

A PROSPECTIVE PHASE II STUDY OF DARATUMUMAB IN PREVIOUSLY-TREATED SYSTEMIC LIGHT-CHAIN (AL) AMYLOIDOSIS

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Abstract: S851

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Background

Daratumumab (DARA), is a novel, high-affinity, IgG1κ human monoclonal antibody that specifically recognizes CD38. It has emerged as a breakthrough targeted therapy for patients with multiple myeloma. Monoclonal plasma cells in AL amyloidosis (AL) are similar to plasma cells in myeloma and express CD38.

Aims

We report here the preliminary results of a prospective multi-center, phase II study of DARA in AL (NCT02816476).

Methods

Forty patients will be recruited in this trial. Patients aged ≥ 18 years with evaluable AL amyloidosis, who have received ≥ 1 prior therapy and are not in very good partial response (VGPR) or better with a measurable plasma cell dyscrasia with dFLC > 50 mg/L (difference between involved and uninvolved free light chain levels), with at least one major vital organ involvement, with ECOG performance status 0, 1 or 2, no chronic atrial fibrillation, a supine blood pressure > 100 mmHg and NT-proBNP < 8500 ng/L are eligible. They receive DARA intravenously in a standard schedule and dose: 16 mg/kg weekly during the first two 28-day cycles and every other week during cycles 3 through 6 for a total of six 28-day cycles. Hematologic responses are measured after 1 injection of DARA, at day 1 of each cycle and at the end of treatment visit. The objectives are to assess hematologic responses, organ responses and safety.

Results

To date 38 of the 40 planned patients have been enrolled in 11 French and 1 Italian centers. Here are the characteristics of the 36 patients included at data cut-off (Nov 13th, 2017). The median age is 69 years (range, 45-83). The median number of organ system involvement is 2 (range, 1-5). Twenty-three patients (64%) have cardiac and 21 patients (58%) renal involvement. The median time from diagnosis to enrolment is 24 months (range, 3.5-122). Median number of prior therapies is 3 (range, 1-5), 20 patients (56%) have received Melphalan and Dexamethasone, 34 patients (94%) bortezomib, and 19 patients (53%) lenalidomide. Nineteen patients (53%) have received 3 or more lines of treatment. There were two on-study deaths due to cardiac progression and lung cancer. Three other patients have discontinued study treatment before 6 cycles due to disease progression. Nine patients (25%) experienced at least one grade ≥ 3 AE (any cause) and only one was considered as drug related (lymphopenia). The most common drug-related AEs were infusion reaction seen in 11 patients (30%), all grade I or II. Very good partial response or better (VGPR) was observed in 14 of 32 evaluable (completing at least 1 cycle) patients (44%), and partial response in 5 patients (16%). The overall response rate is 59%. Responses were usually very rapid, after a single DARA injection, all 17 patients, with available dFLC measurement, who finally reached partial response or better had a dFLC decrease of more than 35 % with a median dFLC decrease after only 1 injection in these 17 responding patients of 70% (range 35-96).

Conclusion

Monotherapy with DARA demonstrates encouraging efficacy in previously-treated patients with AL amyloidosis with deep and rapid hematological responses. The administration of DARA in these patients is associated with a good safety profile and non-severe adverse events occurring mostly after the first infusion. The data, in particular hematological and organ responses, will be updated at the meeting. A prospective randomized international phase III study (AMY3001) in naive patients with DARA in combination with bortezomib, cyclophosphamide and dexamethasone is ongoing.

Session topic: 14. Myeloma and other monoclonal gammopathies - Clinical

Keyword(s): Amyloidosis, chemotherapy