Review Article **www.ijcps.com**

International Journal of
Chemical and Pharmaceutical Sciences
2026, Mar., Vol. 17 (1)

ISSN: 0976-9390
IJCPS

Redefining ES-SCLC Outcomes: Durvalumab's Journey Beyond Platinum-Etoposide from Trial to Therapeutic Revolution

Preethika K, Bhupalan MR, Hari Prasath S and *Thirugnanam TS.

Department of Pharmacy Practice, The Erode College of Pharmacy, Veppampalayam, Vallipurathampalayam (PO), Erode – 638112, Tamil Nadu, India

***Corresponding Author:** E-Mail: drtsthirugnanampharmd@gmail.com

Received: 8th Jan2026, Revised and Accepted: 11th Feb 2026

ABSTRACT

It evaluates the evolution of first-line treatment for extensive-stage small-cell lung cancer (ES-SCLC), noting the significant advancements made by combining immunotherapy with traditional chemotherapy regimens. Historically, etoposide plus carboplatin or cisplatin was the standard of therapy, although overall survival remained low. Recent advances show that adding durvalumab, a PD-L1 inhibitor, to platinum-etoposide chemotherapy greatly improves outcomes for ES-SCLC patients, as seen by the phase III CASPIAN trial, which saw median overall survival increase from 10.3 to 13.0 months. Durvalumab inhibits immune checkpoint signaling, which restores anti-tumor T-cell function, according to mechanistic insights. The paper also addresses significant trials—CASPIAN, MYSTIC, PACIFIC, TOPAZ-1, DUO-E, and AEGEAN—which demonstrate durvalumab's involvement in lung, biliary, and endometrial malignancies. Safety profiles show controllable immune-mediated adverse effects and non-severe nonhematological toxicities. Cost analyses support the regimens.

Keywords: Platinum-Etoposide; Lung cancer; ES-SCLC patients.

1. INTRODUCTION

In accordance with the extremely aggressive characteristics that small-cell lung cancer (SCLC) and its potential for early, widespread metastases that are around three quarters of patients who present with SCLC have extensive-stage SCLC (ES-SCLC) [1]. years following diagnosis, fewer than 5% of ES-SCLC patients are still alive. Until recently, there hasn't been much progress in improving outcomes for people with ES- SCLC. For almost thirty years, etoposide in conjunction with either carboplatin or cisplatin (EP) has been the standard first-line treatment. However, it has been demonstrated that patients with ES-SCLC have a longer overall survival (OS) when platinum-based chemotherapy is combined with immunotherapy that targets the programmed cell death-1 (PD-1)/programmed cell death ligand-1 (PD-L1) pathway [2]. inhibitors of programmed cell death 1 (PD-1) and its ligand (PD-L1) have been noticed as brand-new rehabilitation opportunities. Durvalumab is an everyday treatment for ES-SCLC, as it has been associated with enhanced overall survival while combination with conventional chemotherapy [2]. For the first-line treatment of patients with ES-SCLC, the phase 3 CASPIAN trial sought to evaluate the safety and effectiveness of durvalumab, a selective human IgG1 monoclonal antibody directed against PD-L1, in combination with etoposide plus either carboplatin or cisplatin (platinum–etoposide) and tremelimumab, a human monoclonal IgG2 antibody targeting CTLA-4. With a hazard ratio (HR) of 0·73 in comparison to 0·59–0·91; p=0·0047), durvalumab plus platinum–etoposide treatment was linked to an essential and clinically relevant improvement in overall survival compared to platinum–etoposide alone at the planned interim analysis. Durvalumab + platinum-

etoposide enabled a median overall survival of 13·0 months compared to 10·3 months with platinum-etoposide alone [3].

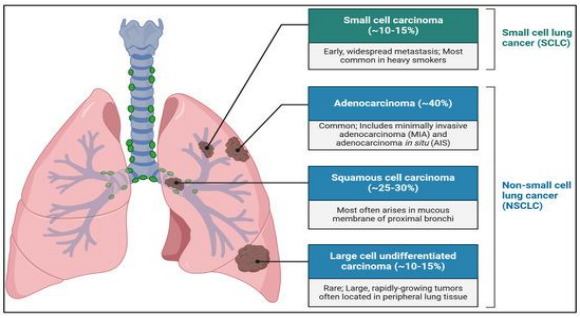
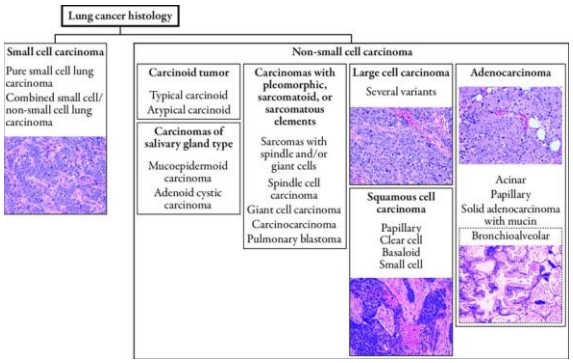


Figure 1. Adenocarcinoma, squamous cell carcinoma, and big cell carcinoma are the three primary subtypes of non-small cell lung cancer (NSCLC), typically arises from the epithelial cells of the lung [4].

2. CLASSIFICATION



Lung cancer histological categorization. There are two types of lung cancer: small cell lung cancer and non-small cell lung cancer. Small cell lung cancer has a 15% distribution, while non-small cell lung cancer has a 75%–80% distribution. The rest fall into different categories [5].

3. HISTORY

3.1. CLINICAL TRIALS

3.1.1. DURVALUMAB

Durvalumab with tremelimumab has shown some activity in non-small cell lung cancer (NSCLC) in a phase I clinical trial. The FDA has designated advanced metastatic bladder (Study 1108) as a breakthrough treatment based on phase I findings. A phase I experiment that combined durvalumab and gefitinib in lung cancer patients "showed promise" based on preliminary data. Durvalumab combined with a TLR 7/8 agonist (MEDI 9197) is presently being used in a phase I clinical trial for solid tumors. Durvalumab and an HPV DNA vaccine (MEDI 0457) are being used in a phase 1b/2a trial for patients with HPV-associated recurrent or metastatic head and neck cancer [6].

3.1.2. MYSTIC TRAILS

Patients with epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) wild-type locally advanced or metastatic (Stage IV) first-line non-small cell lung cancer (NSCLC) are being treated with Imfinzi monotherapy or Imfinzi in combination with tremelimumab versus SoC in the MYSTIC trial, a randomized, open-label, multi-centre, worldwide Phase III trial. Imfinzi is not authorized for use in lung cancer.

167 locations in 17 countries—including the US, Canada, Europe, portions of Asia, including Japan, Korea, Thailand, Taiwan (China), and Vietnam, as well as Russia and Australia—are hosting the trial. OS and PFS are primary objectives [7].

3.1.3. CASPIAN

There has already been a description of the open-label phase III CASPIAN trial's design (NCT03043872). 1, 6 In short, patients with World Health Organization (WHO) performance level 0/1 and treatment-naïve ES-SCLC were randomly assigned 1:1:1 to either EP, durvalumab plus EP, or durvalumab plus tremelimumab plus EP. Four cycles of EP plus durvalumab 1500 mg, with or without tremelimumab 75 mg, were administered to patients in the immunotherapy arms every three weeks [8]. Durvalumab 1500 mg was then maintained every four weeks until the disease progressed. After the EP treatment, patients in the durvalumab plus tremelimumab + EP group received an additional dose of tremelimumab. Patients in the EP group were given up to six cycles of EP along with the option for prophylactic cranial irradiation. If there were signs of efficacy, immunotherapy treatment could be continued beyond progression. Survival was examined every two months after medication was discontinued [8].

3.1.4. PACIFIC

Durvalumab, a programmed cell death-ligand 1 [PD-L1] inhibitor, was administered for up to 12 months to patients with unresectable, stage III non-small-cell lung cancer (NSCLC) whose disease had not progressed after platinum-based concurrent chemoradiotherapy (CRT). This improved overall survival (OS; stratified hazard ratio [HR], 0.68; 95% CI, 0.53 to 0.87; P = .00251; March 22, 2018 data cutoff [DCO]) and progression-free survival (PFS; stratified HR, 0.52; 95% CI, 0.42 to 0.65; P < .0001; February 13, 2017 DCO) in the phase III, placebo-controlled PACIFIC trial. 1–3 At later updates, this level of durvalumab versus placebo benefit stayed constant.

Historically, CRT combined with observation alone was the conventional standard of care; however, this approach was associated with low long-term survival rates. Increasing the radiation dose, consolidating chemotherapy with additional

systemic anticancer medicines, or inducing or consolidating chemotherapy did not appear to increase survival. The treatment of this population has advanced significantly with PACIFIC, the first study to show a survival advantage with immunotherapy in a curative-intent scenario[9].

3.1.5. TOPAZ-1

In the randomized, double-blind, placebo-controlled, multiregional trial TOPAZ-1 (NCT03875235), 685 patients with histologically proven locally advanced, incurable, or metastatic BTC who had not previously received systemic therapy for advanced illness were include to assess efficacy .The following were the trial's demographics: The demographics were as follows:50% male and 50% female; median age was 64 years (range 20-85); 47% were 65 years or older; 56% were Asian, 37% were White, 2% were Black, and 4% were of other races; 7% were Hispanic or Latino. Gallbladder cancer affected 25%, extrahepatic cholangiocarcinoma affected 19%, and intrahepatic cholangiocarcinoma affected 56%.

The primary effectiveness endpoint was overall survival (OS). Tumour assessments were performed every 6 weeks for the first 24 weeks, followed by 8 weeks until objective disease progression was observed. Participants assigned to durvalumab with gemcitabine and cisplatin had a statistically significant improvement in OS when compared to those randomized to placebo with gemcitabine and cisplatin. The median OS was 12.8 months (95% CI: 11.1, 14) and 11.5 months (95% CI: 10.1, 12.5) in the durvalumab and placebo arms, respectively (hazard ratio 0.80; 95% CI: 0.66, 0.97, p=0.021) [10].

3.1.6. DUO-E

The DUO-E/GOG-3041/ENGOT-EN10 experiment (NCT04269200) was a randomized, double-blind, placebo-controlled multicenter phase III trial that took place in 22 countries. Eligible patients were 18 years or older and had newly diagnosed advanced (FIGO measurable stage III/newly diagnosed stage IV [2009 staging method]) or recurrent endometrial cancer of epithelial histology (excluding sarcomas). Surgery had a low chance of curing recurring disease, and previous systemic anticancer treatment was only permitted if given in the adjuvant setting and at least 12 months between the last dosage and subsequent relapse [11].

3.1.7. AEGEAN

AEGEAN is a phase III, double-blind, placebo-controlled, multicenter, international trial that will evaluate the pathology and long-term clinical results of durvalumab + CT prior to surgery, followed by durvalumab monotherapy after surgery in adults with resectable stage II/III NSCLC. The trial will enroll patients from around 275 locations in over 25 countries worldwide. Approximately 800 patients will be randomly assigned (1:1) to receive durvalumab plus platinum-based doublet CT (carboplatin/paclitaxel, cisplatin/gemcitabine, pemetrexed/cisplatin, or pemetrexed/carboplatin) prior to surgery, followed by durvalumab monotherapy after surgery [12].

In addition to receiving an intravenous infusion of 1500 mg durvalumab or a placebo, patients will get platinum-based doublet CT scans every three weeks (q3w) for a maximum of four cycles. Following this, the attending surgeon will decide whether to do a lobectomy, bilobectomy, or sleeve resection. According to other studies that have assessed durvalumab in combination with chemotherapy in both metastatic non-small cell lung cancer and small-cell lung cancer, using a dose and regimen of durvalumab 1500 mg q3w during the neoadjuvant phase is in line with the typical chemotherapy schedule for this disease setting (q3w for 4 cycles). Additionally, prior pharmacokinetic modelling has not revealed any clinically significant variations in drug levels between q3w and q4w dosing schedules [13].

Following surgery, patients will receive an additional mg)/placebo q4w, which is 12 cycles of durvalumab (1500mg)/placebo q4w, which is consistent with other studies that incorporate a durvalumab monotherapy portion of the regimen and minimizes the number of patient visits required. Treatment will commence as soon as clinically feasible post surgery. Interim safety reviews of unblinded data will be carried out by an independent data monitoring committee [14].

3.1.8. CISPLATIN

MILESTONES OF CISPLATIN [17]

Italian chemist Michele Peyrone originally described the chemical cis-[Pt $(NH_3)_2Cl_2$] in 1845. It has traditionally been referred to as Peyronie's salt. Alfred Werner deduced the structure in 1893. Michigan State University researchers Barnett Rosenberg, Van Camp, and others found in 1965 that electrolysis of platinum electrodes produced a soluble platinum complex that prevented binary fission in Escherichia coli (E. coli) bacteria. The bacteria grew as filaments up to 300 times their typical length, but their cell division was stopped even while their growth persisted. It was discovered that the octahedral Pt (IV) complex cisplatin was successful in inducing filamentous growth in E. coli cells, but not the trans isomer. It was discovered that the square planar Pt (II)

complex, cis-[PtCl2(NH3)2], was much more successful in inducing filamentous development [15].

Because of this discovery, it was discovered that cis-[PtCl2(NH3)2] was in fact quite successful in regressing the mass of sarcomas in rats. The use of cisplatin in medicine began with the confirmation of this finding and the expansion of testing to other tumour cell lines. The United States Food and Drug Administration authorized cisplatin on December 19, 1978, for use in ovarian and testicular malignancies, and in 1979 in the United Kingdom (as well as in a number of other European nations). The first to be created was cisplatin. Roger Packer, a paediatric oncologist, started using cisplatin in adjuvant chemotherapy for childhood medulloblastoma in 1983.

The disease-free survival rates for patients with medulloblastoma increased significantly, reaching approximately 85%, as a result of the new procedure he created. Medulloblastoma is now commonly treated with the Packer Protocol. Similarly, cisplatin has been shown to be especially successful in treating testicular cancer, increasing the cure rate to over 90%, making it one of the most effective chemotherapy agents in oncology.

4. METHADOLOGIES

4.1. Demographics and the investigation design

CASPIAN is a multinational, multicentre, sponsor-blind, open-label, randomized phase III study. The significant report comprises a comprehensive overview of the trial methodology, and the effectiveness and safety results from this interim analysis (data cutoff: March 11, 2019) were previously released. According to Response Evaluation Criteria in Solid malignancies, version 1, eligible patients necessitate to be at least 18 years old, show ES-SCLC that was histologically or cytologically verified as treatment-naïve, possess a World Health Organization (WHO) performance status score of 0 or 1, and have realizable disease. The public with brain metastases who were asymptomatic or stable throughout treatment and were no longer using steroids and anticonvulsants at least one month before enrolled in in the trial were eligible [18].

In order to participate in the trial, each patient signed an informed consent form. The study was conducted in adherence with the Declaration of Helsinki, the International Conference on Harmonization's good clinical practice guidelines, and any applicable local regulations. The methodology of the research and all modifications were approved by the appropriate ethics committees and regulatory authorities. An impartial data monitoring committee implemented the purposeful interim efficacy assessment and periodic safety monitoring [19].

The study design and the interventions:

Within 1 to 42 days adhering to chemoradiotherapy, patients underwent randomization in a 2:1 ratio to receive either complemented placebo every two weeks as consolidation therapy for a maximum of 12 months or durvalumab intravenously at a dose of 10 mg according kilogram of body weight. Age (less than 65 vs. beyond 65), sex, and smoking history (current or past smoker vs. never smoked) were used to categorize the patients. During randomization on day 1, as soon as the patient's eligibility to participate was confirmed, the study medication was administered. In the event of verified illness progression, the start of an alternate anticancer treatment, intolerable toxic side effects, or consent withdrawal, the study supplements was terminated. Unless they experienced rapid tumour growth or symptomatic progression necessitating rapid intervention, patients could receive the study medicinal products until the disease grew. If disease control had been accomplished at the end of the 12-month

period but the disease could progress, they might be given the experimental drug yet again [20].

4.2. End points and assessments

We existing long-term follow-up for the two main end-points of operating system (time about the randomization until death from any cause) for durvalumab plus EP versus EP and durvalumab plus tremelimumab plus EP versus EP; OS rates at 12, 18, 24, and 36 months; and OS in patient subgroups based on predetermined baseline factors in this organized preliminary study (DCO 22 March 2021). Since progression-free survival (PFS) were sufficiently established (87% data maturity6), additionally progression nor response data had been collected after the prior DCO. Because further safety data was not collected following a previous DCO, serious adverse events (SAEs), including adverse events (AEs) that contributed to death, were investigated [21].

Age, sex, Eastern Cooperative Oncology Group Performance Status (ECOG-PS), smoking history, metastasis status, PFS, OS, efficacy metrics particularly objective response rate (ORR) and disease control rate (DCR), toxicity data, including undesirable reactions (AEs) and immune-related adverse events (irAEs), blood investigation results, regimen administration details, and dosage at start-up were all taken from the electronic medical records. OS served as the main goal, while PFS, ORR, and safety assessments served as the supplementary endpoints. Based on the data collected, the OS and PFS subgroup analyses were carried out [22].

4.3. Analogical statistical information

Evaluating the protocol's safety in treating elderly patients with ES-SCLC was the primary objectives of this study. A predetermined statistical the criteria wasn't meant for the present research to be confirmatory. As a consequence, the target number of participants to be enrolled during an 18-month period was set at 40 people Assume five participants were ineligible, the statistical power needed to identify adverse events was assessed for 35 patients. There was an 83.4% chance that one or more participants would experience adverse events with a probability of 5% or higher [23]. An independent-sample T-test was utilized for continuous variables and a chi-square test for noncontinuous variables to investigate the distribution of characteristics between the durvalumab and CCRT-alone groups. The Kaplan-Meier method was utilized for calculating survival outcomes, and Cox regression analysis was employed to conduct univariate and multivariate analyses to attempt to figure out the clinical characteristics correlated with each oncologic outcome [24]. A log-rank test was implemented for exploratory univariate analyses. The statistical tests' significance level was picked at $p < 0.05$. Each of the CI and p-value that was expressed had two-tailed. Frequency counts and percentages were employed to summarize AEs. IBM SPSS Statistics, version 24 has been utilized during all statistical analyses [25].

4.4. MECHANISM OF ACTION

4.4.1. Durvalumab

Inflammatory signals and cytokines may regulate the expression of PD-L1 on tumor cells and malignant-associated immune cells within the tumor microenvironment. By interacting with PD-1 and CD80 (B7.1), PD-L1 inhibits T-cell function and activation and decreases cytotoxic T-cell activity, proliferation, and cytokine generation. Durvalumab is a human antibody G1 kappa monoclonal antibody that inhibits immunological responses by blocking PD-L1 from binding to known PD-1 and CD80 (B7.1) without causing antibody-dependent cell-mediated cytotoxicity [26].

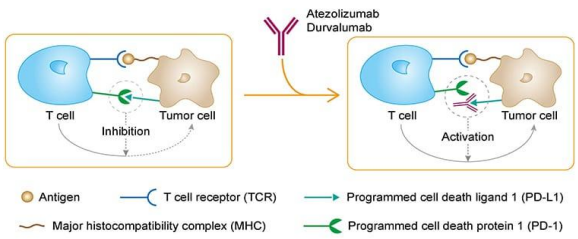


Figure - 2: Mechanism of durvalumab [27].

4.4.2. ETOPOSIDE

Topoisomerase II gets inhibited by etoposide. The late S and G2 periods in the cell cycle are where it mostly acts. Topoisomerase II simultaneously breaks both DNA helix strands. During the replication process, it generates and repairs double-stranded DNA breaks. Etoposide inhibits DNA re-ligation, the reaction's second stage, and poisons the topoisomerase II cleavage complexes. The etoposide-topoisomerase II combination, which performs better in tumour cells with larger numbers of topoisomerase II enzymes, triggers a mutagenesis and cell death pathway [28].

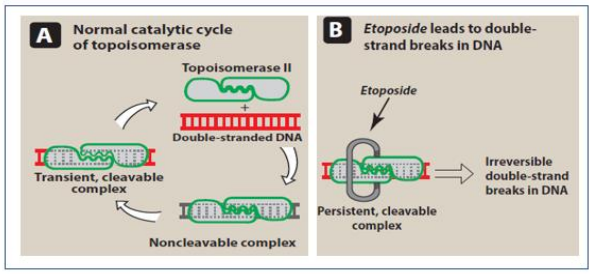


Figure - 3: Mechanism of action [28]

4.4.3. Cisplatin

Through the formation of cross-links (bonds between atoms in the DNA) that prevent DNA from being separated for synthesis or the process of transcription ,attachment of alkyl groups to DNA bases that causes the DNA to be fragmented by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA, and 3) induction of mispairing of the nucleotides leading to mutations [30].

4.4.4. SAFETY

Neither study arm experienced any adverse events that resulted in treatment cessation or death. In the durvalumab plus EP arm, 4 (22%) patients experienced immune-mediated adverse events of any grade; in the EP arm, no immune-mediated adverse events were observed. Grade 3 was one type 1 diabetes mellitus immune-mediated adverse event. According to toxicity management guidelines, corticosteroids or endocrine medication were used to treat the remaining immune-mediated adverse events, which were grade 1 or 2 in severity and included one case each of hyperthyroidism, hypothyroidism, and interstitial lung disease (T)[31].[18] Of the 40 patients treated with durvalumab plus PE, 39 (97.5%) experienced adverse events of any cause and level. Three patients (7.5%) experienced AEs that resulted in medication termination, while 26 patients (65.0%) experienced AEs of grade 3 or higher. Neutropenia was the most frequent grade 3 or higher adverse event. In general, nonhematological toxicities were not severe. The incidence of adverse events (AEs) did not differ between individuals fewer than 70 and those over 70. Two patients who had PS 2 and 3 at the start of treatment, respectively, passed away (5.0%) due to an adverse event of any kind. Five patients (12.5%) experienced immune-mediated adverse events, and two of them stopped taking durvalumab after contracting encephalitis and bullous pemphigoid, respectively [32].

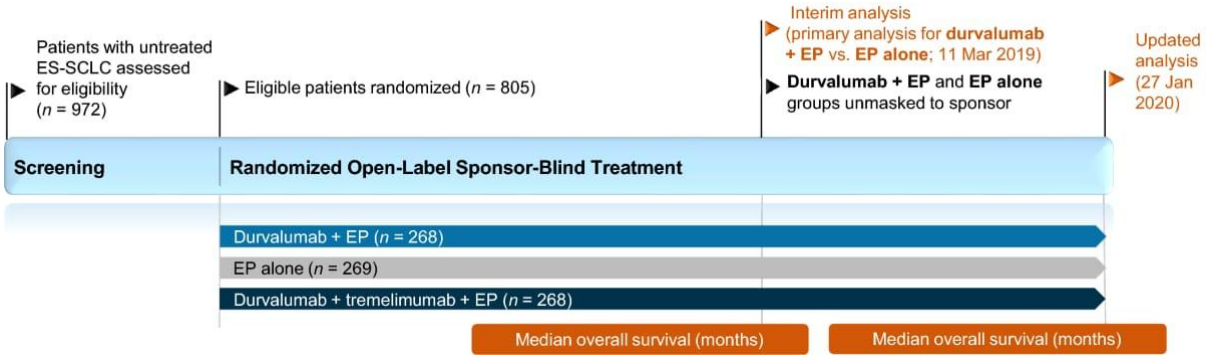


Figure 4: Study Design and Efficacy Outcomes of the Phase III CASPIAN Trial in Extensive-Stage Small Cell Lung Cancer

4.4.5. EFFICACY

In the open-label (unmasked to patients and investigators, but not to sponsors), multicenter, phase III CASPIAN trial, the effectiveness of durvalumab in combination with etoposide with either carboplatin or cisplatin in adults with untreated ES-SCLC is examined. The design of the randomized, open-label, sponsor-blind, multicenter, phase III CASPIAN trial for adults with untreated, advanced small cell lung cancer is illustrated in (figure1). The animated figure (available online) reports the efficacy data for durvalumab plus EP against EP alone; findings from the unapproved combination of durvalumab plus tremelimumab plus EP are not included. HR hazard ratio, ES-SCLC extensive-stage small cell lung cancer, and EP platinum-etoposide [33].

Figure 4: This study describes the design of the multicenter, randomized, open-label, sponsor-blind, phase III CASPIAN trial for adults with untreated, advanced small cell lung cancer. The animated figure (available online) reports the efficacy data for durvalumab plus EP against EP alone; findings from the unapproved combination of durvalumab plus tremelimumab plus EP are not included. HR hazard ratio, ES-SCLC extensive-stage small cell lung cancer, and EP platinum-etoposide [33]

13.0 days was the median follow-up period (95% CI: 8.0–22.2 months). To assess the effectiveness of the treatment, the patients had computed tomography (CT) scans at intervals of typically two to three months. Three patients (7.5%) had a complete response (CR), 25 patients (62.5%) had a partial response (PR), three patients (7.5%) had stable disease (SD), and four patients (10.0%) had progressive illness (PD) (Table 1). Due to either stopping treatment or reaching the cutoff date prior to treatment evaluation, five patients were not given a response assessment. Table 2 shows that the DCR was 88.6% (95% CI: 73.3–96.8%) and the ORR was 80.0% (95% CI: 63.1–91.6%). 13.0 days was the median follow-up period (95% CI: 8.0–22.2 months) [34].13.0 days was the

median follow-up period (95% CI: 8.0–22.2 months). To assess the effectiveness of the treatment, the patients had computed tomography (CT) scans at intervals of typically two to three months. Three patients (7.5%) had a complete response (CR), 25 patients (62.5%) had a partial response (PR), three patients (7.5%) had stable disease (SD), and four patients (10.0%) had progressive illness (PD) (Table 1). Due to either stopping treatment or reaching the cutoff date prior to treatment evaluation, five patients were not given a response assessment. Table 2 shows that the DCR was 88.6% (95% CI: 73.3–96.8%) and the ORR was 80.0% (95% CI: 63.1–91.6%) [34].

Table – 1: Best response rate and DCR (n=40)

THERAPEUTIC EFFICACY	VALUES
Response, n	-
CR	3[7.5]
PR	25[62.5]
SD	3[7.5]
PD	4[10.0]
NE	5[12.5]
ORR [%] [95%C I]	80.0[63.1-91.6]
DCR [&] [95%CI]	88.6[73.3-96.8]

SD stands for stable disease; PD for progressing illness; NE for not evaluable; DCR for disease control rate; CR for complete response; PR for partial response; CI is for confidence interval; ORR stands for overall response rate. [34]

Radiation therapy for superior vena cava (SVC) syndrome was administered concurrently to one patient who had an SD response to treatment. The subsequent treatment rates for each PS were as follows: 100% (3 of 3) for PS 0, 80% (8 of 10) for PS 1, 0% (0 of 2) for PS 2, and 100% (3 of 3) for PS 3. Amrubicin (AMR) was the second-line treatment for 14 (77.8%) of the 18 patients whose illness progressed. During durvalumab maintenance therapy, four patients experienced oligometastatic disease-related illness progression. They underwent radiation therapy for the oligometastatic location and continued receiving durvalumab therapy [35].

4.4.6. COST ESTIMATES

Purchasing, administering, and treating adverse events were all considered direct medical costs [20]. Durvalumab was prescribed for four treatments in our trial, at a dose of 1,500 mg every 21 days. Durvalumab was then maintained, to be used every four weeks until advancement. Etoposide 90 mg/m^2, carboplatin area under the curve (AUC) of 5 mg/ml/min, cisplatin 80 mg/m^2, and topotecan 1.5 mg/m^2/d were supposed to be incorporated in a one-cycle dose of the chemotherapeutic medication [36]. Following four rounds, patients received 1,500 mg of intravenous durvalumab every four weeks as maintenance therapy. Patients in the platinum/etoposide group could be given an extra two cycles of platinum/etoposide (up to six total). For the chemotherapy dose, we utilized a conventional AUC of 6 mg/mL/min and assumed male sex, 65 years old, 70 kg weight, 70 cm height, 1.84 m^2 body surface area, and a blood creatinine level of 1 mg/dL [37].

The 2020 Medicare practitioner fee schedule was used to determine the administration and radiation costs. Durvalumab single-drug infusion lasted one hour, while the chemotherapy drug infusion lasted three hours. As a result, the immunotherapy group needed a total of 4 hours for each cycle, compared to 3 hours for the chemotherapy group. The product of the unit cost of drug administration for each chemotherapy regimen and the average number of cycles was used to calculate the overall cost of medication administration per patient [38].

4.4.7. Exposure to Treatment and Subsequently Therapy

As previously reported, the durvalumab plus EP group had a longer median total period of treatment and received more durvalumab doses than the durvalumab plus tremelimumab plus EP arm (Table 2). The exposure to chemotherapy and tremelimumab remained constant from the previous analysis. Durvalumab was given for ≥2 and ≥3 years to 12% and 9% of patients in the durvalumab plus EP arm, and 11% and 8% in the durvalumab plus tremelimumab plus EP arm. At DCO, 27 (10%) and 19 (7%) patients continued on durvalumab in the durvalumab plus EP and durvalumab plus tremelimumab + EP groups, respectively [39].

Atezolizumab was administered to 78% of patients, compared to 22% for durvalumab. Following initial chemoimmunotherapy, the therapeutic response was 3% CR (one patient), 64% PR, and 33% SD. All patients underwent CTRT to the primary and subsequent regional nodes, with 56% receiving maintenance immunotherapy [40].

Table – 2: Exposure to treatment and subsequently therapy [40]

Parameter	Durvalumab plus EP (n=265)	Durvalumab plus tremelimumab plus EP(n=266)
Median number of durvalumab doses(range)	7.0[1-52]	6.0[1-46]
Total duration of durvalumab exposure, n [%]	NA	NA

≥ 1 years	54 [20.4]	49[18.4]
≥2 years	32[12.1]	30[11.3]
≥3 years	24[9.1]	21[7.9]
Median total duration of Durvalumab weeks[range]	28.0[0.3-198.7]	23.1[0.1-190.0]
Durvalumab dose delays n [%]	152[57.4]	157[59.0]
Durvalumab dose interruptions n [%]	4[1.5]	4[1.5]

4.4.8. SUCCESSFUL TREATMENTS

In untreated patients with extensive disease—small cell lung cancer (SCLC)—combination therapy with durvalumab, etoposide, and platinum agents produced a significant survival benefit over conventional therapy with etoposide and platinum agents, according to the recent phase III trial CASPIAN study [41]. For these individuals, this care has been the norm up until this point. Here, we describe the successful treatment of a patient with recurrent SCLC using a combination of durvalumab, etoposide, and cisplatin. A 65-year-old man was diagnosed with SCLC, with cT1bN2M0, stage IIIA (limited disease) as the clinical stage and the left upper lobe as the primary site. In addition to concurrent accelerated hyper fractionated thoracic irradiation and preventive cerebral irradiation, he underwent treatment with etoposide with cisplatin. His illness returned within the irradiation field a year after he had started treatment. Systemic chemotherapy was thought to be appropriate since there was no indication for repeated curative irradiation. He was therefore given second-line treatment with durvalumab, etoposide, and cisplatin, which resulted in a partial tumour response with negligible side effects. For over seven months, there was a positive response to this treatment [42].

4.4.9. FUTURE DIRECTIONS

Integrate Clinical Impact and Future Directions

Highlight how the introduction of durvalumab has changed clinical practice for ES-SCLC, referencing real-world data and guidelines. Discuss implications for patient survival, quality of life, and long-term outcomes and propose avenues for future research, such as biomarkers for responses, combination therapies, and new immunotherapy agent.

Expand on Comparative Analysis

It Include comparison results with other immunotherapy treatments (such as atezolizumab) and combinations that were utilized in studies for ES-SCLC or NSCLC, with an emphasis on cost-effectiveness, safety, and efficacy. Describe how the possibilities for first-line and maintenance therapy are changing.

Improve the Mechanisms

The mechanisms by which PD-L1 suppression differs from that of other immune checkpoints. Provide tables or diagrams that highlight the signaling pathways impacted by important drugs, and talk about current research on resistance mechanisms and countermeasures.

Enrich Clinical Trials Section

Summarize outcomes, patient populations, and notable secondary endpoints for key trials (CASPIAN, PACIFIC, MYSTIC, etc.), ideally using visual timelines or comparison tables. Highlight differences in inclusion criteria, geographic scope, and methodology across landmark studies.

Expand Safety Profiles and Adverse Events

Provide additional data on adverse event profiles, long-term toxicity, and management strategies for immune-related events. Discuss how safety outcomes inform clinical decision-making in older adults and those with comorbidity.

5. REFERENCE

1. Yuanbin Chen, Mikhail Dvorkin, Dmytro Trukhin , Galina Statsenko Patient-reported outcomes with first-line durvalumab plus platinum-etoposide versus platinum-etoposide in extensive-stage small-cell lung cancer (CASPIAN): a randomized, controlled, open-label, phase III study Volume 149 November 2020 https://www.sciencedirect.com/science/article/pii/S0169500220306000#bib0005
2. Hotta, K., Nishio, M., Saito, H., Okamoto, I., Nakahara, Y., Hayashi, H., Hayama, M., Laud, P., Jiang, H., Paz-Ares, L., & Azuma, K. (2021). First-line durvalumab plus platinum-etoposide in extensive-stage small-cell lung cancer: CASPIAN Japan subgroup analysis. International Journal of Clinical Oncology, 26(6), 1073–1082. https://doi.org/10.1007/s10147-021-01899-8

3. Hotta, K., Nishio, M., Saito, H., Okamoto, I., Nakahara, Y., Hayashi, H., Hayama, M., Laud, P., Jiang, H., Paz-Ares, L., & Azuma, K. (2021). First-line durvalumab plus platinum-etoposide in extensive-stage small-cell lung cancer: CASPIAN Japan subgroup analysis. International Journal of Clinical Oncology, 26(6), 1073–1082. https://doi.org/10.1007/s10147-021-01899-8
4. Garg, P., Singhal, S., Kulkarni, P., Horne, D., Malhotra, J., Salgia, R., & Singhal, S. S. (2024b). Advances in Non-Small Cell Lung Cancer: Current insights and future directions. Journal of Clinical Medicine, 13(14), 4189. https://doi.org/10.3390/jcm13144189
5. N. Mollberg · M. Surati · C. Demchuk · R. Fathi · A. K. Salama · A. N. Husain · T. Hensing · R. Salgia Mind-Mapping for Lung Cancer: Towards a Personalized https://www.researchgate.net/publication/49851292
6. Wikipedia contributors. (2025, August 5). Durvalumab. Wikipedia. https://en.wikipedia.org/wiki/Durvalumab
7. AstraZeneca reports initial results from the ongoing MYSTIC trial in Stage IV lung cancer. (2017, July 27). https://www.astrazeneca.com/media-centre/press-releases/2017/astrazeneca-reports-initial-results-from-the-ongoing-mystic-trial-in-stage-iv-lung-cancer-27072017.html#!
8. Paz-Ares, L., Chen, Y., Reinmuth, N., Hotta, K., Trukhin, D., Statsenko, G., Hochmair, M., Özgüroğlu, M., Ji, J., Garassino, M., Voitko, O., Poltoratskiy, A., Musso, E., Havel, L., Bondarenko, I., Losonczy, G., Conev, N., Mann, H., Dalvi, T., Goldman, J. (2022). Durvalumab, with or without tremelimumab, plus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer: 3-year overall survival update from CASPIAN. ESMO Open, 7(2), 100408. https://doi.org/10.1016/j.esmoop.2022.100400
9. Spigel, D. R., Faivre-Finn, C., Gray, J. E., Vicente, D., Planchard, D., Paz-Ares, L., Vansteenkiste, J. F., Garassino, M. C., Hui, R., Quantin, X., Rimner, A., Wu, Y., Özgüroğlu, M., Lee, K. H., Kato, T., De Wit, M., Kurata, T., Reck, M., Cho, B. C., Antonia, S. J. (2022c). Five-Year survival outcomes from the PACIFIC trial: Durvalumab after chemoradiotherapy in stage III Non–Small-Cell lung cancer. Journal of Clinical Oncology, 40(12), 1301–1311. https://doi.org/10.1200/jco.21.01308
10. Research FDA approves durvalumab for locally advanced or metastatic biliary tract cancer. U.S. Food And Drug Administration. https://web.archive.org/web/20220906053710/https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-durvalumab-locally-advanced-or-metastatic-biliary-tract-cancerhttps://web.archive.org/web/20220906053710/https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-durvalumab-locally-advanced-or-metastatic-biliary-tract-cancer
11. Westin, S. N., Moore, K., Chon, H. S., Lee, J., Pepin, J. T., Sundborg, M., Shai, A., De La Garza, J., Nishio, S., Gold, M. A., Wang, K., McIntyre, K., Tillmanns, T. D., Blank, S. V., Liu, J., McCollum, M., Mejia, F. C., Nishikawa, T., Pennington, K., .Woliver, T. (2023). Durvalumab plus Carboplatin/Paclitaxel followed by maintenance Durvalumab with or without olaparib as First-Line treatment for advanced endometrial cancer: the Phase III DUO-E trial. Journal of Clinical Oncology, 42(3), 283–299. https://doi.org/10.1200/jco.23.02132
12. Heymach, J. V., Mitsudomi, T., Harpole, D., Aperghis, M., Jones, S., Mann, H., Fouad, T. M., & Reck, M. (2021). Design and Rationale for a Phase III, Double-Blind, Placebo-Controlled Study of Neoadjuvant Durvalumab + Chemotherapy Followed by Adjuvant Durvalumab for the Treatment of Patients with Resectable Stages II and III non-small-cell Lung Cancer: The AEGEAN Trial. Clinical Lung Cancer, 23(3), e247–e251. https://doi.org/10.1016/j.cllc.2021.09.010
13. Mauro, G. (2024, September 10). Perioperative Durvalumab regimen upholds EFS benefit in resectable NSCLC. OncLive. https://www.onclive.com/view/perioperative-durvalumab-regimen-upholds-efs-benefit-in-resectable-nsclc?utm_source=chatgpt.com.
14. eymach, J. V., Mitsudomi, T., Harpole, D., Aperghis, M., Jones, S., Mann, H.Reck, M. (2022). Design and rationale for a Phase III, double-blind, placebo-controlled study of neoadjuvant durvalumab plus chemotherapy followed by adjuvant durvalumab for the treatment of patients with resectable stages II and III non-small-cell lung cancer: The AEGEAN trial. Clinical Lung Cancer, 23(3), e247–e251. https://www.sciencedirect.com/science/article/pii/S1525730421002655?utm_source=perplexity

15. Kauffman, G. B., Pentimalli, R., Doldi, S., & Hall, M. D. (2010). Michele Peyrone (1813–1883), discoverer of Cisplatin. Platinum Metals Review, 54(4), 250–256. https://doi.org/10.1595/147106710x534326
16. Wikipedia contributors. (2025b, August 15). Cisplatin. Wikipedia. https://en.wikipedia.org/wiki/Cisplatin#History
17. Sumit Ghosh Cisplatin: The first metal based anticancer drug Volume 88, July 2019, 102925 https://www.sciencedirect.com/science/article/abs/pii/S0045206818311969?via%3Dihub
18. Jonathan W. Goldman, jwgoldman@mednet.ucla.edu, Marina Chiara Garassino, Yuanbin Chen, Norah Shire Patient-reported outcomes with first-line durvalumab plus platinum-etoposide versus platinum-etoposide in extensive-stage small-cell lung cancer (CASPIAN): a randomized, controlled, open-label, phase III study https://www.lungcancerjournal.info/article/S0169-5002(20)30600-0/fulltext
19. Hotta, K., Nishio, M., Saito, H., Okamoto, I., Nakahara, Y., Hayashi, H., Hayama, M., Laud, P., Jiang, H., Paz-Ares, L., & Azuma, K. (2021). First-line durvalumab plus platinum-etoposide in extensive-stage small-cell lung cancer: CASPIAN Japan subgroup analysis. International Journal of Clinical Oncology, 26(6), 1073–1082. https://doi.org/10.1007/s10147-021-01899-8
20. Antonia, S. J., Villegas, A., Daniel, D., Vicente, D., Murakami, S., Hui, R., Yokoi, T., Chiappori, A., Lee, K. H., De Wit, M., Cho, B. C., Bourhaba, M., Quantin, X., Tokito, T., Mekhail, T., Planchard, D., Kim, Y., Karapetis, C. S., Hiret, S., Özgüroğlu, M. (2017). Durvalumab after Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer. New England Journal of Medicine, 377(20), 1919–1929. https://doi.org/10.1056/nejmoa1709937
21. L. Paz-Ares, Y. Chen, N. Reinmuth, K. Hotta, D. Trukhin, Durvalumab, with or without tremelimumab, plus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer: 3-year overall survival update from CASPIAN https://pmc.ncbi.nlm.nih.gov/articles/PMC9161394/pdf/main.pdf
22. Yuta Yamanaka, Yukiko Okuno , Keisuke Kamisako ,Yuta Okazaki Efficacy and Safety Evaluation of Immune Checkpoint Inhibitors in Combination with Chemotherapy for Extensive Small Cell Lung Cancer: Real-World Evidence https://pmc.ncbi.nlm.nih.gov/articles/PMC11656376/pdf/CAM4-13-e70480
23. Ishii, H., Azuma, K., Shimose, T., Yoshioka, H., Kurata, T., Shingu, N., Okamoto, M., Kawashima, Y., & Okamoto, I. (2022). Phase II study of durvalumab (MEDI 4736) plus carboplatin and etoposide in elderly patients with extensive stage small cell lung cancer: Study protocol of turtle study (LOGIK 2003). Thoracic Cancer, 14(1), 105–107. https://doi.org/10.1111/1759-7714.14727
24. Jang, J. Y., Song, S. Y., Shin, Y. S., Kim, H. U., Choi, E. K., Kim, S., Lee, J. C., Lee, D. H., Choi, C., Yoon, S., & Kim, S. S. (2024). Contribution of Enhanced Locoregional Control to Improved Overall Survival with Consolidative Durvalumab After Concurrent Chemoradiotherapy in Locally Advanced Non-Small Cell Lung Cancer: Insights from Real-World Data. Cancer Research and Treatment, 56(3), 785–794. https://doi.org/10.4143/crt.2023.1014
25. Liu, C., Liao, J., Wu, X., Zhao, X., Sun, S., Wang, H., Hu, Z., Zhang, Y., Yu, H., & Wang, J. (2022). A phase II study of anlotinib combined with etoposide and platinum-based regimens in the first-line treatment of extensive-stage small cell lung cancer. Thoracic Cancer, 13(10), 1463–1470. https://doi.org/10.1111/1759-7714.14414
26. Raedler, L. A. (n.d.). Imfinzi (Durvalumab) a new PD-L1 inhibitor approved for the treatment of advanced or metastatic urothelial cancer. American Health & Drug Benefits. https://www.ahdbonline.com/issues/2018/april-2018-vol-11-ninth-annual-payers-guide/imfinzi-durvalumab-a-new-pd-l1-inhibitor-approved-for-the-treatment-of-advanced-or-metastatic-urothelial-cancer
27. Durvalumab overview. (2023, August 27). https://www.creativebiolabs.net/durvalumab overview.htmhttps://www.creativebiolabs.net/durvalumab-overview.htm
28. Reyhanoglu, G., & Tadi, P. (2023, July 4). Etoposide. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK557864/#:~:text=Etoposide%20is%20also%20one%20of,highly%20bound%20to%20plasma%20proteins.
29. https://images.app.goo.gl/ycuHMkMjaHPpSBdQ9
30. Drug Bank. (2024, January 5). Cisplatin (DB00515). In DrugBank 6.0: the Drug Bank

Knowledgebase for 2024. Nucleic Acids Research, 52(D1), D1265–D1275. https://go.drugbank.com/drugs/DB00515 dev.drugbank.comDrugBank

31. Hotta, K., Nishio, M., Saito, H., Okamoto, I., Nakahara, Y., Hayashi, H., Hayama, M., Laud, P., Jiang, H., Paz-Ares, L., & Azuma, K. (2021b). First-line durvalumab plus platinum-etoposide in extensive-stage small-cell lung cancer: CASPIAN Japan subgroup analysis. International Journal of Clinical Oncology, 26(6), 1073–1082. https://doi.org/10.1007/s10147-021-01899-8
32. Misawa, K., Watanabe, K., Seike, M., & Hosomi, Y. (2023). Durvalumab plus platinum-etoposide chemotherapy for extensive-stage small cell lung cancer: a retrospective real-world study. Translational Lung Cancer Research, 0(0), 0. https://doi.org/10.21037/tlcr-24-128
33. Al-Salama, Z. T. (2021). Durvalumab: A review in Extensive-Stage SCLC. Targeted Oncology, 16(6), 857–864. https://doi.org/10.1007/s11523-021-00843-0
34. Misawa, K., Watanabe, K., Seike, M., & Hosomi, Y. (2023b). Durvalumab plus platinum-etoposide chemotherapy for extensive-stage small cell lung cancer: a retrospective real-world study. Translational Lung Cancer Research, 0(0), 0. https://doi.org/10.21037/tlcr-24-128
35. Nesbit, E. G., Leal, T. A., & Kruser, T. J. (2019). What is the role of radiotherapy for extensive-stage small cell lung cancer in the immunotherapy era? Translational Lung Cancer Research, 8(S2), S153–S162. https://doi.org/10.21037/tlcr.2019.05.01
36. Eckardt, J. R., Von Pawel, J., Pujol, J., Papai, Z., Quoix, E., Ardizzoni, A., Poulin, R., Preston, A. J., Dane, G., & Ross, G. (2007). Phase III study of oral compared with intravenous topotecan as Second-Line therapy in Small-Cell lung cancer. Journal of Clinical Oncology, 25(15), 2086–2092. https://doi.org/10.1200/jco.2006.08.3998
37. Zhang, L., Hang, Y., Liu, M., Li, N., & Cai, H. (2020). First-Line Durvalumab plus Platinum-Etoposide versus Platinum-Etoposide for Extensive-Stage Small-Cell Lung Cancer: A Cost-Effectiveness Analysis. Frontiers in Oncology, 10. https://doi.org/10.3389/fonc.2020.602185
38. Tsai, S., Tsai, J., Chen, L., & Yang, S. (2025). Cost-effectiveness of durvalumab after chemoradiotherapy in limited-stage small-cell lung cancer. JTO Clinical and Research Reports, 100879. https://doi.org/10.1016/j.jtocrr.2025.10087
39. L. Paz-Ares, lpazaresr@seom.org ,Y. Chen,N. Reinmuth· T.B. Dalvi, H. Jiang, J.W. Goldman Durvalumab, with or without tremelimumab, plus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer: 3-year overall survival update from CASPIAN Volume 7, Issue 2100408 https://www.esmoopen.com/article/S2059-7029(22)00029-1/fulltext
40. Li, L., Yang, D., Min, Y., Liao, A., Zhao, J., Jiang, L., Dong, X., Deng, W., Yu, H., Yu, R., Zhao, J., & Shi, A. (2023). First-line atezolizumab/durvalumab plus platinum–etoposide combined with radiotherapy in extensive-stage small-cell lung cancer. BMC Cancer, 23(1). https://doi.org/10.1186/s12885-023-10784-8
41. L. Paz-Ares, Y. Chen,N. Reinmuth T. Dalvi, H. Jiang, J.W. Goldman Durvalumab ± tremelimumab + platinum-etoposide in first-line extensive-stage SCLC (ES-SCLC): 3-year overall survival update from the phase III CASPIAN study Volume 32, Supplement 5S1338 https://www.annalsofoncology.org/article/S0923-7534(21)04446-X/fulltext
42. P8-107: Successful treatment with durvalumab, etoposide, and cisplatin in relapsed small cell lung cancer: A case report. (2021). Respirology, 26(S3), 330. https://doi.org/10.1111/resp.14150_619