**Background**

- Folate receptor (FR) is a cell-surface protein, encoded by the frtl1 gene, which is expressed on a variety of epithelial tumors, including ovarian cancer and lung adenocarcinoma (LUAD).
- AZD5335 is a potent, selective, folate-receptor α (FRα) targeting drug.
- AZD5335 + AZD5305 may therefore result in synthetic lethality and lead to antitumour effect.
- AZD5335 was also active in patient-derived xenograft (PDX) models of ovarian cancer, where tumour growth inhibition was >90% at an oral dose of 5 mg/kg.
- AZD5335 was also active in a poly(adenosine diphosphate[ADP]ribose) polymerase (PARP) inhibitor that potently and selectively inhibits and traps PARP1 at sites of DNA damage, leading to replication stress and double-strand breaks at replication forks.

**Methods**

**Methods overview**

- **Study design**: The FONTANA study will evaluate AZD5335 as monotherapy in patients with ovarian cancer or LUAD (Module 1); or AZD5335 in combination with AZD5305 in patients with ovarian cancer (Module 2).
- **Enrolment** began in May 2023, with primary completion anticipated in November 2027.
- **Objectives**: The primary objective is to evaluate the antitumour activity of AZD5335 and AZD5335 + AZD5305 in patients with ovarian cancer or LUAD.
- **Secondary objectives** include the use of PDX models in preclinical studies, a single dose of AZD5335 was active in mice xenograft models of high FRα-expressing breast cancer.

**References**


**Acknowledgements**

Medical writing support for the development of this paper, under the direction of the authors, was provided by Amra Khan, freelance medical writer, for Menarini Asia-Pacific, with funding provided by Menarini Asia-Pacific.

**Sponsorship**

This study was sponsored by AstraZeneca.

**Disclosures**

Funda Meric-Bernstam, Ema Jain, Barret Stoller, Anna Maruty, Armidas Vaskauskas, David Spier, David Hong, Mark Pretorius, Hong Zhang, Ward Betschart, Mary Pelle, Pauline Ng, Robert Kollmann, Türker Gusevs, Zeinab Mostoafa, Myoung Hee, Sung Hoon Lee, Min Jung Kim, Sa-Min Yeon, Aruna Pratiksha, Metin Ozmen, Magda Lemos, Danielle M. Daley, and Mariana Guimaraes received honoraria for participation in advisory boards, data monitoring, steering committees, scientific meetings, and other tasks. In addition, several persons served in scientific advisory boards and held positions on the editorial boards of various journals. They also received research grants from relevant companies and received payments for development of educational materials. Lastly, the study was supported by AstraZeneca.

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**Presented at**

European Society for Medical Oncology (ESMO) Congress 2023, 20–24 October 2023, Madrid, Spain.