Front-line chemotherapy with or without NGR-hTNF in non-small cell lung cancer

V. Gregorč1, N. Zilembo2, F. Grossi3, T. De Pas4, F. Pietrantonio2, M. Giovannini4, G. Rossoni1, A. Bulotta1, A. Lambiase5, C. Bordignon5
1 Instituto Scientifico San Raffaele, Milan; 2 IRCCS Fondazione Istituto Nazionale Tumori, Milan; 3 Istituto Nazionale Ricerca sul Cancro, Genova; 4 Istituto Europeo di Oncologia, Milan; 5 MolMed, Milan, Italy

Background

- NGR-hTNF (asparagine-glycine-arginine human tumor necrosis factor) selectively damages CD13-overexpressing tumor vessels1
- Overexpression of CD13 in NSCLC has been associated with poor prognosis and increased angiogenesis2
- NGR-hTNF was safely given at 0.8 μg/m2 in combination with cisplatin 80 mg/m2, with promising activity shown in phase Ib trial3
- There is a restriction of use for most antiangiogenic agents in squamous non-small cell lung cancer (NSCLC) due to occurrence of severe pulmonary hemorrhage or tumor-related bleeding4
- Significant associations have been observed for chemotherapy between histological subtype and outcome, with improved overall survival (OS) reported for cisplatin/pemetrexed in nonsquamous and cisplatin/gemcitabine in squamous NSCLC

Study design

- Open-label, randomized phase II
- Chemo-naïve, stage IIIb/IV NSCLC
- ECOG performance status (PS) 0-1
- Brain metastases, if adequately treated
- Primary study endpoint - progression free survival (PFS)
- Secondary study endpoints - response rate, safety, OS
- Stratification factors - PS (0 vs 1)
- - histology (squamous vs nonsquamous)
- Treatment plan - cisplatin 80 mg/m2 d1 plus either
- - pemetrexed 500 mg/m2 d1 (nonsquamous)
- q3w for 6 cycles
- - gemcitabine 1,250 mg/m2 d1,8 (squamous)
- q3w for 6 cycles, with or without
- NGR-hTNF 0.8 μg/m2 d1 q3w until PD

Conclusions

- NGR-hTNF was safely given to NSCLC patients, including those with squamous cell histology and treated brain metastases
- In unselected nonsquamous NSCLC, evidence of activity was noted in patients who were never or light former smokers
- In squamous NSCLC, the potential clinical benefit of NGR-hTNF needs to be evaluated in larger sample size trial

References

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Acknowledgements (MolMed)

Cristina Ammannati, Shalini Colombo, Simona Santucci, Antonella Troysi, Elena Lungagnani

Abstract # 1251P