Selinexor Efficacy and Safety are Independent of Renal Function in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL): Subset Analysis from Pivotal Phase 2b SADAL Study

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Conflict of Interest Disclosure

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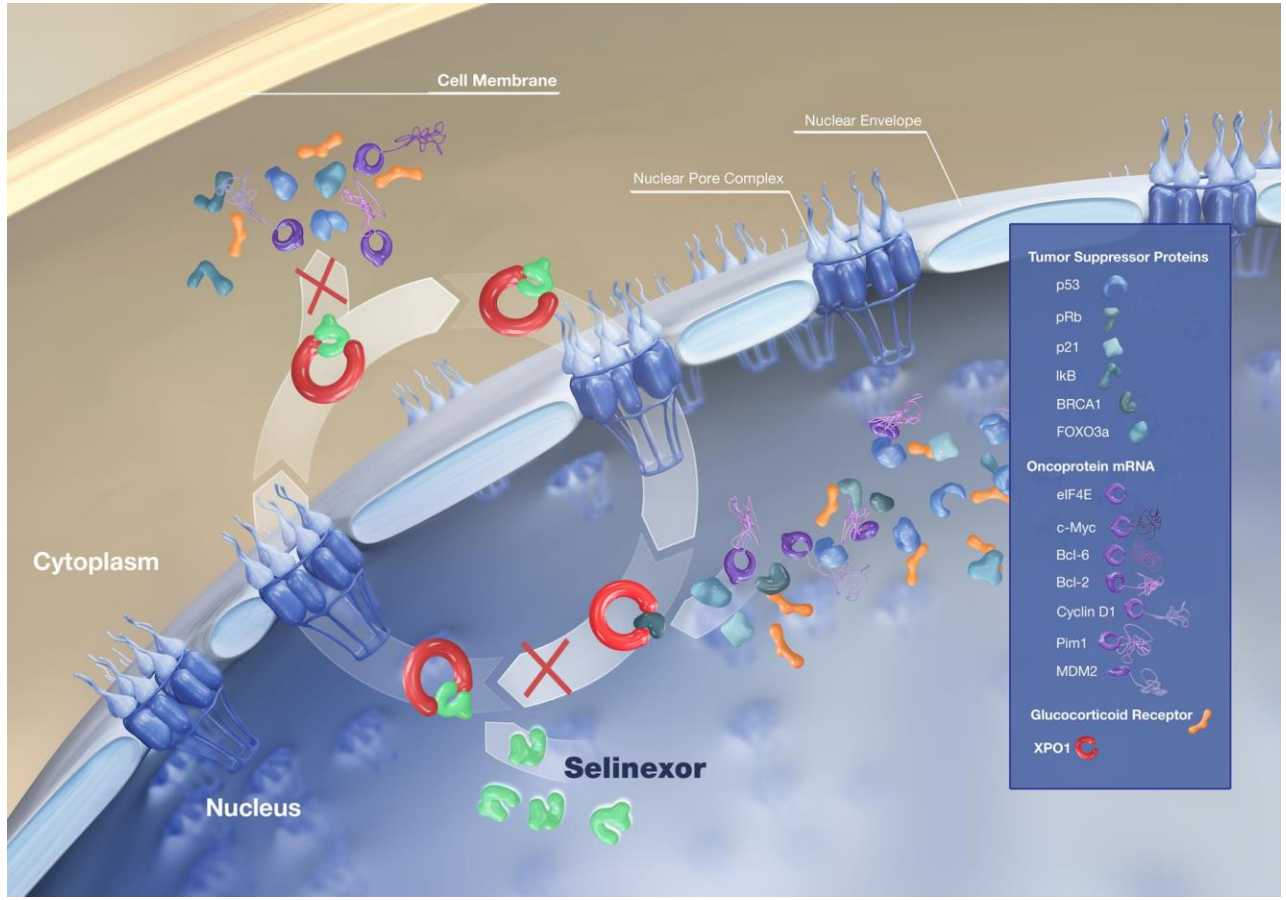
Selinexor: First-in-Class, Oral Selective Inhibitor of Nuclear Export and Reactivates Tumor Suppressor Proteins

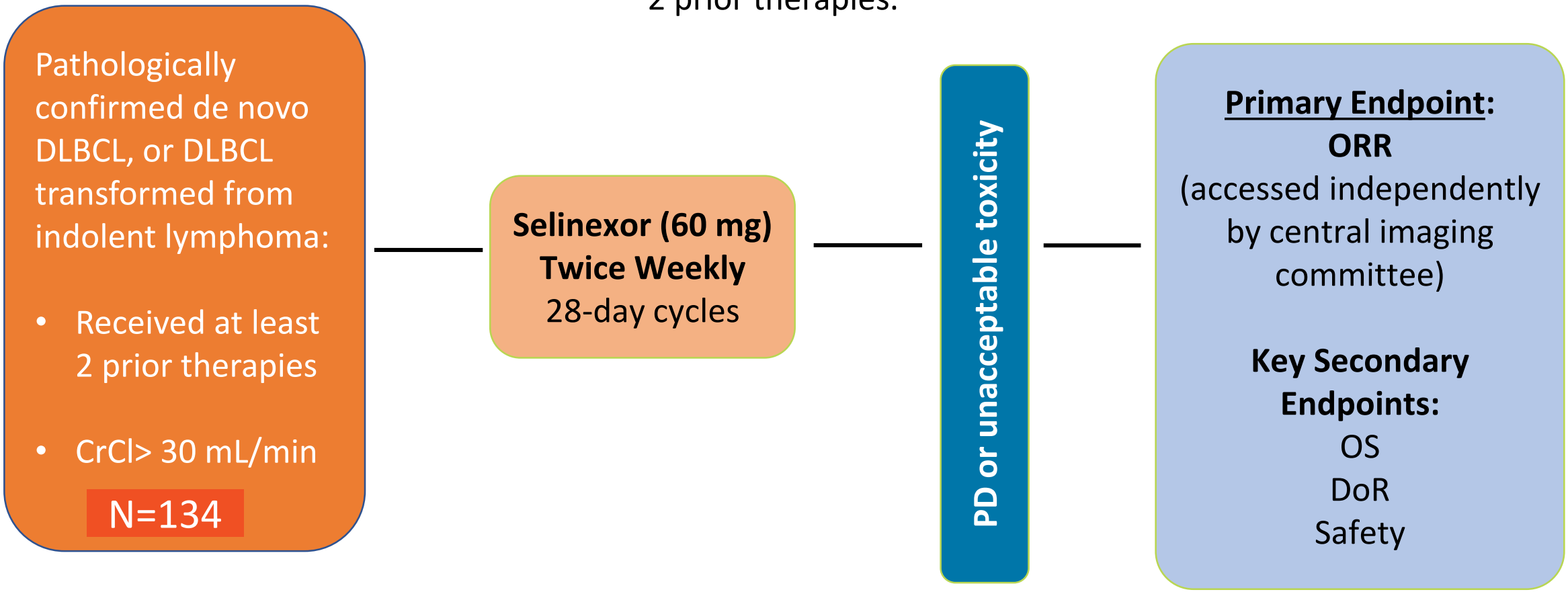


- Selinexor selectively binds and inactivates exportin 1 (XPO1)
  - Forcing the **nuclear retention and reactivation of cell cycle regulators** such as p53, FOXO, IkB, and Rb
  - **Reducing oncoproteins** known to play critical roles in NHL (c-Myc, Bcl2, Bcl6, BclXL)
  - XPO1 overexpression in DLBCL **correlates with poor prognosis**
  - Selinexor in combination with dexamethasone (Sd) has been approved by the FDA for patients with relapsed / refractory multiple myeloma.

Selinexor, oral, single agent, is approved by the FDA for the treatment of patients with relapsed or refractory DLBCL, de novo or transformed from follicular lymphoma after ≥2 prior therapies

SADAL Trial Design

SADAL Trial: 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, and having received at least 2 prior therapies.



DoR = duration of response, OS = overall survival, PD = progressive disease, ORR= overall response rate.

SADAL Overall Efficacy Results

	Response per IRC [a], (n=134)	Median DOR per IRC, months (95% CI)[c] (n=39)
Overall Response Rate (ORR)[b], (95% CI)	**39 (29.0)** (22.0, 38.0)	**9.3** (4.9, NE)
Complete Response (CR), n (%)	18 (13.0)	23.0 (10.4, NE)
Partial Response (PR), n (%)	21 (15.7)	4.4 (1.9, NE)
Stable Disease (SD), n (%)	11 (8.2)	--
Progressive Disease (PD) / Not Evaluable (NE), n (%)	84 (62.7)	--

- Median time to PR or better: 8.1 weeks (range: 6.7 – 16.4)

a. Responses were adjudicated according to the Lugano 2014 Criteria (Cheson BD, et al. *J Clin Oncol*. 2014;32(27):3059-3068. doi: 10.1200/JCO.2013.54.8800) by an Independent Radiologic Committee (IRC) and confirmed by an Independent Oncologist Reviewer. The Deauville criteria (a 5-point scale) was used to grade response using PET-CT. PET-CT results were prioritized over CT results.
b. Includes CR + PR.
c. Median follow up 11.1 months
XPOVIO® [package insert]. Cambridge, MA: Karyopharm Therapeutics, Inc.; 2020; Unpublished data.

Methods: Subset Analysis based on Renal Function

We performed post-hoc analyses of the SADAL study to determine if there are differences in efficacy and safety among patients by baseline renal function, defined as patients with creatinine clearance (CrCl) ≤60 mL/min vs. >60 mL/min.

Total Patients Enrolled	**N=134**
CrCl ≤60 mL/min	**N=37 (28%)**
CrCl >60 mL/min	**N=97 (72%)**

Baseline and Disease Characteristics by Renal Group

	CrCl ≤60 mL/min (n=37)	CrCl >60 mL/min (n=97)
Median Age, Years (range)	**74** (52, 91)	**65** (35, 83)
Median CrCl at Baseline, (range)	**48.5** (6, 60)	**85.3** (61, 180)
Male, n (%)	**14** (37.8)	**65** (67.0)
Female, n (%)	**23** (62.2)	**32** (33.0)
DLBCL Type, n (%)		
De novo	**29** (78.4)	**74** (76.3)
Transformed	**8** (21.6)	**23** (23.7)
DLBCL Subtype, n (%)		
GCB	**15** (40.5)	**48** (49.5)
non-GCB	**21** (56.8)	**45** (46.4)
Non-Classified	**1** (2.7)	**4** (4.1)
Number of Prior Regimens, Median (range)	**2** (2-5)	**2** (2-5)
Prior ASCT, n (%)	**13** (35.1)	**50** (51.5)

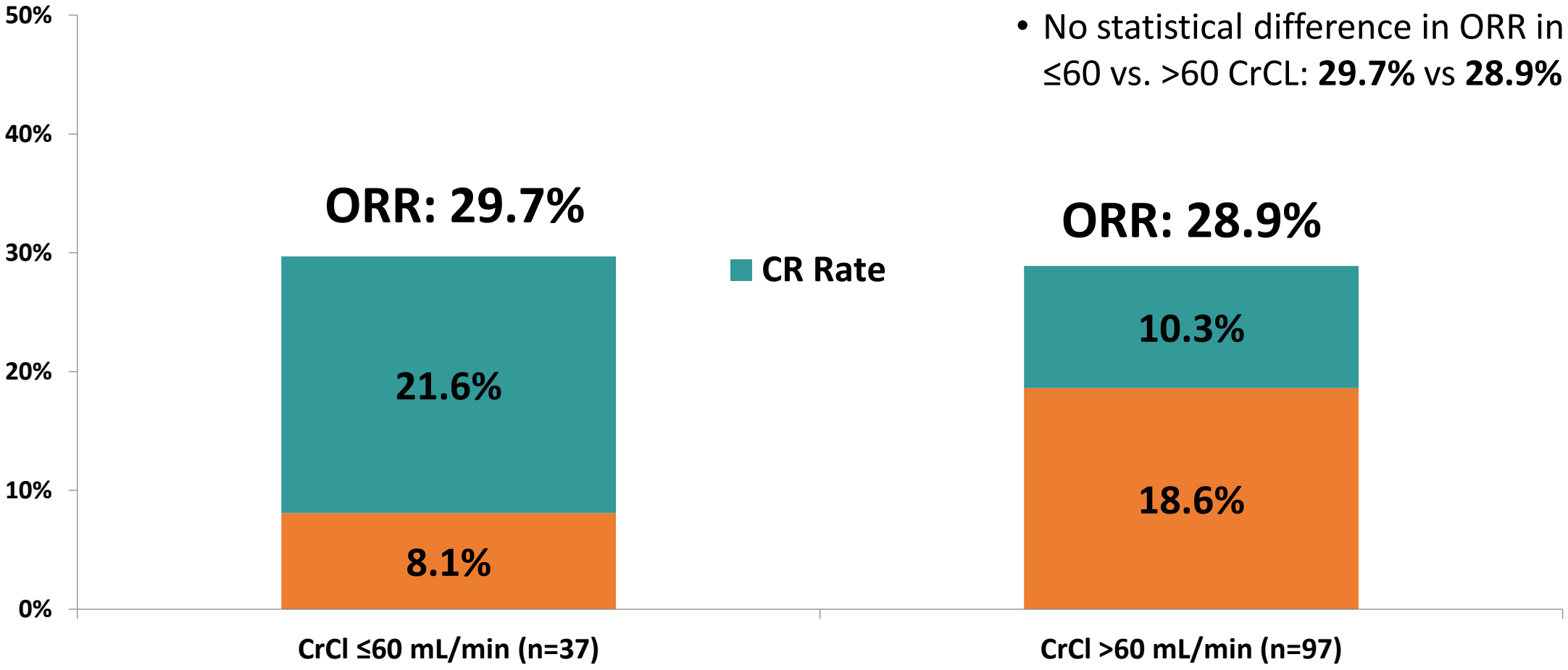
Related Adverse Events, ≥10% Overall

Adverse Events, ≥10% overall	CrCl ≤60 mL/min (n=37)	CrCl >60 mL/min (n=97)
Thrombocytopenia	21 (56.8)	51 (52.6)
Nausea	19 (51.4)	50 (51.5)
Fatigue	14 (37.8)	36 (37.1)
Decreased Appetite	12 (32.4)	34 (35.1)
Anemia	17 (45.9)	27 (27.8)
Neutropenia	10 (27.0)	31 (32.0)
Vomiting	12 (32.4)	23 (23.7)
Weight Decreased	9 (24.3)	20 (20.6)
Diarrhea	11 (29.7)	17 (17.5)
Asthenia	7 (18.9)	14 (14.4)
Constipation	3 (8.1)	11 (11.3)
Dizziness	5 (13.5)	8 (8.2)
Patients with ≥1 Serious Adverse Event	**8 (21.6)**	**20 (20.6)**

- The incidence of treatment-related AEs was comparable between both groups: The most common grade ≥3 treatment-related AEs for patients with reduced versus normal CrCl were thrombocytopenia (45.9% vs. 38.1%), nausea (5.4% vs. 6.2%), and fatigue (8.1% vs. 11.3%).
- There was no clinically significant increase in treatment-related serious adverse events (21.6% vs. 20.6%) and adverse events leading to discontinuation (10.8% vs. 7.2%) in patients with reduced or normal CrCl, respectively.

Efficacy – ORR, OS

- No statistical difference in ORR in patients ≤60 vs. >60 CrCL: **29.7%** vs **28.9%** (p=0.999)



Renal Group	n	OS, median (months)
CrCl ≤60 mL/min	37	**7.8**
CrCl >60 mL/min	97	**9.1**

Conclusions

- Selinexor had **similar response rates in patients regardless of severity of renal function**.
  - Treatment with selinexor demonstrated a similar ORR in patients with a baseline reduced CrCl (**29.7%**) vs normal CrCl (**28.9%**)
  - The OS was comparable in reduced vs normal renal patients: **7.8** vs **9.1** months
  - Selinexor is effective in de novo DLBCL (26.2% ORR) or transformed lymphoma patients (38.7% ORR)
- The incidence of treatment-related **AEs was comparable between both groups**

Oral Selinexor is approved and important option for patients with relapsed DLBCL including patients with renal dysfunction