FPN # 743P: A Phase 1b Dose Escalation Study of CD137 mAb Agonist OC-001 as Monotherapy in Patients with Advanced or Metastatic Cancer

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Background

OC-001 is a CD137 mAb agonist designed to show differential agonistic activity from that of competitor antibodies. OC-001 provided T cell activation that results in antitumor efficacy in humanized mouse tumor models *in vivo*.

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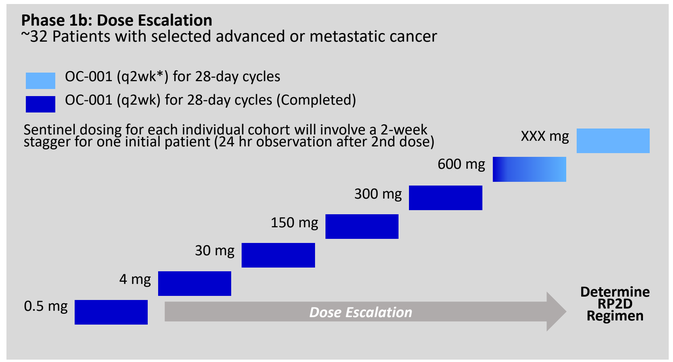
Objectives

Primary objective: to assess the safety and tolerability of OC-001 administered as a monotherapy in patients with selected locally advanced or metastatic cancer.

Secondary objective: to evaluate the PK of OC-001 after single and multiple dose administration.

Overall Study Design

Patients received OC-001 i.v. Q2W (0.5 mg, 4 mg, 30 mg, 150 mg, and 300 mg) in 28-day cycles in a 3+3 dose escalation design. The assessment of a 600 mg i.v. Q2W dose is currently ongoing.



This is study NCT04260802

Patient Population

Up to 32 patients with selected locally advanced or metastatic cancer, including triple negative breast cancer (TNBC), gastric cancer, cervical cancer, ovarian cancer, hepatocellular carcinoma (HCC), sarcomas, squamous cell carcinoma of the head and neck (SCCHN), urothelial cancer, non-small cell- lung cancer (NSCLC), renal cell carcinoma (RCC) and possibly other tumor(s) of interests.

Median age was 60.0 years, 70% were female, 45% had an ECOG status of 1 and 55% had 0, and 55% had received ≥3 lines of prior therapy.

Results

Safety Evaluation

- Nineteen subjects have been treated in 5 dose cohorts
- No trends in LFTs have been observed
- No trends in other chemistry, hematology observed
- No trends observed in the AE profile to date.

Conflicts of interest W. Miller: Advisory Board/Consulting Fees (paid to Dr Miller): Merck, BMS, Roche, GSK, Novartis, Amgen, Mylan, EMD Serono, Sanofi; Honoraria/Speaker's Bureau (paid to Dr Miller): BMS, Merck, Roche, GSK, Novartis, Amgen, Mylan, EMD Serono, Sanofi; Grants (to institution): Merck, CIHR, CRS, Terry Fox Research Institute, SWCRF, CCSRI; Clinical Trials (to institution): Merck, MiMic, Astellas, BMS, Novartis, GSK, Incyte, Pfizer, Sanofi, Ocellaris Pharma, Alkermes, Genentech, Array, Exelixis, VelosBio, Esperas Pharma

Summary

OC-001 did not show any liver safety, hematology or blood chemistry concerns.

Linear PK profiles are observed for the 0.5 mg, 4 mg, 30 mg, 150 mg and 300 mg OC-001 dose levels.

No apparent time dependence of PK between Cycle 1 and Cycle 2.

C_{max} and AUC exposures appear dose proportional over the dose range of 0.5 mg to 300 mg OC-001.

Based on C_{min} values, steady-state appears to be reached between Cycle 2 Day 15 and Cycle 4 Day 1 with C_{min} accumulation ratios of 2.7 or lower.

Accumulation based on C_{max} and AUC is approximately 2.2 or lower.

Conclusions

OC-001 was well tolerated at doses up to 300 mg Q2W.

Liver toxicity was not observed.

OC-001 may be a potential combination therapy with other immuno-oncology agents.

Acknowledgements

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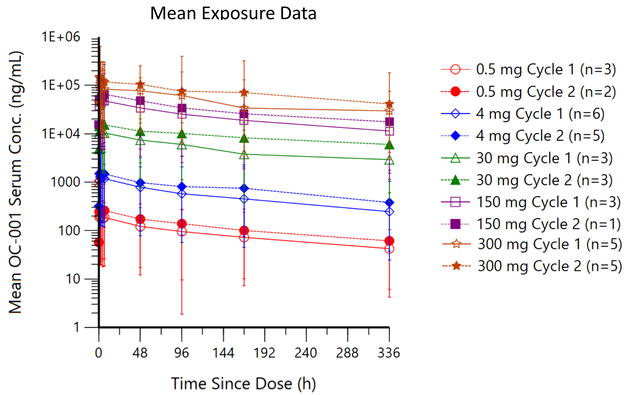
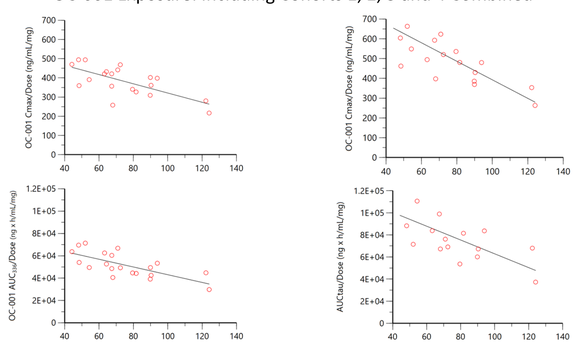
Pharmacokinetics Evaluation



Relationship Between Body Weight and Dose-Normalized OC-001 Exposure: Including Cohorts 1, 2, 3 and 4 Combined

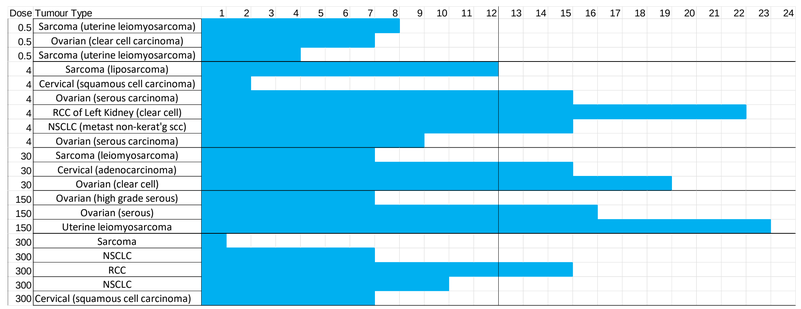


- Presented as Geometric Mean (CV%)[n]*

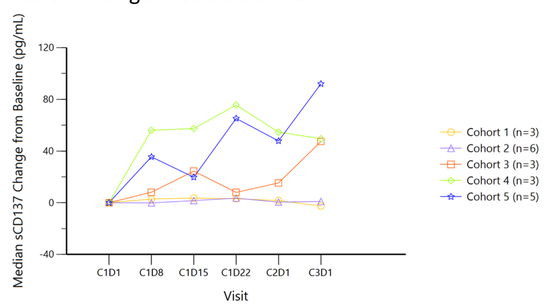
PK Parameter	Cohort 1 (0.5 mg)	Cohort 2 (4 mg)	Cohort 3 (30 mg)	Cohort 4 (150 mg)	Cohort 5 (300 mg)
	Cycle 2 D1	Cycle 2 D1	Cycle 2 D1	Cycle 2 D1	Cycle 2 D1
C_{max} (ug/mL)	0.240, 0.332 [2]*	1.67 (32.7%)[5]	16.0 (12.8%)[3]	68.4 (29.5%) [3]	160 (34.6%) [5]
$AUC_{0\text{-}336h}$ (ug x h/mL)	41.8, 35.7 [2]	248 (32.5%)[5]	3000, 3320 [2]	10600 (6.9%) [3]	24700 (35.5%) [4]
AUC_{inf} (ug x h/mL)	NA	NA	NA	NA	NA
C_{avg} (ug/mL)	0.124, 0.106 [2]	0.739 (32.5%)[5]	8.83, 9.88 [2]	31.4 (6.9%) [3]	73.4 (35.5%) [4]
$t_{1/2}$ (h)	274, 115 [2]	220 (32.5%)[5]	244, 370** [2]	226 (47.4%) [3]	209 (43.3%) [4]
CL (mL/h/kg)	0.127, 0.269 [2]	0.210 (9.2%)[5]	0.150, 0.167 [2]	0.154 (22.6%) [3]	0.186 (18.4%) [4]
Vss (mL/kg)	49.8, 40.6 [2]	65.1 (38.1%)[5]	51.9, 87.0** [2]	48.8 (43.2%) [3]	58.3 (27.9%) [4]

Abbreviations: CV, coefficient of variation; n, number of patients; NA, not applicable.
*Individual values are presented if less than three values are available for summary.
**For this parameter calculation, the calculated half-life is longer than collection interval (value will be excluded from final summary stats).

Duration on OC-001 Monotherapy



Median Change in soluble CD137



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