A novel and selective oral PI3Kα/δ inhibitor, TQ-B3525, in patients with relapsed and/or refractory follicular lymphoma: A phase II, single-arm, open-label study.

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Background: TQ-B3525 is a novel and selective oral PI3K α/δ inhibitor. In an earlier Phase I trial, TQ-B3525 achieved outstanding efficacy in subjects with refractory/relapsed follicular lymphoma (R/R FL) (2020 ASCO Abstract #8058). Here, we report the result from a single-arm, open-label, phase II registration study evaluating the safety and efficacy of TQ-B3525 in R/R FL patients. **Methods:** This phase II study included exploratory stage 1 and confirmatory stage 2. Patients with R/R FL after ≥2 lines therapies received oral 20 mg TQ-B3525 once daily in a 28-day cycle until disease progression or intolerable toxicity. Primary endpoint was independent review committee (IRC)-assessed objective response rate (ORR). Secondary endpoints were ORR by investigator assessment; the IRC- and investigator-assessed disease control rate (DCR), time to response (TTR), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety. **Results:** Based on results (ORR, 88.0%; DOR, 11.8 months; PFS, 12.0 months) in 25 patients at stage 1, second stage study was initiated and included 82 patients for efficacy/safety analysis.Patients received a median of 3 prior lines, with 56.1% refractory to previous therapies; 73.2% experienced POD24 at baseline. At stage 2, ORR was 86.6% (71/82; 95% CI, 77.3%-93.1%), with 28 (34.2%) complete responses. Seven (8.5%) had stable disease for DCR of 95.1%. Median TTR was 1.8 months. Among 71 responders, median DOR was not reached; 18-month DOR rate was 51.6%. At median follow-up of 13.3 months, median PFS was 18.5 (95% CI, 10.2-not estimable) months; estimated 24-month OS rate was 86.1%. Response rates and survival data were consistent across all subgroups. Grade 3 or higher treatment-related adverse events occurred in 63 (76.8%) patients, with neutrophil count decreased (22.0%), hyperglycemia (19.5%), and diarrhea (13.4%) being common. **Conclusions:** TQ-B3525 exhibited favorable efficacy and manageable safety profiles, supporting its potential as a valuable treatment modality for heavily pretreated Chinese R/R/ FL patients. Clinical trial information: NCT04324879. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd. (Nanjing, China); National Natural Science Foundation of China; 81872902, 82073917, and 82070206; National Natural Science Foundation of Guangdong Province; 2023A1515011525; the Lymphoma Research Fund of China Anti-Cancer Association; the Sun Yat-sen University Cancer Center Clinical Research 308 Program; 2014-fxy-106 and 2016-fxy-079; Tianjin Key Medical Discipline (Specialty) Construction Project; TJYXZDXK-053B.

Summary of TQ-B3525 efficacy in the ITT at stage 2.

Efficacy	IRC-Assessed (n=82)	Investigator-Assessed (n=82)
Median DOR#, months (95% CI)	NR (9.2-NE)	14.8 (9.2-20.4)
12-month DOR rate (%, 95% CI)	60.2% (44.3%-72.9%)	51.5% (36.0%-65.0%)
18-month DOR rate (%, 95% CI)	51.6% (30.6%-69.2%)	41.0% (23.5%-57.7%)
Median PFS, months (95% CI)	18.5 (10.2-NE)	18.4 (11.0-22.0)
12-month PFS rate (%, 95% CI)	58.3% (44.0%-70.1%)	52.8% (38.8%-65.0%)
18-month PFS rate (%,95% CI)	58.3% (44.0%-70.1%)	52.8% (38.8%-65.0%)
Median OS, months (95% CI)	Not reached	
12-month OS rate (%, 95% CI)	91.8% (82.5%-96.3%)	
24-month OS rate (%, 95% CI)	86.1% (72.3%-93.3%)	

Data were presented as n (%) or n (%, 95% confidence interval). NE, not estimable # DOR was assessed in 71 patients achieving responses.