Rituximab and Ibrutinib (RI) versus Dexamethasone, Rituximab and Cyclophosphamide (DRC) as initial therapy for Waldenstrőm's macroglobulinaemia (WM) (RAINBOW): a randomised phase II/III study (NCT04061512).

Rebecca Auer[1], Roger Owen[2], Ruth de Tute[2], Suzanne Arulogan[3], Shirley D'Sa[3], Guy Pratt[4], Jaimal Kothari[5], Adefiola Olabode[6], Anthony Lawrie[6], William Wilson[6], Charlotte Tyson[6].

[1]Barts Health NHS Trust, London, [2]St James's University Hospital Leeds, [3]University College London Hospital, [4]University Hospitals Birmingham NHS Foundation Trust, [5]Oxford University Hospitals, [6]CRUK and UCL Cancer Trials Centre, London, UK.

Rituximab-based immunochemotherapy regimens remain the standard of care in the first-line treatment of patients despite the approval of BTK inhibitors (BTKi) across all lines of therapy. In the phase III randomised iNNOVATE study, ibrutinib, in combination with rituximab, demonstrated superior progression free survival (PFS) compared to single agent rituximab in patients with WM. We initiated the RAINBOW trial to evaluate rituximab with ibrutinib in previously untreated patients with WM.

Between February 2020 and September 2024, 148 symptomatic treatment-naïve patients were enrolled into this prospective randomised (1:1), multicentre phase III study and stratified according to the International Prognostic Scoring System for WM.

Patients were treated with RI (Rituximab 375mg/m^2 i.v. days 1, 8, 15, 22 cycles 2 and 5 only with ibrutinib 420 mg daily continued until progression or not tolerating) or DRC (Dexamethasone 20 mg i.v day 1, Rituximab 375mg/m^2 i.v. day 1 and Cyclophosphamide 100 mg/m^2 BD oral days 1-5) for 6 cycles repeated every 21 days. The primary endpoint was investigator assessed PFS. A previously developed sensitive WM-specific flow cytometry assay (limit of detection 0.004% of leucocytes) was used to assess bone marrow (BM) response at the end of RI/DRC treatment. First results from this trial will be presented.