

A Phase Ib/II Study of Atamparib, a PARP7 inhibitor, in Patients with Advanced Solid Tumors

X. Chen¹, C. Zhou¹, J. Zhao², D. Iv³, Y. Zhang⁴, J. Shi⁵, Y. Zhao⁶, Z. Huang⁷, X. Wang⁸, X. Pu⁹, J. Li¹⁰, CW Yip¹², F. Carbone¹¹, Y. Huang¹², L. Mahnke¹³

¹Shanghai East Hospital, Shanghai, CN; ²Peking University Cancer Hospital, Beijing, CN; ³Taizhou Hospital of Zhejiang Province, Taizhou, CN; ⁴Shandong Cancer Hospital, Jinan, CN; ⁵Linyi Cancer Hospital, Linyi, CN; ⁶Henan Cancer Hospital, Zhengzhou, CN; ⁷Fujian Cancer Hospital, Fuzhou, CN; ⁸The First Affiliated Hospital of Guangdong Pharmaceutical University, Guangzhou, CN; ⁹Hunan Cancer Hospital, Changsha, CN; ¹⁰Sichuan Cancer Hospital, Chengdu, CN; ¹¹Nerviano Medical Sciences Srl, Milan, IT; ¹²Nerviano Medical Sciences (Shanghai) Ltd., Shanghai, CN; ¹³Nerviano Medical Sciences, Inc. (US), Boston, MA, USA



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Background

- PARP7 (TIPARP or ARTD14) is a mono-ADP-ribosyltransferase regulates transcription, immune signaling, and stress responses.
- Atamparib (RBN-2397, ONO-7119) is a first-in-class, highly potent, selective, orally bioavailable PARP7 inhibitor, triggers FRA1 degradation, thereby blocking signaling downstream of KRAS and other oncogenes¹.
- A unique dual mechanism of antitumor activity of atamparib¹:
 - (i) tumor-intrinsic transcriptional reprogramming leads to cancer cell death;
 - (ii) activation of innate immune signaling promotes antitumor immunity.
- In the previous 3 clinical trials (NCT04053673, NCT05127590, jRCT2031210373)²⁻⁴, 239 patients who received ≥1 dose of atamparib as monotherapy or in combination with ICI, safety profile was favourable.
- Preliminary anti-tumor activity was observed in late-line NSCLC adenocarcinoma patients with prior standard chemotherapy and immunotherapy failure, with *KRAS* mutation and *KRAS* wild-type. Especially PR was observed in one patient with *KRAS* G12V and *STK11* and *KEAP1* mutation with DOR about 4 months.
- Based on favorable safety profile and emerging evidence suggesting higher exposure is required for efficacy across tumor types harboring different genetic alternations, the ongoing trial is exploring higher dose levels to generate proof of concept in selected populations and then to expand broader genetic subgroups.

Method: Study Design

- PRP7A-ATA-001 (NCT07374419, CTR20260092)⁵ is a phase Ib/II, open-label, multi-center trial conducted in China. It comprises 2 parts:

Phase Ib

- Primary objectives: to assess safety and tolerability, MTD and RP2D.
- Secondary objectives: to characterize PK and antitumor activity.

Phase II

- Primary objective: to assess antitumor activity at RP2D.
- Secondary objectives: to evaluate additional antitumor efficacy, safety and PK.

Exploratory biomarker endpoints to access treatment response, pharmacodynamic effects, ctDNA dynamics and DDI.

Method: Key Eligibility Criteria

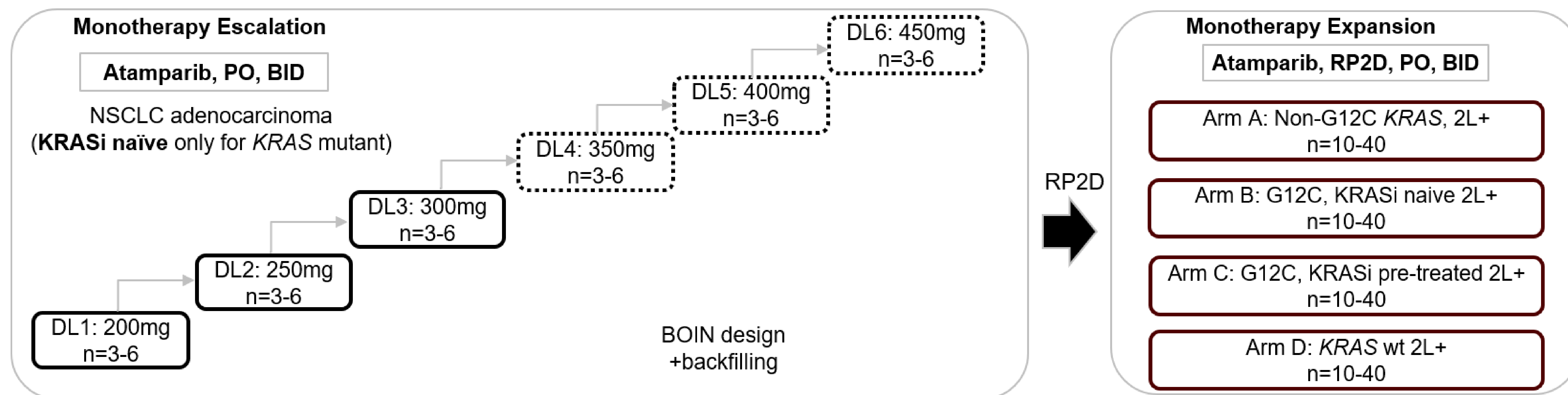
Inclusion

- Participants must be ≥18 years of age.
- Histologically confirmed diagnosis of unresectable advanced or metastatic NSCLC adenocarcinoma.
- Documented *KRAS* mutation status at study entry.
- Pre-treated with ≥1 line of standard therapy and experienced radiographic tumor progression and have failed institutional SOC.
- Have measurable tumor lesions.
- ECOG PS of 0-1.

Exclusion

- Mixed histology of non-adenocarcinoma NSCLC.
- With oncogenic driver mutation other than *KRAS* for which an approved therapy is available but not adequately treated.
- Symptomatic, or unstable CNS lesions.

Method: Study Schema



Phase Ib

- N (escalation) =18-36
- Three different planned dose level cohorts: 200mg; 250mg; 300mg;
- Dose level: 350mg; 400mg; 450mg may also be explored.
- BOIN design with backfilling is followed.
- SMC conducts reviews on safety data for decision on escalation of each dose level.
- Backfilling: if a dose level is deemed safe by SMC, additional participants may be enrolled.

Study procedures

- Screening period of 28 days, treatment period and (28-day safety and survival [expansion only]) follow up period
- Enrolled participants would receive atamparib orally twice daily with continuous dosing in 21-day cycles.
- Safety is evaluated per NCI CTCAE v6.0.
- Tumor assessments per RECIST v1.1 is performed once every 6 weeks for the first 6 months, then reduced to once every 9 weeks.
- Treatment continues until radiographic PD, unacceptable toxicity, or withdrawal from the study.

Summary

- Atamparib is a first-in-class, highly potent and selective PARP7 inhibitor currently in clinical development.
- A clear PARP7 dependency in NSCLC adenocarcinoma and atamparib's unique dual mechanism of action, point to new indications both as single agent and in combination.
- Monotherapy trial is ongoing and expected to enroll up to 200 participants.
- Currently enrolling DL3: 300mg BID. DL1: 200mg BID and DL2: 250mg BID were cleared with no DLTs.
- Emerging preliminary data on safety, PK, and efficacy is expected to be presented at a future conference meeting.

References & Acknowledgements

References

- Degani G, et al. Abstract 3049: Atamparib: First-in-class PARP7 inhibitor for treatment of NSCLC adenocarcinoma in monotherapy and in combination with standards of care. Cancer Res 2026; 86 (7_Supplement): 3049.
- Clinical trial NCT04053673: A Phase 1, First-in-human Study of the Safety, Single- and Multiple-Dose Pharmacokinetics, and Preliminary Activity of Escalating Doses of RBN-2397, an Oral PARP7 Inhibitor, in Patients With Solid Tumors; Trial countries: US, Spain.
- Clinical trial NCT05127590: A Phase 1b/2, Multicenter, Single Arm Study of RBN-2397 in Combination With Pembrolizumab in Patients With Squamous Cell Carcinoma of the Lung; Trial countries: US, Israel, Spain, UK.
- Clinical trial jRCT2031210373: A Phase I, open-label, uncontrolled, dose escalation and expansion study to evaluate the tolerability and safety of ONO-7119 alone and in combination with ONO-4538 in patients with unresectable advanced or recurrent solid tumors; Trial country: Japan.
- Clinical trial NCT07374419: Atamparib in Patients With Advanced Solid Tumors; CTR20260092.; Trial country: China.

Abbreviations

ICI=Immune Checkpoint Inhibitor; NSCLC=Non-small Cell Lung Cancer; PR=Partial Response; DOR=Duration of Response; SOC=Standard of Care; BOIN=Bayesian Optimal Interval; MTD=Maximum Tolerated Dose; RP2D=Recommended Phase II Dose; PK=pharmacokinetics; DDI=drug-drug interaction; ECOG PS=Eastern Cooperative Oncology Group Performance Status; CNS=Central Nervous System; DL=Dose Level; SMC=Safety Monitoring Committee; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events; RECIST=Response Evaluation Criteria in Solid Tumors; PD=Progression of Disease.

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Yaling Huang, MD PhD
CMO site head China
yaling.huang@nervianoms.com

Lisa Mahnke, MD PhD
CMO
lisa.mahnke@nervianoms.com