Carflizomib With and Without Ibrutinib in Frontline and Relapsed / Refractory WM (CZAR01)

Meletios Dimopoulos, Maria Gavriatopoulou, Efstathios Kastritis, Christian Buske. (from the European Consortium of Waldenstrom's Macroglobulinemia.

In WM chemoimmunotherapy induces only low CR / VGPR rates. Thus, innovative approaches are needed. Ibrutinib has high activity in WM and relatively low toxicity. However, the CR / VGPR rates remain relatively low. In addition, activity of Ibrutinib depends on the genotype: compared to patients with MYD88mut/CXCR4WT, single agent therapy with Ibrutinib induces lower response rates in patients with the MYD88mut/CXCR4mut or the MYD88WT/CXCR4WT genotype (major response. Phase II data have indicated that the proteasome inhibitor Carfilzomib is able to overcome the inferior prognosis of Ibrutinib in MYD88mut/CXCR4mut and MYD88WT/CXCR4WT patients. Based on this we hypothesize that addition of Carfilzomib to Ibrutinib will increase the VGPR / CR rate compared to Ibrutinib alone in patients with WM, especially in patients with CXCR4mut and MYD88WT. Both newly diagnosed and previously treated patients were randomized to receive either single agent Ibrutinib continuously until disease progression or Ibrutinib with Carfilzomib, the later agent given for two years. The primary endpoint of the study was achievement of CR / VGPR at 12 months and 24 months. Secondary endpoints include time to best response, time to first response, time to treatment failure, remission duration, progression free survival, cause specific survival, overall survival, safety, quality of life. The accrual of patients was completed in June 2024.