Adoption and early clinical outcomes of atezolizumab (atezo) + carboplatin and etoposide (CE) in patients with extensive-stage small-cell lung cancer (ES-SCLC) in the real-world (RW) setting

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BACKGROUND

- Atezo + CE was approved by the United States (U.S.) Food and Drug Administration and European Medicines Agency in 2019 for first-line (1L) treatment of ES-SCLC based on the IMpower133 trial that demonstrated a statistically significant improvement in overall survival and progression-free survival (PFS) with the addition of atezo to CE.[1]
- This study investigated clinical characteristics, treatment patterns, and early outcomes of the atezo + CE regimen in a RW community oncology setting.

METHODS

- Retrospective study of patients with ES-SCLC who received 1L atezo + CE on or after 25-Sep-2018 (after IMpower133 publication in NEJM)[1] through 30-April-2020 and followed until 30-April-2020. Data from the nationwide Flatiron Health electronic health record–derived deidentified U.S. database were used. Additional information from patient-level unstructured data, including thoracic radiotherapy (TRT) and prophylactic cranial irradiation (PCI) was also included. PCI was defined as brain radiotherapy in the absence of documented prior brain metastasis.
- The IMpower133 eligible–like cohort (subgroup of the main trial study cohort) was defined as:
  - Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-1 at baseline
  - Carboplatin as platinum therapy
  - Starting with atezo + CE as first cycle
  - No central nervous system (CNS) metastasis before start of treatment (patients with CNS metastasis were excluded as it was not possible to differentiate active from treated asymptomatic lesions)
  - Normal laboratory values
- Descriptive analyses of patient characteristics, treatment patterns, and early outcomes were conducted, with Kaplan–Meier methods used to assess time to last administration as a proxy for treatment duration, the cumulative incidence of CNS metastases, and real-world PFS (rwPFS).[2]
- Overall survival was not explored because of the expected short median follow-up.

Table 1. Baseline characteristics of patients with ES-SCLC: Comparison of RW study and IMpower133[1]

Variable	RW (N = 493)	RW IMpower133 trial eligible–like (n = 162)	IMpower133 study population (N = 201)[1]
Age group, y, n (%)			
<65	173 (35.1)	60 (37.0)	111 (55.2)
≥65	320 (64.9)	102 (63.0)	90 (44.8)
Gender, n (%)			
Female	234 (47.5)	73 (45.1)	72 (35.8)
Male	259 (52.5)	89 (54.9)	129 (64.2)
ECOG PS, n (%)			
0	97 (19.7)	66 (40.7)	73 (36.3)
1	178 (36.1)	96 (59.3)	128 (63.7)
2+	104 (21.1)	0 (0.0)	0 (0)
Not reported	114 (23.1)	0 (0.0)	0 (0)
Smoking status, n (%)			
History of smoking	481 (97.6)	158 (97.5)	192 (95.5)
No history	12 (2.4)	4 (2.5)	9 (4.5)
CNS metastasis, n (%)			
Yes	97 (19.7)	0 (0)	17 (8.5)
No	396 (80.3)	162 (100.0)	184 (91.5)
Liver metastasis, n (%)			
Yes	216 (43.8)	68 (42.0)	77 (38.3)
No	277 (56.2)	94 (58.0)	124 (61.7)
SCLC stage at diagnosis, n (%)			
Extensive disease	475 (96.3)	157 (96.9)	187 (93.0)
Limited disease	18 (3.7)	5 (3.1)	13 (6.5)

RESULTS

Study cohorts

- RW cohort included 493 patients with ES-SCLC initiated on 1L atezo + CE.
- IMpower133 trial eligible–like cohort included 162 patients.

Patient characteristics

- Patients in the RW cohort compared with the IMpower133 study population were older (65% vs 45% were aged ≥65 y) and had a higher proportion of females (48% vs 36%).
  - Patients in the RW cohort had worse prognostic baseline characteristics than those in the IMpower133 study population
  - ECOG PS 2+ 21% vs 0%
  - CNS metastasis 20% vs 8%

Treatment patterns in the RW cohort receiving 1L atezo + CE

- 493 patients were treated with atezo + platinum and etoposide.
  - 4% (22/493) of patients had ≥1 cycle of chemotherapy before initiating atezo + CE.
  - Very few (7 out of 493) patients received cisplatin.
- Among patients who reached maintenance treatment, 30% (76/252) received TRT regardless of intent (consolidative or other palliative intent).
  - We cannot discriminate consolidative or other palliative intent retrospectively, a limitation of using RW data.
- Among patients enrolled at least 12 months before study end, 17% (26/155) of patients had >4 cycles of chemotherapy.

CNS metastasis in the RW cohort

- 20% (97/493) of patients presented with CNS metastasis at baseline
  - Of these, 49% (48/97) received CNS treatment before commencing atezo + CE.
  - Treatments received by these patients included whole brain radiation therapy: 81% (n = 39), craniotomy/metastasectomy: 17% (n = 8), stereotactic radiosurgery: 10% (n = 5), surgery: 2% (n = 1), and radiotherapy: 2% (n = 1).
- Cumulative incidence of new CNS metastasis at 6 months was 19% (95% CI, 15%-23%) for patients who were CNS metastasis-free at baseline vs 38% (95% CI, 28%-49%) for those with CNS metastasis at baseline.
- In the maintenance setting, 13% (27/200) of patients with no prior CNS metastasis were treated with PCI.

Clinical outcomes

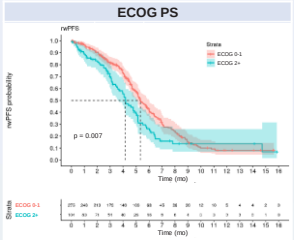
Median rwPFS was 5.2 months (95% CI, 5.0-5.5) in the RW cohort and 5.8 months (95% CI, 5.2-6.7) in the trial eligible–like cohort.

Table 2. Comparison of clinical outcomes: RW study and IMpower133

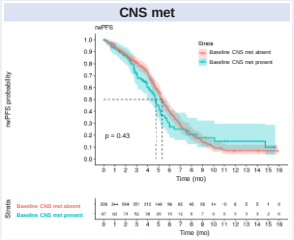
Variable	RW (N = 493)	RW IMpower133 trial eligible-like (n = 162)[a]	IMpower133 study population (N = 201)[1]
Follow-up, median, mo	6.9	7.6	13.9
Tx duration, median (95% CI), mo	5.7 (5.1, 6.7)	6.2 (5.5, 7.8)	4.7 (range, 0-21)[b]
rwPFS, median (95% CI), mo	5.2 (5.0, 5.5)	5.8 (5.2, 6.7)	5.2 (4.4, 5.6)[c]
Sensitivity analysis	n=137	n=51	
Follow-up, median, mo[d]	14.4	14.1	
Tx duration, median (95% CI), mo[d]	4.8 (4.1, 5.5)	5.5 (4.8, 7.1)	
rwPFS, median (95% CI), mo[c]	4.8 (4.1, 5.4)	5.8 (4.7, 7.9)	

CI, confidence interval; mo, months; Tx, treatment.
[a]A subgroup of RW patients comprising IMpower133 trial-eligible patients.
[b]Not based on Kaplan-Meier methodology.
[c]PFS was measured as a primary endpoint in IMpower133.
[d]Includes only patients initiating treatment at least 12 months before study end.

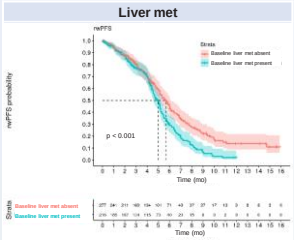
Figure 1. rwPFS—Stratifications in the real-world cohort by baseline characteristics



ECOG PS	N	Median (95% CI), mo
ECOG 0-1	275	5.3 (5.1-6.0)
ECOG 2+	104	4.2 (3.6-5.1)



CNS met	N	Median (95% CI), mo
Absent	396	5.3 (5.1-5.8)
Present	97	4.7 (4.1-5.6)



Liver met	N	Median (95% CI), mo
Absent	277	5.7 (5.1-6.1)
Present	216	5.0 (4.5-5.2)

CI, confidence interval; met, metastases; mo, months
P value is from log-rank test.

CONCLUSIONS

- Despite shorter follow-up in the RW cohort and differences in implementation of atezo + CE, in patient characteristics, and in clinical outcomes, the RW cohort aligns with RW IMpower133 trial eligible-like and IMpower133 cohorts. Sensitivity analyses with longer follow-up show similar results.
- Patients with CNS metastasis at baseline had numerically (but not statistically) lower median rwPFS.
- Cumulative incidence of new CNS metastasis at 6 months was higher for patients with CNS metastasis at baseline. About half of these patients received CNS treatment before commencing atezo + CE.
- Median rwPFS was higher in patients with ECOG PS 0-1 vs 2+ and those without vs with liver metastasis.
- The impact of PCI on brain metastasis in this population needs further research.
- This study shows that TRT is often performed during treatment with the atezo regimen. However, this study cannot address the impact of TRT due to limitations of retrospectively differentiating TRT with consolidative or other palliative intent.

REFERENCE

1. Horn L, et al. N Engl J Med 2018;379(23):2220–2229.
2. Griffith SD, et al. Adv Ther 2019;36(8):2122–2136.

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DISCLOSURES

David C. C. Tsui is an employee of the University of Colorado, Aurora, CO.

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