A Phase I/II Study of CR011-vcMMAE, an Antibody-Drug Conjugate Targeting GPNMB in Patients with Advanced Melanoma

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BACKGROUND

• Antibody drug conjugates allow targeted delivery of drug to tumor
• Increase therapeutic index
• Induce tumor cell death and release novel antigens

• CR011, an IgG, antibody, targets the extracellular domain of GPNMB, a glycoprotein expressed in melanoma and other cancers.

• CR011 is conjugated to the dolastatin-like tubulin inhibitor monomethylauristatin-E (MMAE) via a valine-citrulline-enzyme-cleavable linker.

THREE DOSE ESCALATION

• 32 patients treated for a total of 132 cycles

• CR011-vcMMAE is generally well-tolerated

PHASE II RESULTS

Primary endpoint has been met
• 34 patients evaluable for response

• 2 patients withdrew consent prior to efficacy evaluation

• Median duration of follow-up: 3.4 months

• 5 responses observed (1 unconfirmed)

• Median duration 5.3 months

• 20 patients had RECIST-defined stable disease

• Median duration 4.8 months

PHASE I RESULTS: TOXICITY

Primary endpoint has been met
• 34 patients evaluable for response

• Most common toxicity was rash

• Two patients with dose limiting toxicities (rash/desquamation) at 2.63 mg/kg

• One confirmed partial response observed in Phase I

• Generally well-tolerated

PHASE II RESULTS: ACTIVITY

Primary endpoint has been met
• 34 patients evaluable for response

• Most common toxicity was rash

• Two patients with dose limiting toxicities (rash/desquamation) at 2.63 mg/kg

• One confirmed partial response observed in Phase I

CONCLUSIONS

• Patients with the highest degree of positive staining (>90%; 1+ to 3+) in paraffin-embedded tissues from 13 patients (36%) were evaluated immunohistochemically for expression of GPNMB using biotinylated CR011 antibody.

• Samples were scored based on percentage of tumor cells staining positive and on intensity of staining (1+ to 3+)

• In the 2 patients (15%) with GPNMB-negative tumors, PFS was 2.1 and 2.8 months, respectively

• Patients with any positive staining for GPNMB (1-100%, 1+ to 3+) had a median PFS of 4.5 months (range 4.1-7.9 months) (representative image below).

• Summary of IHC for GPNMB in Phase II Patients (n=13)

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PHASE II: DEMOGRAPHICS

PHASE II: GPNMB EXPRESSION

PHASE II: TOXICITY

PHASE II RESULTS

Patient Status as of April 30, 2009

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