FutureBridge

2024 ASCO® ANNUAL MEETING

POST-CONFERENCE REPORT

ABSTRACT CAPSULE

Non-Small Cell Lung Cancer and Breast Cancer Insights

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01

EVOKE-01 Study

Sacituzumab Govitecan vs Docetaxel In Patients With Metastatic Non-small Cell Lung Cancer Previously Treated With Platinum-based Chemotherapy And PD(L)-1 Inhibitors

– Presented by
Luis G. Paz-Ares, MD

Response to novel therapies likely to differentiate segments in PD(L)-1 progressor populations in NSCLC

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Clinical Trial Overview

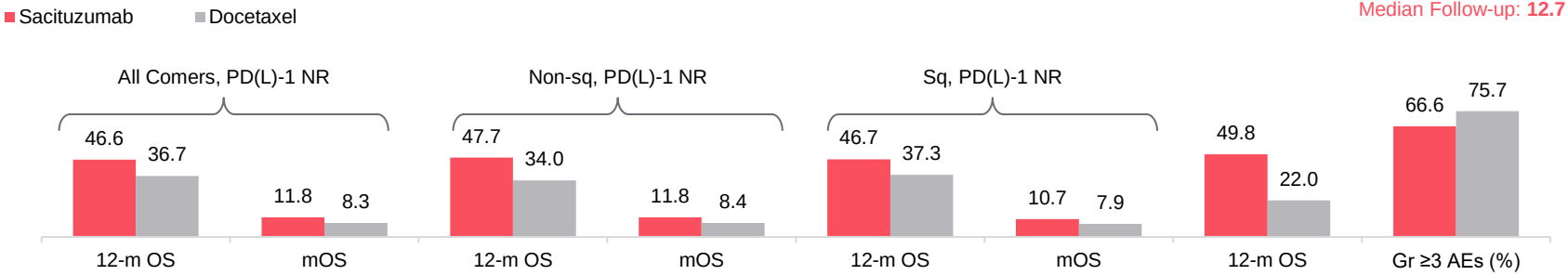
Trial Significance	This phase 3 study is treating **PD(L)-1 progressors** with Sacituzumab govitecan-hziy in **2L+ NSCLC patients**	
Trial Design	Experimental arm: Sacituzumab govitecan Comparator arm: Docetaxel	Primary endpoint: Overall survival (OS)
	Current SOC: Docetaxel OR Docetaxel + Ramucirumab	Enrollment : 603
Target Patient Population	2L+ NSCLC patients progressed on or after platinum-based chemotherapy plus PD(L)-1 Immunotherapy	

Trial ID	NCT05089734
Sponsor	GILEAD
Trial Location	Global

Level of Unmet Need in Current Setting

Low | Medium | **High**

Key Findings & Outcomes



NR: Non-Responder; PD-1: Programmed Cell Death 1; PD-L1: Programmed Cell Death-Ligand 1; Source: Abstract #: LBA8500

Response to novel therapies likely to differentiate segments in PD(L)-1 progressor populations in NSCLC

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Study Conclusion

1. Sacituzumab shows meaningful OS improvement in subgroup analysis for patients who are non-responders to anti-PD(L)-1 therapy. However, a larger clinical study validation is warranted.
   a. PD(L)-1 progressors constitute a growing population, of which non-responders constitute a large portion (~60%).
   b. Chemotherapy remains the only SOC treatment for these patients, thus, reflecting a huge unmet need.
2. Overall, Sacituzumab has demonstrated a favorable safety profile compared to Docetexal.
3. Sacituzumab combination studies are being evaluated in front-line NSCLC setting.

FutureBridge Views

1. Segregation of PD(L)-1 responders and non-responders in future through proof-of-concept trials can highlight early efficacy discrepancies in these sub-populations.

ASCO Attendees Sentiments

> Despite the study failure, the findings of the study in PD(L)-1 non responders are worth considering and may lay a foundation for separate largeer trials in these patients. We are looking forward to a better response with Sacituzumab in PD(L)-1 progressors in NSCLC – *US KOL*

02

LAURA Study

Osimertinib After Definitive Chemoradiotherapy in Patients with Unresectable Stage 3 Epidermal Growth Factor Receptor-Mutated (EGFRm) NSCLC: Primary Results of the Phase 3 LAURA Study

– Presented by
Suresh S. Ramalingam, MD

Osimertinib likely to set new standards of care treatment in early settings, expanding meaningful clinical benefits

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Clinical Trial Overview

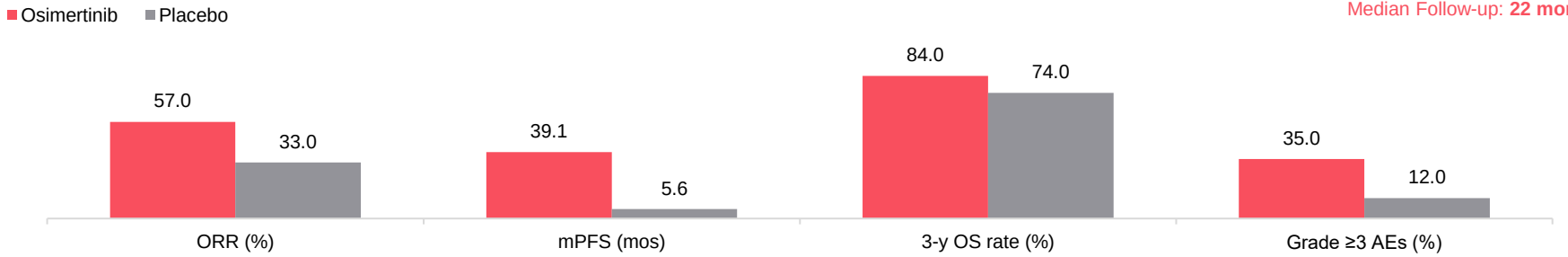
Trial Significance	LAURA is a global Phase 3 study assessing **unresectable Stage 3 EGFR-mutant NSCLC patients, with a stable disease after platinum-based chemoradiotherapy**	
Trial Design	Experimental arm: cCRT → Osimertinib Comparator arm: cCRT → Placebo	Primary endpoint: Progression-Free Survival (PFS)
	Current SOC: cCRT	Enrollment : 216
Target Patient Population	Unresectable Stage 3 EGFR-mutant NSCLC Post CRT Consolidation	

Trial ID	NCT03521154
Sponsor	AstraZeneca
Trial Location	Global

Level of Unmet Need in Current Setting

Low | Medium | **High**

Key Findings and Outcomes



cCRT: Concurrent Chemoradiotherapy; ORR: Objective Response Rate; OS: Overall Survival; Source: Abstract #: LBA4

Osimertinib likely to set a new standard of care treatment in early settings, expanding meaningful clinical benefits

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Study Conclusion

1. This study establishes Osimertinib as a highly effective post-CRT consolidation therapy, significantly improving outcomes for patients with unresectable stage 3 EGFR-mutant NSCLC, showing remarkable improvement in median PFS and better tolerability.

2. Osimertinib will become the new standard treatment for unresectable EGFR-mutant stage 3 NSCLC patients who are stable post-CRT and will lead to the generation of an Osimertinib progressors population soon.

FutureBridge Views

1. The LAURA trial, building on the PACIFIC trial's groundwork, marks a pivotal shift in NSCLC treatment by emphasizing the importance of combatting progression.

2. Osimertinib's success as a post-CRT consolidation therapy underscores the need for innovative approaches to manage emerging Osimertinib progressors.

ASCO Attendee Sentiments

This post-CRT therapeutic approach is a win-win situation for stage 3 EGFR positive patients, and this label expansion will solidify Osimertinib’s pivotal role in addressing the existing unmet needs – *US KOL*

So far, the study shows a dramatic improvement in PFS, nonetheless, OS results would explain the actual acceptance in the real-world. We are waiting for the long-term survival data – *UK KOL*

03

Checkmate 77T Study

Clinical Outcomes with Perioperative Nivolumab by Nodal Status Among Patients with Stage 3 Resectable NSCLC

– Presented by
Mariano Provencio, MD, PhD

Peri-operative PD(L)-1 inhibitors improving survival and quadruple responders' percentage to resection in NSCLC

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Clinical Trial Overview

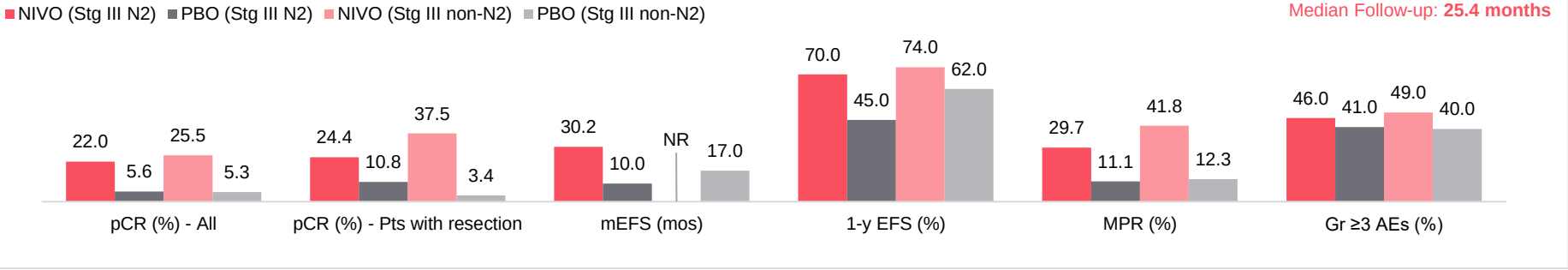
Trial Significance	This Phase 3 study aims to determine whether peri-operative immunotherapy can prolong event-free survival (EFS) and ultimately overall survival in early-stage NSCLC.	
Trial Design	Experimental arm: Nivolumab (NIVO) + Pt Chemo → Surgery → Adj NIVO Comparator arm: Placebo + Pt Chemo → Surgery → Adj Placebo	Primary endpoint: EFS
	Current SOC: Pembrolizumab + Pt Chemo → Surgery → Adj. Pembrolizumab	Enrollment : 482
Target Patient Population	Peri-operative treatment for Stage IIA (> 4 cm) to IIIB (T3N2) NSCLC without EGFR or ALK alterations	

Trial ID	NCT04025879
Sponsor	Bristol Myers Squibb
Trial Location	Global

Level of unmet needs in current settings

Low | **Medium** | High

Key Findings and Outcomes



EFS: Event-Free Survival; MPR: Major Pathological Response; pCR: Pathological Complete Response; Pt: Platinum; Source: Abstract #: LBA8007

Peri-operative PD(L)-1 Inhibitors improving survival and quadruple responders' percentage to resection in NSCLC

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Study Conclusion

1. Peri-operative NIVO significantly provides clinical benefits in terms of median EFS and pCR over placebo with resectable NSCLC, including stage 3N2 patients who have a poor prognosis.

2. Study outcomes support NIVO as a potential new treatment for resectable patients, building upon the standard of care of using chemoimmunotherapy. Perioperative nivolumab will likely gain regulatory approval based on these results.

3. Until data maturity, the selection of perioperative NIVO or Pembrolizumab will be based on physicians' choice and bias. The clinical adoption of perioperative therapies will transform later line treatments and change the patient demographics available for clinical trials.

FutureBridge Views

1. Perioperative NIVO results in high surgical feasibility and substantial nodal downstaging, which will lead to better long-term outcomes.

2. NIVO-Chemo is already approved in Stage I-IIIA as neoadjuvant treatment, Durvalumab as adjuvant post-CRT consolidation, and with the likely future approval of NIVO in perioperative settings for resectable patients, a high unmet need will arise for PD(L)-1 progressor populations across frontlines and beyond.

ASCO Attendee Sentiments

> Results are really encouraging, however, identifying the specific patient population who might be most likely to benefit from NIVO combination, both in neo-and/or-adjuvant setting, is crucial in bringing a maximum benefit to the patients – *DE KOL*

04

postMONARCH Study

Abemaciclib Plus Fulvestrant Vs Fulvestrant alone for HR+, HER2- Advanced Breast Cancer Following Progression on a Prior CDK4/6 Inhibitor Plus Endocrine Therapy: Primary Outcome of the Phase 3 postMONARCH Trial

– Presented by
Kevin Kalinsky, MD, MS

Emerging Abemaciclib plus Fulvestrant treatment extends survival benefit to advanced Breast Cancer Patients, and supports Sequencing of CDK4/6 Inhibitors

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Clinical Trial Overview

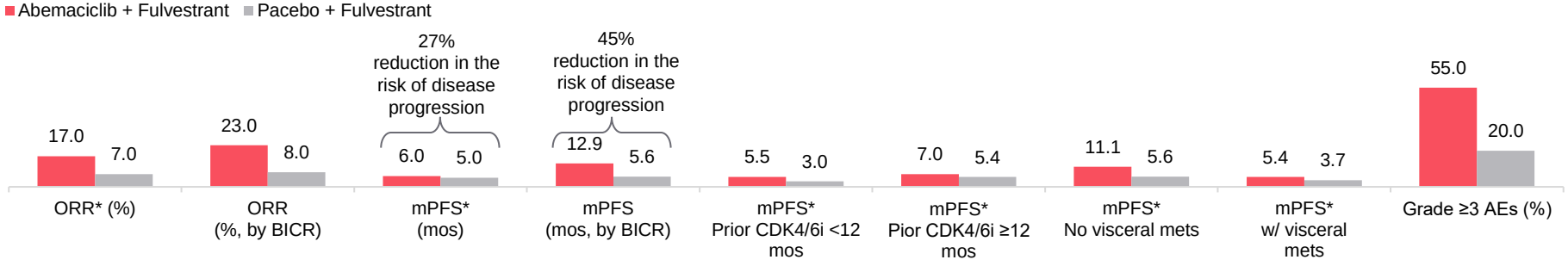
Trial Significance	Phase 3 global study for **HR+, HER2- advanced Breast Cancer (aBC) patients** who progressed/recurred **after CDK4/6 inhibitor plus aromatase inhibitor/ endocrine therapy** (AI/ET)	
Trial Design	Experimental arm: Abemaciclib + Fulvestrant Comparator arm: Placebo + Fulvestrant	Primary endpoint: Progression-Free Survival (PFS)
	Current SOC: Chemotherapy/Fulvestrant	Enrollment : 368
Target Patient Population	HR+/HER2-, 1L-2L Breast Cancer patients who progressed on a CDK4/6 Inhibitor plus aromatase inhibitor/endocrine therapy	

Trial ID	NCT05169567
Sponsor	Lilly
Trial Location	Global

Level of Unmet Need in Current Setting

Low | Medium | **High**

Key Findings and Outcomes



*By Investigator Assessment; ORR: Objective Response Rate Source: Abstract #: LBA1001

Emerging Abemaciclib Plus Fulvestrant treatment extends survival benefit to advanced Breast Cancer patients and supports Sequencing of CDK4/6 Inhibitors

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Study Conclusion

1. With its unique approach of continued CDK4/6 inhibition beyond progression on CDK4/6 inhibitor, this study offers a targeted therapy option of Abemaciclib combination and demonstrated an improved PFS to HR+/HER2- aBC patients after their adjuvant/ first-line therapy across all biomarker subgroups.

2. The study results guide the sequencing of CDK4/6 inhibitors to maximize their benefit in HR+/HER2- advanced breast cancer.

FutureBridge Views

1. CDK4/6 inhibitors plus AI/ET will remain a gold standard for HR+/HER2- aBC; Adding Abemaciclib to ET offers a treatment strategy for continuing CDK4/6 inhibition at progression.

2. The study strengthens the treatment trail by demonstrating a significant improvement in the patient outcomes after first-line palbociclib treatment, irrespective of biomarkers or duration of CDK4/6i use.

3. Introduction of Abemaciclib extends the clinical benefits of CDK4/6 inhibitors in HR+/HER2- aBC by driving the sequencing of treatment therapies.

ASCO Attendee Sentiments

> This regimen would definitely offer new and effective treatment options, especially for biomarker-negative population, i.e., in patients with or without ESR1 mutations and PIK3CA alterations – *US KOL*

05

DESTINY-Breast06 Study

Trastuzumab Deruxtecan vs. Physician's Choice of Chemotherapy in Patients with Hormone Receptor-positive, Human Epidermal Growth Factor Receptor 2-Low or-ultralow Metastatic Breast Cancer with Prior Endocrine Therapy

– Presented by
Giuseppe Curigliano, MD, PhD

HER2-Low/-Ultralow Metastatic Breast Cancer patients benefits from Trastuzumab Deruxtecan through By-stander Effects

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Clinical Trial Overview

Trial Significance	This phase 3 study is evaluating Trastuzumab deruxtecan (T-DXd) in **1L+ HR+/ HER2-low** or **HER2-ultra low** (IHC 0-2/ISH) metastatic Breast Cancer (mBC) patients **with prior endocrine therapy** (ET)	
Trial Design	Experimental arm: Trastuzumab deruxtecan Comparator arm: Capecitabine OR Paclitaxel OR Nab-paclitaxel	Primary endpoint: PFS
	Current SOC: Chemotherapy	Enrollment : 866
Target Patient Population	HR+ HER2-low and HER2-ultra low mBC with progression on at least 1 prior ET plus a CDK4/6 inhibitor (Chemo-naïve)	

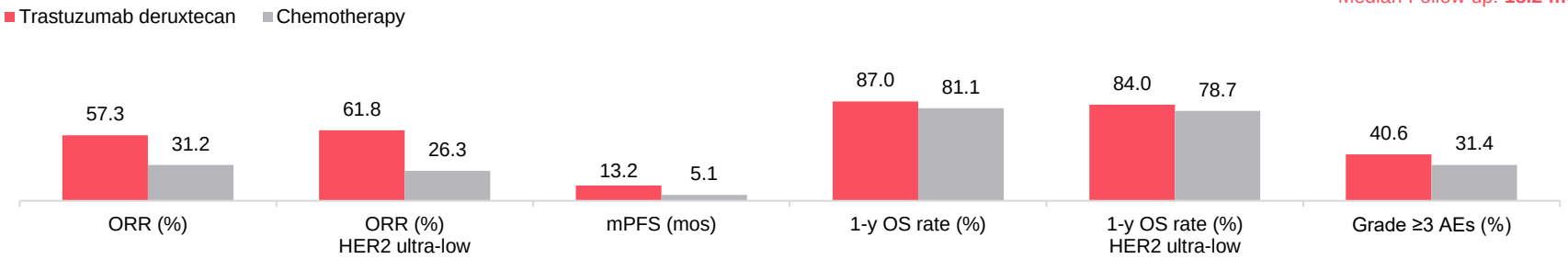
Trial ID	NCT04494425
Sponsor	AstraZeneca, Daiichi-Sankyo
Trial Location	Global

Level of Unmet Need in Current Setting

Low | **Medium** | High

Key Findings and Outcomes

Median Follow-up: **18.2 months**



ORR: Objective Response Rate; OS: Overall Survival; PFS: Progression-Free Survival; Source: Abstract #: LBA1000

HER2-Low/-Ultralow Metastatic Breast Cancer patients benefits from Trastuzumab Deruxtecan through By-stander Effects

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Study Conclusion

1. A significant clinical benefit in PFS and ORR reported by T-DXd in HER2-low/ultralow mBC which had progressed on ET (≥1 lines) will likely translate to meaningful clinical OS, addressing high unmet needs in mBC (~80% are HR+/HER2-low/ultralow population).
   – Notably, improving the sensitivity of assays to distinguish HER2-low/ultralow pool may help in better identifying the patient pool that benefits from Tx that is efficacious in HER2-low/ultralow populations.

2. Emerging novel modalities like ADCs may benefit patient populations even if the targeted antigen is expressed in low amounts. Potential translation to other tumors is possible. HER2-low/-ve pts in tumors like NSCLC, gastric, etc. are excluded in trials upfront based on current assays.

FutureBridge Views

1. T-DXd has yielded positive outcomes in terms of PFS and ORR among HER2-low/ultralow mBC patients, although it comes with higher toxicity compared to SoC.

2. Moreover, it has sparked discussions about the need for personalized testing of HER2 levels and the accuracy of HER2 detection tests to target those who would benefit most.

ASCO Attendee Sentiments

> It is exciting to see how Trastuzumab showing high responses in HER2 ultralow population, though have associated toxicities like ILD that may restrict its use to some patients only… besides identifying this new patient class HER2-ultralow and Chemo-naïve will need focus on HER testing in routine practice – *US KOL*

Thank you

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