**Development of a regional expert clinic for the evaluation and treatment of patients with renal complications of Tuberous Sclerosis Complex (TSC)**

Tuberous Sclerosis Complex (TSC) is a rare autosomal dominant condition caused by mutations in the TSC1 gene on chromosome 9 (coding for hamartin) or the TSC2 gene on chromosome 16 (coding for tuberin). These proteins act as suppressors of the kinase mTOR. Loss of this regulation can lead to benign tumours of the brain, kidneys, lungs, heart and skin. There is a high rate of new mutation (75%) and the disease phenotype and presentation are highly variable. The most common renal features of TSC are angiomyolipomata or AMLs (75%) and cysts; renal cell carcinoma and oncocytomas are rare complications. AMLs can lead to end-stage renal disease, pain or bleeding. The latter is clearly correlated to size and can be potentially life threatening. In June 2016, based on positive trial data with the mTOR inhibitor everolimus, NHS England approved its use to treat adult TSC patients with prescribing restricted through eight regional centres. The main criteria was lesions of >3cm with evidence of interval growth on MR or CT imaging or history of previous bleeding. A mandated requirement for treatment continuation beyond 6 months is evidence of lesion stability by imaging.

We established a new renal clinic at Sheffield to evaluate and treat adult TSC patients across Yorkshire and Humber in November 2016. The clinical team includes nephrologists, a clinical nurse specialist and a clinical geneticist. Collaboration was initiated with radiology and medical physics to develop suitable MRI sequences to evaluate changes in 3D volumes of AMLs from baseline and at 6-12 months after initiation of everolimus. Written patient information is provided and discussed prior to initiation. Patients are followed up monthly until stable on treatment and then every 2-3 months depending on clinical need. Trough everolimus levels are monitored at each visit for dose titration and measured at a central laboratory (St. Georges, London).

To date, ten patients (6 male, 4 female) have been initiated on everolimus. Their mean age was 40yr (24-75yr) with mean baseline eGFR of 74ml/min/1.73m2 (26-114). Eight patients remain on everolimus although 5 required dose reductions due to deranged LFTs, anaemia, reduced appetite or mouth ulcers. One patient developed T2DM whilst on treatment. Two patients were discontinued permanently, one due to ESRD and recurrent respiratory infections and another due to intolerable mouth ulcers. No increase in AML size has been observed on treatment. Several patients have remarked on the significant improvement in their facial skin lesions (adenoma sebaceum) and appearance. Future planned developments are to establish a regular MDT (neurology, neurosurgery, oncology, urology, dermatology, clinical genetics), a regional transition clinic from paediatric to adult care and a regional shared care model for TSC patients across Yorkshire and Humber.