New and Emerging Strategies for the Treatment of Small Cell Lung Cancer

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Small Cell Lung Cancer (SCLC) is a very aggressive cancer that comprises 15 to 25% of all lung cancers and has its highest occurrence in smokers [1-4]. Although it is generally considered to be very responsive to chemotherapy in the limited stage, it has a high incidence of recurrence. Despite its overall response rate which has been reported to be as high as 75 to 85%, patients with extensive stage disease are often refractory to the initial treatment. The long-term survival rate for SCLC for the limited disease state is approximately 15% while the advanced stage disease is often fatal in less than 1 year. Due to the asymptomatic characteristics of SCLC it often goes undiagnosed until it has progressed into the extensive stage. For the past several decades the chemotherapeutic standard of care, cisplatin or carboplatin plus etoposide has remained essentially unaltered. The development of new treatments including off-label use of existing therapies and new chemical entities has fallen well behind therapeutic advances for other forms of cancer. While chemotherapy is a powerful tool in the clinicians’ arsenal against cancer, a positive impact on improving survival can be made by improvements in prevention and early detection.

Newer chemotherapeutics such as amrubicin, picoplatin and temozolomide have currently been studied in clinical trials and have shown potential as effective therapies [5-7]. Of these, amrubicin, a DNA topoisomerase II inhibitor has been evaluated as a single agent and in combination scenarios with good activity against SCLC [8-12]. This agent has also been granted fast track approval by the US Food and Drug Administration for SCLC following first line therapy, Picoplatin, a new generation of platinum based chemotherapy designed to overcome platinum resistance, had only modest results as a single-agent therapeutic in a Phase II trial [13]. Temozolomide has been evaluated in several Phase II trials for patients with brain metastases from SCLC due to its ability to penetrate the central nervous system [14,15]. Additionally, therapeutic agents which function as inhibitors of angiogenesis and BCL-2 inhibitors have shown very limited or no benefit against SCLC in clinical trials [16-18]. As the field of scientific knowledge related to the pathophysiology and biology of lung cancer grows, scientists will be better equipped to design additional targeted therapies and vaccines in the treatment of SCLC. Unlike traditional vaccines which are commonly thought of as preventing disease, cancer vaccines for lung cancer are designed to treat cancer by boosting the immune response of the body against cancer cells. Another approach to improving therapeutic outcomes lies in advances and accessibility in diagnostics for early detection of SCLC. The rationale behind this is that current therapeutic agents are most effective when SCLC is in its early development phase. Early detection would allow for therapeutic intervention before the disease reaches the extensive stage. To this end, recent advances in imaging with fluorescence bronchoscopy and low-dose spiral CT (helical CT) will provide clinicians with improved ability for early detection once appropriated and affordable screening guidelines are further developed. Other early detection modalities utilizing blood-based tests devised from proteomic research are being evaluated to identify diagnostic biomarkers which may be present in the blood at the very early stages of tumor development [19,20]. In addition to improvements in therapy and early detection perhaps the greatest opportunity to combat lung cancer is prevention. Progress in prevention of lung cancer has focused on reduction in exposure to environmental factors (e.g. asbestos, radon and second hand cigarette smoke), smoking deterrence and cessation, diet, and overall nutrition. Strategies related to environmental factors have targeted identification and avoidance of exposure to carcinogens that cause SCLC in both the home and work place. Smoking cessation approaches have been aimed at nicotine replacement therapies (e.g. patches, gum or nasal spray) or other therapeutics (e.g. varenicline, bupropion) designed to reduce/eliminate smoking/nicotine addiction. While there is currently no conclusive data relating the prevention of SCLC to a healthy and nutritious diet, some studies suggest that a diet high in fruits and vegetables that follows the American Cancer Society dietary recommendation may offer some protection.

While there is currently no magic bullet for the prevention, detection and cure of SCLC, the key most probably lies in the improvement and advancement of strategies in each of these areas. Therefore, efforts should be expanded in the development of new and more effective agents, but time, money, and energy should also be directed towards prevention and early detection.

References


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