TAGRISSO® osimertinib

MARIPOSA Competitive Workshop Prework Worksheet

Overview: This Preread is designed to prepare you for active participation in the MARIPOSA Competitive Workshop. Read the information below, complete all question prompts, then bring your completed worksheet with you to the workshop.

Evolving *EGFR*m mNSCLC Treatment Landscape

TAGRISSO Treatment Landscape

TAGRISSO® (osimertinib) is the current standard of care (SOC) treatment for metastatic non-small cell lung cancer (mNSCLC) with epidermal growth factor receptor (EGFR) mutations in the first-line (1L) or second-line (2L) setting.

1L Therapy → **2L Therapy**

Ex19del and L858R *EGFR*m mNSCLC

FLAURA trial (phase 3): TAGRISSO monotherapy

FDA — Approved April 2018

NCCN Guidelines: Category 1 other recommened therapy

FLAURA2 trial (phase 3):
TAGRISSO in combination with chemotherapy

FDA — Approved Februrary 2024

NCCN Guidelines: Category 1 other recommened therapy

S768I, L861Q, and/or G719X *EGFR*m mNSCLC

TAGRISSO monotherapy

NCCN Guidelines: Category 2A therapy[a]

T790M (resistance mutation) *EGFR*m mNSCLC

AURA3 trial (phase 3) and AURA trial (phase 1/2): TAGRISSO monotherapy

FDA — Approved March 2017

NCCN Guidelines: Category 1 therapy[a]

Ex19del and L858R *EGFR*m mNSCLC

Continued TAGRISSO monotherapy after progression on TAGRISSO

NCCN Guidelines: Category 2A therapy[a]

[a] National Comprehensive Cancer Network® (NCCN®) make no warranties of any kind whatsoever regarding their content, use, or application, and disclaims any responsibility for their application or use in any way. All recommendations are category 2A unless otherwise indicated. This is a simplified treatment algorithm based on NCCN Guidelines, and not all scenarios or therapeutic options are listed.

1L, first-line; **2L,** second-line; ***EGFR*(m),** epidermal growth factor receptor; **ex19del,** exon 19 deletion; **FDA,** Food and Drug Administration; **(m)NSCLC,** (metastatic) non-small cell lung cancer; **NCCN,** National Comprehensive Cancer Network.

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Evolving *EGFR*m mNSCLC Treatment Landscape *(continued)*

RYBREVANT Treatment Landscape

RYBREVANT® (amivantamab-vmjw) is a bispecific antibody targeting extracellular regions of EGFR and MET proto-oncogene (MET) on the surface of cells. The antibody inhibits both molecular pathways independent of their cancer-driving or treatment-acquired mutations. Recall that RYBREVANT is an approved targeted therapy option for *EGFR* exon 20 Insertion mutations, but not for *MET* exon 14 skipping mutations or the evolving *MET* amplification biomarker.

Additionally, the MARIPOSA regimen involves the combination of RYBREVANT and lazertinib for patients with *EGFR* exon 19 deletions or L858R mutations.

1L Therapy → **2L Therapy**

***EGFR* exon 20 insertion mutation mNSCLC**

PAPILLON trial: RYBREVANT in combination with chemotherapy

FDA — Approved March 2024

NCCN Guidelines: Category 1 other recommened therapy[a]

***EGFR* exon 20 insertion mutation mNSCLC**

CHRYSALIS multicohort trial: RYBREVANT monotherapy

FDA — Approved May 2021 (Accelerated Approal)

NCCN Guidelines: Category 2A therapy[a]

Ex19del and L858R *EGFR*m mNSCLC

MARIPOSA trial: RYBREVANT in combination with lazertinib

Approval pending

Ex19del and L858R *EGFR*m mNSCLC

MARIPOSA-2 trial: RYBREVANT in combination with chemotherapy

Approval pending

NCCN Guidelines: Category 1 preferred therapy[a]

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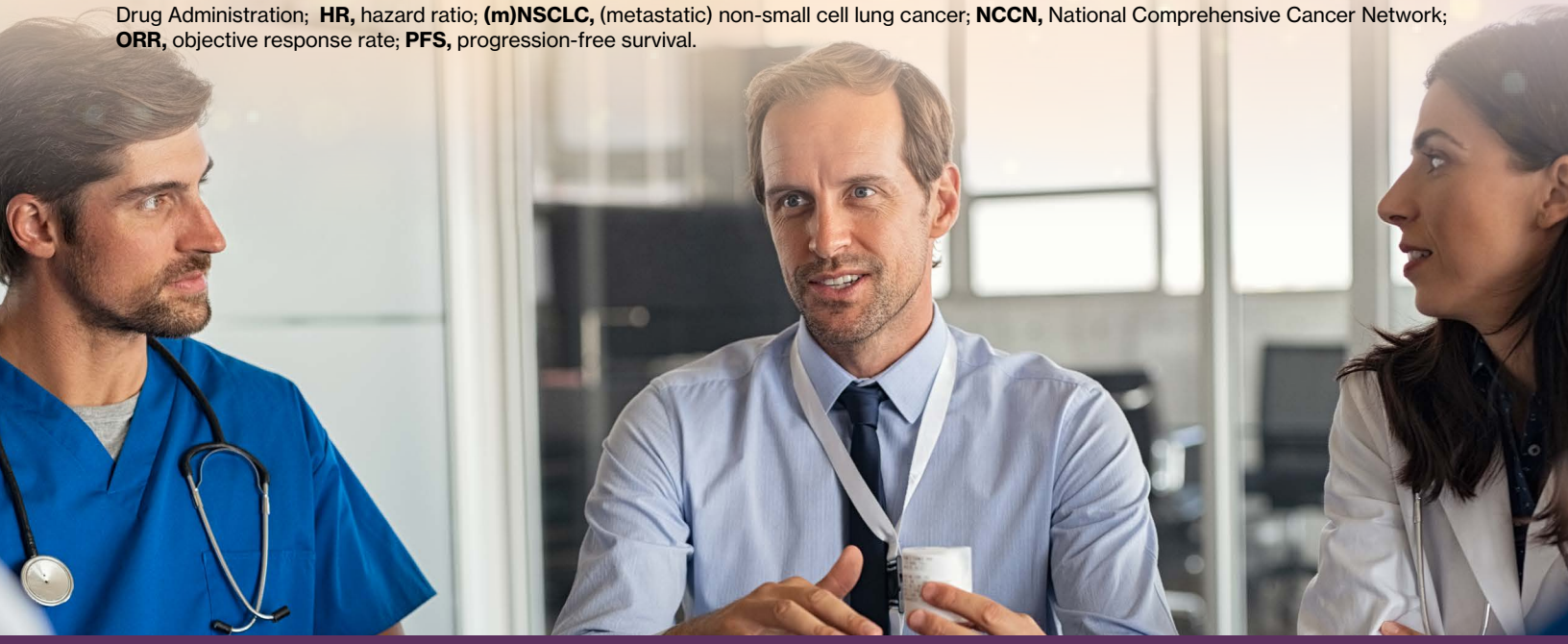
1L, first-line; **2L,** second-line; **CI,** confidence interval; ***EGFR*(m),** epidermal growth factor receptor; **ex19del,** exon 19 deletion; **FDA,** Food and Drug Administration; **HR,** hazard ratio; **(m)NSCLC,** (metastatic) non-small cell lung cancer; **NCCN,** National Comprehensive Cancer Network; **ORR,** objective response rate; **PFS,** progression-free survival.



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MARIPOSA Competitive Workshop Prework Worksheet

MARIPOSA Trial Overview

Study Design[a]

- MARIPOSA is a randomized, multiarm, open-label, phase 3 trial of RYBREVANT plus LECLAZA® (lazertinib) versus TAGRISSO monotherapy for 1L treatment of patients with mNSCLC with EGFR exon 19 deletion or L858R mutations.a
- In the experimental arm, patients received RYBREVANT infusions lasting 2-8 hours weekly for the first 4 weeks followed by every other week, in addition to oral lazertinib once daily.

Study Results (RYBREVANT + Lazertinib Versus TAGRISSO)

- MARIPOSA met the primary endpoint of PFS by BICR (RYBREVANT + lazertinib versus TAGRISSO: HR, 0.70 [95% CI, 0.58-0.85]).
- Relative improvement in PFS was not different between patients with a history of brain metastasis (HR, 0.69; 95% CI, 0.53-0.92) and patients without a history of brain metastasis (HR, 0.69; 95% CI, 0.53-0.89).
- At an interim analysis of OS (median follow-up of 22.0 months; 55% of projected deaths at final OS analysis), early survival data show a trend favoring RYBREVANT plus lazertinib.

Safety

- The most common AEs in the RYBREVANT plus lazertinib arm were paronychia (68%), IRRs (63%), rash (62%), hypoalbuminemia (48%), increased alanine aminotransferase (36%), and peripheral edema (36%).
- AESIs for patients in the RYBREVANT plus lazertinib arm included 37% of patients who experience any VTE event and 15% who experienced grade ≥3 rash.
    - Recent case reports of patients who received RYBREVANT as SOC treatment or as a participant in clinical trials developed significant dermatologic adverse events, including scalp ulcerations. To view images of these case reports, click here and here. (Note that the photos are graphic in nature.)

[a] Lazertinib monotherapy was included to assess the contribution of drug components but was not a part of the main study analysis.

1L, first-line; **AE(SI),** adverse event (of special interest); **BICR,** blinded independent central review; **CI,** confidence interval; ***EGFR*(m),** epidermal growth factor receptor; **ex19del,** exon 19 deletion; **FDA,** Food and Drug Administration; **HR,** hazard ratio; **IRRs,** Infusion-related reactions; **(m)NSCLC,** (metastatic) non-small cell lung cancer; **NCCN,** National Comprehensive Cancer Network; **OS,** overall survival; **PFS,** progression-free survival; **VTE,** venous thromboembolism.

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Customer Scenarios and Strategic Planning

HCP Scenario #1 | Read each of the HCP scenarios below and respond to the question prompts.

"My patients are hesitant to use chemo because of the side effects and MARIPOSA is chemo free, so I'm going to use that as my go-to combination regimen."

Customer Insights

Based on what you know, what do you think is the current mindset of this customer?

What main objective do you want to illustrate to this customer that they may currently be resisting?

CLARIFY

What purposeful questions will you ask to drive traction toward the objective?

What data, insights, and concrete value will you bring to demonstrate the benefit of TAGRISSO? Be sure to relate these concepts back to how you will help overcome resistance to mindset change.

Summarize the small steps you can help the customer make towards understanding the objective. Consider the HCP mindset, their priorities, and how you can help overcome resistance to mindset change.

ADVANCE

Summarize how you will effectively position TAGRISSO to gain commitment and overcome resistance to mindset change. Consider an impactful open, the key data, and a compelling call to action.

HCP, healthcare professional.

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Customer Scenarios and Strategic Planning

HCP Scenario #2 | Read each of the HCP scenarios below and respond to the question prompts.

"How do I know which patients are more appropriate for TAGRISSO plus chemotherapy than TAGRISSO monotherapy?"

Customer Insights

Based on what you know, what do you think is the current mindset of this customer?

What main objective do you want to illustrate to this customer that they may currently be resisting?

CLARIFY

What purposeful questions will you ask to drive traction toward the objective?

What data, insights, and concrete value will you bring to demonstrate the benefit of TAGRISSO? Be sure to relate these concepts back to how you will help overcome resistance to mindset change.

Summarize the small steps you can help the customer make towards understanding the objective. Consider the HCP mindset, their priorities, and how you can help overcome resistance to mindset change.

ADVANCE

Summarize how you will effectively position TAGRISSO to gain commitment and overcome resistance to mindset change. Consider an impactful open, the key data, and a compelling call to action.

HCP, healthcare professional.

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Customer Scenarios and Strategic Planning

HCP Scenario #3 | Read each of the HCP scenarios below and respond to the question prompts.

"I'm going to use the MARIPOSA regimen because it demonstrated better efficacy than TAGRISSO. Why wouldn't I use that first?"

Customer Insights

Based on what you know, what do you think is the current mindset of this customer?

What main objective do you want to illustrate to this customer that they may currently be resisting?

CLARIFY

What purposeful questions will you ask to drive traction toward the objective?

What data, insights, and concrete value will you bring to demonstrate the benefit of TAGRISSO? Be sure to relate these concepts back to how you will help overcome resistance to mindset change.

Summarize the small steps you can help the customer make towards understanding the objective. Consider the HCP mindset, their priorities, and how you can help overcome resistance to mindset change.

ADVANCE

Summarize how you will effectively position TAGRISSO to gain commitment and overcome resistance to mindset change. Consider an impactful open, the key data, and a compelling call to action.

HCP, healthcare professional.

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Customer Scenarios and Strategic Planning

HCP Scenario #4 | Read each of the HCP scenarios below and respond to the question prompts.

"Both FLAURA2 and MARIPOSA require infusions and pills, so the dosing is similar."

Customer Insights

Based on what you know, what do you think is the current mindset of this customer?

What main objective do you want to illustrate to this customer that they may currently be resisting?

CLARIFY

What purposeful questions will you ask to drive traction toward the objective?

What data, insights, and concrete value will you bring to demonstrate the benefit of TAGRISSO? Be sure to relate these concepts back to how you will help overcome resistance to mindset change.

Summarize the small steps you can help the customer make towards understanding the objective. Consider the HCP mindset, their priorities, and how you can help overcome resistance to mindset change.

ADVANCE

Summarize how you will effectively position TAGRISSO to gain commitment and overcome resistance to mindset change. Consider an impactful open, the key data, and a compelling call to action.

HCP, healthcare professional.

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Customer Scenarios and Strategic Planning

HCP Scenario #5 | Read each of the HCP scenarios below and respond to the question prompts.

"I prefer to use a treatment targeting both EGFR and MET, which are two important biomarkers in NSCLC."

Customer Insights

Based on what you know, what do you think is the current mindset of this customer?

What main objective do you want to illustrate to this customer that they may currently be resisting?

CLARIFY

What purposeful questions will you ask to drive traction toward the objective?

What data, insights, and concrete value will you bring to demonstrate the benefit of TAGRISSO? Be sure to relate these concepts back to how you will help overcome resistance to mindset change.

Summarize the small steps you can help the customer make towards understanding the objective. Consider the HCP mindset, their priorities, and how you can help overcome resistance to mindset change.

ADVANCE

Summarize how you will effectively position TAGRISSO to gain commitment and overcome resistance to mindset change. Consider an impactful open, the key data, and a compelling call to action.

HCP, healthcare professional.

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