

Efficacy and safety of selpercatinib in advanced RET-altered thyroid cancers: A meta-analysis and systematic review.

- Muhibullah, Nouman Shafique, Navneet Kaur, Jawad Ahmed, Sarmad Zain, Syed Mujtaba Ali Naqvi, Shammass Bajwa, Hassan Nawaz, Atta Ur Rehman, Ali Haider, Ali Ghaffar, Zainab Javeed, Abdul Ghani Iqbal, Amna Ehsan, Prajwal Khanal, Adeena Shafique, Iqra Shafiq, Besham Kumar, Rida Hussain, Umer Rizwan, Nishtar Medical College and Hospital, Multan, Pakistan; University of Louisville, Louisville, KY; North Alabama Medical Center, Florence, AL; Dow University of Health Sciences, Karachi, Pakistan; Mayo Clinic, Rochester, MN; University of Arkansas for Medical Sciences, Little Rock, AR; AdventHealth Orlando, Orlando, FL; Nishtar Medical University, Multan, Pakistan; Nishtar Medical University Multan, Multan, Pakistan; UNC Nash General Hospital, Rocky Mount, NC; Nishtar Hospital, Multan, Pakistan; Aga Khan University, Karachi, Pakistan; CMH Institute of Medical Sciences, Bahawalpur, Pakistan; West Virginia University Camden Clark Medical Center, Vienna, WV; West Virginia University Camden Clark Medical Center, Parkersburg, WV; Camden Clark Medical Center, Parkersburg, WV

Background: Selpercatinib is a highly selective RET inhibitor that is used for the treatment of RET-mutant medullary thyroid cancers, but its efficacy and safety is not fully understood. Our objective is to summarize available literature on the safety and efficacy profile of Selpercatinib.

Methods: A search was conducted on PubMed, Embase and Cochrane from foundation to 31st January 2024. Patients aged above 18 with Advanced RET-Altered Medullary Thyroid Cancers who received Selpercatinib were identified. Data abstraction was done based on objective response rate, complete response rate, any grade adverse effect (AE) and grade ≥ 3 AE. Analysis was done using R (v.4.3) and reported as proportions with respective 95% confidence intervals (CI) on forest plots. **Results:** Four studies were identified that reported the use of Selpercatinib in Advanced RET-Altered Medullary Thyroid Cancers. Our analysis showed that the pooled proportion of objective response rate and complete response rate was 74.8% (95% CI: 70.1% – 79%) and 4.9% (95% CI: 3.1% – 7.7%) respectively. Pooled proportion of patients experiencing any grade AE and grade ≥ 3 AE was 93.4% (95% CI: 90.4% – 95.6%) and 46.2% (95% CI: 41.1% – 51.3%) respectively. **Conclusions:** Selpercatinib is a novel RET inhibitor which has potential use against RET-Altered Thyroid Cancers. It has an overall acceptable safety and efficacy profile. However it requires further studies to establish its adverse effects and clinical application. Research Sponsor: None.

Objective response rate.

Study	OR	Estimate (95% C.I.)
Illini, 2021	0.680	[0.533, 0.805]
Rotow, 2023	0.500	[0.211, 0.789]
Zhou, 2023	0.836	[0.770, 0.890]
Drilon, 2020	0.694	[0.612, 0.768]
Overall ($I^2 = 77\%$, $p < 0.01$)	0.748	[0.701, 0.790]
Complete Response Rate		
Study	OR	Estimate (95% C.I.)
Illini, 2021	0.080	[0.022, 0.192]
Rotow, 2023	0.000	[0.000, 0.265]
Zhou, 2023	0.075	[0.040, 0.128]
Drilon, 2020	0.014	[0.002, 0.049]
Overall ($I^2 = 45\%$, $P = 0.14$)	0.049	[0.031, 0.077]
Any Adverse Event		
Study	OR	Estimate (95% C.I.)
Illini, 2021	0.860	[0.733, 0.942]
Rotow, 2023	0.714	[0.419, 0.916]
Zhou, 2023	1.000	[0.977, 1.000]
Drilon, 2020	0.910	[0.851, 0.951]
Overall ($I^2 = 36\%$, $P = 0.20$)	0.934	[0.904, 0.956]
Grade ≥ 3 adverse effects		
Study	OR	Estimate (95% C.I.)
Illini, 2021	0.240	[0.131, 0.382]
Rotow, 2023	0.357	[0.128, 0.659]
Zhou, 2023	0.703	[0.625, 0.773]
Drilon, 2020	0.285	[0.213, 0.366]
Overall ($I^2 = 95\%$, $P < 0.01$)	0.462	[0.411, 0.513]