Phase II study of plitidepsin in pretreated patients with locally advanced or metastatic non-small cell lung cancer.

OBJECTIVE: To evaluate the progression-free rate (PFR) at 3 months (13+/−1 weeks), antitumor response, time-to-event efficacy endpoints, and toxicity profile of plitidepsin administered as a 3-h continuous i.v. infusion at a dose of 5mg/m², every 2 weeks, to patients with chemotherapy pretreated advanced non-small cell lung cancer (NSCLC). PATIENTS AND METHODS: This was a multicenter, non-randomized, exploratory, phase II study. Treatment lasted until disease progression, unacceptable toxicity, patient refusal or treatment delay for>2 weeks. PFR (primary efficacy endpoint) and objective response rate (secondary efficacy endpoint) were evaluated according to RECIST, while the toxic profile of plitidepsin was assessed using the NCI-CTC, version 2.0. RESULTS: A total of 21 patients with a median age of 61 years and with locally advanced or metastatic non-resectable NSCLC, who had previously received only one line of chemotherapy in an advanced setting, received a total of 54 cycles of treatment (median of two cycles per patient; range: 1-8). Antitumor activity was seen in 3 (1 PR, 2 SD) out of 17 evaluable patients according to RECIST. One patient was responder for the primary (PFR at 13+/−1 weeks) and secondary efficacy endpoint (stable disease according to RECIST). Other two patients were
non-responders for the primary efficacy endpoint, but had stable disease (not confirmed at weeks 13+/−1 due to previous withdrawal due to adverse events). With a median follow-up of 12.3 months, the median time to progression (TTP) and the median overall survival (OS) were 1.2 months and 4.3 months, respectively. The incidence of plitidepsin-related toxicities was low and most of them were mild-to-moderate in severity. The most common side effects were anemia, and asymptomatic and non-cumulative increases of gamma-glutamyltransferase (GGT) and liver transaminase levels.

CONCLUSION: This study shows that plitidepsin 3-h continuous i.v. infusion (5mg/m²) every 2 weeks, was feasible and well tolerated in patients with pretreated NSCLC. The lack of evidence of antitumor activity precludes further studies with this plitidepsin schedule in this tumor setting.