A Sequential Cohort Study Comparing KappaMab Alone To KappaMab, Lenalidomide And Low Dose Dexamethasone In Kappa-Restricted Relapsed Refractory (RR) Multiple Myeloma (AMaRC 01-16)

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KappaMab is a chimeric IgG1 monoclonal antibody specific for Kappa Myeloma antigen (KMA), a tumour specific cell antigen exclusively expressed on the surface of kappa restricted MM cells. Early safety and efficacy signals seen with single-agent treatment in phase I/II studies in conjunction with observations that IMiD treatment upregulates the KMA target and enhances effector cell cytotoxicity, providing rationale for this proof of principle immune-oncology (IO) approach in a minimally pretreated MM population.

The primary aim of this study was to establish the clinical benefit rate (CBR) of KappaMab alone (Stage 1) and in combination with lenalidomide (LEN) and low dose dexamethasone (DEX) (Stage 2). Secondary aims: to determine the safety of KappaMab in combination with LEN and DEX, in particular, the incidence of immunological adverse events (AEs); and to evaluate the kinetics of response and loss of response (time to response (TTR), time to disease progression (TTP), overall survival (OS)).

METHODS

Investigator initiated, phase IIb, multicentre, open label sequential cohort study comparing KappaMab alone to KappaMab in combination with LEN and DEX in RR MM (funded by the Victorian Cancer Agency, Australia). Key inclusion criteria were kappa restricted myeloma, 1-3 prior lines of therapy but no prior LEN.

Recruitment is planned for 60 patients in total, with an initial intention to treat 30 patients per stage. In Stage 1, patients received KappaMab (10mg/kg IV infusion) weekly for 852 (induction), then every 4/2 (maintenance). (One cycle = 28d). For patients in Stage 2, KappaMab dosing was at the same stage 1 dose, with the addition of LEN (25mg D1-21) and DEX 40mg weekly. In cycle 1 of Stage 2, LEN and DEX commenced 1.5/2 prior to KappaMab. (Cycle 1 was of 35 days duration: LEN 25mg D1-28 and DEX 40mg weekly D1, 8, 15, 22, 29).

Treatment continued until toxicity/progression. This is a planned interim analysis of the primary endpoint (CBR).

RESULTS & DISCUSSION

Of the 60 patients included in this analysis, 27 patients remain on study (Stage 1=40, Stage 2=27).

26 have progressed: (Stage 1=16, Stage 2=10),
• 6 withdrew consent (3 each stage),
• 2 other and
• 5 patients are known to have died (Stage 1=2, Stage 2=3).

Estimated median potential follow-up was 4.71m in Stage 1 (UQ=9.23m) and 5.49m in Stage 2 (UQ=8.41m).

Swimmer plot (by stage) of the status of patients (n=39) enrolled on the study and included in analysis
• Green diamond - time of achievement of OR (i.e. PR or better)
• Red diamond - time to progression
• Black dot - time to death

Follow-up by stage (Stage 1=Max, Stage 2=Red)

Observed CBR (Table 3) in Stage 1 was 5.3% (1/19, PR=1) compared to 77.5% in Stage 2 (31/40, CR=1, VGPR=6; PR=20, MR=4). (Response assessments are ongoing). Proof of concept (PoC) criteria were not met for Stage 1 (Table 4a), but were met for Stage 2 (Table 4b): observed CBR ≥ 55%, and the posterior probability (PP) that the true CBR exceeds 35% was ≥ 95% (PP=0.999).

ORR for Stage 1 (Table 5a) was 5.3% (1/19) compared to 67.5% (27/40) for Stage 2.

Median TDoR was not reached in Stage 1 (95% CI: 4.6m and above), and was 1.84m in Stage 2 (95% CI: 1.18 – 2.17m) (p=0.001).

BACKGROUND & OBJECTIVE

CONCLUSIONS

In a patient population with high prior IMiD (thalidomide) exposure and a median of 1 prior line of therapy, KappaMab combined with LEN and DEX demonstrated an ORR of 67.5% and was well tolerated.

This novel immune-oncology combination may represent a promising new therapeutic option. This trial is ongoing.