LENALIDOMIDE PLUS METRONOMIC CYCLOPHOSPHAMIDE FOR HEAVELY PRETREATED CLASSICAL HODGKIN LYMPHOMA. A PHASE II TRIAL

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Aim: Relapsed or refractory (R/R) classical Hodgkin lymphoma (cHL) after autologous stem cell transplantation (ASCT) remains a challenge. For these patients (pts) treatments with different mechanism of action rather than classical chemotherapy (CHT) are needed.

Methods: Pts with R/R cHL after ASCT or refractory to two CHT regimens were recruited in a phase II trial (EUDRA CT: 2009-016588-12). Lenalidomide (L) was administered at 20 mg/day for 21 days and cyclophosphamide at 50 mg/day for 28 days (cycles every 28 days). If no grade ≥2 toxicity appeared, L could be escalated to 25 mg/day for 28 days. In 2009 we considered that this treatment would be promising if response rate (ORR) were over 60%. A Simon two stage binomial design was used to calculate the sample size. A total of 46 pts were planned but the trial would be stopped if less than 7 responses after 4 cycles were obtained in the first 16 pts.

Results: Between 11/2010 and 12/2011, 16 pts were included. The trial was closed early because we observed only 5 responses after 4 cycles. Median age was 34 years (18-77). The median number of previous lines was 5 (2-6). Ten pts were primary refractory and 11 were refractory at inclusion. Twelve pts were R/R a median of 5 months after ASCT and 4 pts never had achieved a chemosensitive status. Five pts had also received aloSCT. Twelve pts presented with extranodal disease at inclusion. A total of 110 cycles were administered, with serious (grade ≥3) toxicity in 43 cycles (39%). The most frequent serious toxicities were neutropenia (14% of cycles) and thrombocytopenia (7% of cycles). A toxic death was observed after a septic shock in a non neutropenic pt. An ORR of 38% (1 CR and 5 PR) was observed and 10 pts (62%) achieved clinical benefit (response or disease stabilization for more than 6 months). Median progression free survival (PFS) and overall survival (OS) were 7 and 19 months. With a median follow-up of 19 months (3–38+) and 37 months for pts alive, 3 years PFS and OS were 6% and 31%.

Conclusions: The optimistic assumptions of this trial led to an early closure. However, this combination deserves further study as an outpatient palliative treatment as it has succeeded in controlling the progression of the disease for more than 6 months in almost two thirds of a very poor prognosis group of pts.

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