P385

P385 -Using long term outcome data to redefine proteinuria and eGFR endpoints for lupus nephritis trials: proteinuria targets need not be so stringent

Dr Hannah R. Wilson[1], Dr Tabitha Turner-Stokes[1], Dr Iara Santos[1], Dr Hannah Beckwith[1], Dr Neeru Agarwal[1], Dr Sofia Correia[1], Dr Camilla Pillay[1], Dr Andrew Porter[1], Dr Megan Griffith[1], Prof Jeremy Levy[1], Dr Thomas Cairns[1], Prof Terence Cook[1], Prof Liz Lightstone[1]

[1]*Imperial College Lupus Centre, Hammersmith Hospital, London, United Kingdom*

Background

Lupus Nephritis (LN) is a common and severe manifestation of systemic lupus erythematosus (SLE) that can lead to kidney failure (ESRF). Clinical trials tend to assess outcomes at 1 year, however what matters to patients far more, is long-term outcomes. It needs to be determined therefore if our standard 1 year measures are predictive of these longer-term outcomes. Recent analysis of the Euro-Lupus Nephritis and MAINTAIN cohorts suggests a less stringent cut off of proteinuria at 1 year (<0.8g/d and <0.7g/d respectively) better predicted good renal outcomes at 7 years than usual complete remission (CR) criteria of <0.5g/d. This cut-off has yet to be validated using urinary protein creatinine ratio (uPCR) or in a larger real world cohort.

Methods

Data were reviewed for LN biopsies 1/1/1996 to 1/1/2016. Standard definition CR: uPCR (mg/mmol) <50 and estimated glomerular filtration rate (CKD-EPI) (eGFR mls/min/1.73m2) ≥60, or if <60 at screening, not fallen by >20%; Partial remission (PR): uPCR <300 with a ≥50% improvement and eGFR as for CR; Non-remission (NR): no PR by 1 year. Factors affecting and predicting good long term outcome, defined as 1-46year survival with eGFR >60, assessed by multiple logistic regression correcting for relevant variables, and receiver operating characteristic (ROC) curves.

Results

Population: 470 patients had 797 biopsies over the 20 years. Median age at diagnosis: SLE 29 years; LN 32 years. Female: 82%. Ethnicity: 32% South Asian, 27% Black, 26% White and 3% SE Asian.

Outcomes: At latest follow-up since diagnosis LN (median 9years (0-46): majority, 270 (62%) had good renal outcome; ESRF: 66 (15%), median time to ESRF: 5years (0-43); died: 38 (9%), median time to death: 6years (0-30).

Logistic regression identified 1 year eGFR and proteinuria as key predictors of good outcome at latest follow-up: eGFR odds ratio (OR) 3 (95% CI 2.3-4.2) p<0.001 for each rise 10 mls/min/1.73m2; uPCR OR 0.5 (0.2-0.9) p=0.03 for increase between ranges (0-50, 50-300, 300+ mg/mmol).

ROC curves identified 1year uPCR <74mg/mmol (AUC 0.70, p<0.0001, sensitivity 68%, specificity 66%) and eGFR >84ml/min/1.73m2 (AUC 0.84, p<0.0001, sensitivity 78%, specificity 77%) as predictive of good outcome.

Standard CR or NR definitions fail to predict good outcomes; in contrast, achieving the thresholds of uPCR and eGFR identified by ROC curve analysis strongly predicted a good outcome OR 10.5 (95% CI 4.6-23.6, p<0.001); OR good outcome if not achieved 0.1 (95% CI 0.04-0.22, p<0.001).

Conclusions

Our “real world” data, the largest to date, using an unselected, variably treated, multi-ethnic cohort, support the data from long-term follow-up of the Eurolupus and MAINTAIN cohorts, that proteinuria thresholds at one year are too stringent. Our data also suggest that more attention needs to be paid to preservation of excellent renal function. In this study, a proteinuria threshold of <74mg/mmol and eGFR threshold of >84ml/min/1.73m2 at 1 year, better predicted long term renal survival than current trial

endpoints. As this is the key renal outcome that matters to patients, we argue it is time to change the definition of success of treatments being trialled in LN.