRELLA team at UCL have collaborated with the English National Cancer Registration and Analysis Service (NCRAS) to compare data from the IMPORT study with publicly available data in the NCRAS 'Get Data Out' programme.

This is the first time that NCRAS have published data on a childhood solid tumour as part of their 'Get Data Out' (GDO) programme. We compared the numbers of patients with Wilms tumour in each dataset, the proportions receiving surgery/chemotherapy/radiotherapy and the overall survival rates. We could estimate the proportion of all patients (aged 0-19 years) diagnosed with WT in England with the number registered in the IMPORT study over a matching 5 year time-period (2014-2018). This shows that only 80% of the population incident cases were recruited into IMPORT, a fall from the previous proportion of >90% in the last two trials (UKW3 & SIOP WT 2001). This is something we need to understand in more detail to try to improve, noting that the time-period is pre-COVID.

We also found that the proportion of children receiving any form of radiotherapy was about the same in each dataset (~40%). This is higher than previous proportions documented in the UKW3 trial era and could either be due to under-reporting of RT in the UKW3 trial or to new risk stratification criteria allocating more children to receive RT or both.

Overall survival at 3 years (~93%) was almost identical in the two datasets, demonstrating that the IMPORT study is representative of the overall population. This study provides strong evidence for the use of routine health care data to follow the outcomes of children with Wilms tumour. It also sets a precedent for similar studies of other paediatric cancers if the GDO programme could publish similar datasets by aggregating time periods to mitigate small-number publication restrictions.

Updates From Radiotherapy & Radiology Studies

A UK wide study led by the Radiotherapy lead Dr Daniel Saunders and Dr Michelle Li using IMPORT patients' data sets has concluded that some Wilms Tumour patients with localised disease received delayed radiotherapy post-surgery where it was indicated. The median time to RT was 40 days. With a follow up of 50 months it was found that EFS and OS were impacted if RT was commenced 35 days or more post-surgery. The optimal timing of RT requires rapid evaluation in a larger cohort and is being planned with the SIOP-RTSG.

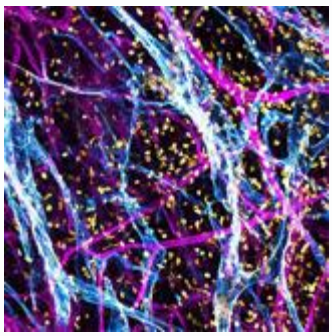
Dr Dan Saunders, Dr Michelle Li and Reem Al-Saadi

In a recent radiology project led by Dr Harriet Rogers and Dr Chris Clark, we assessed whether an imaging biomarker (Apparent Diffusion Coefficient (ADC)), could non-invasively identify stromal histological subtypes using MRIs with Diffusion-weighted imaging data from different hospitals. We expanded a previous single-centre analysis showing that stromal subtypes have increased ADC values compared to other subtypes.

The new multi-centre MRI study confirmed a high sensitivity (70%) and specificity, despite varying DWI acquisition techniques. Pre-surgical recognition may avoid unnecessary extension of pre-operative chemotherapy and aid surgical planning.

News and Successes

Members of the UMBRELLA research team, in conjunction with research groups based at UCL GOS ICH won GOSH's "Moment of Discovery" Award.
During innovative research to reveal lymphatic networks in kidney and WT, this image (right) was generated using 3-D visualisation and new staining methods. Where traditional staining techniques struggle to capture the complexity of lymph networks, this staining method allowS the visualisation of lymph networks (blue) within a Wilms tumour, potentially identifying differences on a 3D level. Visualisation of the network along with blood vessels (purple) and immune cells (gold), offers a unique insight into how these systems become dysregulated/hijacked in cancer, potentially elucidating mechanisms to metastases.
The winning entries were well publicised, with both the BBC and Nature writing about the competition.



21 abstracts have been presented this year across several national and international conferences.

Professor Sam Behjati Winner of the 2023 Foulkes Foundation Academy of Medical Sciences Medal

Congratulations to Professor Sam Behjati, who has been recognised for his pioneering work in advancing the understanding and diagnosis of childhood cancers. His lecture "Finding the origins of childhood cancer" was delivered in receipt of the Foulkes Foundation Academy of Medical Sciences medal, 2023, and included several mentions of Wilms tumour. You can read more on Sam's award here.

Our Research Assistant Aleksandra donated over 14 inches of hair to the Little Princess Trust. Alongside this Aleks raised over £500 for the charity making sure that the hair she donated can be turned into wigs for children suffering from cancer by the wig making wizards at the Little Princess Trust. Incredible!!

Meetings & Conferences In 2024

- January - RSIG Focus Group Meeting
- 22-23rd April - CCLG Conference, Milton Keynes
- 13-17th May - SIOP Europe, Milan
- 5-7th June - Renal Tumours Biology Meeting, New York, USA
- 16-18th September - Annual RTSG meeting, Porto, Portugal
- 15-20th October - Honolulu, HARMONICA + SIOP 2024
- November – Open RSIG meeting, *TBC*

Many thanks to the Histopathology and Radiology departments at Great Ormond Street Hospital for their continued support over the last year, it is truly appreciated!

Thank you to all our supporters, contributors, and funders over the last year! Without you, our continued success and achievements would not be possible.

The UMBRELLA team would like to wish you the best for 2024!

UCL GREAT ORMOND STREET INSTITUTE OF CHILD HEALTH

Little Princess Trust

Children's Cancer and Leukaemia Group

Bethany's Wish Wilms' tumour research fund

NHS Great Ormond Street Hospital for Children NHS Foundation Trust

Contact us: gos-tr.umbrella@nhs.net

Papers published in 2023

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