S179 RANDOMIZED COMPARISON BETWEEN KRD AND KTD INDUCTION, FOLLOWED BY K MAINTENANCE OR OBSERVATION IN TRANSPLANT NON-ELIGIBLE PATIENTS WITH NDMM (AGMT-MM02 TRIAL)

Author(s):
Heinz Ludwig, Thomas Melchardt, Siegfried Sormann, Niklas Zojer, Johannes Andel, Bernd Hartmann, Christoph Tinchon, Eberhard Gunsilius, Klaus Podar, Alexander Egle, Wolfgang Willenbacher, Ewald Wöll, Martin Schreder, Reinhard Ruckser, Boris Bozic, Maria-Theresa Krauth, Andreas Petzer, Clemens Schmitt, Sigrid Machherndl-Spandl, Hermine Agis, Michael Fillitz, Wolfram Pönisch, Stefan Knop, Bruno Paiva, Richard Greil

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Background:
Carfilzomib (K)-based combinations have been established as effective frontline and relapse regimens in pts with multiple myeloma (MM).

Aims:
In this randomized phase II trial we evaluated the impact of either Revlimid (R) or Thalidomide (T) as combination partner for K and dexamethasone (KRd or KTd) on outcome in pts with newly diagnosed MM (NDMM) not eligible for autologous transplantation (TNE). Further, we evaluated the role of one year K maintenance therapy compared to observation.

Methods:
One hundred twenty two pts have been enrolled (ITT population). Median age was 75 yrs, ISS stage I/II/III: 29 (23.8%)/48 (39.3%)/45 (36.9%), ECOG stage 0/1: 64 (52.5%) / 58 (47.5%). t(4;14) ± del17p was noted in 15 (16.3%) of 92 pts with results available. Pts were randomized to 9 cycles of KRd or KTd, and 107 pts received at least one full cycle. Carfilzomib (K) was started with 20mg/m2 at d 1 of cycle 1, and was continued with 27mg/m2 for the first 2 cycles (d 1+2, 8+9, 15+16 schedule); followed by K administration at 57mg/m2 once weekly for a 28 d cycle. Thalidomide 100mg/d (50mg in pts >75 yrs of age), d 1-28, or Revlimid 25mg/d (15mg in pts ³75 yrs of age) d 1-21. Dexamethasone 40mg (20mg in pts ³75 yrs of age) once/week. After induction, pts with ³SD were randomized to K maintenance (d 1 and 15) for 12 cycles or observation. MRD was assessed by NGF with a sensitivity of 10-6 in pts with ≥VGPR. Survival estimates were calculated according to Kaplan-Meier and survival curves were compared with

the log-rank test. PFS and OS results presented are given for the ITT population. This trial is registered on clinicaltrials.gov (NCT02891811).

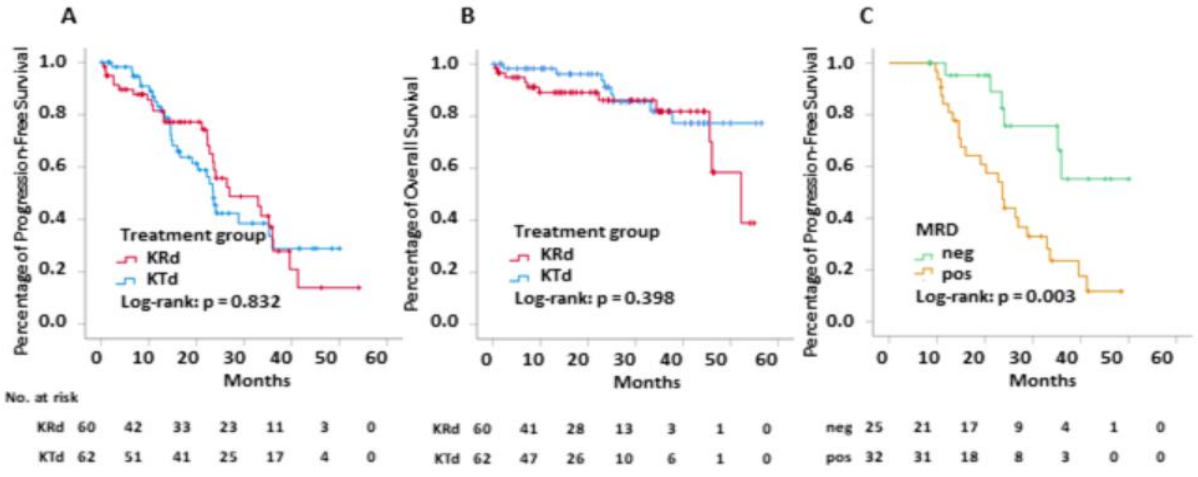
Results:

Median follow-up was 25.3 mos, 15 pts discontinued therapy within the first cycle due to patient (3) or investigator (1) decision, AE/toxicity (8), death or progressive disease (2) or other reason (1). Overall response rate was 91.3% in the entire group with available data (n=115). Results for sCR, CR, VGPR, PR, and ORR for KRd and KTd were similar between both groups (7.3%/10.0%, 27.3%/33.3%, 38.2%/35.0%, 14.5/16.7%, 87.3%/95.0%, respectively). Minor response was noted in 4 (3.5%), stable disease in 5 (4.3%) and progressive disease in 1 (0.8%) pts.

PFS (median 26.9 and 23.5 mos, p=0.832) and OS (not reached vs 52.2 mos, p=0.398) were similar between the KRd and KTd group, respectively. The OS rate at 36 mos was 82% in both groups. MRD testing was performed in 57 pts at time of CR/VGPR. Of those, 43.9%, (20.5% of the ITT group) pts were found to be MRDneg. PFS was significantly longer in MRDneg vs. MRDpos pts (p=0.003). Seventy six pts were randomized to K maintenance therapy or observation. Median PFS was numerically higher in the pts with K maintenance treatment (median 33.0 vs 24.0, p=0.714), but the difference was not statistically significant. Data on OS are not mature yet (only 9 events).

Grade 3/4 hematologic AEs were anemia (4.1%), leukopenia (0.8%), thrombocytopenia (7.4%), while non-hematologic grade 3/4 AEs were infection (20.5%), GI-disorders (7.4%), hypertension (7.4%), renal and cardiac impairment/failure (6.6% and 8.2% respectively).

Figure 1: Progression-free survival (A) and overall survival (B) with KRd and KTd, and PFS in MRD^{neg} and MRD^{pos} patients (C) with TNE NDMM



Conclusion:

Our data show similar high efficacy of KRd and KTd in elderly NTE NDMM pts, including no difference in ORR (KRd and KTd, 87.3% and 95%, respectively), PFS and OS. Overall survival rate at 3 yrs was 82%. Median PFS was significantly longer in MRDneg pts. PFS was numerically, but not statistically longer in pts on K maintenance vs observation. Treatment was associated with an acceptable tolerance profile.

Keyword(s):

Clinical outcome, Clinical trial, Multiple myeloma, Randomized