Phase I/II Study Evaluating the Safety and Preliminary Efficacy of Amulirafusp Alfa (IMM0306) in Combination with Lenalidomide in Patients with Relapsed/ Refractory CD20-Positive Follicular Lymphoma

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INTRODUCTION

- Follicular lymphoma (FL) , the second most common type of non-Hodgkin lymphoma(NHL), is characterized by a relapsing and incurable course, usually requiring multiple lines of therapy and disease control remains largely insufficient with conventional chemo- immunotherapy.
- The length of progression-free survival (PFS) with subsequent treatments sharply decreases after the first relapse. The unmet medical needs for patients with rrFL remain to improve durability and tolerability.
- Amulirafusp alfa (IMM0306) consists of anti-CD20 mAb fused with the CD47 binding domain of signal regulatory protein α (SIRPα). It exerts potent anti-cancer efficacy by activating both macrophages and NK cells via blockading of CD47- SIRPα interaction and FcγR engagement.
- The study is to investigate the efficacy and safety of IMM0306 in combination with Lenalidomide in rrFL failed to at least one line of chemoimmunotherapy.

AIM

- The primary endpoint was investigator-assessed objective response rate (ORR).
- Secondary endpoints included PFS, safety, and pharmacokinetics/pharmacodynamics (PK/PD).

METHOD

- Patients with CD20-positive FL (grade 1-3a) and requiring treatment after ≥ 1 prior systemic therapy including an anti-CD20 mAb, were enrolled in this open-label, multi-center phase I/II study (NCT05771883).
- Amulirafusp alfa (1.6 mg/kg) was intravenously administered QW up to 2 years with lenalidomide 20 mg po QD Cycle 1 to 12 on Days 1 to 21 in each 28-day cycle in phase II study.
- Safety was evaluated per CTCAE version 5.0.
- Tumor assessments performed by Lugano 2014.

RESULTS

As of July 10, 2025, 38 patients with FL were enrolled in phase II.

- Median age was 54 years with 57.9% males.
- 42.1% intermediate- or high-risk FLIPI; 92.1% stage III-IV disease; and 26.3% with positive bone marrow involvement.
- 52.6% were refractory to prior anti-CD20 mAb, defined as no response to or progression within 6 months of completion of the last dose of anti-CD20 mAb therapy.

Table 1. Baseline Characteristics

Baseline Characteristic	Patients (N=38)
Age, years	
Median (range)	54 (32-74)
Gender, n (%)	
Male	22 (57.9)
Female	16 (42.1)
ECOG PS, n (%)	
0	18 (47.4)
1	20 (52.6)
Intermediate- or high-risk FLIPI, n (%)	16 (42.1)
Ann Arbor stage III-IV, n (%)	35 (92.1)
Bulky disease (≥7cm), n (%)	3 (7.9)
Refractory to previous anti-CD20 therapy	20 (52.6)
Positive Bone marrow involvement, n (%)	10 (26.3)
Histology, n (%)	
Grade 1 or 2	25 (65.8)
Grade 3a	13 (34.2)
Prior systemic anti-cancer therapy, n (%)	
Median (range)	1 (1-5)

EFFICACY

- 34 patients were efficacy-evaluable in phase II. The CR rate, and ORR were 67.6% and 91.2%, respectively.
- With median follow-up of 9.02 months, the median PFS was not reached, the PFS rate at 6 months was 91.2% (95% CI, 75.1-97.1).

Table 2. Efficacy

	CD20-refractory (N=18)	Total (N=34)
ORR, n (%)	**16 (88.9)**	**31 (91.2)**
CR, n (%)	12 (66.7)	23 (67.6)
PR, n (%)	4 (22.2)	8 (23.5)
PFS, months, median (95% CI)	**NR (NR, NR)**	**NR (NR, NR)**
6-month rate,%	88.9 (62.4, 97.1)	91.2 (75.1, 97.1)

Figure 1. Swimmer Plot for Duration of Response

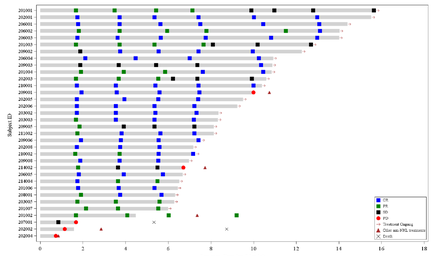
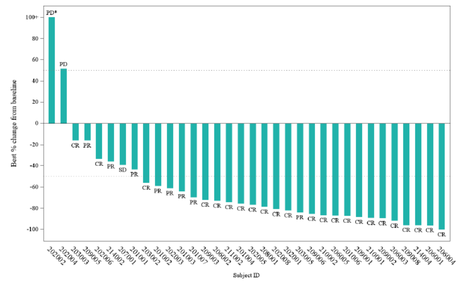


Figure 2. Best Percentage Change in Target Lesion



SAFETY

- The safety-evaluable population included 47 FL patients, of whom 9 patients were in phase Ib and 38 patients were in phase II.
- 44 (93.6%) patients had Grade ≥3 treatment related adverse events (TRAEs) .
- 11 (23.4%) patients had Treatment-related serious adverse events (SAEs).
- 2 (4.3%) patients experienced TRAE leading to the study drug discontinuation, one patient due to Type I hypersensitivity and one patient (discontinued lenalidomide only).
- No TRAE led to death.
- The most frequent TRAEs (≥ 20%) were neutrophil count decreased, white blood cell count decreased, platelet decreased, and anemia, lymphocyte count decreased, infusion-related reactions, blood bilirubin increased, upper respiratory tract infection, hypoalbuminaemia, and asthenia.

Table 3. Overview of TRAEs

Overview of TRAE, n(%)	Patients (N=47)
All grade TRAE	47 (100.0)
≥ G3 TRAE	44 (93.6)
TRAE leading to dose reduction	21 (44.7)
TRAE leading to amulirafusp alfa dose reduction	10 (21.3)
TRAE leading to lenalidomide dose reduction	21 (44.7)
Treatment-related SAE	11 (23.4)
TRAE leading to treatment discontinuation	2 (4.3)
TRAE leading to death	0

Table 4. TRAEs Occurred in ≥ 20% Patients

TRAE, n(%)	Patients (N=47)	
	All Grades	Grade 3-4
Neutrophil count decreased	38 (80.9)	29 (61.7)
White blood cell count decreased	36 (76.6)	20 (42.6)
Platelet decreased	33 (70.2)	10 (21.3)
Anemia	28 (59.6)	0
Lymphocyte count decreased	26 (55.3)	20 (42.6)
Infusion-related reactions	16 (34.0)	0
Blood bilirubin increased	15 (31.9)	0
Upper respiratory tract infection	11 (23.4)	1 (2.1)
Hypoalbuminaemia	11 (23.4)	0
Asthenia	10 (21.3)	1 (2.1)

CONCLUSIONS

Amulirafusp alfa in combination with lenalidomide showed a high rate of response and a well-tolerated safety profile in patients with R/R FL. This phase I/II study is still ongoing.

CONTACT INFORMATION

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