Background and methods

- The selective antivascular agent NGR-hTNF quickly and transiently modulates the systemic release of cytokines and chemokines, with antitumor effects at low dose driven by an early tumor vessel stabilization that increases intratumoral chemotherapeutic uptake.1
- Intravenous infusion of NGR-hTNF is typically characterized by onset of an early on-target adverse effect consisting of short-lived chills.
- By means of an individual patient pooled analysis of patients enrolled in 8 trials conducted in 7 tumor types, we assessed the impact of the onset of the chills on the treatment effect of NGR-hTNF.
- Dataset included 344 patients who had received NGR-hTNF 5 μg/m² every 3 weeks (n=162) or every week (n=181) either as single agent (n=143; mesothelioma, colon and liver cancer) or combined with doxorubicin (n=97; ovarian cancer, sarcomas and SCLC; gemcitabine (n=26); mesothelioma and NSCLC) or vinorelbine (n=35; mesotheliomas).
- In all trials, tumor response by RECIST was assessed every 6 weeks. Endpoints of interest were response rate (complete response plus partial response, CR/PR) and progression-free survival (PFS).

Baseline characteristics

- Odds ratios (OR) and hazard ratios (HR) were derived from logistic and Cox proportional-hazards regression models, respectively.

Occurrence of chills on treatment

- The incidence of chills was higher in pretreated patients compared to non-pretreated patients.

Tumor response rate

- The response rate was similar between patients with and without chills.

Multivariate model for PFS

- The model was significant for PFS and included the following variables: ECOG PS, Gender, Prior regimens, Chills, Grade 1-3 vs 0, and Chills and Grade 1-3 vs 0 in the combination model.

Conclusions

- Around 60% of patients transiently experienced mild-to-moderate chills during the first infusions of NGR-hTNF, more frequently when given as single agent than in combination.
- Patients reporting chills had a 2-10 fold increased tumor response and a 40-70% improved PFS.
- The impact on treatment effect was more marked when NGR-hTNF was given in pretreated patients, as single agent and in combination with doxorubicin.
- Early onset of chills may easily identify patients who are more likely to gain benefit from NGR-hTNF.