P169

Long-term outcome of low dose cyclophosphamide (CYC) and plasma exchange (PLEX) induction in ANCA-associated vasculitis (AAV)

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Introduction.— Adverse events to the treatment of AAV are the greatest threat for 1-year’s outcome. The use of PLEX in AAV is not commonly accepted in patients (pts.) with creatinine < 500 μmol/L. We combined low dose of CYC and PLEX in order to minimize the infection/sepsis rate, which mostly is due to the immunosuppression.

Patient.— A prospective cohort study of all AAV pts. referred between 2000–2010 was performed. All pts. had AAV based on positive ANCA and a compatible clinical syndrome. The use of PLEX was decided on severity of renal biopsy and ANCA titres. Immunosuppression consisted of prednisolone 1 mg/kg/day and a low dose of daily oral CYC (100 mg/day in pts. < 65 years and 50 mg/day in pts. > 65). AZA/MMF was given for maintenance of remission.

Results.— One hundred and thirty-two pts. were admitted and 118 followed for a mean of 5.7 years (range 0.2–12.3; 676 pts. years). Fifty-seven percent were male, 47% were MPO-ANCA positive. Thirty-six (11.5%) pts. died during CYC treatment (two sepsis, two AMI, one lung haemorrhage, all on HD). In total 111 pts. (9%) died within 1 year and 14 more pts. died < 5 years. The total number of deaths was 33 (28%) with an expected 12 years patient survival of 62% (Kaplan Meier). Twenty-seven pts. (23%) developed ESRD, with an expected 12 years kidney survival of 75% (K.M). Forty-three pts. (36%) died or developed ESRD during the study, resulting in an expected 12 years dialysis free patient survival of 62% (K.M.). Pts. aged < 65 or < 500 mg had significantly better dialysis free survival. 29 pts. (23%) had infection < first 4 months, 15 (13%) being leucopenic. Forty-one (34%) relapses occurred during the 12 years of follow up.

Conclusion.— The use of low dose CYC and PLEX for induction resulted in a high survival rate and good preservation of renal function together with low rate of complications. As the septicemia and mortality was low, the combination of PLEX and low CYC seems to be less toxic, than the conventional AAV induction treatment regimen.

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P170

Longitudinal ANCA measurements for predicting a relapse in patients with ANCA-associated vasculitis

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Introduction.— To assess the predictive value of longitudinal anti-neutrophil associated antibody (ANCA) measurements for a relapse in a community-based cohort of patients with ANCA associated vasculitis.

Patients.— All ANCA-positive patients who visited the clinic in Maastricht between 1–1–2000 and 1–10–2011, with a diagnosis of primary ANCA associated vasculitis were evaluated. Disease severity was classified as limited or severe according to the WGET Research group. Patients were routinely tested by indirect immunofluorescence (IIF) and first generation solid phase ANCA tests for MPO- and PR3-ANCA.

Results.— One hundred and one patients with severe disease (65 PR3-ANCA, 36 MPO-ANCA) and 52 patients with limited disease (36 PR3-ANCA, 16 MPO-ANCA) were included at first-time remission. During an average follow-up of 49.8 months (SD 31.4) and an average of 15.1 ANCA measurements (SD 13.7), 71 relapses were recorded (27 major, 44 minor). At the time of diagnosis of a relapse, all patients with major and minor relapses were ANCA positive, whereas 22 of 27 (81.5%) major relapses and 21 of 44 (47.7%) minor relapses were preceded by an ANCA rise. An ANCA rise is more predictive as measured by the first generation ANCA test [HR 2.712 (95%CI 1.559–4.715)] than by IIF [HR 2.280 (95%CI 1.310–3.969)]. Upon stratification in disease severity, an ANCA rise is clearly predictive in patients with severe disease [HR 4.722 (95%CI 2.364–9.432)], while non-significant in patients with limited disease.

Conclusion.— Longitudinal ANCA measurements to predict a relapse are useful in patients with severe disease but not in patients with limited disease.

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P171

Low %CD5+ B cells in patients with ANCA vasculitis portends a shorter time to relapse after rituximab

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Introduction.— We recently reported that CD5+ B cells, as a surrogate marker of B regulatory cells, are decreased in active ANCA-small vessel vasculitis (ANCA-SVV) and normalize during disease remission [1]. After B cell depletion with rituximab, we found that patients who repopulated with a low or decreasing %CD5+ B cells and were on low maintenance immunosuppression had a shorter time to relapse than patients on similar levels of immunosuppression but normalized %CD5+ B cells or patients with similarly low %CD5+ B cells but on full dose maintenance immunosuppression. To assess the predictive value of longitudinal anti-neutrophil associated antibody (ANCA) measurements for a relapse in a community-based cohort of patients with ANCA associated vasculitis.

Discussion.— We present data that confirm the %CD5+ B cells, as a component of the human B regulatory cell phenotype, is an indicator of future relapse. Moreover, a low %CD5+ B cells correlates with a shorter time to relapse regardless of immunosuppression dose. Monitoring whether CD5+ B regulatory cells contribute to B cell repopulation

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