Persistent prevention of CIPN using calmangafodipir (PledOx): Results from a placebo-controlled randomized phase II study (PLIANT) in patients with metastatic colorectal cancer (mCRC).

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Abstract Disclosures

Abstract:

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a major problem after oxaliplatin treatment. Calmangafodipir (CaM) has shown promising activities in model systems in preventing oxaliplatin-induced adverse effects. In a dose-escalating phase I study including 11 patients, doses up to 10 μmol/kg were well tolerated and had promising preventive effects on CIPN (Glimelius, MASCC 2015). A randomized placebo-controlled multicenter phase II study (NCT 01619423) assessed safety and efficacy of CaM in ameliorating CIPN. **Methods:** The PLIANT study included 173 mCRC patients treated with the FOLFOX-6 regimen (oxaliplatin 85 mg/m^2, calciumfolinate 200 mg/m^2, 5FU bolus 400 mg/m^2, 5FU infusion 2400 mg/m^2) every fortnight either in first or second-line. Ten minutes prior to each chemotherapy cycle CaM 2 and 5 (initially 10) μmol/kg or placebo was given intravenously during 5 minutes. The primary endpoint was neurotoxicity according to the Oxaliplatin Sanofi Specific Scale (OSSS) each cycle up to cycle 8. Secondary endpoints included the patient reported outcomes Cold Allodynia Test (CAT) and the Leonard Scale (LS) at end-of-treatment (EOT) and during follow-up

(FU) every 3 month (mo), tumor evaluations after 4 and 8 cycles and overall survival (OS). **Results:** CaM was well tolerated. CIPN according to OSSS was clearly less in patients treated with 5 μmol/kg after the 3rd up to the 8th cycle (OR (90%CI) 0.57(1.13), p=0.15). CaM had a dose-dependent and significant effect on persistent CIPN measured as mean sensory score on the LS at 3 and 6 mo FU. See table for further details (**†** p<0.1, * p<0.05, ******p=0.01 vs. placebo). **Conclusions:** The activity of the chemoprotector CaM is promising in preventing acute and persistent CIPN without any detectable negative influence on the antitumor activity of an oxaliplatin-5FU combination in patients with mCRC. A phase III trial using the 5 μmol/kg dose will be initiated. Clinical trial information: NCT 01619423.

Placebo (n=60)	**PledOx 2 μmol (n=57)**	**5 μmol (n=45)**	**5+10 μmol (n=56)**
OSSS ≥2 (OR) 1.00	0.84	0.57	0.55
CAT (EOT) 2.4	1.3†	1.5†	1.6
LS (3 mo) 5.8	2.8	1.9**	1.6**
LS (6 mo) 5.0	2.6	1.4*	1.2**
ORR (%) 27	40*	27	30
OS (mo) >16	>16	>17	>17