Lung Cancer

The OncoAlert Network:	"Hello all, welcome and we go live in 15 minutes"
Biagio Ricciuti, MD, PhD:	Hello everyone! Looking forward to this session!
Gil Morgan:	"Hello Biagio, Greetings and a pleasure to have you here as moderator"
The OncoAlert Network:	"Good Day Dr. Ricciuti and Dr. Morgan, a pleasure to have you both here"
The OncoAlert Network:	We would like to inform our viewers that with any problems please reach out to us
The OncoAlert Network:	OncoAlertNetwork@OncoAlert360.com
The OncoAlert Network:	Dear Colleagues welcome to the Colloquium
The OncoAlert Network:	Greetings colleagues
The OncoAlert Network:	I would like to introduce our moderator Dr. Biagio Ricciuti
The OncoAlert Network:	looking forward to a great presentation from Dr. lopes on early NSCLC
Gil Morgan:	"Hi Biagio, Hi Gilberto!"
Biagio Ricciuti, MD, PhD:	"Recent advances in immunotherapy and targeted therapies for early-stage lung cancer offer promising new treatment options, potentially improving survival and reducing recurrence. However, many open questions remain, including optimal patient selection, resistance mechanisms, and long-term outcomes."
The OncoAlert Network:	Thank you Dr. Ricciuti
Biagio Ricciuti, MD, PhD:	Great to hear Dr. Lopes reviewing this topics.
Gil Morgan:	"In 2024, significant advancements in the treatment of early non-small cell lung cancer (NSCLC) emerged, particularly in targeted therapies and immunotherapy. New data have provided insights into the benefits of combining immunotherapy with chemotherapy in both neoadjuvant and adjuvant settings, with the first evidence of improved overall survival (OS) in these strategies."
Biagio Ricciuti, MD, PhD:	"Adjuvant ICI has not shown an OS benefit, which is the ultimate endpoint for patients with early stage lung cancer. Neoadjuvant/perioperative should be favored in this setting."

Biagio Ricciuti, MD, PhD:	ALINA has changed our SoC for ALK+ NSCLC. However chemotherapy was not given to patients in the Alectinib arm. Not sure we are ready to abandon adjust chemo (which has an OS benefit) in all comers
The OncoAlert Network:	Alectinib has been established as the standard adjuvant treatment in the US and several other countries for patients with ALK-positive NSCLC.
Gil Morgan:	"Additionally, the use of osimertinib has expanded to include consolidation therapy after chemoradiation in locally advanced (LA) disease, further enhancing treatment outcomes."
Gil Morgan:	"wow, 22-74%"
Biagio Ricciuti, MD, PhD:	"Impressive PFS with osimertinib in the LAURA trial, with an HR of 0.16. Mature OS data certainly warranted."
Gil Morgan:	Thats the Money SLIDE
Gil Morgan:	Loads of great Practice changing trials this past year
Gil Morgan:	Thank you GIlberot
Gil Morgan:	GIlberto
Biagio Ricciuti, MD, PhD:	Amazing talk! Question is if we should extrapolate from LAURA and apply the same strategies to very rare drivers for which we will not have randomized trials
The OncoAlert Network:	Thank you Dr. Lopes
The OncoAlert Network:	and Now We welcome Dr. Charu Aggarwal
The OncoAlert Network: put here	Please remember that if you have Any questions or comments you can
Gil Morgan:	"In this phase 3, double-blind, placebo-controlled trial, patients with unresectable stage III EGFR-mutated non-small-cell lung cancer (NSCLC) who had not progressed after chemoradiotherapy were randomly assigned to receive osimertinib or placebo. Osimertinib significantly improved progression-free survival, with a median of 39.1 months compared to 5.6 months for placebo (hazard ratio for disease progression or death, 0.16; P<0.001). At 12 months, 74% of patients on osimertinib remained progression-free, ver"
Gil Morgan:	https://www.nejm.org/doi/full/10.1056/NEJMoa2402614
Gil Morgan:	"So in summation: Osimertinib significantly improved progression-free survival compared to placebo in patients with unresectable stage III EGFR-mutated NSCLC following chemoradiotherapy, with a favorable safety profile."

Biagio Ricciuti, MD, PhD: "Important to see appropriate cross-over in LAURA (81%). Critical to interpret OS data, when available."

The OncoAlert Network: "Thank you very much Dr. Morgan, with a breakdown of LAURA and link to the publication"

The OncoAlert Network: "Absolutely, VERY Important Point Dr. Ricciuti"

Gil Morgan: Lorlatinib Versus Crizotinib in Patients With Advanced ALK-Positive Non–Small Cell Lung Cancer: 5-Year Outcomes From the Phase III CROWN Study

Gil Morgan: https://ascopubs.org/doi/10.1200/JCO.24.00581

Gil Morgan: "After 5 years of follow-up in the phase III CROWN study, lorlatinib demonstrated unprecedented outcomes in patients with previously untreated advanced ALK-positive NSCLC, with median progression-free survival (PFS) not yet reached compared to 9.1 months for crizotinib (hazard ratio, 0.19)."

Biagio Ricciuti, MD, PhD: "CROWN has changed my practice with 5-year PFS rates of 60%. However, lorlatinib is associated with significant toxicity, making long-term therapy particularly challenging for patients expected to remain on treatment for many years."

Gil Morgan: "The 5-year PFS rate was 60% with lorlatinib versus 8% with crizotinib, and lorlatinib also showed superior intracranial efficacy. No new safety concerns emerged, and no new ALK resistance mutations were detected. Lorlatinib's results represent the longest PFS reported for a single-agent targeted therapy in NSCLC, setting a new standard for ALK-targeted treatments."

Biagio Ricciuti, MD, PhD: New ALK inhibitors (4th gen) promise to be as effective (or more) and possibly safer

Gil Morgan: "So in Summary: After 5 years of follow-up, lorlatinib significantly outperformed crizotinib in progression-free survival and intracranial efficacy, setting a new benchmark for targeted therapy in advanced ALK-positive NSCLC."

Gil Morgan: Multi-site randomized trial of stepped palliative care (PC) for patients with advanced lung cancer.

Gil Morgan: https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.12000

Gil Morgan: This is the abstract presented at ASCO

Gil Morgan: "In summary : The stepped palliative care (SPC) model for advanced lung cancer maintained quality of life with fewer visits compared to

early palliative care (EPC), offering a scalable approach to delivering patient-centered care."

Gil Morgan: Here is MARIPOSA2 in Annals of Oncology

Gil Morgan: Amivantamab plus chemotherapy with and without lazertinib in EGFR-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study☆

Gil Morgan: https://www.annalsofoncology.org/article/S0923-7534(23)04281-3/fulltext

Gil Morgan: "MARIPOSA-2 trial evaluated the efficacy of amivantamab plus chemotherapy, with and without lazertinib, in patients with EGFR-mutated advanced NSCLC after progression on osimertinib. Results showed that both amivantamab–chemotherapy and amivantamab–lazertinib–chemotherapy significantly improved progression-free survival (PFS) and intracranial PFS compared to chemotherapy alone, with hazard ratios of 0.48 and 0.44, respectively ($P < 0.001$ for both)."

Gil Morgan: "Additionally, both amivantamab-containing regimens demonstrated higher objective response rates (64% and 63% vs. 36%). The predominant adverse events were hematologic, EGFR-, and MET-related toxicities, with amivantamab–chemotherapy showing fewer hematologic side effects. These findings suggest that these combinations offer promising treatment options for patients with limited alternatives after osimertinib progression."

Gil Morgan: "So in summary: Amivantamab combined with chemotherapy, with or without lazertinib, significantly improved progression-free survival and intracranial PFS in patients with EGFR-mutated advanced NSCLC after osimertinib progression, with manageable side effects."

Gil Morgan: A Great presentation by Dr. Aggarwal

Biagio Ricciuti, MD, PhD: "MARIPOSA-2 has established a new standard of care in the second-line setting for patients with EGFR mutations following osimertinib. However, for those who receive first-line chemotherapy plus osimertinib, the benefit of additional chemotherapy remains uncertain."

The OncoAlert Network: "We Now have Dr. Naidoo covering SCLC, however we must apologise that due to technical problems, her presentation was cut short however the full presentation will be available on demand"

Biagio Ricciuti, MD, PhD: We now have 5-y survival data from the Impower 133: https://pubmed.ncbi.nlm.nih.gov/39306923/

Biagio Ricciuti, MD, PhD: "he three-, four-, and five-year overall survival (95 % CI) estimates were 16 % (11 %-21 %), 13 % (8 %-18 %), and 12 % (7 %-17 %), respectively."

The OncoAlert Network: "As we anticipated this, These are the top finding in SCLC by Dr. Naidoo"

The OncoAlert Network:	"Summary of SCLC ES SCLC - 1L Chemo-IO current SOC: IMpower133 (Atezo+EP); CASPIAN (Durva + EP) - 2nd line options: lurbinectedin, tarlatamab • LS SCLC • ADRIATIC: 10 consolidation is a new SOC - LU005: concurrent 1O with chemoRT not associated with OS benefit • Future Directions - DELPHI-305: 1st line maintenance tarlatamab - Other novel agents in development (e.g. iDXD)"
The OncoAlert Network:	The same for Mesothelioma
The OncoAlert Network:	Mesothelioma Background: Occupational disease; difficult to diagnose I Treatment of Localized Disease: ?No longer a surgical disease- perhaps for a subset. Role of RT also needs re-evaluation. New systemic therapies have changed landscape Treatment of Adv Disease: 1L: Ipi/Nivo; Pem-Chemo? Potential new option
Gil Morgan:	We Look forward to watching the FULL Presentation On Demand
Gil Morgan:	DeLLphi-301: Tarlatamab phase 2 trial in small cell lung cancer (SCLC)—Efficacy and safety analyzed by presence of brain metastasis.
Gil Morgan:	https://ascopubs.org/doi/10.1200/JCO.2024.42.16_suppl.8015
Biagio Ricciuti, MD, PhD:	Tarlatamab is a preferred second-line option for SCLC. Ongoing biomarker analyses will help identify patients more likely to respond or develop CRS.
Gil Morgan:	"We Apologise for the cut off, but as Mentioned, the full presentation will be found on demand"
The OncoAlert Network:	NOW we have the Radiation Oncology Updates by Dr. Willlers and Dr. Keane of Mass General
Henning Willers, MD:	Dr Keane and I are glad to be part of this event!
Gil Morgan:	"Excellent, GREETINGS Henning and Katie!"
Jarushka Naidoo:	"Thanks all for tuning in, sorry for the tech issues"
Biagio Ricciuti, MD, PhD:	Welcome Dr. Keane Willers
Katie Keane, MD:	Happy to be here!
The OncoAlert Network:	"Welcome Dr. Willers and Dr. Keane, glad to have you here!"
The OncoAlert Network:	Please feel free to comment on any specific points in your presentations
The OncoAlert Network:	Dr. Ricciuti and Dr. Morgan and viewers please feel free to chime in
The OncoAlert Network:	comments or questions always welcome
Biagio Ricciuti, MD, PhD:	"Dr. Keane the negative results of PACIFIC2 have been ascribed to different patient population, increased toxicity but some speculates

negative changes in the TME. Any comments on these potential reasons?"

Katie Keane, MD (Presenter): "Thank you Dr. Ricciuti. Yes, PACIFIC 2 joins multiple additional trials where concurrent chemoRT with IO has led to negative results"

Katie Keane, MD (Presenter): There is interest in lymph node sparing radiotherapy with the thought that radiotherpy may be immunosuppressive

Biagio Ricciuti, MD, PhD: Thank you for the insight!

Katie Keane, MD (Presenter): "For the early-stage population, PACIFIC 4 used IO in the consolidative setting after SBRT. It will be interesting to see if that is positive as the MERCK and SWOG trials were both negative (but also used concurrent IO)"

Henning Willers, MD: Certainly some kind of local treatment intensification in LA-NSCLC is needed. Maybe ICB in select pts. SBRT to primary and PET SIB are promising options to study.

Gil Morgan: Osimertinib after Chemoradiotherapy in Stage III EGFR-Mutated NSCLC

Gil Morgan: https://www.nejm.org/doi/full/10.1056/NEJMoa2402614

Gil Morgan: "Summation:A total of 216 patients who had undergone chemoradiotherapy were randomly assigned to receive osimertinib (143 patients) or placebo (73 patients). Osimertinib significantly improved progression-free survival compared to placebo in patients with unresectable stage III EGFR-mutated NSCLC, with no new safety concerns identified."

Biagio Ricciuti, MD, PhD: "Agree, several retrospective studies showed higher rate of micrometastatic spread even in stage I-III (by imaging only) EGFR+ NSCLC"

Henning Willers, MD: We urgently need better approaches to tackle micrometastatic disease in this population. Local treatment intensification will not be the answer here.

Katie Keane, MD (Presenter): "Intervening at time of maximal response to TKI is an area of particular interest, especially as systemic therapies improve."

Katie Keane, MD (Presenter): How to best identify maximal response (PET? ctDNA?) is a question

Gil Morgan: Durvalumab after Chemoradiotherapy in Limited-Stage Small-Cell Lung Cancer

Gil Morgan: https://www.nejm.org/doi/full/10.1056/NEJMoa2404873

Gil Morgan: "In a phase 3 trial, adjuvant therapy with durvalumab significantly improved both overall survival and progression-free survival compared

	to placebo in patients with limited-stage small-cell lung cancer who had no disease progression after standard chemoradiotherapy, with manageable safety outcomes."
Biagio Ricciuti, MD, PhD:	"ADRIATIC (consolidation durvalumab x2y after concurrent chemo-RT) is now our new SoC with unprecedented benefit in PFS/OS in SCLC. However, high recurrence rates in 3-6 are also noted. how this will impact subsequent treatment choice and efficacy is unclear."
Henning Willers, MD:	Dr Keane what is the role of PCI here? unchanged?
Katie Keane, MD (Presenter):	Thank you Dr. Willers. I would say that is an ongoing question. The benefit of IO was seen in both subgroups (PCI vs. no PCI)
Katie Keane, MD (Presenter):	An assessment of patterns of failure (and whether patients who did not receive PCI had primary progression in the CNS) will be important
Katie Keane, MD (Presenter):	There are ongoing trials looking at PCI vs. MRI surveillance
Katie Keane, MD (Presenter):	"If patients do not receive PCI, they should all receive MRI every 3 months with restaging scans given significant risk of brain metastases"
Katie Keane, MD (Presenter):	Thank you for the opportunity to participate
The OncoAlert Network:	Thank you very Much Dr. Keane and Dr. WIllers
The OncoAlert Network:	a pleasure to have you here
The OncoAlert Network:	Next up is Dr. Malapelle who had an emergency to attend to
The OncoAlert Network: welcome	So Dr. Ricciuti and Dr. Morgan any comments you may have are always
Gil Morgan:	Thank you
Gil Morgan:	Great to see the colloquium adopting a true muldidisciplnary approach not with our friends the pathologists
Gil Morgan:	only way to learn
Biagio Ricciuti, MD, PhD:	"Critical point made by Dr. Malapelle. False negative for less common alterations (e.g. rare exon 20 insertion, uncommon fusions or splicing site variants). Right reference = correct diagnosis == right therapy"
Amira Ahmed:	CAN EGFR TEST DONE ON BLOOD SAMPLE OR JUST TISSUE SAMPLE
The OncoAlert Network:	Great Question Dr. Ahmed
Biagio Ricciuti, MD, PhD:	Both tissue and blood. We tend to do this in parallel given the shorter turnaround time of plasma NGS (or ddPCR for rapid EGFR testing for example)
Gil Morgan:	Biagio is there ever a situation where if you have to use one or the other

Gil Morgan:	Tissue is always best right?
Biagio Ricciuti, MD, PhD:	"Yes tissue is better in general but very important in the setting of acquired resistance to targeted therapies. Tissue allows to detect alterations we would not be able to see using blood (e.g. histologic transformation). Also plasma NGS is less sensitive for gene amplification (e.g. MET, HER2)"
Biagio Ricciuti, MD, PhD:	A good approach is to run these in parallel (when possible). Plasma NGS on the other hand can detect genomic heterogeneity (vs a tissue NGS done on a single lesion)
Gil Morgan:	Thank you Umberto and thank you BIagio
The OncoAlert Network:	Indeed Thank you Dr. Malapelle
The OncoAlert Network:	Now we have Dr. Wardill and Dr Bossi who will be discussing mucositis
The OncoAlert Network:	This is part of the MASCC presentations in Supportive care
Paolo Bossi:	Present!
The OncoAlert Network:	Greetings Dr. Bossi!
The OncoAlert Network:	Welcome to the colloquium
The OncoAlert Network:	Please feel free to chime in with any highlights on the presentations
The OncoAlert Network:	Dr. Wardill will be giving us the pre clinical
The OncoAlert Network:	and Dr. Bossi will give us the clinical
Gil Morgan:	Welcome Paolo! A pleasure to have you here
Gil Morgan:	"I have a question I have from the wards, as Dr. Wardill just mentioned mucositis covers the entire GI tract, is there different way of treating depending on the location"
Paolo Bossi:	Yes! I would say that prevention and teratment of mucositis depends on the sites (oral different from lower GI) and on the teratment (chemo; RT; targeted agents; immunoTx).
Gil Morgan:	is there anything our younger colleagues can be looking out for before the Chemo and RT of who might be more likely to be affected with greater tox with mucositis
Paolo Bossi:	"Mucositis remains one of the most difficult and debilitating adverse effects from cancer therapy. We know that no imporvement wil be psosible without a strict connection between preclinical and clinical research. That's the reason why microbiome is becoming so appealing: preclinical research explains that microbiome diversity and composition is fundamental to reduce oral mucositis induced by chemoradiation;

	similarly, the first randomized trial showed how SSk12 is effective in preventing this side effects!"
Paolo Bossi:	it is important to evalaute the risk profile of patients before starting the teratment. Pts at higher risk are:
Paolo Bossi:	"- very young and older"
Paolo Bossi:	"- with bad oral hygiene; - with concurent infection (candida in particular); - with use of antibiotics before"
Paolo Bossi:	"- using drug that causes xerostomia (a lot of drugs indeed!)"
Gil Morgan:	"Agree completely, regarding oral hygiene and RT it is almost a team effort between the radiation oncologist and the oral hygienist"
Gil Morgan:	Dr. Bossi How would you think technology and biology will impact on the development of new strategies to rpevent oral mucositis?
Paolo Bossi:	"that's true. Indeed, not all the patients may afford expensive dental care"
Paolo Bossi:	#technology: new teratment with proton therapy could theoretically reduce oral mucositis
Gil Morgan:	"Yes, in that case, we are lucky in Sweden. Every patient has to go to the hygienist before and during and even subsidised cost after with chemo radio"
Paolo Bossi:	#biology: radiotherapeutic treatment that will be modulated on hypoxia (with FMISO PET) could tailor the intensity of the treatment and reduce toxicity of RT
Biagio Ricciuti, MD, PhD:	"Dr. Bossi, we are seeing many patients with G2-3 mucositis from ADCs (e.g. dato-DxD). In some countries last therapy is used routinely with significant improvements. However, this is not standard in many US and EU centers. What are your thoughts about this?"
Biagio Ricciuti, MD, PhD:	*laser therapy
Paolo Bossi:	"we have not yet substantial data about laser therapy in preventing mucosits induced by ADC (Dato-DxD in particular). However, the theoretical benefit exists, as this treatment may reduce the inflamatory environment"
Gil Morgan:	"with all of this discussion on microbiome modulation, are we ready for it?"
Gil Morgan:	are we there yet
Biagio Ricciuti, MD, PhD:	Thank you for your insight!

Paolo Bossi:	"we are close to be ready! We know its importance and we may use probiotics and postbiotics, but the right formulation is not yet approved"
Gil Morgan:	Thank you soo much Paolo
The OncoAlert Network:	Thank you very much Dr. Wardill and Dr. Bossi for that wonderful year in review for mucositis
The OncoAlert Network:	The final of the MASCC sessions on supportive care
The OncoAlert Network:	ADC Tox I Solid Tumors
The OncoAlert Network:	by Dr. Maryam Lustberg of Yale Cancer Center
Gil Morgan:	"Early recognition and intervention are crucial for managing complications, requiring therapy interruption, steroid initiation, and close monitoring."
Gil Morgan:	Both patients and healthcare teams must be aware of potential complications.
Gil Morgan:	"I Think these recommendations, is something that we can all do better in mentioning to patients"
Biagio Ricciuti, MD, PhD:	Agree. There is a lot of interest in wearable devices that can help with early detection of ADC toxicities such as ILD. But we are not ready yet for prime time.
Gil Morgan:	"and that is in countries like the US,"
Gil Morgan:	with so many resources
Gil Morgan:	"echallenge may be considered for fully resolved grade 1 events, but there is no safe protocol for rechallenge in unresolved cases or grade 2 events. Combining treatments, such as with immunotherapy, introduces additional considerations for safety and management."
Gil Morgan:	Rechallenge
Gil Morgan:	"I wonder why one of the risk factors is female sex, do you know Biagio?"
Gil Morgan:	https://www.sciencedirect.com/science/article/pii/S2589537023002900
Gil Morgan:	Toxicity profile of antibody-drug conjugates in breast cancer: practical considerations
Biagio Ricciuti, MD, PhD:	great question.
Biagio Ricciuti, MD, PhD:	"Sex differences in AEs may have several explanations. One possibility is that, due to average differences in body type, women receive a

	relatively higher dose. However, this analysis accounted for body type by adjusting for obesity status. Some evidence suggests that adherence to oral therapies varies by sex, though this may be less relevant in a clinical trial setting. Additionally, reporting or interpretation biases could exist, or men and women might report AEs differently due to sex-related variations i"
Biagio Ricciuti, MD, PhD:	"Additionally, reporting or interpretation biases could exist, or men and women might report AEs differently due to sex-related variations in symptom perception. Notably, in this study, objectively assessed hematologic AEs were also more common in women. Pharmacokinetics and pharmacodynamics may also contribute. The literature on systemic therapies presents mixed findings, but some studies indicate that women have a lower capacity to clear fluorouracil compared to men."
Gil Morgan:	"That makes alot of sense, thank you!"
Biagio Ricciuti, MD, PhD:	We certainly need more studies and ultimately the goes is to predict who is at higher risk to implement monitoring strategies (and develop preventive approaches)
Gil Morgan:	Very True
The OncoAlert Network:	Thank you Dr. Lustberg
Gil Morgan:	Thank you Biagio
Gil Morgan:	Thank you all