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Presentation Abstract

Abstract Number:	A73
Presentation Title:	**A Phase I first-in-human (FIH) study of SAR566658, an anti CA6-antibody drug conjugate (ADC), in patients (Pts) with CA6-positive advanced solid tumors (STs) (NCT01156870)**
Presentation Time:	Sunday, Oct 20, 2013, 12:30 PM - 3:00 PM
Location:	Exhibit Hall C-D
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Abstract Body:	**Background**: SAR566658 (SAR) is a maytansinoid-loaded ADC (huDS6-SPDB-DM4) targeting CA6, a specific glycol-epitope of MUC-1 over-expressed in solid tumors (pancreas 26%, ovary 55%, breast 30%, bladder 60%) and rarely in normal tissues. This FIH study was designed to assess the safety, dose limiting toxicities (DLTs)/recommended dose (RD) and pharmacokinetic following SAR administration in Pts with CA6-expressing STs. Trial is funded by Sanofi. **Methods**: This Phase I study explored escalating intravenous doses of SAR administered as single agent every 3 weeks (q3w). An accelerated dose escalation scheme was used for the two first dose levels (DL), followed by a standard 3+3 dose escalation scheme. **Results**: 34 heavily pretreated Pts were enrolled including: 11M/23F, median age 58 years (range, 32-77), ECOG-PS $\leq$1, with a variety of advanced STs including ovary (13), pancreas (10) and breast (4). A total of 114 cycles (cy), median 2, (range,1-14) of SAR was administered across 9 DLs ranging from 10 to 240 mg/m². DLTs were observed at the highest DL of 240 mg/m² and included grade (Gr) 3 diarrhea at cy1 in 1 Pt and Gr3 keratitis at cy2 in 2 Pts. Anticipated toxicity was cornea, peripheral neuropathy, hematological and pulmonary. So far the number of Pts with these toxicities are:

keratitis (all Gr: 11 Pts, including 2 Pts with Gr3), peripheral neuropathy (5 Pts, no Gr≥3), neutropenia (Gr3, 2 Pts), interstitial pneumonitis (1 Pt). Other than late occurrence of reversible corneal adverse events (AE) at 150 mg/m², no dose-dependent AE was observed. Exposure to SAR (Cmax and AUC) increased with no major deviation from dose proportionality over doses of 20 to 240 mg/m². Clearance was roughly constant over the doses with a low to moderate total variability. SAR 190 mg/m² fulfills the criteria for RD: no DLT and manageable ocular AE versus highest DL. Clinical benefit was observed at doses ≥120 mg/m²: 1 partial response (breast), 1 PR to be confirmed (ovary), 3 stable disease (SD)>6months and 11 SDs were noted. A significant decrease in tumor marker was noted in 1 Pt. **Conclusions**: SAR has a favorable safety profile and encouraging antitumor activity. SAR at 190mg/m² q3w was selected as the RD and is being confirmed in an ongoing extension cohort.

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