A phase II study of NGR-hTNF, a novel vascular targeting agent (VTA), administered as single agent at low dose in patients with colorectal cancer refractory to standard regimens

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ABSTRACT

Background: NGR-mTNF has shown antitumor activity in preclinical models also when administered at doses in the picogram range (equivalent to a dose of 0.2 µg/m² in humans) (Figure 3). NGR-hTNF combines activity on tumour vascular permeability and direct anticancer activity. In preclinical models, NGR-hTNF showed antitumor activity at both low and high doses.

Phase I trials

In a phase I trial evaluating the maximum tolerated dose (MTD) of NGR-hTNF at 0.8 µg/m², 2 (6%) achieved a confirmed partial response lasting 5 months and 9/16 pts (56%) had disease stabilization lasting 6 months.

Methods

Primary endpoint: Progression-free survival with restaging performed every 6 weeks according to RECIST criteria. Secondary objectives: disease control rate, overall survival, safety and evaluation of dose limiting toxicities (DLTs) and MTD. Treatment regimen: NGR-hTNF given at 0.8 µg/m² as 1-hour intravenous infusion every 3 weeks (q3w).

Results

Of 111 cycles of therapy were administered with a median of 2 cycles (range 1-10) and 13 pts received 6 cycles (range 2-10). Antitumor activity at low doses of NGR-mTNF and mTNF in preclinical model had a 2-stage design with 16 and 27 pts to be enrolled in stage 1 and 2, respectively.

Conclusions

No significant differences were detected between patients previously treated with <3 and ≥3 regimens (HR=0.74; 95% CI, 0.34-1.54; p=.40) and between patients with prior number of regimens administered <3 (n=15) and ≥3 lines (n=17) (p=.09).

References

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