

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

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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



Clinical case – Elizabeth

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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)

- Crizotinib¹
 - Capmatinib¹
 - Tepotinib¹
 - Savolitinib (China)²
- } 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)^{1,2}

- Amivantamab

Osimertinib + MET-TKI (oral)¹

- Crizotinib
- Capmatinib
- Tepotinib

Diagnosis and biomarkers

- **Chest X-ray/CT:**
 - 5 cm opacity in right upper lung
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- **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

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 (accessed 27 September 2024).