Urinary CD163 Predicts Complete Renal Response with Zetomipzomib Treatment in Phase 2 Study in Patients with Lupus Nephritis

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Introduction

• Complete renal response (CRR) defined by ACR/EULAR guidelines as a desirable clinical outcome associated with long-term preservation of kidney function in patients with lupus nephritis (LN)
• Urinary CD163 (uCD163), a protein released from macrophages in the kidney, is a promising biomarker that correlates with histologic inflammation and has been observed to predict clinical response to therapy

Methods

• In the MISSION Phase 2 (Amendment 4) study, patients with active proliferative LN (Class III or IV a v b) received 60 mg of zetomipzomib subcutaneously once weekly (first dose 30 mg) in addition to stable background therapy for 24 weeks
• End-of-treatment (EOT) was at Week (W) 25, and end-of-study (EOS) occurred at W37
• uCD163 was measured as an exploratory endpoint in 13 patients and was normalized to the urine creatinine for analysis
• uCD163 data at W13 and W25 were used to model a predictive association with CRR at W25 & W37, respectively
• ROC analysis results from the MISSION study suggests that uCD163 levels may be able to predict CRR endpoints up to 3 months later
• There was an apparent separation in uCD163 values between CRR and non-CRR, and uCD163 data maintains its low value in CRR responders even after EOT at W25 for the following 12 weeks at W37 (EOS). Decrease in uCD163 was also observed among non-CRR or non-responders throughout the study visits

Results

• Summary of uCD163 and UPCR
  For the 13 patients who consented to urine biomarker analysis, baseline 24-hour UPCR was mean=2.8 mg/mg, SD=3.3, median=1.8 mg/mg, range=0.93-13.4; uCD163: mean=1.7 mg/mmol, SD=2.3, median=0.97 mg/mmol, range 0.28-8.9
  Clinically relevant CRR was observed in the MISSION Ph 2 study of the 21 patients enrolled in MISSION Phase 2 (Amendment 4), 17 reached EOT and EOS. CRR was achieved in 35% (6/17) and 41% (7/17) of patients at W25 and W37
  • 4 additional patients achieved UPCR <0.5 at W37 although did not meet the daily steroid criteria (≤10 mg/day) for CRR
• Correlation of uCD163 with UPCR and CRR
  Anti-inflammatory potential of zetomipzomib was demonstrated by reduction of uCD163, which was strongly correlated with UPCR improvement at W13, W25 and W37 (Figure 1)

• ROC (Receiver operating characteristic) analysis
  ROC analysis results from the MISSION study suggests that uCD163 at W25 values of ≤0.13 and ≤0.09 at W25 are more likely to achieve a CRR at W25 and W37 respectively

Conclusions

• Post-hoc analysis of data from the MISSION Phase 2 study showed that uCD163 levels may be able to predict CRR endpoints up to 3 months later

References


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