

# Precision targeting of MET in NSCLC: A multidisciplinary approach



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# Expert MDT panel



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# Discussion 1

Targeting *MET*ex14 skipping mutations:  
Patient identification through molecular analysis

Dr Xiuning Le

*Thoracic medical oncologist*



Dr Christine Argento

*Interventional pulmonologist*



Prof. Albrecht Stenzinger

*Molecular pathologist*



# Clinical case – Elizabeth

## Patient history

- Female
- 81 years old
- Never-smoker



## Diagnosis

- **Chest X-ray/CT/PET scans:**
  - Left pleural effusion
  - Tumour: 4 cm diameter in left lower lobe
  - Liver metastasis: 3 cm nodule
  - Multiple hypermetabolic masses in the left lung and lymph nodes
  - Hypermetabolic activity in the right supraclavicular region
- **MRI:** No brain metastases
- **ECOG-PS at diagnosis:** 2
- **Liquid biopsy:**
  - Stage IV NSCLC (adenocarcinoma)

## Biopsy and biomarkers

- **Liquid biopsy:**
  - No actionable oncogene driver mutations detected

## Treatment options

## Discussion 2

### Managing *MET*ex14 skipping mutations: Clinical insights and strategies

Dr Xiuning Le

*Thoracic medical oncologist*



Dr Sandra Cuellar

*Clinical oncology pharmacist*



Ms Stephanie McDonald

*Oncology nurse practitioner*



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  - Stage IV NSCLC (adenocarcinoma)

## Biopsy and biomarkers

- **Liquid biopsy:**
  - No actionable oncogene driver mutations detected

## EBUS-FNA

## DNA and RNA NGS

- **METex14 skipping mutation**

## Treatment options

### MET-TKIs (oral)

- Crizotinib<sup>1</sup>
  - Capmatinib<sup>1</sup>
  - Tepotinib<sup>1</sup>
  - Savolitinib (China)<sup>2</sup>
- } NCCN

CT, computed tomography; EBUS-FNA, endobronchial ultrasound-guided fine-needle aspiration; ECOG-PS, Eastern Cooperative Oncology Group performance status; MRI, magnetic resonance imaging; NGS, next-generation sequencing; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; PET, positron emission tomography; TKI, tyrosine kinase inhibitor.

1. NCCN. Non-small cell lung cancer. Version 10.2024 (accessed 27 September 2024); 2. Yu Y, et al. *Lancet Respir Med.* 2024:S2213-2600(24)00211-X.

# Discussion 3

Metastatic challenges:  
Exploring *MET* amplification in refractory disease

Dr Xiuning Le

*Thoracic medical oncologist*



Dr Christine Argento

*Interventional pulmonologist*



Prof. Albrecht Stenzinger

*Molecular pathologist*





# Clinical case – Andrew

## Patient history

- Male
- 77 years old
- Former-smoker



## First-line treatment

- Osimertinib monotherapy  
(2 years)



## Disease progression



## Treatment options (NCCN)



## Diagnosis and biomarkers

- **Chest X-ray/CT:**
  - 5 cm opacity in right upper lung
  - Solitary 4.5 cm radiodense mass
- **EBUS-FNA:**
  - Cytology consistent with NSCLC
- **Surgical core biopsy:**
  - Infiltrative tumour
  - IHC indicates adenocarcinoma
- **NGS:**
  - *EGFR*ex19 deletion



## Follow-up

- **Clinical assessment:**
  - Increased cough, dyspnoea, pain and weight loss
- **CT scan:**
  - >20% increase in lesion diameter

# Discussion 4

## Navigating resistance: MET-targeted treatment strategies for refractory NSCLC

Dr Xiuning Le  
*Thoracic medical oncologist*



Dr Sandra Cuellar  
*Clinical oncology pharmacist*



Ms Stephanie McDonald  
*Oncology nurse practitioner*



# Clinical case – Andrew

## Patient history

- Male
- 77 years old
- Former-smoker



## First-line treatment

- **Osimertinib monotherapy**  
(2 years)



## Disease progression

- Platinum-based chemotherapy considered if there are no targetable resistance mutations

## Treatment options (NCCN)

### EGFR/MET bi-specific Ab (IV)<sup>1,2</sup>

- Amivantamab

### Osimertinib + MET-TKI (oral)<sup>1</sup>

- Crizotinib
- Capmatinib
- Tepotinib

## Diagnosis and biomarkers

- **Chest X-ray/CT:**
  - 5 cm opacity in right upper lung
  - Solitary 4.5 cm radiodense mass
- **EBUS-FNA:**
  - Cytology consistent with NSCLC
- **Surgical core biopsy:**
  - Infiltrative tumour
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- **NGS:**
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## Follow-up

- **Clinical assessment:**
  - Increased cough, dyspnoea, pain and weight loss
- **CT scan:**
  - >20% increase in lesion diameter

## EBUS-FNA

- **Histology:**
  - No small cell or squamous transformation
  - Confirmed adenocarcinoma

## DNA and RNA NGS

- ***MET* amplification:**
  - >10 copies

Ab, antibody; CT, computed tomography; EBUS-FNA, endobronchial ultrasound-guided fine-needle aspiration; EGFR, epidermal growth factor receptor; IHC, immunohistochemistry; IV, intravenous; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor.

1. NCCN. Non-small cell lung cancer treatment guidelines. Version 10.2024 (accessed 27 September 2024); 2. US Food and Drug Administration. Amivantamab-vmjw prescribing information. 2024. Available at: [www.accessdata.fda.gov/drugsatfda\\_docs/label/2024/761210s004lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761210s004lbl.pdf) (accessed 27 September 2024).