EFFICACY AND SAFETY OF LURBINECTEDIN (PM1183, ZEPSYRE®) IN SMALL CELL LUNG CANCER (SCLC): RESULTS FROM A PHASE 2 STUDY

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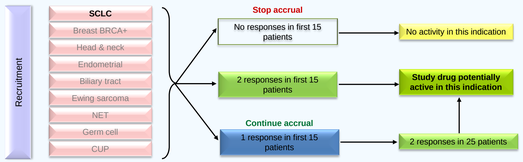
BACKGROUND

SCLC is a deadly cancer and despite initial 80% response, almost all patients will relapse and die of this disease. Limited options exist after failure of first line, with a median time to progression (TTP) of around 3.5 months. New therapeutic agents are needed. Lurbinectedin is a new anticancer drug that blocks transcription and induces DNA double-strand breaks, leading to apoptosis.

METHODS

A multicenter phase 2 basket trial to assess the efficacy and safety of lurbinectedin in several types of advanced solid tumors, including SCLC, is ongoing. In the SCLC cohort, 15 adult patients without brain metastases, who had received one prior chemotherapy line, were recruited. If at least one confirmed response was observed, **recruitment would be increased to 100 patients** to reject the null hypothesis of <=15% vs the alternative of >=30%. If the number of responders is ≥ 23, then null hypothesis can be rejected.

Study Design



Treatment: PM1183 3.2 mg/m^2, 1h iv infusion, q3wks

OBJECTIVES

Primary: Overall response rate (ORR), by RECIST v1.1

Secondary:

- Duration of response
- Clinical benefit: response or stable disease (SD) ≥ 4 months
- Progression free survival (PFS)
- Overall survival (OS)
- Safety of PM1183 in this patient population
- Pharmacokinetics of PM1183
- Pharmacogenomic and pharmacogenetic analyses

RESULTS

Baseline Characteristics (N=68)		
Age (years)	Median (range)	60.5 (40-83)
Gender	Male / Female	43/25
ECOG PS	0/1/2	21/43/4
Limited / Extended*	N (%)	16 (23%) / 49 (72%)
Sites of disease involvement	Median (range)	3 (1-5)
	< 3 / ≥ 3	29/39
Bulky disease (>50 mm)	N (%)	46 (68%)
Known CNS at baseline	N (%)	1 (1.5%)
PCI	N (%)	34 (50%)
Prior lines[§]	Median	1 (1-2)
Best response to last chemotherapy line	CR-PR	42 (62%)
	SD	12 (17%)
CTFI*	≥90 d/ <90d	34/33
Median CTFI* (months)	Median (range)	3.0 (0.0-12.5)
Prior Chemotherapy	CDDP/Etoposide N(%)	68 (100%)
Prior immunotherapy/inv drugs	N(%)	11(16.1%)

* Data not complete for all patients.

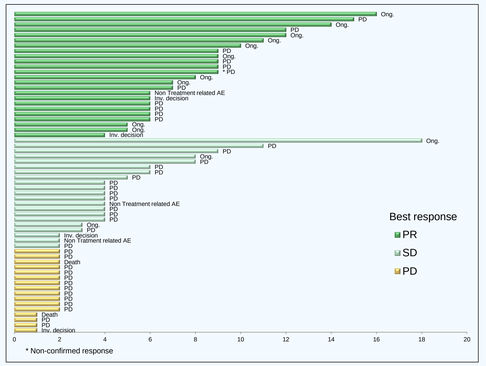
EFFICACY

Response by Chemotherapy-Free Interval (CTFI) (n=61)

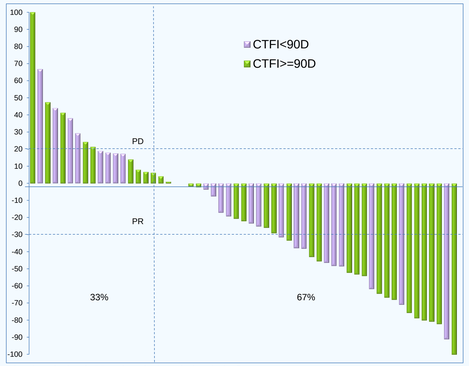
Response	CTFI<90d (n=27)		CTFI>=90d (n=34)		Total (N=61)	
	N	%	N	%	N	%
PR	9	33.3	15	44.1	24	39.3
SD>=4 m	3	11.1	4	11.8	7	11.5
SD<4 m	5	18.5	9	26.5	14	23.0
PD	10	37.0	6	17.6	16	26.2
ORR (95% CI;%)	33.3 (16.5-54)		44.1 (27.2-62.1)		39.3 (27.1-52.7)	
Clinical Benefit (95% CI;%)	44.4 (25.5-64.7)		55.9 (37.9-72.8)		50.8 (37.7-63.9)	
DCR (95% CI;%)	63 (42.4-80.6)		82.4 (65.5-93.2)		73.8 (60.9-84.2)	
DOR (95% CI;%)	4.1 (1.3-5.1)		6.2 (5.3-NR)		6.2 (3.0-8.8)	
PFS (95% CI;%)	3.4 (1.2-5.7)		4.2 (2.6-7.4)		4.1 (2.6-5.7)	
OS (95% CI;%)	8.1 (4.4-14.0)		15.8 (9.6-17.6)		11.8 (9.6-15.9)	

DCR: disease control rate; percentage of patients with PR+SD. Clinical benefit; percentage of patients with PR + SD>4 months.

Swimmer Plot of Outcome in SCLC Patients (n=61)

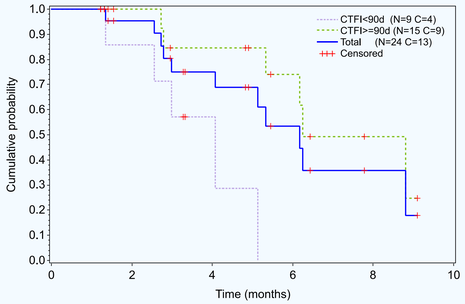


Waterfall Plot of the Maximum Change in Tumor Size (n=57)



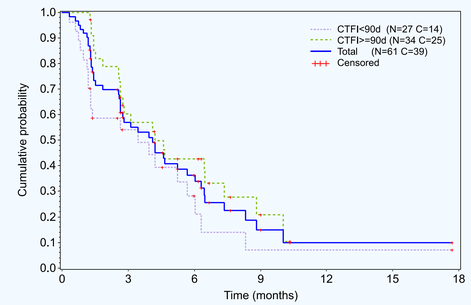
3 patients had early PD and one had new lesions in the first tumor assessment

Duration of Response by CTFI (n=24)



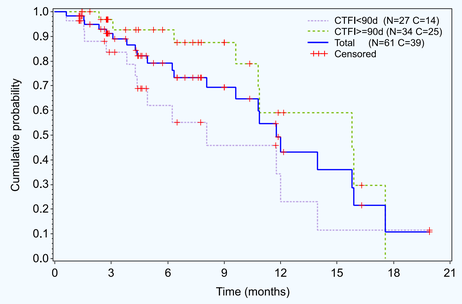
Duration of Response by CTFI (n=24)	CTFI<90d (N=9)	CTFI>=90d (N=15)	Total (N=24)
Median	4.1 (1.3-5.1)	6.2 (5.3-NR)	**6.2 (3.0-8.8)**
DOR at 4 m 95%CI	57.1% (20.5-93.8)	84.6% (65.0-100)	75.0% (56.0%-94.1%)
DOR at 6 m 95%CI	--	74.0% (48.1-99.9)	53.5% (28.7%-78.3%)

Progression Free Survival by CTFI (n=61)



Progression Free Survival by CTFI (n=61)	CTFI<90d (N=27)	CTFI>=90d (N=34)	Total (N=61)
Median	3.4 (1.2-5.7)	4.2 (2.6-7.4)	**4.1 (2.6-5.7)**
PFS at 4 m 95%CI	44.3% (24.2-64.3)	56.9% (39.7-74.0)	51.1% (38.0-64.2)
PFS at 6 m 95%CI	28.1% (8.7-47.6)	42.8% (25.2-60.4)	36.3% (23.2-49.5)

Overall Survival by CTFI (n=61)



Overall Survival by CTFI (n=61)	CTFI<90d (N=27)	CTFI>=90d (N=34)	Total (N=61)
Median	8.1 (4.4-14)	15.8 (9.6-17.6)	**11.8 (9.6-15.9)**
OS at 6 m 95%CI	61.9% (40.2-83.6)	92.7% (83.0-100)	79.3% (67.6-91.0)
OS at 12 m 95%CI	22.9 (0-48.7)	59.1% (31.0-87.3)	43.1% (22.5-63.7)

SAFETY

Adverse Events (N=66)

MedDRA Preferred term	NCI-CTC Grade		
	G1-2	G3	G4
	N - %	N - %	N - %
Anemia	57 - 86.4%	4 - 6.1%	.
Neutropenia	21 - 31.8%	11 - 16.7%	15 - 22.7%
Febrile neutropenia	.	2 - 3.0%	4 - 6.1%
Thrombocytopenia	21 - 31.8%	2 - 3.0%	3 - 4.5%
ALT increased	38 - 58.5%	3 - 4.6%	.
AST increased	24 - 36.9%	.	.
AP increased	16 - 24.6%	.	.
Bilirubin increased	6 - 9.4%	.	.
Fatigue	34 - 51.5%	3 - 4.5%	.
Vomiting	12 - 18.2%	.	.
Nausea	21 - 31.8%	.	.
Diarrhea	6 - 9.1%	.	.
Constipation	7 - 10.6%	.	.
Anorexia	11 - 16.7%	.	.

Myelosuppression was the most common adverse event: 39% neutropenia grade 3/4, 9% febrile neutropenia, 8 patients had dose delay due to neutropenia and 10 had dose reduced because of neutropenia. G-CSF was given to 11 pts.

CONCLUSIONS

- Lurbinectedin as a single agent shows compelling activity as second line treatment in SCLC
- Safety in this patient population was acceptable and well tolerated
  - No unexpected toxicity or drug related deaths occurred
- These results suggests lurbinectedin as a single agent can be considered as an alternative therapy for patients with relapsed SCLC

ACKNOWLEDGEMENTS

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