**Background**

- The Tarextumab phase 1 study enrolled 49 patients with metastatic pancreatic cancer, and included patients with synchronous and metachronous disease, and with or without previous chemotherapy.

- Tarextumab is a novel antibody that targets Notch2/3 and has demonstrated significant anti-tumor activity in preclinical models and early clinical trials.

- Notch inhibition is a promising strategy for the treatment of pancreatic cancer, as Notch activation is known to mediate tumor growth and survival.

**Study Schema and Objectives**

- **Objectives**: The primary endpoint of the study was to determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D) of Tarextumab in combination with nab-paclitaxel and gemcitabine.

- **Safety**: The study aimed to evaluate the safety and tolerability of the combination regimen.

- **Efficacy**: The study also aimed to assess the anti-tumor activity of the combination regimen.

- **Patient Selection**: Patients with untreated metastatic pancreatic cancer were enrolled in the study.

**AEs Occurring in >25% of Pts (n=40)**

- **TRXT in Combination with Nab-P+Gem in Patient-Derived Pancreatic Tumor Xenografts**

  - **Mouse Model**: Using a mouse model of pancreatic cancer, the study evaluated the efficacy of Tarextumab in combination with nab-paclitaxel and gemcitabine.

  - **Results**: The combination regimen demonstrated significant anti-tumor activity, with tumor volume reductions of up to 80% in some cases.

**AEs Related to Tarextumab Occurring in ≥10% of Pts (n=40)**

- **TRXT (anti-Notch2/3) in combination with Nab-P+GEM was well tolerated up to 15 mg/kg Q2W**

  - **Toxicities**: The most common toxicities observed included fatigue, nausea, and diarrhea.

  - **Management**: Dosage adjustments were made in some cases to manage these toxicities.

**Subject Time on Study (n=37 evaluable)**

- **Therapy Duration**: The median therapy duration was 27 weeks, with a range of 2-70 weeks.

**Baseline Characteristics (n=40)**

- **Patient Population**: The study enrolled 40 patients with untreated metastatic pancreatic cancer.

**Study Outcomes**

- **Phase 2 Dose of TRXT in combination with Nab-P+GEM is 15 mg/kg Q2W**

- **Clinical Activity**: The combination regimen demonstrated significant clinical activity, with partial responses observed in 7 patients.

- **Safety Profile**: The regimen was well tolerated, with the most common toxicities being fatigue, nausea, and diarrhea.

**Summary**

- **Tumor Notch3 Level and Recurrent Pts**

  - **Notch3 Analysis**: Notch3 expression was analyzed in tumor samples from recurrent pancreatic cancer patients.

  - **Outcome**: Patients with high Notch3 expression showed improved clinical outcomes following treatment.

- **Conclusion**: Tarextumab in combination with nab-paclitaxel and gemcitabine is a promising combination regimen for the treatment of metastatic pancreatic cancer, with potential clinical activity and a manageable safety profile.