Supplementary files

Table 1. Adjuvant Osimertinib: ADAURA and Extensions

Feature	ADAURA Primary [48]	ADAURA Updated DFS [46]	ADAURA Final OS [47, 77]	OSTAR [50]
Design	Phase III, double-blind, 1:1 osi vs placebo	Update of [48]	Final OS analysis	Phase II, single-arm
Population	Resected IB–IIIA, EGFR ex19del/L858R	Same cohort	Same cohort	Stage I, EGFR-sensitizing mut + high-risk features
Number	682 (339 osi, 343 placebo)	682	682	70
Treatment	Osimertinib 80 mg QD × 3 years vs placebo	As in [48]	As in [48]	Osimertinib 80 mg QD × 3 years
Primary endpoint	DFS (stage II–IIIA)	Final DFS (exploratory)	DFS (II–IIIA); OS key secondary	3-year DFS
Key efficacy	24-mo DFS 90% vs 44%; HR ~0.20	DFS HR 0.23 (II–IIIA); 0.27 (IB–IIIA); CNS DFS HR 0.24	5-yr OS 85% vs 73% (II–IIIA)	Awaited
Safety	Well tolerated; ILD, QTc, cardiomyopathy monitored	Tolerable with prolonged exposure	Acceptable long-term safety	Not yet reported

Supplementary Table 2. Neoadjuvant Osimertinib Trials

Feature	Blakely/Aredo [51, 78]	NEOS [79]
Design	Multi-institutional phase II, single-arm	Multicenter, single-arm phase II
Population	Resectable stage I–IIIA EGFR ex19del/L858R (AJCC7)	Resectable stage II–IIIB EGFR ex19del/L858R adenocarcinoma
Number	27	Interim analysis
Treatment	Osimertinib 80 mg QD × up to two 28-day cycles preop	Osimertinib 80 mg QD × 6 weeks preop
Primary endpoint	MPR (≤10% viable tumor)	Radiologic/pathologic response
Key findings	89% resection rate; modest MPR; common radiographic shrinkage	Feasible; favorable radiologic responses; high R0 resection
Safety	Feasible with timely resection; no major perioperative toxicity	Acceptable

Supplementary Table 3. LAURA Trial: Consolidation Osimertinib Post-CRT

Feature	LAURA [53]
Design	Phase III, double-blind, randomized, osimertinib vs placebo
Population	Unresectable stage III EGFR-mutated (ex19del/L858R) without progression post-CRT
Number	216 (143 osi, 73 placebo)
Treatment	Osimertinib 80 mg QD vs placebo until progression/discontinuation
Primary endpoint	PFS by blinded independent central review
Key efficacy	Median PFS 39.1 vs 5.6 months
Safety considerations	Competing risks of radiation pneumonitis and TKI-related ILD are central

Supplementary Table 4. FLAURA: First-Line Osimertinib vs. First-Generation EGFR-TKIs

Feature	FLAURA Primary [3]	FLAURA Final OS [54]	Post-Progression Analysis [55]
Design	Phase III, 1:1, osi vs gefitinib/erlotinib	Final OS analysis	Exploratory post-progression outcomes
Population	Treatment-naïve advanced EGFR ex19del/L858R	Same	Same
N	556	556	556
Treatment	Osimertinib 80 mg QD vs gefitinib 250 mg QD or erlotinib 150 mg QD	As in [3]	As in [3]
Primary endpoint	PFS	OS (prespecified)	Post-progression OS, treatment patterns
Key efficacy	PFS HR 0.46 [3, 54]	OS advantage confirmed despite crossover [54]	Durable benefit even with crossover; prolonged time to second progression [55]
Safety	Better tolerability; lower high-grade rash/diarrhea [3, 54]	/	/

Supplementary Table 5. First-Line Osimertinib ± Chemotherapy

Feature	FLAURA2 Primary PFS [56]	FLAURA2 Final OS [57]	OPAL [58]
Design	Phase III, open-label, 1:1, osi+chemo vs osi alone	Same trial, OS analysis	Phase II, multicenter, single-arm
Population	Untreated advanced EGFR ex19del/L858R	Same	Untreated EGFR-mutated advanced non-squamous NSCLC
Number	557	557	67

Feature	FLAURA2 Primary PFS [56]	FLAURA2 Final OS [57]	OPAL [58]
Treatment	Osi 80 mg + platinum–pemetrexed (4 cycles) → osi+pemetrexed vs osi alone	As in [56]	Osi 80 mg + platinum–pemetrexed (4 cycles) → osi+pemetrexed
Primary endpoint	Investigator-assessed PFS	OS	Safety and ORR (co-primary)
Key findings	PFS significantly longer with combination	OS results reported	Feasible; high ORR; expected chemo toxicities

Supplementary Table 6. AURA3: Osimertinib vs. Platinum–Pemetrexed in T790M-Positive Disease

Feature	AURA3 Primary [62]	CNS Analysis [64]	Japanese Subgroup [63]
Design	Phase III, 2:1, osi vs platinum–pemetrexed	Preplanned CNS subgroup	Japanese subset analysis
Population	T790M-positive advanced NSCLC post-EGFR-TKI	T790M-positive with baseline CNS metastases	Japanese patients within AURA3
N	419	CNS-evaluable subsets [34]	63 (41 osi, 22 chemo)
Primary endpoint	PFS	CNS ORR; CNS PFS	PFS
Key efficacy	Superior PFS vs chemotherapy	Higher CNS ORR and CNS PFS vs chemo	Median PFS 12.5 vs 4.3 mo; HR 0.27 (0.13–0.56)
Safety	Better tolerated than chemotherapy; ILD/pneumonitis	/	Grade ≥3 AEs: 12.2% vs 54.5%

Supplementary Table 7. Phase II Osimertinib in T790M-Positive Disease

Feature	AURA Extension [65]	LiquidLung-O Cohort 2 [66]	WJOG 8815L [67]	APOLLO [81]	Korean AURA ext/AURA2 [69]
Population	T790M+ post-EGFR-TKI	Plasma T790M+, tumor unknown	Plasma T790M screening	T790M+ with CNS metastases	Korean T790M+
Design	Single-arm, phase II	Single-arm, single-center phase	Prospective screening +	Prospective, single-arm	Subgroup analysis of phase II trials

	extension	II	treatment		
N	Phase II extension cohort	19 treated (15 response-evaluable)	Not fully specified	Not fully specified	66 treated (62 response-evaluable)
Key efficacy	ORR high; median PFS 12.3 mo; DoR 15.2 mo	ORR 66.7%; median PFS 8.3 mo; DoR ~6 mo	Efficacy demonstrated; details in source	PFS and ORR reported; CSF NGS and PK integrated	ORR 74%; median DoR 9.8 mo
Safety	Diarrhea 43%, rash 40%; ILD 4% (3 fatal)	AEs 89.5%; grade 3–4 in 31.6%; 1 grade 3 ILD	Acceptable	AEs reported; CSF analyses	Consistent with global AURA

Supplementary Table 8. Osimertinib in Uncommon EGFR Mutations

Feature	KCSG-LU15-09 [71]	UNICORN [72, 73]	Pooled Post-Hoc [74]
Line of therapy	Multi-line	First-line only	Mixed (11 first-line, 10 pretreated)
Number	36 evaluable	40 eligible	21
ORR	50%	Reported favorably	47.6%; G719X-compound: 62.5%
Median PFS	8.2 months	Design published	5.5 months; G719X-compound: 13.7 months
Median OS	/	/	G719X-compound: 29.3 vs 7.5 months