



ROCKBRUTINIB, A NOVEL BTK INHIBITOR, DEMONSTRATES SAFETY AND EFFICACY IN RELAPSED/REFRACTORY NON-GCB DIFFUSE LARGE B CELL LYMPHOMA

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INTRODUCTION

Approximately 40% of patients with diffuse large B-cell lymphoma (DLBCL) either fail to respond to initial standard therapy or experience a relapse, resulting in a dismal prognosis. Non-germinal center B-cell-like (GCB) DLBCL has an even worse outcome. The early data of covalent bruton's tyrosine kinase inhibitor (cBTKi) in R/R non-GCB DLBCL showed an overall response rate (ORR) of 20-40%. Rocbrutinib (LP-168) is a highly selective, new-generation BTKi with superb bioavailability and unique dual binding mode: covalent binding, otherwise non-covalent with C481 mutation.

AIM

To evaluate the safety and efficacy of Rocbrutinib monotherapy in the R/R non-GCB DLBCL following ≥ 2 prior lines of therapy of an ongoing phase 1 study (NCT04993690) in B-cell malignancies

METHOD

- Patients with R/R non-GCB DLBCL after ≥ 2 prior lines of therapy including ≥ 1 anti-CD20 antibody-containing regimen were enrolled
- Adverse events (AEs) were graded using CTCAE v5.0 and responses of patients with R/R non-GCB DLBCL were assessed per Lugano 2014

RESULTS

Patient Characteristics

- Between 30 July 2021 and 31 May 2024, 33 R/R non-GCB DLBCL were enrolled and efficacy evaluable
- Subjects were dosed at 100mg (n=2), 150mg (n=23), 200mg (n=6) and 300mg (n=2) QD respectively till progressive disease or unacceptable toxicities
- Baseline characteristics are summarized in Table 1

Table 1. Baseline Characteristics of Subjects (N=33)

Characteristics	All subjects (N=33)
Age, median (range), years	59 (21-73)
Gender, n (%)	
Male	20 (60.6)
Female	13 (39.4)
ECOG performance status, n (%)	
0	4 (12.1)
1	29 (87.9)
Stage (Lugano), n (%)	
Stage I-II	9 (27.3)
Stage III	7 (21.2)
Stage IV	17 (51.5)
IPI at study entry, n (%)	
0~1	7 (21.2)
2	9 (27.3)
3	11 (33.3)
4~5	6 (18.2)
No. of prior therapies, median (range)	2 (2-5)
2	23 (69.7)
≥ 3	10 (30.3)
Bulky disease (> 5cm), n (%)	10 (30.3)
Prior CD20 antibody-based therapy, n (%)	33 (100)
Prior BTKi exposure, n (%)	8 (24.2)
Refractory to any previous therapy, n (%)	29 (87.9)
Refractory to last previous therapy, n (%)	28 (84.8)

Safety

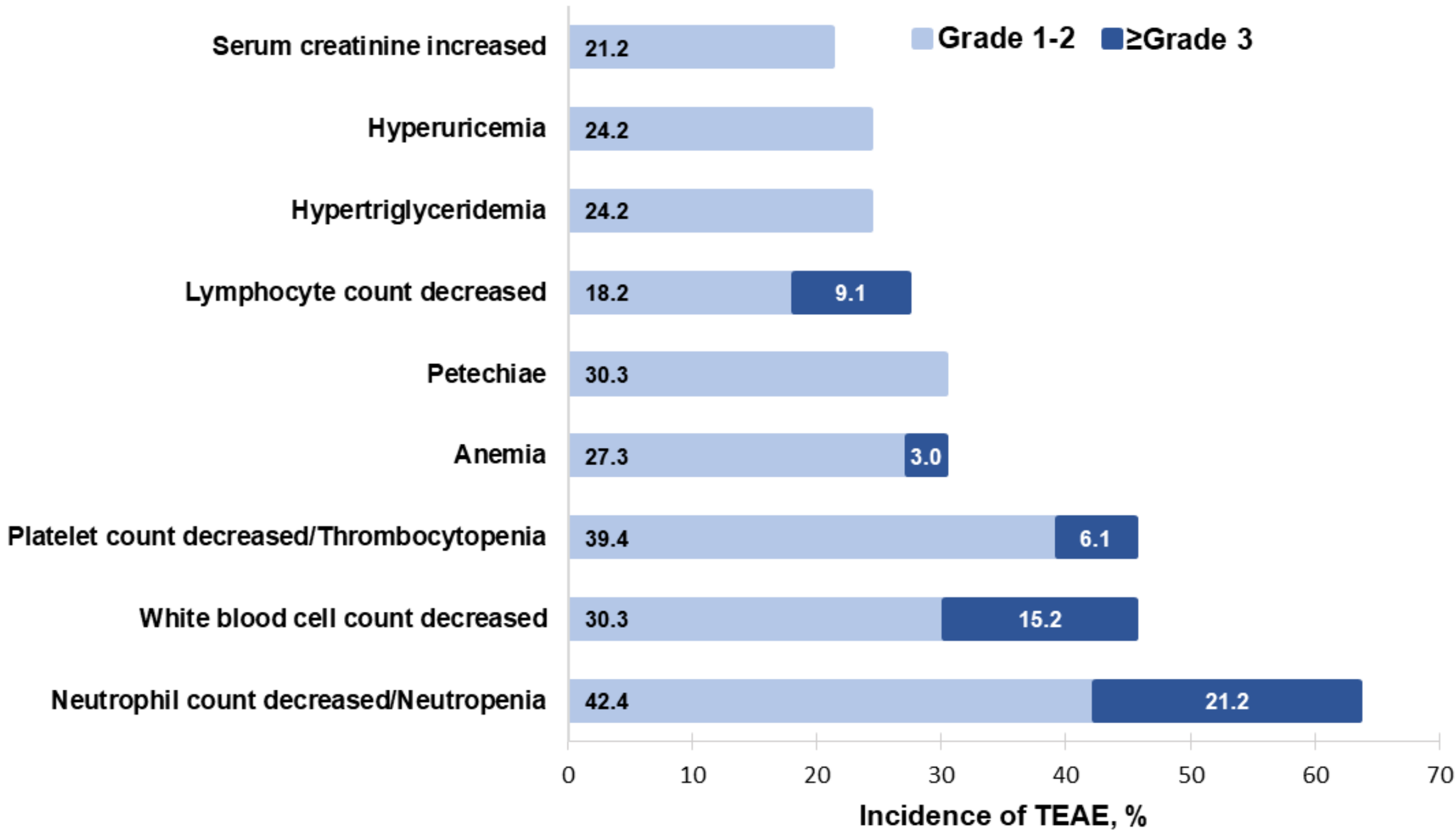
- Grade 3 or higher Treatment Emergent Adverse Events (TEAE) were seen in 14 (42.4%) subjects
- Serious AE (SAE) (lung infection, Grade 3) occurred in 2 (6.1) subjects
- Dose interruptions due to AE occurred in 8 subjects (24.2%), but no AE had led to dose adjustment or drug discontinuation
- AE leading to death was reported for one patient (lung infection, not related to rocbrutinib)

Table 2. Overview of Adverse Events (N=33)

Adverse Event, n (%)	N=33
TEAE of Any Grade	32 (97.0)
Grade ≥ 3 TEAE	14 (42.4)
SAE	2 (6.1)
AEs leading to dose interruption	8 (24.2)
AEs leading to dose adjustment	0
AEs leading to drug discontinuation	0
Grade 5 TEAE	1 (3.0)

- The most common TEAEs occurring in $\geq 20\%$ subjects neutrophil count decreased or neutropenia, white blood cell count decreased, platelet count decreased or thrombocytopenia, anemia, petechiae, lymphocyte count decreased, hypertriglyceridemia, hyperuricemia and serum creatinine increased, most of which were Grade 1

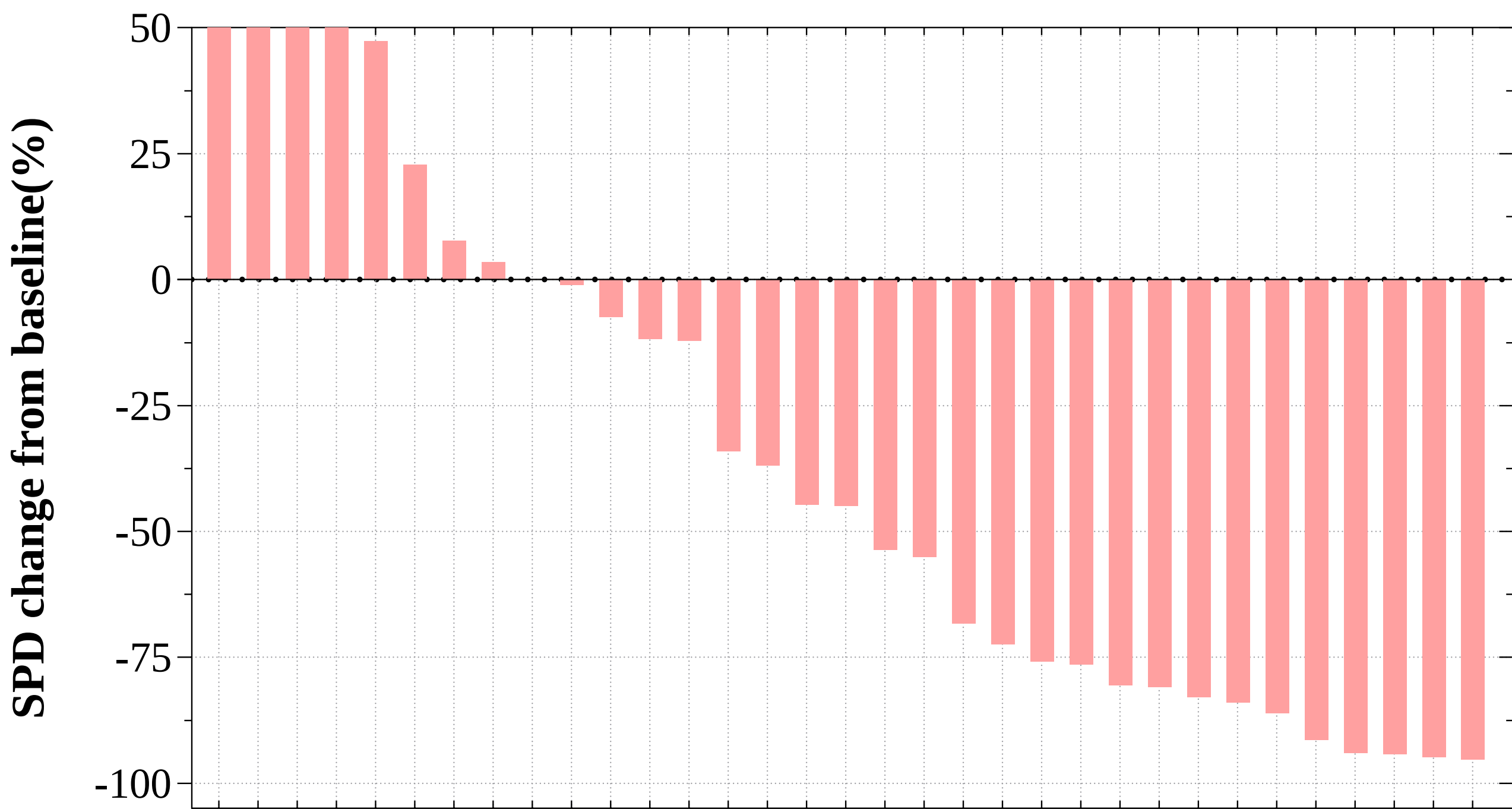
Figure 1. Common TEAEs (incidence $\geq 20\%$)



Efficacy

- Of 33 efficacy evaluable patients with median follow-up of 6.7 months (range: 1.8-26.9), 20 (60.6%) achieved response including 11 (33.3%) complete response (CR). Overall response rates are shown in Table 3
- For the 10 patients who had received ≥ 3 lines of therapy previously, the ORR and CR rate was 90% and 50%, respectively.
- The response rate of rocbrutinib in patients refractory to last prior therapy (n=28) was 57.1%, with CR rate of 28.6%
- The median time to response (TTR) was 2 (range 1-2)
- As of data cut-off, duration of response (DOR), progression-free survival (PFS), and overall survival (OS) are not mature yet

Figure 2. SPD change from baseline of non-GCB DLBCL patients (N=33)



CONCLUSIONS

- Rocbrutinib has demonstrated a high CR and response rate in heavily pre-treated R/R non-GCB DLBCL with favorable safety profiles
- Based on the encouraging data, China CDE (center of drug evaluation) granted rocbrutinib breakthrough therapy designation for the treatment of patients with non-GCB DLBCL who have received at least 2 lines of prior therapies
- Further development of rocbrutinib as monotherapy and in combination with other anti-tumor treatment is ongoing

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