Daratumumab – a CD38 mAb – for the Treatment of Relapsed /Refractory Multiple Myeloma Patients: Preliminary Efficacy and PK Data from a Multicenter Phase I/II Study

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Background: Daratumumab (HuMax™-CD38) is a human CD38 monoclonal antibody with broad-spectrum killing activity; it effectively kills CD38-expressing tumor cells via antibody-dependent cell-mediated cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC) and apoptosis. The objectives of this ongoing first-in-human (FIH) dose-escalation study (ClinicalTrials.gov CT00574288) are to establish the safety profile and MTD. In addition efficacy and pharmacokinetics are evaluated. Preliminary data from this FIH study has shown that daratumumab has an acceptable safety profile[1].

Methods: Pts ≥18 years and previously diagnosed with MM requiring systemic therapy and considered relapsed or refractory (RR) to at least two different prior lines of therapy and not eligible for salvage ASCT were enrolled. The design of this study encompasses an accelerated dose-escalation based on a classical 3+3 design. Daratumumab is administrated over a 9 wk period encompassing 2 pre-doses and 7 full-doses. The doses range from 0.005 mg/kg to 24 mg/kg. Evaluation of efficacy data was performed by TP and Genmab according to Rajkumar[2]. The results presented in this abstract are based on preliminary data analyzed before database lock.

Results: Data from 29 pts including the 16 mg/kg group are collected. Preliminary efficacy evaluation is based on best paraprotein response as reflected by change in serum and/or urine M-component or FLC[2]. Eighteen of 29 patients achieved a response according to Rajkumar[2] and for dose cohort ≥ 4mg/kg 7/9 patients responded to daratumumab as monotherapy; and five of those patients achieved ≥ MR. All patients in dose cohorts ≥ 4mg/kg with bone marrow plasma cells above normal range at baseline decreased the number of plasma cells to normal levels when treated with daratumumab during 9 weeks.

The plasma level of daratumumab is as expected for IgG and no accumulation of daratumumab has been observed during the treatment period. The toxicity was manageable.

Conclusion: Daratumumab treatment resulted in marked response rate and reduction of bone marrow plasma cells in pts with RR MM. No accumulation of daratumumab has been observed and the toxicity has been manageable.

1. Gimsing: ASH 2011 abstract 1873
2. Rajkumar: Blood 2011;117:4691-5