**Aim:** PM01183 is a promising new agent. It exerts antitumor activity through inhibition of trans-activated transcription and modulation of tumor microenvironment. PM01183 single-agent recommended dose (RD) is 5 mg D1 & 8 q3wk, with activity observed in PaC and MBC, but limited in pretreated CRC, and reversible myelosuppression as its main dose-limiting toxicity (DLT). Preclinical synergism/additivity in combination with 5FU/XEL was reported, thus prompting this phase I study.

**Methods:** Adult MBC, CRC or PaC pts ≤ 75 years (y) old, with ECOG PS 0-1, adequate major organ function and ≤ 3 prior lines were included following a 3 + 3 design. Dose level (DL) #1 was PM01183 2 mg on D1 & 8 + XEL 1650 mg/m² b.i.d. from D1 to 14 q3wk. The highest DL with < 1/3 of pts having DLTs in Cycle 1 would be the RD. Prior adjuvant XEL was allowed if relapse >6 months after discontinuation.

**Results:** As of 20 April 2014, 14 pts were treated at 2 DLs; 8 (57%) were males, median age: 55 y (r: 35-74), median BSA: 1.9 mg/m² (r: 1.5-2.2). Median prior lines was 1.5 (r: 0-2) and 10 (71%) pts received prior XEL or infusional 5FU. DL#2 (PM01183 3 mg/ D1& 8) was the maximal dose reached, as 2 of 5 evaluable pts had DLT as grade (G)4 neutropenia >3 D or delay of Cycle 2 for >15 D due to neutropenia. DL#1 was expanded to 9 evaluable pts and none had DLT, defining it as the RD. Common G1/2 toxicities across DLs in ≥15% of pts were: nausea, diarrhea, fatigue and HFS. G3 toxicities (other than reversible neutropenia) at any DLs were: anemia, pulmonary embolism, rash and DVT (1 each). One pt had G4 thrombocytopenia; no other G4 toxicities were reported. Antitumor activity: CRC (n = 6): 2 partial responses (PR) and 3 stable diseases for >4 months (SD4); MBC (n = 3): one PR; PaC (n = 4): 2 SD4. Globally 23% response rate (RR) and 62% of 13 evaluable pts had clinically meaningful benefit from the combination. Median time to progression (TTP) was 32 wks (95%CI: 13-34).

**Conclusions:** The combination of PM01183 and XEL is tolerable, with no DLT occurring at the RD of PM01183 2 mg on D1 & 8 + XEL 1650 mg/m² b.i.d. q3wk. Promising activity was observed. A simplest schedule without the D8 infusion is being explored. Dose escalation is ongoing.

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