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Where to next in limited-stage small cell lung cancer? The role of immune checkpoint inhibitors

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

Primary endpoint: Safety (N=28)

	% of patients
Grade ≥3 TRAEs	96.4%*
TR pneumonitis	14.3% (all grade 2)
TR immune-mediated lung disease	3.6% (grade 2)

Median follow-up: 29.4 months

Efficacy

ORR	92.9%
mPFS	17.9 months
mOS	NR

Median follow-up 29.4 months

Atezolizumab (NRG-LU005)[2]

Atezolizumab + CRT followed by atezolizumab maintenance vs CRT alone

Median follow-up: 21.0 months

Primary endpoint: Efficacy

	A + CRT (n=274)	CRT (n=270)	
mOS (months)	33.1	39.5	p=0.7640
mPFS (months)	12.0	11.5	p=0.9542

Safety

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

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

Durvalumab (ADRIATIC)[3]

Durvalumab ± tremelimumab vs placebo consolidation

Data cut-off: 15 Jan 2024

Primary endpoint: Efficacy

	D (n=264)	P (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

Safety

	D (n=262)	P (n=265)
Grade 3/4 AEs	24.4%	24.2%
Pneumonitis†	38.2%	30.2%
Grade 3/4 pneumonitis	3.1%	2.6%

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

*All events with incidence of ≥10% were haematological toxicities; †refers to pneumonitis and radiation pneumonitis collectively.

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Practical guidance for the application of ICIs in LS-SCLC

2025 NCCN guidelines for LS-SCLC[4]

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,[5–7] as the **pneumonitis aetiology has potential implications for directing clinical management**, including corticosteroid dose and the decision to restart or indefinitely discontinue ICI treatment.[5,6]

Clinical considerations for CT imaging:

RT- and IR-pneumonitis often manifest as **ground glass opacities and consolidations** on CT imaging[5]

RT-pneumonitis is usually, but not always, **contained within the portion of the radiation field**[6–8]

IR-pneumonitis tends to be **bilaterial, involving more lobes** of the lung, **with consolidations and opacities not specifically located within the radiation field**[5–7]

Bronchoscopy with bronchoalveolar lavage is another diagnostic test to confirm pneumonitis aetiology[8]

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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.[9]
Therefore, it is recommended that patients are closely monitored for 12 months following the final dose of immunotherapy.[10]

2022 ESMO Clinical Practice Guideline: Management of toxicities from immunotherapy[11]

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 AEs[9]

Grade 2 irAEs:

- 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.

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