Abstract # EP-1244

# Effect of Prior Therapy on the Efficacy and Safety Of Oral Selinexor in Patients With Relapsed/Refractory (R/R) Diffuse Large B-cell Lymphoma (DLBCL): A Post-hoc Analysis of the SADAL Study

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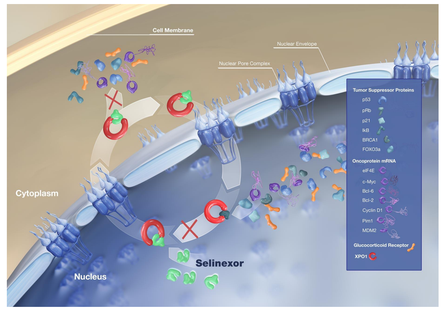
## Introduction

**Diffuse large B-cell lymphoma (DLBCL)**

- DLBCL is a heterogeneous disease with clinically and molecularly distinct subtypes.
- Patients who have received ≥2 lines of therapy, including those with relapse after ASCT or who are not candidates for ASCT, have very poor prognosis.
- There is a critical unmet need to develop new treatment strategies for patients with DLBCL with ≥2 lines of prior therapy.
- The nuclear export protein exportin 1 (XPO1) is overexpressed in many cancers, including DLBCL, and elevated levels are correlated with poor prognosis.
- Selinexor is an oral, small-molecule inhibitor of XPO1 that induces accumulation of tumor suppressor proteins in the nucleus (e.g., p53, p21, IkB, and FOXO), reductions in several oncoproteins (e.g., c-Myc, Bcl-xL, cyclins), cell cycle arrest, and apoptosis of cancer cells.
- XPO1 blockade in DLBCL re-establishes the tumor-suppressing and growth-regulating effects of multiple TSPs by forcing their nuclear retention, and potentially reverses chemotherapy resistance.



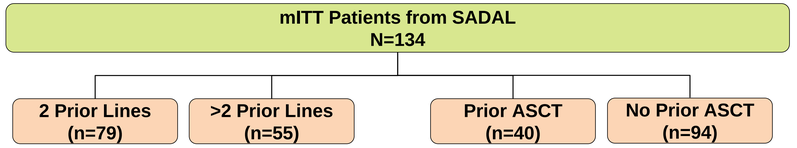

- Selinexor has been approved by the FDA in combination with dexamethasone (Sd) for patients with relapsed/refractory multiple myeloma.[1]
- A Phase 1 study in heavily pretreated DLBCL demonstrated that single agent selinexor resulted in an overall response rate of 32%, with complete response in 9.3% of patients, supporting the broad activity of selinexor in multiple hematologic malignancies including myeloma and DLBCL.

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

- The SADAL (Selinexor Against Diffuse Aggressive Lymphoma) study was an 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 data to compare the safety and efficacy of selinexor in patients based on the number (2 vs. >2) and type (ASCT vs. no ASCT) of prior lines of therapy received.**




- Comparison of ORRs used the Cochran–Mantel–Haenszel method. The Kaplan-Meier method and log-rank test were used for survival analysis.

## Results

**Table 1. Patient Demographics and Disease Characteristics**

| | All (n=134) | 2 Prior Lines (n=79) | >2 Prior Lines (n=55) | Prior ASCT (n=40) | No Prior ASCT (n=94) |
|---|---|---|---|---|---|
| Age (years), median (range) | 67 (35, 91) | 69 (45, 86) | 66 (35, 91) | 64 (41, 77) | 69.5 (35, 91) |
| ≥70 years (%) | 60 (44.8) | 38 (48.1) | 22 (40.0) | 13 (32.5) | 47 (50.0) |
| Male, n(%) | 79 (59.0) | 46 (58.2) | 33 (60.0) | 27 (67.5) | 52 (55.3) |
| Weeks since last disease progression event, median (range) | 7.3 (1.9, 406.3) | 6.4 (1.9, 406.3) | 9.6 (2.3, 134.6) | 6.9 (2.7, 406.3) | 7.5 (1.9, 134.6) |
| **DLBCL type, n (%)** | | | | | |
| *De novo* DLBCL | 103 (76.9) | 61 (77.2) | 42 (76.4) | 32 (80.0) | 71 (75.5) |
| Transformed DLBCL | 31 (23.1) | 18 (22.8) | 13 (23.6) | 8 (20.0) | 23 (24.5) |
| **DLBCL subtype, n (%)** | | | | | |
| GCB | 63 (47.0) | 36 (45.6) | 27 (49.1) | 25 (62.5) | 38 (40.0) |
| Non-GCB | 66 (49.3) | 39 (49.4) | 27 (49.1) | 13 (32.5) | 53 (56.4) |
| Unclassified | 5 (3.7) | 4 (5.1) | 1 (1.8) | 2 (5.0) | 3 (3.2) |

**SADAL Study (n=134)**

| | |
|---|---|
| **Overall response rate, n (%)** | **39 (29.1)** |
| Complete response rate, n (%) | 18 (13.4) |
| Duration of response, median (months) | 9.3 |
| Duration of response in patients with CR, median (months) | 23.0 |
| **Overall survival, median (months)** | **9.0** |

**Table 2. Efficacy by Number of Prior Therapies**

| | 2 Prior Lines (n=79) | >2 Prior Lines (n=55) | *p - value* |
|---|---|---|---|
| Overall response rate, n (%) | 22 (27.8) | 17 (30.9) | *0.85* |
| Complete response rate, n (%) | 12 (15.2) | 6 (10.9) | *0.65* |
| Duration of response, median (months) | 10.4 | 8.4 | *0.40* |
| Overall survival, median (months) | 9.1 | 8.2 | *0.77* |

**Table 3. Efficacy by Prior ASCT**

| | Prior ASCT (n=40) | No Prior ASCT (n=94) | *p - value* |
|---|---|---|---|
| Overall response rate, n (%) | 17 (42.5) | 22 (23.4) | *0.04* |
| Complete response rate, n (%) | 6 (15.0) | 12 (12.8) | *0.94* |
| Duration of response, median (months) | 8.4 | 9.7 | *0.93* |
| Overall survival, median (months) | 10.9 | 7.8 | *0.19* |

**Table 4. Treatment-Related Adverse Events**

| | All (n=134) | 2 Prior Lines (n=79) | >2 Prior Lines (n=55) | Prior ASCT (n=40) | No Prior ASCT (n=94) |
|---|---|---|---|---|---|
| **Grade ≥3 Adverse Events, ≥5% overall, n (%)** | | | | | |
| Thrombocytopenia | 54 (40.3) | 29 (36.7) | 25 (45.5) | 25 (62.5) | 29 (30.9) |
| Neutropenia | 33 (24.6) | 18 (22.8) | 15 (27.3) | 11 (27.5) | 22 (23.4) |
| Anemia | 20 (14.9) | 13 (16.5) | 7 (12.7) | 5 (12.5) | 15 (16.0) |
| Fatigue | 14 (10.4) | 8 (10.1) | 6 (10.9) | 3 (7.5) | 11 (11.7) |
| Nausea | 8 (6.0) | 5 (6.3) | 3 (5.5) | 3 (7.5) | 5 (5.3) |
| Hyponatremia | 7 (5.2) | 4 (5.1) | 3 (5.5) | 0 | 7 (7.4) |
| Leukopenia | 7 (5.2) | 5 (6.3) | 2 (3.6) | 4 (10.0) | 3 (3.2) |
| **Serious Adverse Events, n (%)** | 28 (20.9) | 18 (22.8) | 10 (18.2) | 9 (22.5) | 19 (20.2) |
| **Dose Reduction, n (%)** | 52 (38.8) | 27 (34.2) | 25 (45.5) | 20 (50.0) | 32 (34.0) |
| **Discontinuation, n (%)** | 12 (9.0) | 7 (8.9) | 5 (9.1) | 4 (10.0) | 8 (8.5) |

## Conclusions

- **Single agent selinexor demonstrated durable responses regardless of number of prior lines of therapy or prior treatment with high dose chemotherapy with ASCT.**
- **Notably, ORR was 42.5% in patients who received prior ASCT therapy.**
- **Tolerability of selinexor in the analyzed subgroups were similar to those observed in the overall study population.**
- **Selinexor may represent a treatment option in patients with relapsed or refractory 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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