

Practice aid for LS-SCLC

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Efficacy and safety data for ICIs in LS-SCLC in phase III development

Adebrelimab (NCT04691063)¹

Adebrelimab with cCRT followed by adebrelimab maintenance

> Data cut-off: 31 Oct 2023

Atezolizumab (NRG-LU005)²

Atezolizumab + CRT followed by atezolizumab maintenance vs CRT alone

> Median follow-up: 21.0 months

Durvalumab (ADRIATIC)3

Durvalumab ± tremelimumab vs placebo consolidation

Data cut-off: 15 Jan 2024

Primary endpoint: Safety (N=28)

% of patients 96.4%* Grade ≥3 TRAEs

TR pneumonitis 14.3% (all grade 2)

TR immune-mediated lung disease

Median follow-up: 29.4 months

Primary endpoint: Efficacy

A + CRT **CRT** (n=274) (n=270)

mOS (months) 33.1

11.5 p=0.9542 mPFS (months) 12.0

39.5 p=0.7640

3.6% (grade 2)

Primary endpoint: Efficacy

(n=264) (n=266)

mOS (months) 55.9 33.4 p=0.01

Median follow-up: 37.2 months

mPFS (months) 16.6 9.2 p=0.02

Median follow-up: 24.7 months

Efficacy ORR 92.9% **mPFS** 17.9 months mOS NR Median follow-up 29.4 months

Safety A + CRT **CRT** (n=267) (n=254) 86.5% 92.5% Grade 3/4 AEs 15.7% 6.2% Grade 3/4 irAEs 26.2% 11.8% **Pneumonitis**

Reporting window 30 days post CRT and 90 days post end of atezolizumab (11 weeks vs 15 months)

Safety

D (n=262)(n=265)

Grade 3/4 AEs 24.4% 24.2%

30.2% Pneumonitis[†] 38.2%

Grade 3/4 pneumonitis 3.1% 2.6%

Direct comparisons between trials should not be made due to differences in trial design.





Practical guidance for the application of ICIs in LS-SCLC

ICI approvals in LS-SCLC^{4,5}

Durvalumab is FDA-approved as a single agent for the treatment of adult patients with LS-SCLC whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy⁴

2025 NCCN guidelines for LS-SCLC⁵: Durvalumab is the preferred consolidation regimen for patients with LS-SCLC (Category 1 recommendation)

Patients who do not experience disease progression after systemic therapy and concurrent RT may continue durvalumab until disease progression or unacceptable toxicity, or for a maximum of 24 months.

Distinguishing between IR-pneumonitis and RT-pneumonitis

Distinguishing between RT-pneumonitis and IR-pneumonitis is important,^{6–8} as the **pneumonitis aetiology has potential implications for directing clinical management**, including corticosteroid dose and the decision to restart or indefinitely discontinue ICI treatment.^{6,7}

Clinical considerations for CT imaging:



RT- and IR-pneumonitis often manifest as ground glass opacities and consolidations on CT imaging⁶



RT-pneumonitis is usually, but not always, contained within the portion of the radiation field^{7–9}



IR-pneumonitis tends to be **bilaterial**, **involving more lobes** of the lung, **with consolidations and opacities not specifically located within the radiation field**^{6–8}

Bronchoscopy with bronchoalveolar lavage is another diagnostic test to confirm pneumonitis aetiology⁹



Monitoring for and management of irAEs

Monitoring for irAEs

irAEs can occur at any point during or after cessation of treatment with ICIs, including beyond 12 months. 10

Therefore, it is recommended that patients are closely monitored for 12 months following the final dose of immunotherapy. 11

2022 ESMO Clinical Practice Guideline: Management of toxicities from immunotherapy¹²

irAE management consists of four sequential steps:

- i Diagnosis and grading
- ii Rule out differential diagnoses and pre-immunosuppression workup
- (iii) Selecting appropriate immunosuppression for grade 2 events
- iv Active evaluation at 72 hours to adapt treatment

2021 SITC clinical practice guideline on ICI-related AEs¹⁰

Grade 2 irAEs:

- (II) ICIs should be temporarily discontinued
- Patients should be treated with corticosteroids
- Patients can be re-challenged with ICIs if signs/symptoms are resolved or controlled

Grade 3/4 irAEs:

- ICIs should be discontinued
- Patients should be treated with corticosteroids
- The decision to rechallenge with ICIs should be risk-adjusted



Abbreviations and references

Abbreviations

A, atezolizumab; AE, adverse event; cCRT, concurrent CRT; CRT, chemoradiotherapy; CT, computed tomography; D, durvalumab; ESMO, European Society for Medical Oncology; ICI, immune checkpoint inhibitor; IR, immune-related; LS-SCLC, limited-stage small cell lung cancer; m, median; NCCN, National Comprehensive Cancer Network; NR, not reached; ORR, objective response rate; OS, overall survival; P, placebo; PFS, progression-free survival; RT, radiotherapy; SITC, Society for Immunotherapy of Cancer; TR, treatment-related.

References

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