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Myelosuppression Risk From Epidermal Growth Factor Receptor-Tyrosine Kinase Inhibitors, Carboplatin Chemotherapy, or Both in *EGFR*-Mutated Non-small Cell Lung Cancer (NSCLC)

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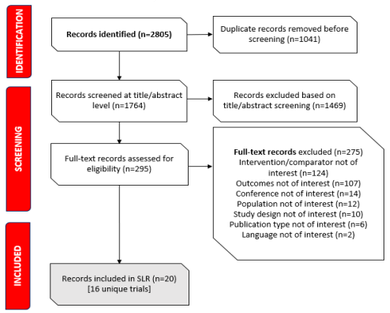
INTRODUCTION

- Approximately 30% of global NSCLC cases are found to have an epidermal growth factor receptor (*EGFR*) mutation[1]
- Tyrosine kinase inhibitors (TKIs) are the standard of care for *EGFR*-mutated NSCLC; however, resistance to TKIs is common and treatment is often supplemented with chemotherapy[2,3]
- The addition of carboplatin-doublet chemotherapy (CBCT) to EGFR-TKIs has been evaluated in *EGFR*-mutated NSCLC; however, both classes of agents are associated with myelosuppression including neutropenia, anemia, and/or thrombocytopenia[3]
- A systematic literature review was conducted to summarize rates of myelosuppressive events following treatment with EGFR-TKIs alone or in combination with CBCT

METHODS

- Systematic searches were conducted on June 19, 2023, in Embase (Elsevier), MEDLINE (National Library of Medicine), CENTRAL and the Cochrane Database of Systematic Reviews via Ovid® (Wolters Kluwer) to identify publications of interest
  - Additional hand searches of conference proceedings from five key meetings were also conducted
- Eligible studies were clinical trials published between 2010 and 2023 that evaluated safety outcomes following administration of the treatments of interest in patients with advanced/metastatic NSCLC with a confirmed *EGFR* mutation
- Key safety outcomes included any grade and grade 3+ neutropenia, anemia, and thrombocytopenia

FIGURE 1: PRISMA study attrition

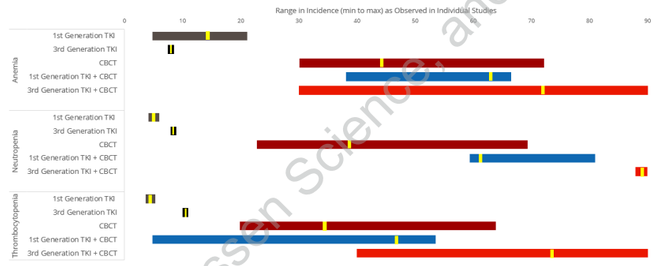


SLR, systematic literature review

RESULTS

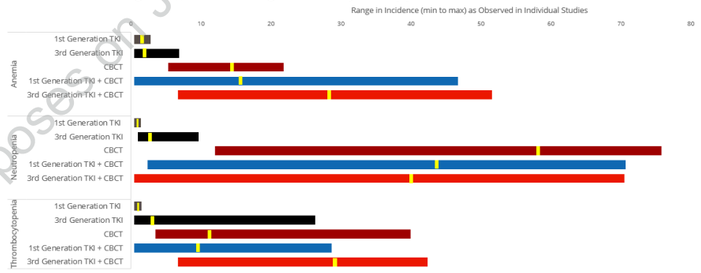
- A total of 1764 unique publications were screened, of which 20 were included representing 16 unique clinical trials (14 of which were randomized controlled trials) in the review (**Figure 1**)
- Twelve trials evaluated first-line treatments, and 4 evaluated second-line or later treatments
  - All of the included trials assessed first- and third-generation TKIs; none assessed second-generation TKIs
- The number of events and participants evaluated across the included trials were used to calculate the weighted average incidence of anemia, neutropenia, and thrombocytopenia
  - This was calculated as total events across all trials divided by the total number of participants across all trials
- The average incidence of any-grade myelosuppressive events for first-generation TKIs plus CBCT versus CBCT alone was estimated to be 63.4% versus 44.7% for anemia, 61.8% versus 38.9% for neutropenia, and 48.2% versus 35.1% for thrombocytopenia
- The average incidence for any-grade myelosuppressive events for third-generation TKIs plus CBCT was 71.7% for anemia, 88.7% for neutropenia, and 73.6% for thrombocytopenia (**Table 1**)
- The average incidence of grade 3+ events followed a similar trend with increased rates of anemia and thrombocytopenia for those treated with third-generation TKIs plus CBCT versus CBCT or third-generation TKIs alone (**Table 1**)

FIGURE 2: Range in incidence of any grade myelosuppression events (%)



CBCT, carboplatin-based chemotherapy; TKI, tyrosine kinase inhibitor. Yellow bars indicate average incidence across included studies.

FIGURE 3: Range in incidence of grade 3+ myelosuppression events (%)



CBCT, carboplatin-based chemotherapy; TKI, tyrosine kinase inhibitor. Yellow bars indicate average incidence across included studies.

TABLE 1: Average incidence of any grade and grade 3+ myelosuppression events

			Anemia	Neutropenia	Thrombocytopenia
Treatment category	**Grade**	**No. of studies**	**Mean (%)**	**Mean (%)**	**Mean (%)**
First-generation TKI	Any	2	15.7	4.7	4.7
	3+	5	1.1	0.3	0.0
Third-generation TKI	Any	1	7.5	7.9	10
	3+	3	1.2	2.9	2.6
CBCT	Any	2	44.7	38.9	35.1
	3+	5	15.3	57.2	12.2
First-generation TKI + CBCT	Any	2	63.4	61.8	48.2
	3+	7	16.1	42.0	9.1
Third-generation TKI + CBCT	Any	2	71.7	88.7	73.6
	3+	5	28.5	39.2	29.2

CBCT, carboplatin-based chemotherapy; TKI, tyrosine kinase inhibitor.

- The incidence of any-grade (**Figure 2**) and grade 3+ (**Figure 3**) myelosuppression events ranged widely across trials
  - Most studies did not evaluate cytopenic events during the first 14 days of treatment when the rate of cytopenia is highest
- When EGFR-TKIs were added to CBCT, the rates of myelosuppression increased compared with that of TKI alone
- Treatment with first-generation TKIs plus CBCT resulted in similar average rates of grade 3+ myelosuppression when compared to CBCT alone. Average rates of any grade events were higher
- The risk of cytopenic events was highest for third-generation TKIs in combination with CBCT, especially for neutropenia and thrombocytopenia

REFERENCES:

1. Werutsky G, et al. *J Thorac Oncol.* 2016;11(10):S184–S185. 2. Cho BC, et al. *J Thorac Oncol.* 2019;14(1);99–106. 3. Koulouris A, et al. *Cancers (Basel).* 2022;14(14);3337.

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KEY TAKEAWAY

Treatment with EGFR-TKIs in combination with CBCT results in higher rates of cytopenic events than seen with CBCT or TKI monotherapy. The rate of events was observed to be highest for third-generation TKIs plus CBCT

CONCLUSIONS

Third-generation EGFR-TKIs in combination with CBCT resulted in higher rates of myelosuppression than those seen with chemotherapy alone

The above safety signal was not as pronounced for first-generation EGFR-TKIs in combination with CBCT

These trends were consistent for any-grade anemia, neutropenia, and thrombocytopenia, as well as grade 3+ anemia and thrombocytopenia

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DISCLOSURES

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