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Clarivate's top takeaways from the 2025 World Conference on Lung Cancer

Market Event Summary

Charlotte Jago, Ph.D. | September 2025

Tagrisso plus chemotherapy improves OS in first-line metastatic *EGFR*-mutated NSCLC

Context

- AstraZeneca's EGFR TKI Tagrisso is standard of care in multiple *EGFR*-mutated NSCLC settings, including early-stage resectable, stage III unresectable, and metastatic.
- Positive PFS data (HR 0.62) from the Phase 3 FLAURA2 trial of Tagrisso plus chemotherapy, versus Tagrisso monotherapy, secured the combination's approval in first-line metastatic *EGFR*-mutated NSCLC in the major markets in 2024.
- OS data from FLAURA2 were first revealed at WCLC 2025.

Key findings

- Median OS was 47.5 months for Tagrisso plus chemotherapy, versus 37.6 months for Tagrisso monotherapy (HR 0.77; P = 0.020). OS rates at 24 months were 79.7% versus 71.5%, at 36 months were 63.1% versus 50.9%, and at 48 months were 49.1% versus 40.8%.
- The combination showed an OS benefit despite platinum-based chemotherapy being the most common subsequent treatment in both treatment arms.
- For the combination versus the monotherapy, the rate of grade ≥ 3 adverse events was 70% versus 34%, of fatal treatment-related adverse events (TRAEs) was 2% versus 1%, and of adverse events leading to discontinuation of Tagrisso was 12% versus 7%.

Clarivate's takeaways

Competition: The first-line *EGFR*-mutated setting sees competition between Tagrisso monotherapy and two combinations approved by the FDA in 2024: Tagrisso plus chemotherapy and Johnson & Johnson's EGFR × MET antibody Rybrevant plus EGFR TKI Lazcluze.

Medical practice: Earlier in 2025, Rybrevant plus Lazcluze was the first regimen to report improved OS versus Tagrisso in this setting (HR 0.75). However, KOLs interviewed by Clarivate are concerned about this regimen's toxicity and may prefer the more familiar toxicity profile of chemotherapy added to Tagrisso.

Market outlook: The first-line metastatic setting is the largest and most dynamic of the NSCLC treatment settings. Clarivate forecasts sales of $35 billion in 2033 in this setting, with EGFR-targeting agents accounting for $6.5 billion.

Ivonescimab plus chemotherapy fails to improve OS in later-line metastatic *EGFR*-mutated NSCLC

Context

- Akeso and Summit's PD-1 × VEGF bispecific antibody ivonescimab plus chemotherapy was approved in China in 2024 for *EGFR*-mutated metastatic NSCLC after EGFR TKI therapy, based on positive PFS data from the Phase 3 HARMONi-A trial. The Phase 3 HARMONi trial, which comprises the addition of Western-patient cohorts to HARMONi-A, aimed to secure approval outside of China.
- HARMONi met its PFS endpoint in May 2025. However, the co-primary OS endpoint, which the FDA advised would be necessary to support marketing authorization, was not met. Detailed PFS and OS data from HARMONi were revealed at WCLC 2025.

Key findings

- Only a nonsignificant trend toward OS improvement was seen with ivonescimab plus chemotherapy versus chemotherapy; median OS was 16.8 months versus 14.0 months (HR 0.79; P = 0.0570).
- Median PFS was 6.8 months for the combination versus 4.4 months for chemotherapy (HR 0.52; P < 0.0001). PFS rates at 6 months were 54.0% versus 34.7% and at 12 months were 25.4% versus 8.3%. PFS HRs in patients with and without CNS metastases at baseline were 0.34 and 0.59, respectively.
- ORR was 45% versus 34%; DCR was 84% versus 73%; and median DOR was 7.6 versus 4.2 months. Rates of grade ≥ 3 TRAEs were 50.0% versus 42.2%, of fatal TRAEs were 1.8% versus 2.3%, and of TRAEs leading to discontinuation of ivonescimab or placebo were 7.3% versus 5.0%.

Clarivate's takeaways

Regulatory expectations: Given the FDA's stated requirement for positive OS data for approval of ivonescimab in the later-line *EGFR*-mutated setting, Clarivate does not forecast approval of ivonescimab plus chemotherapy based on the current data.

Ongoing studies: Ivonescimab is in Phase 3 development in the first-line *EGFR*-mutated setting: with chemotherapy in HARMONi-3 and as monotherapy for patients with high (≥ 50%) PD-L1 expression in HARMONi-7. Clarivate expects these trials will support approval.

Competition: VEGF inhibition has a long history in NSCLC, with biosimilar versions of bevacizumab available in the major markets. The upcoming patent expiry for Keytruda makes the pairing of biosimilar PD-1 and VEGF inhibitors a possible future alternative to a branded PD-1 × VEGF agent.

Izalontamab brengitecan shows early phase efficacy in later-line *EGFR*-mutated advanced NSCLC

Context

- Sichuan Biokin Pharmaceutical and Bristol Myers Squibb's EGFR- and HER3-targeting ADC izalontamab brengitecan is in Phase 3 development in China for *EGFR*-mutated metastatic NSCLC after EGFR TKI therapy.
- The Phase 1 BL-B01D1-101 and Phase 2 BL-B01D1-203 trials assessed various doses of izalontamab brengitecan in Chinese patients who had previously received EGFR TKIs and may also have received chemotherapy.
- Pooled data from the trials were reported at WCLC 2025.

Key findings

- Across all izalontamab brengitecan dose levels, confirmed ORR was 47.4%, median PFS was 6.9 months, and median OS was 24.8 months.
- In patients receiving izalontamab brengitecan 2.5 mg/kg on days 1 and 8 of each 3-week cycle and who had previously received an EGFR TKI and were chemotherapy-naive (N = 50), confirmed ORR was 56.0%, median PFS was 12.5 months, and median OS was not reached. OS rates at 12 and 18 months were 80.3% and 69.2%, respectively.
- There were no treatment-related fatalities. The rate of TRAEs leading to discontinuation was 1.2%

Clarivate's takeaways

Planned trials: Clarivate is tracking the progress of this drug. The Phase 3 IZABRIGHT-Lung01 trial versus platinum-based chemotherapy in *EGFR*-mutated advanced NSCLC after EGFR TKI treatment is expected to start later in 2025 in the major markets.

Complexities: The first-line *EGFR*-mutated setting is starting to see the evolution of SOC from monotherapy with the TKI Tagrisso to combination regimens, including Tagrisso plus chemotherapy, which may impact the relevance of the design of IZABRIGHT-Lung01.

Regulatory designations: Izalontamab brengitecan recently gained FDA Breakthrough Therapy designation for advanced *EGFR*-mutated NSCLC after both EGFR TKI and platinum-based chemotherapy. Use of this drug at that stage may be a more realistic positioning in the treatment paradigm than the IZABRIGHT-Lung01 setting.

About the author

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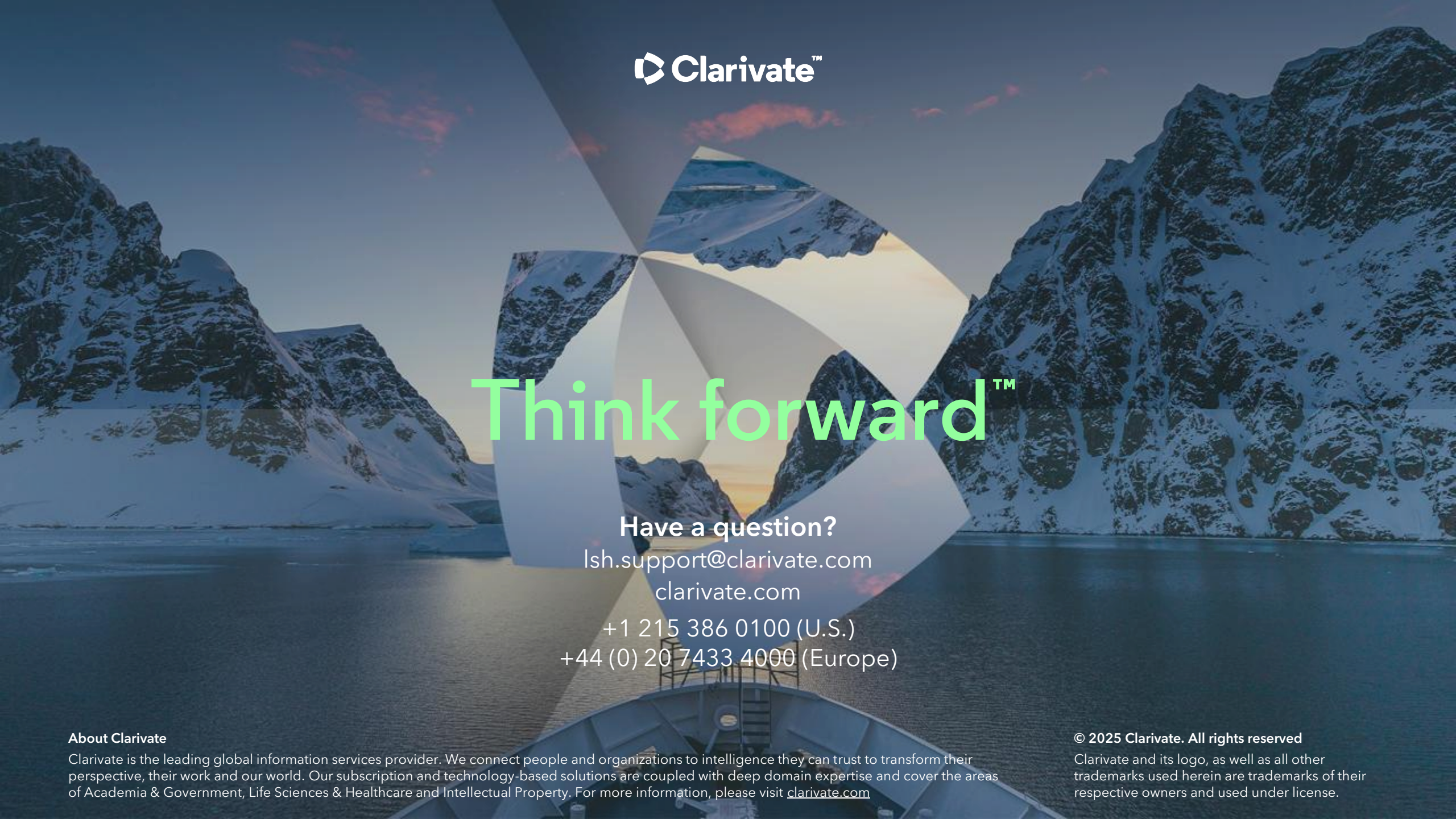
Charlotte Jago is a pharmaceutical industry analyst with more than 20 years' experience, preceded by 5 years of laboratory research in academia (Imperial College London) and industry (Celltech, now UCB). She wrote the flagship Cortellis Drugs to Watch reports in 2013, 2014, 2015, and 2019 and led the improvement in immuno-oncology coverage on the Cortellis Competitive Intelligence platform. She holds a Ph.D. in immunology, a first-class degree in pharmacology, and a postgraduate certificate in journalism.

Clarivate coverage of NSCLC

- NSCLC *Disease Landscape & Forecast* (G7)
  - Provides comprehensive market intelligence with world-class epidemiology, keen insight into current treatment paradigms, and drug forecasts supported by detailed primary and secondary research
- NSCLC *Current Treatment: Physician Insights*: US
  - Provides physician insights on treatment dynamics, prescribing behavior, and drivers of brand use in NSCLC
- NSCLC *Treatment Sequencing*: US
  - Provides sequential treatment patterns in market-relevant treatment scenarios and drug share mapped to treatment journey in NSCLC
- NSCLC *Unmet Need:* US/EU
  - Provides insights into areas of unmet need in specific subpopulations



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