

Safety findings from the phase 2 ALISCA®-Lung1 study of alisertib in patients with small cell lung cancer

Alberto A. Chiappori,^{*1} Robert Jotte,² Amanda Gillespie-Twardy,³ Afshin Dowlati,⁴ Stephen V. Liu,⁵ Benjamin Drapkin,⁶ Kartik Konduri,⁷ Melissa Johnson,⁸ Michael Meshad,⁹ Bindu Potugari,¹⁰ Sandeep Jain,¹¹ Deepa Rangachari,¹² Jacob Sands,¹² Bo Wang,¹³ David Waterhouse,¹⁴ Beth Lowenthal,¹⁵ Judith Bebczuk,¹⁵ Elaine K. Wong,¹⁵ Taofeek K. Owonikoko¹⁶

¹Moffitt Cancer Center, Tampa, FL, USA; ²SCRI Oncology Partners, Rocky Mountain Cancer Centers, Lone Tree, CO, USA; ³SCRI Oncology Partners, US Oncology, Blue Ridge Cancer Center, Blacksburg, VA, USA; ⁴University Hospitals Cleveland Medical Center, Cleveland, OH, USA; ⁵Georgetown University, Washington DC, USA; ⁶University of Texas Southwestern Medical Center, Dallas, TX, USA;

⁷SCRI Oncology Partners, Texas Oncology, Dallas, TX, USA; ⁸SCRI Oncology Partners, Nashville, TN, USA; ⁹SCRI Oncology Partners, Southern Cancer Center, Mobile, AL, USA; ¹⁰Henry Ford Cancer, Detroit, MI, USA; ¹¹SCRI Oncology Partners, Minnesota Oncology Hematology PA, Burnsville, MN, USA; ¹²Dana-Farber Cancer Institute, Boston, MA, USA; ¹³SCRI Oncology Partners, Willamette Valley

Cancer Institute and Research Center, Eugene, OR, USA; ¹⁴SCRI Oncology Partners, OHC Cincinnati, OH, USA; ¹⁵Puma Biotechnology, Inc, Los Angeles, CA, USA; ¹⁶University of Maryland, Baltimore, MD, USA

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Introduction

- Despite advances in treatment options for patients with SCLC, the disease ultimately progresses, resulting in a need for additional therapies. Aurora kinase A (AURKA) is a key regulator of mitosis,^{1,2} AURKA inhibition arrests the growth and proliferation of human SCLC cells,³ and AURKA expression is associated with poor prognosis in multiple solid tumor types.⁴ AURKA and its inhibition therefore represent a target of interest in SCLC.
- Alisertib, an oral small-molecule AURKA inhibitor, is currently under investigation for use in patients with SCLC. Consistent with alisertib's mechanism of interfering with mitosis by disrupting spindle assembly,⁵ the most common AEs in prior studies (e.g., myelosuppression) resulted from damage to rapidly dividing cells.^{6,7}
- Alisertib has been evaluated in >1500 patients to date; in SCLC, in the absence of mandated prophylactic G-CSF, such as in the historical C14007 Study,⁸ the main grade 3/4 AEs were neutropenia and febrile neutropenia, anemia, and thrombocytopenia.
- In the ongoing ALISCA®-Lung1 alisertib monotherapy study in SCLC (PUMA-ALI-4201; NCT06095505), prophylactic G-CSF is mandated with the aim of mitigating neutropenia-related events. Here we report safety findings from the first 88 patients who received alisertib 50 mg and 60 mg BID alongside data from the historical C14007 Study.

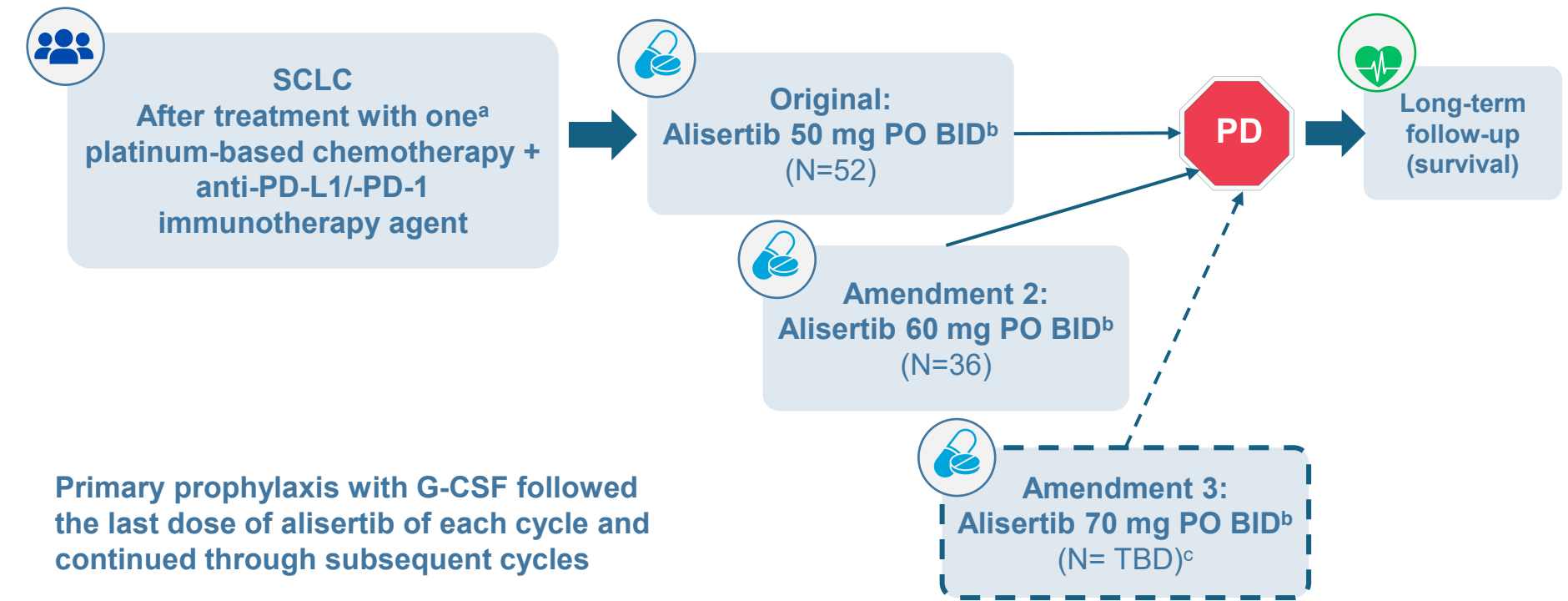
Objectives

- The aim of this presentation is to demonstrate how prophylactic G-CSF helps mitigate grade 3/4 neutropenic events to levels lower than those observed historically in Study C14007.

Methods

- ALISCA-Lung1 is an ongoing phase 2 study of alisertib in patients with pathologically confirmed SCLC following progression on or after treatment with one platinum-based chemotherapy and an anti-PD-L1/-PD-1 immunotherapy agent. Up to one additional systemic anti-cancer therapy for SCLC is allowed, for a total of up to two prior treatment regimens.
- Patients enrolled to date received alisertib 50, 60, or 70 mg PO BID, on Days 1–7 of every 21-day cycle (**Figure 1**). All patients received primary prophylaxis with G-CSF following the last alisertib dose of each cycle, and in subsequent cycles according to product labeling, and clinical practice guidelines and/or institutional guidelines.
- All patients underwent sparse PK sampling to evaluate plasma concentrations of alisertib on Days 1, 7, and 8 of Cycle 1, and Day 1 of every other cycle thereafter (starting on Cycle 3) for population PK analysis.

Figure 1. ALISCA-Lung1 study design



^aUp to one additional systemic anti-cancer therapy for SCLC is allowed, for a total of up to two prior treatment regimens.

^bAlisertib on Days 1–7 of every 21-day cycle.

^cNot shown on this poster due to insufficient follow up.

Results

- A total of 88 patients with metastatic SCLC have been enrolled into two dose cohorts (50 mg BID, 60 mg BID) and are evaluable for efficacy and/or safety (**Table 1**).

Table 1. Patient characteristics by alisertib dose cohort and Study C14007

	50 mg BID (n=52)	60 mg BID (n=36)	Study C14007 50 mg BID (n=60)
Median age, years	63.5	70	62
Sex, n (%)			
Female	26 (50.0)	21 (58.3)	28 (46.7)
Male	26 (50.0)	15 (41.7)	32 (53.3)
VALSG stage at initial diagnosis, n (%)			
Limited	7 (13.5)	8 (22.2)	NR
Extensive	45 (86.5)	28 (77.8)	NR
ECOG performance status at C1D1, n (%)			
0	16 (30.8)	15 (41.7)	13 (21.7)
1	34 (65.4)	21 (58.3)	47 (78.3)
2	2 (3.8)	0	0
Location of disease at enrollment, n (%)			
Visceral	47 (90.4)	33 (91.7)	NR
Not visceral	5 (9.6)	1 (2.8)	NR
Missing	0	2 (5.6)	NR
Metastatic disease location, n (%)			
Brain	21 (40.4)	13 (36.1)	NR
Liver	25 (48.1)	21 (58.3)	NR
No. of prior treatment regimens, n (%)			
1	40 (76.9)	17 (47.2)	25 (41.7)
2	12 (23.1)	19 (52.8)	27 (45.0)
≥3	0	0	8 (13.3)

- A summary of safety outcomes is shown in **Table 2**.
- Grade 3 TEAEs were recorded in 51% of patients (50 mg BID, 40%; 60 mg BID, 67%).
- Grade 4 TEAEs were recorded in 10% of patients (50 mg BID, 8%; 60 mg BID, 14%).

Table 2. Safety summary by alisertib dose cohort and Study C14007

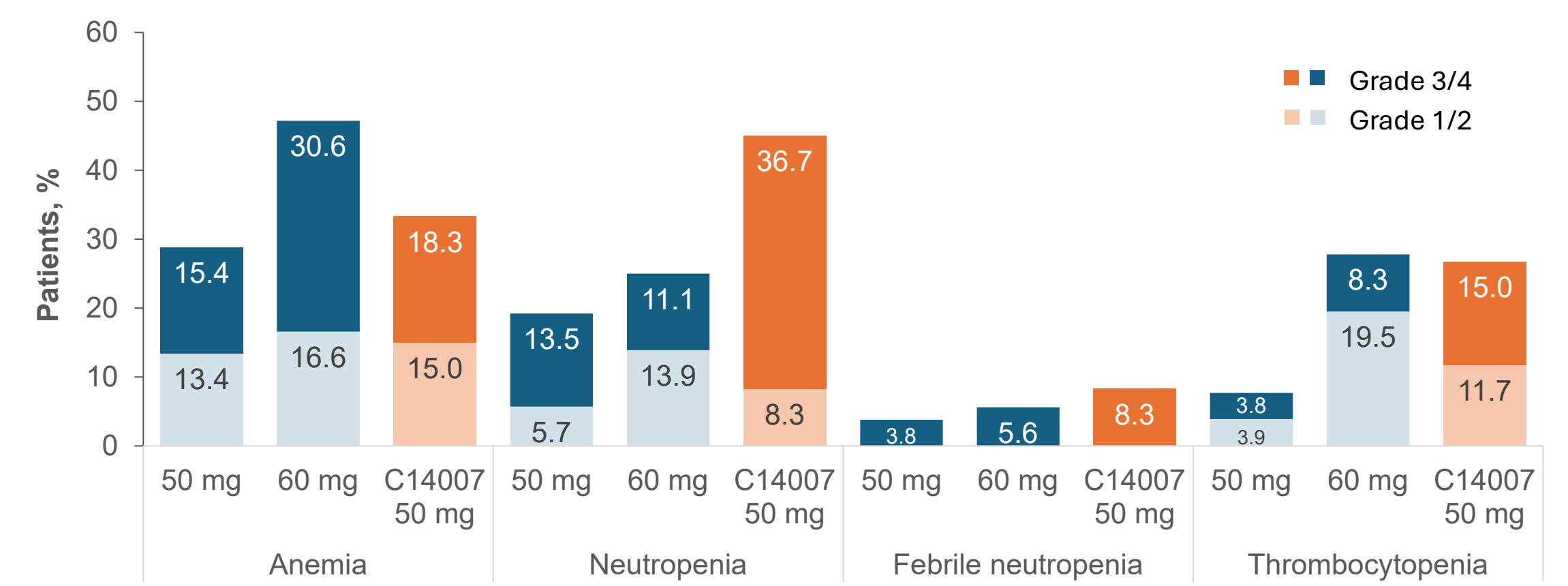
Event, n (%)	50 mg BID (n=52)	60 mg BID (n=36)	Study C14007 50 mg BID (n=60)
Any TEAE	52 (100.0)	36 (100.0)	57 (95.0)
Grade 1	47 (90.4)	35 (97.2)	47 (78.3)
Grade 2	41 (78.8)	36 (100.0)	48 (80.0)
Grade 3	21 (40.4)	24 (66.7)	33 (55.0)
Grade 4	4 (7.7)	5 (13.9)	23 (38.3)
Grade 3 or 4	22 (42.3)	24 (66.7)	40 (66.7)
Serious TEAEs	6 (11.5)	11 (30.6)	28 (46.7)
TEAEs leading to treatment discontinuation	3 (5.8)	6 (16.7)	13 (21.7)
TEAEs leading to dose reduction	5 (9.6)	6 (16.7)	16 (26.7)
TEAEs leading to dose hold	9 (17.3)	14 (38.9)	22 (36.7)
TEAEs leading to hospitalization	6 (11.5)	10 (27.8)	24 (40.0)

- The most common all-grade TEAEs were fatigue, anemia, and alopecia, as shown in **Table 3**. The most common grade 3/4 TEAEs were anemia and neutropenia.
- Incidences of hematologic and nonhematologic TEAEs are shown in **Figures 2 and 3**.

Table 3. TEAEs and AESIs occurring in >15% of patients in ALISCA-Lung1 and Study C14007

Event, n (%)	ALISCA-Lung1 cohort				Study C14007 50 mg BID	
	50 mg BID (n=52)	60 mg BID (n=36)	All grades	Grade 3/4	50 mg BID (n=60)	Grade 3/4
Fatigue	25 (48.1)	1 (1.9)	18 (50.0)	2 (5.6)	28 (46.7)	5 (8.3)
Anemia	15 (28.8)	8 (15.4)	17 (47.2)	11 (30.6)	20 (33.3)	11 (18.3)
Alopecia	14 (26.9)	NA	15 (41.7)	NA	16 (26.7)	NA
Nausea	13 (25.0)	1 (1.9)	12 (33.3)	0	18 (30.0)	0
Decreased appetite	16 (30.8)	0	9 (25.0)	0	18 (30.0)	0
Diarrhea	11 (21.2)	0	13 (36.1)	0	18 (30.0)	2 (3.3)
Stomatitis	7 (13.5)	1 (1.9)	9 (25.0)	3 (8.3)	13 (21.7)	4 (6.7)
Vomiting	12 (23.1)	0	5 (13.9)	1 (2.8)	11 (18.3)	1 (1.7)
Neutropenia	10 (19.2)	7 (13.5)	9 (25.0)	4 (11.1)	27 (45.0)	22 (36.7)
Somnolence	2 (3.8)	0	2 (5.6)	0	9 (15.0)	1 (1.7)

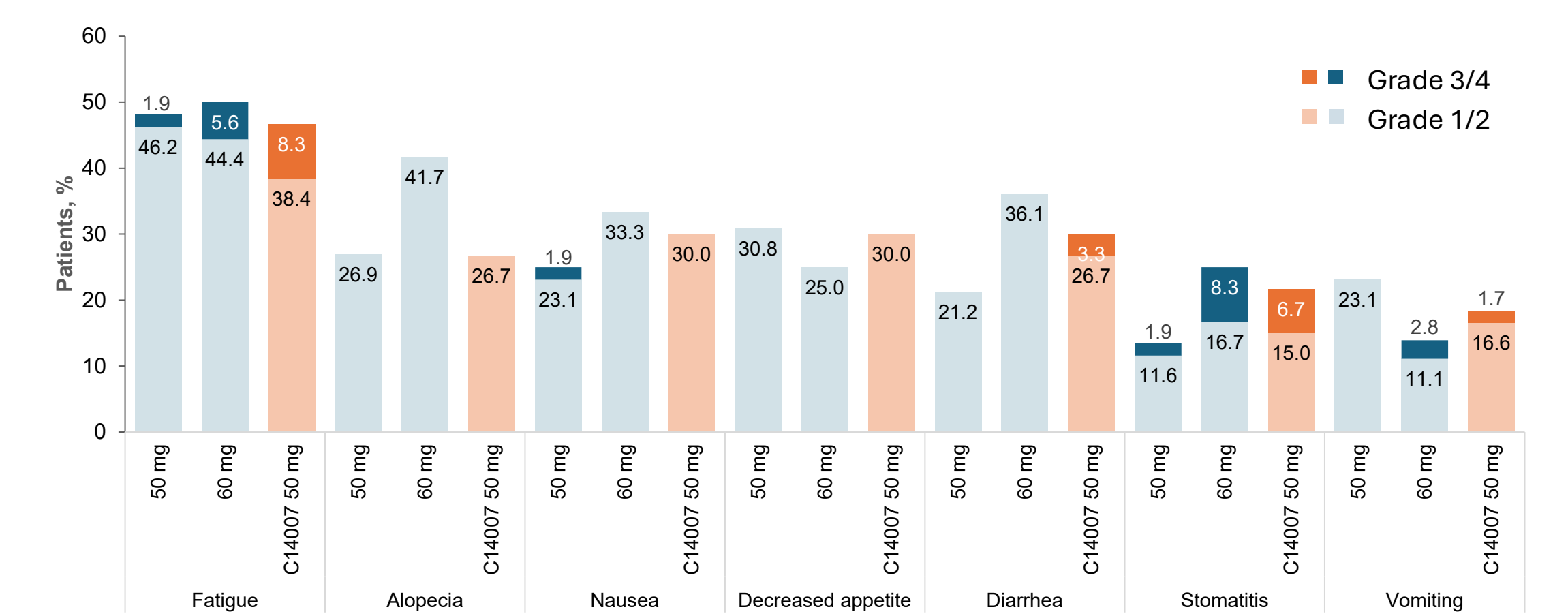
Figure 2. Hematologic AEs in ALISCA-Lung 1 and Study C14007^{a,b}



^aALISCA-Lung1 mandated primary G-CSF prophylaxis; Study C14007 did not.

^bCross-study comparisons are descriptive only. ALISCA-Lung1 and Study C14007 differ in dose range, mandated supportive care (primary G-CSF prophylaxis in ALISCA-Lung1 only), study phase/population, and AE reporting conventions. No statistical comparison is implied.

Figure 3. Nonhematologic AEs in ALISCA-Lung1 and Study C14007^a

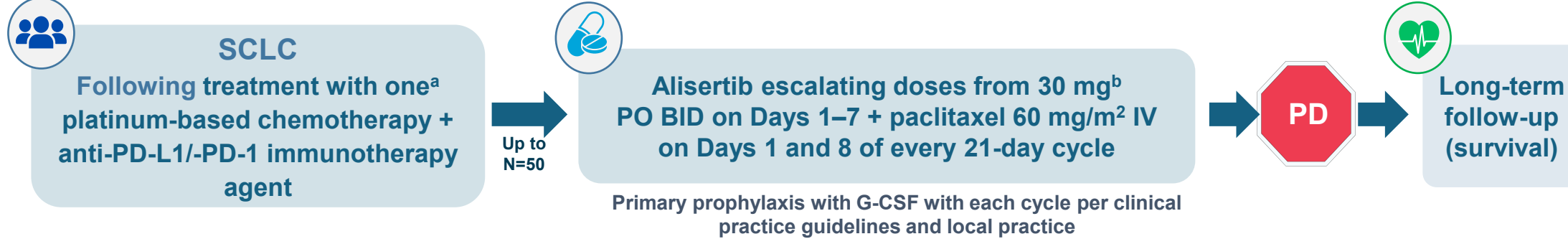


^aCross-study comparisons are descriptive only. ALISCA-Lung1 and Study C14007 differ in dose range, mandated supportive care (primary G-CSF prophylaxis in ALISCA-Lung1 only), study phase/population, and AE reporting conventions. No statistical comparison is implied.

Conclusions

- Early safety data from the ALISCA-Lung1 study did not demonstrate any new safety signals among patients with SCLC treated with alisertib.
- G-CSF prophylaxis has helped mitigate grade 3/4 neutropenic events to levels lower than those observed historically (13.5% for alisertib 50 mg BID vs 36.7% in Study C14007), allowing an increase in alisertib dose to 60 and 70 mg BID.
- Enrollment into the 70 mg BID alisertib monotherapy cohort has commenced.
- The ALISCA-Lung2 (PUMA-ALI-4202) study is investigating increasing doses of alisertib with a fixed paclitaxel dose, plus mandatory G-CSF prophylaxis, in patients with SCLC (NCT07465757; **Figure 4**).

Figure 4. ALISCA-Lung2 study design



^aUp to one additional systemic anti-cancer therapy is allowed, for a total of up to two prior regimens of therapy.

^bFor each subsequent cohort enrolled, patients will take an additional 10 mg PO BID (e.g., patients in Cohort 2 will take alisertib 40 mg PO BID).

Objectives

Primary

- Assess the safety and tolerability of various doses of alisertib administered on Days 1–7 in combination with paclitaxel administered on days 1 and 8 of a 21-day cycle (AEs and serious AEs per NCI CTCAE v5.0).

Secondary

- Determine investigator-assessed efficacy (ORR, DOR, DCR, PFS, and OS) according to RECIST v1.1.

Exploratory

- Evaluate biomarkers of interest in tumor and liquid biopsies.
- Update the population PK profile of alisertib.

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Abbreviations

AE , adverse event	ORR , objective response rate
AESI , adverse event of special interest	PD , progressive disease
AURKA , Aurora kinase A	PD-1 , programmed cell death protein-1
BID , twice per day	PD-L1 , programmed cell death-ligand 1
C1D1 , Cycle 1, Day 1	PFS , progression-free survival
DCR , disease-control rate	PK , pharmacokinetics
DOR , duration of response	RECIST v1.1 , Response Evaluation Criteria in Solid Tumours, version 1.1
ECOG , Eastern Cooperative Oncology Group	SCLC , small cell lung cancer
G-CSF , granulocyte colony-stimulating factor	TBD , to be determined
NA , not applicable	TEAE , treatment-emergent adverse event
NCI CTCAE , National Cancer Institute Common Terminology Criteria for Adverse Events	VALSG , Veterans Administration Lung Study Group
NR , not reported	

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