Study shows white blood cell boosting drugs safe during chemo-radiotherapy of lung cancer

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A late breaking subanalysis of the phase III CONVERT trial presented at the European Lung Cancer Conference (ELCC) shows that white blood cell boosting drugs are safe during concurrent chemo-radiotherapy of small cell lung cancer (SCLC).[1]

"The optimal treatment for limited-stage SCLC is concurrent chemo-radiotherapy," said lead author Dr Fabio Gomes, a medical oncologist at the Christie NHS Foundation Trust, Manchester, UK. "The efficacy of this intensive treatment is balanced by more toxicity, mainly haematological but also oesophageal and pulmonary. Meaning this is not a treatment to be considered for every patient and many more will struggle to stay on track with the planned treatment".

Granulocyte colony-stimulating factors (G-CSFs) are commonly used as a supportive measure to boost the survival, proliferation and differentiation of neutrophils. The expected neutropenia is less severe and patients recover more quickly, reducing their risk for infectious complications. However, its use during concurrent chemo-radiotherapy in SCLC is controversial and the American Society of Clinical Oncology (ASCO) recommends against its routine use.[2] This is due to a randomised trial with 215 eligible patients performed between 1989 and 1991, which showed a significant increase in severe thrombocytopenia, severe anaemia, pulmonary complications and toxic deaths when granulocyte-macrophage CSFs (GM-CSFs) were used during concurrent

chemo-radiotherapy.[3]

Gomes said: "There have been two major changes since this trial was published in 1995 which may affect the safety of CSF in this context. First, the trial tested GM-CSFs which act on more than one blood cell lineage and are not commonly used nowadays. Instead we use G-CSFs, which are more specific and aim for the neutrophil lineage only. Second, modern radiotherapy techniques have evolved significantly since then and are more precise, which reduces the risks of toxicity."

The phase III CONVERT trial enrolled 547 patients with limited-stage SCLC for concurrent chemo-radiotherapy who were randomised to once-daily or twice-daily radiotherapy. There was no difference in overall survival between the two groups.[4]

The trial protocol allowed the use of G-CSF, and around 40% of patients received it at some point during the treatment. For the analysis presented today, the researchers compared the toxicities and outcomes between patients who received G-CSF during concurrent chemo-radiotherapy and those who did not.

They confirmed that the chance of severe thrombocytopenia or anaemia during treatment almost doubled in patients given G-CSF to around 30% and 20%, respectively, however these were lower than previously reported. That was followed by a significantly higher use of further supportive measures such as platelets and blood transfusions. However, there was no difference in the incidence of pulmonary complications or in survival.

Gomes said: "G-CSF had no significant negative impact on the outcomes of these patients, which is a very comforting result. The higher haematological toxicity was balanced by an appropriate supportive care throughout treatment."

He continued: "We can conclude from this analysis that the use of G-CSF during thoracic radiotherapy is safe and should support patients to receive the full planned course of concurrent chemo-radiotherapy and achieve the best possible benefit. These findings should give clinicians the confidence to use G-CSF when needed in this context. We aim to publish a complete analysis later this year which may hopefully help change the current guidelines."

Commenting on the findings, Dr Stefan Zimmermann, Senior Consultant, Medical Oncology Department, HFR - Hôpital Cantonal, Fribourg, Switzerland, said: "Oncologists do need G-CSF to mitigate neutropenia and increase chemotherapy delivery and compliance, but want the beneficial effect of timely concurrent therapy to outweigh the toxic risks."

"In this analysis, the use of G-CSF did not result in an increased risk of pneumonitis, but the incidence of severe thrombocytopenia is a concern," he continued. "The use of G-CSF was not detrimental to progression-free survival or overall survival. We can conclude that primary or secondary prophylaxis of febrile neutropenia with G-CSF is justified, but patients at higher risk for thrombocytopenia should be treated with caution."

More information: 1 Abstract LBA2_PR - 'Use of G-CSF and prophylactic antibiotics with concurrent chemo-radiotherapy in limited-stage small cell lung cancer: results from the phase III CONVERT trial,' will be presented by Dr Fabio Gomes during the Proffered Paper session 'SCLC and early stage NSCLC' on Sunday, 7 May, 09:00 (CEST).

2 Smith TJ, et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015;33(28): 3199-3212.

3 Bunn PA Jr, et al. Chemoradiotherapy with or without granulocyte-macrophage colony-stimulating factor in the treatment of limited-stage small-cell lung cancer: a prospective phase III randomized study of the Southwest Oncology Group. J Clin Oncol. 1995;13(7):1632-1641.

4 meetinglibrary.asco.org/content/165387-176