PROTOCOL TITLE: DAratumumab i**N** combination with Bor**TE**zomib and Dexamethasone in subjects with relapsed or relapsed and refractory Multiple Myeloma and severe renal impairment including subjects undergoing hemodialysis. A phase 2, open-label, multicenter trial

PROTOCOL CODE: GMMG-DANTE

EUDRA-CT: 2016-000433-51

Report GMMG-DANTE Trial

The investigator-initiated multicentric phase II GMMG-DANTE study evaluated the triplet combination treatment of daratumumab, bortezomib and dexamethasone (DVd) in relapsed or refractory (r/r) multiple myeloma (MM) patients with severe renal impairment. r/rMM patients with ≥ 1 prior treatment line and a GFR < 30 ml/min or undergoing hemodialysis were eligible. The trial was planned to include 36 patients in Germany and Greece.
22 patients from 6 German and 1 Greek site were enrolled between January 2017 and January 2020. However, after inclusion of 22 of 36 planned patients the trial was prematurely stopped. The decision to prematurely stop the trial was made due to inferior recruitment as a result of both the broader commercial use of DVd in myeloma patients with renal impairment even without available scientific data on the feasibility, and from early 2020 on the upcoming COVID-19 pandemic with.

Below are the currently available results of the GMMG-DANTE trial.

1 Inclusion/Exclusion Criteria and Screening

No violation of inclusion criteria was observed, actual hemodialysis was not classified as deviation from the inclusion criteria. Regarding exclusion criteria no violation was observed. No unexpected findings were documented were observed.

2 Demography

The average age of patients was 70 years (SD 9 years, range 55-89 years). Twelve out of 21 patients were male (57%), male (69 years) and female age (72 years) was not different.

3 Study arms and stratification criteria

There were no stratification criteria except for study centers.

4 Treatment

All patients started treatment. Patient numbers treated with Daratumumab decreased from Day 1, Cycle 1 (n=21) to Day 1, Cycle 8 (n=12). There was no unexpected variation in doses for this treatment. Dose reduction was performed in one patient in Day 1 of Cycle 1, Cycle 7, and Cycle 8 respectively. For Bortezomib the same decrease of treated patients as for Dexamethasone was observed, for this treatment from cycle 5 a decrease of the average dose was observed. Consistently, cumulative over all cycles, 49 dose reduction were documented, 29 of them in cycles 5 to 8.
Duration of therapy (without maintenance therapy) was between 3 and 110 weeks with a mean of 49 weeks and a median of 28 weeks.

5 Physical Examination and Vital Signs

Body Weight was stable over time, there was a trend to lower average systolic blood pressure, however, individual trajectories showed large heterogeneity. Analogous, but less pronounced results were found for diastolic blood pressure.

6 Primary outcome variable

In 21 patients 14 successes with regard to the primary outcome Overall Response Rate (ORR) according to International Myeloma Working Group (IMWG) criteria, were observed. Of these, 2 patients had complete response (CR), 6 patients had very good partial response (VGPR), and another 6 patients had partial response (PR). Thus, the success criterion of the Simon design was met and the entire study was successful. The exact two-sided 95% CI of success was 43%-85% (software R, procedure binom.test).

7 Secondary outcome variables

The duration of follow up was 28 months. One year overall survival was 0.69 (95% CI ± 0.21), and two year overall survival was 0.50 (95% CI ± 0.24). Median survival was not reached, mean survival (largest censoring time 39 months) was 25.5 (± 7.1) months. One year progression free survival was 0.45 (95% CI ± 0.22), and two year progression free survival was 0.35 (95% CI ± 0.21). Median progression free survival was 10.4 (± 9.3) months, mean progression free survival (largest censoring time 39 months) was 15.8 (± 6.4) months.

8 Safety variables

Among 21 severe adverse events (SAEs) in 10 patients, two events were possibly related to any of the three therapies and one event was possibly related to Dexamethasone only.
No secondary malignancies occurred.