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

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Expert MDT faculty

Dr Lizza Hendriks
Maastricht University Medical Center
Maastricht, The Netherlands

Dr Jacob Sands
Dana-Farber Cancer Institute
Boston, MA, USA

Prof. Suresh Senan
Amsterdam University Medical Center
Amsterdam, The Netherlands

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Experience of using ICIs in SCLC

ES-SCLC

1L PD-1/PD-L1 inhibitors + ChT

CAPSTONE-1 (N=462) adebrelimab + ChT[1]
Significantly improved mOS vs placebo + ChT (p=0.0008)

IMpower133 (N=403) atezolizumab + ChT[2]
Significantly improved mOS vs placebo + ChT (HR 0.76; 95% CI 0.60–0.95; p=0.0154).
Atezolizumab + ChT 5-year OS estimate of 12% (n=18)[3]

CASPIAN (N=805) durvalumab + ChT[4]
Significantly improved mOS vs ChT alone (p=0.0003)

ANSTRUM-005 (N=585) serplulimab + ChT[5]
Significantly improved mOS vs placebo + ChT (p<0.001)

LS-SCLC

STIMULI trial[6]

Consolidation nivolumab + ipilimumab vs observation after CRT in LS-SCLC (N=222)

mPFS not significant: 10.7 vs 14.5 months (HR 1.02; p=0.93)
Median follow-up: 22.4 months

mOS not significant: NR vs 32.1 months (HR 0.95; p=0.82)
Median follow-up: 35 months

STIMULI trial did not meet its primary endpoint of improvement in PFS with nivolumab–ipilimumab consolidation after CRT

Pembrolizumab + concurrent CRT[7]

Single institution study of pembrolizumab + concurrent CRT (N=40)

Adverse events:
grade 5 events, n=0; grade 4 events, n=3; grade 3 events, n=41

Median follow-up: 23.1 months

mPFS: 19.7 months

mOS: 39.5 months

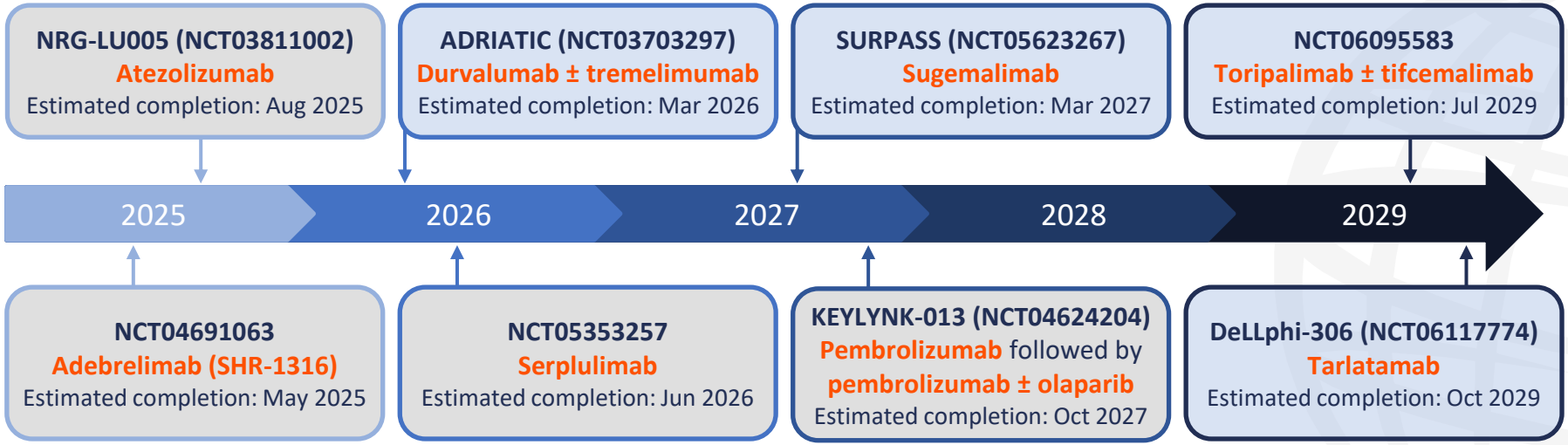
Concurrent CRT and pembrolizumab was well tolerated and OS and PFS were favourable compared to those in the CONVERT trial

1L, first-line; ChT, chemotherapy; CI, confidence interval; CRT, chemoradiotherapy; ES-SCLC, extensive-stage SCLC; HR, hazard ratio; ICI, immune checkpoint inhibitors; LS-SCLC, limited-stage SCLC; m, median; NR, not reached; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFS, progression free survival; SCLC, small cell lung cancer.

1. Cheng Y, et al. *Immunooncol Technol*. 2023;20:100556; 2. Liu SV, et al. *J Clin Oncol*. 2021;39:619–30; 3. Reck M, et al. *Lung Cancer*. 2024:196:107924; 4. Paz-Ares L, et al. *ESMO Open*. 2022;7:100408; 5. Cheng Y, et al. *JAMA*. 2022;328:1223–32; 6. Peters S, et al. *Ann Oncol*. 2022;33:67–79; 7. Welsh JW, et al. *J Thorac Oncol*. 2020:15:1919–27.

Ongoing trials of ICIs in LS-SCLC

Phase III trials



Phase II trials

- **Atezolizumab** (ACHILES; NCT03540420)
- **Durvalumab** (DURVALUNG; NCT05617963)
- **Envafolimab** (NCT05904015)
- **Tislelizumab** (NeoSCLC-001; NCT06375109)
- **TQB2450** (NCT04539977)

Given in combination with CRT

Consolidation therapy
(When disease has not progressed following CRT)

CRT, chemoradiotherapy; ICI, immune checkpoint inhibitor; LS-SCLC, limited-stage small cell lung cancer.
All trials can be found by searching by their NCT number at www.clinicaltrials.gov (accessed 07 November 2024).

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Phase III efficacy and safety data

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)

Efficacy

ORR	92.9%
mPFS	17.9 months
mOS	NR

Adebrelimab with cCRT showed acceptable tolerability and favourable efficacy outcomes

Durvalumab (ADRIATIC)[2]

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
mPFS§ (months)	16.6	9.2	p=0.02

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%

Durvalumab consolidation treatment was well tolerated and demonstrated improvements in OS and PFS vs placebo

Atezolizumab (NRG-LU005)[3]

CRT + atezolizumab followed by atezolizumab maintenance vs CRT alone¶

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%

Concurrent atezolizumab did not improve survival vs standard CRT

Direct comparisons between trials should not be made due to differences in trial design. *Median follow-up 29.4 months; †all events with incidence of ≥10% were haematological toxicities; ‡median duration of follow-up: 37.2 months; §median duration of follow-up 27.4 months; ‖refers to pneumonitis and radiation pneumonitis collectively; ¶median follow-up 21.0 months; **reporting window 30 days post CRT and 90 days post end of atezolizumab (11 weeks vs 15 months). A, atezolizumab; AE, adverse event; cCRT, concurrent CRT; CRT, chemoradiotherapy; D, durvalumab; irAE, immune-related AE; m, median; NR, not reached; ORR, objective response rate; OS, overall survival; P, placebo; PFS, progression free survival; TR, treatment-related.

1. Cheng Y et al. Presented at: ELCC Congress 2024, Prague, Czech Republic. 20–23 March 2024. Abstr. 198P; 2. Cheng Y, et al. *N Engl J Med*. 2024; 391:1313–27; 3. Higgins KA, et al. Presented at: 2024 ASTRO Annual Meeting, Washington, DC, USA. 20 September–2 October 2024. Abstr. LBA02.

Phase II efficacy and safety data

Serplulimab (ASTRUM-LC01)[1]

Single arm: serplulimab consolidation therapy after cCRT and PCI (data cut-off: 7 April 2024)*

Primary endpoint: Efficacy (N=55)

ORR	96.4%
DCR	96.4%
mPFS	NR

Safety (% of patients)

TRAE	72.7%
Grade ≥3 TRAEs	14.6%
Most common grade 3/4 AE	Pneumonitis

Serplulimab consolidation therapy demonstrated response rates of >95% and a manageable safety profile

Toripalimab (GASTO-1052A; NCT04418648)[2]

Toripalimab consolidation vs observation with CR or PR after cCRT†

Primary endpoint: Efficacy

	T (n=31)	O (n=33)	
2-year PFS	61.6%	34.8%	p=0.04
2-year OS	82.7%	59.1%	p=0.23

Safety (% of patients)

	T (n=31)	O (n=33)
Grade ≥2 pneumonitis	16.1%	9.1%
Grade ≥4 TRAEs	0	0

Toripalimab consolidation following definitive cCRT was effective and tolerable in LS-SCLC

Camrelizumab (ChiCTR2000032275)[3]

Camrelizumab plus ChT followed by cCRT plus camrelizumab vs CRT‡

Primary endpoint: Efficacy

	Camrelizumab (n=17)	CRT (n=17)
1-year PFS	54.5%	44.4%
mPFS (months)	NR	14.4

Safety (% of patients)

	Camrelizumab (n=17)	CRT (n=17)
Grade 3/4 TRAEs	58.8%	52.9%
Grade 3/4 radiation pneumonitis	5.9%	5.9%

Addition of camrelizumab to CRT resulted in an encouraging 1-year PFS rate and did not increase incidence of AEs

Direct comparisons between trials should not be made due to differences in trial design. *Median follow-up 9.8 months; †median follow-up 25 months; ‡median follow-up 10.6 months.
AE, adverse event; ChT, chemotherapy; cCRT, concurrent CRT; CR, complete response; CRT, chemoradiotherapy; DCR, disease control rate; LS-SCLC, limited-stage small cell lung cancer; m, median; NR, not reached; O, observation; ORR, objective response rate; OS, overall survival; PCI, prophylactic cranial irradiation; PFS, progression free survival; PR, partial response; T, toripalimab; TRAE, treatment-related AE.
1. Wu Y et al. Presented at: ESMO Congress 2024, Barcelona, Spain. 13–17 September 2024. Poster 1759P; 2. Zhang PX, et al. Presented at: ASCO Annual Meeting 2024, Chicago. IL, USA. 31 May–4 June 2024. Abstr. P8098; 3. Hu M, et al. Presented at: WCLC 2024, San Diego, CA, USA. 7–10 September 2024. Poster P1.13A.05.

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