

No Advantage in Survival With Targeted Therapies as Maintenance in Patients With Limited and Extensive-Stage Small Cell Lung Cancer: A Literature-Based Meta-Analysis of Randomized Trials

Giandomenico Roviello,^{1,2} Laura Zanotti,² Maria Rosa Cappelletti,² Angela Gobbi,² Chiara Senti,² Alberto Bottini,² Daniele Generali^{2,3}

Abstract

Small cell lung cancer (SCLC) is a lethal disease with a very restricted armamentarium of active treatments. In the new era of targeted therapies, several attempts based on the combination of chemotherapy with new compounds has been made but with a low rate of success. The idea of using the new targeted therapies as maintenance treatment after their combination with chemotherapy has been pursued. The aim of the present study was to analyze the available clinical data regarding the effect of the targeted agents as maintenance therapy on survival in patients with SCLC. A literature-based meta-analysis of randomized controlled trials, in accordance with the preferences for reported items in systematic reviews and meta-analyses guidelines, was performed. PubMed, the Cochrane Library, and a search of abstracts presented at American Society of Clinical Oncology meetings were searched for relevant studies. The primary outcome was overall survival (OS). Nine studies, with a total of 1385 patients, were included. The pooled analysis revealed that the new targeted therapies did not improve survival compared with the control arm (placebo, hazard ratio, 1.02; 95% confidence interval, 0.91-1.15; $P = .69$). However, a small advantage in the 1-year OS rate (risk ratio, 1.21; 95% confidence interval, 0.9-1.63; $P = .21$) was observed. Maintenance with targeted therapies failed to improve the survival of patients with SCLC with an increased rate of toxicity. The detected survival advantage suggests that perhaps the maintenance approach could be used to increase the 1-year OS rate. However, this finding requires confirmation in further studies, perhaps of patients selected according to their tumor biologic profile.

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Introduction

Small cell lung cancer (SCLC) accounts for 10% to 15% of all lung cancer patients¹ and is considered a lethal disease with a poor

¹Section of Pharmacology and University Center DIFF-Drug Innovation Forward Future, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

²US Terapia Molecolare e Farmacogenomica, Azienda Socio-Sanitaria Territoriale di Cremona, Cremona, Italy

³Department of Medical, Surgery and Health Sciences, University of Trieste, Trieste, Italy

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Address for correspondence: Giandomenico Roviello, MD, Department of Molecular and Translational Medicine, University of Brescia, Viale Europa 11, Brescia 25123, Italy

E-mail contact: giandomenicoroviello@gmail.com

prognosis. Several reasons can explain this negative trend in survival, including the rapid doubling time and high growth fraction, paraneoplastic endocrinopathy, and the early development of widespread metastases. Therefore, at diagnosis, approximately two thirds of patients will have extensive-stage disease (ED) without total surgical resection possible.^{1,2} In these advanced stages, the combination of different chemotherapeutic drugs, such as cisplatin and etoposide, can achieve a very high response rate but with very poor progression-free survival (PFS) and overall survival (OS).^{3,4}

Nonetheless, the initial response, which mainly results from the high proliferation of the tumor, suggested several therapeutic approaches to prolong the response rate obtained with previous therapy and improve the survival outcomes. Among these, maintenance or consolidation treatments have been extensively studied as

Maintenance Target Therapies for SCLC

possible approaches. However, to date, the results have been contradictory. In 2010, a meta-analysis of all published randomized clinical trials (RCTs)⁵ evaluated the effect of chemotherapy as maintenance or consolidation therapy. A total of 21 RCTs, including 3688 patients, were considered for analysis. Overall, no statistically significant advantage in OS (hazard ratio [HR], 0.93; 95% confidence interval [CI], 0.87-1.00) was reported for maintenance or consolidation therapy.

In the new era of targeted therapy, another possible option to be considered for maintenance therapy for patients with SCLC is the use of novel target agents. These drugs have generally been considered ideal for the maintenance approach, because they have a good toxicity profile, allowing their administration for a long period. However, although several agents targeting different pathways have

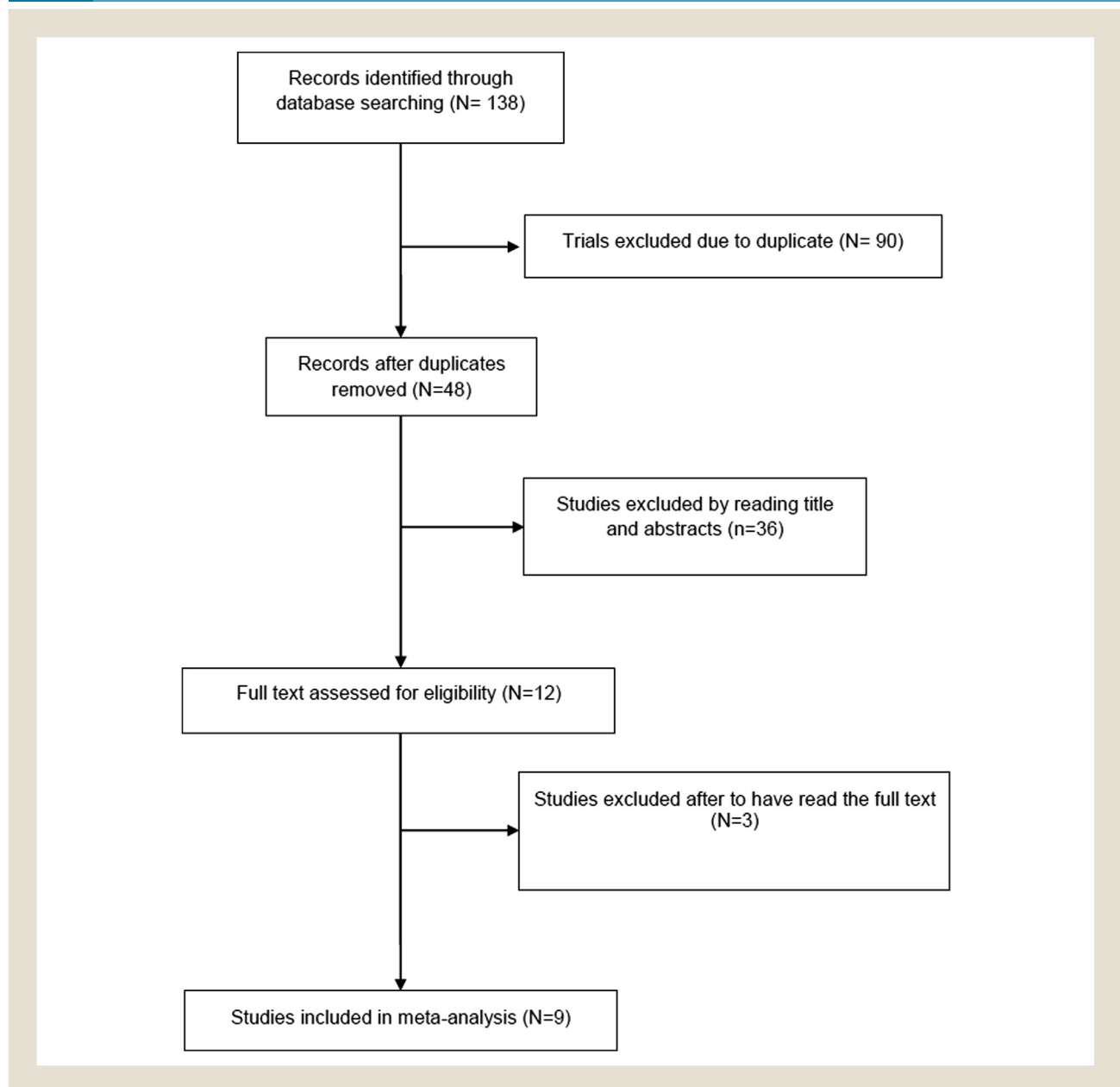
been investigated, the RCTs have reported conflicting results with a doubtful interpretation of their real clinical role. Overall, the issue of a benefit in OS for patients undergoing maintenance therapy with targeted agents for SCLC is unclear and controversial. Therefore, the aim of the present study was to analyze the available clinical data from RCTs to study the effect of targeted agents as maintenance therapy on OS in patients with SCLC.

Materials and Methods

Data Retrieval Strategies

We conducted the present meta-analysis of RCTs in accordance with the preferences for reported items in systematic reviews and meta-analyses guidelines.⁶ PubMed, the Cochrane Library, and the American Society of Clinical Oncology meetings were searched for

Figure 1 Trial Selection Flow Chart



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