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POSITIVE EFFECTS OF TRILACICLIB ON PATIENT MYELOSUPPRESSION-RELATED SYMPTOMS AND FUNCTIONING: RESULTS FROM THREE PHASE 2 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED SMALL CELL LUNG CANCER TRIALS

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Conflict of Interest Disclosure

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- Salary: G1Therapeutics
- Receipt of Intellectual Property Rights/Patent Holder: GlaxoSmithKline
- Ownership Interest (stocks, stock options or other ownership interest excluding diversified mutual funds): G1 Therapeutics, GlaxoSmithKline

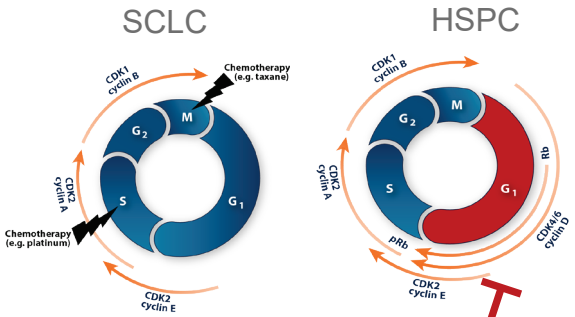
Myelosuppression: despite the availability of interventions like G-CSF, ESAs and transfusions, there is still significant unmet medical need for patients

	1st Line SCLC Incidence of Grade 3/4[1]	2nd Line SCLC Incidence of Grade 3/4[2]	Current Interventions	Current Unmet Needs
Neutropenia 	23%	54% (3% FN)	G-CSF	~70% bone pain (~25% severe[3]) induced by G-CSFs (severe pain treated with NSAIDs, antihistamines, and opioids)
Anemia 	14%	31%	ESA rescue, transfusion rescue	Box warning for shortened overall survival and increased risk of tumor progression; increased risk of thromboembolic disease
Thrombocytopenia 	10%	54%	Transfusion rescue	No options other than transfusions

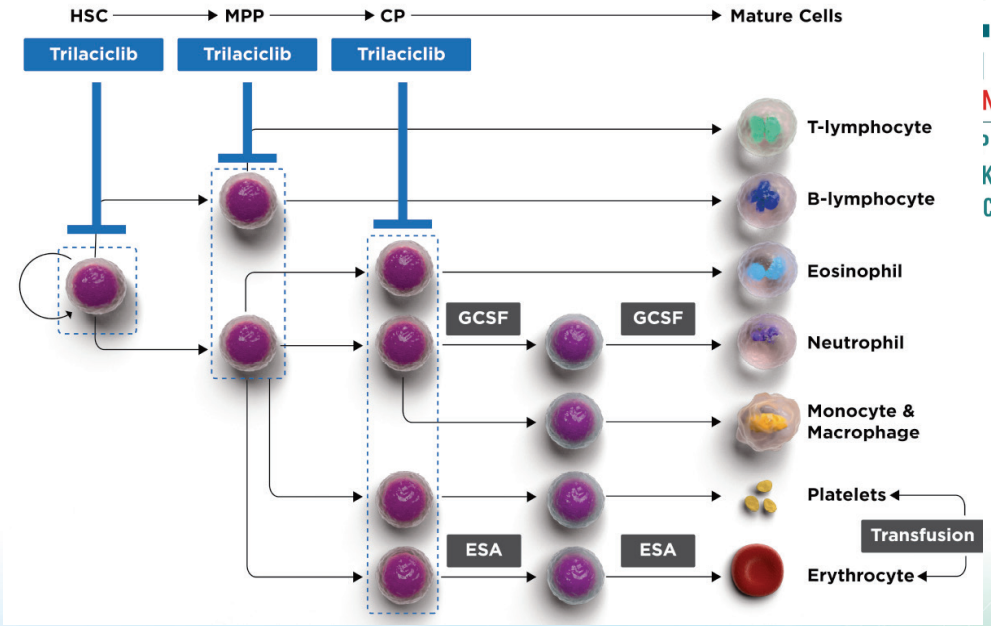
Trilaciclib has the potential to prevent multi-lineage myelosuppression and reduce the need for these interventions and their associated side effects

Sources:
[1]IMpower133 Trial, atezolizumab + E/P arm (n=198), NEJM, 2018; [2]von Pawel J, et al. J Clin. Oncol. 2014;32:4012-4019; [2]Kirshner et al: Prevention of pegfilgrastim-induced bone pain. JCO, 2012

Trilaciclib, a First-in-Class Myelopreservation Agent, Improves Patient Outcomes when Combined with Chemotherapy



Trilaciclib transiently blocks progression through the cell cycle, thereby protecting HSPCs from damage by chemotherapy



- Protection before HSPC damage occurs
- Multi-lineage protection
- Reduces need for supportive care measures

Randomized, Placebo-controlled, Double-blind Phase 2 Studies with ES-SCLC Patients

	1L SCLC	1L SCLC	2L/3L SCLC
Chemotherapy regimen	Etoposide / Carboplatin (E/P) E=100 mg/m^2, P = AUC5 4 to 6 cycles	E/P/Atezolizumab (A) E=100 mg/m^2, P=AUC5, A=1000 mg/m^2 4 induction cycles + maintenance (A)	Topotecan 1.5 mg/m^2 Treat until progression, toxicity, withdrawal of consent
PRO assessments	D1 and D10 of each 21-day cycle	D1 of each 21-day cycle	D1 and D10 of each 21-day cycle
Stratification factors	ECOG (0-1 vs 2)	ECOG (0-1 vs 2) brain metastases (Y/N)	ECOG (0-1 vs 2) brain metastases (Y/N)
Groups	• placebo + E/P (N=37) • trilaciclib + E/P (N=38)	• placebo + E/P/A (N=53) • trilaciclib + E/P/A (N=54)	• placebo + topotecan (N=29) • trilaciclib + topotecan (N=32)

- Use of primary prophylactic colony stimulating factors in Cycle 1 was not allowed; supportive care measures per institution guidelines were permitted throughout the study
- Demographic data and baseline disease characteristics are similar between arms in each study as well as across studies

Trilaciclib Demonstrates Myelopreservation Benefit Across Multiple Lineages in Pooled Analyses of Three SCLC Studies

	Category	Placebo + SOC	Trilaciclib + SOC	2-sided p-value
	Intent to treat population	120	125	
primary endpoints	Mean duration (in days) of severe neutropenia in Cycle 1 (SD)‡	4 (5.2)	1 (2.3)	<0.0001
primary endpoints	Occurrence of severe neutropenia*	64 (53.3%)	16 (12.8%)	<0.0001
primary endpoints	Occurrence of Grade 3/4 anemia (lab data)*	39 (32.5%)	26 (20.8%)	0.0188
	Occurrence of RBC transfusion on/after 5 weeks*	32 (26.7%)	19 (15.2%)	0.0207
	Cumulative incidence of RBC transfusion on/after 5 weeks - event rate per 100 weeks#	3.2	1.5	0.0020
	Occurrence of Grade 3/4 thrombocytopenia (lab data)*	44 (36.7%)	26 (20.8%)	0.0081
	Occurrence of platelet transfusion*	11 (9.2%)	11 (8.8%)	0.8923
	Cumulative incidence of platelet transfusion - event rate per 100 weeks#	1.7	1.1	0.4822

Severe (Grade 4) neutropenia is defined as ANC <500/mm3; RBC = red blood cells, SD = standard deviation,
SOC= etoposide + platinum in G1T28-02, etoposide + platinum + atezolizumab in G1T28-05, and topotecan in G1T28-03. Standard supportive care interventions were allowed for all arms.
‡ p-value was obtained from a nonparametric analysis of covariance (ANCOVA).
* p-value was obtained from a modified Poisson model.
# p-value was obtained from a negative binomial model.

Description of Validated PRO Instruments

- Functional Assessment of Cancer Therapy-Lung (FACT-L)
  - 36-questions
  - Measures generic (e.g., physical well being) and lung cancer-related (e.g., coughing, dyspnea) aspects of quality of life
- Functional Assessment of Cancer Therapy-Anemia (FACT-An)
  - 47-questions
  - Measures fatigue and other aspects of patient's anemia experience (e.g., dyspnea, dizziness)
- Commonalities
  - 1-week recall period
  - Each question is rated on a five-point scale ranging from 0 = "not at all" to 4 = "very much"
  - Higher scores indicate fewer symptoms/better quality of life
  - Both instruments also include the 27 question FACT-General (FACT-G) which assesses HRQoL (physical, functional, emotional, and social/family well-being)
- Specific PRO measure of neutropenia were not included, but fatigue is the most common symptom reported by patients with neutropenia and fatigue is captured by FACT-An

Types of Analyses

Endpoints		Methods
Change from baseline	Change in PRO scores (HRQoL and specific symptoms) at expected end of treatment from baseline	Mixed model repeated measures model (MMRMM)
Deterioration / improvement proportions	Proportion of patients with HRQoL / symptom deterioration and/or improvement using thresholds based on established levels from the literature	Bar charts with rates at each post-baseline assessment
Time to deterioration	Time it takes to reach deterioration threshold based on established levels from the literature	Cox model

Notes on definitions and methods

- **Deterioration** has been defined as a decrease in the baseline score by some clinically meaningful threshold. Clinically meaningful thresholds are calculated through formal psychometric methods and become available in peer reviewed journals
- **Statistical significance** has been defined at the commonly used alpha level of 0.05

FACT-An, FACT-L Analyses Methodology

FACT-An and FACT-L domains and score range	
Outcome	Score range
FACT-G total score	0 – 108
Physical well-being (PWB)	0 – 28
Functional well-being (FWB)	0 – 28
Emotional well-being (EWB)	0 – 24
Social well-being (SWB)	0 – 28
FACT-L total score	0 – 136
Lung cancer subscale (LCS)	0 – 28
Lung-TOI (L-TOI)	0 – 84
FACT-An total score (FACT-AN)	0 – 188
Anemia subscale (AN)	0 – 80
Fatigue subscale (FAT)	0 – 52
Fatigue-symptoms subscale (FAT-SYM)	0 – 20
Fatigue-impact subscale (FAT-IMP)	0 – 32
Non-fatigue subscale (NON-FAT)	0 – 28
Anemia-TOI (AN-TOI)	0 – 126

- Analyses performed for domains shown here, plus selected questions
  - Scores relating to functional impact of SCLC and treatment, as well as symptoms hypothesized to be impacted by chemotherapy (e.g. anemia, neutropenia)
- Focus on FATIGUE as a common symptom reported by patients with neutropenia and anemia
- Responder analyses: by visit using published thresholds to indicate clinically meaningful change
- Time to Confirmed Deterioration (TTCD): log-rank test, Kaplan-Meier curves, and Cox regression model with treatment (T/P) as the only covariate

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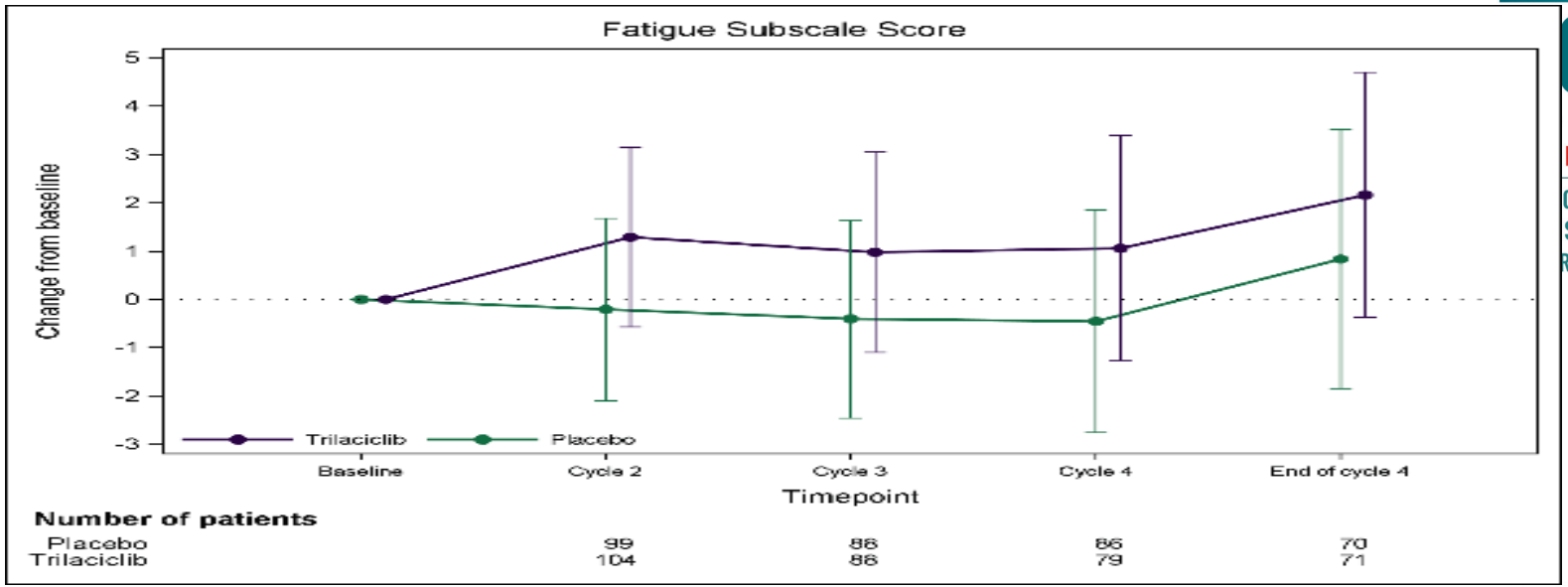
General PRO Observations

- PRO analyses were exploratory endpoints in each study
- PRO completion rates were high across the studies (>80%) for the first 4-6 cycles, the time period for which analyses were performed
- PRO assessments dropped over time due to study attrition in a similar way in both arms in each of the 3 studies
- Enrolled patients had a moderate level of functioning and were moderately symptomatic at baseline as measured by FACT-L and FACT-An instruments in each of the 3 studies
- Baseline FACT-An and FACT-L scores were higher for patients on placebo in all studies which suggests they were less symptomatic at baseline compared to those on trilaciclib

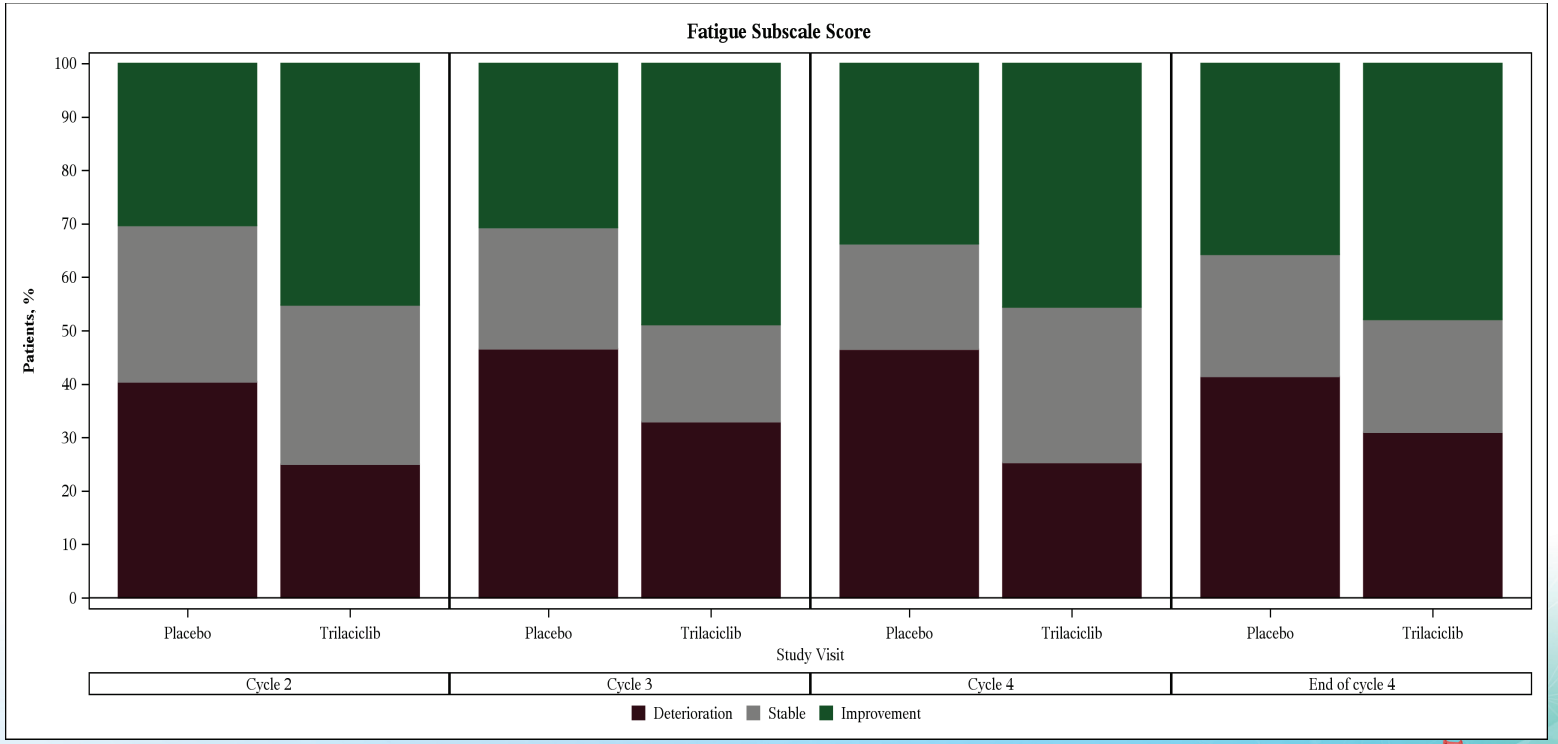
Longitudinal assessment (Change from Baseline over Time in Fatigue)



- Patients on trilaciclib remain stable with some improvement seen at the end of cycle 4, while patients on placebo deteriorate
- Patients on trilaciclib consistently show larger change from baseline, indicating better HRQoL trajectory than placebo patients (clinically meaningful threshold for Fatigue 3-4 points)

Patients on Trilaciclib Had Improved Symptoms of Fatigue Compared to Placebo During the First 4 cycles of Treatment

(pooled analysis across all three SCLC studies)



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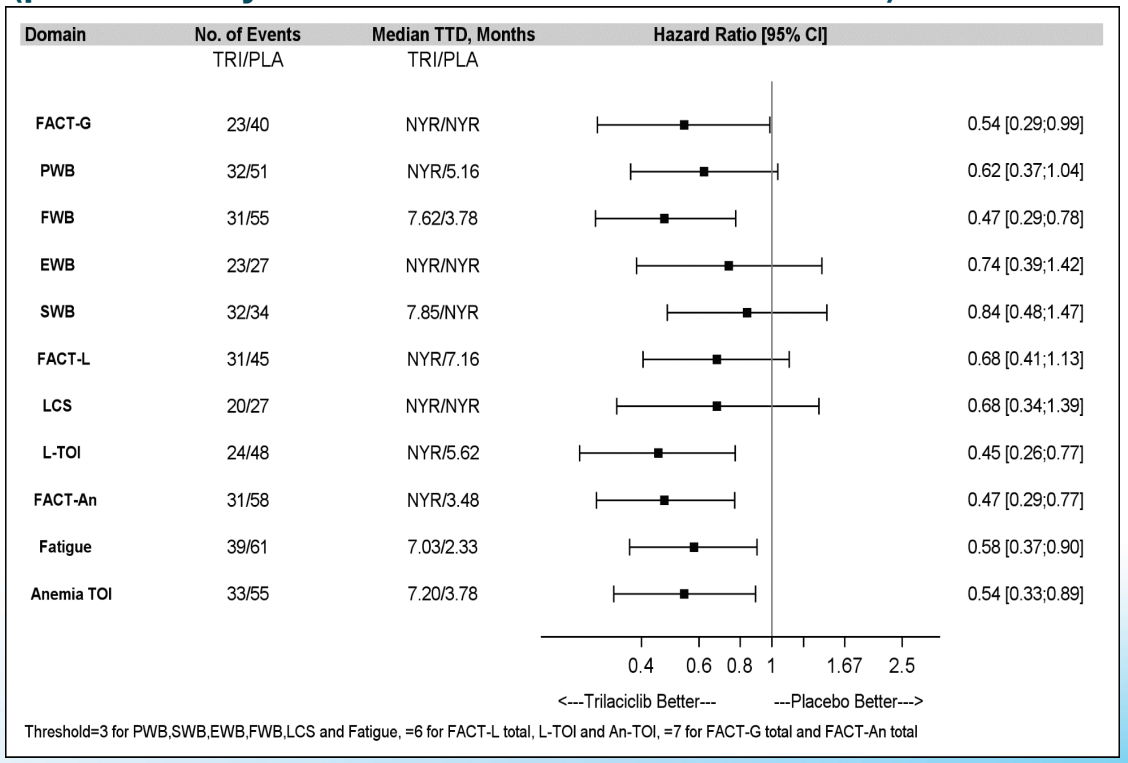
Trilaciclib Delays Time to Confirmed Deterioration in Variety of Symptoms and Functioning Domains of FACT-An, FACT-L

(pooled analysis across all three SCLC studies)



Threshold=3 for PWB,SWB,EWB,FWB,LCS and Fatigue, =6 for FACT-L total, L-TOI and An-TOI, =7 for FACT-G total and FACT-An total

Trilaciclib delayed deterioration of patient functioning and symptom measures over time compared to placebo, for example:

- Median of 4.7 months delay to deterioration for fatigue
- Median of 3.5 months delay for Anemia-TOI
- Median of 4 months delay for functional well-being (FWB)

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Conclusions

- Trilaciclib makes myelosuppressive chemotherapy safer
- Trilaciclib improves the patient experience on chemotherapy
  - Trilaciclib delayed or prevented deterioration in multiple aspects of HRQoL
  - Trilaciclib prevented clinically meaningful increases in fatigue, which are commonly associated with myelosuppression
  - Trilaciclib generally reduced fatigue levels across cycles
  - The effects of trilaciclib on the patient experience were more pronounced for those being treated in the 2nd/3rd line

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