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Matching-adjusted indirect comparison for treatment of NTRK fusion cancer with larotrectinib versus entrectinib

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Background

Information regarding the comparative efficacy and safety of first-generation treatments for Neurotrophic Tropomyosin Receptor Kinase (NTRK) fusion cancer is limited. Although cross-trial comparisons are subject to potential biases, a matching-adjusted indirect comparison (MAIC) can balance observed population characteristics to facilitate comparisons between trials. This study compared larotrectinib and entrectinib using MAIC.

Methods

Adult (≥ 18 years) patient data from larotrectinib trials (LOXO-TRK-14001, SCOUT, and NAVIGATE; data cutoff July 2020) and published aggregate data for entrectinib trials (ALKA-372-001, STARTRK-1, and STARTRK-2; data cutoff October 2018) were used. Patients were matched on available common baseline characteristics (gender, age, race, ECOG score, select tumor types, metastatic disease, NTRK gene, central nervous system metastases, number of prior lines of therapy). Outcomes of interest included overall survival (OS), progression-free survival (PFS), overall response rate (ORR), complete response (CR) rate, duration of response (DoR), any serious treatment-related adverse events (TRAEs), and TRAEs leading to treatment discontinuation. Risk differences (RD) and hazard ratios (HRs) were used to compare treatments.

Results

117 patients from larotrectinib's efficacy population and 147 from its safety population, and 74 from the entrectinib trials were included. Median follow-up was 16.9 months for larotrectinib and 14.2 months for entrectinib. After matching, larotrectinib was associated with longer OS ($p<0.05$) and numerically longer PFS ($p=0.07$, Table). The ORRs were similar ($p=0.61$). The CR rate was higher ($p<0.05$) and DoR was longer for larotrectinib ($p<0.05$). Safety outcomes were comparable and low for both agents.

Conclusions

These findings suggest favorable efficacy of larotrectinib (OS, DoR, and CR) in NTRK fusion cancer compared to entrectinib.Table: 104P

Analysisresults

	Entrectinib Larotrectinib		
	Before matching	After matching	*p-value after matching*
Efficacy Effective sample size (ESS=71.8)			
OS median (95% CI), months	23.9 (16.0, -)	Not reached (NR) (40.7, -)	NR (38.7, -)	<0.05
PFS median (95% CI), months	11.2 (8.0, 15.7)	33.0 (16.6, -)	19.3 (11.1, 55.7)	0.07
DoR median (95% CI), months	12.9 (9.3, -)	41.5 (32.5, -)	32.5 (17.4, -)	<0.05
ORR (95% CI), %	63.5 (51.5, 74.4)	65.0 (56.1, 73.2)	67.6 (55.8, 77.5)	0.61
CR (95% CI), %	6.8 (2.2, 15.1)	19.7 (13.2, 27.5)	20.6 (13.0, 31.1)	<0.05
Safety (ESS=90.7)				
Serious TRAE, %	10.0 (4.2, 20.1)	5.4 (2.5, 9.9)	6.2 (2.9, 12.6)	0.38
TRAEs leading to discontinuation, %	4.0 (0.9, 12.4)	0.7 (0.0, 3.0)	0.5 (0.1, 3.4)	0.15

-: not evaluable

-: not evaluable.

Legal entity responsible for the study

Bayer, Pharmaceuticals Division.

Funding

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Disclosure

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