Abstract # 35371

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OSE279, a PD-1 blocking monoclonal antibody, as future backbone of a bifunctional checkpoint inhibitor platform: Preclinical characterization and early clinical results of a First-In-Human (FIH) study in subjects with advanced malignancies

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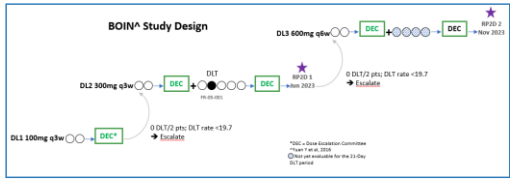
Methodology:

- We have performed preclinical evaluations to support OSE279 development in humans
- A phase I/II study is underway to determine MTD and/or RP2D, efficacy, safety and tolerability, PK and PD profiles of OSE279 in subjects with refractory malignancies, with no standard treatments



Key findings:

- OSE279 has a full antagonist activity against PD-1, similarly to pembrolizumab or nivolumab; simulations showed that trough Receptor Occupancy (RO) would be 94.1±36.9% and 98.3±36.8% at 100 mg and 300 mg, respectively; NOAEL was determined in monkey at 100 mg/kg given for 1 month
- In the FIH study as of September 2023, 13 subjects were treated with at least 2 weeks of follow-up, with 8 tumor types; median age was 62y (range 43-77), 8/13 patients (61.5%) were female, median number of prior metastatic lines was 2 (range 1-6); 2 additional subjects have started treatment in October 2023
- 29 Treatment-Related Adverse Events (TRAEs) occurred in 10 subjects (76.9%); 2 Serious TRAEs (pneumonitis gr2, hepatitis gr3) occurred in 2 patients (15.4%); one (with HCC) of 7 subjects in DL2 (300 mg) had a DLT of gr3 hepatitis
- A confirmed PR* was observed in a Hepatocellular carcinoma (HCC) MSS CPS 3 after one dose of OSE279 300mg; 2 yet Unconfirmed PRs have been reported with 600mg q6w, in subjects with UPS MSI-H and Anal SCC PD-L1 15%; SD>16 weeks was seen in 3 subjects
- Pharmacokinetic (PK) profile showed good exposure and dose-proportionality; RO was maintained and within the boundaries of simulations
- **Conclusions:** OSE279 preclinical data showed efficacy and safety profiles comparable to the EMA/FDA approved anti-PD1 antibodies. In FIH study, OSE279 showed a manageable safety profile with preliminary signs of efficacy in the first 13 subjects treated. A RP2D of 300 mg q3w was selected. 600 mg q6w appears to be a good candidate for the RP2D q6w and 4 additional patients have been enrolled to confirm safety and tolerability. PK and pharmacodynamic profiles were consistent with modelling. Expansion cohorts are planned. Clinical trial information: NCT 05751798.

We thank all investigators and their teams, all study subjects with their families, and all study teams.

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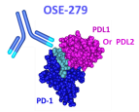
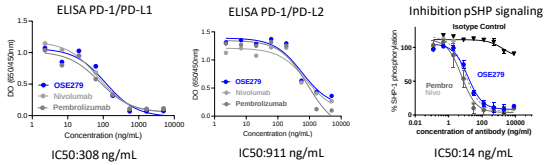
NOAEL=No Observed Adverse Event Level; MSS=Microsatellite Stable; MSI-H=Microsatellite Instability-High; CPS=Combined Positive Score; MTD= Maximum Tolerated Dose; RP2D=Recommended Phase 2 Dose; PR, SD=Partial Response, Stable Disease; DL=Dose Level; DLT=Dose Limiting Toxicity

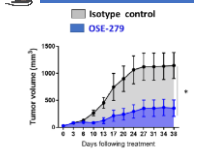
Preclinical assessments



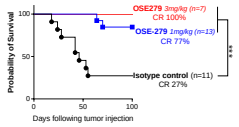
Full antagonist interaction with PD-L1 and PDL2



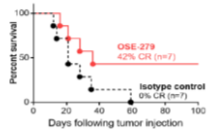
Ectopic colocancer (MC38)



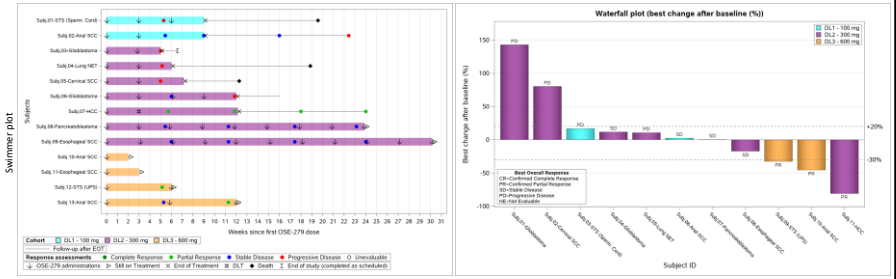
Orthotopic mesothelioma (AK7)



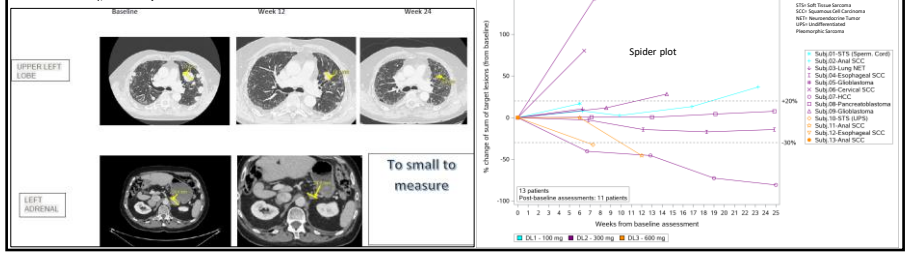
Orthotopic HCC (Hepa1.6)



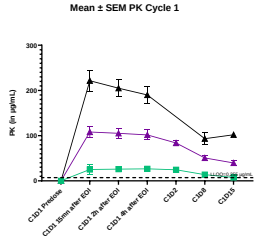
Preliminary efficacy results in treated subjects with at least one tumor assessment



*70 y/o male subject with HCC and PR after one OSE279 administration



Pharmacokinetics



- Subjects in the 3 cohorts were well exposed to OSE279
- Mean PK values at C1 are in the expected range for all dose levels
- Mean OSE279 concentrations for DL3 were 205,5 µg/mL at D1, then decreased as expected to 102 µg/mL at C1D15, showing a good 6-fold and 2-fold dose proportionality compared to DL1 and DL2, respectively

Receptor Occupancy