Second-line pharmacological interventions for advanced non-small cell lung cancer in *MET*ex14 skipping patients: A systematic literature review

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CONCLUSION

- **Evidence on effectiveness of second-line immunotherapy and chemotherapy treatment for patients with previously treated advanced NSCLC with *MET*ex14 skipping is scarce and based on RWD studies with a reduced number of patients. Immunotherapy has limited benefits in this population**
- **For MET-targeted therapies, only Phase I and II clinical trials are available for decision-making and evidence from RWD studies is scarce. No comparative studies assessing MET-inhibitors were identified**
- **In clinical trials, reported second-line OS was numerically higher in the VISION trial (tepotinib) than in the AcSé trial (crizotinib) and comparable to the finding in the PROFILE 1001 trial (crizotinib). However, the available data from the PROFILE 1001 trial included patients in 1L treatment (38%), whereas the first two trials reported outcomes separately for patients in 2L+ treatments. PFS and ORR were numerically higher with tepotinib than with other MET inhibitors**

INTRODUCTION

- *MET*ex14 skipping are primary oncogenic drivers that occur in 3–4% of patients with NSCLC[1,2]
- *MET*ex14 skipping lead to cell invasion, proliferation, and angiogenesis[2]
- Current EMA-approved treatments for adult patients with advanced NSCLC harboring alterations leading to *MET*ex14 skipping who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy include tepotinib and capmatinib[3,4]

OBJECTIVES

- This systematic literature review aims to identify studies assessing pharmacological interventions in adult patients with advanced NSCLC with *MET*ex14 skipping who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy

METHODS

- Longitudinal studies evaluating MET inhibitors, chemotherapy and/or immunotherapy for adult patients with previously treated advanced NSCLC with *MET*ex14 skipping were searched in PubMed, Embase, and CENTRAL databases (May 2024)
- Studies including ≥20 participants per study arm, in which >50% of patients had a diagnosis of locally advanced or metastatic (i.e. stage III–IV) NSCLC, and in which >50% of patients had received 2L+ treatments were eligible for inclusion. Conference abstracts, studies including only Asian populations, studies considering non-pharmacological treatments as comparators and non-English language studies were excluded
- The outcomes analyzed were overall survival (OS), progression-free survival (PFS), and objective response rate (ORR)

RESULTS

Table 1. Studies assessing 2L+ treatments in patients with advanced NSCLC with *MET*ex14 skipping

	N	Treatment line	ORR	PFS	OS
Tepotinib					
VISION (Phase II single-arm CT)[5]	149	2L+	✓	✓	✓
Capmatinib					
GEOMETRY mono-1 (Phase II single-arm CT)[6]	69	2L+	✓	✓	-
Illini et al. (2022) (RWD study)[7]	44	2L+	✓	✓	✓
Crizotinib					
AcSé (Phase II single-arm CT)[8]	25	2L+	✓	✓	✓
PROFILE 1001 (Phase I single-arm CT)[9]	69	1L, 2L+ (62% 2L+)	✓	✓	✓
Offin et al. (2020) (RWD study)[10]	54	1L, 2L+ (NR)	✓	-	✓
Immunotherapy (RWD studies)					
Kolaei et al. (2022)[11]	23	2L	-	✓	✓
Kron et al. (2021)[12]	22	1L, 2L+ (86% 2L+)	-	-	✓
Guisier et al. (2020)[13]	30	1L, 2L+ (87% 2L+)	✓	✓	✓
Sabari et al. (2018)[14]	24	1L, 2L+ (54% 2L+)	✓	✓	✓

Figure 1. PFS results in studies assessing 2L+ treatments in patients with advanced NSCLC with *MET*ex14 skipping

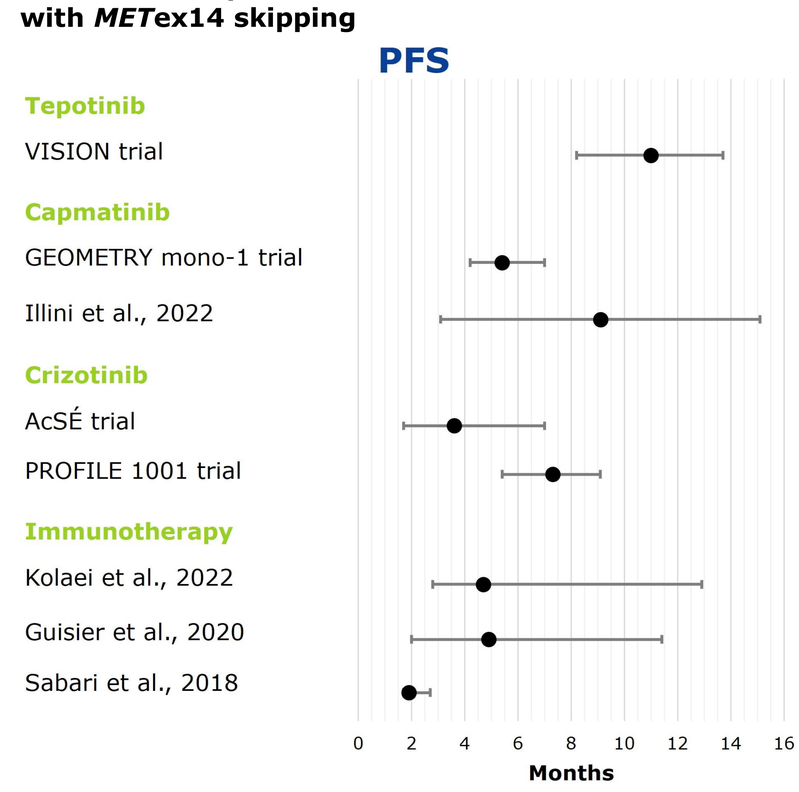
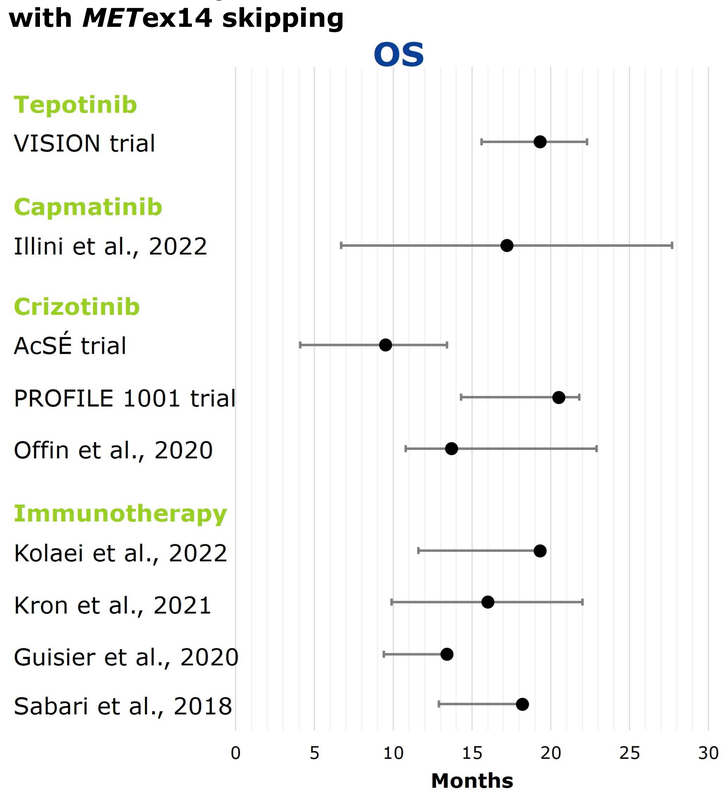


Figure 2. OS results in studies assessing 2L+ treatments in patients with advanced NSCLC with *MET*ex14 skipping



ORR

In clinical trials

ORR was 45% with tepotinib,[5] 40.6% with capmatinib,[6] and 12–32% with crizotinib[8,9]

In RWD studies

ORR was 50% with capmatinib,[7] 31% with crizotinib,[10] and 17–35.7% with immunotherapy[13,14]

PFS

In clinical trials

Median PFS (months) was 11.0 with tepotinib,[5] 5.4 with capmatinib,[6] and 3.6–7.3 with crizotinib[8,9]

In RWD studies

Median PFS (months) was 9.1 with capmatinib[7] and 1.9–4.9 with immunotherapy[11,13,14]

OS

In clinical trials

Median OS (months) was 19.3 with tepotinib[5] and 9.5–20.5 with crizotinib[8,9]

In RWD studies

Median OS (months) was 17.2 with capmatinib,[7] 13.7 with crizotinib,[10] and 13.4–19.3 with immunotherapy[11–14]

Abbreviations: 1L, first line; 2L+, second-or-later line; CT, clinical trial; EMA, European Medicines Agency; MET, mesenchymal–epithelial transition factor; *METex*14, *MET* exon 14; NR, not reported; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RWD, real-world data.

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