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OMX-0407: A novel spectrum-selective small molecule kinase inhibitor in advanced/metastatic solid tumors

Authors and affiliations

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Background

- **OMX-0407, an orally available spectrum-selective kinase inhibitor that targets key oncology-relevant tyrosine kinases and salt-inducible kinases, is being developed as a first-in-class treatment for solid tumor indications with high unmet medical need, such as squamous non small-cell lung cancer (NSCLC), urothelial bladder cancer (UBC), clear cell renal cell carcinoma (ccRCC) and angiosarcoma (AS).**
- **OMX-0407 has demonstrated a dual mode of action by directly inducing cell cycle arrest in tumor cells (Fig. 1) and sensitizing the tumor micro-environment to immune-mediated tumor cell killing in specific tumor types (indications of interest).**
- **Treatment with OMX-0407 in experimental animal models has shown single-agent efficacy in multiple tumor types. *Ex vivo* analyses showed a dose-responsive de-phosphorylation of SRC family kinases (SFKs) associated with cell proliferation inhibition and cell cycle arrest.**
- **Here, we report findings from the dose escalation and expansion parts in ccRCC and AS of a Phase 1a/1b first-in-human study (NCT05826600).**

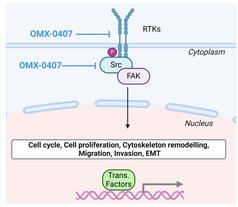

Figure 1. OMX-0407 targets oncology-relevant tyrosine kinases associated with cell proliferation and cell cycle proteins.

Study Design and Status

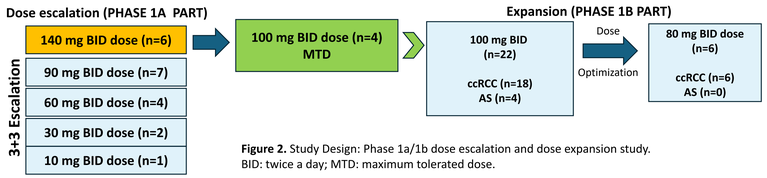

Figure 2. Study Design: Phase 1a/1b dose escalation and dose expansion study.
BID: twice a day; MTD: maximum tolerated dose.

- OMX-0407 was administered orally twice daily in 28-day cycles (**Fig. 2**).
  - **Dose Escalation (DE) Part ("all-comer" population):**
    - Key inclusion criteria: Patients with previously treated, unresectable solid tumors; Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0-2, and measurable disease by RECIST 1.1 criteria.
    - Primary outcomes: incidence of dose-limiting toxicities (DLTs) (by dose level); secondary outcomes: MTD and recommended Phase 2 dose
  - **Expansion Part (Expansion Cohorts in indications of interest):**
    - Key inclusion criteria: ccRCC: 1-3 lines of prior therapy containing anti-PD1 and anti-VEGFR; AS: 1-3 lines of prior therapy containing either taxane or anthracycline. All patients had to show RECIST measurable disease.
    - Primary outcomes: overall response rate; secondary outcomes: progression-free-survival, duration of response, overall survival, quality of life and pharmacokinetic (PK) profile
- The study has completed the phase 1a dose escalation part and is currently enrolling patients in the expansion part

Results

Baseline Characteristics

- At data cutoff (7 May 2025) 53 patients were enrolled: 25 in the DE Part; 4 in the AS and 24 in the ccRCC Expansion Cohorts. For the total safety population, mean age was 60.5 years, nearly 40% female (**Table 1**).

	Dose Escalation Part							Expansion Part	
	10 mg BID (n=1)	30 mg BID (n=2)	60 mg BID (n=4)	90 mg BID (n=8)	140 mg BID (n=6)	100 mg BID (n=4) MTD	Total (n=25)	ccRCC (n=24)	AS (n=4)
Age (ys) [Mean (SD), range*]	70.0 (NC) NA	70.50 (2.1) 69-72	53.3 (9.8) 40-62	59.9 (14.7) 35-78	66.2 56-75	55.3 (24.2) 28-79	60.8 (13.9) 28-79	63.3 (8.4) 48-81	41.3 (24.6) 26-78
Sex [Female (n, %)]	1 (100)	2 (100)	3 (75)	3 (37.5)	2 (33.3)	2 (50)	13 (52)	4 (16.7)	4 (100)
Prior cancer therapies [Median, range*]	3.0 NA	6.5 6-7	2 0-6	4.5 1-7	4 3-7	4 3-6	4 0-7	2 1-4	1.5 1-3
ECOG PS at screening [Median, range*]	0 NA	0.5 0-1	0.5 0-1	0 0-1	0.5 0-1	0.5 0-1	0 0-1	1 0-1	0 0-1

Table 1. Baseline characteristics (sequential order for dose escalation groups).
*Minimum-maximum; NA: not applicable; ys: years.

- The dose escalation part recruited patients with advanced/unresectable solid tumors of different histologies, only colorectal, ovarian, prostate cancer and melanoma patients were recruited more than once.

Safety

Table 2 shows the main related treatment emergent adverse events (TEAEs) for all patients in the two study parts.

- Treatment was well tolerated: related TEAEs were mild to moderate, with the most common being gastrointestinal reactions and fatigue. A possible class effect of fluid retention is under investigation.
- Several cases of anemias were reported as related hematological TEAEs and found to be manageable.
- Two possibly study drug-related serious TEAEs were documented: one grade 2 febrile episode in a visceral AS patient and one grade 3 dyspnea in a ccRCC patient.
- Dose-limiting toxicities: One case of facial swelling secondary to drug allergy at the 90 mg BID dose, and 1 case of fatigue at the 140 mg BID dose.
- A MTD was established at 100 mg BID.

	Dose Escalation Part							Expansion Part		
N patients (%) [Preferred term of TEAEs grade ≥3]	10 mg BID (n=1)	30 mg BID (n=2)	60 mg BID (n=4)	90 mg BID (n=8)	140 mg BID (n=6)	100 mg BID (n=4) MTD	Total (N=25)	ccRCC (n=24)	AS (n=4)	Total (N=28)
Gastrointestinal disorders	0	0	2	3	5	3	13 (52.0)	13 [diarrhea]	3	16 (57.1)
General disorders & administration site conditions	1	1	1	1	5	1	10 (40.0)	9 [fatigue]	3	12 (42.9)
Blood and lymphatic system disorders	0	0	1	2	4 [anemia]	1	8 (32.0)	6 [anemia]	3 [anemia]	9 (32.1)
Metabolism & nutrition disorders	1	0	1	0	3	0	5 (20.0)	8 [hyponatremia]	1	9 (32.1)
Investigations	0	0	0	1	1	1	3 (12.0	4	1	5 (17.9)
Skin and subcutaneous tissue disorders	0	0	0	1	3	1	5 (20.0)	2	0	2 (7.1)
Vascular disorders	0	0	0	0	0	0	0 (0)	3	0	3 (10.7)
Renal and urinary disorders	0	0	0	0	0	0	0 (0)	2 [acute kidney injury]	1	3 (10.7)

Table 2. Related TEAES (in at least 10% of patients in the dose escalation or expansion parts and/or patients with any related TEAE grade ≥3).

PK/Pharmacodynamics (PD)

- PamGene kinase activity profiling revealed OMX-0407-dependent suppression of SRC family kinases (SFKs) and their targets in preclinical tumor models and human PBMCs *ex vivo* (data not shown).
- PamGene analysis of clinical patient PBMCs confirmed PD effects on SFKs with significant correlation to OMX-0407 plasma levels, confirming OMX-0407 pharmacodynamic activity in clinical patients at tested doses.
- Interim PK analysis in the expansion cohort led to dose optimization to 80 mg BID.

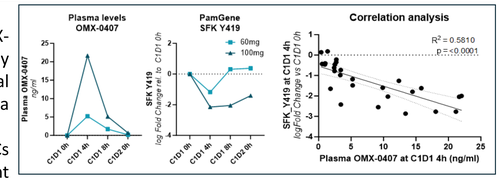

Figure 3. Left) Plasma OMX-0407 levels at PBMC collection timepoints on Cycle 1 Day 1 for exemplary patients treated with 60mg or 100mg dose. **Center)** Log fold change in SFK Y419 (representing SRC Y419 and equivalent phosphosite on other SFKs) signal intensity as measured by PamGene compared to Cycle 1 Day 1 0h pre-dose timepoint . **Right)** Correlation between OMX-0407 plasma levels and SFK Y419 log fold change at C1D1 4h timepoint for dose escalation part patients. Statistical analysis performed using simple linear regression analysis.

Efficacy

We report efficacy data on the Dose Escalation Part ("all comer" population) only as overall follow-up was too short in the Expansion Part in indications of interest. **Figs. 4** and **5** show the patients' time on study and the best change of target lesions from baseline, respectively.

- Most patients discontinued due to progressive disease, 1 patient had a durable complete response (see below), and 1 patient had a stable disease (**Fig. 4**).
- At around the MTD, i. e. at 90 and 100 mg BID, target lesion size seemed to only moderately increase indicating some degree of tumor growth retardation (**Fig. 5**).

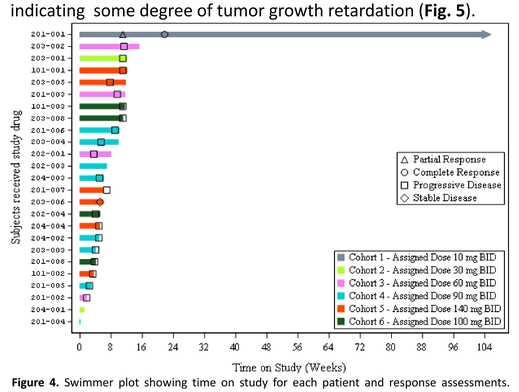

Figure 4. Swimmer plot showing time on study for each patient and response assessments. Reasons for discontinuation other than PD: 201-004, 203-006: withdrawal of consent; 202-003: allergic reaction; 204-001: death.

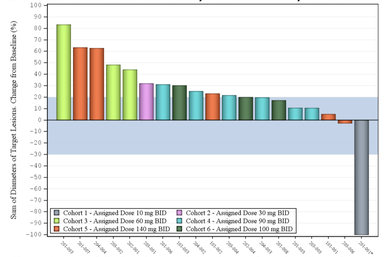

Figure 5. Waterfall plot showing best change from baseline of target lesion size. *: Patient 201-001 was started on 10mg BID then dose – increased to 30 and 60mg, best resonse was recorded during 30 mg BID dosing.

- One patient with a metastatic radiation-induced AS had an exceptional complete response (CR). She started treatment at 10 mg BID and was escalated to 30 mg BID where response started to manifest (**Fig. 6**), she was further dose escalated and is currently receiving OMX-0407 at 60 mg BID:
  - CR was ongoing at the time of data cut, with a current duration of complete response of 21 months.
  - The patient had received previous chemotherapy with doxorubicin, cyclophosphamide and paclitaxel.

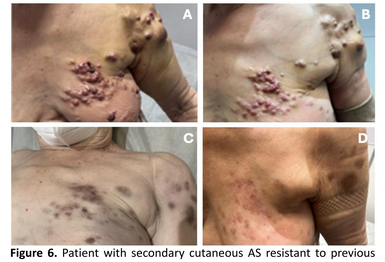

Figure 6. Patient with secondary cutaneous AS resistant to previous chemotherapy (doxorubicin, cyclophosphamide, paclitaxel) treated with OMX-0407. **A)** Baseline. **B)** Cycle 2/Day 1: Dose escalation from 10 mg to 30 mg BID. **C)** Cycle 4/Day 1: 30 mg BID. **D)** Cycle 10/Day 1: 60 mg BID dose (since C9D1).

Conclusions

- **In our study, OMX-0407, a potent and spectrum-selective kinase inhibitor, was well tolerated and demonstrated encouraging anti-tumor activity in a patient with angiosarcoma achieving a durable complete response lasting 21 months and ongoing.**
- **The dose escalation part of the first-in-human clinical study has completed and identified a MTD of 100 mg BID.**
- **OMX-0407 is currently evaluated clinically in the dose expansion Phase 1b part of this study in indications of interest, namely AS and ccRCC, with an optimized dose of 80 mg BID orally.**