**DCE-MRI Results (Cohorts 1-4)**

Study Day showed Cmax and AUC that were dose proportional with no accumulation. Serial DCE-MRI scans with evaluable lesions performed.

- **PK (PD) activity through DCE-MRI, biomarkers of angiogenesis, tumor biopsies and response rate.**
- **0.1-0.4 mg/kg ALN-VSP02 was well-tolerated, with no hepatotoxicity. At 0.7 mg/kg, a patient with pancreatic neuroendocrine tumor. A fall in plasma VEGF levels was observed in.**

**Safety Summary (Cohorts 1-4)**

- **ALN-VSP02 Dose 3 (mg/kg)基の推移を示す。**
- **ALN-VSP02 Phase I Study Demographics (Cohorts 1-4)基の推移を示す。**
- **All patients treated with multiple prior anti-angiogenic and/or chemotherapy regimens. Median age 56 yrs (range 34-78).**

**Summary**

- **ALN-VSP02 Phase I Study**
- **Screening**
- **Baseline (BL) Pre-Dose Day 4 Post-Dose 1 Day 7 Post-Dose 1**
- **Baseline MRI, coronal view of liver**
- **Changes in plasma VEGF and PLGF by dose level.**
- **DCE-MRI baseline and at all post-treatment scans.**
- **Summary of DCE-MRI results for first 4 cohorts.**
- **Peak change in Ktrans for each evaluable tumor following the 2 post-treatment scans. Patients without evaluable liver tumors included those with lesions <2 cm and those whose scans were uninterpretable due to technical limitations (e.g. excessive motion artifact).**
- **13 of 21 tumors (62%) had ↓Ktrans of ≥40%.**
- **19/21 tumors (90%) showed decline in Ktrans**

**Mechanisms for RNAi treatment**

- **For delivery, synthetic siRNA (21 bp) is incorporated into lipid nanoparticles (LNPs).**
- **The particles are taken up by cells via endocytosis and the siRNA is liberated from the LNP.**
- **SiRNA then degrades intracellularly, degrading RNA targets and silencing gene expression.**

**Changes in plasma VEGF and PLGF by dose level.**

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