Clinical Value of Testing for c-Met Protein Overexpression in Patients With Non-Small Cell Lung Cancer

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OBJECTIVE

To evaluate the clinical value of testing patients with advanced/metastatic *EGFR* wild-type non-squamous non-small cell lung cancer (NSCLC) with MET immunohistochemistry (IHC) to identify those with c-Met protein overexpression (OE) or high OE, who would then be eligible for telisotuzumab vedotin (Teliso-V), an antibody-drug conjugate

CONCLUSION

The model findings suggest clinical value in implementing testing for c-Met protein OE among all eligible NSCLC patients as demonstrated by improved outcomes among patients when MET IHC testing is conducted

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Disclosures

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INTRODUCTION

- NSCLC accounts for 81% of all lung cancers in the US[1]
- Guidelines recommend that patients with locally advanced or metastatic NSCLC receive targeted therapy or immunotherapy,[2–4] thus comprehensive biomarker testing in these patients is essential for diagnosis and selection of appropriate treatment
- c-Met OE has emerged in recent years as a clinically relevant and potentially actionable protein biomarker in NSCLC[5]
- c-Met protein targeted agents currently being investigated in NSCLC include the antibody drug conjugates, Teliso-V,[6] telisotuzumab adizutecan,[7] RC108 (NCT05821933), TR1801,[8] SHR-A1403,[9] and the bispecific antibody MCLA-129,[10] with Teliso-V at the most advanced stage in development
- These investigational c-Met protein targeted therapies may require tissue-based biomarker assessment by IHC prior to use as therapy
- Thus, it is important to understand the overall prevalence and prognostic value of c-Met OE as a biomarker

METHODS

- A deterministic decision-tree (for treatment and MET IHC testing allocations) converted into a stochastic partition-survival model (for efficacy-related outcomes) was used to evaluate the clinical utility of MET IHC testing
- The model simulated patients into two cohorts: MET IHC tested or not tested
  - Patients with no testing received a market basket of standard of care (SOC) regimens
  - Patients with testing and c-Met protein OE positivity received Teliso-V, while patients with c-Met low/no OE received SOC
  - Two scenarios were analyzed: c-Met OE or c-Met high OE, assessed by IHC with these thresholds:
    - c-Met high OE (≥50% tumor cells staining at 3+ intensity)
    - c-Met OE (≥25% tumor cells staining at 3+ intensity)
    - c-Met low/no OE (<25% tumor cells staining at ≤3 intensity)
- Prevalence of NSCLC and c-Met protein OE as well as clinical outcomes among patients with c-Met protein OE treated with SOC or Teliso-V were based on published literature (**Table 1**)
- Efficacy inputs (ie, overall survival, progression-free survival) were estimated based on exponential survival curves derived from published clinical and real-world data (**Supplemental Figures 1** and **2**)
- The model estimated expected and incremental life years (LYs) and quality-adjusted life years (QALYs)

METHODS *(CONTINUED)*

Table 1. Model features and parameters

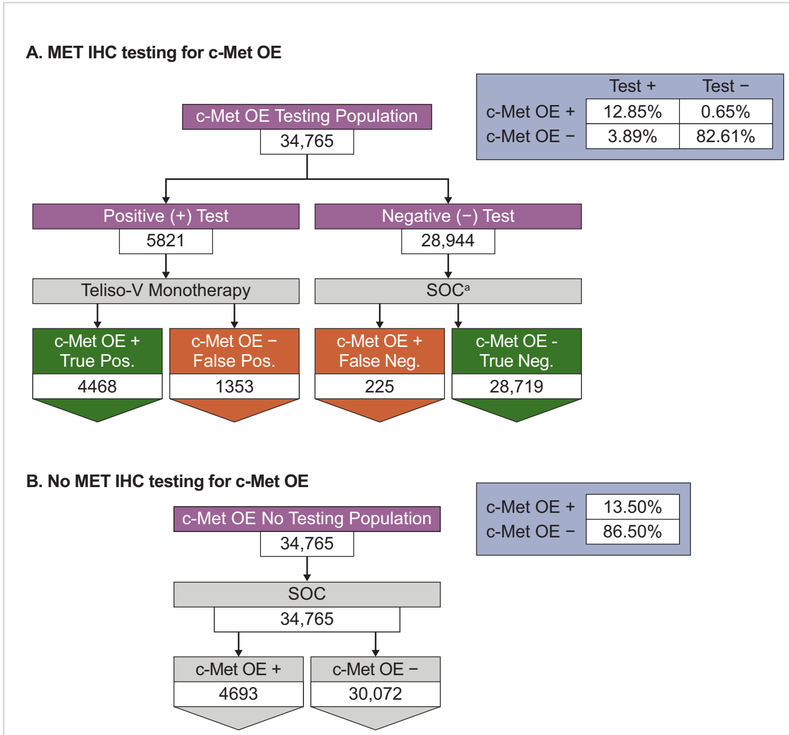
Parameter	Source/input
Prevalence and population	
Prevalence NSCLC among adults	SEER*StatDatabase: Incidence - SEER Research Plus Data, 18 Registries. 2016; BIM
Patients initially diagnosed with locally advanced disease in 1 year	SEER*StatDatabase: Incidence - SEER Research Plus Data, 18 Registries. 2017; BIM
Proportion with advanced/metastatic NSCLC including recurrent disease	Huntzinger 2021 *J Thor Onc* 2021;16(3): S317-S318.
Patients with 2+ lines of therapy	Nadler E, et al. *J Cancer Res Clin Oncol*. 2021; 147(3):671-690.
Percent EGFR wild-type	Dogan S, et al. *Clin Cancer Res*. 2012;18(22):6169-6177.
Population cohort	N = 34,765
Biomarker prevalence: *% c-Met OE, % c-Met high OE*	Camidge DR, et al. *J Clin Oncol*. 2024;42(25):3000-3011.
Efficacy inputs	
Progression-free survival	Camidge DR, et al. *J Clin Oncol*. 2024;42(25):3000-3011. Le 2024 ESMO
Overall survival	Camidge DR, et al. *J Clin Oncol*. 2024;42(25):3000-3011. Le 2024 ESMO
Model analysis year costs	2025 US dollars
Length of analysis	120 months
Comparators	Teliso-V, SOC

BIM, budget impact model; OE, overexpression; SOC, standard of care; teliso-V, telisotuzumab vedotin.

RESULTS

- The deterministic decision-tree for c-Met high OE is illustrated in **Figure 1**, which demonstrates the testing vs no testing strategies and highlights the sensitivity and specificity of the MET IHC test to identify patients with c-Met high OE

Figure 1. Decision tree for c-Met high OE scenario



[a]SOC includes a market basket of immunotherapies (eg, atezolizumab, pembrolizumab, nivolumab), chemotherapies (eg, docetaxel with or without nintedanib), and targeted therapies (eg, ramucirumab + docetaxel).
OE, overexpression; SOC, standard of care.

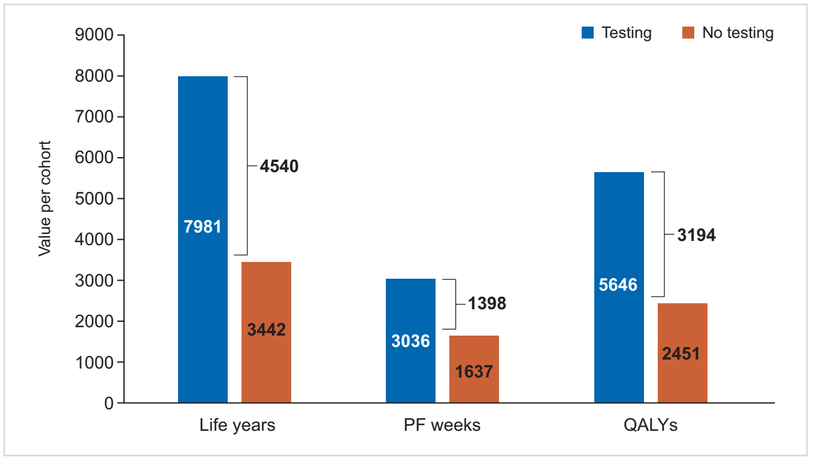
c-Met high OE scenario

- Based on results obtained from the model, the c-Met high OE tested cohort had an incremental improvement of 4540 LYs and 3194 QALYs relative to patients in the not tested cohort, among all eligible patients in the US (**Figure 2**).
- Among patients who would have tested positive for c-Met high OE in both the tested and non-tested cohorts, those in the tested cohort had a 131.9% and 130.3% incremental improvement in LYs and QALYs, respectively

c-Met OE scenario

- Similar trends were observed for patients in the c-Met OE scenario:
  - Among all eligible patients in the US who would have tested positive for c-Met protein OE in the tested cohort, an incremental improvement of 6154 LYs and 4363 QALYs was observed relative to the non-tested cohort
  - Among patients who would have tested positive for c-Met protein OE in both the tested and non-tested cohorts, those in the tested cohort had a 79.0% and 79.9% incremental improvement in LYs and QALYs, respectively

Figure 2. Incremental improvement in life years, progression-free survival, and QALYs in tested (and presumed c-Met high OE positive) vs not tested cohorts



c-Met high OE positive for the testing cohort is the sum of patients on Teliso-V who tested positive and those who tested negative but were actually c-Met high OE positive and received SOC.
PF, progression-free; QALYs, quality-adjusted life years.