INTRODUCTION

Patients with recurrent OC are faced with the inevitable development of platinum resistance.\(^1\) Outcomes for these patients are poor; there remains a high unmet need in this setting.\(^2\)

CDH6, a cell-adhesion protein that is minimally expressed in healthy tissues,\(^3,4\) is expressed in ~65–85% of ovarian cancers.\(^5\)

CDH6 expression is consistent across primary and recurrent OC tumors. CDH6 expression is observed across all epithelial OC histological subtypes and not limited to high-grade serous OC.\(^6\)

R-DXd is a novel CDH6-directed ADC composed of 3 parts: a humanized CDH6 antibody covalently linked to a potent topoisomerase I inhibitor payload (DXd) via a plasma-stable linker.\(^7,8\) (Figure 1)\(^{b}\)

In the first-in-human study of R-DXd in patients with heavily pretreated OC (NCT04707248), doses of 4.8–6.4 mg/kg showed promising efficacy with a manageable safety profile.

- Confirmed ORR was 48.6% (95% CI, 31.9–65.6), median DOR was 11.2 months (95% CI, 3.1–NE), DCR was 97.4% (95% CI, 86.2–99.9), and PFS was 8.1 months (95% CI, 5.3–NE).\(^7\)

- Grade ≥3 TEAEs were reported in 44.4% of patients.\(^7\)

- Preliminary biomarker assessment indicates that R-DXd antitumor activity is observed in patients with OC with a wide range of CDH6 expression.\(^8\)

The REJOICE-Ovarian1 Phase 2/3 study (NCT06161025) is ongoing to evaluate the efficacy and safety of R-DXd in patients with platinum-resistant OC.\(^8\)

Figure 1. R-DXd was designed with 7 key attributes

Humanized CDH6 IgG1 mAb

Cleavable tetrapeptide-based linker

Topoisomerase I inhibitor payload (DXd)

Deruxtecan\(^7\)

METHODS

- **REJOICE-Ovarian1** is a Phase 2/3 study of R-DXd in patients with previously treated platinum-resistant high-grade OC (NCT06161025; EudraCT: 2023-507914-28-00; ENGOT-ov7; GOG-3096).

- The Phase 2 dose-optimization part of the study intends to identify the RP3D of R-DXd based on safety and efficacy criteria.

- The Phase 3 study will compare R-DXd with ICC (weekly paclitaxel, PLD, gemcitabine, or topotecan) to further evaluate the efficacy and safety profile of R-DXd.

**Table 1. Study endpoints**

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<thead>
<tr>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Dual primary endpoints</th>
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<tbody>
<tr>
<td>ORR assessed by BICR(^a)</td>
<td>ORR assessed by BICR(^a)</td>
<td>OS assessed by BICR(^a)</td>
</tr>
<tr>
<td>TEAEs</td>
<td>OS</td>
<td>OS</td>
</tr>
<tr>
<td>PFS2, assessed by Investigator(^b)</td>
<td>ORR assessed by Investigator(^a)</td>
<td>OS</td>
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<td>DCR assessed by Investigator(^a)</td>
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<td>DCR assessed by BICR and Investigator(^a)</td>
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**Key secondary endpoints**

- **TCR**
- **QoL**
- **CA-125**
- **TEAEs**
- **Correlation between CDH6 expression and efficacy**

The first patient was dosed on April 2, 2024, at Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Japan, by Dr Mayu Yonemura.

Further enrollment is ongoing and planned in countries across Asia, Europe, and North and South America, including Australia, Brazil, Canada, China (Mainland), Czech Republic, France, Germany, Greece, Italy, Japan, Poland, Portugal, Republic of Korea, Spain, Taiwan, Turkey, UK, USA.

**REFERENCES**


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