Abstract # EP-1226

Efficacy and Safety of Single Agent Oral Selinexor in Patients with Primary Refractory Diffuse Large B-Cell Lymphoma (DLBCL): A Post-Hoc Analysis of the SADAL Study

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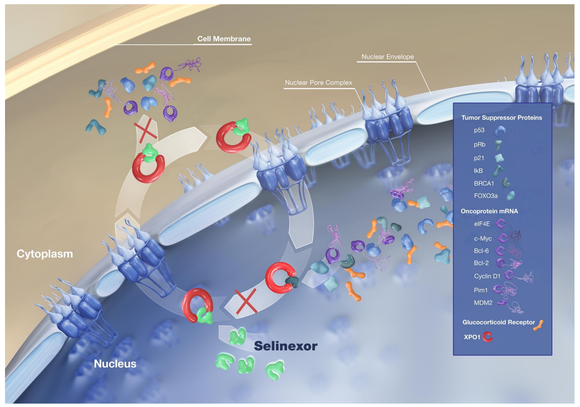
Introduction

Diffuse large B-cell lymphoma (DLBCL)

- Patients with primary refractory DLBCL, defined as those who progress within one year of their frontline immunochemotherapy, have especially poor outcomes.
- Primary refractory disease that progresses after two or more prior therapies portends an extremely dismal outcome.
- A critical unmet need exists for the development of new treatment strategies for patients with primary refractory DLBCL who relapsed after ≥2 lines of prior therapy.

Selinexor

- Selinexor is a first-in-class Selective Inhibitor of Nuclear Export (SINE) compound that selectively binds and inactivates exportin 1 (XPO1), therefore forcing the nuclear retention and reactivation of cell cycle regulators such as p53, FOXO, IkB, and Rb.
- XPO1 overexpression in DLBCL correlates with poor prognosis.
- Selinexor in combination with dexamethasone (Sd) has been approved by the FDA for patients with relapsed / refractory multiple myeloma.[1]

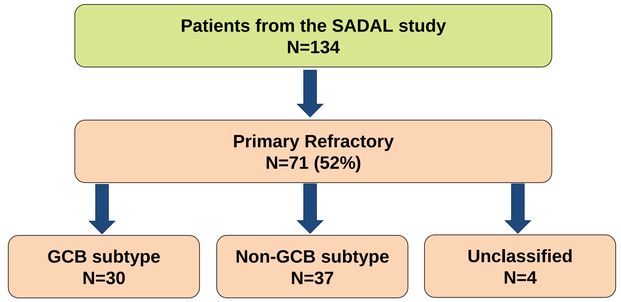


Selinexor Treatment of Diffuse Large B-cell Lymphoma: SADAL Study

- The SADAL (Selinexor Against Diffuse Aggressive Lymphoma) study was a multi-center, open-label Phase 2b study which enrolled patients with previously treated, pathologically confirmed *de novo* DLBCL, or DLBCL transformed from previously diagnosed indolent lymphoma, with a performance status of ≤2 and having received at least 2 prior therapies.[2]
- Selinexor (60 mg) was administered orally on days 1 and 3 weekly until disease progression or unacceptable toxicity.

Methods

We performed post-hoc analyses of the SADAL study to determine if there are differences in efficacy and safety among patients with primary refractory disease, defined as patients who progressed during or within one year of their first line systemic treatment for DLBCL.



Results

Overall Efficacy Results (N=134)

- Single agent oral selinexor showed a 29.1% overall response rate (ORR), median duration of response of 9.3 months and median overall survival of 9 months in 134 patients with previously treated, pathologically confirmed *de novo* DLBCL, or DLBCL transformed from previously diagnosed indolent lymphoma, after at least two lines of chemo-immunotherapy.

Table 1. Demographics and Disease Characteristics - Primary Refractory Population

	Primary Refractory DLBCL (n=71)
Age (years), median (range)	65 (35.0, 83.0)
≥70 years (%)	26 (36.6)
Male, n (%) Female, n (%)	45 (63.4) 26 (36.6)
Weeks since last disease progression event, median (range)	7.6 (1.9, 134.6)
DLBCL type, n (%)	
De novo	57 (80.3)
Transformed	14 (19.7)
Number of prior regimens, median (range)	2 (2-5)
2	43 (60.6)
>2	28 (39.4)
Prior ASCT	17 (23.9)

Table 2. Efficacy in Patients with Primary Refractory DLBCL

	n	ORR n (%)	DOR (months)	OS (months)
Primary Refractory	71	18 (25.4) CR: 7 (10)	4.8 CR: 10.4	7.8 Not Reached
DLBCL subtype				
GCB	30	9 (30.0)	4.4	7
non-GCB	37	6 (16.2)	Not Reached	7.8
Unclassified disease	4	3 (75.0)	1.9	28

Table 3. Treatment-Related Adverse Events

	All (n=134)	Primary Refractory DLBCL (n=71)
Grade ≥3 Adverse Events, ≥5% overall, n(%)		
Thrombocytopenia	54 (40.3)	28 (39.4)
Neutropenia	33 (24.6)	21 (29.6)
Anemia	20 (14.9)	11 (15.5)
Fatigue	14 (10.4)	8 (11.3)
Hyponatremia	7 (5.2)	6 (8.5)
Leukopenia	7 (5.2)	6 (8.5)
Nausea	8 (6.0)	4 (5.6)
Serious Adverse Events	28 (20.9)	13 (18.3)

Conclusions

- **In patients with primary refractory DLBCL (progression on or within 1 year of initial therapy, N=71) treated with at least 2 prior regimens, oral selinexor monotherapy demonstrated an ORR of 25.4% with a CR rate of 10% vs. ORR 29.1% in the entire SADAL population (N=134). Responses were observed in both GCB and non-GCB DLBCL.**
- **Safety in the primary refractory group was comparable to that observed in the overall SADAL trial population (see Abstract #2728).**
- **Treatment with selinexor could provide benefit to patients who progressed during or within one year of their first line systemic treatment for DLBCL.**

References

[1]Chari, A. et al. Oral Selinexor-Dexamethasone for Triple-Class Refractory Multiple Myeloma. *N Engl J Med*. 2019 Aug 22;381(8):727-738.

[2]Kalakonda, N. et al. Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL): a single-arm multinational phase 2 trial. *Lancet Hematology*. (In press)

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