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PLAIN LANGUAGE SUMMARY

Place in therapy of key treatments for platinum-sensitive, relapsed, extensive-stage small cell lung cancer with a focus on lurbinectedin: a narrative review with case studies

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Background

About 2 out of 3 individuals who present to a doctor with symptoms of small cell lung cancer (SCLC) will be diagnosed with advanced disease. Standard treatment with platinum-etoposide plus atezolizumab or durvalumab is highly effective; however, virtually all patients who respond to this primary (first-line) treatment will become resistant to platinum and relapse. For patients who can progress to secondary (second-line) treatment, factors that inform the choice of therapy include:

- Length of time between relapse and last dose of first-line chemotherapy (known as the chemotherapy-free interval; CTFI)
- The patient's general physical condition
- Expected efficacy of the regimen (how well it works)
- Expected safety of the regimen (how well it is tolerated)
- Administration schedule (number of days the drug/s is administered per cycle)
- The patient's preferences

What is this review about?

Key second-line regimens used to treat relapsed SCLC with a CTFI of at least 90 days (i.e. platinum-sensitive) include platinum rechallenge (reusing the first-line regimen), topotecan, a cyclophosphamide-doxorubicin-vincristine (CAV) combination regimen, and lurbinectedin (also irinotecan and tarlatamab in the United States). To better understand the characteristics of each regimen relative to the others, we reviewed the results of recent clinical studies which investigated the efficacy and safety of these regimens in patients with platinum-sensitive relapsed SCLC.

What did the evidence review indicate?

Platinum rechallenge is more effective than topotecan for outcomes such as overall response rate (reduction in size or disappearance of the tumour) and progression-free survival (length of time before the disease becomes worse) and causes fewer cases of severe (grade 3) or life-threatening (grade 4) adverse effects that affect the blood and blood-forming organs such as bone marrow. Platinum-etoposide is administered intravenously on days 1 to 5 of 3-week cycles. During platinum rechallenge, patients may need to take another type of medication (e.g. granulocyte-colony stimulating factor, G-CSF) that helps the bone marrow to produce new white blood cells.

Topotecan is less effective than platinum rechallenge and not as well tolerated. The efficacy of topotecan is similar to that of CAV. Topotecan is administered intravenously or by mouth on days 1 to 5 of 21-day cycles. G-CSF is often required to prevent low blood cell counts.

The efficacy of CAV is similar to that of topotecan; however, patients may not be able to tolerate full doses of CAV due to adverse events (e.g. to the nerves and nervous system). CAV is administered intravenously over approximately 2 hours on day 1 of 21-day cycles.

Compared with platinum rechallenge (phase III study), lurbinectedin (phase II study) may prolong survival and is better tolerated. Lurbinectedin is better tolerated than topotecan or CAV (phase III study), also in patients older than 65 years. Lurbinectedin is administered intravenously over 1 hour on day 1 of 3-week cycles.

Conclusion

Based on its efficacy, tolerability and ease of administration, lurbinectedin appears to be a useful alternative to platinum rechallenge, topotecan and CAV in patients with platinum-sensitive relapsed SCLC.