SAKK 57/16 Nab-Paclitaxel And Gemcitabine in soft tissue sarcoma (NAPAGE): results from the phase Ib part of a phase Ib/II trial

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Abstract: #4465

Background

The outcome for patients with locally advanced or metastatic soft tissue sarcoma (STS) is poor. Following failure from first-line doxorubicin based chemotherapy no standard therapy has been established [1]. Combination treatment with docetaxel/gemcitabine (gem) has emerged as an effective regimen but administration is limited to fit patients only due to the toxicity profile [2,3,4]. However, nanoparticle albumin bound paclitaxel (nab-PC) was designed to avoid the toxicities related to polyethylated castor oil [5,6,7]. In this context, we want to evaluate toxicity and antitumor effect of biweekly nab-PC/gem administration in STS patients.

Methods

We conducted this proof-of-concept phase Ib trial to assess the safety of biweekly nab-PC 150mg/m^2 and gem 1000mg/m^2 administration in the 2nd and 3rd line setting of STS.

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Results

As of 1 April 2019, 6 pts with advanced STS were treated within the phase Ib trial. Three pts were male (50%); median age was 67 yrs (range 44 – 72) (see Table 1). The current total number of biweekly doses received is 29 (median biweekly doses per patient is 5, range 2 – 7). One dose reduction due to skin toxicities occurred. 3 pts remain on study, 3 stopped treatment due to treatment unrelated reasons (refusal, death unrelated to progression or toxicity and investigator's decision). The most common treatment-related AEs were fatigue (3 pts), alopecia (3 pts), and neutropenia (2 pts) (see Table 2). There were no dose-limiting toxicities or discontinuations due to AEs.

Table 1. Patient characteristics (N = 6)

Characteristic	Summary measure *
Age	67 (44 – 72)
Female sex	3 (50%)
ECOG performance status	
0	3 (50%)
1	2 (33%)
2	1 (17%)
Previous chemotherapy	
1st line	6 (100%)
2nd line	0
Sarcoma subtype	
Leiomyosarcoma	3 (50%)
Liposarcoma	1 (17%)
Synovial Sarcoma	1 (17%)
Undifferentiated pleomorphic sarcoma	1 (17%)

* median (range) for continuous variables, frequency (percent) for categorical

Discussion

We were able to confirm the tolerability of the regimen and are currently accruing patients to a prospective single arm phase II trial. Treatment will be given biweekly until progression, unacceptable toxicity or patient withdrawal. Re-staging using contrast-enhanced computer tomography will be performed every 6-12 weeks. The primary endpoint of the trial is progression-free rate (PFR) at 12 weeks. Secondary endpoints are PFS, overall survival adverse events and symptom-specific quality of life. A total of 8 Swiss sites will participate for a total of 37 patients, as required by Simon's two-stage design. The trial is estimated to be completed by end of 2021.

Table 2. Adverse events (N = 6)

Adverse event	Frequency (%)
Fatigue	3 (50%)
Alopecia	3 (50%)
Alanine aminotransferase increased	2 (33%)
Neutrophil count decreased	2 (33%)
Myalgia	2 (33%)
Rash maculo-papular	2 (33%)
Anemia	1 (17%)
Dry mouth	1 (17%)
Nausea	1 (17%)
Edema limbs	1 (17%)
Fever	1 (17%)
Aspartate aminotransferase increased	1 (17%)
White blood cell decreased	1 (17%)
Anorexia	1 (17%)
Pain in extremity	1 (17%)
Peripheral sensory neuropathy	1 (17%)
Hypertension	1 (17%)

Conclusion

These preliminary results indicate that biweekly administration of nab-PC/gem is well tolerated. The phase Ib-established dose and schedule were selected for further evaluation in a phase II trial.

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