NGR-hTNF in previously treated patients with malignant pleural mesothelioma (MPM)

F. De Vincenzo1, G. Rossoni2, A. Santoro3, V. Gregoric4, P. A. Zucali5, G. Citterio6, M. Simonelli7, G. Petrella8, F. Caligaris-Cappio9, A. Lambla3, C. Bordignon3
1Istituto Clinico Humanitás, Rozzano, Italy; 2Istituto Scientifico San Raffaele, Milan, Italy; 3Istituto Ortopedico Rizzoli, Bologna, Italy; 4University of Ferrara, Italy; 5University of Pavia, Italy; 6University of Modena and Reggio Emilia, Italy; 7University of Genoa, Italy; 8University of Florence, Italy; 9University of Milan, Italy

Background and methods

Proclinical, TNP-α has shown potent antitumor and antivascular activity.
• However, the clinical use has been hampered by severe systemic toxicity with HTS significantly lower than ED^3

NGR-hTNF consists of TNF-α fused with the tumor-homing peptide NGR

CD13 expression in AML

NGR-hTNF is Human Tumor Navigating Recombinant Peptide

Malignant pleural mesothelioma (MPM) is a devastating disease with increasing incidence worldwide.
• The combination of gemcitabine and cisplatin is standard-of-care as front-line regimen with median survival of 12.1 months^1

However, patients who failed first line have an aggressive disease with median PFS of 3.5 months, disease control of 16%, and median survival of 6.4 months reported in the re-treatment of a phase 3 trial^2

Recently, an improved approach for non-widely-accepted 2nd line are currently available.
• We report the long-term results of a phase 2 trial testing NGR-hTNF in MPM patients who failed a pembrolizumab-based regimens

Conclusions

NGR-hTNF is well tolerated in patients pre-treated with pembrolizumab.
• Disease control achieved in half of patients and maintained for a median time ≥4 months with triweekly schedule and ≥9 months with weekly schedule

Based on first tumor reassessment, disease control (v progression) associated with longer survival time

Two double-blind, placebo-controlled randomized trials with NGR-hTNF 0.8 µg/m2 weekly are currently open to accrual:
• A phase 2 trial as maintenance treatment in patients who did not progress after 8 cycles of first-line therapy (NGR09 trial - www.clinicaltrials.gov NCT0135800)
• A phase 3 study testing best investigator choice with or without NGR-hTNF in relapsed patients (NGR015 trial - www.clinicaltrials.gov NCT0198266)

Results

OS by disease status (2-month landmark analysis)

- OS by neutrophil-to-lymphocyte ratio (NLR)
  - NLR^≥ 2.5 (v)  vs (NLR^< 2.5 (v)  median survival 16.7 vs 5.0 months)**
  - **median survival 16.7 vs 5.0 months**

References

3. Zucali PA et al. JCO 2010; 28:3654
5. JCO 2008 ; 26:1698