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623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Subgroup Analysis from a Phase 2, Single-Arm Trial of the Oral PI3Kδ Inhibitor Linperlisib in Patients with Relapsed or Refractory Follicular Lymphoma

Tingyu Wang[1], Xiuhua Sun[2], Lihua Qiu[3], Hang Su[4], Junning Cao[5], Zhiming Li[6], Yuqin Song, MD[7], Li Zhang[8], Dengju Li[9], Huijing Wu, MD[10], Wei Zhang[11], Junmin Li[12], Keshu Zhou, MD[13], Hui Zhou[14], Yu Yang[15], Zhifeng Li[16], Hong Cen[17], Zhen Cai[18], Zhihui Zhang, MD[19], Weijun Fu[20], Jie Jin IV[21], Fei Li[22], Weixin Wu[23], Xuekui Gu[24], Weiliang Zhu[25], Lihong Liu[26], Zengjun Li[27], Shuhua Yi[28], Hanying Bao[29], Zusheng Xu[29], Lugui Qiu[1,30]

[1] State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology& Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, China
[2] The Second Hospital of Dalian Medical University, Dalian, China
[3] Tianjin's Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, National Clinical Research Center for Cancer, Tianjin Medical University Cancer Institute and Hospital, Tianjin Medical University, Tianjin, China
[4] 307 Hospital Affiliated To the Academy of Military Medical Sciences, Beijing, CHN
[5] Department of Lymphoma, Fudan University Shanghai Cancer Center, Shanghai, China
[6] State Key Laboratory of Oncology in South China, Guangzhou, China
[7] Department of Lymphoma, Key laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital & Institute, BEIJING, China
[8] West China Hospital, Sichuan University, Chengdu, China
[9] Department of Hematology, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China
[10] Hubei Cancer Hospital, Wuhan, China
[11] Chinese Academy of Medical Sciences & Peking Union Medical College, Department of Hematology, Beijing, China
[12] Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China
[13] Department of Hematology, Cancer Hospital Affiliated to Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China
[14] Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China
[15] Fujian Provincial Cancer Hospital, The Affiliated Tumor Hospital of Fujian Medical University, Fuzhou, China
[16] Department of Hematology, The First Affiliated Hospital of Xiamen University and Institute of Hematology, School of Medicine, Xiamen University, Xiamen, Xiamen, China
[17] Affiliated Tumor Hospital of Guangxi Medical University, Nanning, China
[18] Bone Marrow Transplantation Center, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China
[19] Sichuan Cancer Hospital and Institute, Chengdu, China
[20] Shanghai Fourth People's Hospital, School of Medicine, Tongji University, Shanghai, China
[21] The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China
[22] The First Affiliated Hospital of Nanchang University, Nanchang, China
[23] Zhongshan Hospital, Xiamen University, Xiamen, China
[24] Department of Hematology, The First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China
[25] Zhujiang Hospital of Southern Medical University, Guangzhou, China
[26] The Fourth Hospital of Hebei Medical University, Shijiazhuang, China

[27] State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences & Peking Union Medical Colleg, Tianjin, China
[28] Tianjin Institutes of Health Science, Tianjin, China
[29] Shanghai Yingli Pharmaceutical Co., Ltd., Shanghai, China
[30] State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Haihe Laboratory of Cell Ecosystem, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences&Peking Union Medical College, Tianjin, China

Background
In our previous phase 2 trial (NCT04370405), linperlisib, an oral phosphatidylinositol 3-kinase delta (PI3Kδ) inhibitor, demonstrated encouraging activity and manageable safety in adult patients with relapsed/refractory (R/R) follicular lymphoma (FL) who had received at least 2 prior systemic therapies. It's crucial to note that FL patients with bone marrow involvement (BMI) generally present more unfavorable prognosis. Here, we present a subgroup analysis from this phase 2 study, which is specifically focused on BMI at baseline.
Methods
Details of the trial design and study population have been previously reported. In brief, eligible patients (age > 18 years; histologically confirmed relapsed or refractory FL; disease progression post at least 2 prior systemic therapies) received 80 mg linperlisib tablets daily in a 28-day cycle, until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) assessed by independent review committee (IRC); secondary endpoints included the duration of response (DOR), disease control rate (DCR), progression free survival (PFS), overall survival (OS) and safety profile. For this subgroup analysis, patients were grouped based on the presence or absence of BMI at baseline. For those with baseline BMI, biopsies were evaluated to confirm complete responses. Evaluations of antitumor response were conducted every 2 treatment cycles, following the guidelines of the International Research Working Group.
Results
As previously reported, 84 patients included in the full analysis set (FAS). By subgroup, 25 had baseline BMI and 59 did not. Baseline characteristics by subgroup are shown in Table 1.
In this subgroup analysis, a trend toward higher response rate was seen in R/R FL patients with BMI compared to those without such involvement: ORR based on IRC assessment was 88.0% vs 76.3%; best overall response (BOR) of CR was 24.0% vs 11.9%; BOR of PR was 64.0% vs 64.4%. Patients with BMI had DCR that was consistent with those without BMI (92.0% vs 93.2%). The median DOR and PFS were similar across this subgroup (DOR: 11.7 months vs 13.0 months; PFS: 13.3 months vs 13.7 months) (Table 2). Although the median OS was not reached, 12-month OS rates for patients with and without BMI was 91.7% and 91.5%, respectively (Table 2).
Safety was evaluated in all R/R FL patients who had received ≥1 dose of linperlisib. Rates of any-grade treatment-related adverse events (TRAEs) were similar across this subgroup and comparable with the overall population (Table 2). When compared to the overall population, patients without BMI experienced fewer grade ≥3 TRAEs, while a marginally higher incidence of grade ≥3 TRAEs was observed in patients with BMI (Table 2).
Conclusions
This subgroup analysis indicated that linperlisib is an effective and well-tolerated treatment option for patients with R/R FL, irrespective of BMI. Although minor differences were observed in this subgroup, their significance is limited due to the small sample sizes and probably do not alter the overall clinical benefit of linperlisib. Nevertheless, these findings warrant further investigation.

Disclosures Fu: *Takeda Pharmaceutical Company Limited.:* Research Funding; *Shanghai Changzheng Hospital:* Other: WJF is a former staff of Shanghai Changzheng Hospital and now is a staff of Shanghai Fourth People's Hospital affiliated to Tongji University. .

Table 1 Demographic and disease characteristics

Characteristics	With BMI N=25	Without BMI N=59	All patients N=84
Age, median (range), years	51.0 (34.0-78.0)	50.0 (29.0-78.0)	51.0 (29.0-78.0)
Sex, n (%)			
Female	15 (60.0)	15 (25.4)	30 (35.7)
Male	10 (40.0)	44 (74.6)	54 (64.3)
Cotswolds-modified Ann Arbor stage, n (%)			
I	0 (0.0)	1 (1.7)	1 (1.2)
II	0 (0.0)	5 (8.5)	5 (6.0)
III	0 (0.0)	20 (33.9)	20 (23.8)
IV	24 (96.0)	30 (50.8)	54 (64.3)
Relapsed/ Refractory status, n (%)			
Relapsed	12 (48.0)	27 (45.8)	39 (46.4)
Refractory & Relapsed	8 (32.0)	23 (39.0)	31 (36.9)
Refractory	5 (20.0)	9 (15.3)	14 (16.7)
Prior lines of therapy, n (%)			
≥ 3	19 (76.0)	46 (78.0)	65 (77.4)
< 3	6 (24.0)	13 (22.0)	19 (22.6)
Prior radiation, n (%)	4 (16.0)	11 (18.6)	15 (17.9)

BMI, bone marrow involvement

Table 2 Efficacy and safety by subgroup

	With BMI	Without BMI	All patients
Efficacy			
DOR[a], % (95% CI)	N=22	N=45	N=67
6 mo	72.7 (46.3, 87.6)	82.9(67.5, 91.5)	80.0 (67.4, 88.1)
12 mo	43.2 (18.0, 66.3)	60.6(42.9, 74.3)	55.3 (40.6, 67.8)
Median, months	11.7 (3.0, NE)	13.0(9.2, NE)	12.2 (9.2, 15.9)
PFS[a], % (95% CI)	N=25	N=59	N=84
6 mo	80.6 (56.1, 92.3)	77.9 (64.4, 86.8)	78.6 (67.5, 86.3)
12 mo	50.2 (25.2, 70.9)	53.9 (38.9, 66.7)	53.1 (40.3, 64.3)
Median, months	13.3 (8.8, NE)	13.7 (9.1, 16.6)	13.3 (11.0, 16.6)
OS[b], % (95% CI)	N=25	N=59	N=84
6 mo	95.8(73.9, 99.4)	98.3 (88.6, 99.8)	97.6 (90.7, 99.4)
12 mo	91.7(70.6, 97.8)	91.5 (80.8, 96.4)	91.6 (83.1, 95.9)
Median, months	NE (25.9, NE)	NE (NE, NE)	NE (NE, NE)
Safety, n (%)	N=25	N=59	N=84
Any-grade TRAEs	24 (96.0)	55 (93.2)	79 (94.0)
Grade ≥3 TRAEs	16 (64.0)	30 (50.8)	46 (54.8)

a: data for DOR and PFS was cutoff on October 26, 2021; b: data for OS was cutoff on April 30, 2023.

BMI, bone marrow involvement; NE, not evaluable; TRAEs, treatment-related adverse events.

Figure 1

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