IMPACT OF TRILACICLIB ON MULTILINEAGE CHEMOTHERAPY-INDUCED MYELOSUPPRESSION EVENTS IN PATIENTS WITH EXTENSIVE-STAGE SMALL CELL LUNG CANCER: POST-HOC ANALYSES OF DATA FROM RANDOMIZED CLINICAL TRIALS

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BACKGROUND

- Myelosuppression, which commonly manifests as neutropenia, anemia, and/or thrombocytopenia, is a major dose-limiting complication of chemotherapy for patients with extensive-stage small cell lung cancer (ES-SCLC)[1-4]
- Chemotherapy-induced myelosuppression (CIM) places a substantial burden on patients and the health care system, owing to an increased risk of morbidity and mortality and of poor health-related quality of life[3-6]
- Trilaciclib is an intravenous short-acting cyclin-dependent kinase 4/6 inhibitor administered prior to chemotherapy for multilineage myeloprotection
  - Approved in Feb 2021 by the US Food and Drug Administration to decrease the incidence of CIM in adult patients when administered prior to a platinum/etoposide- or topotecan-containing chemotherapy regimens for ES-SCLC[7]
  - Added as a prophylactic option in two National Comprehensive Cancer Network guidelines to manage chemotherapy-induced myelosuppression in patients with ES-SCLC[8,9]

PURPOSE

- Trilaciclib demonstrated efficacy in reducing occurrence of CIM events separately for neutrophil, red blood cell, and platelet lineages among ES-SCLC patients in its phase 2 trials[10-12]
- This post-hoc trial analysis further evaluated the impact of trilaciclib on the occurrence of single and concurrent multilineage CIM events among ES-SCLC patients

METHODS

- Data from phase 2 clinical trials of trilaciclib in the first-line (1L) chemotherapy setting (G1T28-02 and G1T28-05) and second/third-line (2/3L) chemotherapy setting were used in this analysis (**Table 1**)
  - Analyses were conducted separately by line of chemotherapy
- Severe (Grade ≥ 3 per National Cancer Institute Common Terminology Criteria for Adverse Events definition) CIM events of neutropenia (SN), anemia (SA), and thrombocytopenia (ST) were assessed
- The proportion of patients with severe single and concurrent multilineage CIM events and incidence rate were estimated per cycle and during the first four cycles of chemotherapies
  - Concurrent CIM events were defined as having 2 or 3 lineage-specific CIM events overlap for ≥ 1 day
  - The start date of a CIM event was used to determine whether the event occurred in a given treatment cycle. For concurrent CIM events, the earliest start date of the concurrent events was used to determine the corresponding cycle

Table 1. Clinical Trials of Trilaciclib

Study	Population	Treatment schedule
G1T28-02 (NCT02499770)[10] Proof of concept	Newly diagnosed (1L) ES-SCLC (n=75)	• Trilaciclib 240 mg/m^2 or placebo IV prior to chemotherapy on days 1-3 of each 21-day cycle • **Chemo backbone:** E/P therapy, including standard-of-care etoposide (100 mg/m^2) IV on days 1-3 and carboplatin AUC 5 on day 1 of each 21-day cycle
G1T28-05 (NCT03041311)[11] Pivotal trial	Newly diagnosed (1L) ES-SCLC (n=105)	• Trilaciclib 240 mg/m^2 or placebo IV prior to chemotherapy on days 1-3 of each 21-day cycle for up to four cycles, followed by atezolizumab monotherapy (without trilaciclib or placebo) • **Chemo backbone:** E/P/A therapy, including standard-of-care etoposide (100 mg/m^2) on days 1-3, carboplatin AUC 5 on day 1, and atezolizumab (1200 mg) IV on day 1 of each 21-day cycle
G1T28-03 (NCT02514447)[12]	Previously treated (2/3L) ES-SCLC (n=60)	• Trilaciclib 240 mg/m^2 or placebo IV prior to chemotherapy on days 1-5 of each 21-day cycle • **Chemo backbone:** topotecan 1.5 mg/m^2 IV on days 1-5 of each 21-day cycle

Abbreviations: A, atezolizumab; AUC, area under the plasma concentration-time curve; E, etoposide; ES-SCLC, extensive-stage small cell lung cancer; IV, intravenous infusion; NCT, National Clinical Trial; P, carboplatin.

RESULTS

1L settings

- During cycles 1-4 of 1L chemotherapies, fewer patients receiving trilaciclib experienced single-lineage and multilineage CIM events compared with patients receiving placebo (**Figure 1**)
- In addition, compared to patients receiving placebo, patients treated with trilaciclib had lower incidence rates of CIM events across single and multiple lineages (**Table 2**)
- The 1L results were broadly consistent across individual and 1L pooled data from G1T28-05 and G1T28-02
- For placebo arm, SN generally occurred more frequently in earlier cycles for placebo (pooled data, cycles 1, 2, 3, 4 = 41.1%, 27.9%, 22.9%, 16.3%) whereas SA (1.1%, 5.8%, 8.4%, 10.0%) and ST (0.0%, 4.7%, 6.0%, 7.5%) tended to occur later (**Table 3**)
- For trilaciclib, the proportions of patients with CIM were consistently below 8% without prominent patterns over cycles (**Table 3**)

2/3L settings

- A similar trend was found between the 1L and 2/3L settings, with lower proportions of trilaciclib patients having experienced single and multilineage CIM events during cycles 1-4 of the 2/3L chemotherapies compared to placebo (**Figure 1**, **Table 3**)
- Incidence rates of single and multilineage CIM events also followed a similar pattern (**Table 2**)

Trilaciclib helps protect against **CIM** in multiple cell lineages when given to **ES-SCLC patients** prior to chemotherapy

Figure 1. Proportion of Patients with Single or Multilineage Severe (Grade ≥3) CIM during Cycles 1-4

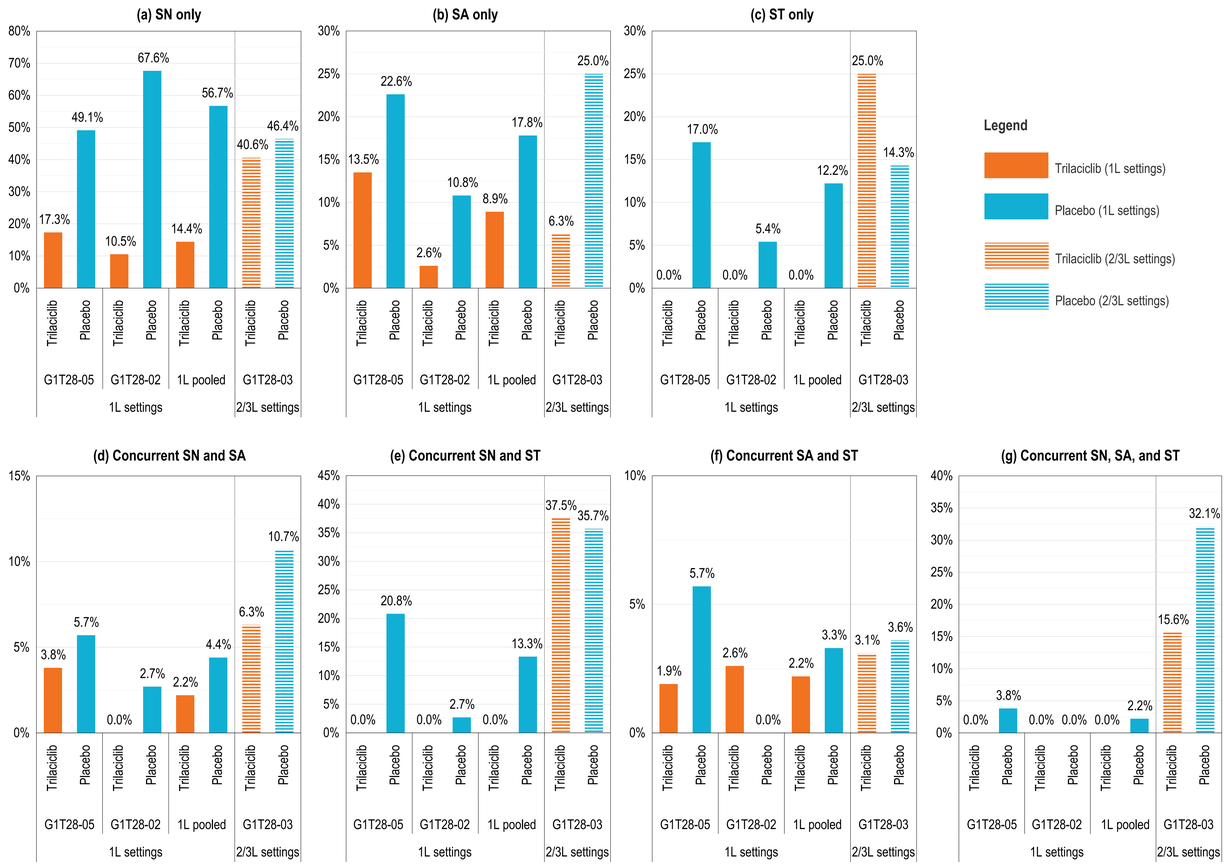

Table 2. Incidence Rate of Single and Multilineage Severe (Grade ≥3) CIM during Cycles 1-4

Incidence rate of CIM events per cycle	1L						2/3L	
	G1T28-05		G1T28-02		Pooled (G1T28-05 and G1T28-02)		G1T28-03	
	Trilaciclib (n=52)	Placebo (n=53)	Trilaciclib (n=38)	Placebo (n=37)	Trilaciclib (n=90)	Placebo (n=90)	Trilaciclib (n=32)	Placebo (n=28)
SN only	0.046	0.178	0.048	0.259	0.047	0.212	0.158	0.207
SA only	0.041	0.067	0.007	0.031	0.028	0.052	0.018	0.078
ST only	0.000	0.051	0.000	0.019	0.000	0.038	0.070	0.059
Concurrent SN and SA	0.009	0.013	0.000	0.006	0.006	0.010	0.018	0.030
Concurrent SN and ST	0.000	0.055	0.000	0.006	0.000	0.035	0.119	0.105
Concurrent SA and ST	0.009	0.017	0.007	0.000	0.008	0.010	0.018	0.010
Concurrent SN, SA, and ST	0.000	0.013	0.000	0.000	0.000	0.008	0.044	0.114

Abbreviations: SN, severe neutropenia; SA, severe anemia; ST, severe thrombocytopenia

Table 3. Proportion of Patients with Single or Multilineage Severe (Grade ≥3) CIM per Cycle

	Cycle	1L						2/3L	
		G1T28-05		G1T28-02		Pooled (G1T28-05 and G1T28-02)		G1T28-03	
		Trilaciclib (n=52)	Placebo (n=53)	Trilaciclib (n=38)	Placebo (n=37)	Trilaciclib (n=90)	Placebo (n=90)	Trilaciclib (n=32)	Placebo (n=28)
SN only	Cycle 1	3.8%	34.0%	7.9%	51.4%	5.6%	41.1%	34.4%	28.6%
	Cycle 2	3.8%	22.0%	3.0%	36.1%	3.5%	27.9%	15.4%	36.4%
	Cycle 3	6.4%	18.4%	3.0%	29.4%	5.0%	22.9%	11.8%	25.0%
	Cycle 4	6.8%	14.6%	6.9%	18.8%	6.8%	16.3%	14.3%	25.0%
SA only	Cycle 1	1.9%	1.9%	0.0%	0.0%	1.1%	1.1%	0.0%	10.7%
	Cycle 2	1.9%	6.0%	0.0%	5.6%	1.2%	5.8%	3.8%	4.5%
	Cycle 3	6.4%	10.2%	0.0%	5.9%	3.8%	8.4%	5.9%	12.5%
	Cycle 4	6.8%	14.6%	3.4%	3.1%	5.5%	10.0%	0.0%	8.3%
ST only	Cycle 1	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	9.4%	3.6%
	Cycle 2	0.0%	6.0%	0.0%	2.8%	0.0%	4.7%	15.4%	9.1%
	Cycle 3	0.0%	8.2%	0.0%	2.9%	0.0%	6.0%	0.0%	18.8%
	Cycle 4	0.0%	10.4%	0.0%	3.1%	0.0%	7.5%	7.1%	0.0%
Concurrent SN and SA	Cycle 1	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.6%
	Cycle 2	1.9%	2.0%	0.0%	0.0%	1.2%	1.2%	3.8%	4.5%
	Cycle 3	2.1%	4.1%	0.0%	0.0%	1.3%	2.4%	0.0%	6.3%
	Cycle 4	0.0%	0.0%	0.0%	3.1%	0.0%	1.3%	7.1%	0.0%
Concurrent SN and ST	Cycle 1	0.0%	15.1%	0.0%	0.0%	0.0%	8.9%	28.1%	28.6%
	Cycle 2	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	11.5%	4.5%
	Cycle 3	0.0%	6.1%	0.0%	0.0%	0.0%	3.6%	11.8%	6.3%
	Cycle 4	0.0%	4.2%	0.0%	3.1%	0.0%	3.8%	0.0%	8.3%
Concurrent SA and ST	Cycle 1	0.0%	0.0%	2.6%	0.0%	1.1%	0.0%	0.0%	0.0%
	Cycle 2	1.9%	2.0%	0.0%	0.0%	1.2%	1.2%	3.8%	4.5%
	Cycle 3	0.0%	4.1%	0.0%	0.0%	0.0%	2.4%	0.0%	0.0%
	Cycle 4	2.3%	2.1%	0.0%	0.0%	1.4%	1.3%	7.1%	0.0%
Concurrent SN, SA, and ST	Cycle 1	0.0%	1.9%	0.0%	0.0%	0.0%	1.1%	6.3%	21.4%
	Cycle 2	0.0%	2.0%	0.0%	0.0%	0.0%	1.2%	0.0%	9.1%
	Cycle 3	0.0%	2.0%	0.0%	0.0%	0.0%	1.2%	17.6%	6.3%
	Cycle 4	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	25.0%

Abbreviations: SN, severe neutropenia; SA, severe anemia; ST, severe thrombocytopenia

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