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Commentary Open Access

First-Line Platinum-Based Chemotherapy Re-challenge in Sensitive Small Cell Lung Cancer (SCLC): A Standard Treatment?

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Commentary

Small cell lung cancer (SCLC) has typically high sensitivity to chemotherapy and radiotherapy, although greater part of patients with limited disease (LD) and all patients with extended disease (ED) will develop disease relapse or progression, with an overall survival of 2-4 months in case of only best supportive care [1]. Based on response yielded by first-line therapy and relapse-free interval (RFI), interval between first-line treatment completion and disease progression, SCLC are generally divided in two categories: resistant and sensitive. Sensitive patients are those with response to first-line therapy and RFI of 90 days, while resistant patients have no response to first-line chemotherapy or shorter RFI [2].

Resistant patients have worse prognosis and usually treated with topotecan, the only drug approved as second-line treatment for recurrent SCLC but with modest results in survival and quality of life (QoL) [3-6]. Amrubicin, a synthetic 9-amino-anthracycline, in phase II trials showed promising results but a phase III trial failed to show the superiority of this drug in comparison to topotecan [7-9]. In sensitive subgroup a rechallenge of first-line chemotherapic regimen is reasonable approach, but with modest evidence due to the little clinical experiences, mainly represented by a small retrospective mono-institutional series. At ASCO 2014 Goto et al. presented results of a randomized prospective trial where sensitive SCLC patients were treated with topotecan or a rechallange with platinum, etoposide associated to a third drug such as irinotecan with a support of granulocyte colony-stimulating factor. Patients treated with polichemotherapy had a better outcome in comparison to control arm, although experimental arm had a higher incidence of side effects in particular: febrile neutropenia, anemia, thrombocytopenia and diarrhea [10].

Similarly Nakamura et al. presented a phase II randomized trial where sensitive SCLC patients were treated with rechallange of platinum doublet chemotherapy or amrubicin: monochemotherapy yielded a higher response rate in comparison to rechallenge (67% vs 43%) but disease control rate (85% vs 80%) and PFS (5.4 vs 5.0 months) were similar in both arms [11]. These experiences are reviewed in American College of Chest Physicians (ACCP) and National Comprehensive Cancer Network (NCCN) guidelines where authors suggest to offer rechallenge for responding patient with long RFI [12,13]. Our experience albeit retrospective has the advantage of being the most robust multi-centre case series published so far: not only allowed us to verify what rechallange produced in terms of survival but also allowed to recognize other exploring analysis. Stratifying patients according to RFI duration, we noted that those who had a longer interval, were those in which the rechallange produced a longer PFS, although these results did not reach statistical significance nor an advantage in OS.

This is probably due to the design and the statistical power of our study, the rarity of cases of sensitive SCLC makes it difficult to build up robust series that allow definitive conclusions. Another feature emerged from our study is that in some patients disease retained a kind of platinum-sensitivity for subsequent lines of therapies, almost as treatments do not exert a selection of resistant clones progressively regimens containing platinum group metals. Even in this case we cannot be extracted definitive conclusions for the small number of patients analysed at failure of first-line rechallange. In conclusion rechallange of first-line platinum based chemotherapy in patients with tumor response and controlled disease for a long period of time, may be a reasonable treatment option. The results yielded by this strategy look attractive. Furthermore, the data available would seem to suggest that the higher the better RFI appears the result produced by rechallange and that even in selected patients the disease long preserve a kind of platinum-sensitivity.

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